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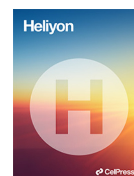
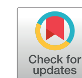


Research article

Performance of the BioFire Blood Culture Identification 2 panel for the diagnosis of bloodstream infections



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HIGHLIGHTS

- Blood cultures have long turnaround times preventing early targeted therapy in sepsis.
- BCID2 is a multiplex PCR for pathogens and resistances on positive blood culture.
- BCID2 showed excellent agreement with conventional methods.
- BCID2 significantly reduced time to results as compared to culture-based methods.
- Rapid diagnostic methods may lead to early treatment and improved outcomes in sepsis.

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Bloodstream infection
Sepsis
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ABSTRACT

Background: Conventional blood cultures methods are associated with long turnaround times, preventing early treatment optimization in bloodstream infections. The BioFire Blood Culture Identification 2 (BCID2) Panel is a new multiplex PCR applied on positive blood cultures, reducing time to pathogen identification and resistant markers detection.

Methods: We conducted a prospective observational study including positive blood cultures from Intensive Care Units and Emergency Departments and performed BCID2 in addition to conventional testing. Concordance between the two methods was assessed and BCID2 performance characteristics were evaluated. Resistance markers detected by BCID2 were confirmed by in-house PCR. Whole genome sequencing was performed in discordant cases.

Results: Among 60 monomicrobial blood cultures, BCID2 correctly identified 55/56 (91.7%) on-panel pathogens, showing an overall concordance of 98%. In 4/60 cases BCID2 did not detect any target and these all grew BCID2 off-panel bacteria. Only one discordant case was found. Sensitivity and specificity for Gram-positive bacteria on monomicrobial samples were 100% (95% CI 85.8–100%) and 100% (95% CI 90.3–100%) respectively, while for Gram-negatives 100% (95% CI 87.7–100) and 96.9% (95% CI 83.8–99.9%), respectively. Among two polymicrobial blood cultures, full concordance was observed in one case only. BCID2 identified antimicrobial resistance genes in 6/62 samples, all confirmed by in-house PCR (3 *mecA/C S. epidermidis*, 3 *bla*$_{CTX-M}$ *E. coli)*. Estimated time to results gained using BCID2 as compared to conventional testing was 9.69 h (95% CI: 7.85–11.53).

Conclusions: BCID2 showed good agreement with conventional methods. Studies to assess its clinical impact are warranted.

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1. Introduction

Bloodstream infections and sepsis are associated with high morbidity and mortality, in particular in the intensive care setting [1] and early antimicrobial treatment has been shown to improve survival [2].

Considerable efforts have been made to shorten the time to results of blood cultures-based methods. The widespread implementation of matrix-assisted laser desorption ionization–time-of-flight (MALDI-TOF) mass spectrometry has offered a significant advance. When applied to early subcultures, MALDI-TOF can shorten the time to pathogen identification to a few hours from BC positivity, although the process still requires subsequent bacterial isolation and confirmation [3].

Based on these considerations, a few other technologies have emerged for the rapid diagnosis of bloodstream pathogens, aimed at further reducing turnaround times and simplifying the laboratory workflow. The BioFire Blood Culture Identification Panel (BCID, bioMérieux France) is an emerging molecular assay for the rapid diagnosis of bloodstream infections from positive blood cultures. It is based on a multiplex PCR able to detect the most common pathogens and resistance genes. The instrument is fully automated, requires minimal sample manipulation and has a turnaround time of about 1 h.

A panel based on the identification of 24 microorganisms and 3 antimicrobial resistance genes (*mecA*, *vanA/B* and *KPC*) was previously shown to have good performance [4, 5, 6, 7] and a positive impact on patients' management has been suggested by some studies [8, 9].

A new version of this assay has been recently released (BioFire Blood Culture Identification 2 Panel, bioMerieux, France) resulting in a broader panel including 33 pathogens (26 bacterial genera/species and 7 fungal species) and 10 resistance markers; few studies have evaluated the performance of BCID2 on clinical samples so far [10, 11, 12, 13, 14].

