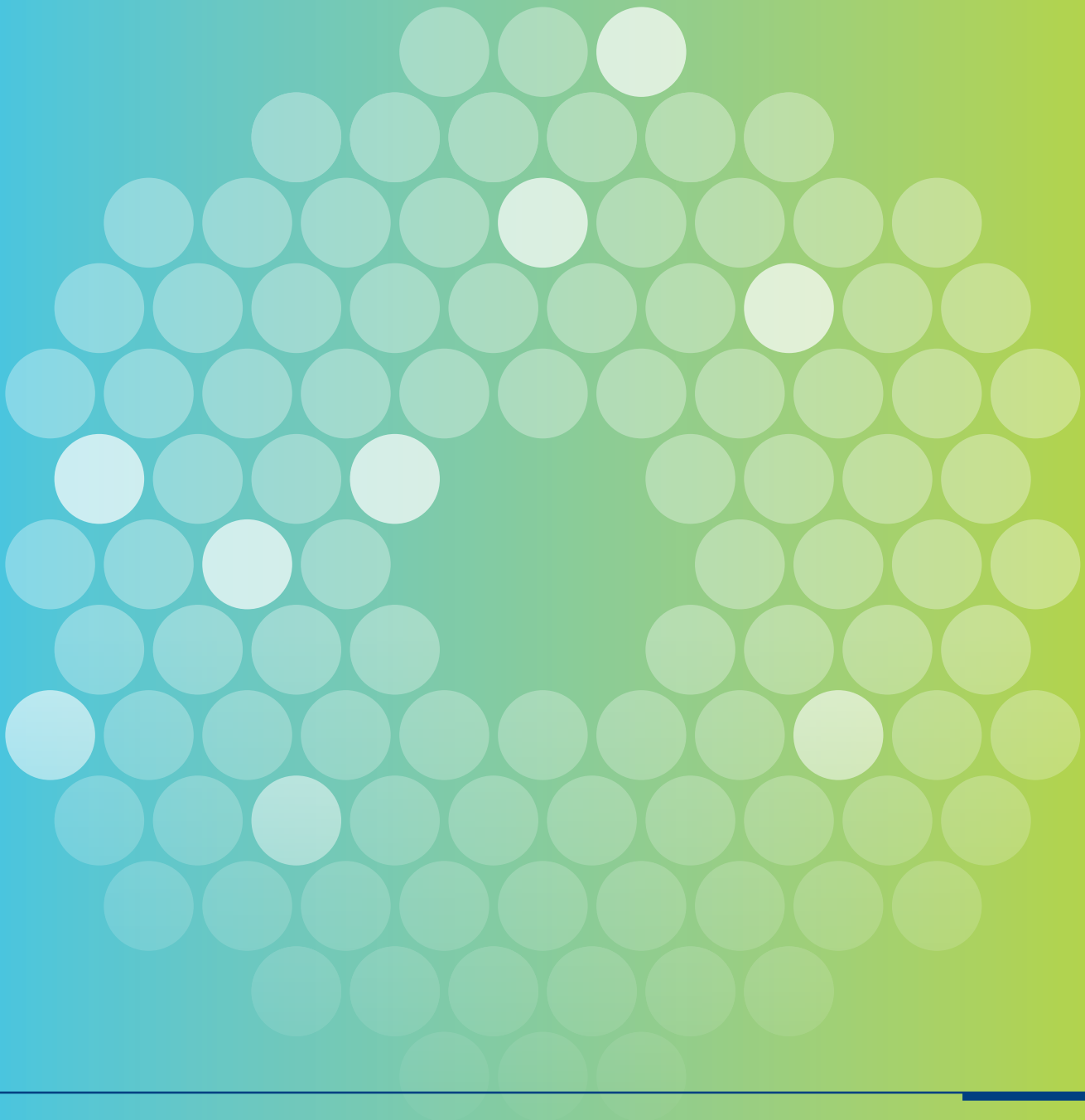
BIOMÉRIEUX

BIOFIRE® FILMARRAY®

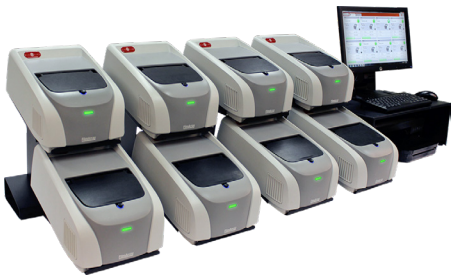
SELECTION OF PUBLICATIONS

2023 EDITION



PIONEERING DIAGNOSTICS

BIOFIRE® FILMARRAY® INSTRUMENTS



BIOFIRE® FILMARRAY® 2.0
FDA cleared
and CE marked

BIOFIRE® FILMARRAY® TORCH
FDA cleared
and CE marked

BIOFIRE® PANELS

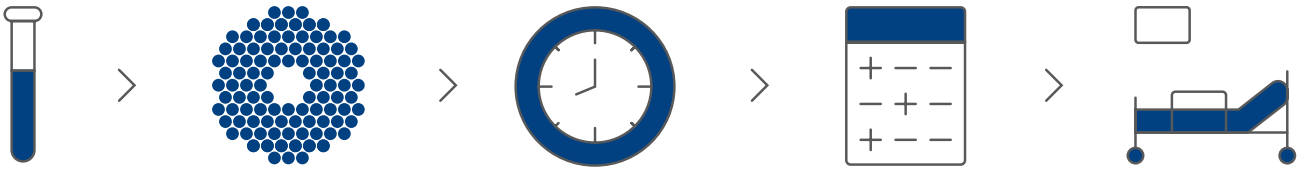
- Respiratory 2.1 (RP2.1) Panel*
- Respiratory 2.1 *plus* (RP2.1*plus*) Panel†
- Respiratory 2.1-EZ (RP2.1-EZ) Panel‡
- Pneumonia (PN) Panel*,†
- Pneumonia *plus* (PN*plus*) Panel†
- Blood Culture Identification 2 (BCID2) Panel*,†
- Gastrointestinal (GI) Panel*,†
- Meningitis/Encephalitis (ME) Panel*,†
- Joint Infection (JI) Panel*,†

* FDA cleared † CE 2797 ‡ Emergency Use Authorization (EUA)

‡This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories; This product has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms; and, The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

INTRODUCTION

Syndromic testing is a symptom-driven broad grouping of probable pathogens into one rapid test that maximizes the chance of getting the right answer in a clinically relevant timeframe.



One sample

One comprehensive test

Takes about an hour for results

Multiple results in one report

Improves patient management

BIOFIRE® syndromic testing allows simultaneous detection of multiple pathogens with a turnaround time of about an hour. Results aid in making vital decisions regarding admission, isolation, cohorting, targeted therapy, and appropriate use of antivirals and antibiotics.

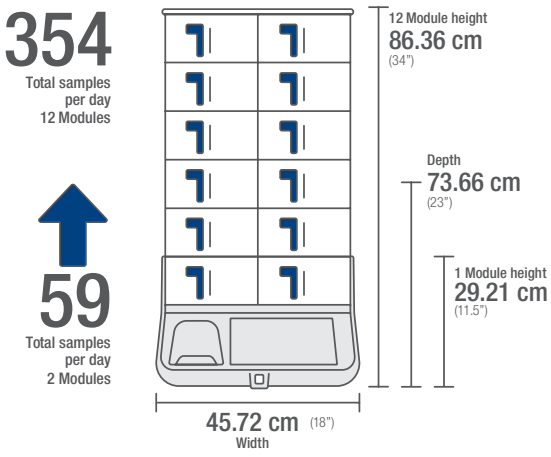
Reduced Length of Stay

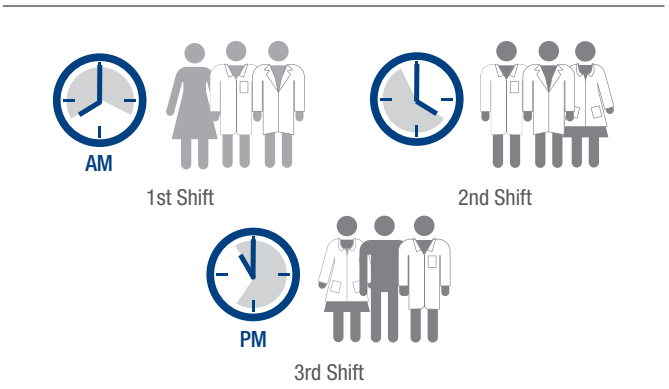
Appropriate Use of Antibiotics

Enhanced Infection Control

The BIOFIRE® FILMARRAY® Systems offer high-quality testing any time, by any tech, and at any size institution.

The BIOFIRE® FILMARRAY® TORCH instrument





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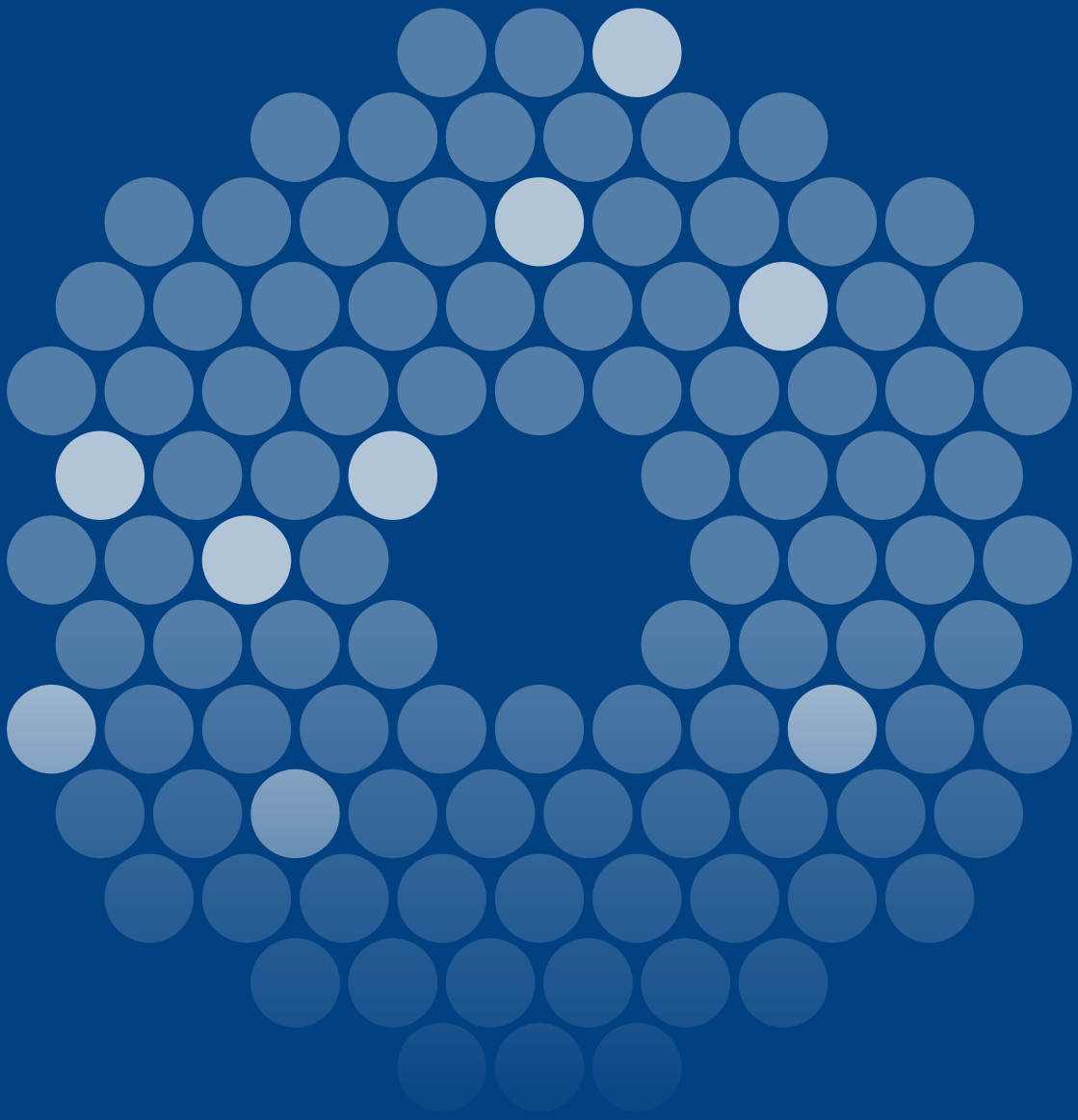


BIOFIRE® RESPIRATORY PANELS

JOURNAL OF INFECTION AND CHEMOTHERAPY, August 2019, pii: S1341-321X(19)30218-1. doi: 10.1016/j.jiac.2019.07.014.

The impact analysis of a multiplex PCR respiratory panel for hospitalized pediatric respiratory infections in Japan

Kitano T, Nishikawa H, Suzuki R, Onaka M, Nishiyama A, Kitagawa D, Oka M, Masuo K, Yoshida S

STUDY DESCRIPTION

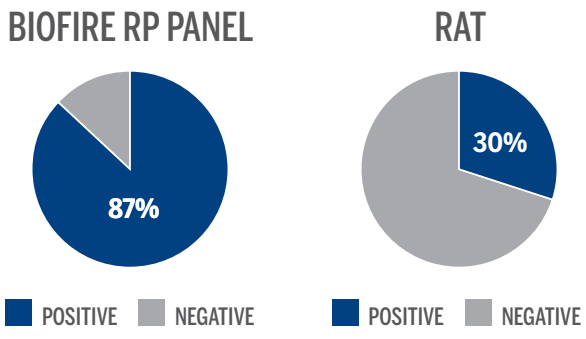
This is a pre-post study of pediatric inpatients with symptoms of respiratory infection at a community hospital in Japan after rapid antigen testing (RAT) was replaced by the BIOFIRE® FILMARRAY® Respiratory (RP) Panel. 1132 patients in the RAT group (March 2012 to March 2018) were compared to 149 patients in the BIOFIRE RP Panel group (March 2018 to April 2019) to evaluate changes in diagnostic yield, antimicrobial treatment, and hospital costs.

The primary outcomes were antimicrobial days of therapy (DOT) and hospital length of stay (LOS). The secondary outcomes were hospital cost, pathogen detection rate and treatment failure rate. Patients were well matched for most demographic measures. However, patients in the BIOFIRE RP Panel group were younger, and more likely to have a general diagnosis of "others."

SUMMARY OF RESULTS AND DISCUSSION

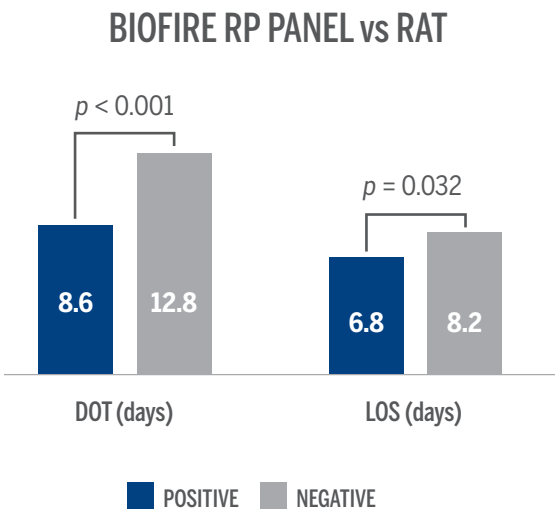
In the BIOFIRE RP Panel group, 210 patients were initially tested. Of these patients, 38 were excluded for a diagnosis other than respiratory infection, and 2 patients were excluded for previous treatment with antimicrobials. The remaining 21 excluded patients were discharged after availability of the test result, indicating that 10% of patients avoided admission based on BIOFIRE RP Panel testing. Of note, the impact of avoided hospital admission was not factored into the results of the study, leading to an underestimation of the overall cost savings.

Testing with the BIOFIRE RP Panel produced an 87% positivity rate compared to 30% for the RAT group as depicted in the figure below. The most common pathogens detected were rhinovirus/enterovirus (≈30%), respiratory syncytial virus (≈27%), and parainfluenza virus (≈14%).



SUMMARY OF RESULTS AND DISCUSSION (cont.)

As shown in the graph below, patients in the BIOFIRE® RP Panel group had reductions in both DOT and LOS. For DOT, there was a mean decrease of about 4 DOT compared to the RAT group ($p < 0.001$), with reductions seen for the following antibiotic classes: macrolides, 3 days; cephalosporins, 1 day; tetracyclines, 0.4 days. For LOS, patients tested with the BIOFIRE RP Panel had a mean reduction of about 1.5 days compared to the control group. Difference in cost was evaluated between the two groups with an average overall hospital cost savings of approximately $135 USD per case seen in the BIOFIRE RP Panel group. There was no significant difference in treatment failure rate between the groups (BIOFIRE RP Panel 2.1%; RAT, 2.6%, p = 0.661).



