

# Implementation of a Rapid Multiplex Polymerase Chain Reaction Pneumonia Panel and Subsequent Antibiotic De-escalation

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**Background.** Net effects of implementation of a multiplex polymerase chain reaction (PCR) pneumonia panel (PNP) on antimicrobial stewardship are thus far unknown. This retrospective study evaluated the real-world impact of the PNP on time to antibiotic de-escalation in critically ill patients treated for pneumonia at an academic medical center.

*Methods.* This retrospective, quasi-experimental study included adult intensive care unit (ICU) patients with respiratory culture results from 1 May to 15 August 2019 (pre-PNP group) and adult ICU patients with PNP results from 1 May to 15 August 2020 (PNP group) at Nebraska Medical Center. Patients were excluded for the following reasons: any preceding positive coronavirus disease 2019 PCR test, lack of antibiotic receipt, or non-respiratory tract infection indications for antibiotics. The primary outcome was time to discontinuation of anti-methicillin-resistant *Staphylococcus aureus* (MRSA) therapy. Secondary outcomes included time to discontinuation of antipseudomonal therapy, frequency of early discontinuation for atypical coverage, and overall duration (in days) of antibiotic therapy for pneumonia.

**Results.** Sixty-six patients in the pre-PNP group and 58 in the PNP group were included. There were significant differences in patient characteristics between groups. The median time to anti-MRSA agent discontinuation was 49.1 hours in the pre-PNP and 41.8 hours in the PNP group (P = .28). The median time to discontinuation of antipseudomonal agents was 134.4 hours in the pre-PNP versus 98.1 hours in the PNP group (P = .47). Other outcomes were numerically but not significantly improved in our sample.

**Conclusions.** This early look at implementation of a multiplex PNP did not demonstrate a statistically significant difference in antibiotic use but lays the groundwork to further evaluate a significant real-world impact on antibiotic de-escalation in ICU patients treated for pneumonia.

Keywords. antimicrobial stewardship; pneumonia; pneumonia panel; rapid diagnostic tests.

Better diagnostics for evaluation of pneumonia etiology are needed. Risk factors for antimicrobial resistance remain unclear, broad-spectrum empiric antibiotics are often initiated, and respiratory cultures are often negative. Many institutions have implemented rapid diagnostics, such as methicillinresistant *Staphylococcus aureus* (MRSA) nares polymerase chain reaction (PCR), to help guide and encourage prompt

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antibiotic de-escalation [1]. BioFire Diagnostics (bioMérieux) developed a multiplex PCR pneumonia panel (PNP) with improved pathogen detection in pneumonia. This tool can be used on both sputum and bronchoalveolar lavage (BAL) samples, producing results in approximately 75 minutes for numerous bacterial, viral, and resistance gene targets [2]. Rapid detection of the causative agent in pneumonia could allow faster optimization of antimicrobial therapy [2–6], and several studies have suggested that the PNP provides information that could lead to earlier discontinuation or de-escalation of empiric therapy [2–5]. This could be counteracted by the increased sensitivity of the PNP for microorganisms and reporting of semiquantitative results, which could potentially lead to increased antibiotic use [2–7].

The net effects of PNP implementation on actual antimicrobial use are thus far unknown. Several study groups have performed theoretical analyses comparing hypothetical PNP-directed antimicrobial use with traditional culture-driven antimicrobial use and have identified numerous potential opportunities for changes

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to antimicrobial prescribing [3–5, 8–11]. However, there are limited data on actual antimicrobial changes made in response to PNP results [12–17] and very little data comparing clinical antimicrobial changes informed by PNP with those informed by conventional microbiologic methods [18]. Therefore, we initiated a pilot study aiming to evaluate antibiotic de-escalation immediately following implementation of the PNP in critically ill patients treated for pneumonia at our institution before widespread education on the tool and compare this with antibiotic de-escalation practices before PNP.