In this study we assess the performance of the BCID2 panel compared to conventional culture methods for the diagnosis of bloodstream infections from positive blood culture specimens in patients admitted to the Intensive Care Unit and Emergency Departments.

2. Methods

2.1. Study design and study setting

This was a prospective observational study performed at the Pathology Queensland Central Laboratory and the University of Queensland Centre for Clinical Research (UQCCR), located at the Royal Brisbane and Women's Hospital, Brisbane, Australia. The laboratory provides diagnostic microbiology services for 12 hospitals in South-East Queensland, including large tertiary referral hospitals as well as smaller regional facilities.

Blood cultures collected from Intensive Care Units or Emergency Departments, which flagged positive by the BacT/Alert Virtuo (bioMérieux, France) from June 1st, 2021, to July 1st, 2021, were included in the study. The BCID2 was run daily during business hours, therefore only BC flagging positives in the previous 8 h were included in the evaluation, as per manufacturer instruction samples should be assessed within 8 h from positivity.

2.2. Traditional blood culture methods

Blood culture bottles (bioMerieux A FA Plus, FN Plus and PF Plus media) were incubated and identified as positive by the BacT/Alert Virtuo. After blood cultures flagged positive, a Gram stain and wet-preparation were performed, and blood culture media was sub-cultured into appropriate agar plates. Plates were then incubated for a maximum of 48 h. Moreover, one drop from positive blood cultures was also applied to a chocolate agar plate and incubated for at least 4 h (CHOC spot).

Microorganisms growing on the plates, including those from early sub-cultures (CHOC spot), underwent pathogen identification using the MALDI-TOF MS system (VITEK MS, bioMérieux, France).

Susceptibility testing was performed by automated microdilution with VITEK 2 (bioMérieux, France), using the appropriate testing cards, including the VITEK 2 AST-N246 card for Gram-negatives, the AST-P656 card for *Staphylococcus aureus* and the AST-P643 for enterococci. Disk diffusion susceptibility and E-test were used where required. Susceptibility to *Candida* spp. was assessed with VITEK 2 AST-Y08 card and broth microdilution (Yeast sensititre).

2.3. BioFire Blood Culture Identification 2 (BCID2) panel testing

BioFire Blood Culture Identification 2 (BCID2) Panel (bioMérieux, France) testing was conducted as per manufacturer's TGA-approved instructions on one positive BC bottle per patient. Specifically, 200 μL of the positive blood culture sample was mixed with the supplied sample dilution buffer. An aliquot of the sample solution obtained was then inoculated in the panel pouch, which had been previously hydrated with the supplied hydration solution. The BioFire BCID2 pouch was then loaded on to the BioFire FilmArray TORCH System for nucleic acid extraction, amplification, and analysis.

BioFire BCID2 Panel was run within 8 h from BC flagging positive according to manufacturer's instructions.

In the case of a failed run, the test was repeated. Targets included in the BCID2 panel are listed in Table 1.

2.4. BCID2 performance assessment

Concordance between BCID2 and MALDI-TOF for pathogen identification was assessed, for monomicrobial and polymicrobial blood cultures. Moreover, antimicrobial resistance markers detected by the BCID2 were confirmed by in-house real-time TaqMan PCR (UQCCR) and compared to antimicrobial susceptibility results according to VITEK 2 and other conventional methods utilized. In case of discordant results for pathogen identification or resistance markers detection between BCID2 and conventional testing, whole genome sequencing was performed.

Sensitivity and specificity with 95% confidence intervals were calculated for each BCID2 target for monomicrobial samples, with conventional culture methods as reference gold standard, using Stata, version 16.1 (StataCorp, TX, USA) and MedCalc version 19.1.7 (MedCalc Software Ltd, Ostend, Belgium).

