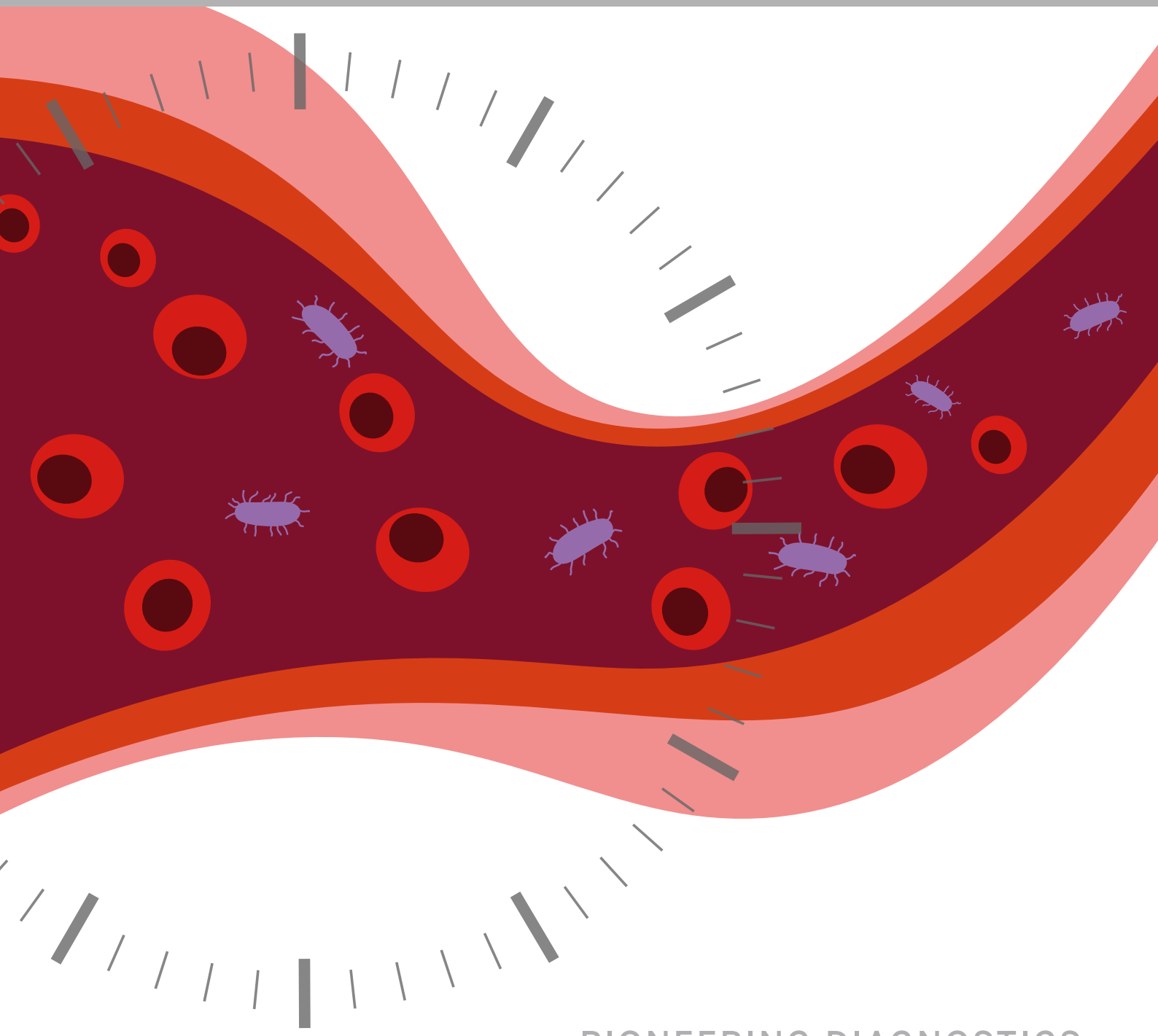
BIOMÉRIEUX

EVIDENCE-BASED DIAGNOSTICS FOR BLOODSTREAM INFECTION MANAGEMENT

Selection of publications

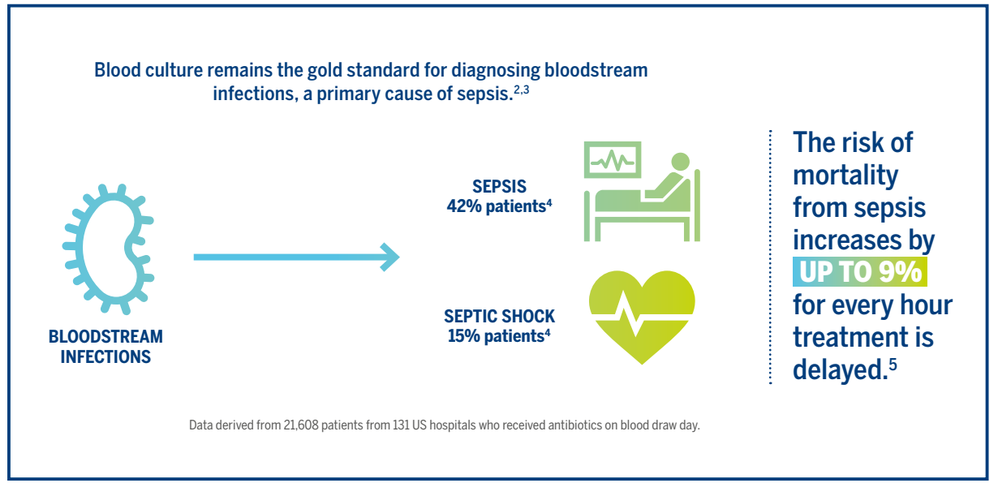
2026 EDITION



PIONEERING DIAGNOSTICS

“Utilization of rapid diagnostics is a critical tool for the minimization of time to target therapy and improved sepsis outcomes.”[1]

Figure 1. Bloodstream infection diagnostic tools are critical for optimal management of sepsis[2-5]
Source: bioMérieux



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PREFACE

Sepsis is a major global health challenge, responsible for life-threatening organ dysfunction and contributing significantly to mortality worldwide. In many cases, **sepsis** is the final common death pathway for severe infectious diseases, including bacterial bloodstream infections, diarrheal disease, lower respiratory tract infections, malaria, dengue, and systemic fungal infections.[6] In 2017 alone, an estimated **49 million cases of sepsis** occurred globally, leading to **11 million potentially avoidable deaths** - accounting for approximately **20% of all annual deaths worldwide**.[7] Despite its profound impact, awareness and recognition of sepsis remain insufficient across healthcare systems.

Our understanding of **sepsis** and its systemic effects has evolved over time, with advances in medical knowledge, pathophysiology, and diagnostics shaping modern clinical practice. The latest international consensus, published in 2016 and incorporated into the **2021 Surviving Sepsis Campaign** guidelines, defines **sepsis** as “life-threatening organ dysfunction caused by a dysregulated host response to infection”.[8,9] For clinical operationalization, organ dysfunction is identified as an acute increase of **two or more points in the Sequential Organ Failure Assessment (SOFA) score**.[8]

Since delays in recognition and treatment significantly increase mortality, **early diagnosis and timely intervention** are critical for improving clinical outcomes.[10] Rapid initiation of appropriate antimicrobial therapy has been shown to reduce morbidity and mortality in bacterial infections.[11] As blood cultures remain the gold standard for diagnosing bloodstream infections, integrating **rapid diagnostic technologies** for pathogen identification and antimicrobial susceptibility testing has dramatically improved the time to targeted therapy.[12]

This **selection of publications** highlights the **latest scientific evidence** supporting the role of **Rapid Diagnostic Tests (RDTs)** in improving clinical outcomes and healthcare efficiency. RDTs are essential tools for laboratories, Antimicrobial Stewardship Programs (ASP), and frontline clinicians, ensuring timely and appropriate antimicrobial use to improve patient survival, shorten hospital stays, and reduce healthcare-associated costs.

We hope this document supports clinicians in **integrating rapid diagnostics into routine care**.

Professor Ignacio Martin-Loeches, MD, PhD, FJFICMI,

Trinity College Dublin, School of Medicine,
Consultant in Intensive Care Medicine St James’s Hospital,
Dublin, Ireland

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INTRODUCTION

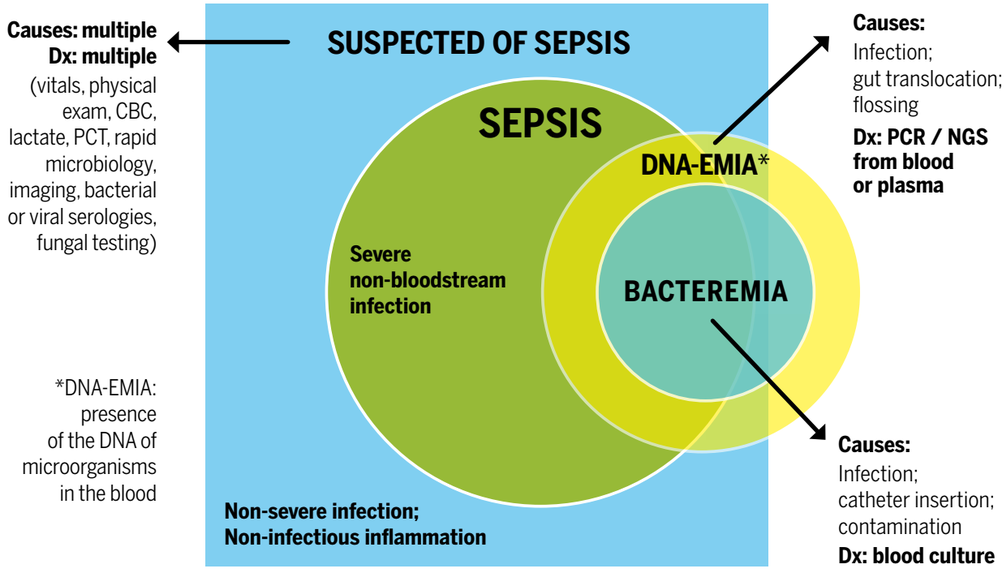
SEPSIS AWARENESS AND EARLY INTERVENTIONS

Sepsis is a preventable, life-threatening condition in which timely and appropriate care management is critical to improving clinical outcomes. However, the heterogeneous presentation of sepsis often makes early recognition challenging. **Screening tools**—combining vital signs, laboratory tests, and AI-driven algorithms—can aid in **early sepsis detection and risk stratification**, potentially enhancing clinical decision-making and prompting timely interventions.[13,14]

Early treatment, particularly with **antibiotics**, is crucial for improving patient outcomes. However, **empiric broad-spectrum antibiotics** are often prescribed to ensure broad initial coverage, increasing the risk of toxicity and **long-term antimicrobial resistance**. To optimize therapy, it is essential to rapidly identify the infection site, determine the **causative pathogen**, and establish **appropriate antimicrobial coverage**, enabling **early de-escalation or discontinuation** of empiric regimens when possible.[1]

Given the systemic nature of sepsis and its frequent association with **bloodstream infections (BSI) (Figure 2)**,[11] **blood cultures** remain a cornerstone of sepsis diagnostics and are strongly recommended in international guidelines.[9,15] Studies have consistently shown that **time to appropriate antimicrobial therapy** is directly correlated with **sepsis mortality (Figure 3)**.[16,17] Therefore, **rapid identification of the causative pathogen and its antimicrobial susceptibility** is imperative to guide **effective, targeted therapy**, ultimately improving patient outcomes and reducing unnecessary antimicrobial exposure.

Figure 2. Conceptual relationship between sepsis and bacteremia, showing overlap[11]
Reproduced with permission from Sweeney TE, *et al*. *Expert Rev Mol Diagn*. 2019;19(11):959-962



CBC: complete blood count; DNA: deoxyribonucleic acid; Dx: diagnostics; NGS: next-generation sequencing; PCR: polymerase chain reaction; PCT: procalcitonin

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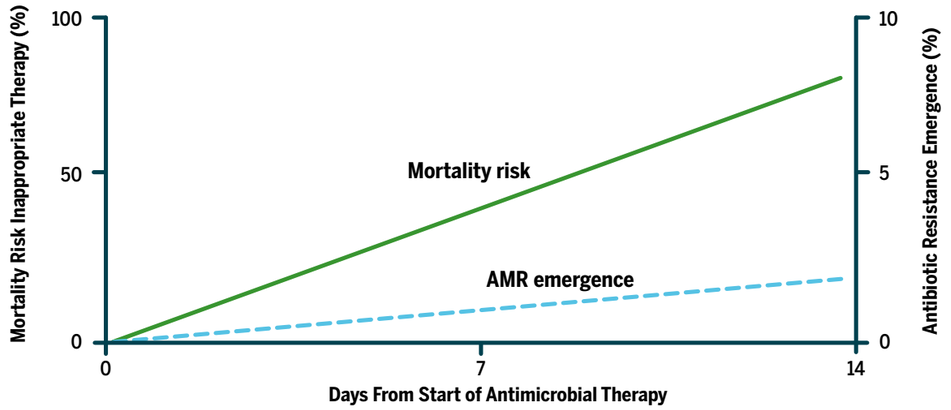
Figure 3. Increasing risk of mortality for each day that inappropriate therapy is continued after start of treatment[16]
Reproduced from Kollef MH, *et al*. *Crit Care* 2021;25(1):360. Open Access CC BY 4.0



IMPACT OF RAPID AND INTEGRATED DIAGNOSTICS ON CLINICAL OUTCOMES

The **prompt administration of antibiotics** for life-threatening infections must be balanced with the **selection of appropriate antimicrobial therapy**, i.e., an antimicrobial regimen proven to have *in vitro* activity against the causative pathogens. Numerous observational studies, both retrospective and prospective, along with one randomized trial in patients with Gram-negative bacterial bloodstream infections, have demonstrated that **delays in appropriate antimicrobial therapy** are associated with **increased mortality**.[16,18-22] This relationship holds true across community-acquired and hospital-acquired infections, including **sepsis, septic shock, bloodstream infections**, and **nosocomial pneumonia**.

