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Point-of-care nucleic acid amplification testing for bloodstream infection: Diagnostic performance, clinical utility and future perspectives

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Abstract

Bloodstream infection (BSI) and sepsis require rapid pathogen identification and timely antimicrobial optimisation, yet conventional blood culture is limited by prolonged turnaround time and imperfect sensitivity. Rapid molecular technologies have therefore emerged as complementary diagnostic approaches for accelerating pathogen detection and, in selected platforms, resistance-marker identification. This narrative review synthesises evidence on two clinically important technologies: culture-independent T2 magnetic resonance (T2MR) testing, represented by T2Bacteria and T2Candida, and culture-based multiplex Polymerase Chain Reaction (PCR), represented by the BioFire Blood Culture Identification 2 (BCID2) panel. Evidence indicates that T2MR can substantially reduce time to pathogen detection and antimicrobial optimisation compared with conventional blood culture, while BCID2 demonstrates high sensitivity and specificity for several clinically important bloodstream pathogens and selected resistance determinants. Real-world studies suggest that rapid molecular results can support antimicrobial escalation, de-escalation and stewardship decisions; however, clinical benefit depends on panel coverage, baseline laboratory turnaround, local epidemiology and effective stewardship infrastructure. These technologies should not be considered replacements for conventional blood culture, which remains essential for broad organism recovery, phenotypic antimicrobial susceptibility testing and detection of pathogens outside molecular panels. An integrated diagnostic pathway combining rapid molecular testing with conventional culture may therefore provide the greatest clinical value. Future priorities include expanded pathogen and resistance coverage, prospective multicentre outcome studies, cost-effectiveness analyses and implementation research in resource-limited settings.

Keywords: *Bloodstream infection, Sepsis, Point-of-care testing, Nucleic acid amplification test, T2 magnetic resonance, BioFire BCID2, Multiplex PCR, Antimicrobial stewardship*

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1. Introduction

Bloodstream infection and sepsis remain among the most time-critical conditions encountered in acute clinical

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practice (Evans *et al.*, 2021; Timbrook *et al.*, 2017). The diagnostic pathway must simultaneously establish whether infection is present, identify the causative organism and support selection of effective antimicrobial therapy. Conventional blood culture remains the reference approach for microbiological diagnosis because it permits recovery of viable organisms followed by identification and phenotypic antimicrobial susceptibility testing. However, blood culture is inherently time-dependent: microbial growth must first become detectable, after which additional steps are required for organism identification and susceptibility testing. Diagnostic yield may also be reduced by prior antimicrobial exposure, low organism burden and fastidious or otherwise difficult-to-culture pathogens. These limitations create a clinically important interval during which antimicrobial treatment is necessarily empirical.

The need to shorten this interval has driven the development of molecular rapid diagnostic technologies that detect pathogen nucleic acids rather than waiting for visible microbial growth (Nguyen *et al.*, 2019; Mylonakis *et al.*, 2015; Tang *et al.*, 2019; Peri *et al.*, 2022). Among the technologies that have reached clinical use are culture-independent T2 Magnetic Resonance (T2MR) assays, which can detect selected pathogens directly from whole blood, and multiplex PCR platforms such as the BioFire Blood Culture Identification 2 (BCID2) panel, which are applied to positive blood culture bottles. These approaches are related in their objective but differ substantially in workflow, pathogen coverage and the point at which they enter the diagnostic pathway.

T2MR testing is designed to bypass the requirement for a positive blood culture signal (Berinson *et al.*, 2021; Cortazzo *et al.*, 2021). The T2Bacteria panel targets selected bacterial pathogens, whereas T2Candida targets clinically important Candida species. In contrast, BCID2 is triggered after a blood culture bottle becomes positive and provides rapid identification of a broad group of pathogens together with selected antimicrobial resistance markers. Consequently, T2MR has its greatest conceptual advantage when a clinically important organism must be detected before blood culture positivity, whereas BCID2 functions as a rapid identification and resistance-characterisation step after culture positivity.

Published evidence has increasingly moved beyond technical diagnostic performance toward questions of clinical utility, including time to pathogen identification, time to appropriate or targeted therapy, antimicrobial escalation and de-escalation, length of stay and mortality (D'Onofrio *et al.*, 2020; Giannella *et al.*, 2021). However, these outcomes are not interchangeable, and the strength of evidence differs between platforms. The present review therefore focuses on the clinical meaning of rapid molecular diagnosis rather than treating all molecular rapid diagnostic tests as a single homogeneous intervention.

Research gap: Although rapid molecular platforms have accumulated substantial diagnostic and implementation evidence, their clinical roles remain difficult to compare because culture-independent and culture-based technologies enter the diagnostic pathway at different stages and are supported by different evidence bases. A clinically oriented synthesis that considers diagnostic performance, turnaround time, antimicrobial stewardship, patient outcomes, limitations and implementation context is therefore needed.