2.5. In-house PCR and whole genome sequencing

For in-house real-time TaqMan PCR (UQCCR), in-house designed 1.0 μM forward and reverse primers and 0.25 μM probe were prepared in a reaction mix with 10.0 μL QuantiTect Probe PCR (QIAGEN), 2.0 μL DNA, total reaction 20 μL. Reactions were run on Rotor-Gene Q real-time PCR thermocycler (QIAGEN) under the following conditions: 95 °C for 15 min, 45 cycles at 95 °C for 15 s, 60 °C for 30 s. PCR results were analysed with the Rotor-Gene 6000 Series software, *mecA/C* was undertaken as described by Ciesielczuk et al [15]. using GoTaq Reaction Mix.

Whole genome sequencing was undertaken on the Illumina MiniSeq platform with Nextera DNA Flex Library Prep Kit, library quality and quantification by TapeStation using High Sensitivity D1000 and Qubit fluorometer High Sensitivity 1x dsDNA. Pooled library was loaded into a 300 cycle High Output Reagent Cartridge.

3. Results

3.1. BCID2 performance for pathogen identification and resistance markers detection

Sixty-two positive blood cultures were included in the study during the study period, of which 60 yielded monomicrobial results according to conventional methods and 2 polymicrobial results. The monomicrobial results consisted of 32 Gram-negative bacteria, 26 Gram-positive and 2 yeasts, with the most common species identified being *Escherichia coli* (n

Table 1. BioFire BCID2 panel; MRSA, methicillin-resistant *Staphylococcus aureus*.

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Gram positives	*Staphylococcus spp* *Staphylococcus aureus* *Staphylococcus epidermidis* *Staphylococcus lugdunensis* *Streptococcus spp.* *Streptococcus agalactiae* *Streptococcus pyogenes* *Streptococcus pneumoniae* *Enterococcus faecalis* *Enterococcus faecium* *Listeria monocytogenes*
Gram negatives	*A. calcoaceticus-baumannii complex* *Bacteroides fragilis* *Haemophilus influenzae* *Neisseria meningitidis* *Pseudomonas aeruginosa* *Stenotrophomonas maltophilia* *Enterobacterales spp.* *Escherichia coli* *Enterobacter cloacae complex* *Klebsiella aerogenes* *Klebsiella oxytoca* *Klebsiella pneumoniae group* *Proteus spp.* *Salmonella* *S. marcescens*
Yeast	*Candida albicans* *Candida auris* *Candida glabrata* *Candida krusei* *Candida parapsilosis* *Candida tropicalis* *Cryptococcus neoformans/gattii*
Antimicrobial resistance markers	*mecA/C* *mecA/C and MREJ (MRSA)* *van A/B* *CTX-M blaKPC* *blaIMP* *blaOXA-48* *blaNDM* *blaVIM* *mcr-1*

= 23), followed by *Staphylococcus aureus* (n = 7). The 2 polymicrobial samples were positive for *E. coli* and *Enterococcus faecalis,* and *E. coli* and *Proteus mirabilis* respectively.

Hands on time required for sample preparation for the BCID2 was only a few minutes; pathogen identification and resistance markers detection were expected in 65 min from instrument load.

Among 60 monomicrobial blood cultures, BCID2 correctly identified 55/60 (91.7%) pathogens at a genus level and 47/60 (78.3%) at a species level. Pathogens correctly identified at a genus level only included species not detected by the BCID2 panel. Discrepancy among culture and BCID2 result was observed in one case only where BCID2 identified enteric bacteria, while *Bacillus cereus* was grown according to traditional culture methods and confirmed by whole genome sequencing. Four isolates from monomicrobial blood cultures were not detected by the BCID2 and they all included BCID2 off-panel pathogens (*Campylobacter jejuni* in two cases, *Bacteroides cellulosilyticus, Actinomyces* spp.). In one case, the BCID2 run failed, however, when repeated, it correctly performed pathogen identification (*E. coli*). Overall, concordance between culture methods and BCID2 for on-panel pathogens in monomicrobial blood cultures was 98% (55/56). Sensitivity and specificity for Gram-positive bacteria were 100% (95% CI 85.8–100%) and 100% (95% CI 90.3–100%) respectively, while for Gram-negatives 100% (95% CI 87.7–100%) and 96.9% (95% CI 83.8–99.9%), respectively.