Antimicrobial susceptibility testing (AST) is essential for guiding **targeted antimicrobial therapy**. AST is crucial in ensuring effective treatment coverage and combating **antimicrobial resistance (AMR)** — a major contributor to both **community- and hospital-acquired sepsis**. Globally, AMR is responsible for more than **700,000 deaths annually**, a figure projected to reach **10 million by 2050** if left unaddressed.[23]

To optimize treatment, **timely de-escalation of empiric broad-spectrum antibiotics** should be based on **microbiology results** and **patient response**. Unnecessary prolonged use of broad-spectrum agents must be avoided, as **each additional day of antibiotic exposure increases the risk of resistance emergence and potentially negatively impacts patient outcomes**.[24,25] Implementing **risk factor identification** alongside **fast AST technologies** can enhance antimicrobial optimization and stewardship efforts.[26,27,28]

In recent years, several **novel RDTs** for bloodstream infections and sepsis have emerged, significantly **reducing the time to pathogen identification**. Traditional methods typically take 2 to 3 days, whereas modern RDTs can deliver results within hours when performed **directly on positive blood cultures (Figure 4)**.[29] Over the past decade, these technologies have shown significant benefits, including **improved antimicrobial use, better clinical outcomes, and healthcare cost savings**.

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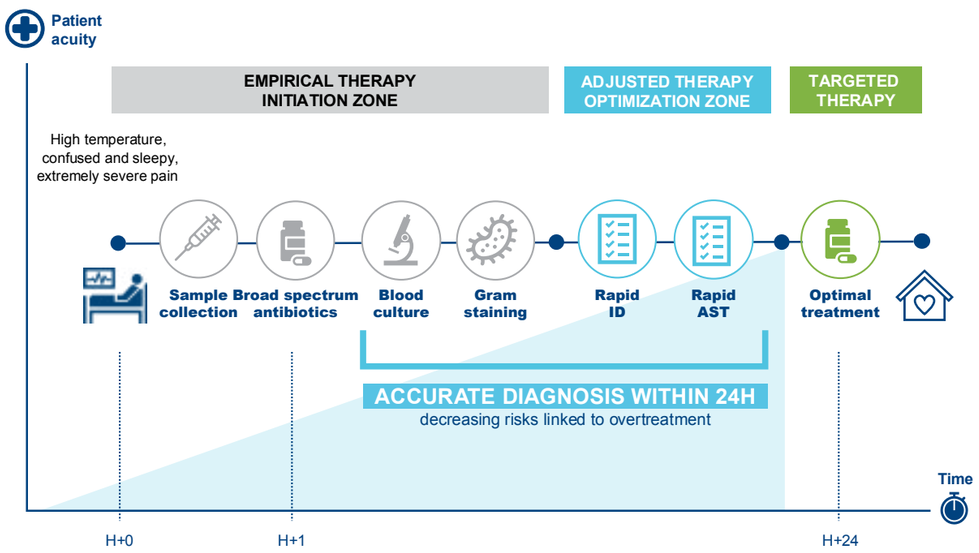
A 2017 meta-analysis by Timbrook *et al*. demonstrated that **RDTs**, when used in combination with **ASP**, were associated with **reduced mortality and shorter hospital stays**.[30] More recently, **Peri *et al***. reviewed 88 studies comparing **RDTs and conventional blood cultures**, both with and without **ASP integration**, in patients with BSI. Their findings confirmed that **RDT implementation improved clinical outcomes** even in centers with well-established ASPs.[31]

Clinical guidelines - including those from the Infectious Diseases Society of America **(IDSA)** and the Society for Healthcare Epidemiology of America **(SHEA)**, as well as the European Respiratory Society **(ERS)**, European Society of Intensive Care Medicine **(ESICM)**, European Society of Clinical Microbiology and Infectious Diseases **(ESCMID)** and Latin American Thoracic Association **(ALAT)** - recommend **the systematic integration of RDTs within stewardship workflows** to **enhance diagnostic accuracy and optimize antimicrobial therapy**.[27,32]

In 2025, the American Society for Microbiology **(ASM)** published the first evidence-based laboratory medicine practice guidelines for the **diagnosis of bloodstream infections using rapid tests**. The expert committee made a series of eight recommendations and **strongly recommended using rapid diagnostics combined with active communication by ASPs, in order to decrease the time to targeted therapy and length of stay**.[33]

Figure 4. Reduced time to optimal treatment through fast diagnostic pathway
Source: bioMérieux



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ECONOMIC BURDEN OF SEPSIS AND THE ROLE OF RAPID DIAGNOSTIC TESTING IN COST-EFFECTIVE SEPSIS MANAGEMENT

Given the high costs associated with sepsis, interventions that **improve patient outcomes while reducing hospital resource consumption** are essential. Strategies such as reducing hospital length of stay, minimizing unnecessary diagnostic tests, and optimizing treatment regimens have significantly lowered healthcare-associated costs related to sepsis and bloodstream infections. A study by Ferrer *et al*. demonstrated that prompt administration of appropriate antibiotic therapy significantly reduces mortality in septic patients.[10] However, **ensuring early and targeted therapy remains a challenge** due to delays in pathogen identification and AST.

The introduction of **RDTs** has been **a game changer in sepsis management**. **RDTs** have been associated with substantial cost savings by accelerating pathogen detection, enabling faster clinical decision-making, and improving antimicrobial stewardship. Perez ***et al***. found that implementing RDTs reduced hospital length of stay by a median of 8 days in patients with Gram-negative bacteremia, leading to estimated savings of approximately $26,298 per patient.[34] Similarly, other studies have shown that the use of RDTs leads to earlier de-escalation of broad-spectrum antibiotics, reducing the risk of AMR while optimizing hospital resources.[35,36]

The **utility of rapid identification and AST** is closely linked to **timely modifications in antimicrobial therapy**. Rapid diagnostics not only improve the accuracy and speed of pathogen identification but also significantly contribute to the cost-effectiveness of healthcare. By reducing hospital stays, minimizing unnecessary treatments, and optimizing resource utilization, these tools play a crucial role in controlling healthcare expenditures.

Furthermore, sepsis management must also take into account the rising challenge of AMR. The overuse and misuse of broad-spectrum antibiotics have driven the emergence of resistant pathogens, increasing the complexity and costs of treatment. **Effective ASPs, supported by rapid diagnostics**, enable more precise and responsible antibiotic use, ultimately **reducing both mortality and financial strain on healthcare systems**.

Integrating these advanced diagnostic tools into routine clinical practice is a crucial step toward enhancing sepsis management. The **combined impact of RDTs and antimicrobial stewardship strategies** holds great promise in improving patient survival, curbing AMR, and ensuring cost-effective, high-quality care.

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Cooper L, Yu K, Van Benten K, Patkar A, Ye G, Gregory S, Ai CE, Gupta V.

MICROBIOLOGY SPECTRUM 2024;12(8):e0040224 https://doi.org/10.1128/spectrum.00402-24

Retrospective evaluation of rapid genotypic ID and phenotypic AST systems on positive blood culture turnaround time and simulated potential impacts on bloodstream infection management. 51

Yuceel-Timur I, Thierry E, Chainier D, Ndao I, Labrousse M, Grélaud C, Bala Y, Barraud O.

JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY 2024;79(Suppl 1):i26-i31 https://academic.oup.com/jac/article/79/Supplement_1/i26/7762031

Explorative cost-effectiveness analysis of a rapid ID and rapid AST solution for patients with bloodstream infection. 53

Boughazi HE, Textoris J, Vandepitte S.

VALUE IN HEALTH 2023;26(12):S176 https://www.valueinhealthjournal.com/article/S1098-3015(23)04034-2/fulltext

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MacVane SH, Dwivedi HP.

JOURNAL OF ANTIMICROBIAL THERAPY 2024;79(Suppl 1):i13-i25 https://doi.org/10.1093/jac/dkae282

RECOMMENDED READING / RESOURCES

The American Society for Microbiology's evidence-based laboratory medicine practice guidelines for the diagnosis of bloodstream infections using rapid tests: a systematic review and meta-analysis.

Wolk DM, Parrott JS, Babady NE, Mochon AB, Tom R, Diel C, Dien Bard J, Harrington A, Hata DJ, Roberts AL, Boyce L, Johnson JK.

CLINICAL MICROBIOLOGY REVIEWS 2025;16:e0013724 https://doi.org/10.1128/cmr.00137-24

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021.

Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM,*et al*.

INTENSIVE CARE MEDICINE 2021;47(11):1181-1247 https://doi.org/10.1007/s00134-021-06506-y

Hospital Sepsis Program Core Elements References and Resources.

Centers for Disease Control and Prevention (CDC) https://www.cdc.gov/sepsis/hcp/core-elements/resources.html

Updated on 31/01/2025. Accessed on 22/09/2025.

CLINICAL VALUE OF APPROPRIATE BLOODSTREAM INFECTION MANAGEMENT

OVERVIEW OF BENEFITS OF FASTER TIME TO THERAPY

TIMING OF ANTIBIOTIC THERAPY AND MORTALITY

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CRITICAL CARE
2021;25:360. doi: 10.1186/s13054-021-03787-z

Timing of antibiotic therapy in the ICU.

Kollef MH, Shorr AF, Bassetti M, Timsit J-F, Micek ST, Michelson AP, Garnacho-Montero J.

OBJECTIVE

This review aimed to examine time-related variables affecting antibiotic optimization and their impact on the treatment of life-threatening infections in the ICU. It also highlights the importance of antibiotic timing in the ICU through the use of advanced molecular microbiology testing and artificial intelligence/machine learning (AI/ML) tools to minimize the unnecessary use of these agents.

KEY STUDIES AND CONCLUSIONS

- **EPIC III Study by Vincent *et al.* (2020)**: This international point prevalence study examined the occurrence of infections in ICUs and highlighted the impact of antibiotic-resistant pathogens on patient outcomes.
- **Bassetti *et al.* (2020)**: A systematic review that confirmed the positive impact of appropriate antibiotic therapy on reducing mortality and length of stay in patients with severe bacterial infections.
- **Vazquez-Guillamet *et al.* (2014)**: This analysis emphasized the importance of appropriate antibiotic therapy in septic shock, showing that timely administration can significantly improve survival.
- **DALI Study by Roberts *et al.* (2014)**: This multicenter study described the variability in achieving pharmacokinetic/pharmacodynamic targets for β-lactam antibiotics in critically ill patients, highlighting the need for prolonged or continuous infusions.
- **Kumar *et al.* (2006)**: This study demonstrated that each hour delay in administering appropriate antibiotics for septic shock significantly increases mortality.

CONCLUSIONS AND FUTURE PERSPECTIVES

The timing of appropriate antibiotics in patients with life-threatening infections, including sepsis and septic shock, is now recognized as one of the most important determinants of survival for infected critically ill patients.

Advances in artificial intelligence (AI) and machine learning (ML) can aid in early identification of sepsis and prediction of antimicrobial resistance patterns, potentially improving the timing and appropriateness of antibiotic therapy.

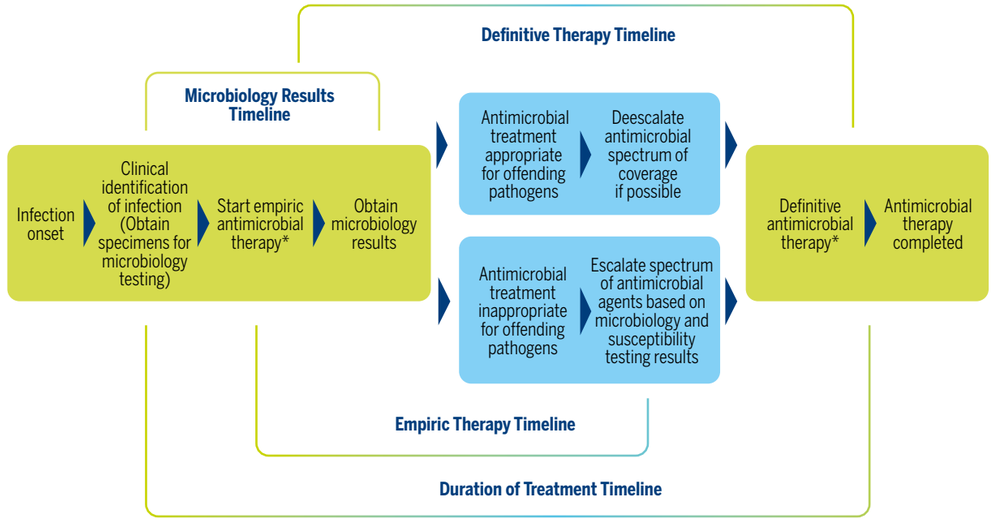
The integration of fast molecular diagnostics and AI/ML algorithms is expected to enhance the timely administration of appropriate antibiotics and minimize the use of unnecessary broad-spectrum agents.

"Avoidance of unnecessarily prolonged administration of broad-spectrum agents, based on available pathogen identification and susceptibility testing, should be routinely performed as the risk of resistance emergence increases incrementally with each day of antibiotic administration without a demonstrable ceiling effect."

KEY FINDINGS

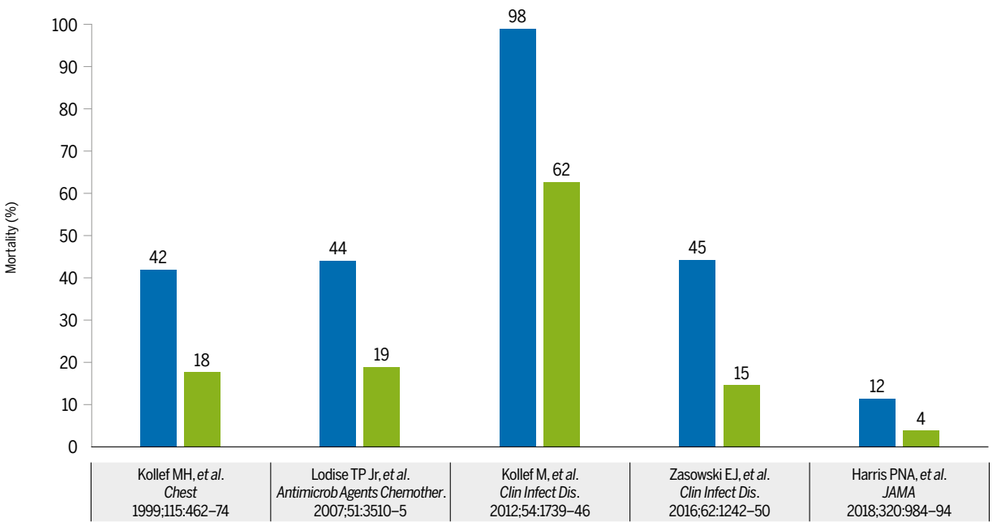
- Timely administration of antibiotics is crucial for improving outcomes in patients with life-threatening infections, such as sepsis and septic shock.
- Delays in antibiotic therapy can significantly increase mortality rates.
- The selection of appropriate antibiotics, which are effective against the offending pathogens, is essential. Both the timing and appropriateness of the antibiotic regimen influence patient survival.
- Early modification of broad-spectrum antibiotic therapy based on microbiology results and clinical response is recommended to prevent the development of antimicrobial resistance and reduce unnecessary antibiotic exposure.