The objective of this narrative review is to synthesise the available evidence on point-of-care and near-patient nucleic acid amplification testing for bloodstream infection, with particular emphasis on T2MR and BCID2, and to interpret how these technologies can be integrated with conventional blood culture to improve early clinical decision-making.

2. Literature identification and scope of the review

This article is presented as a narrative review rather than a formal systematic review or new meta-analysis. The literature base was derived from the source manuscript's structured search and reference-list screening, which focused on PubMed/MEDLINE and related biomedical indexing sources using combinations of terms covering point-of-care testing, nucleic acid amplification, T2 magnetic resonance, T2Bacteria, T2Candida, BioFire, blood culture identification, multiplex PCR, bloodstream infection, sepsis, diagnostic accuracy, antimicrobial therapy and antimicrobial stewardship. Reference lists of relevant reviews and meta-analyses were also examined for foundational and implementation studies.

Published evidence from approximately 2020-2026 was emphasised, while earlier pivotal studies were retained where they provided foundational diagnostic accuracy data that continued to underpin later clinical and implementation studies (Lucignano *et al.*, 2022; Bonura *et al.*, 2024; Unic-Stojanovic *et al.*, 2026). The

evidence base includes controlled and observational studies, diagnostic accuracy studies, systematic reviews and meta-analyses, as well as real-world implementation reports. Published pooled estimates from the two major meta-analyses identified in the source material are reported as previously published estimates and are not presented as a new quantitative synthesis.

This approach is intended to provide a transparent narrative synthesis while avoiding the methodological overstatement that would arise from describing the present article as a new systematic review and meta-analysis. Where individual studies provide more recent or context-specific evidence, their findings are discussed alongside the pooled literature.

3. Conventional blood culture and the need for rapid diagnosis

Blood culture remains indispensable in the diagnosis of BSI because it provides viable isolates for definitive organism identification and phenotypic antimicrobial susceptibility testing. Nevertheless, the time required for microbial growth and subsequent laboratory processing can delay targeted treatment. The clinical consequence is particularly important in patients with severe sepsis or septic shock, in whom the initial antimicrobial regimen may need to cover a broad range of organisms and resistance phenotypes before microbiological information becomes available.

Rapid molecular testing addresses a different part of this diagnostic problem. Rather than waiting for organism growth, molecular assays detect predefined nucleic-acid targets and can therefore provide actionable information within hours. Their main limitations arise from the same feature that makes them rapid: they can only detect organisms and resistance determinants included in the assay design. A negative molecular result therefore cannot automatically exclude BSI, particularly when the causative organism is outside the panel.

The optimal diagnostic strategy is consequently complementary. Conventional blood culture provides broad recovery and phenotypic information, while rapid molecular testing can accelerate the first clinically actionable identification step. The relative value of each technology depends on the patient's acuity, the organisms prevalent in the local setting, baseline laboratory turnaround time and the capacity of the clinical team to act on rapid results.

4. Major point-of-care and near-patient NAAT platforms

4.1. Culture-independent T2 magnetic resonance testing

T2MR is a culture-independent molecular platform that uses nucleic-acid amplification followed by magnetic resonance-based detection. The technology is designed to detect selected pathogen targets directly from whole blood and therefore does not require a blood culture bottle to become positive before generating a result. The T2Bacteria panel targets six bacterial pathogens, while T2Candida targets five clinically important Candida species. In the source evidence, results are available within approximately three to five hours of sample collection.

The principal clinical advantage of T2MR is therefore temporal. When the suspected pathogen is included on the panel, detection can occur substantially earlier than conventional blood culture. This is potentially most valuable in high-acuity situations in which early pathogen information can influence antimicrobial selection before conventional culture becomes positive.

4.2. Culture-based multiplex PCR and BCID2

BCID2 represents a different diagnostic model. The assay is applied to a blood culture bottle after it has flagged positive and uses multiplex PCR to identify a broad group of bacterial and fungal pathogens together with selected antimicrobial resistance markers. The source manuscript describes identification of 33 pathogens and ten resistance markers in approximately one hour after a positive blood culture signal.

Because BCID2 requires culture positivity, it cannot eliminate the initial blood-culture incubation interval. Its value lies in compressing the time between culture positivity and actionable organism or resistance information. This distinction is important when interpreting claims of 'rapid diagnosis': T2MR can provide direct-from-blood information, whereas BCID2 accelerates the post-positivity identification phase.