Table 2 summarizes the performance characteristics of the BCID2 compared to conventional culture for monomicrobial samples.

Among the two polymicrobial blood cultures, full concordance was observed in one case only, where *E. faecalis* and *E. coli* were correctly identified both by standard methods and BCID2. The second polymicrobial sample was positive for *E. coli* and *P. mirabilis* according to standard methods while BCID2 reported *E. coli* and *E. faecalis* (see Table 3). However, when whole genome sequencing was performed, it confirmed results from the BCID2 (*E. coli* and *Enterococcus* spp.)

BCID2 identified pathogens harbouring antimicrobial resistant genes in 6/62 monomicrobial blood cultures. These included *S. epidermidis* harbouring *mecA/C* (n = 3) and *E. coli* harbouring $bla_{CTX\text{-}M}$ (n = 3). In-house PCR confirmed the presence of all the 6 resistance genes.

Conventional antimicrobial susceptibility testing confirmed oxacillin resistance in the case of *S. epidermidis* harbouring *mecA/C* (cefoxitin screen and oxacillin MIC on VITEK 2 susceptibility panel), and 3rd generation cephalosporin resistance in the case of *E. coli* harbouring $bla_{CTX\text{-}M}$ (confirmed by combination disk testing). A fourth *E. coli* isolate from a monomicrobial blood culture was found to exhibit resistance to 3rd generation cephalosporin according to antimicrobial susceptibility testing while no resistance marker was detected by BCID2. Whole genome sequencing was performed detecting the presence of bla_{CMY} and confirming the absence of $bla_{CTX\text{-}M}$. The presence of bla_{CMY} in the isolate was also confirmed by in-house PCR. Overall, the agreement between BCID2 and in-house PCR for on panel resistance markers was 100% (6/6).

In the remaining microorganisms identified by BCID2, no resistance markers were detected, including *mecA/C* and *MREJ* in *S. aureus*, van A/B in *Enterococcus* spp. and carbapenemases or *mcr-1* in Gram-negatives. Standard antimicrobial susceptibility testing confirmed the absence of oxacillin and vancomycin resistance in all the remaining Gram-positive isolates as well as the absence of carbapenem resistance in all Gram-negatives. Susceptibility to colistin is not routinely tested in isolates susceptible to carbapenems.

Table 4 summarizes results about detection of antimicrobial resistance by conventional cultures, BCID2 and in-house PCR.

3.2. Time to results

Mean time from blood cultures collection to positivity was 18.59 h (range 1.3–64.7).

Mean time from blood cultures flagging positive to pathogen identification with MALDI-TOF MS for blood cultures positive for BCID2 on-panel pathogens was 11.19 (±7.18) hours (median 10.76 h, IQR 7.46–11.83).

We estimated that if BCID2 had been implemented in the workflow of Pathology Queensland Central Laboratory for clinical purposes, and performed real time after blood cultures flagged positive, pathogen identification would have been available 1.5 (±0.2) hours after blood culture positivity, with this estimate being in line with studies assessing the use of BCID2 in the clinical setting [11]. According to this estimate, we estimated that if BCID2 had been implemented in the clinical workflow, its results would have been available 9.69 (95% CI: 7.85 to 11.53) hours sooner as compared to MALDI-TOF pathogen identification, potentially translating to shorter time to optimal antimicrobial treatment.

Mean time from blood cultures flagging positives to antimicrobial susceptibility testing performed by VITEK 2 for BC growing BCID2 on-panel pathogens was 27.23 (±8.46) hours (median 26.84, IQR 22.57–31) and mean time to antimicrobial susceptibility testing for the 6 isolates harbouring antimicrobial resistance genes was 29.05 (±5.26) hours (median 28.3, IQR 26.54–30.17). Assuming again a mean time from BC positivity to BCID2 results of 1.5 (±0.2) hours, we estimate that if BCID2 had been implemented in the clinical workflow, the resistance genes would have been detected 27.8 (95% CI: 23.05 to 32.55) hours earlier as compared to antimicrobial susceptibility testing provided by VITEK 2.

