

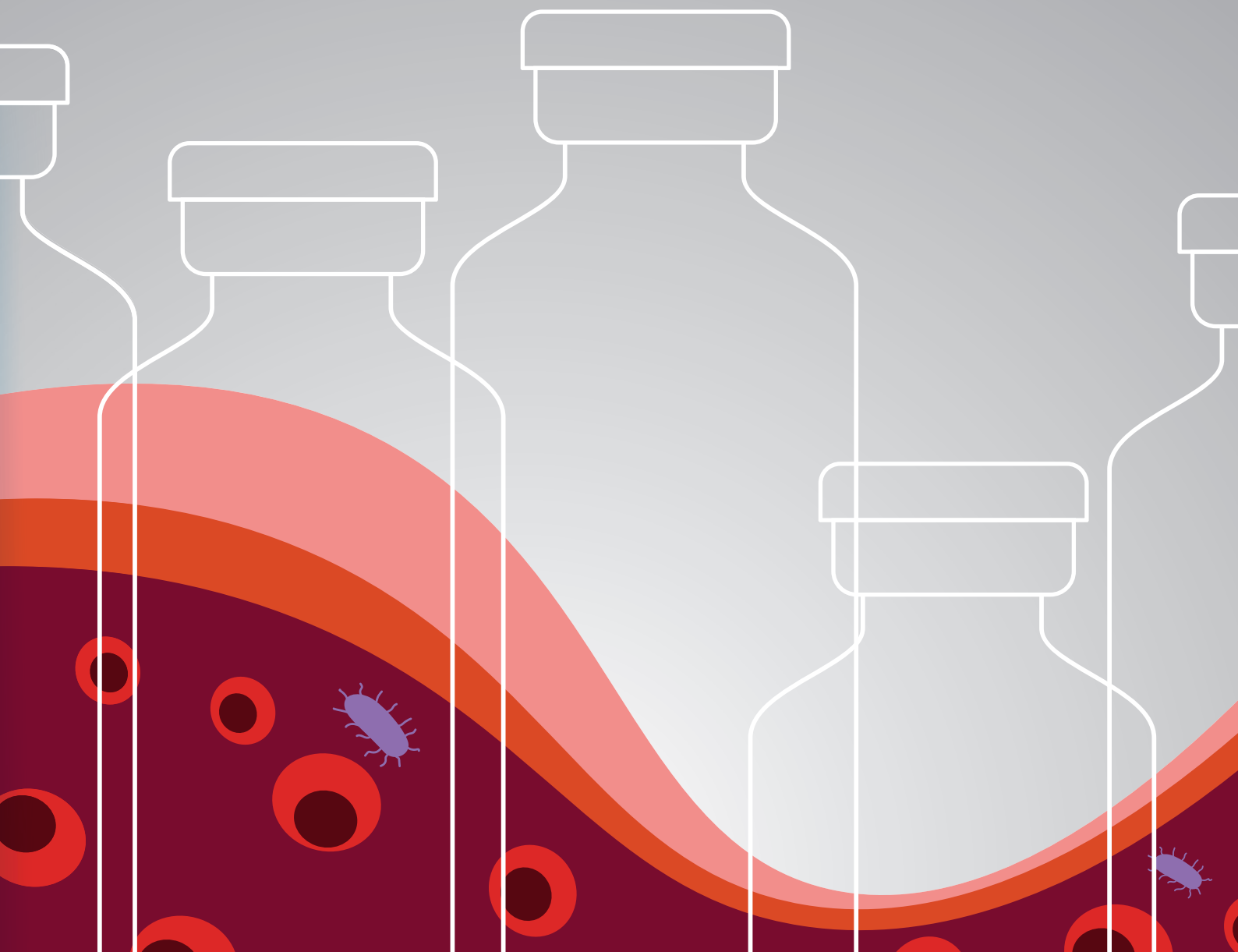


BIOMÉRIEUX

BACT/ALERT®

Selection of publications

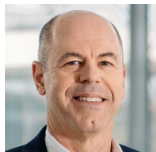
2026 EDITION



PIONEERING DIAGNOSTICS

INTRODUCTION

“Blood cultures remain the foundational diagnostic step upon which all subsequent tests for bloodstream infections and sepsis rely, making their rigorous execution essential to ensure accurate and reliable results.”



Dr. Charles K. Cooper,
Executive Vice President, Chief Medical Officer, bioMérieux

BLOODSTREAM INFECTIONS

Bloodstream infections are life-threatening conditions that occur when microorganisms present in the blood trigger systemic signs of infection. The presence of bacteria or fungi in the bloodstream, whether associated with active disease or not, is referred to as bacteremia or fungemia.¹ When this bacteremia or fungemia is accompanied by systemic signs of infection such as fever, chills or hypotension, the condition is defined as a bloodstream infection (BSI).²

BSIs represent a clinical situation in which fast and accurate diagnosis is essential to identify the causative pathogen. The pathogens most frequently associated with bloodstream infections include *Escherichia coli*, *Staphylococcus aureus*, coagulase-negative staphylococci, *Klebsiella pneumoniae* and *Candida albicans*.³

BSIs are also a major gateway to sepsis, a life-threatening organ dysfunction caused by a dysregulated host response to infection.⁴ Sepsis is a complex inflammatory process that remains largely underrecognized and a major cause of morbidity and mortality worldwide, with an estimated 166 million cases and 21.4 million sepsis-related deaths globally in 2021, including 15.5 million deaths associated with underlying infectious diseases.⁵ This substantial global burden highlights the need for early detection of bloodstream infections to guide clinical management and prevent progression to severe outcomes.

Early treatment, particularly with antimicrobials, is crucial for improving patient outcomes in cases of BSI or sepsis. Therefore, 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 adaptation of empiric antimicrobial therapy.⁶

BLOODSTREAM INFECTION DIAGNOSIS

Blood culture is the standard microbiological method for diagnosing BSIs. By inoculating a patient’s blood into culture media, microorganisms can be detected and identified. Because bloodstream infections are pathogen specific, a positive blood culture result provides clinically actionable information.⁷⁻⁹

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Three essential goals of blood culture¹⁰

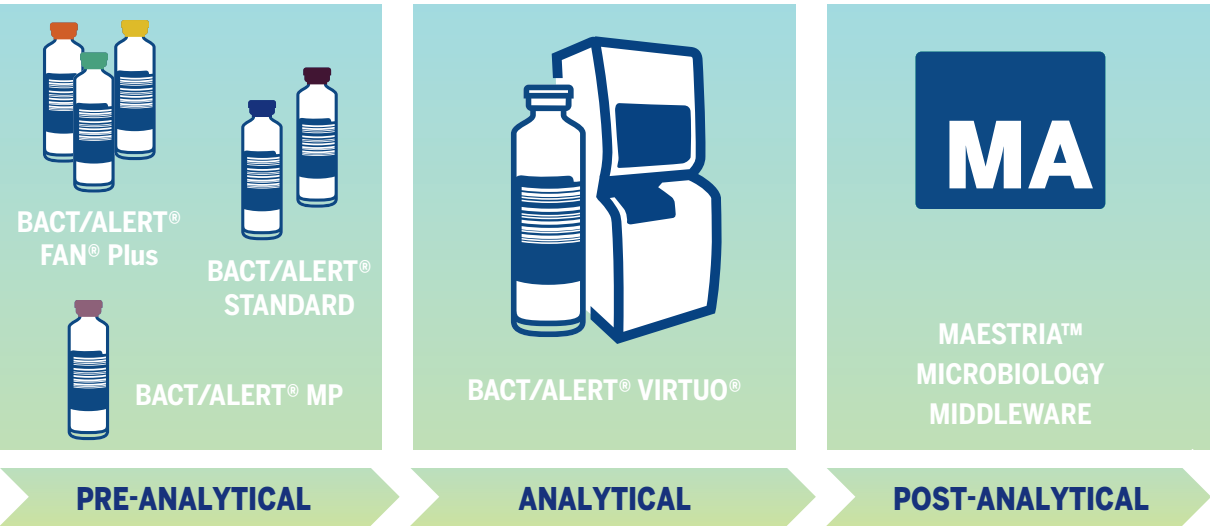
CONFIRM INFECTIOUS ETIOLOGY BY IDENTIFYING THE PRESENCE OF MICRO-ORGANISMS IN THE BLOOD

IDENTIFY THE ETIOLOGICAL AGENT AND HELP DETERMINE THE SOURCE OF INFECTION

GUIDE ANTIMICROBIAL THERAPY THROUGH ORGANISM ISOLATION, IDENTIFICATION, AND SUSCEPTIBILITY TESTING

To preserve diagnostic accuracy, blood samples should be collected as early as possible after symptom onset, ideally before antimicrobial administration.¹¹ Blood cultures obtained after treatment initiation can experience up to a 50 percent reduction in pathogen recovery.¹² Microorganism recovery is improved when blood is inoculated into bottles containing antimicrobial neutralizing media, which helps counteract the effect of prior antimicrobial exposure. This challenge is particularly relevant in clinical practice, since one-third to two-thirds of patients suspected of sepsis receive antibiotics prior to blood culture collection.¹³ bioMérieux, with over 60 years of experience in microbiology, provides integrated and reliable BACT/ALERT® blood culture solutions (Figure 1) enabling medical teams to accurately diagnose patients with bloodstream infections and sepsis.

Figure 1: BACT/ALERT® range* supports pre-analytical, analytical and post-analytical excellence to enable better patient care



*Non exhaustive list of BACT/ALERT® products.

The BACT/ALERT® FAN® Plus bottles use high-capacity resin technology to neutralize broad spectrum antimicrobials and improve microorganism recovery, even under antibiotic exposure. By relying on three optimized bottles, aerobic, anaerobic and pediatric, laboratories can cover all clinical conditions while reducing the complexity of bottle management for laboratory teams and blood sampling for nurses.