Table 1: Comparison of major rapid molecular diagnostic approaches for bloodstream infection

Diagnostic stage	Direct from whole blood	After blood culture positivity	Conventional culture pathway
Representative platform	T2Bacteria/T2Candida	BioFire BCID2	Blood culture with identification and AST
Main information	Selected pathogen targets	Pathogens + selected AMR markers	Broad organism recovery + phenotypic AST
Turnaround advantage	Hours from specimen collection	Approximately 1 h after positivity	Typically substantially longer
Main strength	Can bypass culture positivity	Broad post-positivity panel and rapid AMR-marker information	Broadest recovery and definitive phenotypic susceptibility testing
Main limitation	Limited to on-panel organisms	Requires a positive culture first; limited to on-panel targets	Slow and may miss low-burden/fastidious infection
Best conceptual role	Early high-acuity detection	Rapid acceleration of positive cultures	Reference/complementary microbiological pathway

5. Diagnostic performance of rapid molecular platforms

5.1. T2MR diagnostic accuracy

Foundational diagnostic accuracy studies provide the basis for interpreting more recent T2MR implementation evidence. A prospective multicentre study conducted across 11 United States hospitals evaluated T2Bacteria and reported per-patient sensitivity and specificity of approximately 90% for proven bloodstream infection caused by organisms covered by the panel, with a negative predictive value of 99.7%. A separate pooled analysis of eight studies involving 2,717 subjects evaluated T2Candida and reported pooled sensitivity of 91% and specificity of 94%, with a diagnostic odds ratio of 133.65 and a summary receiver operating characteristic area under the curve of 0.970.

More recent clinical studies have generally supported the central value proposition of rapid detection while illustrating the importance of patient population and panel coverage. In a paediatric cohort, T2Bacteria sensitivity and specificity were 84.2% and 85.9%, respectively, while T2Candida sensitivity and specificity were 100% and 94.1%. Definitive microorganism identification was available in a mean of 4.4 hours for T2Bacteria and 3.7 hours for T2Candida, compared with 65.7 and 125.5 hours for blood culture, respectively. The study also reported 100% T2Bacteria sensitivity with blood volumes below 2 mL in neonates and infants, highlighting a potential practical advantage where obtaining larger blood volumes is difficult.

A 2024 single-centre evaluation of T2MR in septic patients further reported shorter turnaround and substantial concordance with conventional blood culture, while a 2026 intensive-care study comparing rapid molecular diagnostics with conventional blood cultures reported high diagnostic performance for organisms covered by the T2Bacteria/T2Resistance panels. Complementary clinical evidence includes an emergency-department study evaluating early T2Bacteria initiation (Voigt *et al.*, 2020), prospective evaluation of T2MR for complicated candidemia (Posteraro *et al.*, 2018), diagnostic evaluation of the T2Resistance panel for selected resistance determinants (Ashcraft *et al.*, 2025), and a descriptive intensive-care experience in which T2Bacteria/T2Resistance results were associated with changes in antimicrobial therapy (Giacobbe *et al.*, 2022).

5.2. BCID2 diagnostic accuracy

The principal pooled diagnostic accuracy evidence for BCID2 comes from a 2022 systematic review and meta-analysis covering nine studies and 2,005 blood cultures. The pooled estimates demonstrate high performance for several major pathogen groups. Sensitivity and specificity were 98.2% and 98.3% for Enterobacterales, 96.0% and 99.5% for Staphylococcus aureus, and 96.7% and 99.5% for Streptococcus species. Sensitivity was somewhat lower for less frequently represented targets such as Pseudomonas aeruginosa and Enterococcus faecalis, for which confidence intervals were wider.

Performance for selected antimicrobial resistance markers was also high (Holma *et al.*, 2022; Rhoads *et al.*, 2023). Pooled sensitivity and specificity were 94.9% and 99.4% for blaCTX-M, 94.9% and 99.7% for carbapenemases, and 93.9% and 99.6% for mecA/C and MREJ. These findings illustrate the clinical advantage of combining pathogen identification with early resistance-marker information, but molecular detection should not be equated automatically with full phenotypic susceptibility. Resistance genes are selected targets and do not capture every mechanism or every clinically relevant phenotype.

The diagnostic accuracy evidence also demonstrates an important statistical and clinical principle: pooled headline accuracy is strongest for targets that are common in the underlying dataset. Less common organisms may have fewer contributing observations and therefore wider uncertainty. Consequently, local epidemiology and the prevalence of off-panel organisms remain important when interpreting the apparent performance of any multiplex assay.

Table 2: Selected diagnostic performance findings from major rapid molecular platforms