Table 2. Performance characteristics of the BCID2 compared to conventional culture shown for each target for monomicrobial samples.

Microorganism	TP (n) [BC+/BCID2+]	FP (n) [BC-/BCID2+]	FN (n) [BC+/BCID2-]	TN (n) [BC-/BCID2-]	SE (%)	95% CI (%)	SP (%)	95% CI (%)
Staphylococcus spp.	12[a]	0	0	48	100	73.5–100	100	92.6–100
S. aureus	7	0	0	53	100	59–100	100	93.3–100
S. epidermidis	3	0	0	57	100	29.2–100	100	93.7–100
S. lugdunensis	0	0	0	60	NA	-	100	94.1–100
Streptococcus spp.	9[b]	0	0	51	100	66.4–100	100	93–100
S. agalactiae	0	0	0	60	NA	-	100	94.1–100
S. pyogenes	1	0	0	59	100	2.5–100	100	93.9–100
S. pneumoniae	4	0	0	56	100	39.8–100	100	93.6–100
E. faecalis	2	0	0	58	100	15.8–100	100	93.8–100
E. faecium	1	0	0	59	100	2.5–100	100	93.9–100
L. monocytogenes	0	0	0	60	NA	-	100	94.1–100
Gram positives, overall	**24**	**0**	**0**	**36**	**100**	**85.8–100**	**100**	**90.3–100**
A. calcoaceticus-baumannii	0	0	0	60	NA	-	100	94.1–100
Bacteroides fragilis	1	0	0	59	100	2.5–100	100	93.9–100
H. influenzae	0	0	0	60	NA	-	100	94.1–100
N. meningitidis	0	0	0	60	NA	-	100	94.1–100
P. aeruginosa	1	0	0	59	100	2.5–100	100	93.9–100
S. maltophilia	0	0	0	60	NA	-	100	94.1–100
Enteric bacteria	26	1[c]	0	33	100	86.8–100	97.1	84.7–99.9
E. coli	23	0	0	37	100	85.2–100	100	90.5–100
E. cloacae complex	0	0	0	60	NA	-	100	94.1–100
K. aerogenes	0	0	0	60	NA	-	100	94.1–100
K. oxytoca	1	0	0	59	100	2.5–100	100	93.9–100
K. pneumoniae	1	0	0	59	100	2.5–100	100	93.9–100
Proteus spp.	1	0	0	59	100	2.5–100	100	93.9–100
Salmonella spp.	1	0	0	59	100	2.5–100	100	93.9–100
S. marcescens	0	0	0	60	NA	-	100	94.1–100
Gram negatives, overall	**28**	**1**	**0**	**31**	**100**	**87.7–100**	**96.9**	**83.8–99.9**
C. albicans	1	0	0	59	100	2.5–100	100	93.9–100
C. auris	0	0	0	60	NA	-	100	94.1–100
C. glabrata	0	0	0	60	NA	-	100	94.1–100
C. krusei	0	0	0	60	NA	-	100	94.1–100
C. parapsilosis	1	0	0	59	100	2.5–100	100	93.9–100
C. tropicalis	0	0	0	60	NA	-	100	94.1–100
C. neoformans/gattii	0	0	0	60	NA	-	100	94.1–100
Yeasts, overall	**2**	**0**	**0**	**58**	**100**	**15.8–100**	**100**	**93.8–100**

TP = True Positives; FP = False Positives; FN = False Negatives; TN = True Negatives; BC = Blood Culture; BCID2 = Blood Culture Identification 2 Panel; SE = Sensitivity; SP = Specificity; CI = Confidence Interval.

[a] Including 2 off-panel species (*S. hominis* and *S. capitis*).