# METHODS

#### **Study Population**

This retrospective, quasi-experimental study included adult intensive care unit (ICU) patients with respiratory culture results from 1 May to 15 August 2019 (pre-PNP cohort) and adult ICU patients with PNP and paired respiratory culture results from 1 May to 15 August 2020 (PNP cohort) at Nebraska Medical Center, a 718-bed academic hospital in Omaha, Nebraska. Patients included had a clinical diagnosis of pneumonia according to clinician documentation in the electronic medical record and were admitted to the medical, surgical, or cardiovascular ICU. Patients were excluded for age  $\leq 18$  years, a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) PCR test result, receipt of antibiotics for an indication other than pneumonia or no receipt of any antibiotics, and death or transition to comfort measures while receiving antibiotics for pneumonia. If multiple respiratory cultures or PNPs were performed during the same course of therapy for pneumonia, only the first result was included. Sputum samples were excluded if they were rejected for culture owing to poor specimen quality (ie, <25 white blood cells and  $\geq 10$  epithelial cells per low-power field).

# **Patient Consent**

The design of this work was reviewed and deemed exempt research by the University of Nebraska Medical Center Institutional Review Board Office of Regulatory Affairs. Written patient consent was not required owing to the retrospective nature of the current study.

## Intervention

The PNP was implemented in May 2020, with ordering restricted to the ICU setting or to pulmonary and infectious diseases (ID) providers outside the ICU. The institutional antimicrobial stewardship program (ASP) published a PNP guidance document on their website (https://www.unmc.edu/intmed/\_documents/id/ asp/clinicmicpneumonia-panel-guideline.pdf) to help clinicians make treatment decisions based on PNP results and local susceptibility trends. This guideline was distributed to ICU, ID, and pulmonary physicians via email, but no formal instruction was provided owing to the demands of the coronavirus disease 2019 (COVID-19) pandemic on both the ASP and ICU clinicians. Institutional pneumonia guidelines were updated to recommend PNP use in patients with hospital-acquired or ventilator-associated pneumonia, severe community-acquired pneumonia (CAP), or CAP treated empirically with expanded-spectrum therapy, and in patients not improving despite receipt of typical CAP therapy.

Conventional culture and susceptibility testing methods were also performed on the samples sent for PNP. In patients in whom a PNP was ordered, the use of urinary antigen testing and other respiratory rapid diagnostics was discouraged; MRSA nares PCR is not currently used at our center. The ASP reviewed PNP results as part of routine prospective audit and feedback during weekday business hours and made recommendations to optimize therapy when applicable. Recommendations were communicated to primary teams via secure messaging and/ or phone calls.

#### Outcomes

The primary outcome was time to discontinuation of anti-MRSA therapy in hours. Secondary outcomes included time to discontinuation of antipseudomonal therapy (in hours), frequency of early discontinuation of atypical coverage (defined as receipt of <1500 mg of azithromycin or <5 days of doxycycline, levofloxacin, or a combination of agents with atypical antimicrobial activity), duration of therapy for pneumonia (in days), and total antibiotic days of therapy. The ASP intervention acceptance rate, frequency of ID consultation, and incidence of therapy changes (including escalation, de-escalation, and discontinuation) were also collected.

## **Statistical Analyses**

Continuous variables were compared using the 2-sample t test or Mann-Whitney U test as appropriate, and categorical variables were compared using the Fisher exact test. Two-tailed P values <.05 were considered to indicate statistical significance.

## RESULTS

A total of 441 respiratory samples were reviewed, of which 40 were duplicates, leaving 401 samples fully evaluated. These samples were collected from 162 ICU patients in the preintervention period and 239 ICU patients in the intervention period. After review, 66 pre-PNP and 58 PNP patients were included (total n = 124), with 277 excluded. Reasons for exclusion included positive SARS-CoV-2 PCR result (n = 102 [37%]), non-respiratory tract infection indication for antibiotics (n = 72 [26%]), death or transition to comfort measures (n = 44 [16%]), no antibiotic therapy prescribed (n = 26 [9%]), and other (n = 33 [12%]).