KEY POINTS

- There was a much higher detection rate in the BIOFIRE RP Panel group compared to the RAT group (87.2% vs 30.2%)
- Patients tested with the BIOFIRE RP Panel showed a reduction in average antimicrobial days of therapy (8.56 vs 12.82) and average length of stay (6.83 vs 8.18) vs control.
- After implementation of the BIOFIRE RP Panel, overall hospital costs were reduced by about $135 per patient case.

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RP CLINICAL UTILITY

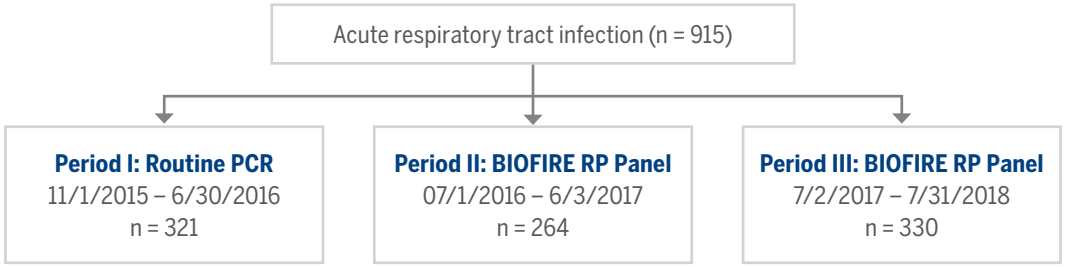
Antibiotics, March 2021; 10(283):1-10

Rapid Molecular Tests for Detecting Respiratory Pathogens Reduced the Use of Antibiotics in Children

Kim Y., Lee J., Kim S., *et al.*

STUDY DESCRIPTION

A retrospective pre/post observational study assessed the clinical efficacy of the BIOFIRE® FILMARRAY® Respiratory (RP) Panel in children who underwent testing for respiratory pathogens at a hospital in South Korea. During Period I, patients were tested with routine PCR and during Period II and III patients were tested using the BIOFIRE RP Panel. Periods II and III were split to check whether medical practices changed after the initial introduction period of the BIOFIRE RP Panel.



SUMMARY OF RESULTS AND DISCUSSION

Positive detection rates between routine testing (71.3%) and the BIOFIRE RP Panel (83.3%) were significantly different ($p<0.001$). There was a significant decrease in wait time, turnaround time and lead time between routine PCR and the BIOFIRE RP Panel. Length of Stay (LOS) was significantly shorter during Period III (3.0 days) vs Period I (3.2 days) ($p=0.004$); however, there was no significant difference during Period I vs Period II (3.5 days) and Period I vs Period II-III (3.2 days). Frequency of IV antibiotic use was reduced from Period I (51.7%) vs Period III (39.4%) ($p=0.002$), but there was no significant difference during Period I vs Period II (52.7%) and Period I vs Period II-III (45.3%). Duration of IV antibiotic use was different in Period I (1.7 days) vs Period III (1.2 days) ($p<0.001$) and Period I vs Period II-III (1.4 days) ($p=0.015$), but there was no significant difference during Period I vs Period II (1.7 days). Duration of IV + oral antibiotic use was shorter in Period III (2.7 days) vs Period I (3.4 days) ($p=0.019$), and there was no significant difference during Period I vs Period II (3.8 days) and Period I vs Period II-III (3.1 days).

KEY POINTS

- There was a significant decrease in wait time, turnaround time and lead time between routine PCR and the BIOFIRE RP Panel
- Antibiotic use and length of stay were significantly decreased in Period II compared to Period I, but not in Period II compared to Period I
- There was a delay between when diagnostic tests are implemented and changes clinical practices

Journal of Clinical Microbiology May 2022; 60(5):e0006622

Multicenter Evaluation of the BioFire Respiratory Panel 2.1 (RP2.1) for Detection of SARS-CoV-2 in Nasopharyngeal Swab Samples

Berry G.J., Zhen W., Smith E., *et al.*

STUDY DESCRIPTION

A multicenter prospective study (3 sites) was performed in the U.S over a period of approximately 4 months in 2020 (July-October). A total of 524 residual nasopharyngeal swab (NPS) specimens were collected from subjects of all ages and from geographically and demographically diverse U.S. populations. The primary outcome was to assess the positive percent agreement (PPA) and negative percent agreement (NPA) of the BIOFIRE® Respiratory 2.1 (RP2.1) Panel SARS-CoV-2 assay. Performance of the panel was determined by comparing BIOFIRE RP2.1 Panel results to a composite of the emergency use authorization (EUA) tests used as the standard point-of-care assay at each individual site for the detection of SARS-CoV-2.

SUMMARY OF RESULTS AND DISCUSSION

To establish a reference, researchers considered concordance between at least two of the three standard point-of-care tests to be the final result. BIOFIRE RP2.1 Panel results were compared to these composite results and were considered true positive or true negative only if the results were in agreement. When a BIOFIRE RP2.1 Panel result disagreed with the composite comparator result, the result of the BIOFIRE RP2.1 Panel was considered false positive or false negative.

A high concordance of SARS-CoV-2 detection was observed between the composite results and the BIOFIRE RP2.1 Panel results with a PPA of 98.4% (61/62) and a NPA of 98.99% (457/462). Analysis of discordant results suggested that concentrations of SARS-CoV-2 in those samples were near the limit of detection (LoD) for both the BIOFIRE RP2.1 Panel and the comparator assays.

The BIOFIRE RP2.1 Panel detected one or more targets in 19.3% (101/524) of specimens tested with only three analytes detected: SARS-CoV-2 in 66/101 (65%), human rhinovirus/enterovirus in 33/101 (33%) and adenovirus in 3/101 (3%), with one coinfection of SARS-CoV-2 and adenovirus. SARS-CoV-2 was the predominant organism detected in age groups 19-40, 41-60 and 61+ age groups, and human rhinovirus/enterovirus was the predominant detected organism in the 0 to 18 years age group.

KEY POINTS

- BIOFIRE RP2.1 Panel has an excellent PPA (98.4%) and NPA (98.99%) compared to a composite standard of care for the detection of SARS-CoV-2 in NPS specimens.
- Discordant results between BIOFIRE RP2.1 Panel and the composite comparator occurred primarily in samples near the LoD.

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RP SYSTEMATIC REVIEW/META-ANALYSIS

Antibiotics, Sep 2022; 11(9):1192

Point-of-Care and Rapid Tests for the Etiological Diagnosis of Respiratory Tract Infections in Children: A Systematic Review and Meta-Analysis

Brigadoi G., Gastaldi A., Moi M., *et al.*

STUDY DESCRIPTION

A meta-analysis including 57 studies on pediatric populations (ED, inpatient, and outpatient) with randomized trials (14.0%), non-randomized observational studies (47.4%) and quasi-experimental studies (38.6%) was performed to assess the effect of point-of-care rapid influenza tests (POCTs) and rapid tests, including the BIOFIRE® FILMARRAY® Respiratory (RP) Panel. The primary outcome was the effect of POCTs and rapid tests on antibiotics prescriptions and the secondary outcomes were the impact of the tests on the rate of prescriptions, days of therapy, length of stay, and reduction of cost.

SUMMARY OF RESULTS AND DISCUSSION

According to the NIH Quality Assessment Tool, 82.5% (47/57) of the studies were assessed as fair, 3.5% (2/57) as poor, and 14% (8/57) as good. 93% of the studies were performed in high income countries (43.9% NORAM, 33.3% Europe, 14.0% Asia) and 82.5% were published after 2007. The most frequently studied tests in the articles were the rapid influenza diagnostic tests (22/57, 38.6%) and the BIOFIRE RP Panel (22/57, 38.5%).

Of the 49 studies that assessed antibiotic prescription rates after implementation of rapid tests or POCT, 65.3% found a statistically significant reduction. An overall reduction in antibiotic prescription was observed when comparing the BIOFIRE RP Panel to standard testing, but not when compared to clinical diagnosis. Of studies that reported impact on oseltamivir prescription, 12 of 20 (60%) reported a significant increase with POCT. The length of stay significantly decreased with POCT in 16 of the 34 studies (47.1%) which included this outcome. 11 of the 18 studies (61%) which measured days of therapy reported a significant reduction after implementing rapid testing or POCT. Finally, the meta-analysis noted a significant reduction in costs for three of the eight studies (37.5%) which included cost as an outcome.

KEY POINTS

- 1st systematic review evaluation of rapid tests and POCTs in pediatric setting worldwide and their impact on antimicrobial prescription, healthcare costs, and patient outcomes.
- Implementation of rapid tests and POCTs could be a valuable tool for the improvement of antimicrobial prescription rates.
- More well-designed studies of implementation (well-structured antimicrobial stewardship programs) of rapid tests and POCTs are needed to improve patients' outcomes in high and low-middle income countries.

THE PEDIATRIC INFECTIOUS DISEASE JOURNAL, March 2020, 39 (3): 188-191 doi: 10.1097/INF.0000000000002544

Performance and Impact of a CLIA-waived, Point-of-care Respiratory PCR Panel in a Pediatric Clinic

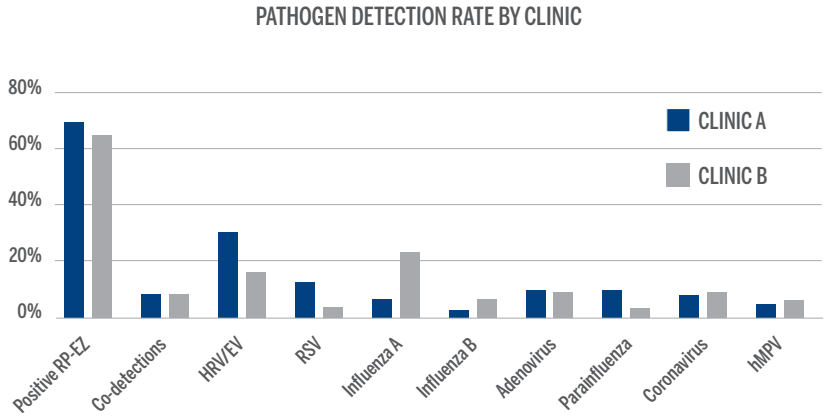
Beal SG, Posa M, Gaffar M, Reppucci J, Mack JA, Gurka MJ, Rand K, Houck H, Kelly MN

STUDY DESCRIPTION

This is a prospective study to evaluate the impact of using the BIOFIRE® FILMARRAY® Respiratory EZ (RP EZ) Panel in a pediatric outpatient clinic. At Clinic A, patients for whom respiratory pathogen testing was deemed appropriate by the clinician were tested on-site using the BIOFIRE RP EZ Panel and/or rapid antigen tests. Use of the BIOFIRE RP EZ Panel was encouraged and prescriptions for antimicrobials were delayed until test results were available. At Clinic B, on-site testing was limited to rapid antigen tests, however, residual respiratory samples were frozen and later tested for definitive pathogen identification. The primary study aim was to determine the proportion of patients that received appropriate antimicrobial therapy based on pathogen detection. Patients with positive rapid antigen results for strep throat were excluded because antibiotic use would be unrelated to the results of the BIOFIRE RP EZ Panel. The study also evaluated the impact to clinic workflow.

SUMMARY OF RESULTS AND DISCUSSION

During the one year study period, a total of 430 samples (298 at Clinic A and 132 at Clinic B) were tested with the BIOFIRE RP EZ Panel. As shown in the figure below, the overall positivity rate and co-detection rates were similar. Patients tested at Clinic A were significantly younger (3.19 vs 5.89, p<0.0001), had lower detection rates for influenza A and B, and a higher detection rate for RSV and HRV/EV. Continued use of rapid antigen tests at Clinic A (350 additional samples) likely contributed to the differences in pathogen detection rates as samples with positive rapid antigen results may have been excluded from testing with the BIOFIRE® RP EZ Panel at Clinic A. The high positivity rate at both sites indicates appropriate use of diagnostic testing at both locations. Importantly, 51% (153/298) and 36% (48/132) of samples tested at Clinic A and Clinic B had pathogens detected by the BIOFIRE RP EZ Panel that cannot be detected by rapid antigen tests.



SUMMARY OF RESULTS AND DISCUSSION (cont.)

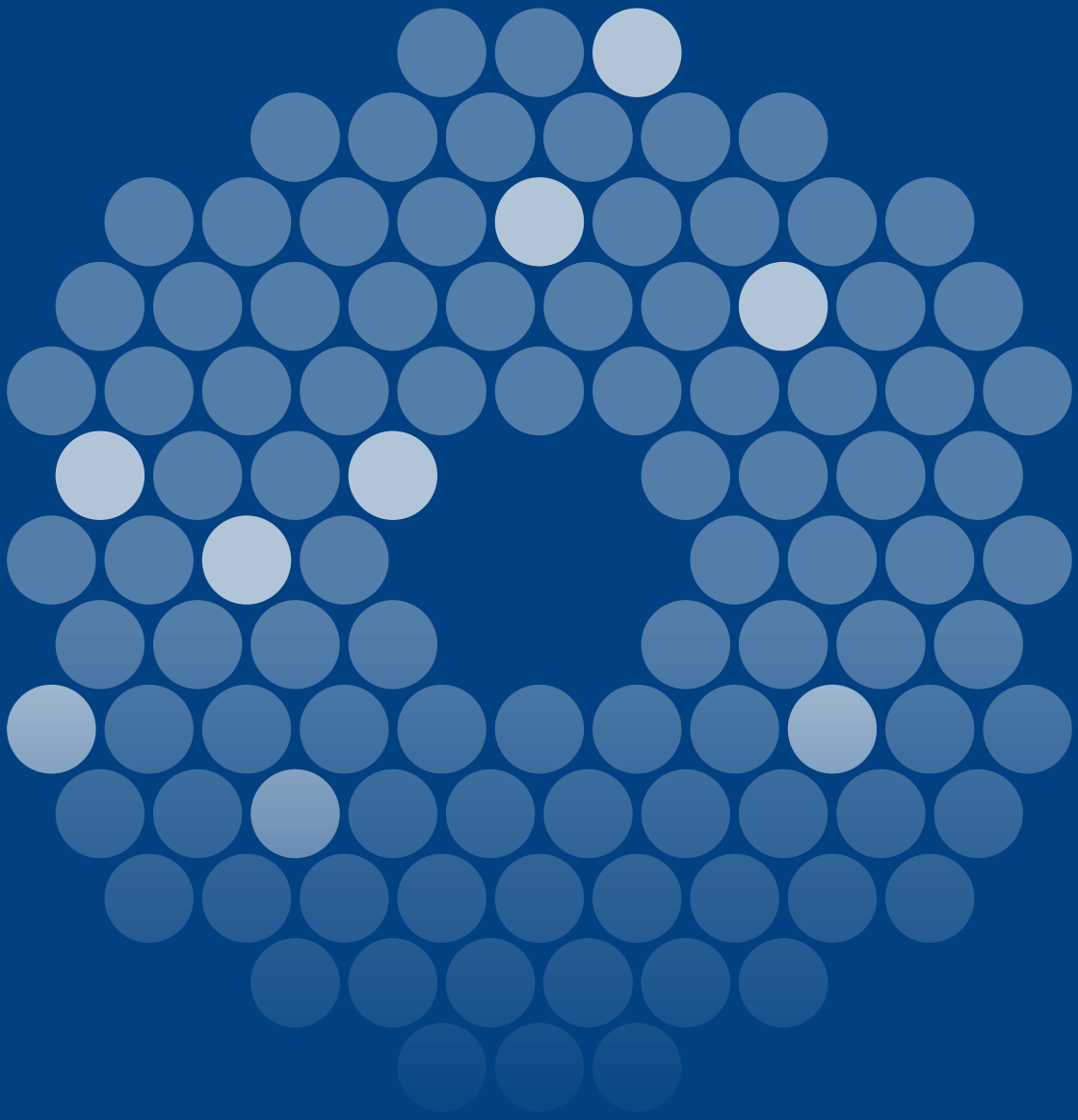
Appropriate use of antimicrobials was determined by comparing antimicrobial prescriptions to detected pathogens. Both clinics had high rates of appropriate use of antibiotics indicating strong antimicrobial stewardship. However, use of the BIOFIRE® RP EZ Panel demonstrated a significant improvement in the appropriate use of antimicrobials. Specifically, antimicrobials were avoided more often for patients with no pathogen detection (97.6 vs 90.5%) or with viral detections other than influenza or RSV (98.1 vs 94.1%). Clinic B had a higher use of oseltamivir for influenza positive patients, however, a post-hoc analysis of patients with influenza determined that all 55 patients at both clinics were managed appropriately when including factors such as age and duration of symptoms.