Platform/target	Evidence base	Sensitivity	Specificity	Clinical interpretation
T2Bacteria	Nguyen *et al.* (2019); 11 hospitals	90%	90%	Strong foundational performance for on-panel BSI; high NPV reported
T2Candida	Tang *et al.* (2019); 8 studies, 2,717 subjects	91% (88–94%)	94% (93–95%)	High pooled diagnostic performance for selected Candida targets
T2Bacteria in paediatric cohort	Lucignano *et al.* (2022)	84.2%	85.9%	Rapid results; performance influenced by paediatric population and panel coverage
T2Candida in paediatric cohort	Lucignano *et al.* (2022)	100%	94.1%	Rapid fungal identification in paediatric BSI
BCID2: *Enterobacterales*	Peri *et al.* (2022); 9 studies, 2,005 cultures	98.2% (96.3–99.1%)	98.3% (96.5–99.2%)	Excellent pooled performance
BCID2: *S. aureus*	Peri *et al.* (2022)	96.0% (90.4–98.4%)	99.5% (98.7–99.8%)	Excellent pooled performance
BCID2: *Streptococcus spp.*	Peri *et al.* (2022)	96.7% (92.8–98.5%)	99.5% (98.8–99.8%)	Excellent pooled performance
BCID2: blaCTX-M	Peri *et al.* (2022)	94.9% (85.7–98.3%)	99.4% (97.8–99.8%)	Strong resistance-marker performance
BCID2: *Carbapenemases*	Peri *et al.* (2022)	94.9% (83.4–98.6%)	99.7% (98.9–99.9%)	Strong resistance-marker performance
BCID2: mecA/C and MREJ	Peri *et al.* (2022)	93.9% (83.0–98.0%)	99.6% (98.6–99.9%)	Strong resistance-marker performance

6. Clinical utility: From faster detection to better therapy

6.1. Pooled evidence for T2MR

The strongest quantitative evidence for the clinical impact of T2MR comes from a published 2021 systematic review and meta-analysis of 14 controlled studies. The pooled evidence showed a mean reduction of approximately 81 hours in time to pathogen detection and 77 hours in time to species identification compared with blood culture. Among patients with positive T2MR results, time to targeted antimicrobial therapy was reduced by approximately 42 hours. Time to empirical de-escalation among patients with negative T2MR results was reduced by approximately 7 hours.

The same meta-analysis reported shorter length of stay. Mean intensive care unit stay was approximately 5.0 days shorter and mean hospital stay approximately 4.8 days shorter in the T2MR group. Mortality, however, did not differ significantly between groups: the pooled risk ratio was 1.02 (95% CI 0.81-1.29). The absence of a pooled mortality benefit is important because it prevents the review from equating faster microbiological information with guaranteed survival improvement.

Interpretation of the time-based outcomes requires caution because heterogeneity was very high for time to detection, species identification and targeted therapy. Such heterogeneity is clinically understandable: the

absolute advantage of a rapid test depends partly on how long the local blood culture workflow normally takes. In contrast, length-of-stay outcomes showed low heterogeneity, suggesting that downstream resource utilisation may be more stable across settings than absolute time savings.

Table 3: Published pooled clinical outcomes associated with T2MR compared with blood culture

Outcome	Studies	Pooled estimate (95% CI)	Interpretation
Time to detection	13	−81 h (−93 to −69)	Large time advantage for T2MR; very high heterogeneity
Time to species identification	7	−77 h (−114 to −41)	Large time advantage; very high heterogeneity
Time to targeted therapy	4	−42 h (−62 to −23)	Nearly two-day reduction among T2MR-positive patients
Time to empirical de-escalation	4	−7 h (−13 to −1)	Modest benefit; negative molecular result may not be sufficient alone
ICU length of stay	3	−5.0 days (−9.6 to −0.5)	Shorter ICU stay; lower heterogeneity
Hospital length of stay	3	−4.8 days (−9.4 to −0.3)	Shorter hospital stay; no heterogeneity reported
Mortality	4	RR 1.02 (0.81–1.29)	No significant overall mortality difference

6.2. Real-world T2MR implementation

Real-world studies extend the pooled evidence into clinical settings with different patient populations and laboratory workflows. A retrospective intensive-care study from Belgrade reported 100% diagnostic accuracy for the on-panel organisms evaluated and identified all cases of K. pneumoniae, A. baumannii and P. aeruginosa in a small cohort, while conventional blood culture detected 9 of 12 such cases. A retrospective study from Palermo reported 81% concordance between T2Bacteria and blood culture and 88% pathogen coverage among culture-positive cases, with shorter turnaround time.

Another clinical experience illustrates how diagnostic utility may extend beyond analytical performance: rapid molecular results can lead to antimicrobial therapy changes when they are incorporated into clinical decision-making.

The paediatric evidence is particularly illustrative of the time advantage. T2Bacteria and T2Candida produced definitive microorganism identification within hours rather than the much longer blood-culture intervals described above. Additional clinical evidence includes an emergency-department study evaluating early T2Bacteria initiation, prospective evaluation of T2MR for complicated candidemia, and diagnostic evaluation of the T2Resistance panel for selected resistance determinants.

A separate critically ill cohort reported pathogen identification by T2Bacteria in 26% of tested episodes, detection of resistance determinants by T2Resistance in 11%, and treatment changes attributable to these results in 21% of episodes.

