

Opportunities for Point-of-Care Diagnostics in Outpatient Pediatric Centers to Influence Antibiotic Prescribing Patterns

Antibiotics are frequently prescribed to treat a variety of conditions in patients who benefit from their use.¹ Although beneficial, antibiotic use can lead to common adverse effects that include rashes and diarrhea in addition to less common events, such as severe allergic reactions and *Clostridium difficile* infection.¹ Unnecessary antibiotic prescribing is a risk factor for antibiotic resistance, which can result in increased healthcare costs, morbidity, and mortality.¹ In 2016, to combat the growing threat of antibiotic resistance, the president's National Action Plan called for a goal of reducing antibiotics prescribed for acute respiratory conditions by 50% in 2020.² Efforts to measure antibiotic prescribing patterns help encourage antibiotic prescribing only for infections that warrant their use, ensure correct dosing and duration, and minimize the occurrence of misdiagnoses. All of these steps are fundamental to reducing inappropriate antibiotic prescribing.¹

Antibiotic Prescribing Patterns for Acute Respiratory Infections

Bronchitis, otitis media, pharyngitis, sinusitis, tonsillitis, pneumonia, and the common cold are among some of the most frequently diagnosed acute respiratory infections for which antibiotics are prescribed.³ Among ambulatory care visits in the United States, only 50% of antibiotic prescriptions for acute respiratory infections (ARIs) were estimated to be appropriate.⁴ Using ICD-9-CM diagnosis codes to identify children (< 18 years) who had 5 specific ARIs (ie, acute otitis media, sinusitis, bronchitis, upper respiratory infection, and pharyngitis), a retrospective analysis was conducted using data collected from the National Ambulatory Medical Care Survey from 2000 to 2010 to determine rates of outpatient visits and antimicrobial prescribing.⁵ Additionally, bacterial prevalence rates for the 5 ARIs were estimated from a meta-analysis

of studies published from 2000 to 2011.⁵ A mean of 56.9% (95% CI, 50.8%–63.1%) of ARI visits led to overall antibiotic prescribing while the overall expected prescribing rate of the 5 ARIs was 27.4% (95% CI, 26.5%–28.3%), based upon the estimated prevalence rates.⁵ This difference in prescribing compared with the expected prescribing rate represents approximately 11.4 million unnecessary antibiotic prescriptions to pediatric patients annually.⁵

Factors Contributing to Inappropriate Antibiotic Prescribing Patterns

Most antibiotic healthcare expenditures in the United States result from prescribing in the outpatient setting, although antibiotic use is not always necessary.⁶ The decision-making process used by physicians to prescribe antibiotics is complex and can be influenced by both clinical and nonclinical factors.⁶ These factors include:

- *Pressure from parents.* Clinicians feel pressured by parents to prescribe antibiotics to pediatric patients; pediatricians express that they have prescribed antibiotics, even when they are not clinically indicated as a result of the “culture of expectations” held by parents.⁷
- *Time constraints.* Busy appointment schedules, especially during peak seasons of respiratory illness, leave little time for clinicians to spend with each patient. Pediatricians report that it is quicker to prescribe an antibiotic than to explain to parents why it is not necessary.⁷
- *Diagnostic uncertainty regarding the type of infection (eg, bacterial or viral).* Clinicians indicate that despite treatment guidelines, they are not always confident of whether the infection is bacterial; they sometimes prescribe antibiotics to avoid undertreating the infection.⁸ ▶

Diagnostic Testing

Diagnostic testing is useful to clinicians in determining if an infection is bacterial or viral, which contributes to prescribing decisions.⁶ Although molecular-based respiratory panels are often used in hospitals and emergency department settings, the cost and extensive turn-around time associated with these diagnostics result in infrequent use in outpatient practices.⁹ Cost-effective, accurate, and sensitive diagnostic testing that can provide rapid results through an on-demand platform would be beneficial in the ambulatory setting to minimize inappropriate antibiotic prescribing, further improving the quality of patient care.^{1,10}

Onsite Respiratory Testing

Traditionally, clinical care of respiratory tract infections is designed around syndromic disease management and centralized laboratory testing.¹¹ Now, laboratory testing is shifting to decentralized, near-patient settings, creating a simplified process with faster results.¹² With the shift toward value-based care, syndromic testing from BioFire Diagnostics, LLC contributes to doing what is best for the patient while reducing untimely and expensive send-out tests. The BioFire® FilmArray® Respiratory EZ (RP EZ) Panel, which is cleared for use with the BioFire® FilmArray® 2.0 EZ System, tests for a comprehensive set of 14 respiratory targets, facilitating rapid near-patient molecular diagnostic testing. Attributes of the BioFire® FilmArray® 2.0 EZ System Configuration include:

- Designed for use with the BioFire RP EZ Panel in CLIA-waived testing sites, including clinics and physician offices
- Enables decentralized molecular testing throughout a provider network
- Features a simplified and intuitive interface and results report

Exploring the Real-world Use of the BioFire RP EZ Panel

The real-world use of the BioFire RP EZ Panel was investigated and results were published in *The Pediatric Infectious Disease Journal* (March 2020, 39 (3): 188-191 doi: 10.1097/INF.0000000000002544).⁹ The following is a summary of the key findings from that study.

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

Study Description

This is a prospective study to evaluate the impact of using the BioFire 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 1-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 1**⁹, the overall positivity rate and co-detection rates were similar.