BIOFIRE RP EZ PANEL DETECTION	STUDY DEFINED	CLINIC A	CLINIC B	P VALUE
None	Appropriate Treatment	83/85 (97.6%)	38/42 (90.5%)	0.0923
Influenza	No antibiotics or antivirals	6/19 (31.6%)	27/369 (75%)	0.0018
RSV	Oseltamivir	37/38 (97.4%)	3/3 (100%)	1.0000
Virus other than influenza/RSV	No antibiotics or antivirals	5152/155 (98.1%)	48/51 (94.1%)	0.16727
Atypical Bacteria	No antibiotics or antivirals	1/1 (100%)	0/0 -	-
Total	Appropriate antibiotic	249/298 (93.6%)	116/132 (87.9%)	0.0445

An evaluation of clinic workflow at Clinic A found that the average duration of appointment times was shorter (mean 48.0 vs 53.7, p=0.0009) for patients tested with the BIOFIRE RP EZ Panel compared to those that were not tested. Results for the BIOFIRE RP EZ Panel were called to the patients after the test results were available.

KEY POINTS

- Approximately 50% of respiratory pathogens detected by the BIOFIRE RP EZ Panel are not detectable by rapid antigen testing due to the limited number of pathogens.
- Use of the BIOFIRE RP EZ Panel significantly increased appropriate use of antimicrobials even in a setting with strong antimicrobial stewardship.
- Use of the BIOFIRE RP-EZ Panel reduced appointments times and subjective feedback from the clinical staff was positive.



BIOFIRE® FILMARRAY® PNEUMONIA PANELS

The Journal of Infection Dec 2022; 85(6):625-633

Molecular point-of-care testing for lower respiratory tract pathogens improves safe antibiotic de-escalation in patients with pneumonia in the ICU: results of a randomised controlled trial

Poole S., Tanner A.R., Naidu V.V., *et al.*

STUDY DESCRIPTION

A monocentric randomized controlled trial performed in the UK between 2019 and 2021. Critically ill adults in the intensive care unit (ICU) with a working diagnosis of community acquired pneumonia (CAP), hospital acquired pneumonia (HAP), or ventilator associated pneumonia (VAP) were enrolled in this trial. 100 patients were randomly assigned to an intervention arm where the BIOFIRE® FILMARRAY® Pneumonia plus (PN*plus*) Panel was used for testing and clinical advice including antimicrobial stewardship was given immediately based on test results (PN*plus* group). The 100 patients randomly assigned to the control arm receive standard clinical care and microbiologic examinations. The primary outcome was the proportion of patients who received results-directed antimicrobial therapy within 48 hours of a respiratory tract result. The secondary outcomes were the proportion of patients with a causative organism identified and the time to result of microbiological investigations. Clinical and safety outcomes were also measured.

SUMMARY OF RESULTS AND DISCUSSION

Baseline characteristics were well matched between groups.

Samples collected and pneumonia types: 125 (63%) endotracheal aspirate, 57 (29%) sputum, 8 (4%) undirected bronchoalveolar lavage (BAL) and 7 (4%) directed BAL. The tests provided working diagnoses of the types of infections: 85 CAP, 69 HAP, and 46 VAP.

Primary outcome: 80 (80%) of the 100 patients in the PN*plus* group received results-directed therapy compared to 29 (29%) of the 99 patients in the control arm (difference of 51%, 95% CI 39 to 63, p<0.0001).

Secondary outcomes: A credible pathogen identification was obtained in 71 (71%) of 100 patients in the PN*plus* group, compared to 51 (51%) of 100 in the control group (difference of 20%, 95% CI 7 to 33; p=0.004). Additional organisms were detected in 43 (43%) of 100 patients who were intubated at recruitment and 29 (39%) of 75 patients who were not intubated. The time to test result was 1.7 hours [1.6 to 1.9] in the PN*plus* group vs 66.7 hours [56.7 to 88.5] in the control group (difference of -65.0 hours, 95% CI -68.0 to -62.0; p<0.0001). Safety was measured by the time to hospital and critical care discharge, the proportion of patients who received mechanical ventilation, and mortality. No differences between the groups were observed.

KEY POINTS

- BIOFIRE PN*plus* Panel led to increased diagnostic yield.
- BIOFIRE PN*plus* Panel led to more rapid time to result.
- Actionable results impact antimicrobial stewardship and appropriate treatment.

Microbiology Spectrum, Nov. 2021; 9(3): e0069521

Diagnosis and Treatment of Bacterial Pneumonia in Critically Ill Patients with COVID-19 Using a Multiplex PCR Assay: A Large Italian Hospital's Five-Month Experience

Posteraro B., Cortazzo V., Liotti F.M., *et al.*

STUDY DESCRIPTION

This study was conducted in an Italian ICU on ventilated patients. 212 respiratory samples from SARS-CoV-2 positive patients were analyzed. The aim was to compare the bacterial identification and the antimicrobial resistance (AMR) pattern between the BIOFIRE® FILMARRAY® Pneumonia *plus* (PN*plus*) Panel and the standard of care (SoC), which included culture and antimicrobial susceptibility testing (AST). The impact of the BIOFIRE PN*plus* Panel on antimicrobial therapy management for bacterial pneumonia was measured.

SUMMARY OF RESULTS AND DISCUSSION

The positive percent agreement of the BIOFIRE PN*plus* Panel compared to culture and AST was 100% for all evaluable targets. The negative percent agreement for all species was 99.2% (98.7-99.5; IC 95%) and 99.7% for AMR genes (98.8-100; IC 95%).

In the quantitative analysis of 202 bacterial organisms, the agreement between the BIOFIRE PN*plus* Panel and SoC culture methods was 35.1% (71/202). 56% (113/202) did not exceed 1log10 copies/mL of difference and 8.9% (18/202) exceeded 1log10 copies/mL of difference.

Of 120/212 samples that had positive detections on the BIOFIRE PNplus Panel, antibiotics were administered in 72.5% (87/120). Of 92 samples that had negative detections, antibiotics were not administered in 87% (80/92). Of 98 positive samples that were concordant between the BIOFIRE PN*plus* Panel and culture, 93 had appropriate antimicrobial escalation/initiation, 10 had de-escalation and 5 had no intervention. Of 90 concordant negative samples, 5 had appropriate antimicrobial discontinuation and 85 had no intervention. The BIOFIRE PN*plus* Panel prevented unnecessary antibiotics administration in 88.9% of cases with SoC-negative results and allowed appropriate therapy for 94.3% of cases with SoC-positive results.

In the concordant results group the time to intervention was 6.4±6.6h for the BIOFIRE PN*plus* Panel and 72h for cultures. Implementation of the BIOFIRE PN*plus* Panel significantly increased the number of patients receiving antibiotics within 6 hours (86.1% vs 19.3%; P<0.001). 52/120 antimicrobial interventions were for detection of carbapenem-resistant *A. baumannii* (confirmed by AST). 63.9% (78/122) of bacterial pneumonia cases were caused by antimicrobial-resistant organisms.

KEY POINTS

- The BIOFIRE PN*plus* Panel had a high PPA and NPA for bacterial identification and AMR pattern.
- The BIOFIRE PN*plus* Panel impacted antibiotics stewardship in COVID-19 patients with bacterial pneumonia and high antimicrobial resistance.
- The BIOFIRE PN*plus*Panel results led to escalation, de-escalation and discontinuation of antibiotics.

Thorax, Jan 2022; doi: 10.1136/thoraxjnl-2021-216990

Multicentre Evaluation of Two Multiplex PCR Platforms for the Rapid Microbiological Investigation of Nosocomial Pneumonia in UK ICUs: The INHALE WP1 Study

Enne V., Aydin A., Baldan R., *et al.*

STUDY DESCRIPTION

This study compared the performance of two automated PCR-based syndromic test systems, the BIOFIRE® FILMARRAY® Pneumonia (PN) Panel and Unyvero Hospitalized Pneumonia (HPN) Panel, for microbiological diagnosis of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). Surplus routine lower respiratory tract samples from 15 intensive care units in the UK were collected to assess this purpose. In addition, this independent comparison was designed to select a panel for a randomized controlled trial (RCT) based on a scoring system that compared concordance, sensitivity, time to result, number of targets, cost per test, footprint, failure rates, and overall user experience.

SUMMARY OF RESULTS AND DISCUSSION

Of 652 eligible samples, 260 were from patients with suspected HAP and 392 from patients with suspected VAP. Most samples were from adults and 72 were from children. Sample types were 299 endotracheal aspirates, 272 sputa, 67 bronchoalveolar lavages, and 14 unspecified. Concordance analysis compared machine and routine microbiology results, and Bayesian latent class (BLC) analysis estimated the sensitivity and specificity of each test while taking into account the imperfection of "gold standard" culture. PCR tests identified pathogens in considerably more samples compared with routine microbiology: 60.4% and 74.2% by the Unyvero HPN Panel and the BIOFIRE PN Panel respectively vs 44.2% by routine microbiology ($p<0.0001$). The BIOFIRE PN Panel had 91.7%–100.0% sensitivity and 87.5%–99.5% specificity. The Unyvero HPN Panel had 50.0%–100.0% sensitivity and 89.4%–99.0% specificity. BLC analysis indicated that routine microbiology had low sensitivity compared to PCR, ranging from 27.0% to 69.4%.

The BIOFIRE PN Panel scored 105 points vs 68 for the Unyvero HPN Panel. The Unyvero HPN Panel had more concordance but less sensitivity, and more targets but more failed tests. The BIOFIRE PN Panel performed better on other characteristics such as turnaround time and user experience and was chosen accordingly for the INHALE RCT.

KEY POINTS

- PCR-based diagnostics detected significantly more potential pathogens in respiratory samples from HAP/VAP patients than routine culture ($p<0.001$), and the prevalent organisms were consistent across methods.
- The BIOFIRE PN Panel had 91.7%–100.0% sensitivity and 87.5%–99.5% specificity.
- The BIOFIRE PN Panel was chosen for the INHALE RCT.

International Journal of Infectious Diseases, March 2020, In-Press Journal Pre-Proof

Evaluation of the BIOFIRE® FILMARRAY® Pneumonia Panel for rapid detection of respiratory bacterial pathogens and antibiotic resistance genes in sputum and endotracheal aspirate specimens

Yoo I.Y., Huh K., Shim H.J., Yun S.A., Chung Y.N., Kang O.K., Huh H.J., and Lee N.Y.

STUDY DESCRIPTION

A retrospective study of the BIOFIRE® FILMARRAY® Pneumonia (PN) Panel for detection of respiratory bacterial pathogens and antibiotic resistance (AMR) markers in sputum and endotracheal aspirates (ETA) from patients in the Republic of Korea. Specimens were screened for quality by Gram stain. Performance of the BIOFIRE PN Panel was assessed by comparing results to routine microbiological methods and antimicrobial susceptibility testing (AST). Correlation of BIOFIRE PN Panel semi-quantitative results (bins) were compared to bacterial counts using culture methods. Retrospective chart review assessed the potential impact of BIOFIRE PN results on antibiotic treatment adjustments.

SUMMARY OF RESULTS AND DISCUSSION

Sputum and ETA specimens were collected from March to July 2019. A total of 100 samples (31 sputum and 69 ETA) from 97 patients were included: 65 pathogen positive samples, 27 selected no-growth samples, and 8 normal throat flora. The BIOFIRE PN Panel and culture were concordantly positive in 64 specimens, concordantly negative in 26 specimens, and 9 specimens had discordant results. Of the discordant results, 8 were positive only by the BIOFIRE PN Panel and 1 only positive by culture. As shown in the table, sensitivity for individual pathogens was 100% for 8 of 9 reported pathogens while specify ranged from 88.3-99.0%.

Polymicrobial detections were increased when using the BIOFIRE PN Panel. Culture detected one pathogen in 59 specimens and two pathogens in 6 specimens, while the BIOFIRE PN Panel yielded one pathogen in 29 specimen, two pathogens in 23 specimens, three pathogens in 12 specimens, and four or more pathogens in 9 specimens.

AMR detections included 21 mecA/C and MREJ, 16 CTX-M, and 5 carbapenemase gene positive specimens. The BIOFIRE PN Panel identified a corresponding resistance gene in 94.4% (17/18) of phenotypically resistant organisms. Additionally, the BIOFIRE PN Panel detected 25 resistance genes in 22 specimens that were not identified by AST. Discrepant analysis by sequencing confirmed the BIOFIRE PN Panel AMR detections in 80% of cases (20/25).

ORGANISMS	BIOFIRE PN + CULTURE +	BIOFIRE PN + CULTURE -	BIOFIRE PN - CULTURE +	BIOFIRE PN - CULTURE -	SENSITIVITY % (95% CI)	SPECIFICITY % (95% CI)
Gram-Negative Bacteria						
ACB	21	9	0	69	100 (80.8–100)	88.5 (78.7–94.3)
ECC	2	7	0	90	100 (19.8–100)	92.8 (85.2–96.8)
Escherichia coli	3	8	0	88	100 (31.0–100)	
Haemophilus influenza	0	5	0	94	-	91.7 (83.8–96.1)
Klebsiella aerogenes	1	3	1	94	50.0 (2.7–97.3)	94.9 (88.1–98.1)
Klebsiella oxytoca	0	1	0	98	-	96.9 (90.6–99.2)
Klebsiella pneumoniae	5	12	0	82	100 (46.3–100)	87.2 (78.4–92.9)
Moraxella catarrhalis	0	1	0	98	-	99.0 (93.7–99.9)
Proteus spp.	0	1	0	98	-	99.0 (93.7–99.9)
Pseudomonas aeruginosa	19	9	0	71	100 (79.1–100)	88.8 (79.2–94.4)
Serratia marcescens	0	3	0	96	-	97.0 (90.8–99.2)
Gram-Positive Bacteria						
Staphylococcus aureus	16	14	0	69	100 (75.9–100)	83.3 (73.0–90.1)
Streptococcus agalactiae	1	4	0	94	100 (5.5–100)	95.9 (89.3–98.7)
Streptococcus pneumoniae	1	3	0	95	100 (5.5–100)	96.9 (90.1–99.2)

ACB, *Acinetobacter calcoaceticus-baumannii complex*; ECC, *Enterobacter cloacae* complex

SUMMARY OF RESULTS AND DISCUSSION (cont.)

The BIOFIRE® PN Panel semi-quantitative bin results (≥106 copies/mL) and bacterial culture (significant growth) were concordant in 88.2% (67/76) of specimens.

Retrospective chart review was performed to evaluate the potential impact of the BIOFIRE PN Panel on therapy modifications in 46 clinically suspected pneumonia cases. Initial empiric therapy could have been changed in 23 (50.0%) cases, with antibiotic escalation in 13 (28.3%) and antibiotic de-escalation in 10 (21.7%).

KEY POINTS

- BIOFIRE PN Panel demonstrated a high sensitivity for detection of typical respiratory bacteria and antibiotic resistance genes with additional detection of 25 AMR genes.
- There was good correlation between semi-quantitative analysis and culture for samples with significant bacterial growth.
- Antibiotic treatment modifications were indicated in 50% of pneumonia cases.

Open Forum Infectious Diseases, 2020 Nov; 8(1):0faa560

Performance of a Semiquantitative Multiplex Bacterial and Viral PCR Panel Compared with Standard Microbiological Laboratory Results: 396 Patients Studied with the BIOFIRE Pneumonia Panel

Rand K, Beal S, Cherabuddi K, *et al.*

STUDY DESCRIPTION

This study was performed in a clinical microbiology laboratory on 396 unique endotracheal or bronchoalveolar lavage specimens. The aim was to compare the qualitative and quantitative results of the BIOFIRE® FILMARRAY® Pneumonia (PN) Panel with conventional microbiology methods (gram stain, culture, mass spectrometry and antibiotic susceptibility testing). Methods were compared for identification of bacteria and resistance. The relationship between semi-quantitative copy number / culture growth or white blood cell (WBC) level on gram stain was also measured.

SUMMARY OF RESULTS AND DISCUSSION

In 396 patients, the BIOFIRE PN Panel detected 98.3% (173/176) of isolates and identified 409 specimens. Using culture as the "gold standard", by specimen the sensitivity was 98.6% (CI 95%, 94.8–99.8), the specificity was 69% (CI 95%, 62.9–74.6), the positive predictive value (PPV) was 63% (CI 95%, 58.6–67.1), and the negative predictive value (NPV) was 98.9% (CI 95%, 95.7%–99.7%). Compared to culture, the BIOFIRE PN Panel detected bacterial pathogens in 20% more cases (35% vs. 55%, $p<0.00001$). False positive detections compared to culture were confirmed for 39 cases by independent PCR. Taking these adjudicated results into account gave a 97.8% sensitivity (95% CI, 94.3%–99.4%), 80.4% specificity (95% CI, 74.5%–85.4%), PPV 80% (95% CI, 75.5%–84%), and NPV 97.8% (95% CI, 94.3%–99.1%).