There were significant differences in patient characteristics between groups (Table 1). The pre-PNP group was predominantly male, while the PNP group was predominantly female. A significantly higher proportion of patients in the PNP group

 
 Table 1. Patient Characteristics and Description of Therapy Changes and Interventions

	Patients, No. (%) <sup>a</sup>		
Characteristic	Pre-PNP Group (n = 66)	PNP Group (n = 58)	<i>P</i> Value
Male sex	47 (71.2)	26 (44.8)	<.01
Age, mean (SD), y	61.9 (13.0)	60.4 (13.5)	.53
ICU			
CVICU	18 (27.3)	7 (12.1)	.04
MICU	37 (56.1)	50 (86.2)	<.01
SICU	11 (16.7)	1 (1.7)	<.01
Pneumonia type			
CAP	34 (51.5)	41 (70.7)	.04
HAP	16 (24.2)	5 (8.6)	.03
VAP	16 (24.2)	12 (20.7)	.67
Ventilation status at time of respiratory culture			
Ventilated	51 (77.3)	47 (81)	.66
Not ventilated	15 (22.7)	11 (19)	
Specimen source			
Sputum/ET aspirate	41 (62.1)	46 (79.3)	.05
BAL/mini-BAL	25 (37.9)	12 (20.7)	
Change in therapy	57 (86.4)	52 (89.7)	.78
Escalation	5 (7.6)	6 (10.3)	.75
De-escalation	47 (71.2)	40 (69)	.85
Discontinuation	5 (7.6)	6 (10.3)	.75
ASP intervention	5 (7.6)	15 (25.9)	<.01
Accepted	1 (20)	5 (33.3)	>.99
Accepted/modified	2 (40)	2 (13.3)	.25
Rejected	2 (40)	8 (53.3)	>.99
ID consultation	14 (21.2)	15 (25.9)	.67
General ID	7 (10.6)	11 (19)	.21
Transplant ID	4 (6.1)	3 (5.2)	>.99
Oncology ID	3 (4.5)	1 (1.7)	.62

Abbreviations: ASP, antimicrobial stewardship program; BAL, bronchoalveolar lavage; CAP, community-acquired pneumonia; CVICU, cardiovascular ICU; ET, endotracheal; HAP, hospital-acquired pneumonia; ICU, intensive care unit; ID, infectious diseases; MICU, medical ICU; PNP, polymerase chain reaction pneumonia panel; SD, standard deviation; SICU, surgical ICU; VAP, ventilator-associated pneumonia.

<sup>a</sup>Data represent no. (%) of patients unless otherwise specified.

were admitted to the medical ICU compared with the pre-PNP group (86.2% vs 56.1%; P < .01), and lower proportions of PNP patients were admitted to the cardiovascular or surgical ICU. The PNP group also had a significantly higher proportion of patients treated for CAP (70.7% vs 51.5% for the pre-PNP group; P = .04) and a lower proportion of patients treated for hospital-acquired pneumonia (8.6% vs 24.2%; P = .03). The specimen source for the respiratory cultures was more commonly sputum or endotracheal aspirate in the PNP group compared with the pre-PNP group. Similar numbers of patients in the 2 groups were ventilated and were being treated for ventilator-associated pneumonia.

Bacterial organisms identified were similar between groups (Figure 1A). In both groups, approximately 50% of patients had no organism identified. In the PNP cohort, when

comparing numbers of organisms detected with the PNP compared with culture performed on the same specimens, the PNP was found to be more sensitive, detecting more organisms more frequently, which is consistent with the published literature. Haemophilus influenzae, the organism most commonly identified by the PNP, grew less often in culture (identified in culture for 3 of 10 PNP-positive samples). MRSA was detected in 4 of 58 PNP samples (6.9%) and grew from culture in 3 of 58 PNP samples (5.2%) and 3 of 66 pre-PNP samples (4.5%). Pseudomonas aeruginosa was detected in 5 of 58 PNP samples (8.6%) and grew from culture in 5 of 58 PNP samples (8.6%) and 9 of 66 pre-PNP samples (13.6%). The organisms most commonly identified from culture and not by the PNP included Stenotrophomonas maltophilia (n = 4) and Corynebacterium striatum (n = 2). The majority of samples analyzed with the PNP (46 of 58 [79.3%]) were sputum or endotracheal aspirate. Results from these specimens were more frequently polymicrobial compared to PNP results for BAL or mini-BAL samples (30.4% vs 8.3%, respectively).