Figure 1. Important antibiotic-related timelines potentially impacting the outcomes of infected critically ill patients
Reproduced from Kollef MH, *et al. Crit. Care* 2021;25:360. Open Access. CC BY 4.0



*Prolonged infusion duration of antimicrobials to increase antimicrobial drug exposure for the offending pathogen.

Figure 2. Bar graph depicting mortality for patients receiving delayed appropriate antibiotic therapy (blue bars) and those receiving timely appropriate antibiotic therapy (green bars)
Reproduced from Kollef MH, *et al. Crit. Care* 2021;25:360. Open Access. CC BY 4.0



EARLY vs. DELAYED PHENOTYPE-DESIRABLE ANTIMICROBIAL THERAPY

JAMA NETWORK OPEN
2024;7(12):E2451633. doi: 10.1001/jamanetworkopen.2024.51633

Clinical Outcomes of Early Phenotype-Desirable Antimicrobial Therapy for *Enterobacterales* Bacteremia.

Moon RC, MacVane SH, David J, Morton JB, Rosenthal N, Claeys KC.

OBJECTIVE

The objective of this study was to compare the clinical outcomes between patients receiving early versus delayed phenotype-desirable antimicrobial therapy (PDAT[1]) among patients hospitalized with *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae*, or *Proteus mirabilis* bloodstream infections (BSIs), using the Desirability Of Outcome Ranking (DOOR) analysis.

STUDY DESIGN

Retrospective observational cohort study using the Premier PINC AI Healthcare Database (PHD).[2]

Adult inpatients with blood culture isolates belonging to *E. coli, K. oxytoca, K. pneumoniae*, or *P. mirabilis*, and who received effective beta-lactam or select oral antibiotic therapy within 2 days of blood culture collection (BCC) were included.

PDAT was defined as a beta-lactam antibiotic with the narrowest spectrum of activity to effectively treat the causative pathogen **(Figure 1)**. Early PDAT was defined as PDAT within 2 days of BCC (day 0 to 2) and delayed PDAT within 4 days of BCC (day 3 to 4).

RESULTS

- While no difference in mortality was observed, patients receiving delayed PDAT were more likely to be still hospitalized or discharged to a place other than home (34.1% vs. 30.5%) or have a readmission (14.8% vs. 12.3%) within 30 days compared to patients receiving early PDAT.
- The overall length of stay (LOS) (mean, 7.4 vs. 7.0 days) and LOS since BCC (mean, 6.5 vs. 5.4 days) were both longer among patients receiving delayed PDAT than among patients receiving early PDAT.
- Health care costs for both index hospitalization (mean, $31,447 vs. $25,535) and index hospitalization plus 30-day follow-up (mean, $35,691 vs. $29,671) were also higher for patients receiving delayed PDAT than for patients receiving early PDAT.
- It was observed that the overall desirability of the outcome in patients receiving early PDAT was preferable to that in patients receiving delayed PDAT in both unadjusted and inverse-probability weight (IPW) adjusted DOOR analysis **(Figure 2)**.

CONCLUSIONS

This is the first study to compare clinical outcomes between patients with *E. coli, K. pneumoniae, K. oxytoca*, and *P. mirabilis* BSIs receiving early PDAT vs. delayed PDAT using DOOR analysis. The study findings showed that receiving early PDAT was associated with favorable 30-day clinical outcomes among patients hospitalized with *Enterobacterales* BSIs. Starting early PDAT may be important not only for antimicrobial stewardship but also for improving the clinical outcome of affected patients.

1. PDAT: treatment using the agent with the narrowest spectrum of activity that effectively treats the causative pathogen.
2. The PHD is an all-payer hospital administrative database for geographically diverse inpatient and outpatient visits from more than 1,300 US hospitals.

"Receiving early PDAT was associated with favorable 30-day clinical outcomes among patients hospitalized with Enterobacterales BSIs. Starting early PDAT may be important not only for antimicrobial stewardship but also for improving the clinical outcome of affected patients."

KEY FINDINGS

- Receiving early phenotype-desirable antimicrobial therapy (PDAT) was associated with favorable 30-day clinical outcomes among patients hospitalized with *Enterobacterales* bloodstream infections.
- Early PDAT may be important not only for antimicrobial stewardship but also for improving patient outcomes.

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Figure 1. Grid illustrating the DOOR-MAT for the treatment of BSI caused by *E. coli, K. oxytoca, K. pneumoniae*, or *P. mirabilis*
Reproduced with permission from principal author. Moon RC, *et al*. *Microbiol. Spectrum* 2024;7(12):e2451633

	Phenotype according to: 1. Narrow-spectrum β-lactams (S to any Narrow-Spectrum Penicillins or Narrow-Spectrum Cephalosporins) 2. Expanded-Spectrum cephalosporins (S to Intermediate I) 3. Carbapenem (S to any Broad ± Intermediate II) 4. Novel β-lactams/β-lactamase inhibitors (R to Broad)			
Antibiotic received	**S-S-S-S**	**R-S-S-S**	**R-R-S-S**	**R-R-R-S**
Narrow-Spectrum Penicillins or Narrow-Spectrum Cephalosporins (e.g., cefazolin, amoxicillin-clavulanate)	S	R	R	R
Intermediate I or Oral 3rd-Gen Cephalosporins (e.g., ceftriaxone, cefdinir)	S	S	R	R
Intermediate II (e.g., cefepime, piperacillin-tazobactam)	S	S	S	R
Broad (e.g., carbapenems)	S	S	S	R
Broadest (e.g., ceftazidime-avibactam)	S	S	S	S

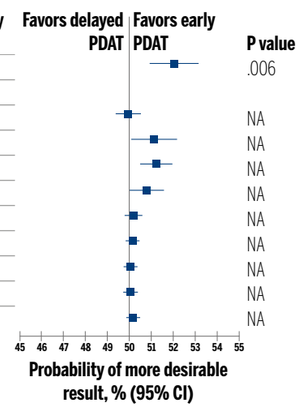
S indicates susceptibility; R indicates resistance

Desirable (PDAT) Potentially appropriate Appropriate but broad Overtreatment Undertreatment

Figure 2. Forest Plot Demonstrating the Inverse Probability Weighted–Adjusted Desirability of Outcome Ranking (DOOR) Analysis for Each Component
Reproduced with permission from principal author. Moon RC, *et al. Microbiol. Spectrum* 2024;7(12):e2451633

	Estimated patients, %			
DOOR	**Early PDAT (N=5033)**	**Delayed PDAT (N=3160)**	**DOOR Probability % (95% CI)**	**P value**
Combined			52.0 (50.9–53.2)	.006
DOOR Components				
• In-hospital mortality	6.4	6.3	49.9 (49.4–50.5)	NA
• Alive in hospital or discharged not to home	28.6	30.8	51.1 (50.1–52.2)	NA
• Readmission	11.5	14.0	51.2 (50.5–52.0)	NA
• Transfer to intensive care unit	14.3	15.8	50.8 (50.0–51.6)	NA
• Acquisition of MDRO	3.3	3.6	50.2 (49.7–50.6)	NA
• Hospital-onset CDI	1.4	1.7	50.1 (49.9–50.4)	NA
• New indication for IMV use	1.3	1.3	50.0 (49.8–50.3)	NA
• New indication for KRT	0.5	0.6	50.0 (49.9–50.2)	NA
• New indication for vasopressor use	1.5	1.8	50.1 (49.8–50.4)	NA

CDI indicates *Clostridioides difficile* infection; IMV, invasive mechanical ventilation; KRT, kidney replacement therapy; MDRO, multidrug-resistant organism; NA, not applicable; and PDAT, phenotype-desirable antimicrobial treatment.



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JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY – ANTIMICROBIAL RESISTANCE
2022;4(5). doi: 10.1093/jacamr/dlac089

Early appropriate diagnostics and treatment of MDR Gram-negative infections.

Bassetti M, Kanj SS, Kiratisin P, Rodrigues C, Van Duin D, Villegas MV, Yu Y.

OBJECTIVE

This article aimed to review the increasing need for rapid diagnosis of bacterial infections and efficient laboratory workflows to confirm diagnoses and facilitate prompt de-escalation to targeted therapy, in line with antimicrobial stewardship (AMS) principles. In addition, fast diagnostic tests and future perspectives for their use are discussed.

RAPID DIAGNOSTIC TESTS (RDTs)

- There is an urgent need for faster diagnostic methods to timely treat acutely ill patients with Gram-negative infections.
- Rapid methods for Gram-negative bacteria (GNB) resistance typing can be divided into two classes:
  - phenotypic antimicrobial susceptibility testing (AST) that indicates bacterial growth or degradation of the antibiotic,
  - molecular methods that detect nucleic acid sequences indicative of resistance genes and their expression.
- The turnaround time of these methods is substantially shorter than traditional culture methods (range, 1–8 h).
- Phenotypic AST is universally applicable, mechanism-independent and has therapeutic relevance.
- Molecular tests can be as fast as 15 min to 1 h, but are limited to the most common genes, and negative results do not necessarily imply that the organism is completely susceptible.

RDT, MULTIDRUG-RESISTANT GNB TREATMENT & PATIENT OUTCOMES

- Multidrug-resistant GNB (MDR-GNB), especially those producing extended specturm beta-lactamases (ESBLs) and carbapenemases, are an increasingly important etiology of ventilator-associated pneumonia (VAP).
- Fast AST tests reduce turnaround time and consequently, antibiotic de-escalation can be made in most patients with nosocomial pneumonia. For patients receiving an inactive regimen, the fast AST methods allow appropriate therapy sooner and have the potential to substantially reduce morbidity and mortality.
- In bloodstream infections (BSI), RDT was associated with significant decreases in mortality risk when combined with an AMS program and also decreased the time to effective therapy and hospital length of stay (LOS).
- The use of inappropriate antibiotic treatment or delays as short as 24 h for MDR infections leads to treatment failure and poor outcomes. Real-world data showed an antibiotic failure rate of 68.3% and a mortality rate of 40.8% among 112 patients with identified MDR infections.
- Difficult-to-treat resistant (DTR) GNB infections are resistant to all fluoroquinolones and beta-lactam categories, including carbapenems, posing a serious challenge to clinicians. They require a more detailed selection of therapy targeting specific pathogen resistance determinants, highlighting the value of RDTs that can inform earlier treatment decisions.
- AMS plays a crucial role for preserving the effectiveness of new agents in the long term and, at the same time, to guarantee their prompt use in those who may benefit the most from their administration.

CONCLUSIONS AND FUTURE PERSPECTIVES

Effective management of MDR-GNB infections requires a multidisciplinary approach, including various diagnostic methods and consensus on algorithms, protocols, and guidelines for selecting optimal antibiotic therapy.
Making such diagnostic tools available to general practitioners (GPs) and patients in the community, and in all regions worldwide, would create a paradigm shift from empirical to evidence-based treatment of infectious diseases.

"The integration of novel and rapid diagnostics for resistance phenotyping in patients has the potential to improve treatments and outcomes of MDR-GNB infections."

KEY FINDINGS

- **Delivering faster resistance results can reduce antibiotic use, other treatment needs and hospital costs.**
- **Delayed appropriate antibiotic therapy is associated with worse outcomes, including increased length of stay, higher in-hospital costs, and a significant increase in the risk of in-hospital mortality.**
- **The need for fast diagnostics to identify phenotypic resistance and specific resistance mechanisms is emphasized to reduce inappropriate early antibiotic therapy and improve patient outcomes.**
- **The integration of RDTs with AMS programs is crucial for optimizing antibiotic therapy, facilitating rapid de-escalation to targeted therapy, and reducing the emergence of resistance.**

OVERVIEW OF BENEFITS OF FASTER TIME TO THERAPY

SUPPORTING EVIDENCE

CLICK TO ACCESS ARTICLE

CLINICAL INFECTIOUS DISEASES
2023;76(3):469-478. doi: 10.1093/cid/ciac727

Association Between Time to Appropriate Antimicrobial Treatment and 30-day Mortality in Patients with Bloodstream Infections: A Retrospective Cohort Study.

Van Heuverswyn J, Valik JK, van der Werff SD, Hedberg P, Giske C, Nauclér P.

OBJECTIVE

The objective of this study was to assess the association between time to appropriate antimicrobial treatment and 30-day mortality in patients with bloodstream infections (BSI) admitted to the Emergency Department (ED).

STUDY DESIGN

Retrospective cohort study using electronic health records from a large academic center in Sweden.
Participants: 10,628 BSI episodes in 9,192 unique adult patients with BSI in the ED or general wards from 2012 to 2019.
Pathogen-antimicrobial combinations were classified as appropriate or inappropriate based on *in vitro* susceptibilities.
Multivariable logistic regression was used to assess the association between appropriate therapy and mortality at pre-specified times (1, 3, 6, 12, 24, 48, and 72 hours).

RESULTS

- The overall 30-day mortality was 11.8%.
- No association in favor of a protective effect between appropriate therapy and mortality was found at the 1, 3, and 6 hours landmark after blood culture collection.
- At 12 hours, the risk of death increased with inappropriate treatment (adjusted odds ratio 1.17 [95% confidence interval {CI}, 1.01-1.37]) and continued to increase gradually at 24, 48, and 72 hours.
- Stratifying by high or low SOFA score generated similar odds ratios, with wider confidence intervals.