The BIOFIRE PN Panel reported resistance genes for 63 patients. Reported mecA/C and MREJ were compared to MRSA "gold standard" culture results and showed 80% sensitivity, 50% specificity, 50% PPV, and 80% NPV.

Semi-quantitative microbiological methods and BIOFIRE PN Panel copy number were strongly related ($p<0.00001$), particularly when copy number was ≥107/mL. When looking at the growth of ≥1 bacterial target on culture, 73.5% (165/216) had a copy number of ≥107/mL. Assessment of the WBCs on gram stain with the BIOFIRE PN Panel results of ≥107 copies/mL showed for 82.4% (70/85) moderate (2+) or many (3+ or 4+) WBCs while only 17.2% (15/85) were reported as having no WBCs.

KEY POINTS

- The BIOFIRE PN Panel had a high sensitivity for bacterial detections.
- Strong association at high copy number between semi-quantitative microbiological methods and BIOFIRE PN Panel semi quantitative copy number.

European Journal of Clinical Microbiology & Infectious Diseases, Aug. 2021; 40(8):1609-1622

Multinational Evaluation of the BIOFIRE® FILMARRAY® Pneumonia *plus* Panel as Compared to Standard of Care Testing

Ginocchio C., Garcia-Mondragon C., Mauerhofer B., *et al.*

STUDY DESCRIPTION

This was a multicenter study including 52 laboratories from 13 European countries and Israel. The authors compared the results from the BIOFIRE® FILMARRAY® Pneumonia *plus* (PN*plus*) Panel to the results from standard of care testing. They looked at the number of pathogens detected and the potential impact of the BIOFIRE PN*plus* Panel on antimicrobial stewardship and patient outcomes.

SUMMARY OF RESULTS AND DISCUSSION

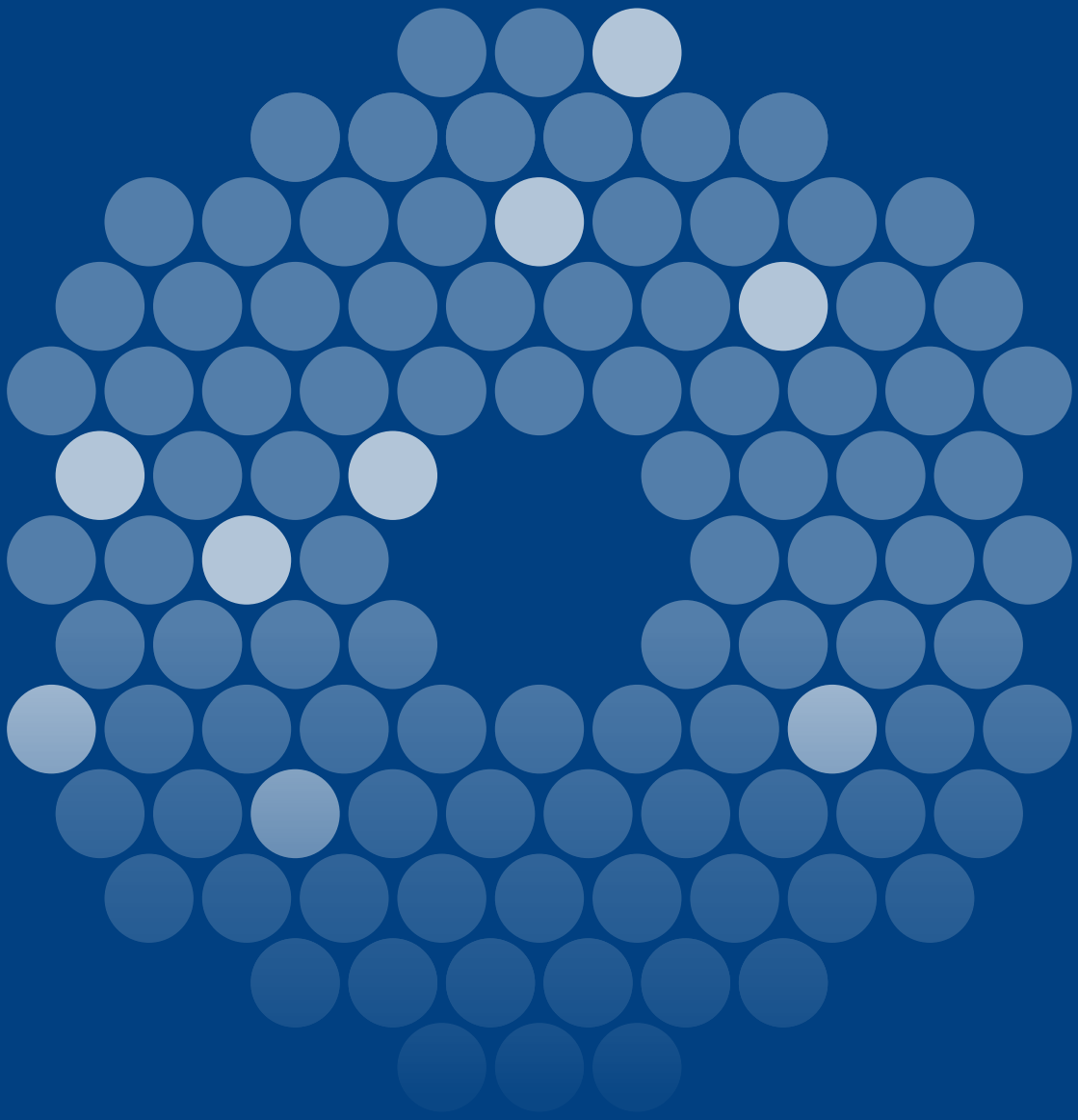
2,476 unique BAL-like and sputum-like samples from adult and pediatric patients suspected of pneumonia were collected and tested using both SOC methods and the BIOFIRE PN*plus* Panel. SOC varied by site and included all bacterial culture and phenotypic susceptibility testing when indicated, as well as any additional test methods performed.

On qualitative assessment one or more pathogens were detected in 76.13% of samples when using the BIOFIRE PN*plus* Panel, while 56.03% had positive results with SOC testing ($p \leq 0.0001$). Co-detections were also evaluated, with the BIOFIRE PN*plus* Panel results showing at least one bacteria in 70.57% of samples, and at least one virus in 20.49% of samples. SOC results showed at least one bacteria in 55.75% of results, and at least one virus in 2.93% of results. There were 649 potential pathogens detected by SOC that are not included in the BIOFIRE PN*plus* Panel target menu. With these pathogen detections included, the panel detected 87.58% and SOC detected 55.59% of potential pathogens.

On quantitative assessment, the BIOFIRE PN*plus* Panel semi-quantitative bin values were less than SOC in 5.1%, equal to SOC in 25.4%, and greater than SOC in 69.6% of results. The BIOFIRE PN*plus* Panel bin values were on average greater than or equal to SOC values. For 58.5% of the results, they were 1–2 logs more than SOC, and 3-4 logs for 11.0% of the results.

KEY POINTS

- The BIOFIRE PN*plus* Panel identified significantly more positive specimens than SOC.
- Semi-quantification may assist in understanding pathogen significance.
- Fast identification and quantification of the pathogens could support antimicrobial stewardship and patient outcomes.



BIOFIRE®
BLOOD CULTURE IDENTIFICATION PANELS

Pathology 2021 Dec 53(7):889-895

Evaluation of the BIOFIRE® Blood Culture Identification 2 Panel and Impact on Patient Management and Antimicrobial Stewardship

Sparks R, Balgahom R, Janto C, *et al.*

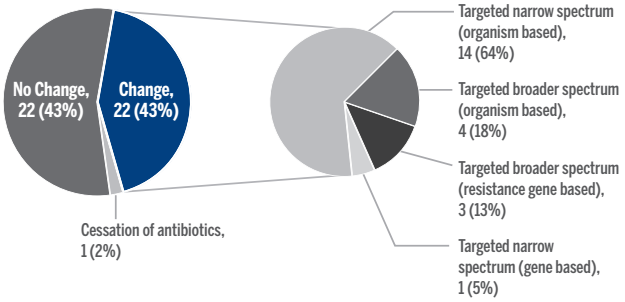
STUDY DESCRIPTION

A prospective study conducted in four Australian hospitals. Positive blood cultures from June to August 2020 were simultaneously tested with standard-of-care (SOC) methods and the BIOFIRE® Blood Culture Identification 2 (BCID2) Panel to determine the diagnostic performance of the BIOFIRE BCID2 Panel as well as the theoretical impact on patient therapy. The BIOFIRE BCID2 Panel was investigational use only at the time of the study, so antimicrobial recommendations were theoretical.

SUMMARY OF RESULTS AND DISCUSSION

A total of 51 positive blood cultures were included in the study. For monomicrobial blood cultures, the BIOFIRE BCID2 Panel identified 39/42 (92.9%) of blood culture isolates to the genus level and 32/42 (76.2%) to the species level. Of the targets available on the BIOFIRE BCID2 Panel, 100% (39/39) concordance was observed between organisms detected by the BIOFIRE BCID2 Panel and culture based SOC. Of the seven polymicrobial blood cultures, concordance was observed in only 2/7 (28.6%) cases. 3 polymicrobial cultures contained organisms not on the BIOFIRE BCID2 Panel, and 1 polymicrobial culture did not detect an organism identified by the BIOFIRE BCID2 Panel. The BIOFIRE BCID2 Panel detected all microorganisms in 52/53 (98.1%) of blood culture isolates available on the panel and identified via conventional methods. As shown in the chart, theoretical alteration in antimicrobial recommendations could be made for 23/51 (45.1%) of patients.

IMPACT OF BIOFIRE BCID2 PANEL RESULTS ON THERAPY, n=51



KEY POINTS

- For monomicrobial blood cultures, 100% (39/39) concordance was observed between on panel organisms detected by conventional methods and the BIOFIRE BCID2 Panel.
- The BIOFIRE BCID2 Panel detected all microorganisms in 52/53 (98.1%) of blood culture isolates available on the panel and identified via conventional methods.
- Theoretical alteration in antimicrobial recommendations could be made for 23/51 (45.1%).

Journal of Infection and Chemotherapy Apr 2022; 28(7):1037-1040

Performance of the new FilmArray Blood Culture Identification 2 Panel and its potential impact on clinical use in patients with Gram-negative bacteremia

Kanda N., Hashimoto H., Suzuki T., *et al.*

STUDY DESCRIPTION

An observational study conducted in a tertiary care center in Japan (from June 2020 to September 2020) that retrospectively evaluated the sensitivity and specificity of the BIOFIRE® FILMARRAY® Blood Culture Identification (BCID) and BIOFIRE® Blood Culture Identification 2 (BCID2) Panels compared to conventional culture methods. The clinical utility regarding antibiotic use was theoretically evaluated for both panels by two infectious disease physicians.

SUMMARY OF RESULTS AND DISCUSSION

Included in this study were hospitalized patients with Gram-negative bacilli bacteremia. Blood cultures were incubated using the BACT/ALERT® VIRTUO® 1, and susceptibility test results were evaluated according to the Clinical and Laboratory Standards Institute (CLSI) breakpoints. The BIOFIRE BCID Panel was used during the study period and the BIOFIRE BCID2 Panel was utilized retrospectively for all enrolled patients. A total of 50 patients were included in the analysis and 52 Gram-negative organisms were identified by blood culture. The BIOFIRE BCID Panel identified 79% (41/52) of organisms, with three samples containing Enterobacteriaceae. The BIOFIRE BCID2 Panel identified 87% (45/52) out of the total organisms, with two organisms identified as Enterobacterales, and identified 100% (45/45) of on-panel organisms. Among the organisms that were not detected by the panels, 91% and 100% were off-panel for the BIOFIRE BCID Panel and the BIOFIRE BCID2 Panel, respectively.

In terms of identification of antimicrobial resistance genes, the BIOFIRE BCID2 Panel detected 5 CTX-M genes, of which 100% were confirmed by AST Extended Spectrum Beta-Lactamase (ESBL) results.

It was retrospectively determined that 8 patients received ineffective antibiotic therapy based on the Gram stain result alone, from which 6 and 7 patients would have received effective treatment if the BIOFIRE BCID Panel and BIOFIRE BCID2 Panel were used, respectively. In addition, 16 (32%) patients for whom BIOFIRE BCID2 Panel results were positive for Enterobacterales and negative for antimicrobial resistance genes could have had antimicrobial de-escalations. Time to optimal therapy and time to de-escalation of therapy was significantly lower in the BIOFIRE BCID2 Panel group compared with the BIOFIRE BCID Panel group (by 8 hours, p=0.0007, and 20 hours, p=0.0005, respectively).

KEY POINTS

- The performance of both panels was higher compared with the standard of care for on-panel organisms, and similar between the two panels.
- The BIOFIRE BCID2 Panel improves on the time to optimal therapy achieved by the BIOFIRE BCID Panel.
- The BIOFIRE BCID2 Panel provides the opportunity for more rapid de-escalation of antimicrobial therapy decisions based on the resistance genes detected. However, these decisions require a more active antimicrobial stewardship evaluation and clinical assessment to obtain effective and safe treatment.

Diagnostic Microbiology & Infectious Disease Feb 2023; 105(2):115858

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

Donnars A., Mahieu R., Declerck C., *et al.*

STUDY DESCRIPTION

This prospective quasi-experimental pre/post-implementation study assessed the effectiveness of the BIOFIRE® Blood Culture Identification 2 (BCID2) Panel for the early administration of appropriate antimicrobial therapy in adult patients from medical wards, emergency rooms and intensive-care units in a French university hospital. The pre-implementation period (P1) was from July 2021 to Nov. 2021 and the post-implementation period (P2) was from Dec. 2021 to Apr. 2022.

SUMMARY OF RESULTS AND DISCUSSION

The study defined time to most appropriate treatment (MAT) as the time from communication of the direct examination, identification, or AST results to a decision made by a clinician, specialist, or clinical microbiologist for the active treatment of the organism with minimal ecological impact on commensal flora. There was no significant difference in the mean age of patients, gender, distribution of wards, or origin of bacteremia between the two periods. Similarly, there was no significant difference in bacteria distribution identified in both periods. Overall, the BIOFIRE BCID2 Panel identified 94.4% of bacteria isolated on solid media.

TAT TIMES FROM GRAM-STAIN TO IDENTIFICATION (H)	ALL POSITIVE BLOOD CULTURES (INCLUDING CONTAMINATED)		POSITIVE BLOOD CULTURES (EXCLUDING CONTAMINATED)	
	Pre-Implementation period (P1)	Post-Implementation period (P2)	Pre-Implementation period (P1)	Post-Implementation period (P2)
Mean time	20.1 +/- 10.2	12.5 +/- 20.3	19.3 +/- 7.2	8.9 +/- 12.9
Median time	19.4	1.25	19.3	1.25
Range	1.75-86.7	1-143.5	1.75-46.8	1-47.2

The proportion of clinicians to prescribe the MAT between P1 and P2 showed a significant difference (26.0% vs 61.4% ($p<0.001$)) for mono-microbial blood cultures with Gram-negative bacteria. Similarly, when only considering those patients with inappropriate empirical treatment, the proportion of clinicians to prescribe the MAT was 50% vs 87.5% ($p<0.001$) between P1 and P2, respectively. For mono-microbial blood cultures with Gram-positive bacteria, the proportion of changes to MAT in P1 vs P2 was 33.0% vs 64.4% ($p<0.01$). When the BIOFIRE BCID2 Panel results were concomitant with direct examination and when the empirical treatment was not appropriate, the study showed that the proportion of clinicians to change to the MAT in P2 was significantly higher than during P1 in the emergency room and in medical wards (this difference was not significant in the ICU).

KEY POINTS

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

Pharmacotherapy Dec 2022; doi:10.1002/phar.2747

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

Britt N.S., Khader K., He T., *et al.*

STUDY DESCRIPTION

A retrospective pre/post-implementation study on the BIOFIRE® FILMARRAY®Blood Culture Identification (BCID) Panel between 2015 and 2020 at the United States Veterans Health Administration (VHA) hospitals with antimicrobial stewardship programs (ASP) and varied in standard practices. The purpose of this study was to evaluate the clinical outcomes among hospitalized adult patients with monomicrobial bloodstream infections.

SUMMARY OF RESULTS AND DISCUSSION

From a total of 4,138 patients, 2,100 were enrolled in the pre-implementation period and 2,038 were enrolled in the post-implementation period. The study found early antimicrobial de-escalation within 48 hours was higher in the post-implementation period, at 38.1% (776/2,038) vs. 34.6% (727/2,100) for the pre-implementation period (p=0.022).

