UK clinicians' attitudes towards the application of molecular diagnostics to guide antibiotic use in ICU patients with pneumonias: a quantitative study

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Background: Molecular diagnostic tests may improve antibiotic prescribing by enabling earlier tailoring of antimicrobial therapy. However, clinicians' trust and acceptance of these tests will determine their application in practice.

Objectives: To examine ICU prescribers' views on the application of molecular diagnostics in patients with suspected hospital-acquired and ventilator-associated pneumonia (HAP/VAP).

Methods: Sixty-three ICU clinicians from five UK hospitals completed a cross-sectional questionnaire between May 2020 and July 2020 assessing attitudes towards using molecular diagnostics to inform initial agent choice and to help stop broad-spectrum antibiotics early.

Results: Attitudes towards using molecular diagnostics to inform initial treatment choices and to stop broad-spectrum antibiotics early were nuanced. Most (83%) were positive about molecular diagnostics, agreeing that using results to inform broad-spectrum antibiotic prescribing is good practice. However, many (58%) believed sick patients are often too unstable to risk stopping broad-spectrum antibiotics based on a negative result.

Conclusions: Positive attitudes towards the application of molecular diagnostics to improve antibiotic stewardship were juxtapositioned against the perceived need to initiate and maintain broad-spectrum antibiotics to protect unstable patients.

Introduction

Rapid molecular diagnostic tests, such as the FilmArray Pneumonia Plus Panel (bioMérieux) ('Pneumonia Panel')[1] might support clinicians' antibiotic prescribing and promote stewardship by enabling earlier tailoring of patients' antimicrobial therapy. These tests can accurately detect multiple respiratory pathogens and antimicrobial resistance genes directly from respiratory secretions, with results in 1–6 h compared with the current, culture-based, turnaround of 48–72 h.[2,3]

Antibiotic prescribing in ICU is complex, where antibiotic decisions are often made under diagnostic uncertainty with high-stake consequences. Poor laboratory sensitivity in terms of pathogen recovery and a *circa* 48–72 h delay between specimen receipt and result exacerbate these challenges.[2] One recent qualitative study highlighted that ICU clinicians often face two

competing, and sometimes contradictory, imperatives: at the personal level, the need to protect the patient and the prescriber against the consequences of not prescribing, versus at the societal level, concerns about antimicrobial resistance.[4] Clinical uncertainty complicated these decisions, whereby clinicians often defaulted to prescribing broad-spectrum antibiotics 'just in case' of infection, to 'err on the side of caution'.

Although molecular diagnostic platforms could support clinicians with complex prescribing decision-making, little is known about clinicians' perceptions of these tests, and the drivers and barriers towards their application particularly around two key behaviours: (i) the initial choosing of an antibiotic; and (ii) stopping a broad-spectrum antibiotic early. Emerging research suggests clinicians' views about these tests are complex and that although clinicians were open to using molecular diagnostic technology as a prescribing decision aid, trust and acceptance of these tests can be low.[5]

The UK Department of Health and Social Care identified a 'lack of engagement to understand frontline needs' as a potential barrier to the clinical adoption of molecular tests.[6] This study seeks to address this by assessing what clinicians' attitudes are towards using rapid molecular diagnostics as an antibiotic prescribing decision aid for suspected hospital-acquired and ventilator-associated pneumonia (HAP/VAP) ICU patients.

Materials and methods

This research is part of the INHALE research programme (ISRCTN16483855), investigating the utility of molecular diagnostics to improve antimicrobial prescribing for ICU patients with suspected HAP/VAP (see trial protocol[7]). The INHALE randomized controlled trial (RCT) was paused during the COVID-19 pandemic's first wave, and a microbiological substudy was conducted at five INHALE sites, examining the utility of the FilmArray Pneumonia Plus Panel ('Pneumonia Panel') test for investigating possible secondary infection in ICU patients with COVID-19. See Table S1 (available as Supplementary data at *JAC* Online) for organisms detected by the 'Pneumonia Panel'.