Empiric therapy selections are summarized in Figure 1*B*. Empiric anti-MRSA therapy was initiated in 55 of 66 patients (83%) in the pre-PNP group and 40 of 58 (69%) in the PNP group (P = .09). Significantly fewer patients in the PNP group were started on empiric antipseudomonal therapy (39 of 58 [67%] vs 59 of 66 [89%] for the pre-PNP group; P < .01), and significantly more patients received empiric atypical coverage (32 of 58 [55%] vs 17 of 66 [26%], respectively; P < .01).

The results of the primary and secondary outcomes are summarized in Table 2. The median time to anti-MRSA agent discontinuation (interquartile range [IQR]) was 49.1 (28.7-104.8) hours in the pre-PNP and 41.8 (20.8-96.2) hours in the PNP group (absolute difference, 7.3 hours; P = .28). Figure 2 shows the percentage of empiric anti-MRSA agents discontinued during each day of therapy. Although there were more discontinuations within the first 24 hours in the PNP group (14 of 40 [35%] vs 10 of 55 [18%] in the pre-PNP group), this difference was not statistically significant (P = .09). An exploratory subgroup analysis was performed on the primary outcome, excluding patients who had MRSA detected on microbiologic testing and would therefore have appropriately received a full course of anti-MRSA therapy. In this subgroup of patients who did not have MRSA detected (n = 89), the median time (IQR) to discontinuation of the anti-MRSA agent was 39.3 (20.5-94.4) hours in the PNP group (n = 37) and 48.9 (28.1–98.0) hours in the pre-PNP group (n = 52), which was not significantly different (P = .22).

An additional exploratory subgroup analysis was performed, excluding patients who had anti-MRSA therapy continued for >72 hours, suggesting that the clinician did not act on respiratory culture or PNP results. In the subgroup of patients who received anti-MRSA therapy for <72 hours (n = 59), the patients in the PNP group (n = 24) had a significantly shorter median time to discontinuation of anti-MRSA therapy than those in



Figure 1. Summary of bacterial organisms identified and empiric therapy. *A*, Percentage of samples in each group with each organism detected by culture or polymerase chain reaction pneumonia panel (PNP). *B*, Percentage of patients in each group who received empiric therapy including the listed antibiotic. Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*, MSSA, methicillin-susceptible *S aureus*; NRF, normal respiratory flora; PSAR, *Pseudomonas aeruginosa*.

the pre-PNP group (n = 35) (21.3 vs 41.3 hours, respectively; P = .02).

There were no statistically significant differences between groups with respect to the secondary outcomes (Table 2).

The median time (IQR) to discontinuation of an antipseudomonal agent was 134.4 (63.5–171.4) hours in the pre-PNP group, compared with 98.1 (46.5–168.9) hours in the PNP group (absolute difference, 36.3 hours; P = .47). Early

#### Table 2. Results for Primary and Secondary Outcomes

Outcome	Pre-PNP Group	PNP Group	P Value
	n = 55	n = 41	
Time to anti-MRSA agent discontinuation, median (IQR), h	49.1 (28.7–104.8)	41.8 (20.8–96.2)	.28
	n = 59	n = 39	
Time to antipseudomonal agent discontinuation, median (IQR), h	134.4 (63.5–171.4)	98.1 (46.5–168.9)	.47
	n = 17	n = 32	
Discontinuation of atypical coverage, no. (%)	8 (47.1)	13 (40.6)	.77
	n = 66	n = 58	
Duration of antimicrobial therapy for pneumonia, mean (SD), d	7.9 (3)	7.6 (3.5)	.61
Antibiotic days of therapy for pneumonia, mean (SD), d	13.4 (6.2)	13.3 (6.6)	.93
Abbreviations: IQR, interquartile range; MRSA, methicillin-resistant Staphylococcus a	ureus; PNP, polymerase chain reaction pr	neumonia panel; SD, standard deviation.	