6.3. Clinical utility of BCID2

BCID2 has accumulated a growing real-world evidence base since its clinical implementation. Earlier rapid molecular diagnostic trials showed that accelerated organism identification can support antimicrobial optimisation, particularly when linked to stewardship interventions (Banerjee *et al.*, 2015; Buss *et al.*, 2018). Clinical evaluations of BCID2 have similarly demonstrated effects on patient management and antimicrobial stewardship (Sparks *et al.*, 2021). A retrospective propensity-score-matched study of critically ill patients with BSI found that BCID2-guided antimicrobial stewardship was associated with shorter time to appropriate antimicrobial therapy and lower day-28 mortality specifically among patients who had initially received inappropriate empirical therapy (Tseng *et al.*, 2024).

In a separate intensive-care study conducted in Taiwan in a setting with a high burden of drug-resistant pathogens, BCID2 produced substantially faster pathogen and resistance-marker information than conventional

culture and influenced antimicrobial stewardship decisions (DelRusso *et al.*, 2023). A community health-system study of 190 patients found that time to de-escalation fell from 59.2 to 35.3 hours after BCID2 implementation, while time to culture identification decreased from 53.1 to 22.4 hours. The study is notable because results were communicated through a standard critical-laboratory notification pathway without direct antimicrobial-stewardship team notification, suggesting that some benefit can be achieved even in settings with limited stewardship resources.

Other implementation evidence is more nuanced. A 2026 academic medical-centre evaluation found no overall reduction in the time from positive blood culture to the first effective or appropriate antibiotic dose, although a shorter time to effective therapy was observed among cultures containing organisms with Gram-negative resistance (Dave and Moy, 2026). False-negative results for on-panel organisms have also been reported, illustrating that molecular assays require cautious interpretation alongside culture and clinical context (Fox-Lewis *et al.*, 2022). Economic evidence indicates that the value of rapid diagnostics is strongly influenced by whether results are coupled with antimicrobial stewardship and by downstream resource utilisation (Pliakos *et al.*, 2018). Studies of stewardship-linked rapid molecular testing also support faster optimisation of antimicrobial therapy in selected bloodstream infections (Rivard *et al.*, 2017).

Paediatric implementation evidence has also supported the practical value of BCID2, with evaluation of the expanded panel in a US children's hospital demonstrating measurable clinical impact (Graff *et al.*, 2021).

Table 4: Representative real-world implementation evidence for rapid molecular diagnostics

Platform/study context	Design	Main finding	Clinical implication
T2MR, Belgrade ICU, 2026	Retrospective comparative	High accuracy for on-panel organisms; rapid molecular detection outperformed culture for selected cases	Supports early detection but small single-centre evidence
T2MR, Palermo, 2024	Retrospective single-centre	81% concordance with culture; 88% pathogen coverage among culture-positive cases; shorter turnaround	Demonstrates practical time advantage
T2Bacteria/T2Resistance, 2022	Retrospective clinical experience	Pathogen identified in 26%; resistance determinant in 11%; therapy changed in 21%	Shows potential for treatment modification
BCID2, Taiwan, 2024	Retrospective propensity-score matched	Shorter time to appropriate therapy; lower day-28 mortality in initially inappropriate therapy subgroup	Potential outcome benefit in high-risk subgroup
BCID2, Taiwan ICU, 2024	Retrospective observational	Faster results and measurable stewardship impact in high AMR burden	Relevant to resistant BSI settings
BCID2, community system, 2023	Retrospective pre/post	De-escalation ~24 h faster; culture identification ~31 h faster	Benefit possible without direct stewardship-team notification
BCID2, academic centre, 2025/2026 report	Retrospective before/after	No overall reduction in time to first effective antibiotic; shorter time in Gram-negative resistance subgroup	Implementation benefit is context-dependent

7. Antimicrobial stewardship and the interpretation of rapid molecular results

Rapid pathogen and resistance-marker information is most clinically valuable when it changes antimicrobial decisions. In the absence of an active stewardship pathway, a molecular result may simply coexist with an empirical regimen that is not modified until conventional culture and susceptibility data become available. Conversely, when rapid results are incorporated into diagnostic stewardship, they can support earlier escalation when resistance is identified, de-escalation when a likely pathogen and susceptibility profile permit narrowing, and avoidance of unnecessary broad-spectrum exposure.

The evidence reviewed here suggests that antimicrobial stewardship is therefore not an optional add-on but an important mediator of clinical benefit. The clearest mortality signal in the BCID2 literature occurred

among critically ill patients who initially received inappropriate empirical therapy, supporting the concept that rapid diagnostics may have their greatest effect when they correct an existing therapeutic mismatch.

Nevertheless, rapid molecular detection must be interpreted within clinical context. Detection of a resistance gene does not necessarily establish the full phenotypic susceptibility profile, while a negative result does not exclude organisms that are absent from the panel. Stewardship teams and treating clinicians should therefore combine molecular results with the patient's clinical syndrome, local resistance epidemiology, Gram-stain information where available, blood-culture growth characteristics and subsequent phenotypic susceptibility testing.

8. Integration of rapid molecular testing into the clinical diagnostic workflow

A practical clinical model is to treat rapid molecular testing and conventional blood culture as complementary layers rather than competing diagnostic systems. The appropriate platform depends on when the clinician needs information and what information is required.