[b] Including 4 off-panel species (*S. intermedius, S. constellatus, S. group C* and *S. group D*).

[c] This sample grew *B. cereus* according to traditional methods confirmed by whole genome sequencing.

4. Discussion

Agreement between BCID2 and traditional culture methods was high in our study, with an overall concordance for on-panel pathogens on monomicrobial blood cultures of 98%, in line with existing reports [10, 11, 13, 16, 17]. This is a promising concordance rate, although it should be acknowledged that not all BCID2 targets were detected in our samples, therefore their performance could not be evaluated.

Concordance between conventional testing and BCID2 for polymicrobial blood cultures is reported to be lower than that for monomicrobial blood cultures by some of the available performance studies [10, 11]. Specifically, Berinson et al reported a concordance rate for polymicrobial samples of 61.3% [10] while Sparks et al of 28.6%, although in the latter study most disagreement was due to the culture-based identification of BCID2 off-panel pathogens, and possibly affected by a laboratory contamination [11]. Differently, Cortazzo et al obtained a concordance rate of 100% between BCID2 and conventional testing for pathogen identification on 35 archived polymicrobial blood culture samples [16]. In our study concordance between culture methods and BCID2 in polymicrobial samples, was of 3/4 isolates (1 out of 2 samples). However, when whole genome sequencing was performed, it confirmed the results of BCID2, likely suggesting an agreement of BCID2 with the clinical sample content of 100%.

Compared to the previous version of the test, BCID2 has introduced 16 new targets, many of which have been detected in our study, including *E. faecalis, E. faecium, S. epidermidis, Bacteroides fragilis, Salmonella* spp., as well as and $bla_{\text{CTX-M}}$. The importance of broadening the BioFire FilmArray BCID panel had been highlighted by a study by Ny et al where a subset of bacteraemia cases caused by organisms not detected by the previous version of the test were associated to adverse clinical outcomes and mainly caused by anaerobes [18]. Moreover, despite we did not detect any carbapenem resistant Gram-negatives due to their low prevalence in the Australian setting, the new capability of BCID2 of detecting carbapenemases is going to be extremely relevant in settings with high prevalence of antimicrobial resistance, both for treatment adjustment and for prompt implementation of infection prevention and control practices [19].

Table 3. Concordance between BCID2 and traditional methods for polymicrobial blood cultures.

Polymicrobial blood cultures	Results according to conventional methods	Results according to BCID2	Concordant results
1	*Escherichia coli* *Enterococcus faecalis*	*Escherichia coli* *Enterococcus faecalis*	100%
2	*Escherichia coli* *Proteus mirabilis*	*Escherichia coli* *Enterococcus faecalis*[a]	50%
Overall concordance for isolates from polymicrobial blood cultures			**3/4 (75%)**

[a] Whole genome sequencing confirmed *Enterococcus* spp.

With the use of the new version of the test, only 6% (4/62) of pathogens causing bloodstream infections in our study remained unidentified due to isolates not included in the BCID2 panel, while the missed coverage rate with the use of the previous version of the test has been reported as high as 12–30 % [6, 8, 20, 21, 22]. Notably, 2 out of 4 of the unidentified pathogens by BCID2 in our study were identified by conventional culture methods as *C. jejuni*, and in these cases a rapid diagnosis of the ongoing infection to guide treatment was made by multiplex PCR performed on faeces, before growth in the BC bottles was identified.

The availability of tests for the rapid diagnosis of bloodstream infections has the potential to improve the clinical management of patients with suspected sepsis. Specifically, pre/post interventional studies showed a reduced time to optimal antimicrobial treatment in critically ill and cancer patients with bloodstream infections diagnosed with the previous BCID panel compared to standard blood culture methods [7, 9]. Moreover, a randomized control trial showed how BCID reduced the treatment of contaminants and the use of broad-spectrum antimicrobials, as well as enhanced antimicrobial de-escalation when used in association to antimicrobial stewardship programs [8].