discontinuation of atypical coverage occurred in 47.1% in the pre-PNP group and 40.6% in the PNP group (P = .77). There were no differences between the pre-PNP and PNP groups with respect to the mean duration of therapy for pneumonia (7.9 vs 7.6 days, respectively; P = .61) or antibiotic days of therapy (13.4 vs 13.3 antibiotic days; P = .93).

The most common change in therapy was de-escalation, which occurred with similar frequency in the 2 groups (47 of 66 [71.2%] in the pre-PNP vs 40 of 58 [69%] in the PNP group; P = .85). Escalation and discontinuation both occurred in 5 of 66 patients (7.6%) in the pre-PNP and 6 of 58 (10.3%) in the PNP group (P = .75). In the PNP group, of the 40 antibiotic de-escalations made, 16 were based on PNP results, 12 were based on culture results, and 12 were seemingly unrelated to microbiology results. Of the 6 antibiotic discontinuations made, 5 were based on PNP results, and 1 on culture results. Of the 6 antibiotic escalations made, 4 were based on PNP results, while 2 were unrelated to microbiology results. Of the 4 cases of escalations based on PNP results, 3 had discordant culture results. One case was considered an inappropriate escalation (escalated for MRSA based on PNP but de-escalated again based on methicillin-susceptible S aureus in culture), while the other 2 cases were considered appropriate escalations; 1 of the 2 escalated for detection of bla<sub>CTX-M</sub> gene (CTX-M) on PNP despite non-extended-spectrum β-lactamase-producing Escherichia coli isolated in sputum culture (CTX-M-positive E coli later grew in BAL culture), and 1 escalated for Legionella pneumophilia on PNP (which did not grow in culture).

ASP intervention occurred more frequently in the PNP than in the pre-PNP group (15 of 58 [25.9%] vs 5 of 66 [7.6%], respectively; P < .01). Overall, the ASP intervention acceptance rate was 50% (60% for the pre-PNP and 47% for the PNP group). ID teams were consulted in 14 of 66 cases (21.2%) and 15 of 58 cases (25.9%) in the pre-PNP and PNP groups, respectively (P = .67).

# DISCUSSION

This is the first comparative study assessing the real-world impact of implementation of the PNP on time to discontinuation of anti-MRSA and antipseudomonal therapy, which are commonly used broad-spectrum empiric antimicrobials at our institution for ICU patients with suspected pneumonia. Overall, we did not note any statistically significant impacts on antibiotic de-escalation or earlier discontinuation of anti-MRSA or antipseudomonal therapy; however, this was a pilot study to establish power needed for a larger trial. Still, there were trends noted toward reduction in broad-spectrum antimicrobial use after implementation of the PNP. Numerical reductions in both time to discontinuation of anti-MRSA agent (7 hours) and time to discontinuation of antipseudomonal therapy (36 hours) were noted in the primary analysis. The magnitude of any clinical impact from these signals will be better evaluated in subsequent well-powered trials.

In the current study, there was a high proportion of patients who received empiric vancomycin (83% in the pre-PNP and 69% in the PNP group) despite a relatively low prevalence of MRSA isolated by respiratory culture (4.5% and 5.2%, respectively). This overuse may lead to increased costs and increased risk of acute kidney injury for patients. Although implementation of MRSA nares PCR has been shown to reduce the duration of MRSA therapy by approximately 2 days owing to its high negative predictive value (NPV; 95%-98%) [1], our institution does not currently use this tool. It should be noted the high NPV of MRSA nares PCR is driven primarily by the very low prevalence of MRSA as a cause of pneumonia, and both false-positives and false-negatives do occur depending on the timing of the swab sample in relation to when the suspected pneumonia occurred. One potential concern with using MRSA nares PCR screening is the relatively low positive predictive value (PPV; 36%-57%) and the risk that providers may inappropriately initiate or continue anti-MRSA therapy on the basis of a positive result. In our study, the NPV of the PNP for MRSA was 100% and the PPV was 75%; though MRSA grew in very few cultures, our results suggest that the PPV of PNP for MRSA may be higher than for MRSA nares PCR.