Early appropriate antimicrobial therapy (defined as the administration of ≥1 dose of an antimicrobial to which the related organism was susceptible) was also higher in the post-implementation period vs the pre-implementation period (93.8% vs 91.7%, p=0.008). The median time to appropriate therapy was shorter in the post-implementation period compared with the pre-implementation period (8 h vs 9 h, p=0.005). There was no significant difference between the two periods in the overall 30-day mortality, and similarly no difference for *Clostridium difficile* (*Clostridioides difficile*) infection incidence 90 days after blood stream infection. However, BIOFIRE BCID Panel implementation was associated with lowered 30-day mortality in patients <65 years (6% post-implementation vs. 10% pre-implementation; p=0.01) The sub-analysis showed that median time to appropriate therapy was significantly reduced in different groups in the post-implementation period, but with more benefits in patients with multidrug resistance bacteria (MRSA and VRE). In the same analysis, it was observed that the implementation of the BIOFIRE BCID Panel improved the early appropriate therapy in non-MRSA and VRE cases.

KEY POINTS

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

International Journal of Molecular Sciences Oct 2022; 23(19):11925

Time to Effective Therapy is an Important Determinant of Survival in Bloodstream Infections Caused by Vancomycin-Resistant *Enterococcus* spp

Russo A, Picciarella A, Russo R, *et al.*

STUDY DESCRIPTION

A prospective observational multicenter study to evaluate the clinical impact of early effective antibiotic therapy on the survival of inpatients with monomicrobial enterococcal bloodstream infection (EBSI) caused by vancomycin-resistant enterococci (VRE). Standard of care included testing by MALDI-TOF, Thermo Scientific™ SensiTitre™ system, or VITEK® 2 and the BIOFIRE® Blood Culture Identification 2 (BCID2) Panel. This study was conducted from August 2016 to April 2021 in Rome, Italy.[1]

SUMMARY OF RESULTS AND DISCUSSION

Hospitalized patients with no evidence of endocarditis or hospital-acquired BSI caused by VRE were considered for this study. A total of 103 consecutive patients were enrolled, 79 (76.7%) with *Enterococcus faecium* and 24 (23.3%) with *Enterococcus faecalis*. The time to effective therapy was 3.12 days from blood culture collection. From the total, 55.3% of the patients were treated with early effective therapy (defined as less than 48 hours), and 44.7% of the patients received delayed effective therapy (defined as more than 48 hours). Early effective therapy was associated with improved survival. Patients that received early effective therapy had significantly lower 30-day mortality than patients who received delayed therapy (12.2% vs. 45.6%, $p < 0.001$) (see Figure. 1). A Cox regression analysis revealed the risk factors independently associated with 30-day mortality were age, chronic kidney disease, oncologic disease, and intensive care unit admission. On the contrary, early effective therapy was correlated with survival.

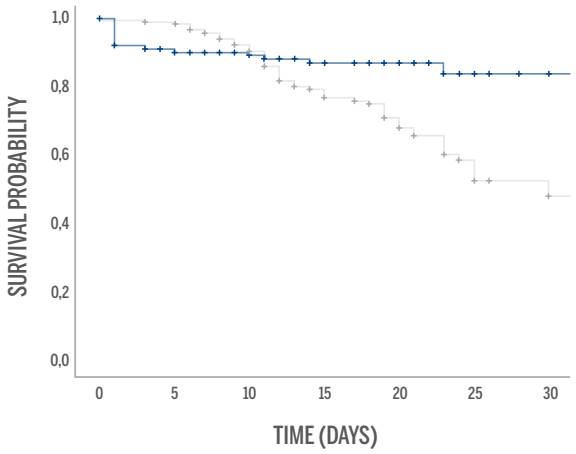
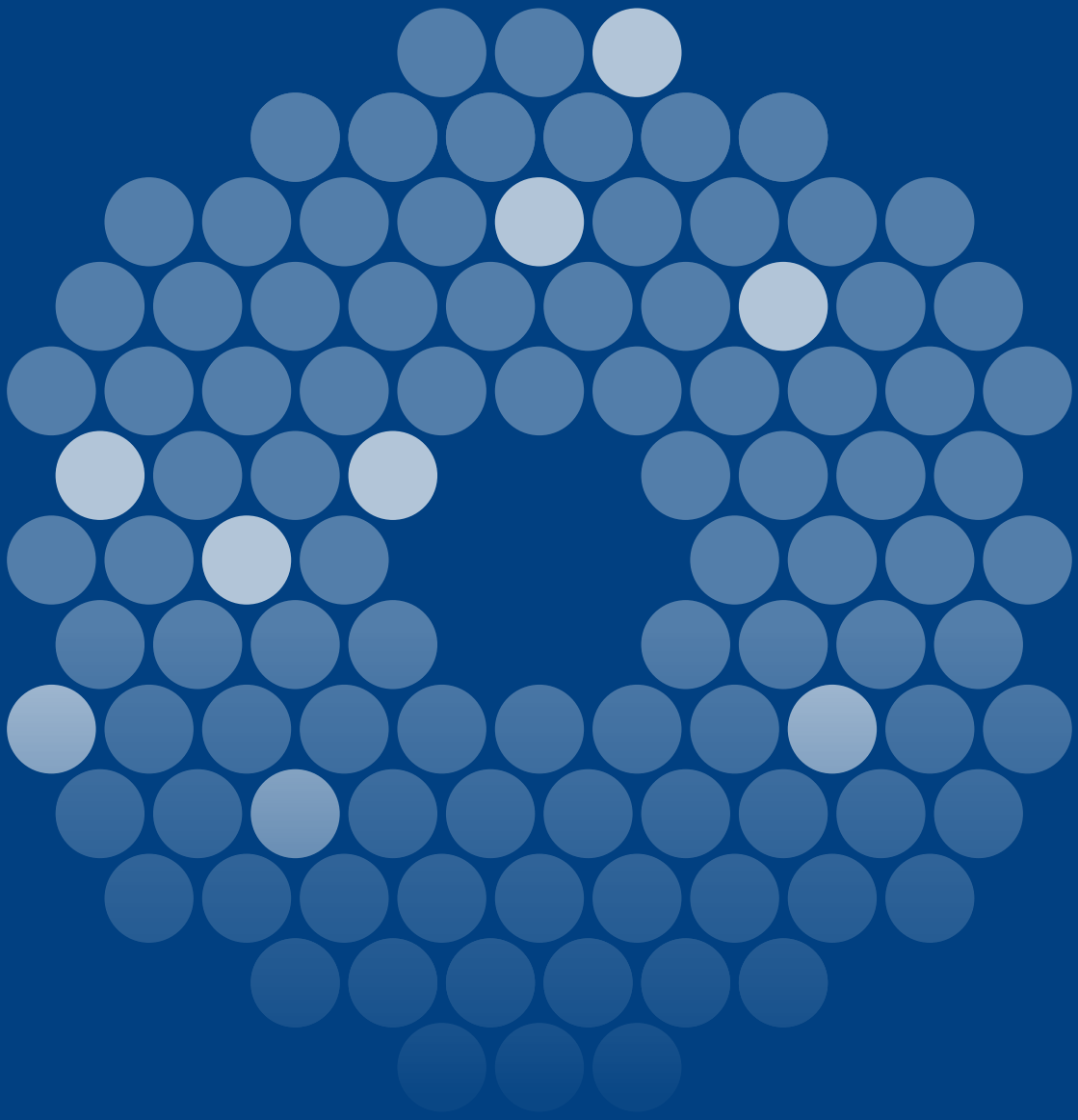


Figure 1. 30-day survival of patients receiving early effective therapy in blue and patients receiving delayed effective therapy in grey.

KEY POINTS

- The administration of effective antibiotic therapy within 48 hours from blood culture collection was related to the decrease of 30-day mortality rates in patients with VRE bacteremia.
- Rapid molecular diagnostic testing to detect both enterococcal species and the presence of vancomycin resistance genes (VanA, VanB) has been shown to reduce the time to appropriate therapy and mortality in patients with EBSI, as well as a reduction in hospital costs, and represents a standard of care in management of BSIs.



BIOFIRE® FILMARRAY® GASTROINTESTINAL PANEL

Scandinavian Journal of Gastroenterology, December 2020; 55(12):1405-1410

Mapping of Aetiologies of Gastroenteritis: A Systematic Review and Meta-Analysis of Pathogens Identified using a Multiplex Screening Array

Meyer J, Roos E, Combescure C, *et al.*

STUDY DESCRIPTION

This is a systematic review and meta-analysis of the literature reporting organisms identified in patients suffering from gastroenteritis (GE) using the BIOFIRE® FILMARRAY ® Gastrointestinal (GI) Panel, to compare the diagnostic yield with traditional microbiological examination of the stools. The systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Out of 111 studies, 14 were selected (excluding studies with 30% of immunocompromised patients, patients suffering from Inflammatory Bowel Diseases, or studies on inpatients only).

SUMMARY OF RESULTS AND DISCUSSION

A total of **17,815** patients (adults and children) with suspected GE and related symptoms from the 14 studies were included. The BIOFIRE GI Panel results were positive in **39.7%** (7,071 patients) for all pooled publications. In publications also reporting traditional methods, the positivity rate of the BIOFIRE GI Panel reached **48.2%** compared to 16.7% for traditional methods. From the pooled detections, the most common pathogens identified were **EPEC: 27.5%** [95%CI: 22.9-32.6%]; ***C. difficile:* 19.3%** [95%CI: 14.6-25%]; and **norovirus: 15.1%** [95%CI :12.2-18.5%]. 13 publications (17,585 patients) reported the number of patients in whom the presence of more than 1 pathogen was identified. The pooled proportion of **co-detections** was **18.1%** [95% CI: 13.4-24%].

	TRADITIONAL MICROBIOLOGICAL EXAMINATION		BIOFIRE GI PANEL	
Studies	Patients tested, n	Patients with ≥1 pathogen(s), n(%)	Patients tested, n	Patients with ≥1 pathogen(s), n(%)
Valenzuela et al.	N/A	N/A	199	133 (68%)
Spina et al.	709	128 (18.1%)	709	384 (54.2%)
Calderaro et al.	1716	396 (23.1%)	1716	958 (55.8%)
Connor et al.	N/A	N/A	388	207 (53.5%)
Buss et al.	N/A	N/A	1556	835 (53.5%)
Keske et al.	N/A	N/A	699	499 (71.4%)
Axelrad et al.	5986	246 (4.1%)	9402	2746 (29.2%)
Khare et al.	230	19 (8.3%)	230	76 (33%)
Beal et al.	594	40 (6.7%)	241	79 (32.8%)
Cybulski et al.	1887	113 (6%)	1887	669 (35.5%)
Pouletty et al.	59	21 (35.6%)	59	58 (98.3%)
Piralla et al.	168	81 (48.2%)	168	92 (54.8%)
Leli et al.	N/A	N/A	183	94 (51.4%)
Stockmann et al.	378	175 (46.3%)	378	244 (64.6%)

Diagnostic yields of the BIOFIRE GI Panel and traditional methods per studies

KEY POINTS

- First systematic review and meta-analysis of the BIOFIRE GI Panel, looking at pooled prevalence providing a complete picture of the etiologies of gastroenteritis
- Positivity rate of the BIOFIRE GI Panel was 39.7% for all pooled publications and 48.2% when compared to 16.7% for traditional methods
- Most common pathogens identified were EPEC, *C. difficile* and norovirus

BMJ Open Gastroenterology, Feb 2021, 8(1): e000553

Accuracy and comparison of two rapid multiplex PCR tests for gastroenteritis pathogens: a systematic review and meta-analysis

Chang LJ, Hsiao CJ, Chen B, *et al.*

STUDY DESCRIPTION

A systematic review and meta-analysis of the literature (up to December 1, 2019) reporting the detection of gastrointestinal infections by the BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel and the Luminex® xTAG® Gastrointestinal Pathogen Panel (GPP)[1] to evaluate the diagnostic value and reliability of both multiplex PCR tests, and to compare the diagnostic accuracy for each pathogen.

SUMMARY OF RESULTS AND DISCUSSION

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the standard guidelines for systematic reviews of diagnostic tests by the Cochrane Collaboration were used. An adult and pediatric cohort with acute diarrhea suspected as secondary to infectious gastroenteritis was tested by multiplex PCR and standard microbiology techniques. A total of 11 studies with a total of 7,085 stool samples were analyzed.

- High discrimination for all pathogens by the two panels (AUROC≥0.96) except for *Yersinia enterocolitica* by xTAG GPP (AUROC:0.91)
- AUROC was higher with the BIOFIRE GI Panel than with xTAG GPP (0.99 vs 0.98, p=0.03)
- High specificity for both panels (0.98 to 1.00), except for *Salmonella* by xTAG GPP (0.97) and *Clostridium difficile* by BIOFIRE GI Panel (0.97), with a high rule-in value
- BIOFIRE GI Panel demonstrated a higher sensitivity and post-test probability than xTAG GPP for most of the pathogens except for Rotavirus A
- Overall BIOFIRE GI Panel showed a higher rule-out value than xTAG GPP
- Variation of post-test probability for positive test among all pathogens: xTAG GPP was in the 11% - 86% range; BIOFIRE GI Panel was in the 68% - 96% range

KEY POINTS

- ► First systematic review and meta-analysis comparatively evaluating the performance of the novel multiplex PCR-based tests xTAG GPP and BIOFIRE GI Panel in detecting each pathogen
- ► Compared with conventional methodologies, xTAG GPP and BIOFIRE GI Panel can detect more than 90% of the common enteropathogens with high sensitivity, specificity and in a shorter turnaround time
- ► BIOFIRE GI Panel demonstrated a higher sensitivity and post-test probability than xTAG GPP for most of the pathogens except for Rotavirus A

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Pediatric Quality and Safety Jan 2022; 7(1):e517

Improving Care for Children with Bloody Diarrhea at Risk for Hemolytic Uremic Syndrome

Burns C.S., Rubin J., Sardesai T., *et al.*

STUDY DESCRIPTION

A retrospective cohort study analyzing the impact of a clinical pathway designed to standardize diagnostic workup procedures, including testing with the BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel and the management of pediatric patients (from 4 months to 19 years of age) with an increased risk of hemolytic uremic syndrome (HUS). Researchers performed a chart review of eligible episodes between September 2015 and July 2020 at an academic tertiary care children's hospital in Seattle, US to determine how the implementation of the clinical pathway in January 2018 impacted the incidence of hospital admission for patients presenting to the emergency department (ED) with bloody diarrhea. Additionally, researchers analyzed changes in IV fluid administration, ED and hospital length of stay (LOS), ED and hospital charges, rates of readmission, stool PCR utilization and the diagnosis of Shiga toxin-producing *Escherichia coli* (STEC), acute kidney injury (AKI), and HUS.

SUMMARY OF RESULTS AND DISCUSSION

The study analyzed data 28 months before and 31 months after the implementation of the pathway. Within the study period, there were 305 encounters with children who visited the ED with bloody diarrhea or other eligible HUS risk factors. One hundred and nine of these encounters occurred prior to the implementation of the clinical pathway, and 196 occurred post-implementation. When the BIOFIRE GI Panel was introduced in May 2017, it was utilized in 83% of episodes and the use of the BIOFIRE GI Panel was sustained throughout the implementation of the pathway. After the implementation of the clinical pathway, there was a decrease in the rate of patients admitted to the hospital (49% to 30%) and an increase in the mean LOS for patients discharged from the ED (209 to 277 minutes) and charges ($2,651 to $3,524) for patients discharged from the ED. There was no significant difference in the length of stay or charge for hospitalized patients, the rate of ED return visits or hospital readmission, or rates of diagnosis of STEC, AKI, or HUS. Mean overall charges, including charges for discharged and hospitalized patients, decreased after implantation, from $7,715 to $6,797. Implementation of stool PCR testing correlated with increased laboratory testing charges but overall decreased healthcare costs.

KEY POINTS

- The implementation of a rapid stool PCR diagnostic test such as the BIOFIRE GI Panel, together with guidelines, may be sufficient to drive behavior changes in patient management.
- The implementation of a clinical pathway and rapid stool PCR diagnostic test led to a decrease in hospitalizations and overall charges, albeit with a modest increase in ED length of stay and charges.
- A clinical pathway guiding decisions to discharge patients from the ED, admit them to the hospital, and discharge them from the hospital did not increase rates of ED revisits or readmission, indicating the criteria were appropriate.