CONCLUSIONS

In BSI, delays in appropriate antimicrobial treatment were associated with increased 30-day mortality after 12 hours from blood culture collection, but not at 1, 3, and 6 hours. These results indicate a benchmark for providing fast microbiological diagnostics and timely appropriate antimicrobial therapy in managing BSIs.

"These results call into question the promotion of aggressive broad spectrum empirical treatment within 3 hours when BSI is suspected, unless there is suspected septic shock or bacterial meningitis."

KEY FINDINGS

- Delays in appropriate antimicrobial treatment beyond 12 hours from blood culture collection are associated with increased 30-day mortality, but no increase was observed within 1 to 6 hours, supporting the use of fast diagnostic tests to allow timely administration of appropriate antimicrobials.
- The point estimates were similar regardless of high or low SOFA score at onset.
- The study was underpowered to draw meaningful conclusions in the subgroup of septic shock patients and was conducted in a context of low resistance.

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CLINICAL INFECTIOUS DISEASES
2024;79(2):502-515. doi: 10.1093/cid/ciae234

Rapid Diagnostic Tests and Antimicrobial Stewardship Programs for the Management of Bloodstream Infection: What is Their Relative Contribution to Improving Clinical Outcomes? A Systematic Review and Network Meta-analysis.

Peri AM, Chatfield MD, Ling W, Furuya-Kanamori L, Harris PNA, Paterson DL.

OBJECTIVE

Evidence about the clinical impact of rapid diagnostic tests (RDTs) for the diagnosis of bloodstream infections (BSIs) is limited, and their superiority over conventional blood cultures (BCs) used within antimicrobial stewardship programs (ASPs) is as yet undetermined. This meta-analysis aimed to compare the clinical impact of RDT to conventional BC, with respect to mortality, length of stay (LOS), and time to optimal therapy (TOT).

STUDY DESIGN

A systematic review and network meta-analysis to compare multiple interventions (RDT on positive BC broth or whole blood, and conventional BC, both assessed with and without ASP) combining direct/indirect evidence across a network of studies.
Inclusion criteria: The review included randomized controlled trials (RCTs) and quasi-experimental studies that compared the clinical impact of RDT and conventional BC, both with and without ASP.
Primary outcomes: Mortality, LOS and TOT.

RESULTS

A total of 88 studies were included. The study confirmed that use of RDTs combined with ASPs leads to a significant reduction in mortality compared to conventional BCs alone. This benefit is also observed when comparing RDT + ASP to BC + ASP.

- **RDT + ASP vs. BC Alone**: Significant reduction in mortality (OR, 0.72; 95% CI, .59–.87).
- **RDT + ASP vs. BC + ASP**: Significant reduction in mortality (OR, 0.78; 95% CI, .63–.96).

RDTs with ASPs significantly reduced TOT compared to BCs alone and BCs with ASPs. This reduction in TOT is crucial for improving patient outcomes and reducing the use of broad-spectrum antibiotics.

- **RDT + ASP vs. BC Alone**: Reduced TOT by 29 hours (95% CI, −35 to −23).
- **RDT + ASP vs. BC + ASP**: Reduced TOT by 18 hours (95% CI, −27 to −10).
- **RDT + ASP vs. RDT Alone**: Reduced TOT by 12 hours (95% CI, −20 to −3).

The study found a limited impact of RDTs and ASPs on LOS. While RDT + ASP reduced LOS compared to BC alone, no significant differences were observed between other groups.

- **RDT + ASP vs. BC Alone**: Reduction in LOS (OR, 0.91; 95% CI, .84–.98).

CONCLUSIONS

Although there are challenges in implementing RDTs and ASPs effectively in clinical practice, RDT was shown to provide clinical benefits for patients with BSIs. The findings support the Infectious Diseases Society of America (IDSA) recommendation to use RDTs within ASPs for managing BSIs to improve clinical outcomes. The study suggests that even institutions with effective ASPs in place can benefit from the introduction of RDTs.

"...the implementation of RDT + ASP may confer a survival benefit even in institutions already implementing conventional culture results through effective ASP, overall supporting the recommendation of the IDSA to use RDT within ASP for the management of BSI."

KEY FINDINGS

- RDTs combined with ASPs significantly reduced mortality, TOT and LOS in patients with BSI, compared to BCs alone.
- Even when both are embedded within ASPs, RDTs still provide a survival benefit over conventional BCs.
- Findings support IDSA recommendation to use RDTs within ASPs for managing BSIs to improve patient outcomes.

IMPACT OF INFORMATION DELAY ON PATIENT OUTCOMES

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CLINICAL INFECTIOUS DISEASES
2023;77(5):680-686. doi: 10.1093/cid/ciad243

Information Delay of Significant Bloodstream Isolates and Patient Mortality: A Retrospective Analysis of 6225 Adult Patients With Bloodstream Infections.

Fidalgo B, Morata L, Cardozo C, del Rio A, Morales J, Fernandez-Pittol M, Martinez JA, Mensa J, Vila J, Soriano A, Casals-Pascual C.

OBJECTIVE

This study evaluated the impact of real-time communication of microbiological information on the clinical and prognostic outcomes of adult patients with bloodstream infections (BSIs).

STUDY DESIGN

Observational, retrospective analysis of all clinical episodes of bacteremia in a teaching hospital in Barcelona, Spain, from January 2013 to December 2019.
The study compared bacteremia-associated mortality when blood culture results were communicated to the infectious diseases specialist (IDS) in real-time (during daytime working hours) and when results were delayed by 8 hours or more (reported the following morning).
Primary outcome: Impact on 30-day mortality of real-time vs. delayed availability of blood culture results.

RESULTS

- A total of 6,225 BSI cases were included.
- 2,130 (34.2%) of BSIs became positive during daytime working hours; 4,095 (65.8%) became positive during night-time working hours. Overnight positivity was reported to the IDS the following morning and therefore not in real-time.
- Of the 6,225 patients included, 625 (10%) died at 30 days. Of the 625 deaths, 193 (30.8%) corresponded to blood cultures that became positive during daytime working hours and 432 (69.2%) became positive during night-time hours.
- Empirical antibiotic treatment was appropriate in 4,661 of 6,015 patients (77.4%).
- Initial analysis including all pathogens did not reveal an association between mortality and delayed information report (odds ratio [OR], 1.18; 95% confidence interval [CI, 0.99–1.42).
- However, information delay of BSIs caused by fast-growing microorganisms such as *Enterobacterales* was associated with a significant increase in the odds of death at 30 days in the univariate and the multivariate analysis (OR, 2.22; 95% CI, 1.50–3.30) and similar results were found with mortality at 14 days and 7 days.

CONCLUSIONS

Early identification of significant bacterial isolates is critical to effectively manage patients with BSIs. This study suggests that real-time reporting of clinically relevant microbiological results from blood culture isolates, particularly for rapidly growing bacteria (e.g., *Enterobacterales*), may impact clinical outcomes. In view of the important prognostic implications, the need for adequate resource allocation (microbiologist/IDS with 24/7 coverage) should be reconsidered, and investigated in future studies.

"Information delivered in real time has prognostic relevance and is likely to improve survival of patients with documented BSIs."

KEY FINDINGS

- Real-time reporting of blood culture results for BSI patients may impact clinical outcomes.
- Information delay of BSIs caused by fast-growing microorganisms such as *Enterobacterales* was associated with a significant increase in the odds of death at 30 days in the univariate and multivariate analysis.
- This study highlights the importance of a rapid collaboration between the microbiology laboratory and the IDS.
- The need for 24/7 hospital coverage by a clinical microbiologist and/or an IDS should be revisited in view of the important prognostic implications.

RDT, AMS & CLINICAL SURVEILLANCE PLATFORM (CSP)

CLICK TO ACCESS ARTICLE

JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY
2024;79(SUPPL 1):I37-I43. doi: 10.1093/jac/dkae277

Getting rapid diagnostic test data into the appropriate hands by leveraging pharmacy staff and a clinical surveillance platform: a case study from a US community hospital.

Frens J, Baumeister T, Sinclair E, Zeigler D, Hurst J, Hill B, McElmeel S, Le Page S.

OBJECTIVE

This study aimed to optimize the post-analytical phase of a rapid diagnostic test (RDT) and evaluate whether combining RDT with real-time Antimicrobial Stewardship team (AST) support and a Clinical Surveillance Platform (CSP) would improve the time to appropriate therapy in bloodstream infections (BSI).

STUDY DESIGN

Single-center study conducted at Cone Health, Greensboro, NC, USA, which includes multiple hospitals and urgent care centers.
2016 – Cone Health enhanced its antimicrobial stewardship by expanding AST, implementing the BIOFIRE® FILMARRAY® BCID panel for fast pathogen and resistance gene identification, and providing real-time treatment recommendations by pharmacists, while daily reviewing positive blood cultures to ensure optimal antibiotic use and tracking physician acceptance of recommendations.
2021 – Adoption of the BIOFIRE® FILMARRAY® Blood Culture Identification 2 (BCID2) panel.
From August 2021 to March 2022, the time to antibiotic administration was evaluated, with VigiLanz (CSP) providing assistance for pharmacists. Quality assurance efforts included defining key performance indicators (KPIs) based on BCID2 results, enabling real-time notifications to the AST. KPIs focused on time to effective and optimal therapy, hospital length of stay, and mortality.

RESULTS

Post-BCID panel implementation (January to April 2018):

- 101 Gram-negative organisms were evaluated, 72% of which were *Escherichia coli*.
- Initial empirical antibiotics included vancomycin plus piperacillin/tazobactam (32%) and ceftriaxone monotherapy (24%).
- Antibiotic therapy was changed to align with AST guidance in 66% of cases.
- Final susceptibility matched AST recommendations 98% of the time, leading to increased physician comfort with BCID results and reduced rejection of recommendations over time.

Post-BCID2 panel implementation evaluation (August 2021 to March 2022):

- The combined mean time from BCID2 result to effective antibiotics was 1.2 hours and to optimal therapy was 7.6 hours.
- Initial empirical antibiotic coverage was 100% for methicillin-susceptible *S. aureus* (MSSA) and *P. aeruginosa*, but low for CTX-M (5%), methicillin-resistant *S. aureus* (MRSA) (40%), and vancomycin-resistant *Enterococcus* (VRE) (25%).
- Mean time to effective therapy was less than 3 hours for CTX-M-positive organisms (2.8 h), MRSA (2.6 h), and VRE (3.0 h).
- Time to effective antibiotic therapy for extended spectrum beta-lactamase (ESBL)-producing organisms not empirically covered decreased from 17.7 to 2.8 hours after BCID2 implementation ($p = 0.0041$).

CONCLUSIONS

Combining RDT, AST support, and information technology optimizes time to appropriate antibiotic therapy for BSIs, with pharmacists effectively communicating results and recommendations. Continuous feedback on microbiological and clinical outcomes reinforces physician confidence in RDT adoption and acceptance of recommendations, supported by high-quality CSP reports.

"The combination of RDT, AST support and IT can greatly aid in optimizing the timing of appropriate therapy in patients with BSIs."

KEY FINDINGS

- One of the first studies to demonstrate that the combination of RDT, AST support and a Clinical Decision System can have an impact on patient outcome.
- After BCID2 implementation, the time to effective antibiotic therapy for ESBL-producing organisms was reduced from 17.7 hours to 2.8 hours and this time was automatically calculated by the CSP.
- Study confirmed that clinical decision support can sustainably improve the quality of antimicrobial prescribing.

CLICK TO ACCESS ARTICLE

ANTIBIOTICS
2022;11(27):1-15. doi: 10.3390/antibiotics11010027

Diagnostic Testing for Sepsis: A Systematic Review of Economic Evaluations.

Rojas-Garcia P, van der Pol S, van Asselt ADI, Postma MJ, Rodríguez-Ibeas R, Juárez-Castelló CA, González M, Antoñanzas F.

OBJECTIVE

The objective was to perform a systematic review of economic evaluations to analyze the cost-effectiveness of diagnostic methods in sepsis and to draw lessons on the methods used to incorporate antimicrobial resistance (AMR) in these studies.

STUDY DESIGN

The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and used the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist for data extraction. The articles included compared at least two different diagnostic strategies for sepsis.

RESULTS

From a total of 306 articles identified, the final review included 16 cost-effectiveness articles (14 of which used a decision model), mostly based on retrospective data and published between January 2000 and December 2020. Some studies focused on cost per case and savings (i.e., considering an identical health impact) without calculating Incremental Cost-Effectiveness Ratios (ICERs), highlighting a gap in comprehensive economic evaluation. Analyses were most often made from the healthcare center's perspective, with a few from the healthcare payer's and societal perspective. The modelled time horizons included length of hospital stay (LOS), periods of 30 days, six months, one year, or projected life expectancy. Although sepsis can have long-term effects on mortality and quality of life, analyses were not able to explore long-term costs and effects beyond two years.

Health economic outcome metrics included average savings per patient, savings in hospital, average savings per case avoided, costs per life year, costs per additional correct diagnosis, costs per death averted, and costs per quality-adjusted life-year (QALY). Diagnostic testing for sepsis, particularly using procalcitonin (PCT) and polymerase chain reaction (PCR) tests, was systematically found to significantly improve clinical outcomes and be cost-effective compared to standard care, which usually consists of a blood culture and initial empiric treatment with broad-spectrum antibiotics.

Selected cost-savings outcomes from a hospital perspective in the review include:

- **Per-patient savings**: Total hospital care costs per patient decreased by up to €9,970 with use of PCR tests, due to the shortening of ICU stay and use of fewer antibiotics.
- **Cost per death averted**: Depending on the LOS decrease (from 0 to 4 days) PCR as an adjunct to the blood cultures was either cost-saving or cost-effective given a willingness to pay of less than $3,000 per death averted.
- **Episode-based savings**: Using PCR tests, each episode saw an estimated saving of €430, on average.
- **Reduced hospital stays**: Diagnostic strategies reduced hospital stays by 4 to 8 days, by saving the use of one type of antibiotic or reducing the broad-spectrum treatment in 80% of the patients (improving the clinical efficacy of antibiotics).

