

Diagnostic Tests

What Physicians Need to Know

BioFire Respiratory Panel for the Detection of Viruses and Bacteria

Nick F. Bennett, DO, MBA, FAAFP, and Ashley L. Bissaillon, DO

Madigan Army Medical Center Family Medicine Residency, Tacoma, Washington

Test	Indication	Population	Cost*
BioFire Respiratory 2.1 Panel	Rapidly detect common viral and bacterial pathogens†	Any patient with signs or symptoms of respiratory tract infection	\$417

*—Reimbursement rate according to the 2023 Centers for Medicare and Medicaid Services clinical laboratory fee schedule. This price is the out-of-pocket cost to the patient.^{10,11}

†—Viruses: adenovirus, coronavirus (229E, HKU1, NL63, OC43), Middle East respiratory syndrome coronavirus, SARS-CoV-2, human metapneumovirus, human rhinovirus/enterovirus, influenza A virus (A/H1, A/H3, A/H1-2009), influenza B virus, parainfluenza virus (1, 2, 3, 4), respiratory syncytial virus. Bacteria: *Bordetella parapertussis*, *B. pertussis*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*.¹

The BioFire Respiratory 2.1 Panel (RP2.1) is a multiplex polymerase chain reaction (PCR) test that identifies nucleic acids from 23 different bacteria and viruses that commonly cause upper and lower respiratory tract infections. It is a point-of-care nasopharyngeal swab that provides quick and accurate results.¹ The U.S. Food and Drug Administration granted the BioFire RP2.1 test emergency use authorization in May 2020 and marketing authorization in March 2021, making it the first test including SARS-CoV-2 to be marketed beyond the height of the pandemic.²

Accuracy

The BioFire RP2.1 tests for 19 viral and four bacterial pathogens. *Table 1* summarizes data from a prospective multicenter study of 1,612 respiratory samples from symptomatic patients in three hospitals and another prospective multicenter study of 524 samples.^{3,4}

This series is coordinated by Natasha Pyzocha, DO, contributing editor.

A collection of Diagnostic Tests published in *AFP* is available at <https://www.aafp.org/afp/diagnostic>.

Author disclosure: No relevant financial relationships.

Benefit

Although the BioFire RP2.1 test allows for identification of many common respiratory tract infections in 45 minutes, there is limited clinical benefit. A 2015 observational study of outpatient respiratory pathogen testing used in 295 adults was notable for a decrease in antibiotic use in those who tested positive for influenza.⁵ However, there was no difference in antibiotic use in those who tested positive for other viruses or negative for all viruses (48.6% and 49.3%, respectively). A 2019 retrospective cohort study of 243 adults discharged from the emergency department and 243 adults who were hospitalized had similar findings.⁶ In patients discharged from the emergency department, antibiotic use was lower only in those who tested positive for influenza, with an average of 0.5 days of antibiotic therapy compared with 2.7 days for those with negative test results and 1.8 days for those negative for influenza. No statistically significant decrease in antibiotic use occurred in hospitalized patients who received respiratory pathogen testing. In a 2019 randomized controlled study of 800 hospitalized adults, adding respiratory pathogen testing to routine real-time PCR reduced the duration of intravenous antibiotics (seven vs. eight days; $P < .001$) and shortened the length of hospitalization (eight vs. nine days; $P < .001$) compared with real-time PCR testing alone.⁷

TABLE 1

Accuracy Data for the BioFire RP2.1 Test Extrapolated From 2018 and 2022 Multicenter Clinical Studies