Table 5: Conceptual clinical workflow for integrating rapid molecular diagnostics with conventional blood culture in suspected bloodstream infection

Suspected BSI/sepsis	Blood culture collected	Rapid molecular pathway selected	T2MR: direct-from-blood or BCID2: after culture positivity	**Pathogen ± resistance information**	Antimicrobial stewardship + clinical reassessment	**Targeted/de-escalated therapy with culture confirmation**

In this framework, the rapid test is used to accelerate the first actionable microbiological decision, while culture continues in parallel. T2MR is most conceptually suited to patients in whom direct-from-blood information is valuable before culture positivity, whereas BCID2 is most suited to rapid interpretation of a positive blood culture. Both pathways should feed into antimicrobial stewardship and clinical reassessment rather than automatically dictating therapy.

9. Comparative clinical application of T2MR and BCID2

The two major platform categories should not be interpreted as interchangeable alternatives. T2MR's distinguishing feature is culture independence, making it particularly attractive when a rapid answer is needed before blood culture becomes positive. Its limitation is a narrower organism menu. BCID2, by contrast, is triggered by a positive blood culture and therefore cannot shorten the initial time to positivity, but it offers broader post-positivity pathogen coverage and resistance-marker information.

Table 6: Practical comparison of T2MR and BCID2 in clinical decision-making

Clinical consideration	T2MR	BCID2
When information becomes available	Within hours of direct blood testing	After blood culture becomes positive, usually within approximately 1 h thereafter
Main clinical question	Can an on-panel pathogen be detected before culture positivity?	Which pathogen and selected resistance markers are present in a positive culture?
Major advantage	Early direct-from-blood detection	Broad post-positivity identification and resistance-marker information
Major limitation	Narrower target coverage	Cannot bypass the blood-culture positivity interval
Role in stewardship	May support earlier targeted therapy or selected de-escalation	May support escalation/de-escalation after culture positivity
Need for conventional culture	Yes	Yes
Best-fit clinical context	High-acuity patients needing early information	Routine acceleration of positive blood-culture management

The practical decision is therefore influenced by clinical acuity and laboratory workflow. In patients with septic shock, febrile neutropenia or another scenario in which even a short delay may be clinically consequential, a culture-independent assay may provide information that conventional culture cannot provide soon enough. In laboratories processing large numbers of positive blood cultures, BCID2 may function as a broad near-patient or near-laboratory accelerator that shortens the interval between culture positivity and treatment optimisation.

Neither technology should be considered a replacement for blood culture. Molecular panels are inherently constrained by their target lists, and negative results require cautious interpretation. Blood culture remains necessary for recovery of off-panel organisms and for phenotypic susceptibility testing. The most defensible clinical model is therefore parallel testing with rapid molecular acceleration followed by culture-based confirmation and completion of microbiological characterisation.

10. Conclusion

Point-of-care and near-patient nucleic acid amplification technologies have substantially changed the diagnostic timeline for bloodstream infection. T2MR can provide direct-from-blood detection within hours, offering an opportunity to identify selected pathogens before conventional blood culture becomes positive. BCID2 provides rapid pathogen and selected resistance-marker identification once a blood culture has flagged positive, thereby accelerating the post-positivity phase of microbiological diagnosis. Published evidence demonstrates meaningful reductions in time to detection and antimicrobial optimisation, while diagnostic accuracy is high for several major targets.

The clinical value of these technologies, however, depends on how rapidly results are communicated and incorporated into treatment decisions. The available evidence does not support replacing blood culture, which remains essential for broad organism recovery and phenotypic susceptibility testing. Instead, the most appropriate model is an integrated diagnostic pathway in which rapid molecular testing accelerates early decision-making and conventional culture provides complementary definitive microbiological information. Future research should prioritise prospective patient-centred outcomes, subgroup analyses of patients with initially inappropriate therapy, formal cost-effectiveness assessment and implementation studies across diverse healthcare settings.

References

Ashcraft, D., St Pierre, J., Davis, H., Scariano, S., Latsis, M., Vortisch, R., Smith, S. and Pankey, G. (2025). Evaluation of the diagnostic accuracy of the T2Resistance panel (research use only) in patients with possible bacterial bloodstream infections. *Ochsner J*, 25(1): 24-33. doi: 10.31486/toj.24.0101.

Banerjee, R., Teng, C.B., Cunningham, S.A., Ihde, S.M., Steckelberg, J.M., Moriarty, J.P. *et al.* (2015). Randomized trial of rapid multiplex polymerase chain reaction-based blood culture identification and susceptibility testing. *Clin Infect Dis*, 61(7): 1071-1080. doi: 10.1093/cid/civ447.