The use of lower respiratory tract specimens to rule out MRSA at the time of suspected pneumonia seems preferable to nasal screening because of closer proximity to the infection;



Figure 2. Time to discontinuation of empiric anti-methicillin-resistant *Staphylococcus aureus* (MRSA) agent. The y-axis represents the percentage of patients with empiric anti-MRSA therapy whose anti-MRSA agent was discontinued within the time period specified on the x-axis. The polymerase chain reaction pneumonia panel (PNP) group included 40 patients, and the pre-PNP group, 55 patients. No differences between groups were statistically significant.

however, it is unclear whether the PNP will have a similar impact on the duration of anti-MRSA therapy. Our subgroup analyses suggest that the PNP did have some impact on the timing of anti-MRSA therapy discontinuation, as evidenced by Figure 2, which shows a shift toward earlier discontinuation of vancomycin. In addition, when we excluded patients in whom anti-MRSA therapy was continued for >72 hours, anti-MRSA therapy was discontinued 20 hours earlier with PNP use. This suggests that when clinicians are open to stopping vancomycin, the PNP results in more rapid de-escalation, particularly in centers that do not use rapid nasal PCR screening for MRSA.

With negative PNP results, our study found high rates of concordant negative culture results (26 of 28 [92.9%]). In the 2 cases in which a negative PNP result was not correlated with a negative culture result, *S maltophilia* was isolated in culture; *S maltophilia* is often a colonizer and may not have been a true pathogen. These results suggest that a negative PNP result could potentially be used to prompt de-escalation and/or discontinuation of therapy, especially if the diagnosis of pneumonia is unclear. Discontinuation and de-escalation occurred in a high proportion of the patients with negative PNP results (21 of 28 [75%]), though this proportion may increase with additional provider education.

There are several potential confounders and limitations to the current study. First, while this is the largest study of PNP impact in patients without COVID-19, the number of patients included in this pilot study was still relatively small, which likely reduced our power to detect a difference in outcomes between groups. Second, this was a retrospective, quasi-experimental study performed during the COVID-19 pandemic, which resulted in some significant differences between the patient populations. In particular, there were differences in ICU locations, types of pneumonia treated, and specimens used for testing, which may have affected clinician decision making. A majority of samples used for PNP testing were sputum samples or endotracheal aspirates, which frequently led to polymicrobial results and may have increased provider uncertainty in antimicrobial selection and/or prevented further streamlining of therapy. In addition, this study was completed very early after implementation of this new tool, accompanied by minimal education for ICU clinicians owing to COVID-19-related work demands. The documented ASP intervention rate was 26% in the PNP group, which is lower than expected. The acceptance rate of ASP intervention was also much lower than in historical institutional experience.

These differences may be due to several factors. First, it is known that antimicrobial overuse was common, especially early during the COVID-19 pandemic [19, 20]. Diagnostic uncertainty and severity of patient illness may have contributed to lower rates of de-escalation. In addition, owing to limited experience with this new tool, there was likely a significant lack of clinician confidence in using the PNP to direct therapy early after implementation, which was demonstrated by the proportions of de-escalations that were still made based on culture results or other factors despite having earlier PNP results. Finally, it has been well demonstrated that rapid diagnostic tools provide the most benefit when combined with ASP intervention and education [21, 22]. While our facility maintains a robust ASP centered on prospective audit and feedback, ASP personnel had added duties during the study period owing to the COVID-19 pandemic and were unable to intervene in a consistent and timely manner. In addition, minimal education was provided for physicians, and no education was provided to

other clinicians, including nurses, advanced practice providers, and pharmacists. Pharmacists are commonly instrumental in improving antimicrobial use for inpatients, and lack of pharmacist familiarity with the PNP may have also limited the effect seen on antimicrobial use early after implementation [22].