Sample and setting

All five ICUs participating in INHALE's COVID-19 microbiological substudy were included: four NHS teaching hospitals, and one NHS general hospital (all in England). Intensivists and microbiologists involved in the treatment of ICU patients with suspected HAP/VAP and COVID-19 were eligible to participate. Research nurses administered the questionnaire to clinicians at opportune times (e.g. end of shift). Data collection occurred between May 2020 and July 2020.

Questionnaire design

Clinicians completed a questionnaire capturing demographic data and their views about the application of rapid molecular diagnostics for ICU patients with HAP/VAP ('Pneumonia Panel') both as a tool to (i) inform the initial choice of agent (reliability $\alpha = 0.64$; 5 items: e.g. 'I prefer NOT to run a molecular diagnostic test on all patients before prescribing a broad-spectrum antibiotic') and (ii) to stop broad-spectrum antibiotics early (reliability $\alpha = 0.85$; 5 items: e.g. 'It is too risky to stop a broad-spectrum antibiotic based on a negative molecular diagnostic result').

One item was included to probe a practical limitation of the diagnostic: 'Lack of sputum often prevents rapid molecular diagnostic tests, where these are clinically indicated'.

Data analysis

To assess clinicians' views about using molecular diagnostics for ICU, frequency counts and percentages for each scale item were calculated for patient cases with and without COVID-19. Mean scores were calculated for attitudes towards applying molecular diagnostics ('Pneumonia Panel') as a tool to (i) inform the initial choice of agent and (ii) stop broad-spectrum antibiotics early. Differences between clinicians' views

Table 1. Clinicians' attitudes towards the application of rapid molecular diagnostics (RMD; 'Pneumonia Panel')

	Yes, *n* (%)	No, *n* (%)	Don't know, *n* (%)
Attitudes towards applying rapid molecular diagnostics (RMD) as a tool to guide the initial choice of antibiotic			
It is NOT too risky to wait more than 24 hours for a RMD test result	21 (40.4)	30 (57.7)	1 (1.9)
I prefer NOT to run a RMD on all patients before prescribing a BSAB	15 (30)	33 (66)	2 (4)
A test identifying a specific pathogen does NOT rule out the need for a BSAB	15 (28.8)	33 (63.5)	4 (7.7)
It is best to prescribe a BSAB without waiting for a 1-hour RMD test result	13 (24.1)	40 (74.1)	1 (1.9)
RMD results are NOT particularly important, even if the patient deteriorates UNEXPECTEDLY	8 (14.5)	45 (81.8)	2 (3.6)
Attitudes towards using RMD as a tool to stop BSAB early			
Sick patients are often too unstable to risk stopping BSAB based on a negative RMD result	35 (66)	18 (34)	0
It is too risky to stop a BSAB, based on a negative RMD result, if the patient is still clinically unwell	31 (63.3)	16 (32.7)	2 (4.1)
A negative RMD result does NOT justify stopping BSAB if the patient's inflammatory markers are still unstable	27 (55.1)	20 (40.8)	2 (4.1)
It is way too risky to stop a BSAB for a sick patient based on a negative RMD result	20 (45.5)	20 (45.5)	4 (9.1)
A negative RMD result does NOT justify stopping BSAB because RMD cannot find 'hidden' pathogens	15 (36.6)	21 (51.2)	5 (12.2)
Practical limitations with applying RMD			
Lack of sputum often prevents RMD tests where these are clinically indicated	27 (60)	16 (35.6)	2 (4.4)