Berinson, B., Both, A., Berneking, L., Christner, M., Lütgehetmann, M., Aepfelbacher, M. *et al.* (2021). Usefulness of BioFire FilmArray BCID2 for blood culture processing in clinical practice. *J Clin Microbiol*, 59(8): e00543-21. doi: 10.1128/JCM.00543-21.

Bonura, C., Graceffa, D., Distefano, S., De Grazia, S., Guzman, O., Bohn, B. *et al.* (2024). Evaluation of T2 magnetic resonance (T2MR) technology for the early detection of ESKAPEc pathogens in septic patients. *Antibiotics (Basel)*, 13(9): 885. doi: 10.3390/antibiotics13090885.

Buss, B.A., Baures, T.J., Yoo, M., Hanson, K.E., Alexander, D.P., Benefield, R.J. *et al.* (2018). Impact of a multiplex PCR assay for bloodstream infections with and without antimicrobial stewardship intervention at a cancer hospital. *Open Forum Infect Dis*, 5(10): ofy258. doi: 10.1093/ofid/ofy258.

Cortazzo, V., D'Inzeo, T., Giordano, L., Menchinelli, G., Liotti, F.M., Fiori, B. *et al.* (2021). Comparing BioFire FilmArray BCID2 and BCID panels for direct detection of bacterial pathogens and antimicrobial resistance genes from positive blood cultures. *J Clin Microbiol*, 59(4): e03163-20. doi: 10.1128/JCM.03163-20.

D'Onofrio, V., Salimans, L., Bedenic, B., Cartuyvels, R., Barisic, I. and Gyssens, I.C. (2020). The clinical impact of rapid molecular microbiological diagnostics for pathogen and resistance gene identification in patients with sepsis: A systematic review. *Open Forum Infect Dis*, 7(10): ofaa352. doi: 10.1093/ofid/ofaa352.

Dave, A.S. and Moy, S.P-1984. (2026). Assessing the clinical impact of the BioFire FilmArray Blood Culture Identification 2 (BCID2) Panel in the selection of effective antibiotic therapy at an academic medical center. *Open Forum Infect Dis*, 13(Suppl 1): ofaf695.2151. doi: 10.1093/ofid/ofaf695.2151.

DelRusso, K., Colmerauer, J. and Premus, J. (2023). Impact of the BioFire FilmArray Blood Culture Identification 2 (BCID2) Panel on time to antimicrobial escalation or de-escalation in a community health system. *Open Forum Infect Dis*, 10(Suppl 2): ofad500.206. doi: 10.1093/ofid/ofad500.206.

Evans, L., Rhodes, A., Alhazzani, W., Antonelli, M., Coopersmith, C.M., French, C. *et al.* (2021). Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. *Intensive Care Med*, 47: 1181-1247. doi: 10.1007/s00134-021-06506-y.

Fox-Lewis, A., Wang, J., Strydom, H., Wright, J., Morpeth, S.C. and Taylor, S. (2022). False negative Escherichia coli result from the BioFire FilmArray Blood Culture Identification 2 panel. *J Clin Microbiol*, 60(11): e02339-21. doi: 10.1128/jcm.02339-21.

Giacobbe, D.R., Crea, F., Morici, P., Magnasco, L., Di Pilato, V., Briano, F. *et al.* (2022). T2Bacteria and T2Resistance assays in critically ill patients with sepsis or septic shock: A descriptive experience. *Antibiotics (Basel)*, 11(12): 1823. doi: 10.3390/antibiotics11121823.

Giannella, M., Pankey, G.A., Pascale, R., Miller, V.M., Miller, L.E. and Seitz, T. (2021). Antimicrobial and resource utilization with T2 magnetic resonance for rapid diagnosis of bloodstream infections: Systematic review with meta-analysis of controlled studies. *Expert Rev Med Devices*, 18(5): 473-482. doi: 10.1080/17434440.2021.1919508.

Graff, K.E., Palmer, C., Anarestani, T., Velasquez, D., Hamilton, S., Pretty, K. *et al.* (2021). Clinical impact of the expanded BioFire blood culture identification 2 panel in a US children's hospital. *Microbiol Spectr*, 9(1): e00429-21. doi: 10.1128/Spectrum.00429-21.

Holma, T., Torvikoski, J., Friberg, N., Nevalainen, A., Tarkka, E., Antikainen, J. *et al.* (2022). Rapid molecular detection of pathogenic microorganisms and antimicrobial resistance markers in blood cultures: Evaluation and utility of the next-generation FilmArray Blood Culture Identification 2 panel. *Eur J Clin Microbiol Infect Dis*, 41: 363-371. doi: 10.1007/s10096-021-04314-2.

Lucignano, B., Cento, V., Agosta, M., Ambrogi, F., Albitar-Nehme, S., Mancinelli, L. *et al.* (2022). Effective rapid diagnosis of bacterial and fungal bloodstream infections by T2 magnetic resonance technology in the pediatric population. *J Clin Microbiol*, 60(10): e00292-22. doi: 10.1128/jcm.00292-22.