A recently published study described implementation of this PNP in ICU patients after a 2-month educational rollout including educational sessions and written communication to ICU providers and pharmacists; its findings demonstrated that the implementation of this tool may shorten both the time to first antibiotic change based on microbiologic data and the time to adequate therapy [18]. This further demonstrated the impact that intensive education can have on provider-driven antimicrobial changes in response to a new tool. Despite these faster changes in therapy, the authors found that changes based on PNP were made in only approximately 50% of cases eligible for change based on the PNP result, suggesting provider hesitancy to trust this tool, which is consistent with our findings. As the previous study did not include targeted antimicrobial stewardship intervention, it is possible that the addition of this aspect will improve provider confidence in decision making based on PNP results, which our ongoing study will address.

With additional clinician experience, education, more aggressive stewardship interventions, and a larger patient population, our study suggests that use of the PNP may result in significant reductions in broad-spectrum antimicrobial therapy. To address the limitations of the current study and better assess the clinical impact of the PNP, a larger, prospective study is currently underway, with assay implementation in combination with a robust clinician education effort and consistent, intensive stewardship intervention.

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Potential conflicts of interest: T. C. V. S. reports receiving investigatorinitiated grants from and consulting for bioMérieux and Thermo Fisher. E. J. S. received investigator-initiated grants from bioMérieux and from Merck unrelated to the current work. J. R. M. is a member of protocol leadership for the National Institutes of Health/National Institute of Allergy and Infectious Diseases/COVID-19 Prevention Network (CoVPN) vaccine study CoVPN 3006/Prevent COVID U and received salary support for this activity, unrelated to the current work. J. R. M. also received a consultative honorarium in 2021 for serving on a Pfizer Global Medical Grants/Mayo Clinic Global Bridges Antimicrobial Stewardship Grant review panel and an honorarium from Pew Charitable Trust in 2022, unrelated to the current work. B. T. A. is an advisory board member for Astellas Pharma and F2G and has received an investigator-initiated grant from Merck, unrelated to the current work. A. B. W. reports consulting for Thermo Fisher, unrelated to the current work. S. J. B. has received honoraria from Pfizer for serving as an advisory board member for antivirals and from bioMérieux for a presentation related to rapid diagnostic testing. All other authors report no potential conflicts.