Pathogen	No. detected	Sensitivity (%)	Specificity (%)	LR+	LR–
Viruses					
Adenovirus	118	94.6	96.9	30.5	0.06
Coronavirus HKU1	16	100	99.2	125.0	0.00
Coronavirus NL63	50	100	99.4	166.7	0.00
Coronavirus 229E	16	91.7	99.7	305.7	0.08
Coronavirus OC43	38	80.5	99.7	268.3	0.20
MERS-CoV	0	NA	100	NA	NA
SARS-CoV-2	524	98.4	98.9	0.0	0.00
Human metapneumovirus	81	97.3	99.5	194.6	0.03
Human rhinovirus/enterovirus	502	97.5	93.5	15.0	0.03
Influenza A	78	100	100	NA	0.00
Influenza A/H1	0	NA	100	NA	NA
Influenza A/H3	4	100	100	NA	0.00
Influenza A/H1-2009	74	100	100	NA	0.00
Influenza B	16	100	99.9	1000.0	0.00
Parainfluenza virus 1	10	100	99.9	1000.0	0.00
Parainfluenza virus 2	54	97.9	99.5	195.8	0.02
Parainfluenza virus 3	53	95.6	99.4	159.3	0.04
Parainfluenza virus 4	16	100	99.6	250.0	0.00
Respiratory syncytial virus	199	99.4	98.3	58.5	0.01
Bacteria					
<i>Bordetella pertussis</i>	3	66.7	99.9	667.0	0.33
<i>B. parapertussis</i>	6	85.7	100	NA	0.14
<i>Chlamydia pneumoniae</i>	6	100	99.9	1000.0	0.00
<i>Mycoplasma pneumoniae</i>	28	95.8	99.7	319.3	0.04

LR+ = positive likelihood ratio; LR– = negative likelihood ratio; MERS-CoV = Middle East respiratory syndrome coronavirus; NA = not available.

Information from references 3 and 4.

In a quasi-randomized trial of 545 hospitalized adults, no statistically significant correlation was identified between respiratory pathogen testing and length of hospitalization or duration of antibiotic use, but there was a decrease in time to first dose of antivirals when using respiratory pathogen testing compared with routine, laboratory-based respiratory PCR and serology testing.⁸ In a 2016 retrospective, case-control study of 2,430 children, there were decreased antibiotic use (four vs. five median antibiotic days; $P < .01$) and fewer chest radiographs ordered (59% vs. 78%; $P < .01$)

for those who underwent respiratory pathogen testing, compared with non-PCR methods.⁹ More than one-half (54.3%) of children whose results were positive for a viral pathogen on respiratory pathogen testing still received antibiotics.

Harms

Although the BioFire RP2.1 test includes 23 different viruses and bacteria, it is not comprehensive. This testing can lead to anchoring bias, and an initial positive result may lead to the absence of a broader differential. Positive results do not

rule out coinfection from other organisms not being tested.

Cost

The BioFire RP2.1 test is authorized for use on the BioFire FilmArray 2.0 and BioFire Torch Systems. The reimbursement rate for the consumable RP2.1 test is \$417, according to the 2022 Centers for Medicare and Medicaid Services clinical laboratory fee schedule; however, respiratory panels testing for six or more pathogens are not eligible for this reimbursement, per Medicare policy.^{10,11} This is in contrast to influenza A and B, SARS-CoV-2, and respiratory syncytial virus multiplex testing, which is fully covered by Medicare at a reimbursement rate of \$143.¹² Additionally, the capital purchase of the BioFire FilmArray and BioFire Torch Systems can cost \$37,500 and \$35,000, respectively (BioFire Diagnostics sales, personal communication, December 29, 2022).

Bottom Line

The BioFire RP2.1 is a rapid and accurate test that can assist with timely antiviral therapy and infection control measures, but evidence is mixed over its clinical benefit in decreasing the length of antibiotic use in adults.⁵⁻⁹ In agreement with the Infectious Diseases Society of America 2018 recommendations, broad respiratory pathogen panels should be used only when they affect patient management, such as to alter empiric antimicrobial therapy or to change infection control measures.¹³ Instead of ordering large multiplex tests, physicians should consider using tests of commonly suspected pathogens based on location, season, and patient history.¹³ However, immunocompromised and critically ill patients with pneumonia and exacerbations of airway disease may benefit from the use of the BioFire RP2.1 test, which is endorsed by the Infectious Diseases Society of America's 2020 diagnostic committee.¹⁴

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army, the U.S. Department of Defense, or the U.S. government.