Transplant Infectious Disease Aug 2022, 24(4):e13873

The role of gastrointestinal pathogen polymerase chain reaction testing in liver transplant recipients hospitalized with diarrhea

Ching C.K., Nobel Y.R., Pereira M.R., *et al.*

STUDY DESCRIPTION

A retrospective cohort study conducted at a medical center in New York, US to assess incidence, predictors, and outcomes of liver transplant recipients who underwent stool pathogen testing using the BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel. Samples were collected between April 1, 2015, and December 31, 2019 from inpatients within a year of liver transplant.

SUMMARY OF RESULTS AND DISCUSSION

One hundred twelve eligible patients underwent BIOFIRE GI Panel testing during the study period, with 14 (12.5%) testing positive for at least one pathogen, including three polymicrobial infections. *Escherichia coli* (n=9) and norovirus (n=5) were the most commonly identified pathogens. Compared to patients with negative BIOFIRE GI Panel results, patients who tested positive tended to be further from liver transplant (74.5 vs 15.5 days, p<0.01) and were tested earlier during their hospitalization (1.0 vs 9.0 days, p<0.01). Additionally, patients with a positive BIOFIRE GI Panel result were more likely to have a change in antimicrobial therapy (71.4% vs 28.6%, p=0.02), had shorter length of stay (7.5 vs 17.5 days, p<0.01), and fewer days to discharge from testing (5.3 vs 8.9 days, p=0.2). There was no statistically significant difference in the rates of readmittance or colonoscopy within 30 days between those with positive and negative BIOFIRE GI Panel results. However, a tendency was observed to decrease the number of re-admissions and colonoscopies in the group with a positive result. In addition, for patients who were tested both via the BIOFIRE GI Panel and PCR testing for *Clostridium difficile* (*Clostridioides difficile*) and Cytomegalovirus (CMV), no statistically significant difference in rates of *C. difficile* or CMV was observed between patients who received a positive or negative result on the BIOFIRE GI Panel.

It was observed that a result from the BIOFIRE GI Panel was more likely to be positive when testing was performed earlier in the admission than in those cases when it was performed later, suggesting that patients with diarrhea as their main complaint may be more likely to have a case of diarrhea with an infectious etiology. In addition, the BIOFIRE GI Panel was also more likely to be positive at least 30 days following liver transplant, suggesting an increased likeliness to be exposed to community-associated pathogens during recovery periods.

KEY POINTS

- The BIOFIRE GI Panel can be a valuable tool for managing diarrhea in hospitalized liver transplant patients, especially when it is used within the first two days of admission and in the 30 days post-transplant period.
- Patients with positive BIOFIRE GI Panel results were more likely to have a targeted antimicrobial regimen, compared to those with negative results.
- Positive results obtained with the BIOFIRE GI Panel were associated with a shorter length of stay, and fewer days to discharge from testing.

The American Journal of Gastroenterology, 2020 Oct. 115(10):1553-55

Use of the Multiplex Diagnostic PCR Panel in Diarrheal Disease: Expert Guidance on the Interpretation of Results with a Focus on Traveler's Diarrhea

Connor BA, Martin GJ, and Riddle MS

STUDY DESCRIPTION

Three case scenarios were presented to address the issue of interpreting positive multiplex PCR results for multiple pathogens, including diarrheagenic *Escherichia coli* (*E. coli*), and how to approach interpretation considering the symptomatology and clinical history in a traveler's diarrhea context.

SUMMARY OF RESULTS AND DISCUSSION

First case study: a 41-year-old woman returned to the U.S. from Asia. She presented diarrhea and abdominal pain on the plane. Upon her arrival symptoms were watery diarrhea, cramps and a high fever. Multiplex PCR identified STEC, ETEC and *Campylobacter* pathogens. The expert suggested that *Campylobacter* was the probable responsible pathogen, with possible STEC/ETEC co-infections. STEC is a concern but low frequency in travelers, and not commonly associated with high fever.

Second case study: a 24-year-old woman returned to the U.S. from Costa Rica. After her arrival she presented diarrhea and a high frequency of bowel movements, not affecting her daily activities. The multiplex results found EAEC and EPEC pathogens. The expert did not suggest antibiotic treatment; instead they focused on treating the symptoms. These pathogens cause prolonged diarrhea in children and the symptoms tend to be mild and self-limited.

Third case study: a 26-year-old man arrived in the U.S. from India after 4 months of traveling. He presented a 4-week watery diarrhea and cramping, with previous antibiotic treatment (azithromycin). The multiplex PCR had positive detections for *Yersinia*, EPEC, *Giardia*, norovirus and sapovirus. The expert suggested there was a high risk of exposure to different pathogens and a possible colonization. Giardia is associated with long and intermittent symptoms; thus, it should be treated.

APPROACH	INTERPRETATION
Is this community-acquired?	Viral pathogens likely to predominate
Is this travel-related?	More likely bacterial or parasitic causes
Are the symptoms persistent?	Consider parasitic or noninfectious causes
Did symptoms develop suddenly?	More likely bacterial or viral
Did symptoms develop insidiously?	More likely parastic or noninfectious
Was there treatment or self-treatment with antibiotics?	Response to treatment

KEY POINTS

- The use of a multiplex panel is well suited to the syndromic approach
- A multiplex approach should consider the interpretation of the results in conjunction with other information such as clinical and epidemiological data
- Multiplex results alone should not be used to monitor treatment and microbiological cure due to the persistence of microbial DNA *in vivo*

BIOFIRE® FILMARRAY®
MENINGITIS/ ENCEPHALITIS PANEL

Antibiotics Jul 2022; 11(8): 1028

Assessment of the Impact of a Meningitis/Encephalitis Panel on Hospital Length of Stay: A Systematic Review and Meta-Analysis

Hueth K., Thompson-Leduc P., Totev T., *et al.*

STUDY DESCRIPTION

A systematic review and meta-analysis of the current literature describing the impact of the BIOFIRE® FILMARRAY® Meningitis/Encephalitis (ME) Panel on hospital length of stay (LOS), duration of acyclovir use, and duration of antimicrobial use.

SUMMARY OF RESULTS AND DISCUSSION

This systematic review analyzed 169 publications published from 2015 onwards in the EMBASE and MEDLINE databases. After a screening of the publications, 11 were retained for meta-analysis and 13 were retained for systematic review, which included a range of study designs: retrospective cohort (n=4), case-control (n=3), pre/post interventional (n=3), cross-sectional (n=1), combination designs (n=1), and randomized control trial (n=1). Five publications reported exclusively on pediatric patients, 1 study did not report ages, and the remaining 7 studies reported on either adults or combined pediatric and adult populations.

All 11 studies reported a reduction in the mean duration of hospital LOS using the BIOFIRE ME Panel compared to standard of care (SOC). There was a statistically significant reduction in mean duration of LOS by 1.2 days (95% CI [-1.96, -0.44]). Both LOS and acyclovir use demonstrated a statistically significant reduction across all 11 studies, with reduced duration of antibiotic administration that did not reach statistical significance.

7 studies reported information on the duration of acyclovir therapy. Meta-analysis of the 7 studies demonstrated a statistically significant reduction in mean duration of acyclovir therapy in the BIOFIRE ME Panel cohorts by 1.14 days (95% CI [-1.78, -0.50), with the strongest effect observed in studies that exclusively included pediatric patients.

Lastly, among the 6 studies which reported duration of antibiotic therapy, 3 studies demonstrated a statistically significant reduction in the mean duration of antibiotic therapy (all of which exclusively evaluated pediatric patients) of 1.85 days (95% CI [-2.50, -1.21]). The overall reduction in mean duration of antibiotic therapy across the 6 studies was not statistically significant, but showed a reduction of 1.01 days (95% CI [-2.39, 0.37]).

KEY POINTS

- BIOFIRE ME Panel associated with faster turnaround time and increased viral yield.
- BIOFIRE ME Panel may lead to reduced unnecessary antimicrobial administration and optimize antiviral therapies among patients with suspected CNS infection.
- BIOFIRE ME Panel implementation is cost-effective, particularly if there is a reduction in length of hospitalization.

BMC Pediatrics Apr 2022; 22(1): 182 Apr 2022; 22(1): 182

FilmArray® Meningoencephalitis panel in the diagnosis of central nervous system infections: stewardship and cost analysis in a paediatric hospital in Chile

Acuña M., Benadof D., Yohannessen K., *et al.*

STUDY DESCRIPTION

Analytical observational pre- and post-implementation study using the BIOFIRE® FILMARRAY® Meningitis/Encephalitis (ME) Panel in children hospitalized with suspected central nervous system (CNS) infection. This study compared the etiology of the associated infection to the hospitalization costs.

SUMMARY OF RESULTS AND DISCUSSION

During the study period (2016-2018), 409 CSF samples from children under 15 years old were analyzed. The study population included patients in outpatient, inpatient, and emergency department settings. Of the included patients, 85.5% required hospitalization at the largest children's hospital in Santiago, Chile in the pre-intervention period (297 patients) and 92.7% in the post-intervention period (112 patients). Of these, hospitalization in the intensive care unit (ICU) was more frequent in the post-intervention period (14.8% vs. 28.6% ($p<0.001$)), however with a median of ICU bed-days used significantly lower (2 days vs. 3.5 days). The overall CSF positivity rate was 9.4% in the pre-intervention period and 26.8% in the post-intervention period ($p<0.001$), mainly impacting the infant population <6 months (from 2.6% to 28.1% after the implementation of the BIOFIRE ME Panel). Viral targets, *S. agalactiae, S. pneumoniae* and *N. meningitidis* were the main detections in this population.

The BIOFIRE ME Panel may also impact the cost effectiveness of treatment through better stewardship of resources resulting from accurate identification of infectious agents and improved time to appropriate treatment. Finally, the cost/benefit ratio the BIOFIRE ME Panel to ICU bed-day is favorable, providing a saving of $2,916 to $12,240 USD based on ICU bed-days.

KEY POINTS

- BIOFIRE ME Panel use significantly increases the rate of etiological identification.
- Turnaround time decreased after implementation of the BIOFIRE ME Panel which facilitated timely clinical decisions.
- Considerable decrease in patient care costs associated with the rate of ICU bed-days.

Open Forum Infectious Diseases, Sep. 2021; 8(10):Ofab467

Impact of a Multiplex Polymerase Chain Reaction Panel on Duration of Empiric Antibiotic Therapy in Suspected Bacterial Meningitis

Choi J, Westblade L, Gottesdjener L, *et al.*

STUDY DESCRIPTION

Retrospective pre-post interventional study conducted to assess the clinical impact of the BIOFIRE® FILMARRAY® Meningitis/Encephalitis (ME) Panel in the emergency department of a New York City academic hospital from 2014 to 2020. This study was composed of a pre-intervention group tested by CSF culture for suspected bacterial meningitis for 3 years preceding BIOFIRE ME Panel implementation and a post-intervention group tested by the BIOFIRE ME Panel. The study included adult patients who presented to the ED with suspected bacterial meningitis, received empiric antibiotic therapy, and had an LP performed in the ED. The primary clinical outcome assessed was the impact on duration of empiric antibiotic therapy for suspected bacterial meningitis. Antimicrobial stewardship teams were not directly involved in communicating positive detections to clinicians.

SUMMARY OF RESULTS AND DISCUSSION

The study evaluated results for 206 patients (137 in the pre-intervention group and 69 in the post-intervention group). The pre-intervention and post-intervention groups had 24 patients and 14 patients with an identified pathogen, respectively. The implementation of the BIOFIRE ME Panel resulted in an average turnaround time reduction of 68.7 hours (2.6 hours vs. 71.3 hours).

The overall median duration of empiric antibiotic therapy in the post-intervention group was reduced by 22 hours (12.3 hours vs. 34.7 hours, $p<0.01$). Interestingly, a similar observation was made regarding the total duration of antibiotic therapy for patients with no pathogens detected, which was reduced in the post-intervention group (16.6 hours vs 39.6 hours, $p=0.02$).

A higher proportion of patients (+46%) had empiric antibiotics discontinued or de-escalated in the post-intervention group (hazard ratio=1.46). Overall, the time to discontinuation or de-escalation of empiric antibiotic therapy did not appear significantly different between groups.

The time to targeted therapy after pathogen identification was lower in the post-intervention group (median 7.0 hours vs. median 59.3 hours, $p<0.001$). The BIOFIRE ME Panel reduced the length of stay in the post-intervention group (median 3 days vs. median 4 days, $p=0.3$).

The hospitalization rates and in-hospital mortality were not significantly different between groups.

KEY POINTS

- Use of the BIOFIRE ME Panel can reduce antibiotic exposure without impacting mortality.
- Antibiotic therapy changes were made in absence of direct involvement of antimicrobial stewards.
- Rapid negative results are an important factor in the earlier discontinuation of antibiotics.

Antibiotics, May 2020, 9(6):282

Impact of a Multiplex Polymerase Chain Reaction Assay on the Clinical Management of Adults Undergoing a Lumbar Puncture for Suspected Community-Onset Central Nervous System Infections

Moffa, M.A., Bremmer, D.N., Carr, D., *et al.*

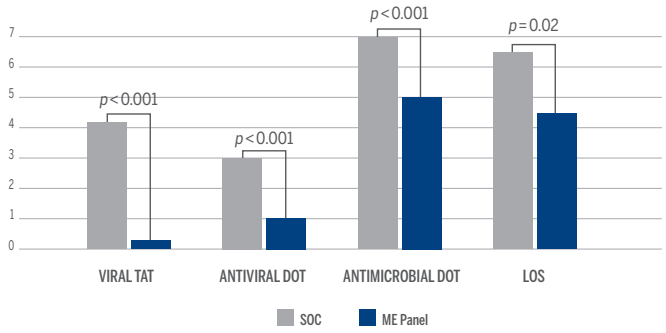
STUDY DESCRIPTION

Pre/post study (n=160) of an adult population at a quaternary academic referral center and community-based teaching hospital to evaluate the impact of reduced turnaround time (TAT) for HSV PCR on antimicrobial therapy duration and length of stay (LOS). TAT for VZV, EV, and CMV were also evaluated. The BIOFIRE® FILMARRAY® Meningitis/Encephalitis (ME) Panel was implemented as the intervention to reduce viral PCR TAT in comparison to standard of care which included sending all viral PCR testing to a reference laboratory.

SUMMARY OF RESULTS AND DISCUSSION

More viral pathogens were identified in the post-intervention period (6.1% vs 7.6%). The impact of testing for viral etiologies in-house compared to sending out to a reference lab on TAT was demonstrated by significant ($p<0.001$) reductions for all viruses evaluated. The median HSV PCR TAT was reduced by more than 3 days (85 vs 4.1 hours). Similar findings were observed for the other viruses evaluated: CMV 94.3 hours, EV 108.3 hours, and VZV 120.0 hours.

Both the median total antiviral and antimicrobial days of therapy (DOT) were significantly ($p<0.001$) reduced by 2 days. Consistently, a reduction of 2.2 days ($p=0.02$) in length of stay was observed.



KEY POINTS

- Testing for viral etiologies by the BIOFIRE ME Panel in-house compared to sending out to a reference lab significantly reduces TAT
- Reduced TAT for viral testing led to a reduction in antiviral DOT, an important consideration for avoiding acute kidney injury
- LOS was significantly reduced by more than 2 days when testing was performed onsite

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ME CLINICAL UTILITY

Diagnostic Microbiology and Infectious Disease, August 2020, 97(4): 115085

Impact of FilmArray meningitis encephalitis panel on HSV testing and empiric acyclovir use in children beyond the neonatal period

Messacar K, Gaensbauer JT, Birkholz M, *et al.*

STUDY DESCRIPTION

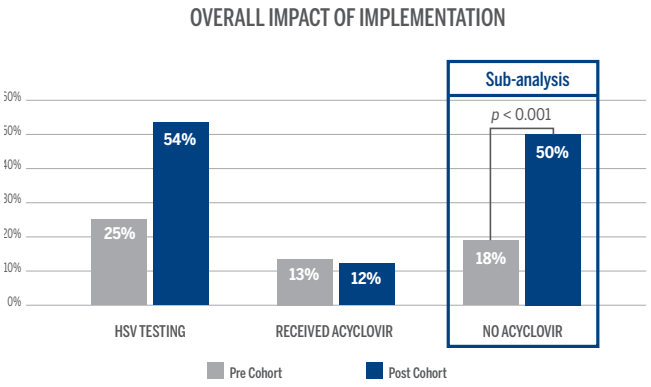
Pre/post study at a U.S. pediatric center evaluating the impact of the BIOFIRE® FILMARRAY® Meningitis/Encephalitis (ME) Panel on acyclovir utilization in infants >60 days old with suspected CNS infection. The study was conducted over an 11-year period (pre n=4,888, post n=408). Testing was encouraged if providers were concerned about >1 pathogen and discouraged in immunocompetent children without encephalitis or pleocytosis (<5 cells/µL). Singleplex HSV PCR testing was available during both periods.