Nine models included **antimicrobial resistance (AMR)** and showed that diagnostic tests enabling targeted antibiotic treatment can reduce the use of broad-spectrum antibiotics and the incidence of resistant infections, demonstrating that incorporating AMR into economic evaluations of sepsis diagnostics is essential to understand the full benefits of diagnostic strategies.

CONCLUSIONS

This first systematic review of the economic evaluation of sepsis diagnostic methods found that using fast, accurate diagnostic techniques to detect sepsis early is generally cost-effective compared to standard care, even when only considering the short-term horizons of sepsis episodes.

"PCR and PCT are more efficient than standard care, as QALY gains have been found together with savings for the health system."

KEY FINDINGS

- Using a diagnostic technique to detect sepsis early on was found to be systematically and significantly cost-effective compared to standard care.
- PCR and PCT tests were shown to provide hospital cost-savings due to improved patient management, and quality-adjusted life year (QALY) gains.
- These findings suggest that investing in early diagnostic tools can save both lives and resources for healthcare systems.

REVIEW OF IMPROVEMENTS IN THE BLOODSTREAM INFECTION DIAGNOSTIC PROCESS

CLICK TO ACCESS ARTICLE

CLINICAL MICROBIOLOGY AND INFECTION
2020;26(2):142-150. doi: 10.1016/j.cmi.2019.11.017

Bloodstream Infections Standard and Progress in Pathogen Diagnostics.

Lamy B, Sundqvist M, Idelevich EA; ESCMID Study Group for Bloodstream Infections, Endocarditis and Sepsis (ESGBIES).

OBJECTIVE

This article reviews the major improvements that have been made in the diagnostic performance of modern blood culture (BC) through actions on pre-analysis and time-to-result (TTR).

PRE-ANALYTICAL ACTIONS

Source: bioMérieux adapted from Lamy B, *et al*. *Clin Microbiol Infect*. 2020;26(2):142-150

BLOOD SAMPLING PROCEDURE	STATE-OF-THE-ART	ACTIONS
Skin preparation	The contamination rate is <3%, optimally <1%	• Monitor the rate of contamination • Promote general and targeted education • Diversion tube diverts the initial first mL of blood to remove any potentially contaminated skin plug • Single sampling strategy - reduces the rate of solitary BC, improves the total volume and sensitivity, and reduce the contamination rate
Bottle-filling (adult patient)	The volume of blood per bottle is 8-10 mL	• Monitor the rate of bottles not reaching the recommended volume of blood (target) • Single sampling strategy point • CMBCS monitors the volume of blood on each bottle, facilitates general and targeted education
No. of bottles / episode (adult patient)	4-6 bottles (4 acceptable if all were properly filled) Rate of solitary BC (2 bottles) below 10%	• Monitor the rate of solitary BC per 24 hour
Specimen transport	<4 hours for most BC; 2 hours if decentralized BC	• Continuous transport system

MODERN ANALYTICAL METHODS*

Source: bioMérieux adapted from Lamy B, *et al*. *Clin Microbiol Infect*. 2020;26(2):142-150

FAST DIAGNOSTIC PROCEDURE	ADVANTAGES	LIMITATIONS
MALDI-TOF ID from positive BC	Very fast ID Easy Low additional cost	• Identification difficulties with some species • Confirmation might be needed • Mixed cultures
MALDI-TOF ID from positive BC using short sub-cultures	Fast ID Very easy Easy to integrate in lab workflow Confirmation usually not needed	• Slow-growing organisms • Mixed cultures
Molecular methods for ID from positive BC	Very fast ID Easy	• High cost • Limited pathogen panel • Confirmation needed
DNA-based ID from whole blood	Time advantage compared to culture Advantage in pathogen detection under antibiotics	• Limited number of pathogens in panel assays • Relatively low sensitivity • Clinical relevance of DNAemia? • High workload • High cost • Highly experienced staff required • Does not substitute culture

*Modern BC methods: species ID result available on same day of BC positivity and preliminary or final AST result available on same day or at latest next day of BC positivity.

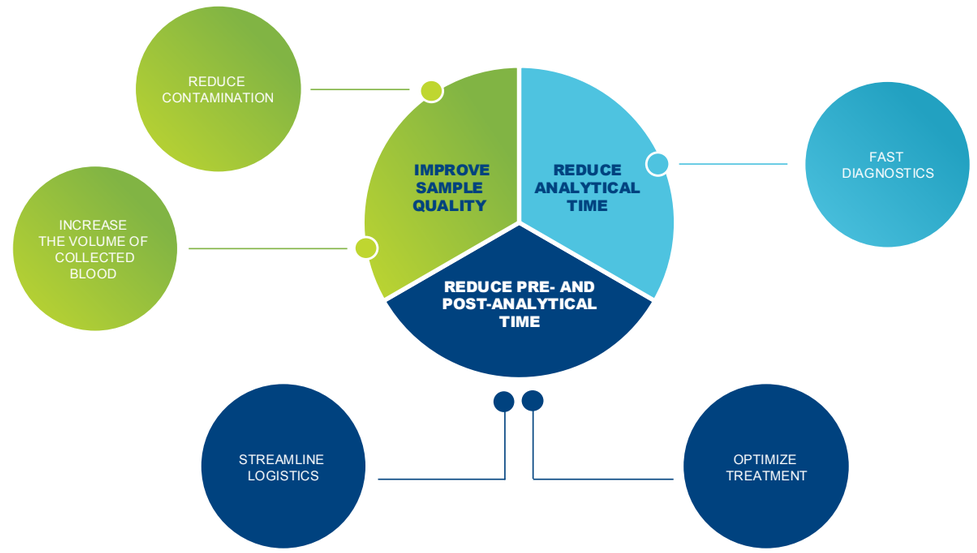
POST-ANALYTICAL

- Organizational issues are hindering the advantages of novel technologies due to current working patterns of most laboratories.
- Workflow modifications, namely decentralizing the BC instruments and/or introducing BC diagnostics 24/7, would improve the TTR, regardless of techniques used in the laboratory.
- All new positive episodes, both identification and antimicrobial susceptibility testing (AST), should be promptly reported to an antimicrobial stewardship team or to clinicians.

CONCLUSIONS

The introduction of these fast diagnostic methods should be accompanied by effective logistics in both pre- and post-analytic steps, in order to reduce the total time from when the patient with suspicion of BSI enters the hospital to when a report is produced. Progress in BSI pathogen diagnostics should be based on a bundle approach **(Figure 1)** that includes optimization of the pre-analytical parameters, rapid start of incubation, the use of fast diagnostics, reorganization (e.g., 24/7, transportation service) and a close involvement of antimicrobial stewardship teams.

Figure 1. A "bundle" approach is the basis of effective bloodstream infection management
Source: bioMérieux adapted from Lamy B, *et al*. *Clin Microbiol Infect*. 2020;26(2):142-150



"Continuous improvement of the whole BSI diagnostic process, based on sampling quality and time to result, should be a priority to improve patient outcome and avoid unnecessary antibiotic treatment."

KEY FINDINGS

- **The implementation of MALDI-TOF MS and molecular approaches for species identification and fast AST techniques can lead to substantial decrease in the time-to-result.**
- **A multifaceted approach is necessary to fully optimize the blood culture output, including pre-analytical, analytical, and post-analytical actions.**

CLINICAL IMPACT OF FAST DIAGNOSTICS ON BLOODSTREAM INFECTION MANAGEMENT

VALUE OF FAST BLOOD CULTURE TESTING

CLICK TO ACCESS ARTICLE

INTERNATIONAL JOURNAL OF ANTIMICROBIAL AGENTS
2024;63(6):107176. doi: 10.1016/j.ijantimicag.2024.107176

Clinical and economic evaluation of blood culture whole process optimisation in critically ill adult patients with positive blood culture.

Dai Y, Zhu X, Chang W, Lu H, Nie Z, Wu Y, Yao H, Chen Y, Xiao Y, Chu X.

OBJECTIVE

The objective of this study was to evaluate the clinical and economic impact of optimizing the entire blood culture process for critically ill adult patients in intensive care units (ICUs) who were diagnosed with bloodstream infections (BSIs). The study examined how process improvements, such as reducing the time for bacterial identification (ID) and antibiotic susceptibility testing (AST), affect patient outcomes, antibiotic use, and healthcare costs.

STUDY DESIGN

The study was conducted at the University Hospital of Hefei, China, and compared two groups of ICU patients:

1. **Pre-optimization group** (March 2019 - February 2020) comprising 122 patients.
2. **Post-optimization group** (November 2021 - October 2022) comprising 179 patients.

The optimization phase aimed at reducing the time from blood sample collection to reporting Gram-stain results, ID, and AST, and included:

- Educational initiatives for medical staff
- Optimization of the blood culture process (addition of an emergency satellite blood culture incubator)
- Conversion to more advanced diagnostic technologies: from BACT/ALERT® 3D to VIRTUO® and from phenotypic ID with VITEK®2 to faster ID using MALDI-TOF/MS (VITEK® MS)
- Improvement of result reporting to the clinician via systematic notification of Gram-stain, ID, and AST results through the Electronic Medical Record (EMR) integrating the Laboratory Information Systems (LIS).

The primary endpoint was the time from admission to targeted antibiotic therapy. Other outcomes were related to laboratory processes, clinical outcomes and health economics. During the whole study period, clinical microbiologists did not interfere with the medication prescribed by the attending clinical physicians.

RESULTS

- **Time efficiency**: The post-optimization group experienced significant reductions in the time required for key processes **(Figure 1)**. The time from patient admission to blood culture prescription, reflecting the impact of medical education, was reduced by 5.94 days. Optimization of laboratory processes enabled the time from blood bottle loading to the final report to be reduced by 18% (17 hours), allowing for quicker, more informed clinical decision-making. Collectively, the time from admission to final ID/AST report was reduced by more than 50% (12.59 days to 5.73 days).
- **Targeted therapy**: In the post-optimization group, the time from admission to targeted antibiotic therapy (following both Gram-stain results and final ID/AST results) was reduced by more than 50%.
- **Detection rates**: The post-optimization group showed a significantly higher positive detection rate of pathogens, including *Staphylococcus aureus*, *Streptococcus* spp., and *Klebsiella* spp., improving the accuracy of diagnosis and treatment (21.13% vs. 16.46%; p=0.005).
- **Health outcomes**: The length of hospital stay was reduced by almost 30% (6.49 days).
- **Cost reduction per patient**: The total hospitalization costs decreased by 58% (from $16,418 to $6,904), including a 44% decrease in laboratory testing costs (from $1,626 to $915) and a 78% decrease in antimicrobial drug costs (from $2,194 to $473) in the post-optimization group.

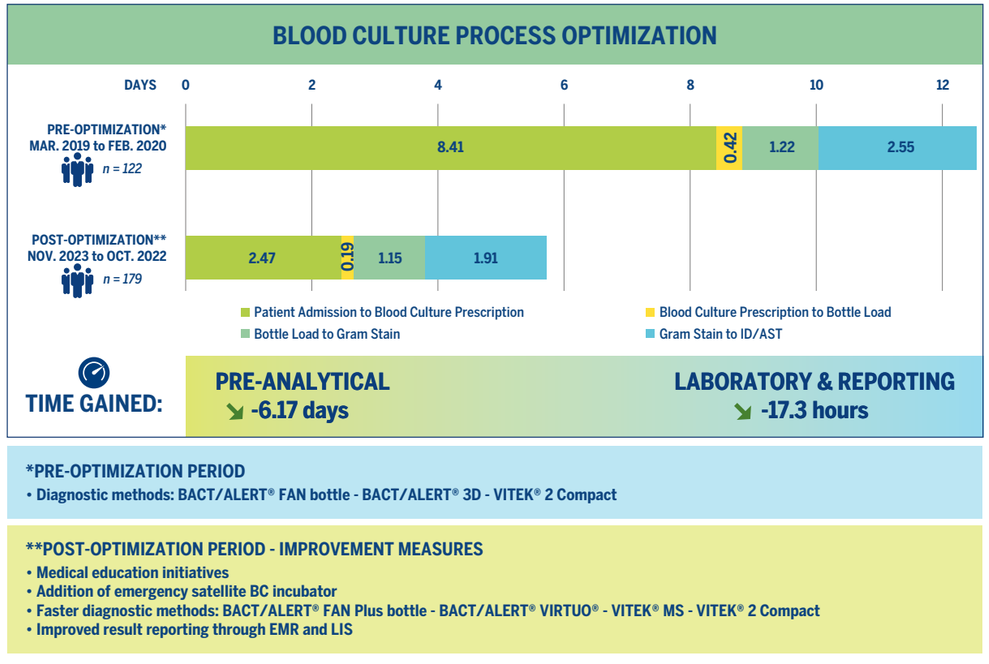
CONCLUSIONS

Optimizing the blood culture process significantly improved clinical outcomes for ICU patients with BSIs by shortening the time to targeted antibiotic therapy, reducing hospital stays, and lowering hospitalization costs. Faster bacterial identification and AST led to earlier, more appropriate antibiotic prescriptions, which likely contributed to better patient outcomes.

From an economic perspective, these improvements resulted in substantial cost savings, particularly in antimicrobial drug use and hospital stay duration. The study stresses the importance of timely, accurate diagnostics in the management of BSIs and highlights the need for further integration of fast microbial testing in critical care settings.

VALUE OF FAST BLOOD CULTURE TESTING

Figure 1. Schematic representation of blood culture process optimization and different time measurements
Source: bioMérieux adapted from Corrigendum to Dai Y, *et al. Intl J Antimicrob Agents* 2024;64(2):107242



"With the advancement of microbiological technology leading to improvements in the speed and accuracy of diagnosing infections, we are moving towards a new paradigm where collaboration between doctors, clinical pharmacists and microbiologists will be imperative."

KEY FINDINGS

Improved process efficiency led to improved health outcomes:

- **Time to targeted antibiotic therapy**: Shortened by more than 50%, improving patient care and reducing patient length of stay by more than six days.
- **Cost efficiency**: In the post-optimization group, total hospitalization costs were reduced by 58%, antimicrobial drug costs by 78%, and laboratory test costs by 44%, demonstrating significant financial savings from faster diagnostics.