#### References

- Parente DM, Cunha CB, Mylonakis E, Timbrook TT. The clinical utility of methicillin-resistant *Staphylococcus aureus* (MRSA) nasal screening to rule out MRSA pneumonia: a diagnostic meta-analysis with antimicrobial stewardship implications. Clin Infect Dis **2018**; 67:1–7.
- Murphy CN, Fowler R, Balada-Llasat JM, et al. Multicenter evaluation of the BioFire FilmArray pneumonia/pneumonia plus panel for detection and quantification of agents of lower respiratory tract infection. J Clin Microbiol 2020; 58:e00128-20.
- Lee SH, Ruan SY, Pan SC, Lee TF, Chien JY, Hsueh PR. Performance of a multiplex PCR pneumonia panel for the identification of respiratory pathogens and the main determinants of resistance from the lower respiratory tract specimens of adult patients in intensive care units. J Microbiol Immunol Infect 2019; 52:920–8.
- 4. Buchan BW, Windham S, Balada-Llasat JM, et al. Practical comparison of the BioFire FilmArray pneumonia panel to routine diagnostic methods and potential impact on antimicrobial stewardship in adult hospitalized patients with lower respiratory tract infections. J Clin Microbiol 2020; 58:e00135-20.
- Yoo IY, Huh K, Shim HJ, et al. Evaluation of the BioFire FilmArray pneumonia panel for rapid detection of respiratory bacterial pathogens and antibiotic resistance genes in sputum and endotracheal aspirate specimens. Int J Infect Dis 2020; 95:326–31.
- 6. Webber DM, Wallace MA, Burnham CA, Anderson NW. Evaluation of the BioFire FilmArray pneumonia panel for detection of viral and bacterial pathogens in lower respiratory tract specimens in the setting of a tertiary care academic medical center. J Clin Microbiol 2020; 58:e00343-20.
- Edin A, Eilers H, Allard A. Evaluation of the BioFire FilmArray pneumonia panel plus for lower respiratory tract infections. Infect Dis (Lond) 2020; 52:479–88.
- Zacharioudakis IM, Zervou FN, Dubrovskaya Y, Inglima K, See B, Aguero-Rosenfeld M. Evaluation of a multiplex PCR panel for the microbiological diagnosis of pneumonia in hospitalized patients: experience from an academic medical center. Int J Infect Dis 2021; 104:3540360.
- Hoover J, Mintz MA, Deiter F, et al. Rapid molecular detection of airway pathogens in lung transplant recipients. Transpl Infect Dis 2021; 23:e13579.
- Erich BJ, Kilic A, Palavecino E, et al. Evaluation of the potential impact of a Multiplex rapid diagnostic panel in critically ill patients with hospital-acquired pneumonia. Cureus 2022; 14:e21716.
- Monard C, Pehlivan J, Auger G, et al. Multicenter evaluation of a syndromic rapid multiplex PCR test for early adaptation of antimicrobial therapy in adult patients with pneumonia. Crit Care 2020; 24:434.
- 12. Molina FJ, Botero LE, Isaza JP, et al. Diagnostic concordance between BioFire\* FilmArray\* pneumonia panel and culture in patients with COVID-19 pneumonia admitted to intensive care units: the experience of the third wave in eight hospitals in Colombia. Crit Care 2022; 26:130.
- Furukawa D, Kim B, Jeng A. Real-life utilization of BioFire\* Filmarray\* pneumonia panel as an antibiotic stewardship tool. Infect Dis (Lond) 2021; 53:308–13.
- Cohen R, Babushkin F, Finn T, et al. High rates of bacterial pulmonary coinfections and superinfections identified by multiplex PCR among critically ill COVID-19 patients. Microorganisms 2021; 9:2483.
- Cohen R, Finn T, Babushkin F, et al. High rate of bacterial respiratory tract coinfections upon admission amongst moderate to severe COVID-19 patients. Infect Dis (Lond) 2022; 54:134–44.
- Maataoui N, Chemali L, Patrier J, et al. Impact of rapid multiplex PCR on management of antibiotic therapy in COVID-19-positive patients hospitalized in intensive care unit. Eur J Clin Microbiol Infect Dis 2021; 40:2227–34.
- Verroken A, Scohy A, Gérard L, Wittebole X, Collienne C, Laterre PF. Co-infections in COVID-19 critically ill and antibiotic management: a prospective cohort analysis. Crit Care 2020; 24:410.
- Esplund JN, Taylor AD, Stone TJ, et al. Clinical impact of a multiplex rapid diagnostic pneumonia panel in critically ill patients. Antimicrob Steward Healthc Epidemiol 2023; 3:e5.
- Rawson TM, Moore LSP, Zhu N, et al. Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis 2020; 71:2459–68.
- Vaughn VM, Gandhi TN, Petty LA, et al. Empiric antibacterial therapy and community-onset bacterial coinfection in patients hospitalized with coronavirus disease 2019 (COVID-19): a multi-hospital cohort study. Clin Infect Dis 2021; 72:e533–41.
- Bauer KA, Perez KK, Forrest GN, Goff DA. Review of rapid diagnostic tests used by antimicrobial stewardship programs. Clin Infect Dis 2014; 59:S134–45.
- Foster RA, Kuper K, Lu ZK, Bookstaver PB, Bland CM, Mahoney MV. Pharmacists' familiarity with and institutional utilization of rapid diagnostic technologies for antimicrobial stewardship. Infect Control Hosp Epidemiol 2017; 38: 863–6.