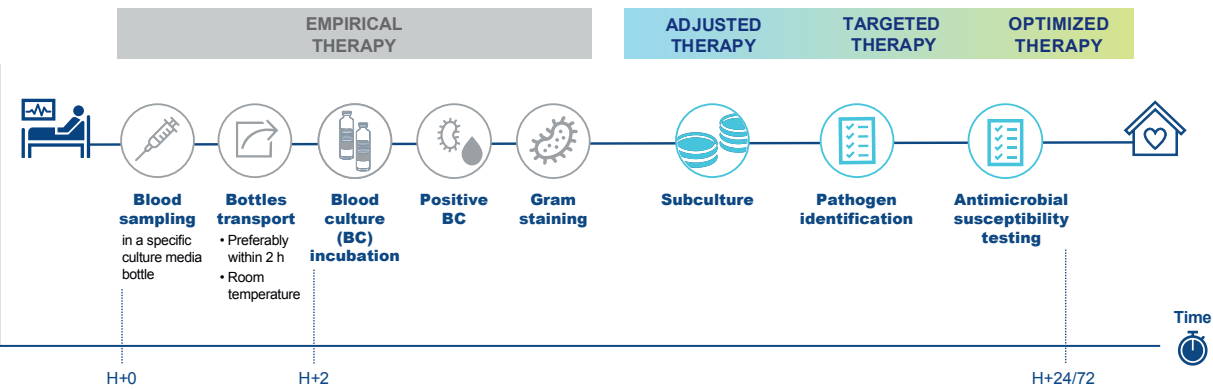
The performance of the diagnostic pathway depends on the robustness of the blood culture system supporting each step of the process, particularly under real-world conditions. The BACT/ALERT® systems use a colorimetric detection technology that offers a clear advantage under delayed entry conditions. By absorbing CO₂ produced by replicating microorganisms, the sensor undergoes an irreversible color change that provides a robust and early growth signal. This direct colorimetric response, supported by dedicated algorithms, enables the system to maintain high performance even with delayed bottle entry, thereby reducing the likelihood of false negative results.¹⁴

BACT/ALERT® VIRTUO®, the fully automated system of the BACT/ALERT® range, strengthens this analytical pathway through rapid and consistent detection of microorganisms. The system uses a Drop and Go loading mechanism that ensures automated and continuous bottle processing, which supports true 24/7 operation and reduces hands-on time for laboratory staff.¹⁵ This reduction in manual tasks helps reallocate technical resources toward higher value-added tasks. BACT/ALERT® VIRTUO® maintains thermal stability throughout incubation and applies sensitive algorithm-based detection, which accelerates positivity signals.

Blood culture is the first step in bloodstream infection management, and its quality, accuracy, and timeliness influence all subsequent microbiological diagnostic steps, including organism identification (ID) and antimicrobial susceptibility testing (AST).

Beyond this initial step, bioMérieux provides an integrated diagnostic pathway for BSI and sepsis management (Figure 2), with automated Gram staining, culture media, immunoassays and solutions for organism ID and AST. Together, these technologies support the microbiological diagnosis of BSI throughout the laboratory workflow.^{16,17}

Figure 2: Integrated diagnostic pathway for BSI and sepsis management



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ABBREVIATIONS & ACRONYMS

The following abbreviations and acronyms are used throughout the Selection of publications.

AST	antimicrobial susceptibility testing
ATCC	American Type Culture Collection
BC	blood culture
BSI	bloodstream infection
CFU	colony-forming unit
CLSI	Clinical and Laboratory Standards Institute
CO ₂	carbon dioxide
Cmax	maximum plasma concentration
DDD	defined daily dose
EMR	electronic medical record
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GN	Gram-negative
GP	Gram-positive
HPLC	high-performance liquid chromatography
HR	hazard ratio
ICU	intensive care unit
ID	identification
IQR	interquartile range
LIS	laboratory information system
LOS	length of stay
MIC	minimum inhibitory concentration
MRSA	methicillin-resistant <i>Staphylococcus aureus</i>
MTBC	<i>Mycobacterium tuberculosis</i> complex
NTM	nontuberculous mycobacteria
PBS	phosphate-buffered saline
PJI	prosthetic joint infection
PSL	peak serum level
sHR	subdistribution hazard ratio
TAT	turnaround time
TTOT	time to optimal therapy
TTD	time to detection
TTP	time to positivity
USD	United States dollar

BROAD SAMPLE AND PATHOGEN COVERAGE

**YEAST
ANAEROBE
OTHER SAMPLES THAN BLOOD**

Efficient Recovery of *Candida auris* and Five Other Medically Important *Candida* Species from Blood Cultures Containing Clinically Relevant Concentrations of Antifungal Agents

Posteraro B, Menchinelli G, Ivagnes V, et al.

OBJECTIVE

To compare antimicrobial drug-neutralizing capability of blood culture (BC) media of BACT/ALERT® FA Plus (FAP) or BACTEC™ Plus Aerobic/F (PAF) bottles with non-neutralizing BC media in BACTEC™ Mycosis IC/F (MICF) bottles for recovery of *Candida* spp. growth in the presence of clinically relevant concentrations of antifungal agents.

STUDY DESCRIPTION

- **Study design:** Experimental *in vitro* comparative study using a clinical BC simulation model.
- **Population:** 117 fungal/antifungal combinations at clinically relevant antifungal concentrations (100%, 50%, or 25% peak serum level (PSL)).
- **Intervention:** BACT/ALERT® VIRTUO® (VIRTUO) system + FAP bottle.
- **Comparators:**
 - BACTEC™ system + PAF, neutralizing media.
 - BACTEC™ system + MICF, non-neutralizing media (control).
- **Outcomes:**
 - Recovery rate of *Candida* spp. with or without of antifungal agents.
 - Mean time to detection (TTD).

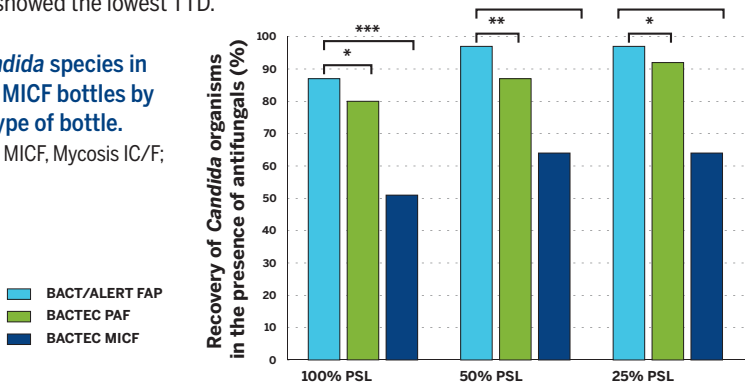
RESULTS

Both FAP and PAF bottles maintained high recovery rates, achieving 100% recovery for *C. auris*, *C. glabrata*, and *C. parapsilosis* even at 100% PSL antifungal concentrations, while slightly lower recovery was observed for *C. albicans*, *C. krusei*, and *C. tropicalis*. Notably, azoles and amphotericin B did not impact *Candida* spp. growth in FAP or PAF bottles, whereas recovery rates under echinocandins were lower (87% for FAP and 70.4% for PAF) particularly for *C. albicans*, *C. tropicalis*, and *C. krusei*.

In contrast, MICF bottles showed reduced performance across all tested antifungal concentrations (recovery rates with echinocandins: 50%, azole: 72.9%, amphotericin B: 53.3%).

Compared with PAF and MICF bottles, FAP bottles showed a significantly higher recovery rate under antifungal conditions (Figure 1). Overall, under antifungal conditions, FAP bottles showed the lowest TTD.

Figure 1. Percentages of overall recovery for *Candida* species in BACT/ALERT® FAP, BACTEC™ PAF, or BACTEC™ MICF bottles by the antifungal concentrations present in each type of bottle. (***, $p < 0.001$; **, $p < 0.01$; and *, $p < 0.05$). FAP, FA Plus; MICF, Mycosis IC/F; PAF, Plus Aerobic/F; PSL, peak serum level.



CONCLUSIONS

BACT/ALERT® FAP blood culture bottles showed good performance for the recovery of *Candida* spp. in the presence of clinically relevant concentrations of antifungal agents.

KEY FINDINGS

- FAP bottles, with optimized micronutrient composition, demonstrated better overall performance, with higher *Candida* recovery compared to PAF and MICF, especially under antifungal exposure.
- Both FAP and PAF bottles were highly efficient for the detection of *C. auris*, *C. glabrata*, or *C. parapsilosis* in the presence of antifungals.
- MICF bottles were considerably less efficient for the detection of *Candida* spp. (excluding *C. auris*), under antifungal exposure, including at low antifungal concentrations.

Routine Use of Anaerobic Blood Culture Bottles for Specimens Collected from Adults and Children Enhances Microorganism Recovery and Improves Time to Positivity

Ransom EM, Burnham CD.

OBJECTIVE

To determine the clinical utility of combining BACT/ALERT® FA Plus (FA Plus) aerobic and FN Plus (FN Plus) anaerobic blood culture bottles with the BACT/ALERT® VIRTUO® (VIRTUO) system.

STUDY DESCRIPTION

- **Study design:** Retrospective cohort study in a central laboratory serving academic and community hospitals (Barnes-Jewish Hospital, St. Louis, USA).
- **Population:** 158,710 blood culture (BC) bottles, including 8,959 positive BCs corresponding to 13,592 positive bottles, of which 551 positive BCs (823 positive bottles) were from pediatric patients.
- **Intervention:** Anaerobic BC bottles + aerobic BC bottles.
- **Comparator:** Aerobic BC bottles alone.
- **Outcomes:** Recovery rate and time to detection (TTD).
- **Time:** November 2018 to October 2019.

RESULTS

Anaerobic BC bottles yielded 403 obligate anaerobes (5.8% of positive anaerobic bottles), and 16 obligate anaerobes in pediatric patients were identified from 389 positive anaerobic bottles (1.8%).

If anaerobic bottles had not been collected, all but 8 obligate anaerobes, all *Cutibacterium* spp., would have gone undetected.

Anaerobic bottles also demonstrated increased recovery and shorter time to detection for selected facultative anaerobes, with significantly improved recovery observed for *Staphylococcus aureus* (1,799 vs. 1,879, $p = 0.009$) and *Streptococcus intermedius* (0 vs. 7, $p = 0.046$), and shorter time to detection for both *S. aureus* (-36 min, $p = 0.027$) and *Proteus mirabilis* (-180 min, $p = 0.039$).

Overall, only a limited number of microorganisms demonstrated improved recovery or faster detection in aerobic bottles.

If only aerobic bottles had been collected, 2,027 additional cultures would have been reported as negative and 7,452 fewer isolates would have been detected, including *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*.