CLICK TO ACCESS ARTICLE

DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
2023;107(4):116085. doi: 10.1016/j.diagmicrobio.2023.116085

Assessment of the impact of centralized bioMérieux BACT/ALERT® VIRTUO® blood culture system implementation on outcomes in patients with gram-negative bacteremia.

Destache C, Boldt D, Anthone J, Velagapudi M, Swaney R, Jerabek J, Malik N, Williams J, Jokomo-Nyakabau R, Vivekanandan R, Cavalieri SJ.

OBJECTIVE

This study evaluated the impact of implementation of BACT/ALERT® VIRTUO® and centralization of blood culture processing by comparing microbiology workflow, antimicrobial utilization, and patient outcomes between study groups.

STUDY DESIGN

Retrospective pre-post intervention study of blood culture processing for patients with Gram-negative BSI admitted to six USA area hospitals (Omaha, NE). These hospitals changed from a decentralized on-site blood culture system at each hospital utilizing BD BACTEC™ 9000 series (pre-intervention group; August-December 2018) to a single consolidated laboratory (staffed 24/7) for blood culture processing utilizing BACT/ALERT® VIRTUO® at an academic medical center that serves all area hospitals (post-intervention group; August-December 2020). During both study time periods, positive blood cultures from all hospitals were tested using the BIOFIRE® Blood Culture Identification (BCID) panel with positive results being communicated to the antimicrobial stewardship team for each hospital. The microbiology laboratory used VITEK® MS and VITEK® 2 during both time periods.

RESULTS

- **Patients**: A total of 370 patients (185 patients in each group) were enrolled in the study. Patient demographics, Charlson comorbidity score, common organisms (53% *E. coli*, 17% *Klebsiella* spp., and *Pseudomonas* spp. 7%), and antimicrobial susceptibilities were comparable between study groups. A similar proportion of patients were admitted to general hospital floors and had Infectious Diseases consultation services in both time periods.
- **Microbiology timing and workflow efficiency**: The average time from hospital admission to blood culture draw and total volume of blood drawn were lower in the post-intervention group. Of note, the average blood culture transportation time was not significantly different between the two time periods (pre-intervention 3.4 ± 5.0 h vs. post-intervention 4.1 ± 3.7 h), despite blood cultures being transported by courier to a single location in the post-intervention group.
- **Antimicrobial utilization and patient outcomes**: Several measures of antimicrobial utilization were improved in the post-intervention group. The time from blood culture draw to treatment change (65.0 ± 46.3 h vs. 52.9 ± 38.3 h, p=0.044) and time from organism identification to treatment change (23.8 ± 33.8 h vs. 15.1 ± 27.4 h, p=0.009) were significantly shorter in the post-intervention group. The duration of targeted antimicrobial therapy (i.e., optimal therapy) was significantly longer in the post-intervention group (4.6 ± 3.7 days) compared to the pre-intervention group (3.6 ± 3.0 days; p=0.032). The average duration of vancomycin therapy (i.e., suboptimal therapy) was shorter in the post-intervention group (14.4 ± 20.1 h) compared to the pre-intervention group (22.2 ± 33.8 h; p=0.048), due to faster discontinuation of unnecessary therapy (i.e., vancomycin for Gram-negative BSI). The total duration of antimicrobial therapy and duration of empiric antimicrobial therapy were unchanged between groups. Time to ID consult, hospital length of stay, and mortality were not different between the study groups.

CONCLUSIONS

Replacement of decentralized BD BACTEC™ 9000 systems in area hospitals with centralized BACT/ALERT VIRTUO at an academic medical center, along with pre-existing fast diagnostics and antimicrobial stewardship, resulted in significant improvement in the care of patients with Gram-negative bacteremia.

"This is the first report of such a fully integrated, consolidated, and optimized microbiology process with robust AMS in a multi-hospital, urban health system setting, to determine the effect on patient outcomes."

KEY FINDINGS

- Blood cultures were reported on average 12 hours earlier (blood culture draw to treatment change) using the BACT/ALERT® VIRTUO® compared to the BACTEC™ 9000 instruments.
- An integrated, consolidated, and optimized microbiology process with robust antimicrobial stewardship can positively impact the care of patients with serious infections.

CLICK TO ACCESS ARTICLE

MICROBIOLOGY SPECTRUM
2022;10(5):e0143622. doi: 10.1128/spectrum.01436-22

Impact of Automated Blood Culture Systems on the Management of Bloodstream Infections: Results from a Crossover Diagnostic Clinical Trial.

Halperin AV, Del Castillo Polo JA, Cortes-Cuevas JL, Cardenas Isasi MJ, Ampuero Morisaki M, Birch R, Sánchez Díaz AM, Cantón R.

OBJECTIVE

Assess the performance of BACT/ALERT® VIRTUO® in comparison to BACTEC™ FX and evaluate the workflow of both systems in a clinical setting.

STUDY DESIGN

Prospective crossover diagnostic clinical trial including blood cultures (BC) from stratum 1 (emergency department, 70% of BC) and stratum 2 (other wards, 30% of BC), switching between VIRTUO and BACTEC FX every 2 weeks over a 6-month period.

TTD (time interval between loading of BC bottles and positivity), TAT (time interval between positivity and Gram stain result), Time to Identification and AST from loading of BC bottles were assessed.

Workflow, process mapping and hands-on-time were assessed by Lab Consultancy team by direct observation of 100 to 430 events per step.

RESULTS

- A total of 9,957 extractions, 4,797 in the VIRTUO arm and 5,160 in the BACTEC™ FX arm (9,538 and 10,204 bottles, respectively), were included.
- Median TTD was significantly shorter with VIRTUO by 1.5 h overall; the difference was greatest for aerobic bottles, with 3.7 h and 4.1 h reductions for significant organisms and contaminants, respectively.
- Median TTD was significantly shorter with VIRTUO among patients who were on antimicrobial treatment at the BC sampling, by 4.5 h (p<10-3) overall and 8.7 h (p<10-4) when considering aerobic bottles only.
- When considering aerobic bottles, the median time to ID and the median time to AST results were reduced by 6.7 hours and 6.6 hours, respectively, and median TAT was 9 hours shorter with VIRTUO (all p<0.05).
- VIRTUO workflow needs 7 fewer manual steps compared to BACTEC FX, thanks to its design and automation features. At this site, processing 110 bottles a day in average with a 17% positivity rate, VIRTUO allowed a 15 minutes saving of hands-on-time per day.

CONCLUSIONS

In a real-world setting, VIRTUO provided shorter TTD and TAT than BACTEC FX and demonstrated better neutralization performance for BACT/ALERT bottles. This could have a positive impact on the faster identification of causative microorganisms of BSIs and antimicrobial stewardship.

"...we have shown in a real-world setting that VIRTUO provides shorter TTD and TAT than BACTEC FX and that the TTD for aerobic bottles is even shorter for patients who have received antimicrobials before blood culture extraction. This could have an important effect on the faster identification of causative microorganisms of BSIs and antimicrobial stewardship."

KEY FINDINGS

- First prospective crossover clinical trial comparing Time to Detection (TTD) and Turn-Around-Time (TAT) of BACT/ALERT® VIRTUO® and BACTEC FX in a real-life setting including 9,957 extractions.
- TTD was significantly shorter with VIRTUO, by 1.5 hours overall and 3.7 hours for aerobic bottles.
- TAT was significantly shorter with VIRTUO, by 2.1 hours overall and 9.0 hours for aerobic bottles.
- VIRTUO design and automation features requires fewer manual steps, saving 15 min hands-on-time a day.

VALUE OF FAST PATHOGEN IDENTIFICATION

CLICK TO ACCESS ARTICLE

MICROBIAL BIOTECHNOLOGY
2022;15(10):2667–82. doi: 10.1111/1751-7915.14124

MALDI-TOF mass spectrometry rapid pathogen identification and outcomes of patients with bloodstream infection: A systematic review and meta-analysis.

Yo CH, Shen YH, Hsu WT, Mekary RA, Chen ZR, Lee WTJ, Chen SC, Lee CC.

OBJECTIVE

The study aimed to evaluate the effectiveness of fast microbial identification by MALDI-TOF MS* from blood cultures isolates with and without antibiotic stewardship teams (AST), on clinical outcomes for patients with bloodstream infections (BSI).

STUDY DESIGN

A systematic literature review and meta-analysis was conducted to compare studies using MALDI-TOF MS for microorganism identification versus conventional phenotypic methods.

Studies were included if they analyzed efficiency measures (e.g., time to bacteriology identification), clinical outcomes (e.g., hospital length of stay), or economic measures (e.g., hospitalization costs).

Studies without a comparison group were excluded.

RESULTS

In total, 21 studies were retained, mostly from North America and Europe, as well as Japan, Korea, and Israel, involving 14,515 patients.

MALDI-TOF MS used to support BSI management was associated with impactful improvements in 3 areas:

- **In-hospital mortality**: Significantly reduced by 23% (risk ratio 0.77, 95% CI 0.66 to 0.90). The highest reductions were observed when restricting analysis to adult studies (31% reduction; RR 0.69, 95% CI: 0.57-0.84; nine studies) or to studies co-implemented with AST (35% reduction; RR 0.65, 95% CI 0.49 to 0.86; 6 studies). The low heterogeneity in mortality outcome estimates enhances the reliability of the pooled effect estimates, supporting the robustness of the findings.
- **Efficiency of patient management**: The use of MALDI-TOF significantly reduced time to pathogen identification by 22.86 hours, time to effective antibiotic therapy by 5.07 hours, and hospital stay duration by 0.73 days, but had no impact on duration of ICU stay.
- **Economic impact**: The technology also resulted in net cost savings, with a net reduction in direct hospitalization costs per patient of $4,140 on average.

CONCLUSIONS

Fast pathogen identification by MALDI-TOF MS from blood cultures isolates, with or without AST, improves clinical outcomes and may be cost-effective for patients with BSI, reducing both the clinical and economic burden. Future studies should focus on formal cost-effectiveness analyses and the implementation of antimicrobial stewardship programs to maximize benefits.

* MALDI-TOF MS: Matrix Assisted Laser Desorption Ionization - Time of Flight Mass Spectrometry

"Implementing rapid microbial identification using MALDI-TOF MS not only improves clinical outcomes but also results in substantial cost savings, and may be cost-effective among patients with BSI."

KEY FINDINGS

Use of MALDI-TOF MS to support bloodstream infection management:

- Reduced mortality in patients with BSI by 23% compared to conventional methods.
- Accelerated identification of microorganisms causing the infection by 22.86 hours, leading to earlier and more accurate treatment decisions.
- Improved time to effective antibiotic therapy by approximately 5.07 hours, enhancing the treatment reponse.

CLICK TO ACCESS ARTICLE

PHARMACOTHERAPY
2023;43(1):24-34. doi: 10.1002/phar.2747

Examining the clinical impact of rapid multiplex polymerase chain reaction-based diagnostic testing for bloodstream infections in a national cohort of the Veterans Health Administration.

Britt NS, Khader K, He T, Willson TM, Effiong A, Timbrook TT, Potter EM, Lodise TP.

OBJECTIVE

The purpose of this study was to evaluate the clinical outcomes among hospitalized adult patients with monomicrobial bloodstream infections.

STUDY DESIGN

A national, multicenter, retrospective, quasi-experimental pre-post implementation study among hospitalized adult patients with monomicrobial bloodstream infections using the BIOFIRE® Blood Culture Identification (BCID) Panel between 2015 and 2020 at the United States Veterans Health Administration (VHA) hospitals with antimicrobial stewardship programs (ASP) and varied standard practices.

RESULTS

From a total of 4,138 patients, 2,100 were enrolled in the pre-implementation period and 2,038 were enrolled in the post-implementation period.

The study found early antimicrobial de-escalation within 48 hours was higher in the post-implementation period, at 38.1% (776/2,038) vs. 34.6% (727/2,100) for the pre-implementation period (p=0.022).

Early appropriate antimicrobial therapy (defined as the administration of ≥1 dose of an antimicrobial to which the related organism was susceptible) was also higher in the post-implementation period vs. the pre-implementation period (93.8% vs. 91.7%, p=0.008).

The median time to appropriate therapy was shorter in the post-implementation period compared with the pre-implementation period (8 h vs. 9 h, p=0.005).

There was no significant difference between the two periods in the overall 30-day mortality, and similarly no difference for *Clostridioides difficile* infection (CDI) incidence 90 days after bloodstream infection. However, BIOFIRE BCID Panel implementation was associated with lower 30-day mortality in patients.

Sub-analysis showed that median time to appropriate therapy was significantly reduced in different groups in the post-implementation period, but with more benefits in patients with multidrug resistant (bacteria: methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *Enterococci* (VRE)). It was also observed that implementation of the BIOFIRE BCID Panel improved early appropriate therapy in non-MRSA and VRE cases.

CONCLUSIONS

Implementation of the BCID Panel was associated with improvements in antimicrobial use in facilities with ASP, which persisted even after taking into account the varying ASP practices. Benefits were most pronounced in those facilities with automatic ID consults for BSI. However, no improvements in hospital LOS, mortality, or CDI were observed post-BCID implementation. The BCID platform may serve as a useful adjunct for BSI management in facilities with ASP.

"In a «real-world» clinical setting, the implementation of the BIOFIRE BCID Panel was associated with clinical improvements in antimicrobial utilization."

KEY FINDINGS

- Implementation of the BIOFIRE® BCID Panel showed an improvement in early antimicrobial de-escalation and median time to appropriate therapy independently of the ASP practices across the different institutions within the VHA.
- A significant benefit in 30-day and in-hospital mortality in the sub-group of patients younger than 65 years old was found, even though the implementation of the BIOFIRE® BCID Panel did not show a significant difference in mortality globally.
- Significant improvements in time to appropriate therapy were observed in those patients with high resistance infections such as VRE and MRSA.

CLICK TO ACCESS ARTICLE

DIAGNOSTICS
2023;13(14):2433. doi: 10.3390/diagnostics13142433

Clinical Impact of the Biofire Blood Culture Identification 2 Panel in Adult Patients with Bloodstream Infection: A Multicentre Observational Study in the United Arab Emirates.