SUMMARY OF RESULTS AND DISCUSSION

Following the implementation of the BIOFIRE ME Panel more patients received HSV testing (25% pre vs 54% post); testing was conducted by the BIOFIRE ME Panel alone most of the time (96%) and by both methods in 4% of cases. A similar proportion of patients received acyclovir in both periods overall (13% pre vs 12% post).

A sub analysis was also performed to compare the impact of an HSV negative result from the BIOFIRE ME Panel compared to singleplex HSV PCR.

Patients testing negative by the BIOFIRE ME Panel were less likely to be started on acyclovir (18% vs 50%, p<0.001) and patients that had therapy initiated had a 3-dose reduction in therapy (2 vs 5, p=0.001), approximately reducing therapy by 24 hours.



KEY POINTS

- Patients testing negative for HSV by the BIOFIRE ME Panel were less likely to be started on acyclovir compared to the singleplex assay, likely a result of the reduced TAT
- Acyclovir therapy duration was reduced by 3 doses in patients testing negative by the BIOFIRE ME Panel

European Journal of Clinical Microbiology and Infectious Diseases, December 2020, 39 (12): 2379-2386

Impact of cerebrospinal fluid syndromic testing in the management of children with suspected central nervous system infection

Posnakoglou L, Siahanidou T, Syriopoulou V, *et al.*

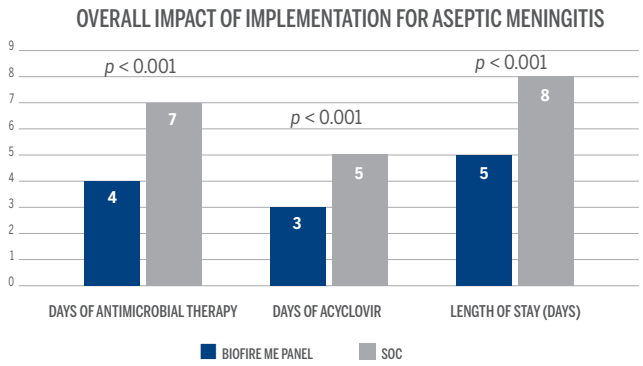
STUDY DESCRIPTION

Prospective randomized study evaluating the impact of the BIOFIRE® FILMARRAY® Meningitis/Encephalitis (ME) Panel on antimicrobial therapy and economic outcomes in a 750-bed pediatric hospital in Greece. The study was conducted over a 1-year period (April 2018-April 2019) with patients ≤16 years with suspected CNS infection and CSF pleocytosis (>15 cells/mm3). 142 CSF samples were tested with the BIOFIRE ME Panel (n=71) or standard of care (SOC) methods (n=71). SOC included bacterial culture and/or singleplex PCR testing, ordered at the discretion of the attending pediatrician.

SUMMARY OF RESULTS AND DISCUSSION

The group tested with the BIOFIRE ME Panel had more positive detections than the control group overall (37 (52.1%) vs 16 (22.5%), $p<0.001$) and more positive viral detections (27/61 (44.2%) vs 11/66 (16.7%) p<0.001). The BIOFIRE ME Panel detected 5 bacterial targets that were not detected by SOC: 2 *N. meningitides*, 2 *S. pneumoniae*, and 1 *E. coli* (all but the *E. coli* detection were confirmed by singleplex PCR). There were no negative detections on the BIOFIRE ME Panel that were positive in bacterial culture.

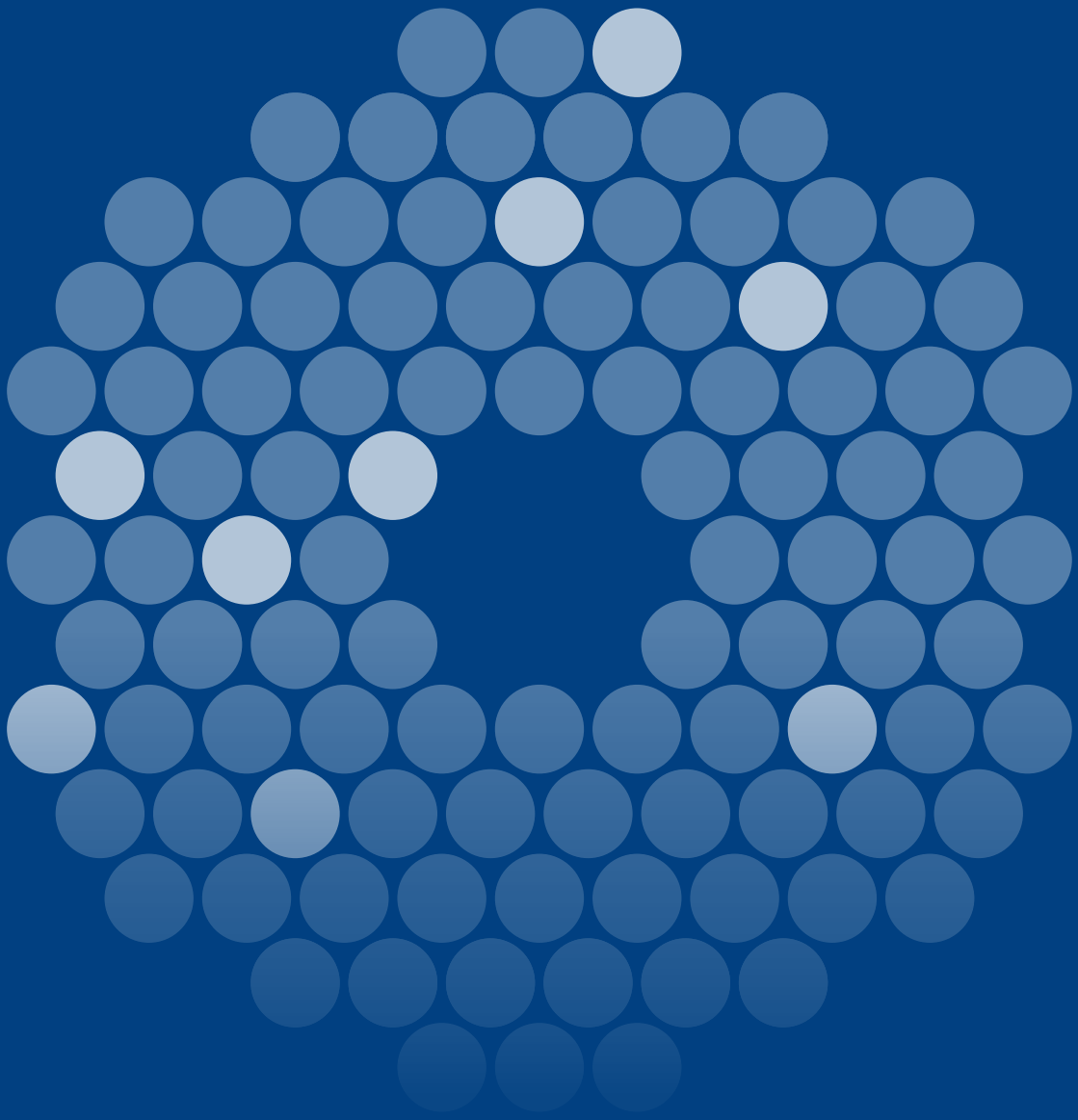
Patients with a positive viral detection by the BIOFIRE ME Panel had fewer days of antimicrobial therapy (4 vs 7), fewer days of acyclovir (3 vs 5), and a reduced duration of hospitalization (5 days vs 7). A sub-analysis of patients ≤ 3 months showed a greater reduction in length of stay (5 days vs 9). All previously mentioned findings were statistically significant with $p<0.001$.



Median hospitalization costs were 31.5% lower overall in the BIOFIRE ME Panel group (€1,042 vs €1,522), and 36% lower for patients ≤ 3 months (€1,042 vs €1,632). Overall cost reduction for the duration of the 1-year study was €22,834.

KEY POINTS

- Patients who were tested with the BIOFIRE ME Panel had reduced cost, reduced antimicrobial therapy, and reduced LOS
- The BIOFIRE ME Panel detected more targets than SOC with no false negative results
- Increased sensitivity to bacterial detection (especially after initiation of empiric antibiotics) was demonstrated and is critical for appropriate treatment of bacterial meningitis



BIOFIRE®
JOINT INFECTION PANEL

European Journal of Clinical Microbiology & Infectious Diseases Feb 2023; 42(2):169-176

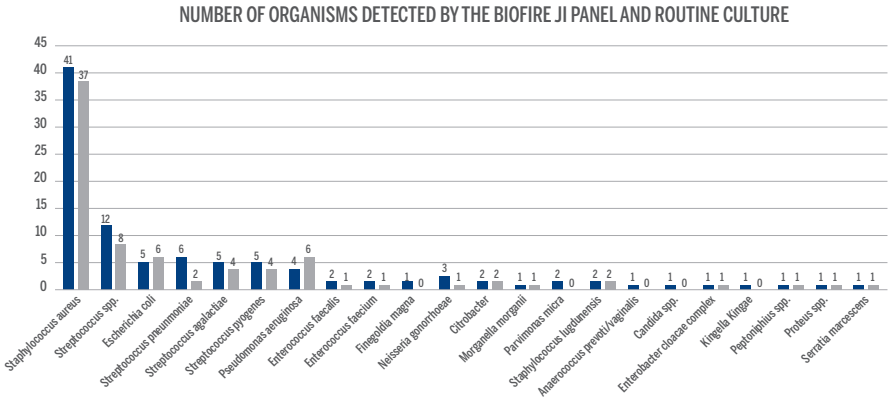
A multicentre evaluation and expert recommendations of use of the newly developed BioFire Joint Infection polymerase chain reaction panel

Saeed K., Marsh M., Aldridge C., *et al.*

STUDY DESCRIPTION

Observational retrospective comparative analysis conducted across 8 hospitals in the UK and Ireland to evaluate the performance of the BIOFIRE® Joint Infection (JI) Panel compared to routine culture methods on synovial fluid samples from March 2021 to March 2022. Additionally, a multidisciplinary team (MDT) discussed the potential clinical impact of the BIOFIRE JI Panel.

SUMMARY OF RESULTS AND DISCUSSION



A total of 399 synovial fluids were tested, originating mainly from knee and hip samples. Patient sample ages ranged from >56 yrs. (67.85%), 19-55 yrs. (29.55%), <18 yrs. (1.65%), and unknown (0.95%). The overall positive percent agreement (PPA) between the BIOFIRE JI Panel and the routine culture results for on-panel organisms was 91.6% [83.6%; 95.9%] and the overall negative percent agreement (NPA) was 93% [89.7%; 95.4%]. The BIOFIRE JI Panel demonstrated high diagnostic yield and detected additional previously missed microorganisms (Fig.1.), including 24 samples when the synovial fluid culture was previously negative. Sixteen synovial fluid cultures were positive for off-panel organisms. The BIOFIRE JI Panel detected resistance markers in 5 samples, 4 of these resistance markers were also identified following routine diagnosis.

The results of MDT's assessment of the BIOFIRE JI Panel recommended 1) to target patients with a clinical suspicion of acute septic arthritis and 2) to be restricted by a specific procedure at site on when to use it. The potential benefits of the BIOFIRE JI Panel are a prompt diagnosis, earlier targeted therapy, and quicker time to a differential diagnosis with negative results.

KEY POINTS

- The PPA and NPA for the BIOFIRE JI Panel and routine culture for on-panel organisms were 91.6% and 93% respectively.
- The BIOFIRE JI Panel detected additional organisms and had 100% detection of resistance markers.
- The MDT assessed the BIOFIRE JI Panel's use in 1) adult and pediatric patient populations, 2) in combination with specialist input, and 3) in practice compared to standard methods. The ability of the BIOFIRE JI Panel to provide rapid results was assessed as having potential clinical impact on patient management.

Journal of Clinical Microbiology Dec. 2022; 60(12):e0112622

Comparison of the BioFire Joint Infection Panel to 16S Ribosomal RNA Gene-Based Targeted Metagenomic Sequencing for Testing Synovial Fluid from Patients with Knee Arthroplasty failure

Azad M., Wolf M., Patel R., *et al.*

STUDY DESCRIPTION

A retrospective study conducted in a US site comparing the sensitivity and specificity of the BIOFIRE® Joint Infection (JI) Panel versus targeted Metagenomic Sequencing (tMGS). The sample pool comprised 60 archived synovial fluid samples from patients diagnosed with prosthetic knee infections (following IDSA Guidelines) and with or without positive cultures. tMGS is a technique that relies initially on PCR amplification of the conserved, bacterial 16S rRNA gene followed by a Next-Generation Sequencing.

SUMMARY OF RESULTS AND DISCUSSION

The results of both methods are presented in Table 1. Among the 60 samples, 41 were culture positive, 18 culture negative, and 1 without a culture sample. 39 out of the 41 culture positive samples were diagnosed as having Prosthetic Joint Infections (PJI).

Among the 18 culture negatives and 1 without culture sample, 5 samples were from patients diagnosed with PJI. Both the BIOFIRE JI Panel and tMGS identified *Staphylococcus aureus* in 3 out of 5 of these samples.

Overall sensitivities for PJI diagnosis were 56% for the BIOFIRE JI Panel (24/43 as 1 BIOFIRE JI Panel was invalid), and 93% (41/44) for tMGS, mainly due to a high number of samples with *Staphylococcus epidermidis*.

Overall sensitivities for culture-positive PJI with on-panel organisms were 91% (21/23) for the BIOFIRE JI panel, and 96% for tMGS (23/24).

Overall specificities for PJI diagnosis were 100% (16/16) for the BIOFIRE JI Panel, and 94% (15/16) for tMGS (false positive with *Streptococcus australis*).

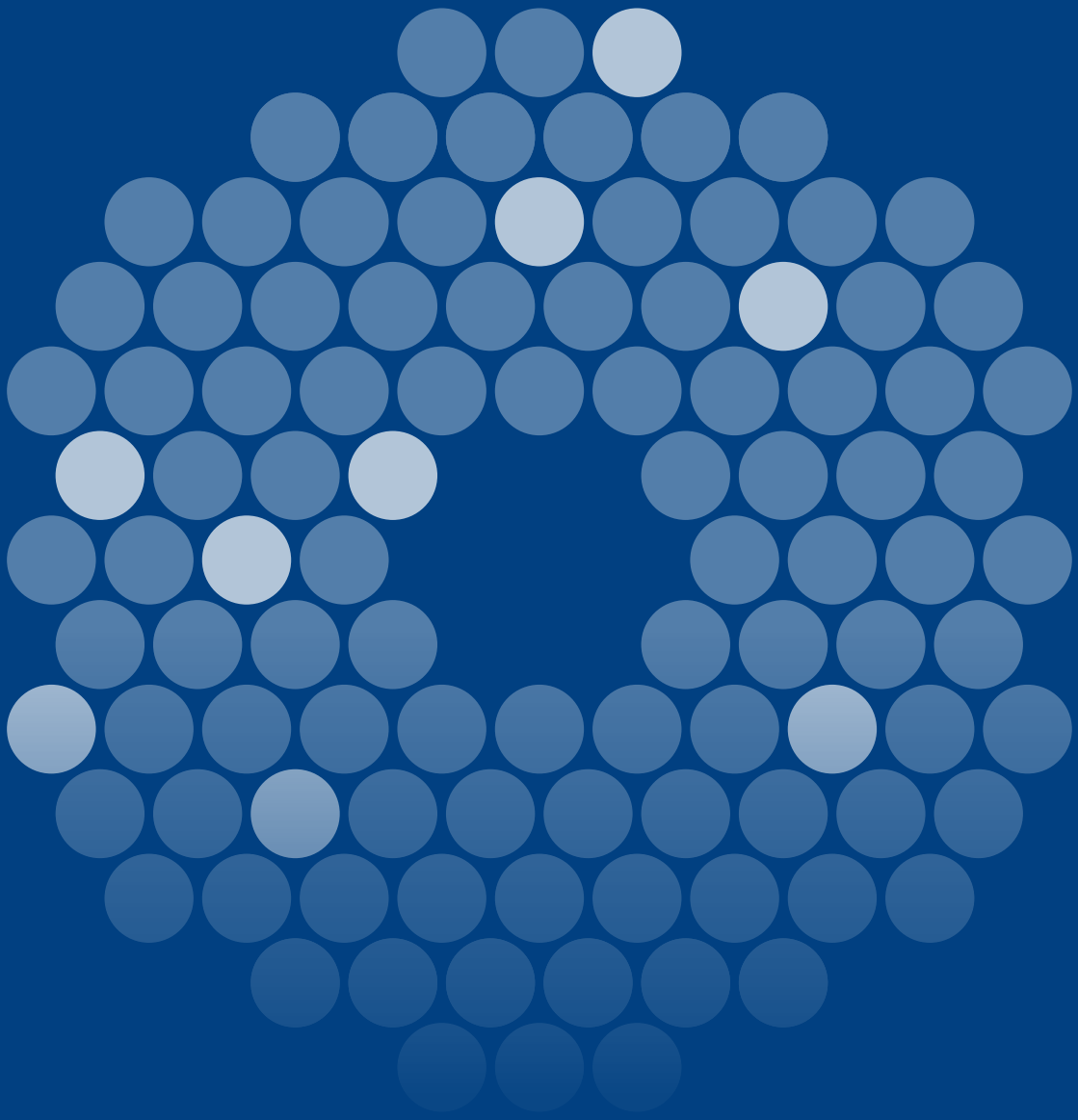
ORGANISM OR GROUP		BIOFIRE JI PANEL	tMGS
On panel	*Staphylococcus aureus*	11/11	12/12
	Enterococcus aureus	1/1	1/1
	Staphylococcus lugdunensis	2/2	2/2
	Streptococcus salivarius group	0/1	1/1
	Streptococcus mitis group	2/2	2/2
	Group C *Streptococcus* species	1/1	1/1
	Pseudomonas aeruginosa	1/1	1/1
	Serratia marcescens	2/2	2/2
	Enterobacter cloacae complex	0/1	1/1
	Candida albicans	1/1	0/1
Off panel	*Staphylococcus epidermidis*	0/12	12/12
	Corynebacterium striatum	0/1	1/1
	Lelliottia species	0/1	1/1
	Haemophilus parainfluenzae	0/1	1/1

Table 1. Organism-specific findings of the BIOFIRE JI Panel and tMGS in PJI cases with culture-positive synovial fluid samples (n=39)

A proposed algorithm for PJI diagnosis suggests use of the BIOFIRE JI Panel after a negative microbiology culture. If the results of BIOFIRE JI Panel are negative, then proceeding to tMGS is suggested.