CONCLUSIONS

The study data support the routine collection of paired aerobic and anaerobic bottles for blood cultures on the VIRTUO system, compared with aerobic-only collection.

KEY FINDINGS

- Almost all obligate anaerobes from this study were only isolated from anaerobic bottles.
- Facultative anaerobes grew comparably and sometimes better in anaerobic bottles.
- Clinically relevant microorganisms would have been missed for both adult and pediatric patients without the anaerobic bottle.

Culturing periprosthetic tissue in BacT/Alert® Virtuo blood culture system leads to improved and faster detection of prosthetic joint infections

Sanabria A, Røkeberg MEØ, Johannessen M, et al.

OBJECTIVE

To evaluate the use of the BACT/ALERT® VIRTUO® (VIRTUO) system with BACT/ALERT® FA Plus (aerobic) and FN Plus (anaerobic) blood culture bottles for culturing periprosthetic tissue specimens.

STUDY DESCRIPTION

- **Study design:** Spiking experiments + prospective study at the University Hospital of North Norway (Tromsø, Norway).
- **Population:** 36 spiked periprosthetic tissue samples with 6 bacterial species (5 ATCC* strains and 1 clinical strain) commonly associated with prosthetic joint infections (PJI). Additionally, 158 clinical periprosthetic tissue samples from 62 patients with suspected PJI (hip, knee, elbow, ankle, or shoulder) were analyzed. Samples were incubated for up to 12 days.
- **Intervention:** VIRTUO with FA Plus and FN Plus bottles.
- **Comparator:** Conventional microbiological culture-based method.
- **Outcomes:** Sensitivity, time to detection (TTD), microorganism identification, agreement between methods.
- **Time:** August 2017 to June 2018.

* American Type Culture Collection

RESULTS

The recovery rate in spiked blood culture (BC) bottles was 100% (n = 36) for both bottle types. The mean TTD was 10.1 ± 2.2 h for FA Plus. For FN Plus bottles, TTD varied markedly between strains, with *Cutibacterium acnes* showing a mean TTD of 209.2 ± 18.1 h compared to 25.2 ± 1.1 h for *Bacteroides fragilis*. No differences were observed between repeats, supporting the reproducibility of the method.

Among clinical samples, 25.3% (80/316) of BC bottles signaled positive, corresponding to 29.1% (46/158) of tissue specimens from 24 patients. Of these, 73.9% of microorganisms were detected in both bottles, 21.8% in aerobic bottles only, and 4.3% in anaerobic bottles only. Two bottles were classified as false positives after negative subculture.

For aerobic bottles, 89% of microorganisms were detected within 24 h and 100% within 40 h, compared to 97% and 100% within 24 h and 31 h, respectively, for anaerobic bottles. The mean TTD was shorter for anaerobic bottles than for aerobic bottles (11.3 h vs. 13.9 h).

Compared with the conventional method, the BC method showed comparable sensitivity (79% vs. 76%, *p* = 0.844) and an overall agreement of 84%. Similar bacterial species were identified in 89% of positive samples. The TTD was markedly reduced using the BACT/ALERT bottles, with more than 80% of microorganisms detected within 20 h compared to up to 5 days using the conventional method.

CONCLUSIONS

The study data showed sensitivity comparable to conventional cultures, whilst enabling faster detection of pathogens, which could facilitate clinical decision-making at an earlier stage in the prosthetic joint infection management.

KEY FINDINGS

- The VIRTUO BC method demonstrated comparable sensitivity to conventional culture for detection of prosthetic joint infection pathogens (79% vs. 76%).
- The BC method provided substantially faster pathogen detection, with 89% of microorganisms detected within 24 h compared with 27% using conventional culture.
- The authors concluded that the VIRTUO system is a reliable and rapid diagnostic approach for culturing periprosthetic tissue, potentially facilitating earlier clinical decision-making in PJI management.

Performance of the BacT/Alert Virtuo Microbial Detection System for the culture of sterile body fluids: prospective multicentre study

She RC, Romney MG, Jang W, et al.

OBJECTIVE

To compare the performance of the BACT/ALERT® VIRTUO® (VIRTUO) system with the BACT/ALERT® 3D (BTA3D) system using BACT/ALERT® blood culture bottles (SA, SN, FA Plus and FN Plus) and conventional culture for the recovery of microorganisms from sterile body fluids.

STUDY DESCRIPTION

- **Study design:** Prospective multicenter comparative study (Los Angeles (USA), Cleveland (USA) and Vancouver (Canada)).
- **Population:** 811 specimens from 655 unique patients were inoculated into 1,257 bottle pairs (443 FA Plus, 499 FN Plus, 139 SA and 176 SN). Specimens included peritoneal, cerebrospinal, pericardial, pleural and synovial fluids from adult patients submitted for routine bacterial cultures.
- **Intervention:** VIRTUO + SA, SN, FA Plus or FN Plus (FAN® Plus).
- **Comparator:** BTA3D + SA, SN, FAN Plus and conventional culture (Gram stained and seeded to solid media).
- **Outcomes:** Recovery rate, time to detection (TTD).
- **Time:** March to September 2013 and May 2015 to April 2016.

RESULTS

VIRTUO and BTA3D showed equivalent recovery of clinically significant microorganisms, with recovery rates of 81.9% (127/155) and 81.3% (126/155), respectively. In contrast, conventional solid media recovered significantly fewer clinically significant microorganisms (61.3% (95/155), *p* < 0.001), notably fewer *Enterobacteriaceae* and enterococci.

Among clinically significant isolates from monomicrobial cultures detected by both automated systems, VIRTUO demonstrated a significantly shorter median time to detection compared with BTA3D: 12.5 h [2.8–101.5] vs. 15.5 h [4.3–78.5], *p* < 0.001.

Direct specimen Gram stain detected the eventual pathogen in 26.1% (30/115) of significant positive specimens, supporting the need for culture-based detection even when initial microscopy is negative.

CONCLUSIONS

VIRTUO demonstrated faster time to detection compared with BTA3D, while maintaining equivalent recovery rates of clinically significant microorganisms from sterile body fluids.

KEY FINDINGS

- VIRTUO showed equivalent recovery of clinically significant microorganisms from sterile body fluids compared with BTA3D (81.9% vs. 81.3%, respectively).
- VIRTUO demonstrated faster TTD than the BTA3D system, likely due to advances in software algorithms and temperature stability.
- The low yield of direct Gram stain highlights the value of continuous-monitoring blood culture systems for pathogen detection in sterile body fluids.

Multicenter matched-pair study comparing BACT/ALERT® MP reagent systems for the recovery of mycobacteria from specimens other than blood

Dwivedi H, MacDonald K, Angaali N, et al.

OBJECTIVE

To evaluate the performance of an improved BACT/ALERT® MP bottle (MP-I) compared with the current MP bottle (MP-C) for the detection and recovery of mycobacteria from clinical specimens other than blood.

STUDY DESCRIPTION

- **Study design:** Multicenter prospective matched-pair study (3 US sites and 1 in India).
- **Population:** 1,488 clinical specimens (sterile and non-sterile, predominantly respiratory) from 1,162 patients and 52 additional seeded samples (with mycobacteria and respiratory flora). Overall, 212 mycobacteria-positive samples. Incubation for up to 42 days.
- **Intervention:** BACT/ALERT® 3D (BTA3D) system + MP-I bottle.
- **Comparator:** BTA3D system + MP-C bottle.
- **Outcomes:** Sensitivity, specificity, recovery rate, false positive and false negative rates, time to detection (TTD).

RESULTS

The MP-I bottle demonstrated improved performance compared with MP-C. Sensitivity was numerically higher with MP-I (86.6% vs. 81.4%), although the difference was not statistically significant ($p = 0.163$). **Specificity was significantly improved (96.8% vs. 93.8%, $p = 0.002$), with a lower false-positive rate (2.3% vs. 4.8%, $p < 0.001$).**

Recovery of mycobacteria was numerically higher with MP-I (94.3% vs. 88.7%, $p = 0.054$), consistently across sites, suggesting a trend toward higher recovery. Among seeded samples, **recovery reached 100% with both bottle types.**

Importantly, MP-I was associated with **shorter mean TTD**, particularly for *Mycobacterium tuberculosis* complex (MTBC), with a mean reduction of **approximately 2.7 days** (11.6 vs. 14.4 days). Differences in TTD were minimal for non-tuberculous mycobacteria (NTM), including rapid growers (7.3 vs. 7.4 days) and slow growers (11.5 vs. 11.8 days).

Table 1. Comparison of parameters between MP-I and MP-C

PARAMETER	MP-I	MP-C	P-VALUE
Sensitivity	86.6%	81.4%	0.163
Specificity	96.8%	93.8%	0.002
Recovery rate	94.3%	88.7%	0.054
False positive rate	2.3%	4.8%	< 0.001
False negative rate	0.1%	0.3%	0.687
Mean TTD, MTBC	11.6 days	14.4 days	
Mean TTD, NTM rapid grower	7.3 days	7.4 days	
Mean TTD, NTM slow grower	11.5 days	11.8 days	

CONCLUSIONS

MP-I bottles showed significantly higher specificity and lower false-positive rates compared with MP-C, with numerically higher mycobacterial recovery and shorter mean TTD for *M. tuberculosis* complex, alongside a trend toward higher sensitivity.

KEY FINDINGS

- MP-I bottles showed significantly higher specificity and lower false-positive rates compared with MP-C, with a trend toward higher sensitivity.
- MP-I showed numerically higher mycobacterial recovery, with an absolute increase of approximately 5.6 percentage points compared with MP-C.
- MP-I reduced time to detection for *M. tuberculosis* complex by approximately 2.7 days compared with MP-C.
- This modified medium includes a nutrient supplement supporting optimal mycobacterial growth.

KEY PERFORMANCE ATTRIBUTES

**FASTER RESULTS
CONSISTENT PERFORMANCE OVER TIME
ADVANCED ANTIMICROBIAL NEUTRALIZATION**

Impact of Implementation of BacT/Alert Virtuo on Blood Culture Time to Positivity in Sepsis Patients

Mazzulli T, Ratkov D, Guglielmin K, et al.