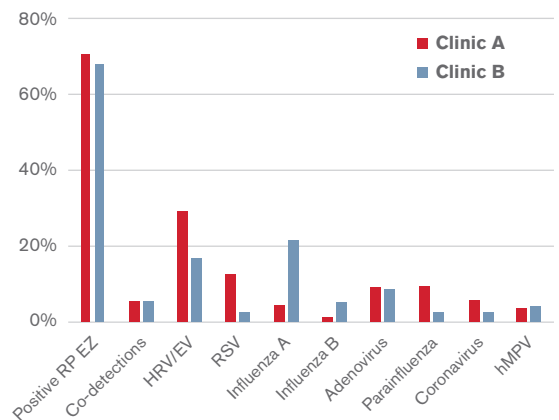


Figure 1. Pathogen Detection Rates by Clinic

EV, enterovirus; hMPV, human metapneumovirus; HRV, human rhinovirus; RP EZ, BioFire RP EZ Panel; RSV, respiratory syncytial virus.

Adapted from: Beal SG, Posa M, Gaffar M, et al. Performance and Impact of a CLIA-waived, Point-of-care Respiratory PCR Panel in a Pediatric Clinic. *Pediatr Infect Dis J.* 2020;39(3):188-191. doi:10.1097/INF.0000000000002544

Table 1. Key Findings of Appropriate Use of Antimicrobials with BioFire® RP EZ Panel Detection

BioFire RP EZ Panel Detection	Study Defined Appropriate Treatment	Clinic A	Clinic B	P value
None	No antibiotics or antiviral	83/85 (97.6%)	38/42 (90.5%)	.0923
Influenza	Oseltamivir	6/19 (31.6%)	27/36 (75%)	.0018
RSV	No antibiotics or antivirals	37/38 (97.4%)	3/3 (100%)	1.0000
Virus other than influenza/RSV	No antibiotics or antivirals	152/155 (98.1%)	48/51 (94.1%)	.16727
Atypical bacteria	Appropriate antibiotic	1/1 (100%)	0/0	--
Total		279/298 (93.6%)	116/132 (87.9%)	.0445

EV, enterovirus; hMPV, human metapneumovirus; HRV, human rhinovirus; RP EZ, BioFire RP EZ Panel; RSV, respiratory syncytial virus.

Adapted from: Beal SG, Posa M, Gaffar M, et al. Performance and Impact of a CLIA-waived, Point-of-care Respiratory PCR Panel in a Pediatric Clinic. *Pediatr Infect Dis J.* 2020;39(3):188-191. doi:10.1097/INF.0000000000002544

Patients tested at Clinic A were significantly younger (3.19 vs 5.89, $P < .0001$), had lower detection rates for influenza A and B, and a higher detection rate for respiratory syncytial virus (RSV) and human rhinovirus/enterovirus. 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.

Appropriate use of antimicrobials was determined by comparing antimicrobial prescriptions to detected pathogens (Table 1⁹). 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.

An evaluation of clinic workflow at clinic A found that the average duration of appointment times was shorter (mean 48.0 vs 53.7, $P = .0009$) 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 rapid antigen tests available for detecting 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.

Clinical and Practical Considerations for BioFire RP EZ Panel Implementation in the Outpatient Setting

Clinics can provide more timely and accurate diagnosis with on-site testing using the BioFire RP EZ Panel. Each test takes just 2 minutes of hands-on time and 1 small sample, helping to streamline workflow and provide results to patients in about an hour.

Rapid and comprehensive test results from the BioFire Panels may help in discussing the efficacy of antibiotics with patients. Accurate and timely diagnosis may increase patient satisfaction while potentially reducing unnecessary antibiotic prescriptions.

Furthermore, when patients have clear answers about what's probably causing their respiratory infection, they may be less likely to seek additional care in the emergency department. ►

Key Takeaways:

How the BioFire® RP EZ Panel Can Benefit a Practice and Patients

- ▶ **Improve Operational Efficiency**
The BioFire RP EZ Panel has been shown to reduce appointment duration.⁹
- ▶ **Reduce Unnecessary Testing**
The BioFire RP EZ Panel offers results in about an hour, potentially enabling faster diagnosis and decreased follow-up care.
- ▶ **Put Confidence in Treatment Plans**
Choosing a syndromic panel means choosing greater accuracy and a higher standard of care. A panel that identifies a broad range of pathogens can better detect co-infections and help to put a name on the pathogen. This can increase confidence in the treatment plan for the patient.
- ▶ **Prescribe the Right Treatment**
The BioFire RP EZ Panel has demonstrated an increase in the occurrence of appropriate treatment.⁹

The BioFire® Respiratory 2.1-EZ Panel (EUA)[†] With SARS-CoV-2

Because a large number of pathogens cause respiratory infections, tests that only identify SARS-CoV-2 or influenza run the risk of missing the real culprit. In fact, SARS-CoV-2 has been detected in respiratory samples less than 10% of the time in the United States,¹³ and many rapid influenza diagnostic tests sacrifice accuracy for speed, with sensitivities ranging from 50% to 70%.¹⁴

That's why the BioFire Respiratory 2.1- EZ Panel (EUA) uses a syndromic approach to accurately detect and identify a wide range of pathogens. The panel identifies a menu of 19 respiratory targets, including SARS-CoV-2, in one multiplex PCR test, with results in about 45 minutes. The BioFire Respiratory 2.1-EZ Panel (EUA) is designed to run on the CLIA-waived BioFire® 2.0 EZ Configuration System. This sample-to-answer respiratory pathogen panel is a frontline solution for clinics of every size.

[†] This test has not been FDA cleared or approved; this test has been authorized by FDA under an EUA for use by authorized laboratories; this test has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms; and this test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics tests 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 authorization is terminated or revoked sooner.

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