Clinicians responded to the above statements for patient cases both with and without COVID-19. There were no significant differences between clinicians' beliefs for COVID-19 and non-COVID-19 cases (all *P* > 0.05), so responses for non-COVID-19 cases are reported here.
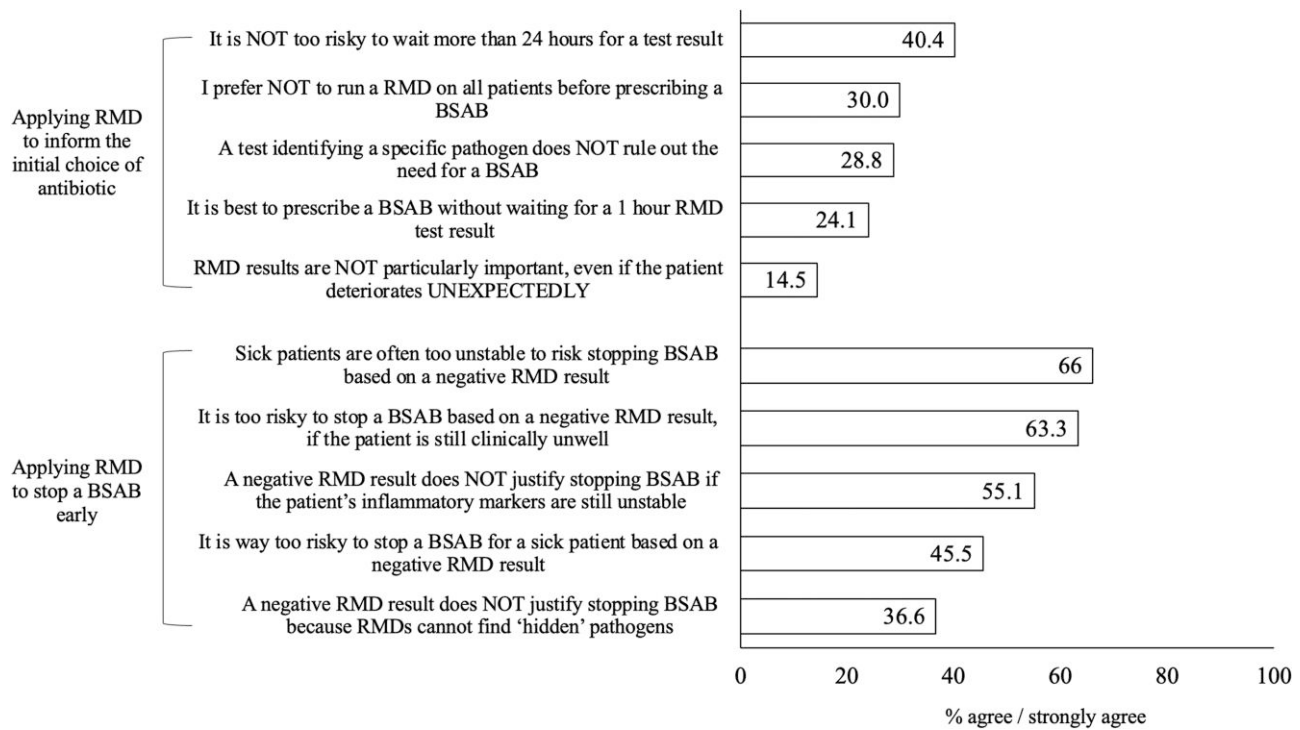
Figure 1. Clinicians' agreement with attitudes towards the application of rapid molecular diagnostics (RMD; 'Pneumonia Panel') as a tool to inform the initial choice of antibiotic and to stop a broad-spectrum antibiotic (BSAB) early.

about the application of molecular diagnostics for patients in ICU with and without COVID-19 infection were compared using McNemar's tests and paired samples *t*-tests.

Ethics

This research received ethical approval from the London—Brighton and Sussex Research Ethics Committee (19/LO/0400). This research used implied informed consent to minimize clinical disruption.

Results

Sixty-three of 197 questionnaires were completed (32% response rate). Participants were ICU consultants ($n = 31$; 49.2%); middle-grade ICU trainees ($n = 9$; 14.3%), early-grade ICU trainees ($n = 7$; 11.1%), consultant clinical microbiologists ($n = 8$; 12.7%), other clinicians ($n = 6$; 9.5%) and two clinicians who did not specify their hospital, grade and specialty (3.2%). See Table S2 for an overview of participant characteristics, and Table S3 for additional demographic data.