OBJECTIVE

To assess the impact of implementing the BACT/ALERT® VIRTUO® (VIRTUO) automated blood culture system on time to positivity (TTP) in intensive care unit (ICU) patients with suspected sepsis.

STUDY DESCRIPTION

- **Study design:** Retrospective pre-post implementation multicenter study in 3 hospitals (Toronto, Canada).
- **Population:** Adult ICU patients (≥ 18 years) with suspected sepsis and at least one positive blood culture for bacteremia or fungemia.
- **Intervention:** VIRTUO + BACT/ALERT® FA Plus and FN Plus bottles.
- **Comparator:** BACT/ALERT® 3D (BTA3D) + FA Plus and FN Plus bottles.
- **Outcomes:** Time to positivity (TTP). Secondary analyses by Gram stain category and isolates requiring antimicrobial susceptibility testing (AST).
- **Time:**
 - **Pre-implementation:** February 2016 to March 2017.
 - **Post-implementation:** May 2017 to April 2018.

RESULTS

A total of 229 positive blood cultures were analyzed (115 processed with BTA3D and 114 with VIRTUO). Similar organism distributions were observed with VIRTUO and BTA3D for both Gram-positive and Gram-negative bacteria. For both VIRTUO and BTA3D, the most frequently isolated organisms were staphylococci other than *Staphylococcus aureus* among Gram-positive bacteria and *Escherichia coli* among Gram-negative bacteria. No yeast isolates were detected during the pre-implementation period.

Median TTP was significantly shorter with VIRTUO compared to BTA3D (16.2 h vs. 21.1 h; *p* < 0.001), and this reduction remained significant after exclusion of fungal isolates (15.5 h vs. 21.1 h; *p* = 0.001).

Among clinically relevant isolates requiring AST, median TTP was also significantly reduced with VIRTUO (11.1 h vs. 16.0 h; *p* = 0.008).

The reduction in time to positivity was more pronounced for Gram-negative organisms (10.2 h vs. 17.1 h; *p* < 0.001). A significant reduction was also observed for Gram-positive bacteria (17.2 h vs. 21.5 h; *p* = 0.003).

CONCLUSIONS

VIRTUO was associated with significantly shorter time to positivity than BTA3D in ICU patients with suspected sepsis. This reduction was observed across Gram-positive and Gram-negative bacteria, with the greatest difference reported for Gram-negative organisms.

KEY FINDINGS

- Median TTP was significantly reduced with VIRTUO (-4.9 h; *p* < 0.001).
- Among clinically relevant isolates requiring AST, TTP was also significantly reduced (-4.9 h; *p* = 0.008).
- Greater reduction observed in Gram-negative organisms (-6.9 h; *p* < 0.001).
- Faster TTP with VIRTUO may support earlier diagnosis and management of sepsis and bloodstream infections in ICU patients.

In vitro Evaluation of BACT/ALERT® VIRTUO®, BACT/ALERT 3D®, and BACTEC™ FX Automated Blood Culture Systems for Detection of Microbial Pathogens Using Simulated Human Blood Samples

Menchinelli G, Liotti FM, Fiori B, et al.

OBJECTIVE

This study compared the performance of the BACT/ALERT® VIRTUO® (VIRTUO), BACT/ALERT® 3D (BTA3D), and BACTEC™ FX (FX) automated blood culture (BC) systems for microbial growth detection and time to detection using simulated human blood samples.

STUDY DESCRIPTION

- **Study design:** *In vitro* comparative study using simulated human BC tested in parallel across three automated systems.
- **Population:** 330 adult and pediatric clinically relevant isolates (140 Gram-negative, 140 Gram-positive, and 50 yeasts) inoculated into 2,610 bottles with 30 colony-forming units per bottle.
- **Intervention:** VIRTUO system + BACT/ALERT® FA Plus, FN Plus and PF Plus bottles.
- **Comparators:** Tested in parallel under standardized conditions.
 - BTA3D system + FA Plus, FN Plus and PF Plus bottles.
 - FX system + Plus Aerobic/F, Plus Anaerobic/F and Peds Plus/F bottles.
- **Outcomes:** Recovery rate and time to detection (TTD).

RESULTS

Of the 2,610 bottles tested, 2,600 (99.6%) signaled positive in all three systems, demonstrating comparable growth recovery rates. Only the FX system failed to detect *Staphylococcus lugdunensis* isolates in anaerobic bottles.

Among adult simulated cultures, median TTDs in aerobic and anaerobic bottles were significantly shorter with VIRTUO compared with BTA3D and FX (11.6 h / 10.1 h vs. 13.3 h / 12.3 h vs. 13.5 h / 12.2 h, respectively; *p* < 0.001 for all comparisons).

Similarly, in pediatric simulated cultures, VIRTUO demonstrated a significantly shorter median TTD compared with FX and BTA3D (11.2 h vs. 12.5 h vs. 13.0 h, respectively; *p* < 0.001).

Overall, VIRTUO enabled faster growth detection for most microbial species tested. Notable examples included *Salmonella* spp. (1.8 h reduction vs. FX) among Gram-negative organisms and *Streptococcus agalactiae* (1.3 h reduction vs. FX) among Gram-positive bacteria. The greatest reductions in TTD (approximately 3 h) compared with FX were observed for Gram-positive bacteria in anaerobic and pediatric bottles (14.0 h vs. 17.0 h and 13.5 h vs. 16.1 h, respectively; *p* < 0.001).

In contrast, yeast organisms showed comparable TTD between VIRTUO and FX in aerobic and pediatric bottles, with no consistent significant differences observed.

CONCLUSIONS

Despite similar recovery rates across all three systems, VIRTUO significantly reduced TTD in both adult and pediatric simulated cultures.

KEY FINDINGS

- VIRTUO significantly reduced TTD compared with both BTA3D and FX systems (-1.7 to -1.9 h overall; *p* < 0.001).
- The greatest reduction in TTD compared with FX was observed for Gram-positive bacteria, particularly in anaerobic and pediatric bottles (up to -3 h; *p* < 0.001).
- VIRTUO detected key bloodstream pathogens, including *Salmonella* spp. and *Streptococcus agalactiae*, earlier than both comparator systems.

Comparative evaluation of BacT/ALERT VIRTUO and BACTEC FX400 blood culture systems for the detection of bloodstream infections

Qin Y, Liao Y, Zhou J, et al.

OBJECTIVE

To compare the clinical performance of the BACT/ALERT® VIRTUO® (VIRTUO) and BACTEC™ FX400 (FX400) blood culture (BC) systems for pathogen detection in patients with suspected bloodstream infections (BSI).

STUDY DESCRIPTION

- **Study design:** Single-center clinical study with paired blood culture testing from the same patients.
- **Population:** 1,772 paired BC specimens collected from patients (≥ 16 years old) in general wards or intensive care unit (ICU) with suspected bloodstream infection or sepsis.
- **Intervention:** VIRTUO system + BACT/ALERT® FA Plus and FN Plus (FAN® Plus) bottles.
- **Comparator:** FX400 system + resin aerobic and lysing anaerobic bottles.
- **Outcomes:** Positivity rate, time to detection (TTD), cumulative positivity rate over time.

RESULTS

Among bottles originating from specimens collected in general wards (1,916), VIRTUO showed a significantly higher positivity rate of 6.7% (128 cases) compared with FX400, 4.2% (80 cases, $p < 0.001$). Among bottles originating from specimens collected in ICUs ($n = 1,628$), positivity rates were also higher with VIRTUO, reaching 8.5% (138 cases) versus 6.4% (105 cases) for FX400 ($p = 0.028$).

VIRTUO also showed higher positivity rates by bottle type. In anaerobic bottles, VIRTUO detected 5.9% positives compared with 3.2% for FX400 ($p < 0.001$). In aerobic bottles, VIRTUO detected 9.1% positives compared with 7.2% for FX400 ($p = 0.043$) (Table 1).

VIRTUO demonstrated a significantly shorter median TTD (14 h [IQR: 9;21]) compared with FX400 (16 h [12; 27]; $p < 0.001$). At 48 hours, VIRTUO achieved a significantly higher cumulative positivity rate than FX400 (97.4% vs. 88.1%, $p < 0.05$), indicating earlier cumulative detection of positive cultures (Figure 1).

Across organism groups, VIRTUO detected more organisms than FX400. This included Gram-positive bacteria, Gram-negative bacteria and yeasts (Table 2). Among system-discordant detections, several key pathogens were more often detected by VIRTUO only than by FX400 only, including *A. baumannii* (42.9% vs. 14.3%), *E. coli* (45.7% vs. 11.4%), and *S. aureus* (44.4% vs. 11.1%).

CONCLUSIONS

In this clinical comparison, VIRTUO demonstrated higher positivity rates than FX400 across clinical settings and bottle types. VIRTUO also showed a shorter median time to detection and detected more organisms across major microbial groups.

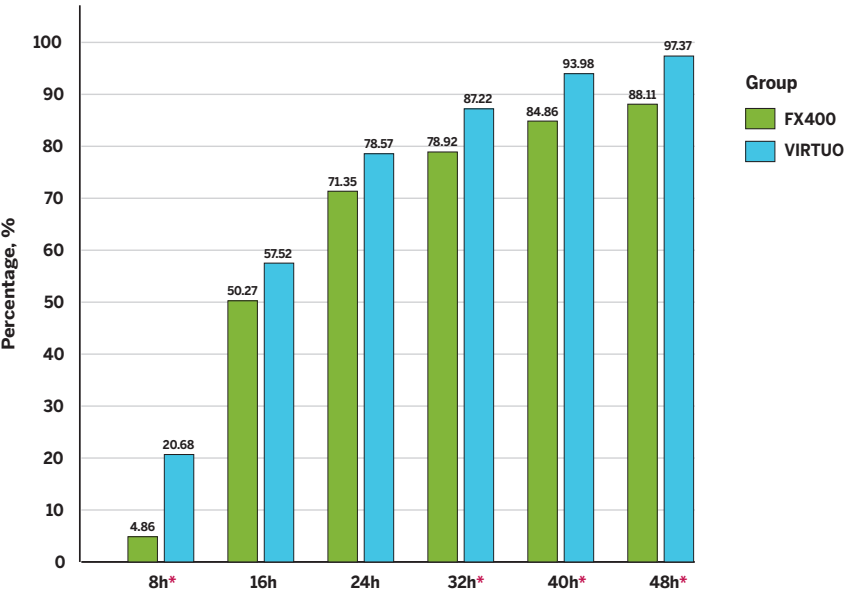
KEY FINDINGS

- VIRTUO showed higher positivity rates than FX400 for aerobic (+1.9 points) and anaerobic (+2.7 points) bottles, across both clinical settings, ICU (+2.1 points) and general wards (+2.5 points).
- VIRTUO consistently showed faster TTD compared with FX400 and achieved a higher cumulative positivity rate by 48h.
- VIRTUO detected a higher number of organisms across all groups, including key BSI pathogens such as *S. aureus*, *A. baumannii*, *E. coli*, as well as anaerobes and yeasts.