Senok A, Dabal LA, Alfaresi M, Habous M, Celiloglu H, Bashiri S, Almaazmi N, Ahmed H, Mohmed AA, Bahaaldin O, Elimam MAE, Rizvi IH, Olowoyeye V, Powell M, Salama B.

OBJECTIVE

This study aimed to evaluate the impact of the BIOFIRE® Blood Culture Identification 2 (BCID2) Panel on earlier targeted antimicrobial therapy, potential reduced exposure to broad-spectrum antimicrobials, and the rate of inappropriate antimicrobial treatment.

STUDY DESIGN

Multicenter observational study in a «real-world» setting in adult populations in the ICU's of three institutions in the United Arab Emirates. Out of a total of 229 patients enrolled, 99/229 were analyzed in the pre-BCID2 group and 86/229 were analyzed in the post-BCID2 group. The study period was 6 months pre- and 6 months post-BCID2 Panel implementation. During the pre-BCID2 implementation period, the standard of care was blood culture, Gram-staining and VITEK® MS and VITEK® 2 systems. Discrepancies were addressed using standard methods as a gold standard.

RESULTS

Pathogen identification and concordance

- In the pre-BCID2 implementation phase pathogen detection was 87/99 (87.9%) compared with 85/86 (98.8%) during the BCID2 implementation phase.
- Most frequent organisms detected by both methods were *Klebsiella pneumoniae*, *Escherichia coli*, and *Staphylococcus epidermidis*.
- *Candida auris* was frequently detected but only during the BCID2 implementation phase.
- Of the 98 organisms detected by the BCID2 Panel, 74/98 (75.5%) were fully concordant with standard methods.
- 3/85 patients had truly discordant results: 2 patients with *Elizabethkingia meningoseptica* identified by conventional culture and *Escherichia coli* and *Candida auris* identified by the BCID2 Panel; and 1 patient with *Streptococcus viridans* identified by conventional culture and *Staphylococcus* spp. identified by the BCID2 Panel.

Time to inform targeted therapy

- Median time from first positive blood culture collection and targeted therapy communicated to the ICU team in the pre- and BCID2 implementation periods was 91.7 hours vs. 28.1 hours, respectively ($p<0.0001$).

Antibiotic treatment

- Median duration of empiric antibiotic treatment was shorter in the BCID2 implementation phase: 2 days vs. 3 days ($p=0.128$).
- Antibiotic de-escalation was comparable in both periods ($p=1.00$).

30-day mortality

- The 30-day mortality rate in the BCID2 implementation group was significantly lower when compared with the pre-BCID2 implementation group: 17.3% vs. 31.6%, respectively ($p=0.019$).

CONCLUSIONS

Implementation of the BCID2 Panel was associated with a significantly shorter time to result leading to earlier targeted therapy and a reduced 30-day mortality, supporting the use of the panel to improve clinical outcome in ICU patients with a bloodstream infection.

"... in addition to conventional microbiological methods and an effective antimicrobial stewardship program, the BIOFIRE BCID2 Panel could improve the clinical outcome of patients admitted to the intensive care unit with a confirmed BSI."

KEY FINDINGS

- Mean time to results gained using the BIOFIRE® BCID2 Panel (in addition to conventional methods) compared to using conventional methods alone was 73.3 h (95% CI: 59.8–88.6; $p<0.0001$).
- 30-day mortality was significantly lower in BCID2 (17.3%) vs. pre-BCID2 (31.6%) patients ($p=0.019$).
- The BIOFIRE® BCID2 Panel enabled identification of a high frequency of resistance genes in clinically relevant pathogens (29.6% of detected pathogens), highlighting its value, particularly in contexts of high prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA).

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DIAGNOSTIC MICROBIOLOGY & INFECTIOUS DISEASE
2023 Feb;105(2):115858. doi: 10.1016/j.diagmicrobio.2022.115858

BIOFIRE® Blood Culture IDentification 2 (BCID2) panel for early adaptation of antimicrobial therapy in adult patients with bloodstream infections: a real-life experience.

Donnars A, Mahieu R, Declerck C, Chenouard R, Lemarié C, Pailhoriès H, Requin J, Kempf M, Eveillard M.

OBJECTIVE

This study assessed the effectiveness of the BIOFIRE® Blood Culture Identification 2 (BCID2) Panel for the early administration of appropriate antimicrobial therapy in adult patients from medical wards, emergency rooms and intensive-care units in a French university hospital.

STUDY DESIGN

Prospective quasi-experimental pre/post-implementation study. The pre-implementation period (P1) was from July 2021 to Nov. 2021 and the post-implementation period (P2) was from Dec. 2021 to Apr. 2022. During P1, positive blood cultures were processed using Gram staining microscopic examination (direct examination), culture on blood agar plates, identification of colonies and antimicrobial susceptibility testing (AST). During P2, multiplex PCR with BCID2 Panel was performed immediately after direct examination. The study defined time to most appropriate treatment (MAT) as the time from communication of the direct examination, identification, or AST results to a decision made by a clinician, specialist, or clinical microbiologist for the active treatment of the organism with minimal ecological impact on commensal flora.

RESULTS

There was no significant difference in the mean age of patients, gender, distribution of wards, or origin of bacteremia between the two periods. Similarly, there was no significant difference in bacteria distribution identified in both periods. Overall, the BCID2 Panel identified 94.4% of bacteria isolated on solid media.

The proportion of clinicians to prescribe the MAT between P1 and P2 showed a significant difference (26.0% vs. 61.4% ($p<0.001$)) for mono-microbial blood cultures with Gram-negative bacteria. Similarly, when only considering those patients with inappropriate empirical treatment, the proportion of clinicians to prescribe the MAT was 50% vs. 87.5% ($p<0.001$) between P1 and P2, respectively.

For mono-microbial blood cultures with Gram-positive bacteria, the proportion of changes to MAT in P1 vs. P2 was 33.0% vs. 64.4% ($p<0.01$). When the BCID2 Panel results were concomitant with direct examination and when the empirical treatment was not appropriate, the study showed that the proportion of clinicians to change to the MAT in P2 was significantly higher than during P1 in the emergency room and in medical wards (this difference was not significant in the ICU).

CONCLUSIONS

In this study, most antimicrobial therapies were considered as accurate as soon as bacterial identification was made - and therefore before obtaining the AST results. By reducing the turnaround time from the time of direct examination to organism identification, the BCID2 Panel demonstrated an effective impact on the timely administration of appropriate antibiotics.

"In this study, we demonstrated that using BIOFIRE BCID2 Panel concurrently to direct microscopic examination for positive blood cultures had a significant impact for timely administration of appropriate antibiotics."

KEY FINDINGS

- The BIOFIRE® BCID2 Panel showed an important decrease in turnaround time when compared to conventional methods.
- Overall, the BIOFIRE® BCID2 Panel demonstrated an excellent percent agreement when compared with conventional blood culture methods for on-panel pathogens.
- The use of the BIOFIRE® BCID2 Panel with direct microscopic examination showed a positive impact on time to administration of appropriate treatment.

VALUE OF FAST ANTIMICROBIAL SUSCEPTIBILITY TESTING

CLICK TO ACCESS ARTICLE

MICROBIOLOGY SPECTRUM
2024;12(8):E2451633 doi: 10.1128/spectrum.00402-24

Hospital mortality and length of stay associated with *Enterobacterales* positive blood cultures: a multicenter analysis.

Cooper L, Yu K, Van Benten K, Patkar A, Ye G, Gregory S, Ai C, Gupta V.

OBJECTIVE

Evaluate the impact of antimicrobial susceptibility testing (AST) result turnaround time (TAT), adequate (AET) and inadequate (IET) empirical antibiotic therapy, and carbapenem susceptible (carb-S) and carbapenem non-susceptible (carb-NS) *Enterobacterales* on post-BSI event mortality and in-hospital length of stay (LOS) for hospitalized adult individuals with positive blood cultures (PBC).

STUDY DESIGN

Retrospective, observational, multicenter study including a total of 29,570 *Enterobacterales* PBC admissions across 161 US sites.

Enterobacterales species evaluated included: *E. coli*, *K. pneumoniae*, *K. oxytoca, K. aerogenes, E. cloacae, S. marcescens, C. freundii, P. mirabilis, P. stuartii*, and *M. morganii*.

AST TAT was calculated as the date/time of first blood pathogen AST results minus the date/time of blood culture collection.

Post-BSI event LOS was the length of time spent in the hospital post-*Enterobacterales* PBC collection.

Post-BSI event mortality was evaluated in the subset of patients with available related data.

RESULTS

- Of the 29,570 admissions evaluated, 4,091 (13.8%) patients received IET, and 415 (1.4%) patients had carb-NS pathogens.
- Carb-NS infections were more likely to receive IET compared to carb-S infections (53.0% vs. 13.3%, respectively).
- The adjusted odds of post-BSI event mortality were 1.61 times higher for the IET group compared to the AET cohort [OR: 1.61 (95% CI, 1.32, 1.98); p<0.0001].
- The average TAT for AST was 60.2 h.
- Compared to the reference AST TAT <40 h, longer AST TAT correlated with higher odds of mortality **(Figure 1)**:
  - 49-63 h AST TAT had OR: 1.32 (95% CI, 1.03, 1.71; (p=0.0307),
  - >63 h AST TAT had OR: 1.48 (95% CI, 1.16, 1.90; (p=0.0017).
- TAT was associated with longer LOS with AST TAT results >65 h from BC collection (p<0.0001) (**Figure 2**).

CONCLUSIONS

These findings showed that overall post-BSI event mortality was 61% higher for patients started on IET compared to AEP.

There are operational workflow opportunities to decrease the AST TAT that may positively affect patient care and may partially mitigate the associated higher LOS and mortality seen in this study.

"Workflows that accelerate AST TAT for Enterobacterales BSIs and facilitate timely and adequate therapy may reduce post-BSI in-hospital mortality rate and LOS."

KEY FINDINGS

- Carbapenem-NS infections were more likely to receive inappropriate antimicrobial therapy compared to carbapenem-S infections (53.0% vs. 13.3%, respectively).
- Inappropriate antimicrobial therapy was associated with 61% higher risk of post-BSI event mortality in patients with *Enterobacterales* BSI.
- Longer AST TAT (compared to <40 h) was correlated with longer LOS and higher odds of mortality, both statistically significant.

Figure 1. Model-estimated (adjusted) odds ratio of in-hospital mortality with positive *Enterobacterales* blood cultures by AST turnaround time (TAT)
Reproduced from Cooper L, *et al*. *Microbiol. Spectrum* 2024;12(8):e2451633 CC-BY 4.0 licence

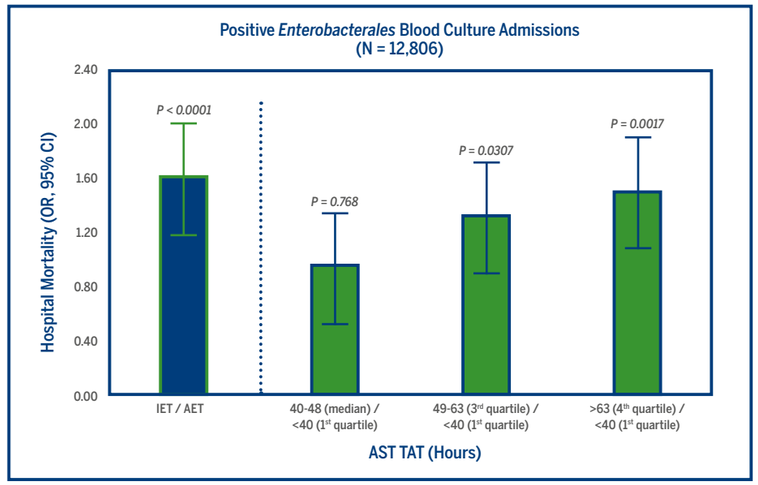

Figure 2. Model-estimated (adjusted) post-BSI event LOS (days) with positive *Enterobacterales* blood cultures by empiric therapy, carbapenem susceptibility, and AST turnaround time (TAT)
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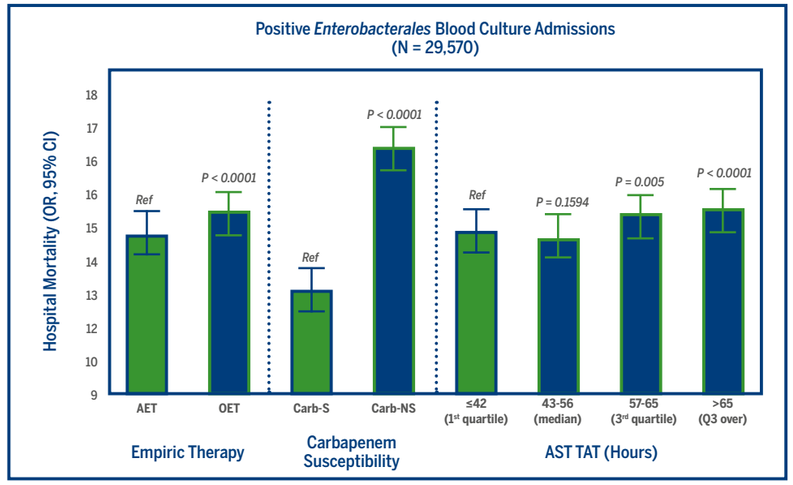

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JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY
2024;79(SUPPL 1):I26-I31. doi: 10.1093/jac/dkae280

Retrospective evaluation of rapid genotypic ID and phenotypic AST systems on positive blood culture turnaround time and simulated potential impacts on bloodstream infection management.

Yuceel-Timur I, Thierry E, Chainier D, Ndao I, Labrousse M, Grélaud C, Bala Y, Barraud O.

OBJECTIVE

This study evaluated the effectiveness of the VITEK® REVEAL™ system on the management of Gram-negative positive blood cultures (PBCs) in comparison to the standard of care (SOC), providing insights into its potential benefits in clinical settings by assessing the improvements in time-to-result (TTR), turnaround time (TAT), and time-to-antibiotic adaptation.

STUDY DESIGN

Retrospective modeling study.