Attitudes towards the application of rapid molecular diagnostics ('Pneumonia Panel') as an aid to prescribing broad-spectrum antibiotics in ICU (Table 1, Figure 1)

To inform the initial choice of antibiotic

Most clinicians endorsed the value of molecular diagnostics; however, many were hesitant about using them to inform the initial choice of antibiotic (Table 1). For example, 40.4% ($n = 21$)

agreed it was 'NOT too risky to wait more than 24 hours for a test result'.

To stop broad-spectrum antibiotics early

Clinicians' attitudes towards using the 'Pneumonia Panel' test to guide the early stopping of broad-spectrum antibiotics were nuanced. As can be seen from Table 1, over half believed that 'sick patients are often too unstable to risk stopping broad-spectrum antibiotics based on a negative rapid molecular diagnostic result' (66.0%; $n = 35$) and that 'it is too risky to stop a broad-spectrum antibiotic, based on a negative molecular diagnostic result, if the patient is still clinically unwell' (63.3%; $n = 31$).

Clinicians' views about applying molecular diagnostics did not significantly differ at the scale level or individual level (all $P > 0.05$) for patients with and without COVID-19.

Discussion

Attitudes towards using molecular diagnostics in ICU were nuanced. Most clinicians saw potential in molecular diagnostics, perceiving their value in aiding the selection of early antibiotics—consistent with previous research suggesting this technology might assist the optimization of antimicrobial therapy.[3,5] However, many were hesitant to use them to help inform the initial choice of antibiotics. Our findings identified an apparent tension between ideas about best practice and the clinical application of these tests to inform treatment of ICU patients. Most clinicians had concerns about their application to stop broad-spectrum antibiotics early, deeming it too risky. These findings corroborate and reinforce the findings of

qualitative studies showing that initiating and continuing broad-spectrum antibiotic prescriptions often reflect a desire to protect both patent and clinician by *erring on the side of caution.*[4]

Findings suggest there is uncertainty about the place of these tests in practice. Prior research has identified a number of factors that may affect the uptake of molecular diagnostics, such as mis-apprehensions and uncertainty about test capabilities, leading to a lack of trust in this technology.[5] Uncertainties around the nature (e.g. viral, bacterial, non-microbial) and primary focus (e.g. lung, central line, abdominal) of the pathology driving a patient's 'septic state'[8] may also undermine clinicians' confidence in molecular tests performed on one sample site.

Limitations

Study recruitment was challenging given clinical pressures during the COVID-19 pandemic. Given 5/10 adult sites were able to participate and only 1/3 of eligible clinicians at these sites completed questionnaires, it is possible our sample was not representative. Further, survey responses may reflect what clinicians thought 'ought to be done' rather than their actual prescribing practice.

Study implications

The varied nature of clinicians' views identified in this study emphasizes the clinical complexity of ICU and prescribing decisions. Molecular diagnostic technologies offer the potential for improving prescribing practices. However, our findings illustrate the unique challenges facing the adoption of these tests into ICU settings, with unanswered questions regarding the place and suitability of these tests in clinical practice.

Findings suggest a disconnect between theory and practice. Most clinicians agreed that molecular diagnostics have the potential to improve patient care and antibiotic stewardship, in principle. However, their application in practice was more nuanced. Here, many clinicians perceived the value of molecular diagnostics in informing the initiation of antibiotics, and continuation was juxtapositioned against the perceived need to prescribe broad-spectrum antibiotics early and continue with treatment, even when test results supported curtailment. Often, the perceived need to continue was linked to the belief that it would be too risky to stop broad-spectrum antibiotics if the patient remained clinically unwell or appeared unstable. These clinicians appeared to be balancing the technological information against their instincts derived from clinical experience: an apparent conflict between the science and the art of medicine.

Conclusions

Clinicians' views about using molecular diagnostics to support antibiotic prescribing decisions for ICU patients with HAP/VAP were nuanced. Positive attitudes towards the application of molecular diagnostics to improve antibiotic stewardship were juxtapositioned against the perceived need to initiate and maintain broad-spectrum antibiotics to protect unstable patients.

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Supplementary data

Tables S1 to S3 are available as Supplementary data at *JAC* Online.

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