Table 1. Positivity rate by BC bottle type

	ANAEROBIC BOTTLES (N = 3,544)			AEROBIC BOTTLES (N = 3,544)		
	FX400 (n = 1,772)	VIRTUO (n = 1,772)	p-value	FX400 (n = 1,772)	VIRTUO (n = 1,772)	p-value
Positive	57 (3.2%)	105 (5.9%)	< 0.001	128 (7.2%)	161 (9.1%)	0.043
Negative	1,715 (96.8%)	1,667 (94.1%)		1,644 (92.8%)	1,611 (90.9%)	

Figure 1. Cumulative TTD distribution for BACT/ALERT VIRTUO and BACTEC FX400



An asterisk (*) denotes significant differences

Table 2. Microorganism recovery by organism group in VIRTUO and FX400

ORGANISM	BOTH, VIRTUO AND FX400 POSITIVE		VIRTUO POSITIVE ONLY		FX400 POSITIVE ONLY	
GP	28	30.4%	51	55.4%	13	14.1%
GN	54	46.6%	43	36.4%	21	17.8%
Yeasts	12	36.4%	15	45.5%	6	18.2%

Effect of delayed entry on performance of the BACT/ALERT FAN PLUS bottles in the BACT/ALERT VIRTUO blood culture system

Adamik M, Hutchins A, Mangilit J, et al.

OBJECTIVE

To determine the impact of delayed loading (“delayed entry”) on the performance of BACT/ALERT® FAN® Plus blood culture bottles (FA Plus, FN Plus, and PF Plus) using BACT/ALERT® VIRTUO® (VIRTUO) system, under simulated clinical conditions representative of sample transport and off-shift laboratory delays.

STUDY DESCRIPTION

- **Study design:** *In vitro* simulated blood culture study.
- **Population:** 1,377 blood culture bottles using human blood spiked with clinically relevant microorganisms (Gram-positive, Gram-negative, anaerobic bacteria and yeast), inoculated at low concentrations (5-84 CFU/bottle) and incubated up to 5 days.
- **Intervention:** Delayed loading after 24 h and 36 h at room temperature (20–25 °C).
- **Comparator:** Immediate bottle loading (“no delay”).
- **Outcomes:** Time to detection (TTD), recovery rate.

RESULTS

When loaded immediately, the overall recovery rate was 100%, with a mean TTD of 13.8 h. Bottles held for 24 h at room temperature also achieved 100% recovery, while bottles delayed for 36 h maintained 99.6% recovery.

The observed TTD decreased after delayed loading, as microbial growth had already started during room-temperature storage prior to instrument loading. However, the total time to detection increased once the pre-incubation delay was included, reaching 32.5 h for the 24 h delay and 42.5 h for the 36 h delay.

Table 1. Summary of the TTD and overall recovery depending on pre-loading delay

PRE-LOADING DELAY	MEAN TOTAL TTD (H)	OVERALL RECOVERY	P-VALUE
0	13.8	100% (460/460)	0.22
24	32.5 (8.5 + 24)	100% (458/458)	
36	42.5 (6.5 + 36)	99.6% (457/459) ^a	

^aTwo bottles inoculated with *Acinetobacter baumannii* were negative, including one confirmed false negative after control testing.

FN Plus and PF Plus bottles demonstrated recovery rates of 100%, whereas FA Plus bottles showed 97.5% recovery, mainly due to reduced recovery of *Acinetobacter baumannii* after 36 h of delayed entry.

CONCLUSIONS

The data demonstrated a recovery rate of 100% with or without delayed loading, except for one sample with *Acinetobacter baumannii* after 36 h of delay. Although the overall recovery rate remained largely unchanged, the total TTD increased with delayed loading.

KEY FINDINGS

- FAN Plus bottles used with VIRTUO maintained 100% recovery rates after delays up to 24 h at room temperature.
- Delays beyond 24 h may negatively impact recovery of some organisms, particularly *Acinetobacter baumannii*, highlighting the importance of timely bottle loading.

Comparative study of antibiotic adsorption capacity of three brands of blood culture bottles

Yuan S, Yang J, Deng N, et al.

OBJECTIVE

To compare three automated blood culture (BC) systems, BACT/ALERT® 3D (BTA3D), BD BACTEC™ (BACTEC), and VersaTREK®, under antibiotic exposure.

STUDY DESCRIPTION

Phase 1: Simulated antibiotic-exposure model.

- **Study design:** Comparative *in vitro* study using simulated blood culture conditions.
- **Population:** 210 simulated BCs using horse blood spiked with 4 bacterial species and exposed to 4 commonly used antimicrobial agents, evaluated under clinically relevant antibiotic concentrations and incubated for up to 5 days.
- **Intervention:** BTA3D system + BACT/ALERT® FA Plus and FN Plus (FAN® Plus) bottles.
- **Comparator:**
 - BACTEC system + BD BACTEC™ Plus Aerobic/F and Lytic/10 Anaerobic/F bottles.
 - VersaTREK system + Aerobic, Anaerobic bottles.
- **Outcomes:** Recovery rate, time to detection (TTD), antibiotic neutralization.

Phase 2: Retrospective clinical evaluation in an intensive care unit (ICU).

- **Study design:** Retrospective observational comparison of BC results from ICU patients.
- **Population:** ICU patients with blood cultures performed.
- **Intervention:** BTA3D system data.
- **Comparator:** Historical VersaTREK data.
- **Outcomes:** Positivity rate, type and number of detected strains, TTD by Gram-stain category.
- **Time:** June 2022 and June 2023.

RESULTS

Under simulated antibiotic exposure, the BTA3D system with FAN Plus bottles demonstrated the highest overall microorganism recovery among the evaluated BC systems. Overall recovery rates were 64.3% (45/70) for BTA3D, compared with 35.7% (25/70) for BACTEC and 18.6% (13/70) for VersaTREK.

In aerobic conditions, FA Plus and BACTEC Aerobic/F Plus bottles showed comparable recovery rates (71.4%), both significantly higher than VersaTREK aerobic bottles (34.3%, *p* = 0.047). Under anaerobic conditions, FN Plus bottles demonstrated markedly higher recovery compared with VersaTREK anaerobic bottles (57.1% (20/35) vs. 2.9% (1/35), *p* = 0.018), whereas no positive bottles were detected in BACTEC anaerobic media.

BACT/ALERT bottles demonstrated better adsorption and neutralization capabilities for most antibiotics tested, particularly cefoperazone/sulbactam, penicillin, and vancomycin. Imipenem demonstrated poor recovery across all systems, although BACT/ALERT remained the only system able to recover microorganisms in its presence.

Regarding time to detection, FA Plus bottles showed shorter mean TTD (24.4 h) compared with BACTEC Aerobic/F Plus (29.5 h) and VersaTREK aerobic bottles (58.5 h). Comparison of anaerobic TTD was limited due to low recovery rates in comparator systems.

In the retrospective ICU analysis, positivity rates increased from 9.1% with VersaTREK to 11.9% with BACT/ALERT system. TTD for Gram-positive bacteria was shorter with BACT/ALERT compared with VersaTREK media (22.2 h vs. 35.9 h) while TTD for Gram-negative bacteria was similar between the two systems.

CONCLUSIONS

In this study, the BACT/ALERT system showed greater recovery of microorganisms in the presence of antibiotics, with higher detection rates and generally shorter times to detection compared with the other blood culture systems evaluated.

KEY FINDINGS

- BTA3D showed the highest overall recovery in simulated blood cultures containing antibiotics: 64.3% vs. 35.7% for BACTEC and 18.6% for VersaTREK.
- The strongest differentiation was observed under anaerobic conditions, with FN Plus recovering 57.1% of tested conditions vs. 2.9% with VersaTREK and 0% with BACTEC anaerobic bottle.
- Retrospective ICU data supported the *in vitro* findings, with BACT/ALERT showing higher positivity rates and shorter TTDs for Gram-positive pathogens than VersaTREK.

Efficient Inactivation of Clinically Relevant Antimicrobial Drug Concentrations by BacT/Alert or Bactec Resin-Containing Media in Simulated Adult Blood Cultures

Menchinelli G, Liotti FM, Giordano L, et al.

OBJECTIVE

To compare the antimicrobial neutralization capability of BACT/ALERT® FA Plus and FN Plus (FAN® Plus) bottles and BACTEC™ Plus Aerobic/F and Plus Anaerobic/F (BACTEC Plus bottles) across 40 antibiotic-bacterium combinations in simulated adult blood cultures (BC).

STUDY DESCRIPTION

- **Study design:** Comparative *in vitro* study using simulated BC spiked with bacterial strains and incubated for up to 120 hours.
- **Population:** 13 commonly used antimicrobial agents for bloodstream infection treatment paired with frequently isolated Gram-negative (n = 4) and Gram-positive (n = 4) bacterial species, resulting in 40 antibiotic-bacterium combinations. Three concentrations were tested: C_{max}, C_{max}/2, and C_{max}/4.
- **Intervention:** BACT/ALERT® VIRTUO® system + FAN Plus bottles.
- **Comparator:** BACTEC™ FX system + BACTEC™ Plus bottles (Plus Aerobic/F and Plus Anaerobic/F).
- **Outcomes:** Time to detection (TTD) and recovery rate.

RESULTS

Overall recovery rates were significantly higher for FAN Plus compared with BACTEC Plus bottles (93.2% (816/876) vs. 88.4% (774/876), *p* < 0.001). After stratification, recovery rates remained higher for BACT/ALERT media in both aerobic (94.2% (418/444) vs. 90.9% (404/444), *p* < 0.001) and anaerobic conditions (92.1% (398/432) vs. 85.6% (370/432), *p* < 0.001) compared with BACTEC Plus bottles. Differences were statistically significant in favor of BACT/ALERT bottles, for *B. fragilis* and *K. pneumoniae* in anaerobic bottles (*p* < 0.05), while no significant differences were observed for other species.