KEY POINTS

- Study limitations include low sample size and the testing of only frozen samples, including numerous samples with *Staphylococcus epidermidis,* thereby potentially biasing the sample pool.
- BIOFIRE JI Panel is a rapid and easy-to-use test with good sensitivity for on-panel organisms and the ability to detect antimicrobial resistance; however, the BIOFIRE JI Panel demonstrated a low sensitivity in PJI due the absence of *Staphylococcus epidermidis*.
- tMGS has excellent overall sensitivities, however it requires a trained microbiologist for results interpretation and careful consideration of organisms that are possible contaminants.



BIOFIRE® SYNDROMIC TRENDS

Open Forum Infectious Diseases, Jun 2022; 9(7):ofac296

Epidemiology of Antimicrobial Resistance Among Blood and Respiratory Specimens in the United States Using Genotypic Analysis From a Cloud-Based Population Surveillance Network

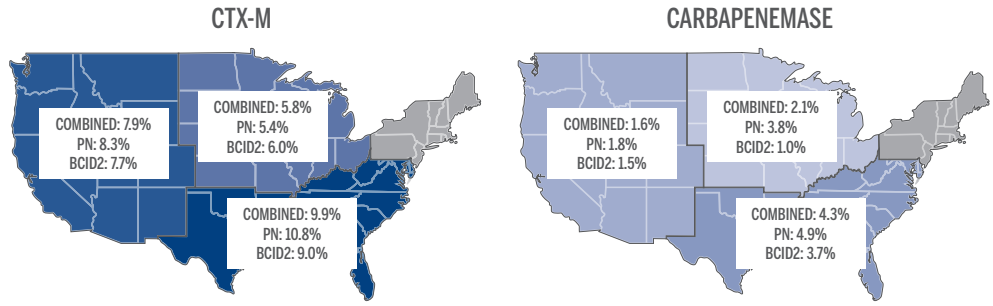
Timbrook T., Olin K., Spaulding U., *et al.*

STUDY DESCRIPTION

A retrospective observational study of the BIOFIRE® FILMARRAY® Pneumonia (PN) Panel and the BIOFIRE® Blood Culture Identification 2 (BCID2) Panel data from BIOFIRE® Syndromic Trends (Trend), a cloud-based population surveillance network. Data were utilized from 2019 to 2021 for both gram-positive and negative organisms along with their antimicrobial resistance (AMR) gene targets as well as the detections of *Candida auris*. Proportions of detections were evaluated by region and panel. Codetections of AMR and proportion of detections per organism were analyzed for gram-negative organisms.

SUMMARY OF RESULTS AND DISCUSSION

In total, 26,912 BIOFIRE Panels were tested. Proportion of AMR detections were greatest in the South and among respiratory specimens. Resistance proportions for gram-negative were 7.0% CTX-M and 2.9% carbapenemases while gram-positive AMR reflected 34.9% for methicillin-resistant *Staphylococcus aureus* and 15.9% for vancomycin-resistant enterococci. Emerging AMR detections occurred with 10 mcr-1 and 4 *C. auris* positives occurring.[1]



KEY POINTS

- Near real-time characterization of these resistance types is important for local guideline development and outbreak detection, regional benchmarking, and informing national public health initiatives.
- Nearly pandrug resistant detections (e.g *mcr-1* and bla_{NDM} codetections) occurred, highlighting the importance of AMR surveillance.

1. This figure is used by permission of *Infectious Diseases Society of America* and *HIV Medicine Association*. Timbrook *et al.* do not endorse the content of this slide. Source material DOI: 10.1093/ofid/ofac296.

JMIR Public Health and Surveillance Aug 2022; 8(8): e34757

Impact of COVID-19 Social Distancing Mandates on Gastrointestinal Pathogen Positivity: Secondary Data Analysis

Palmer T., Benson L.S., Porucznik C., *et al.*

STUDY DESCRIPTION

A retrospective observational study was performed to assess the impact of social distancing policies on gastrointestinal pathogens from January 1, 2019 to August 31, 2020 in the United States. Deidentified test result data from the BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel were acquired from BIOFIRE® Syndromic Trends (TREND), a cloud-based surveillance network. Three pathogens, adenovirus F40 and 41, norovirus GI/GII and *Escherichia coli* O157, representing different transmission routes were chosen for the final analysis. An interrupted time series analysis was used to compare rates of pathogen detection over time.

SUMMARY OF RESULTS AND DISCUSSION

84,223 tests were collected from nine states including California, Colorado, Illinois, Kansas, Michigan, Nebraska, Ohio, Texas, and Wisconsin. Most pathogen positivity rates decreased immediately after social distancing mandates were implemented, except for *E. coli* O157 in Kansas, Michigan, and Nebraska.

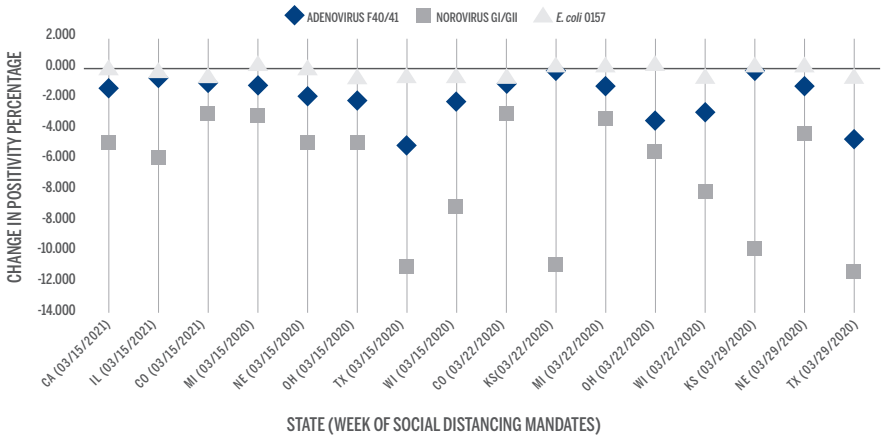


Figure 1. Change in positivity percentage during the week of social distancing mandates.[1]

KEY POINTS

- Norovirus GI/GII had the largest decrease in positivity rates during the study period.
- Social distancing measures had minimal impact on positivity rates of *E. coli* O157.

Open Forum Infectious Diseases, Mar 2021; 8(7): ofab133

The Effects of Social Distancing Policies on Non-SARS-CoV-2 Respiratory Pathogens

Nawrocki J, Olin K, Holdrege M, *et al.*

STUDY DESCRIPTION

A retrospective observational study performed in 2020 in the US. The goal of the study was to assess the impact of social distancing policies on non-SARS-CoV-2 respiratory pathogens from January 1, 2020 to May 1, 2020 in nine states. Detection rates were acquired from BIOFIRE® Syndromic Trends. Social distancing policies included foreign travel and large gathering bans, closures of schools, restaurants, and gyms, as well as stay-at-home orders. Linear mixed-effect models were used to compare observed vs. historical rates of pathogen detection.

SUMMARY OF RESULTS AND DISCUSSION

National pathogen detections rates were lower than historical averages during the months of March and April. National pathogen rates were within the historical average during the first two weeks in March, then showed a reduction after the Foreign Travel Ban was implemented by the US on March 11, 2020.

Human rhinovirus/enterovirus and human metapneumovirus showed a decrease in pathogen detections after March 11, 2020. Adenovirus and parainfluenza virus began to decrease before the Foreign Travel Ban was put into effect. Detection rates also fell for respiratory syncytial virus, influenza A, and non-SARS-CoV-2 coronaviruses. Influenza B rates also decreased during the study period but showed an increase in detections sooner than what has been seen historically. Bacterial detections did not decrease but remained within the historical range. All nine states showed a decrease in pathogen detections, with New York, Nebraska, Kansas, and California seeing the decrease within one week after the Foreign Travel Ban.

The mathematical model showed that all social distancing policies except Federal Guidelines had a statistically significant impact resulting in decreased total pathogen detections. In particular, Stay at Home Orders and Public Closures were associated with statistically significant drops in human rhinovirus/enterovirus and human metapneumovirus. Influenza A detections dropped significantly with the implementation of the Foreign Travel Ban.

It is important to note that mask mandates were not evaluated in the study. Additionally, test utilization rates increased to up to 300% during the study period compared to rates from 2019, but returned to historical levels by May 2021.

KEY POINTS

- 15% reduction in total detection rate from March-April 2020.
- No decrease in detection rate was seen in bacteria.
- Implementing social distancing policies resulted in a decrease of spring seasonal viruses.

PLoS One, Apr 2021; 16(4):e0250767

Real-Time Gastrointestinal Infection Surveillance Through a Cloud-Based Network of Clinical Laboratories

Ruzante J., Olin K., Munoz B., *et al.*

STUDY DESCRIPTION

A retrospective observational study performed in 2019 in the US. The primary aim of the study was to describe the pathogen detection rates of the BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel from January 1, 2016 to October 31, 2018. Additionally, the BIOFIRE GI Panel pathogen detection rates were compared to eight pathogens monitored by the Centers for Disease Control and Prevention Foodborne Diseases Active Surveillance Network (FoodNet). The BIOFIRE GI Panel detection rates were acquired from BIOFIRE® Syndromic Trends.

SUMMARY OF RESULTS AND DISCUSSION

During the study period, 50,192 pathogens were detected. 71% were bacteria, 25% were viruses, and 4% were parasites. The most common detections were *Clostridium difficile* (30%), enteropathogenic *Escherichia coli* (EPEC) (16%), and norovirus (11%). No seasonal trends were seen for sapovirus, adenovirus, *Clostridium difficile*, *Vibrio*, and *Y. enterocolitica*. The winter season showed an increase in detection rates for astrovirus and norovirus, while the months of April and May showed an increase in rotavirus detections. *Camplylobacter*, *Salmonella*, *Plesiomona shigelloides*, EPEC, and *cryptosporidium* had higher positive detection rates in the summer months.

The co-detection rate was 10.2%. Most (80%) co-detections had two pathogens detected; the remaining 20% had three detections. Notably, co-detections were more likely to be seen in *P. shigelloides*, *E. histolytica*, enterotoxigenic E. coli (ETEC) and enteroaggregative *E. coli* (EAEC) cases. Positive correlations were seen between detections of *Shigella*/Enteroinvasive *E. coli* and *E. histolytica* as well as ETEC and enteroaggregative *E. coli* (EAEC), however the correlation is weak. Conversely, negative correlations were observed between *Clostridium difficile* and other pathogens.

The proportion of detections of foodborne pathogens were similar between the BIOFIRE GI Panel and FoodNet. In both cases, *Campylobacter* and *Salmonella* had the highest rates of detection and *Vibrio* and *C. cayetanensis* had the lowest. However, the BIOFIRE GI Panel detected higher proportions of all pathogens except *Campylobacter* and *Salmonella*.

KEY POINTS

- The most commonly detected pathogens were *Clostridioides difficile*, enteropathogenic *Escherichia coli* (EPEC), and norovirus.
- The co-detection rate was 10.2%.
- There was a weak positive correlation between co-detections of *Shigella*/Enteroinvasive *E. coli* and *E. histolytica* as well as enterotoxigenic *E. coli* (ETEC) and enteroaggregative *E. coli* (EAEC).

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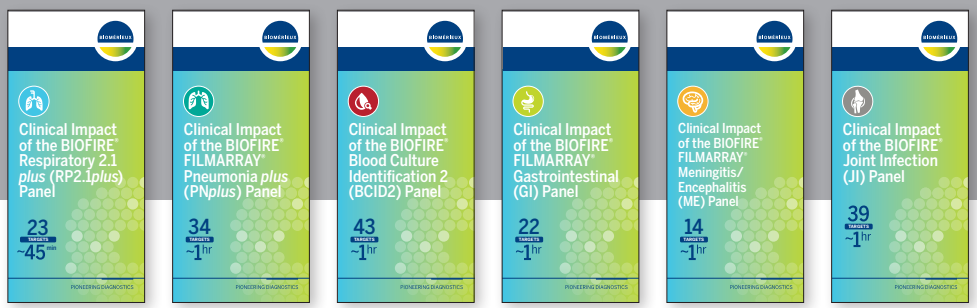

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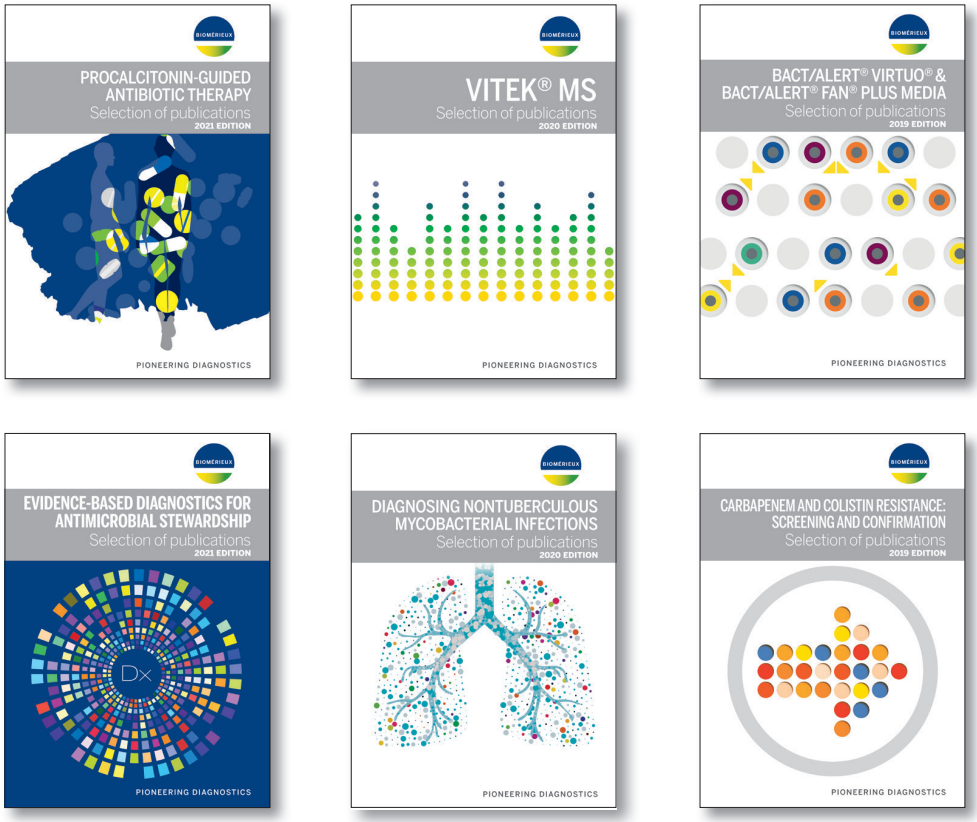

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