Address correspondence to Nick F. Bennett, DO, MBA, FAAFP, at nick.f.bennett.civ@health.mil. Reprints are not available from the authors.

References

1. The BioFire Respiratory 2.1 (RP2.1) Panel. Accessed October 20, 2022. <https://www.biofire.com/products/the-filmarray-panels/filmarrayrp/>
2. U.S. Food and Drug Administration. FDA permits marketing of first SARS-CoV-2 diagnostic test using traditional premarket review process. March 17, 2021. Accessed October 20, 2022. <https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-first-sars-cov-2-diagnostic-test-using-traditional-premarket-review-process>
3. Leber AL, Everhart K, Daly JA, et al. Multicenter evaluation of BioFire FilmArray Respiratory Panel 2 for detection of viruses and bacteria in nasopharyngeal swab samples. *J Clin Microbiol*. 2018;56(6):e01945-e17.
4. Berry GJ, Zhen W, Smith E, et al. Multicenter evaluation of the BioFire Respiratory Panel 2.1 (RP2.1) for detection of SARS-CoV-2 in nasopharyngeal swab samples. *J Clin Microbiol*. 2022;60(5):e0006622.
5. Green DA, Hitoalaj L, Kotansky B, et al. Clinical utility of on-demand multiplex respiratory pathogen testing among adult outpatients. *J Clin Microbiol*. 2016;54(12):2950-2955.
6. Manatrey-Lancaster JJ, Bushman AM, Caligiuri ME, et al. Impact of BioFire FilmArray respiratory panel results on antibiotic days of therapy in different clinical settings. *Antimicrob Steward Healthc Epidemiol*. 2021;1(1):e4.
7. Shengchen D, Gu X, Fan G, et al. Evaluation of a molecular point-of-care testing for viral and atypical pathogens on intravenous antibiotic duration in hospitalized adults with lower respiratory tract infection: a randomized clinical trial. *Clin Microbiol Infect*. 2019;25(11):1415-1421.
8. Andrews D, Chetty Y, Cooper BS, et al. Multiplex PCR point of care testing versus routine, laboratory-based testing in the treatment of adults with respiratory tract infections: a quasi-randomised study assessing impact on length of stay and antimicrobial use. *BMC Infect Dis*. 2017;17(1):671.
9. Subramony A, Zachariah P, Krones A, et al. Impact of multiplex polymerase chain reaction testing for respiratory pathogens on healthcare resource utilization for pediatric inpatients. *J Pediatr*. 2016;173:196-201.e2.
10. The BioFire CodeMap. Accessed October 20, 2022. <https://www.codemap.com/biofire/index.cfm?page=respiratory>
11. United HealthCare. Laboratory services policy, professional. Accessed November 1, 2022. <https://www.uhcprovider.com/content/dam/provider/docs/public/policies/comm-reimbursement/COMM-Laboratory-Services-Policy.pdf>
12. Centers for Medicare and Medicaid Services. 22CLABQ3. Item #87636. Accessed December 29, 2022. <https://www.cms.gov/medicaremedicare-fee-service-payment/clinicalabfeeschedclinical-laboratory-fee-schedule-files/22clabq3>
13. Miller JM, Binnicker MJ, Campbell S, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the Infectious Diseases Society of America and the American Society for Microbiology. *Clin Infect Dis*. 2018;67(6):e1-e94.
14. Hanson KE, Azar MM, Banerjee R, et al. Molecular testing for acute respiratory tract infections: clinical and diagnostic recommendations from the IDSA's Diagnostics Committee. *Clin Infect Dis*. 2020;71(10):2744-2751. ■