Overall TTD was significantly shorter with FAN Plus compared with BACTEC Plus bottles for both Gram-negative bacteria, in aerobic and anaerobic bottles, respectively, (11.1/11.8 h vs. 13.3/14.8 h) and Gram-positive bacteria (11.9/12.1 h vs. 14.3/15.4 h) (all *p* < 0.0001).

At the lowest clinically relevant antibiotic concentration (C_{max}/4), both systems efficiently recovered most organisms. However, *E. coli* exposed to meropenem was not recovered by either system. FN Plus showed improved recovery for challenging combinations, including *K. pneumoniae* with meropenem and *B. fragilis* with metronidazole.

Clinically relevant TTD delays were mainly associated with vancomycin-containing bottles, particularly in BACTEC Plus bottles and across several MRSA-antibiotic combinations.

CONCLUSIONS

In this study, the overall recovery rate was significantly higher for FAN Plus, with similar advantages observed in both aerobic and anaerobic conditions. TTD was significantly shorter for both Gram-positive and negative organisms. These findings also suggest that blood culture performance depends not only on resin technology, but also on the specific bacterium-antibiotic combination tested.

KEY FINDINGS

- FAN Plus bottles achieved significantly higher organism recovery compared with BACTEC Plus bottles, with a 4.8 point absolute increase, (*p* < 0.001).
- BACT/ALERT demonstrated significantly shorter overall TTD for both Gram-positive and Gram-negative organisms.
- At low clinically relevant antibiotic concentrations (C_{max}/4), both systems maintained efficient organism recovery, supporting effective antimicrobial neutralization.
- Vancomycin-containing bottles were associated with the most clinically relevant TTD delays, particularly in BACTEC Plus bottles.

Comparison and evaluation of neutralization of clinically frequently used antimicrobial agents using three different culture media in simulated blood cultures

Hang Y, Xiong J, Hu L, et al.

OBJECTIVE

To compare the antimicrobial neutralization performance of three commercial blood culture (BC) media under simulated blood culture conditions.

STUDY DESCRIPTION

- **Study design:** Comparative *in vitro* study using simulated BC.
- **Population:** Simulated blood cultures using horse blood spiked with 6 clinically relevant microorganism species paired with clinically relevant antimicrobial agents (n = 9), resulting in 9 microorganism-antimicrobial combinations, inoculated at low concentrations (30–100 CFU/bottle) and incubated up to 5 days.
- **Intervention:** BACT/ALERT® 3D (BTA3D) system + BACT/ALERT® FA Plus and FN Plus (FAN® Plus) bottles.
- **Comparators:**
 - DL-Bt BC system + DL bottles.
 - VersaTREK® system + REDOX™ 1 (aerobic) and REDOX™ 2 (anaerobic) bottles.
- **Outcomes:** Recovery rates and time to detection (TTD), including comparison with antimicrobial-free controls (ΔTTD).

RESULTS

Only FAN Plus bottles achieved 100% recovery for most tested antimicrobials, except for carbapenems.

In aerobic conditions, recovery rates were significantly higher for FA Plus compared with DL and REDOX 1 media: 87.5% vs. 42.9% vs. 12.5%, respectively (*p* < 0.001). Similar results were observed under anaerobic conditions with FN Plus compared with other media (91.4% vs. 2.9% vs. 14.3%, *p* < 0.001).

No significant difference in TTD was observed between FA Plus and DL aerobic media. However, FA and FN Plus showed shorter TTD for gentamicin compared with REDOX media (–1.2 h and –1.4 h, respectively; *p* = 0.008). For levofloxacin, FN Plus reduced TTD by 2.8 h compared with DL anaerobic media (*p* = 0.008), whereas FA Plus showed a longer TTD (+3.0 h) compared with DL aerobic media (*p* < 0.008).

Regarding the difference in TTD between antimicrobial-containing samples and controls (ΔTTD), cefoxitin-*S. aureus* showed the highest ΔTTD in FAN Plus media (19.9 h aerobic, 9.1 h anaerobic). In DL media, levofloxacin-*S. aureus* also demonstrated notable ΔTTD (7.8 h aerobic, 10.8 h anaerobic). Negative ΔTTD values were observed for some combinations, notably fluconazole-*C. albicans* (–2.4 h) in FA Plus and meropenem-*B. fragilis* (–7.4 h) in FN Plus.

CONCLUSIONS

This study highlighted that the recovery rate was significantly higher with BTA3D compared with the other systems under antimicrobial exposure. Additionally, although no significant overall difference in TTD was observed, TTD was slightly shorter with BTA3D compared with REDOX and DL media for specific antimicrobial-organism combinations.

KEY FINDINGS

- FAN Plus media demonstrated significantly higher recovery rates than DL and REDOX media in both aerobic (87.5%) and anaerobic (91.4%) conditions under antimicrobial exposure (*p* < 0.001).
- FAN Plus maintained shorter TTD for most tested antimicrobial-organism combinations under antimicrobial exposure, particularly in anaerobic conditions.
- All blood culture bottles showed reduced recovery in the presence of carbapenems, highlighting persistent challenges in antimicrobial neutralization.

Antimicrobial binding and growth kinetics in BacT/ALERT® FA Plus and BACTEC® Aerobic/F Plus blood culture media

Lovern D, Katzin B, Johnson K, et al.

OBJECTIVE

To compare the antimicrobial neutralization capacity of BACT/ALERT® FA Plus (FA Plus) and BACTEC™ Aerobic/F Plus (BACTEC Plus) blood culture (BC) bottles.

STUDY DESCRIPTION

- **Study design:** Comparative *in vitro* study combining kinetic binding analysis (assessed by reverse-phase HPLC) and simulated BC recovery experiments.
- **Population:** Simulated BC using human blood spiked with 4 bacterial species, exposed to high serum concentrations of antimicrobial agents (n = 10), with five replicates for each drug–organism combination and low inoculum levels (~7–30 CFU/bottle).
- **Intervention:** BACT/ALERT® 3D system + FA Plus bottles.
- **Comparator:** BACTEC™ system + BACTEC Plus bottles.
- **Outcomes:** Binding kinetic, recovery rate, time to detection (TTD).
- **Time:** Binding kinetics assessed up to 90 min; recovery experiments incubated up to 5 days.

RESULTS

Pronounced differences were observed in binding kinetics and residual free antimicrobial concentrations between bottle types. **The rate and overall reduction of free antimicrobial consistently favored FA Plus bottles for all antibiotics tested.** For levofloxacin, linezolid, oxacillin, and vancomycin, free antimicrobial concentrations decreased to at or below the minimum inhibitory concentration (MIC) range of the challenge organisms within 10 min in FA Plus bottles; for daptomycin, ampicillin, and piperacillin, sub-MIC concentrations were achieved within 30 min. Although FA Plus also showed better binding kinetics for cefepime and ceftriaxone, neither bottle type reduced drug concentrations below the MIC of the test organisms.

Faster and more effective antimicrobial adsorption translated into enhanced drug neutralization and improved recovery of susceptible test strains. **Overall recovery was significantly higher with FA Plus than with BACTEC Plus bottles (80.0% vs. 46.6%; *p* < 0.001).**

BACT/ALERT FA Plus bottles achieved greater recovery for multiple organism–antibiotic combinations, including:

- *E. faecalis* with ampicillin (5/5 vs. 0/5),
- *E. coli* with ceftaroline (5/5 vs. 2/5), levofloxacin (5/5 vs. 0/5), and piperacillin (5/5 vs. 3/5),
- *S. aureus* with daptomycin (5/5 vs. 1/5),
- *P. aeruginosa* with piperacillin (5/5 vs. 2/5).

Neither FA Plus nor BACTEC Plus bottles recovered *E. coli* or *P. aeruginosa* in the presence of cefepime, or *E. coli* in the presence of ceftriaxone, with 0/5 recoveries in all corresponding conditions.

Five statistically significant differences in TTD were identified. BACTEC Plus showed faster TTD for *S. aureus* with levofloxacin and linezolid, –0.4 h and –0.7 h, respectively. FA Plus showed shorter TTD for *S. aureus* with oxacillin and vancomycin, –4.6 h and –13.7 h, respectively, and for *E. faecalis* with vancomycin, –3.6 h.

CONCLUSIONS

FA Plus bottles demonstrated faster and more effective antimicrobial adsorption and neutralization kinetics than BACTEC Plus bottles, translating into higher microbial recovery and shorter TTD for selected organism–antibiotic combinations.

KEY FINDINGS

- Improved antibiotic adsorption kinetics enabled FA Plus to reduce free drug concentrations to sub-MIC levels within 10–30 minutes for several antibiotics, resulting in more effective antimicrobial neutralization.
- FA Plus bottles achieved a significantly higher overall recovery rate than BACTEC Plus bottles, 80.0% vs. 46.6%, (*p* < 0.001).
- Although TTD differences varied across antibiotic–organism combinations, the largest clinically meaningful reductions favored FA Plus, with detection time shortened by up to 13.7 h for *S. aureus* in the presence of vancomycin.

REAL-WORLD VALUE OF INTEGRATED DIAGNOSTICS

Impact of 24/7 loading of blood culture bottles in a new automated incubator on the diagnosis of bloodstream infections

Péan de Ponfilly G, Benmansour H, Manda V, et al.

OBJECTIVE

To assess the impact of implementing BACT/ALERT® VIRTUO® (VIRTUO), a fully automated blood culture (BC) system, compared with BACT/ALERT® 3D (BTA3D), a semi-automated BC system, on time to results and benefits on bloodstream infection (BSI) diagnosis.