Mylonakis, E., Clancy, C.J., Ostrosky-Zeichner, L., Garey, K.W., Alangaden, G.J., Vazquez, J.A. *et al.* (2015). T2 magnetic resonance assay for the rapid diagnosis of candidemia in whole blood: A clinical trial. *Clin Infect Dis*, 60(6): 892-899. doi: 10.1093/cid/ciu959.

Nguyen, M.H., Clancy, C.J., Pasculle, A.W., Pappas, P.G., Alangaden, G., Pankey, G.A. *et al.* (2019). Performance of the T2Bacteria panel for diagnosing bloodstream infections: A diagnostic accuracy study. *Ann Intern Med*, 170(12): 845-852. doi: 10.7326/M18-2772.

Peri, A.M., Ling, W., Furuya-Kanamori, L., Harris, P.N.A. and Paterson, D.L. (2022). Performance of BioFire Blood Culture Identification 2 Panel (BCID2) for the detection of bloodstream pathogens and their associated resistance markers: A systematic review and meta-analysis of diagnostic test accuracy studies. *BMC Infect Dis*, 22: 794. doi: 10.1186/s12879-022-07772-x.

Pliakos, E.E., Andreatos, N., Shehadeh, F., Ziakas, P.D. and Mylonakis, E. (2018). The cost-effectiveness of rapid diagnostic testing for the diagnosis of bloodstream infections with or without antimicrobial stewardship. *Clin Microbiol Rev*, 31(3): e00095-17. doi: 10.1128/CMR.00095-17.

Posteraro, B., Torelli, R., De Carolis, E., Spanu, T. and Sanguinetti, M. (2018). T2 magnetic resonance contributes to the very early diagnosis of complicated candidaemia: A prospective study. *J Antimicrob Chemother*, 73(7): 1952-1959. doi: 10.1093/jac/dky048.

Rhoads, D.D., Pournaras, S., Leber, A., Balada-Llasat, J.M., Harrington, A., Sambri, V. *et al.* (2023). Multicenter evaluation of the BIOFIRE Blood Culture Identification 2 panel for detection of bacteria, yeasts, and antimicrobial resistance genes in positive blood culture samples. *J Clin Microbiol*, 61(6): e01891-22. doi: 10.1128/jcm.01891-22.

Rivard, K.R., Athans, V., Lam, S.W., Gordon, S.M., Procop, G.W., Richter, S.S. and Neuner, E. (2017). Impact of antimicrobial stewardship and rapid microarray testing on patients with Gram-negative bacteremia. *Eur J Clin Microbiol Infect Dis*, 36(10): 1879-1887. doi: 10.1007/s10096-017-3008-6.

Sparks, R., Balgahom, R., Janto, C., Polkinghorne, A. and Branley, J. (2021). Evaluation of the BioFire Blood Culture Identification 2 panel and impact on patient management and antimicrobial stewardship. *Pathology*, 53(7): 889-895. doi: 10.1016/j.pathol.2021.02.016.

Tang, D.L., Chen, X., Zhu, C.G., Zhu, Z.H., Xia, Y., Wang, S.Y. *et al.* (2019). Pooled analysis of T2 Candida for rapid diagnosis of candidiasis. *BMC Infect Dis*, 19: 798. doi: 10.1186/s12879-019-4419-z.

Timbrook, T.T., Morton, J.B., McConeghy, K.W., Caffrey, A.R., Mylonakis, E. and LaPlante, K.L. (2017). The effect of molecular rapid diagnostic testing on clinical outcomes in bloodstream infections: A systematic review and meta-analysis. *Clin Infect Dis*, 64(1): 15-23. doi: 10.1093/cid/ciw649.

Tseng, H.Y., Chen, C.L., Chen, W.C., Kuo, Y.C., Liang, S.J., Tu, C.Y. *et al.* (2024). Reduced mortality with antimicrobial stewardship guided by BioFire FilmArray Blood Culture Identification 2 panel in critically ill patients with bloodstream infection: A retrospective propensity score-matched study. *Int J Antimicrob Agents*, 64(4): 107300. doi: 10.1016/j.ijantimicag.2024.107300.

Unic-Stojanovic, D., Kangrga, N., Cirkovic, I., Malesevic, I., Djokovic Mrdakovic, I., Petrovic, J. and Bojic, M. (2026). Sepsis diagnosis in the intensive care unit: A comparative study of rapid molecular diagnostics and conventional blood cultures. *Biomedicines*, 14(2): 479. doi: 10.3390/biomedicines14020479.

Voigt, C., Silbert, S., Widen, R.H., Marturano, J.E., Lowery, T.J., Ashcraft, D. and Pankey, G. (2020). The T2Bacteria assay is a sensitive and rapid detector of bacteremia that can be initiated in the emergency department and has potential to favorably influence subsequent therapy. *J Emerg Med*, 58(5): 785-796. doi: 10.1016/j.jemermed.2019.11.028.

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