Between November 2021 and March 2022, 79 Gram-negative monomicrobial PBCs were tested with both VITEK REVEAL and BIOFIRE® Blood Culture Identification 2 (BCID2) panel, as well as the SOC (VITEK® MS and VITEK® 2 for antimicrobial susceptibility testing of isolated colonies).

Two different scenarios were assessed:

- **Scenario 1 (S1)**: VITEK REVEAL used when Gram-stain results were available before noon and SOC initiated otherwise.
- **Scenario 2 (S2)**: VITEK REVEAL used for all PBCs.

Laboratory working hours: 8 AM to 6 PM

RESULTS

Time-to-result (time between run initiation and AST results):

- VITEK REVEAL significantly reduced TTR (7.9 hours in S1; 7.0 hours in S2) compared to SOC (9.6 hours).
- In addition to the AST TTR, SOC required an additional 12.8 hours to obtain isolated colonies, while VITEK REVEAL could be launched directly from PBCs.

Turnaround time (time between PBC and actionable AST [i.e. validated report]):

- VITEK REVEAL significantly reduced TAT (20.1 hours in S1; 15 hours in S2) compared to SOC (31.1 hours).

Impact of extended laboratory working hours:

- Increasing laboratory working hours from 6 PM to 10 PM **(Figure 1)**, increased the proportion of patients with actionable results on the day of BC positivity (Day 0).

Time-to-antibiotic adaptation (time between PBC and antibiotic adaptation):

- VITEK REVEAL was significantly faster (34.9 hours in S1; 26.8 hours in S2) compared to SOC (51.6 hours).
- A higher percentage of antimicrobial adaptations could be made on the day following BC positivity (Day 1) with VITEK REVEAL than with SOC **(Figure 2)**.

CONCLUSIONS

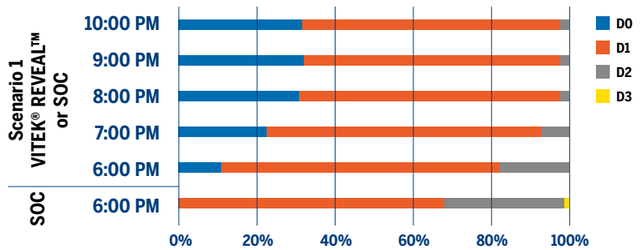
Use of VITEK REVEAL led to significantly shorter TTR and TAT compared to the SOC (MALDI-TOF MS and VITEK 2), which could enable clinicians to make timely adjustments to antimicrobials.

"This study implies that the use of VITEK® REVEAL™ enables swift adaptations of antibiotic treatment strategies. By considerably minimizing the turnaround time, healthcare professionals can promptly make necessary adjustments to therapeutic regimens."

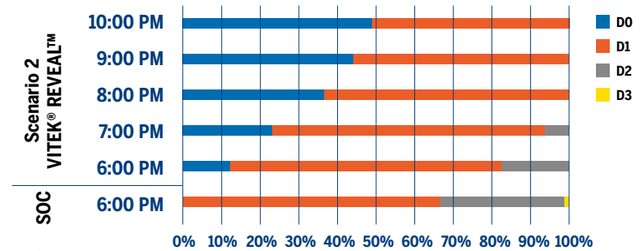
KEY FINDINGS

- VITEK® REVEAL™ yielded better results than the standard of care, significantly shortening the time to result (7.0 h compared to 9.6 h) as well as the turnaround time (15 h compared to 31.1 h) when applied for all isolates.
- These findings underscore the potential of VITEK® REVEAL™ in expediting appropriate antibiotic interventions, even in centers that do not process PBCs around the clock.

Figure 1. Turnaround time by calendar day for extended hospital laboratory hours from 6 PM to 10 PM
Reproduced with permission from Oxford University Press (OUP). Yuceel-Timur I, *et al*. *J Antimicrob Chemother*. 2024;79(Suppl 1):i26-i31



D0: Day 0
D1: Day 1
D2: Day 2
D3: Day 3



D0: Day 0
D1: Day 1
D2: Day 2
D3: Day 3

Figure 2. Time to antibiotic adaptation
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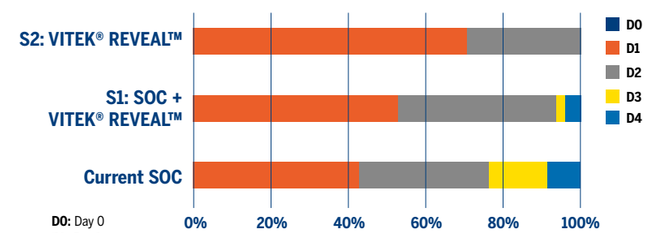

D0: Day 0
D1: Day 1
D2: Day 2
D3: Day 3
D4: Day 4

CLICK TO ACCESS ARTICLE

VALUE IN HEALTH
2023;26(12):S176
POSTER PRESENTED AT THE 2023 ISPOR EUROPE CONFERENCE, COPENHAGEN

Explorative cost-effectiveness analysis of a rapid ID and rapid AST solution for patients with bloodstream infection.

Boughazi HE, Textoris J, Vandepitte S.

OBJECTIVE

This model-based study assessed both the clinical outcomes and the economic impact of implementing a fast identification and antibiotic susceptibility testing (ID/AST) solution versus standard of care (SOC) in the management of patients with bloodstream infections (BSI). The goal was to explore the potential of this faster diagnostic method to help reduce mortality and healthcare costs by enabling earlier administration of appropriate treatment.

STUDY DESIGN

A decision analytic model was developed, from a French payer perspective, to compare the health outcomes and direct healthcare costs for a hypothetical cohort of 20,000 hospitalized patients diagnosed with BSI.

The cohort was divided into two groups:

- **Control arm (SoC)**: Conventional ID/AST methods were used, for which results are typically available within 24 to 48 hours. According to literature, about 19% of these patients received inappropriate antibiotic treatment, and 42% of them progressed to sepsis.[1]
- **Intervention arm (fast ID/AST)**: A fast diagnostic solution was used, providing results within 6 hours, which would enable clinicians to administer appropriate antibiotics within a single work shift. The hypothesis was that this method could reduce the proportion of patients progressing to sepsis to 28.4%.

The model estimated the cost per death averted and used average costs of BSI, sepsis, and septic shock based on data from published literature and expert clinical validation. A short-term time horizon was applied, focusing on the period from the onset of BSI to hospital discharge or death. The robustness of the model was tested through one-way sensitivity analyses.

RESULTS

- Using this explorative model, results* showed potential reductions in the rates of sepsis (-8.9%), septic shock (-4.6%), and mortality (-3.8%) **(Table 1)**. Furthermore, the estimated total net cost savings per patient were €992, with a 1.5-day reduction in average length of hospital stay and a 1.1-day reduction in average Intensive Care Unit (ICU) stay.
- One-way sensitivity analyses confirmed the robustness of these results, showing that the model's outcomes were stable across various assumptions **(Figure 1)**.

* The results shown in Table 1 and Figure 1 have been updated since the published abstract of the 2023 ISPOR poster.

CONCLUSIONS

This analysis provides valuable evidence for healthcare decision-makers, suggesting that investment in fast diagnostic tools not only improves patient outcomes but also generates significant cost savings, thereby enhancing the overall efficiency of healthcare systems. This aligns with global health recommendations, such as those from the World Health Organization (WHO) regarding use of fast AST methods direct from blood culture.[2]

1. Kadri SS, *et al*. *Lancet Infect Dis.* 2021;21(2):241-251 doi 10 .1016/S1473-3099(20)30477-1
2. WHO Global Research Agenda for AMR in Human Health Policy Brief 2023

"The use of a rapid ID/AST solution was cost-saving and life-saving when compared to standard of care in BSI management by starting earlier with appropriate treatment."

Table 1. Differences in main outcomes between SOC arm and fast ID/AST arm
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	STANDARD OF CARE	FAST ID/AST	DIFFERENCE
Health outcomes			
Sepsis cases (%)	27.7	18.8	- 8.9
Septic shock cases (%)	14.3	9.7	- 4.6
Overall mortality (%)	11.7	7.9	- 3.8
Economic outcomes			
Average LoS per patient (days)	11.6	10.1	- 1.5
Average ICU stay (days)	3.4	2.3	- 1.1
Total cost per patient (€)	9,951	8,959	- 992

Figure 1. Tornado diagram – net cost savings per patient when +/- 30% variation is applied for each variable
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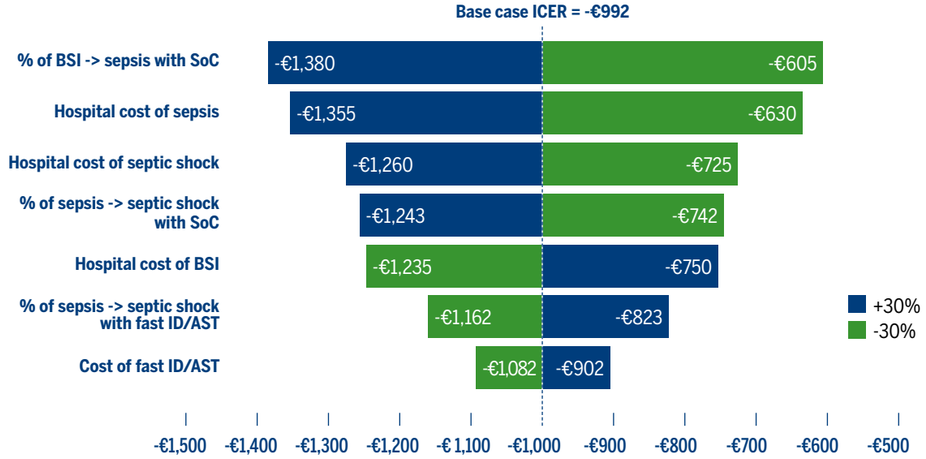

KEY FINDINGS

- Clinical benefits associated with the explorative model:
  - Use of a fast ID/AST solution could reduce the risk of progression from BSI to sepsis and septic shock, by providing timely actionable results.
  - Mortality rates could be lowered by 3.8% when using fast ID/AST compared to SOC.
- Economic benefits associated with the explorative model:
  - Average hospital and ICU length of stay could be shortened, leading to lower healthcare resource utilization.
  - Total cost of care could be reduced by nearly €1,000 per patient.

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JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY
2024;79(SUPPL 1):I13-I25. doi: 10.1093/jac/dkae282

Evaluating the impact of rapid antimicrobial susceptibility testing for bloodstream infections: a review of actionability, antibiotic use and patient outcome metrics.

MacVane SH, Dwivedi HP.

OBJECTIVE

This article reviews metrics to measure the impact of fast AST on actionability, antibiotic use, and patient outcomes for the management of bloodstream infections (BSIs). In addition, it highlights the importance of optimizing processes and workflows to maximize the benefits of fast AST.

IMPACT ON ACTIONABILITY AND CLINICAL DECISION-MAKING

- **Actionability** is defined as the ability of test results to influence clinical decision-making and is often used to assess whether fast AST provides any advantage over conventional phenotypic methods.
- For fast AST, actionability is a measure of how frequent results can lead to quicker and more frequent antibiotic modifications.
- To be actionable, fast AST results must provide sufficient information for clinicians to assess the appropriateness of the patient's current antibiotic therapy and be able to determine which antibiotic regimen is optimal for the patient.

IMPLEMENTATION AND WORKFLOW

- Effective implementation requires validation against reference methods and adjustments in laboratory workflows to optimize testing and reporting of fast results.
- The fast pathogen identification test will need to accompany fast AST implementation, if not included in the same test.
- Adequate training and staffing are essential for timely set-up and reporting of fast AST results.
- Smooth information flow, integration with hospital IT systems, and compliance with cybersecurity requirements is crucial for the implementation of fast AST systems.

REPORTING AND COMMUNICATION

- Whereas fast AST tests are the enabler of actionability, implementation is dependent on the speed of reporting and response of clinical staff. Fast AST results must be communicated promptly to ensure they are actionable.
- Pairing fast AST with AMS programs enhances the impact on antibiotic use and patient outcomes.
- Further studies that compare clinical outcomes and economic impacts with various implementation and notification strategies are needed to help determine where each intervention mechanism best fits into clinical practice.

CLINICAL OUTCOME AND ASSOCIATED METRICS

- Most common metrics used to assess impact of fast AST: antimicrobial exposure, clinical outcomes, length of stay.
- Faster AST results showed benefit in reducing broad-spectrum antimicrobial which is a core element of AMS interventions.
- Decreased mortality rates and increased clinical resolution were associated with fast AST reports.
- Shorter hospital length of stay was also associated with fast AST implementation.

CONCLUSIONS

Fast AST significantly reduces time to results and allows for quicker identification of the most effective antibiotics to treat BSIs.
Fast AST also supports antimicrobial stewardship programs by minimizing the use of broad-spectrum antibiotics and promoting the use of targeted therapies.
The impact of fast AST on patient outcome is limited unless results are reported, communicated, and acted on in timely fashion.

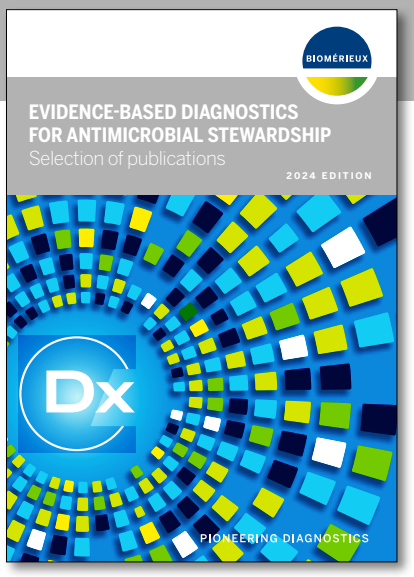
"Randomized controlled trials and observational studies consistently show that rapid AST significantly reduces time to results and improves antimicrobial therapy for patients with BSI across various methods, patient populations and organisms."

KEY FINDINGS

- AST is crucial for managing BSIs to ensure optimal antibiotic therapy.
- Fast AST methods can provide results in under 8 hours, significantly faster than conventional methods.

Other evidence-based Selection of Publications available

Contact your local bioMérieux representative to find out more about other available educational resources, or visit : https://www.biomerieux.com/corp/en/education/medical-education/sepsis.html



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