STUDY DESCRIPTION

- **Study design:** Prospective pre-post implementation study conducted at Lariboisière University Hospital (Paris, France).
- **Population:** BC collected from intensive care unit and emergency department patients, incubated for up to 5 days.
- **Intervention:** Two VIRTUO systems enabling 24/7 loading, one located in the central laboratory and one in the emergency laboratory open during nighttime + BACT/ALERT® FA Plus and FN Plus (FAN® Plus) bottles.
- **Comparator:** BTA3D system with BC bottle loading during central laboratory opening hours, 07:30–18:30, 7/7 + FAN Plus bottles.
- **Outcomes:** Time between collecting blood and loading bottles into the incubator, time to positivity (TTP), time to Gram staining (TTG), positivity rates, number of diagnosed BSI episodes, and BSI incidence density.
- **Time:**
 - **Comparator:** January 1, 2015 to December 31, 2016.
 - **Intervention:** January 1, 2017 to December 31, 2018.

RESULTS

Overall BC activity remained stable across the two periods, while implementation of 24/7 VIRTUO incubation improved diagnostic yield and workflow efficiency, as summarized in Table 1.

Table 1. Impact of 24/7 blood culture incubation on diagnostic performance and workflow

DOMAIN	OUTCOME
BC activity	Stable (~30,000 sets per period)
Diagnostic yield	Positivity rate increased (+1.7 percentage points)
BSI diagnosis	Episodes increased (+189 cases)
BSI incidence	Increased (+0.4 episodes per 1,000 hospital-days)
Time to loading	Reduced, overall –5.3 h; daytime –1.3 h; nighttime –10.0 h

Adapted from Péan de Ponfilly G, et al., Eur J Clin Microbiol Infect Dis. 2021;40(12):2639-2643.

At the microorganism level, TTG was reduced for most major pathogens, with reductions ranging from –4.4 h to –8.1 h, except for yeasts. In contrast, TTP remained largely unchanged for most organisms and was longer for some species, likely reflecting reduced pre-incubation microbial growth before bottle loading after 24/7 implementation.

CONCLUSIONS

Implementation of a 24/7 blood culture incubation workflow with VIRTUO significantly improved BSI diagnostics by reducing time to loading, increasing blood culture positivity rates, and identifying more BSI episodes. Reduced time to loading was associated with shorter time to Gram staining for most major pathogens, supporting more timely management of patients with suspected bloodstream infections.

KEY FINDINGS

- 24/7 VIRTUO implementation improved BSI diagnostic yield, with blood culture positivity rates increasing by 1.7 percentage points and 189 additional BSI episodes identified compared with BTA3D.
- VIRTUO reduced time to loading, with the largest workflow gain observed at night, and was associated with shorter time to Gram staining for most major pathogens.

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, et al.

OBJECTIVE

To compare the performance of BACT/ALERT® VIRTUO® (VIRTUO) and BACTEC™ FX (FX) blood culture (BC) systems and evaluate their impact on clinical workflow in a real-world setting.

STUDY DESCRIPTION

- **Study design:** Prospective crossover clinical trial including blood cultures from two patient strata: the emergency department (approximately 70% of blood cultures) and all other hospital wards (approximately 30%).
- **Population:** 9,957 blood extractions from patients over 16 years old suspected of bacteremia or fungemia.
 - **Intervention:** 4,797 blood samples, corresponding to 9,538 bottles.
 - **Comparator:** 5,160 blood samples corresponding to 10,204 bottles.
- **Intervention:** VIRTUO system + BACT/ALERT® FAN® Plus bottles.
- **Comparator:** FX system + BACTEC™ Plus bottles.
- **Outcomes:**
 - **Primary:** Time to detection (TTD).
 - **Secondary:** Turnaround time (TAT), positivity rate, time to identification and antimicrobial susceptibility testing (AST) from bottle loading, workflow efficiency.
- **Time:** 6-month study with crossover every 2 weeks between VIRTUO and FX.

RESULTS

VIRTUO yielded a significantly higher overall positivity rate than FX (18.2% vs. 15.5%; $p = 0.0003$), while false-positive counts remained low and similar between systems (20 vs. 17).

Median TTD was significantly shorter with VIRTUO by 1.5 h overall ($p < 0.0001$), with the greatest reductions observed in aerobic bottles, reaching 3.7 h for significant organisms and 4.1 h for contaminants.

Median time to identification and time to AST were comparable between systems when all bottle types were analyzed together. Overall median TAT was reduced by 2.1 h with VIRTUO compared with FX ($p = 0.004$). In aerobic bottles, VIRTUO significantly reduced TAT by approximately 9 h, time to identification by 6.7 h, and time to AST by 6.6 h compared with FX (all $p < 0.05$).

Among patients receiving antimicrobial treatment at the time of BC sampling, median TTD was significantly shorter with VIRTUO by 4.5 h overall ($p < 0.001$) and 8.7 h for aerobic bottles ($p < 0.0001$). For first-line antimicrobial therapies (carbapenems, piperacillin-tazobactam, and amoxicillin-clavulanate), VIRTUO shortened median TTD by 11.2 h overall and by 15.6 h in aerobic bottles.

Compared with FX, VIRTUO workflow required 7 fewer manual steps and reduced hands-on time by approximately 15 minutes per day, based on an average processing of 110 bottles per day with a 17% positivity rate.

CONCLUSIONS

Compared with FX, VIRTUO significantly reduced TTD, particularly for aerobic bottles and blood cultures collected from patients receiving antimicrobial therapy. In addition to shortening TAT, VIRTUO improved laboratory workflow efficiency through reduced hands-on time and fewer manual steps, supporting faster bloodstream infection diagnosis and reporting.

KEY FINDINGS

- VIRTUO significantly reduced median TTD versus FX, with the largest improvements observed in aerobic bottles, –3.7 h, and in patients receiving antimicrobial therapy, up to –8.7 h for aerobic bottles.
- Among patients receiving first-line antimicrobial therapies, VIRTUO reduced median TTD by 11.2 h overall and by 15.6 h in aerobic bottles, supporting a substantial advantage in antibiotic-exposed patients.
- VIRTUO improved laboratory efficiency by reducing TAT, decreasing hands-on time by approximately 15 min/day, and reducing manual steps from 11 to 4 compared with FX.

Lab efficiency and improvements in the management of bloodstream infections: a before and after study

Paluch M, Ettahar N, Lagraulet B, et al.

OBJECTIVE

To assess the impact of laboratory conversion, combining lab automation and 24/7 workflow, on laboratory efficiency, timeliness of diagnostic results, and patient outcomes in bloodstream infections (BSI).

STUDY DESCRIPTION

- **Study design:** Monocentric retrospective pre–post observational study conducted at the Centre Hospitalier de Valenciennes (Valenciennes, France).
- **Population:** Adult intensive care unit (ICU) patients with 116 pre-conversion and 128 post-conversion BSI episodes confirmed by positive blood cultures.
- **Intervention:** BACT/ALERT® VIRTUO® (VIRTUO, automated system), WASPLAB® system (automatic inoculation) and 24/7 laboratory organisation.
- **Comparator:** BACTEC™ FX system (semi-automated) with limited operating hours.
- **Outcomes:**
 - **Laboratory efficiency:** Workload, lean indicators, analytical distance.
 - **Timeliness of diagnostic results:** Time to positivity (TTP), time to Gram staining, time to identification (ID), turnaround time (TAT), antimicrobial susceptibility testing (AST) results within 24 h.
 - **Clinical outcomes:** Time to first antibiotic modification, mortality, hospital and ICU discharge.
 - **Antimicrobial consumption:** Defined daily doses per 1,000 hospital-days (DDD/1,000 HD), antibiotic use by category (based on the French Infectious Diseases Society (SPILF) criteria).
- **Time:** January to December 2019 and June 2021 to May 2022.

RESULTS

Laboratory efficiency:

- **Laboratory activity increased by ~30%**, with a higher proportion of samples processed by automated systems (from 45% to 86%).
- Workflow efficiency improved substantially, reflected by an **18-fold reduction in analytical distance and increased high value-added technical activities (40% vs. 21%)**.
- Higher lean scores indicated improved laboratory efficiency, increasing by 14 points on Day 0 and 20 points on Day 1.

Timeliness of diagnostic results:

- For clinically significant episodes, **no significant differences** were observed for time to positivity or Gram staining.
- **TAT was significantly reduced (–3.3 h; $p = 0.004$), particularly for night-shift samples**, with AST results available within 24 h increasing from 0.9% to 18.7% ($p < 0.0001$).

Clinical outcomes:

- **Time to first antibiotic modification was significantly reduced by 19.1 h overall ($p = 0.04$)**, and by 23.6 h among clinically significant episodes ($p = 0.05$).
- No significant difference in hospital length of stay was observed, **while the probability of ICU discharge increased by 51%** (sHR = 1.51; $p = 0.014$).
- A trend towards reduced mortality was observed (adjusted hazard ratio (HR) = 0.65; $p = 0.08$).

Antimicrobial consumption:

- Overall antimicrobial consumption slightly decreased (**1,667 vs. 1,542 DDD/1000 hospital-days**), with reduced use of category 1 (preferred-use) and category 3 (restricted) antibiotics, and increased use of category 2 (limited indications).

CONCLUSIONS

Compared with the pre-conversion workflow, the implementation of a fully automated 24/7 laboratory organization improved laboratory efficiency and supported patient management.

KEY FINDINGS

- **Laboratory automation and reorganization achieved lean management goals by shifting microbiologists' activities toward higher-value tasks, including clinical collaboration and antimicrobial stewardship.**
- **Time to first adaptation was substantially reduced (–19.1 h, $p = 0.04$), likely driven by the increased proportion of AST results available within 24 hours for samples flagged during night shifts (+17.8 percentage points, $p < 0.0001$). These gains occurred in parallel with a 30% increase in overall laboratory activity, underscoring the efficiency of the laboratory transformation.**
- **The optimized workflow was associated with improved patient management, including a higher probability of ICU discharge and a trend toward reduced 30-day mortality.**

Optimizing blood culture diagnostics through laboratory automation: reducing turnaround time and improving clinical outcomes

Qin J, Zhang H, Zhang X, et al.

OBJECTIVE

To evaluate the impact of integrating laboratory automation into the blood culture (BC) diagnostic workflow.