The clinical impact of BCID2 has not been assessed yet in real life scenarios. However, Sparks et al analysed its theoretical impact on clinical management of patients with bloodstream infections, showing that antimicrobial therapy would have been altered in 45.1% of cases if the test results had been made available to treating clinicians [11]. In our study we did not assess any clinical outcomes, however we estimated that BCID2 would have reduced time to pathogen identification and antimicrobial resistance detection of almost 10 h and 27 h respectively compared to traditional culture methods, and this could translate in time gained for antimicrobial treatment optimization, potentially leading to improved outcomes.

Nonetheless, it must be acknowledged that the impact of the BCID2 and of emerging molecular tests applied on positive blood cultures may vary according to the setting where they are implemented. Time gained through the implementation of these tests compared to conventional culture-based methods may be dependent on local practices, including the use of MALDI-TOF on early subcultures or bacterial pellet, rapid AST or other molecular assays [23], as well as on the possibility of running the test 24/7 rather than during business hours only. Moreover, the impact of these assays on clinical decision making is highly reliant on the presence of antimicrobial stewardship programs aimed at a real-time reporting of the tests' results in order to adjust antimicrobial prescriptions [24].

The BCID2 is not the only emerging molecular test for the rapid diagnosis of bloodstream pathogens and associated antimicrobial resistance. Other technologies are emerging, both applied on positive BC and on whole blood [17, 25], each with specific advantages and disadvantages. The BCID2 has the advantage of detecting a large panel of pathogens and antimicrobial resistance genes; however, its turnaround time still depends on BC positivity and is longer compared to that of emerging tests applied directly on whole blood [26]. Moreover, the interaction between genetic and phenotypic determinants of antimicrobial resistance is complex and critical thinking is always required when using molecular tests for detecting resistance genes, whose presence not always translate into a resistant phenotype and whose absence is not necessarily associated to a susceptible profile [27]. In this regard, rapid tests providing minimum inhibitory concentrations (MICs) rather than detecting resistance genes, such as those based on morphokinetic cellular analysis, may be more accurate in predicting the phenotypic AST, although they are associated to longer turnaround times [17].

The advantages of implementing one test over the other have not been extensively assessed, may depend on local settings, and should take into account not only the performance of these assay but also clinical and health economic endpoints.

Table 4. Resistance markers detected by BCID2 and in-house PCR and correlation to bacterial phenotype.

Phenotype according to VITEK 2 and conventional susceptibility testing	Identification of resistance markers according to BCID2	Identification of resistance markers according to in-house PCR	Concordant results
Oxacillin resistance[a]	*mecA/C* *S. epidermidis* (n = 3)	*mecA/C* *S. epidermidis* (n = 3)	3/3
3rd generation cephalosporin resistance	bla_{CTX-M} *E. coli* (n = 3)	bla_{CTX-M} *E. coli* (n = 3)	3/3
3rd generation cephalosporin resistance	None *E. coli* (n = 1)	bla_{CMY} *E. coli* (n = 1)[b]	NA
Overall concordance for on-panel resistance markers			**6/6 (100%)**

NA = Not applicable.
[a] Cefoxitin screening well.
[b] bla_{CMY} was also detected by whole genome sequencing.

5. Conclusion

Agreement of BCID2 with conventional culture-based methods was high. Large and well-designed studies to assess the clinical impact of rapid diagnostic tests in the management of sepsis through patient-centred outcomes are highly warranted.

Declarations

Author contribution statement

Anna Maria Peri, Patrick NA Harris: Conceived and designed the experiments.

Anna Maria Peri, Michelle J Bauer, Haakon Bergh, David L Paterson, Patrick NA Harris. Analyzed and interpreted the data.

Anna Maria Peri, Michelle J Bauer, Haakon Bergh, Dominika Butkiewicz: Contributed reagents, materials, analysis tools or data.

Anna Maria Peri: wrote the paper.

Michelle J Bauer, Haakon Bergh, David L Paterson, Patrick NA Harris: contributed to drafting and revising the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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