STUDY DESCRIPTION

- **Study design:** Single-center pre-post implementation study with retrospective historical and prospective intervention cohorts, conducted at Renji Hospital (Shanghai, China), including three surgical departments.
- **Population:** Adult hospitalized patients (≥ 18 years) with bloodstream infection episodes, including 192 episodes from 110 patients in the pre-optimization cohort and 156 episodes from 112 patients in the post-optimization cohort.
- **Intervention:** Optimized automated BC diagnostic workflow including implementation of BACT/ALERT® VIRTUO® (VIRTUO) system, VPlus 50 automated sample processor, and VITEK® 2 XL Microbiology Analyzer.
- **Comparator:** Historical conventional workflow using BD BACTEC™ FX400 system with manual processing and staged reporting.
- **Outcomes:**
 - **Primary:** Time from BC collection to final report (turnaround time (TAT)).
 - **Secondary:** 28-day mortality, length of stay (LOS), time to optimal therapy (TTOT), and costs related to antibiotics, laboratory tests and hospitalization.
- **Time:**
 - **Comparator:** March 2023 to August 2023 (retrospective).
 - **Intervention:** March 2024 to August 2024 (prospective).

RESULTS

The **BC positivity rate increased** in the post-optimization group (**12.5% vs. 17.2%**), likely related to the use of BACT/ALERT® FN Plus bottles with improved antibiotic adsorption and stable incubation conditions provided by the VIRTUO system.

Optimization resulted in a **significant reduction in TAT, from 96 h to 60.8 h ($p < 0.01$)**. This reduction was **more pronounced for Gram-negative bacteria** compared with Gram-positive bacteria (44.9 h vs. 27.2 h reduction).

Fungal TATs also decreased (113.9 h vs. 108.3 h), although the difference was not statistically significant ($p = 0.94$). In contrast, TATs increased for Gram-positive bacilli (80.3 h vs. 93 h) and anaerobic bacteria (136 h vs. 161.5 h). Additionally, the automated review function reduced reporting time for negative blood cultures by approximately 8 h (135 h vs. 127 h).

Automation was also associated with improvements in antimicrobial management. Optimal therapy was achieved more frequently in the post-optimization group (92.0% vs. 81.8%; $p = 0.02$), with a **shorter TTOT (42.4 h vs. 60.6 h; $p = 0.02$)**. Although the 28-day mortality rate remained unchanged (15.5% vs. 14.3%; $p = 0.81$), patients in the post-optimization group experienced a **significantly shorter LOS (19 vs. 28 days; $p = 0.04$)**.

Healthcare costs were significantly reduced post-optimization vs. pre-optimization ($p < 0.05$ for all comparisons), including antibiotics (USD 269.16 vs. USD 678.59), laboratory tests (USD 1,637.15 vs. USD 2,417.38), and overall hospitalization (USD 14,847.92 vs. USD 24,334.96).

CONCLUSIONS

This study showed that integration of laboratory automation (including VIRTUO system) into the BC diagnostic workflow was associated with increased positivity rates and significantly reduced TAT, particularly for Gram-negative bacteria. Automation was also associated with improved antimicrobial management, with a higher proportion of patients achieving optimal therapy, shorter TTOT, shorter LOS, and reduced healthcare costs.

KEY FINDINGS

- **Integration of lab automation into the BC workflow was associated with increased blood culture positivity (+4.7 percentage points) and a significant reduction in median TAT (–35.2 h; $p < 0.01$).**
- **The optimized workflow increased the proportion of patients receiving optimal therapy (+10.2 percentage points) and reduced median TTOT (–18.2 h; $p = 0.02$).**
- **Workflow optimization was associated with a shorter median hospital stay (–9 days; $p = 0.04$) and lower healthcare-related costs.**

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

Dai Y, Zhu X, Chang W, et al.

OBJECTIVE

To evaluate the clinical and economic impact of optimizing the entire blood culture (BC) process in critically ill adult patients in intensive care units (ICUs) diagnosed with bloodstream infections (BSI).

STUDY DESCRIPTION

- Study design:** Quasi-experimental pre-post study with retrospective pre-optimisation and prospective post-optimisation cohorts conducted at University Hospital of Hefei (Hefei, China).
- Population:** Adult ICU patients with BSIs confirmed by positive blood cultures, including 122 patients before and 179 patients after implementation of the optimized blood culture workflow.
- Intervention:** Post-optimization phase including conversion to the BACT/ALERT® VIRTUO® system + BACT/ALERT® FAN® Plus bottles, combined with:
 - Optimization of blood culture handling and reporting processes;
 - Educational initiatives and workflow reorganization;
 - Rapid identification using MALDI-TOF/MS (VITEK® MS) after short-term incubation;
 - Improved sample logistics and deployment of a satellite incubator.
- Comparator:** Pre-optimization, baseline BC workflow using BACT/ALERT® 3D system + BACT/ALERT® FAN® bottles with conventional blood culture processing and reporting.
- Outcomes:**
 - Primary:** Time from admission to targeted antibiotic therapy.
 - Secondary:** Time to identification and antimicrobial susceptibility testing (AST), clinical outcomes, antibiotic use, and healthcare costs.
- Time:**
 - Comparator:** March 2019 to February 2020.
 - Intervention:** November 2021 to October 2022.

RESULTS

Positivity rates: The post-optimization group showed a significantly higher positivity rate of pathogens, including *Staphylococcus aureus*, *Streptococcus* spp., and *Klebsiella* spp., improving the accuracy of diagnosis and treatment (21.13% vs. 16.46%; $p = 0.005$).

Time efficiency: The post-optimization group experienced significant reductions in the time required for key processes (Figure 1). The time from patient admission to BC prescription, reflecting the impact of medical education, was reduced by 5.94 days ($p < 0.001$). Optimization of laboratory processes enabled the time from blood bottle loading to the final report to be reduced by 18% (-17 hours, $p < 0.001$), allowing for quicker, more informed clinical decision-making. Collectively, cumulative improvements across the diagnostic workflow suggest a reduction of more than 50% in the overall time from admission to final identification/AST reporting (approximately 12.63 to 5.7 days).

Targeted therapy: In the post-optimization group, the time from admission to targeted antibiotic therapy was significantly reduced by more than 50% following both Gram-stain results and final identification/AST results.

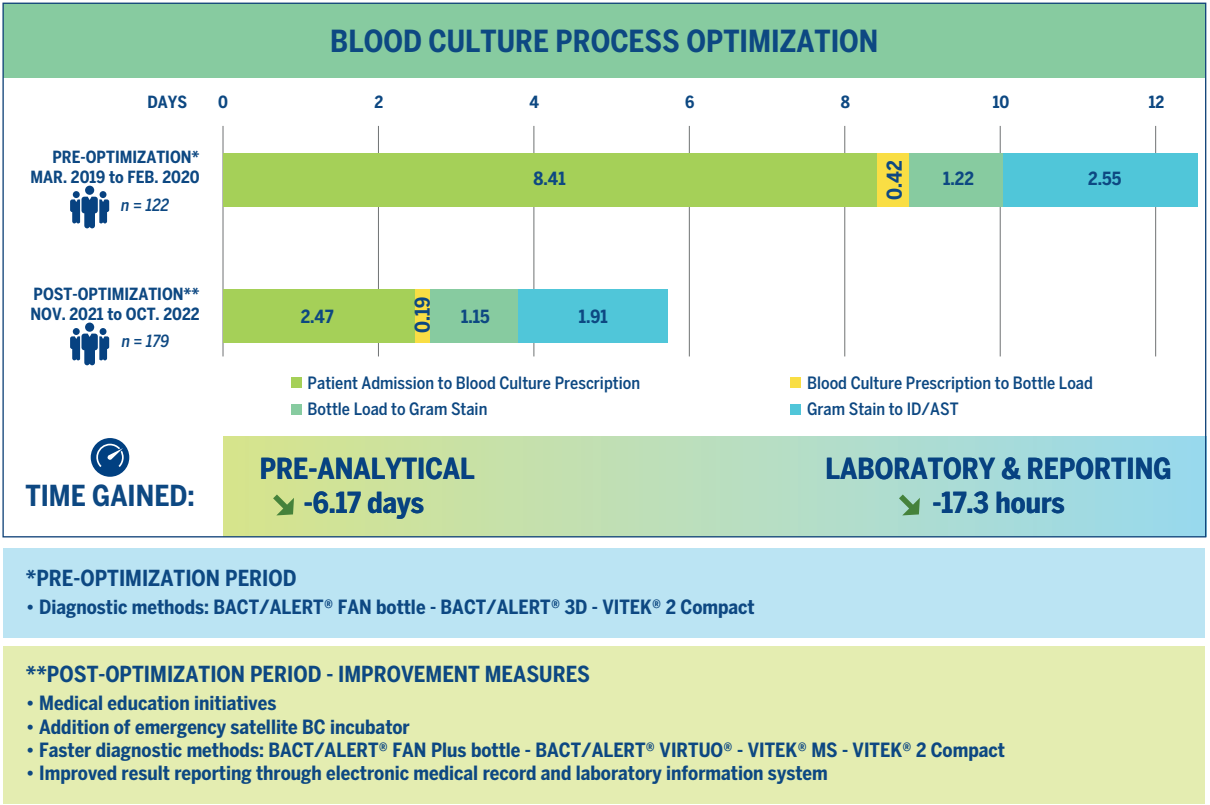
Clinical outcomes: The length of stay was reduced by almost 30% (-6.49 days; 15.84 vs. 22.33 days; $p = 0.001$).

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

Blood culture process optimization improved the management of bloodstream infections in ICU patients by accelerating pathogen identification and antimicrobial susceptibility testing, enabling earlier targeted antibiotic therapy. These improvements were associated with reduced hospital length of stay and healthcare costs, highlighting the clinical and economic value of optimized blood culture workflows.

Figure 1. Schematic representation of blood culture process optimization and different time measurements
Source: bioMérieux adapted from Dai Y, et al. Int J Antimicrob Agents. 2024;63(6):107176



KEY FINDINGS

- Blood culture process optimization substantially accelerated diagnosis, reducing laboratory reporting time by approximately 17 hours and shortening time to targeted antibiotic therapy by more than 50%. These improvements were associated with a 6.49-day reduction in hospital length of stay.
- The optimized workflow improved diagnostic yield, increasing blood culture positivity rates (+4.67 percentage points), supporting earlier and more informed antimicrobial management.
- Faster and more efficient blood culture management was associated with significant economic benefits, reducing total hospitalization costs by 58%, antimicrobial expenditures by 78%, and laboratory testing costs by 44% compared with the pre-optimization period.

NOTES



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