CHIEF SCIENTIST OFFICE

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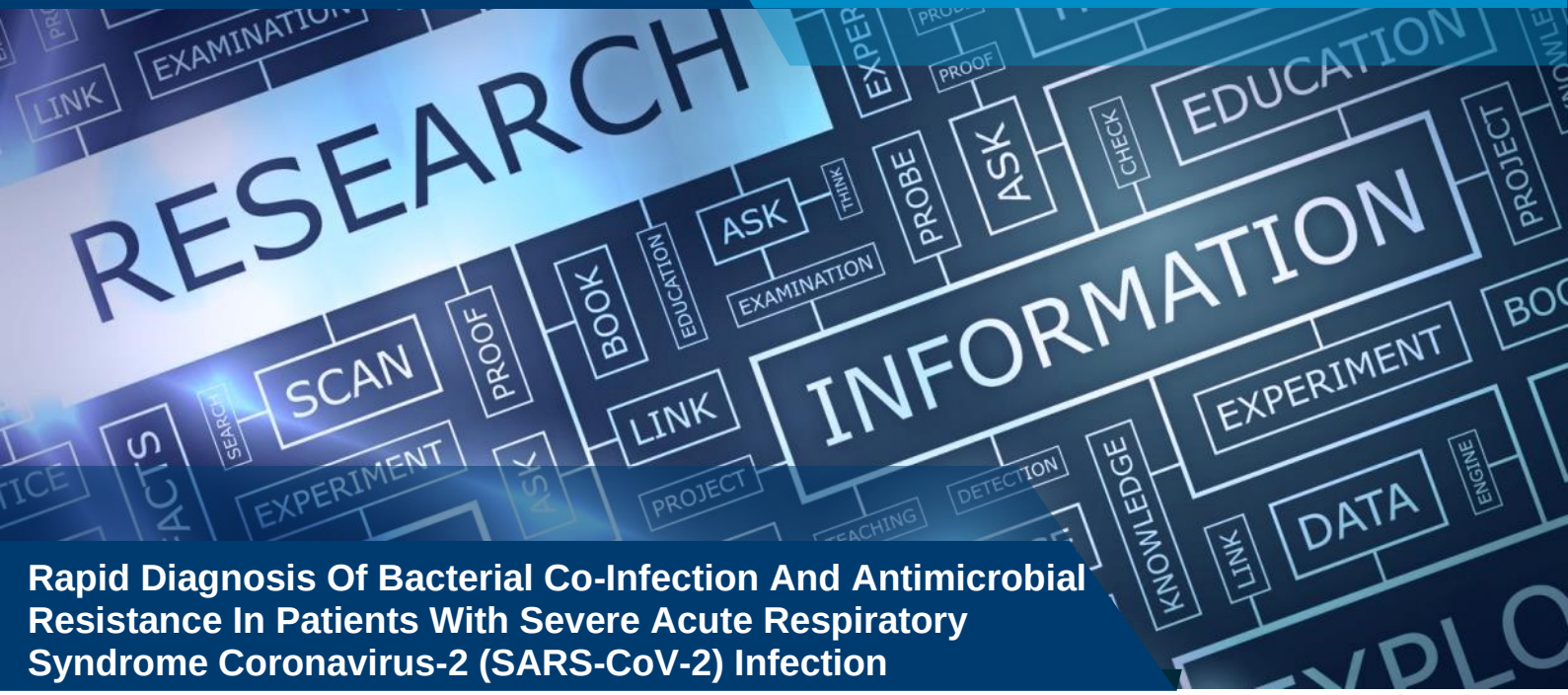
RESEARCH PROJECT BRIEFING



Rapid Diagnosis Of Bacterial Co-Infection And Antimicrobial Resistance In Patients With Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Infection

AIMS

- To identify the frequency of bacterial co-infection in patients hospitalized with suspected and confirmed SARS-CoV-2 infection.
- To identify the most frequent pathogens and the rates of antibiotic resistance.
- To compare three methods of pathogen detection (culture, Polymerase chain reaction (PCR), and a USB device called nanopore sequencing which identifies bacterial DNA) for their ability to detect bacterial pathogens in patients with SARS-CoV-2.

KEY FINDINGS

- An automatic test to detect bacteria called the Biofire was more sensitive than other methods for pathogen detection.
- No significant difference in pathogen distribution between SARS-CoV-2 positive vs negative patients was identified.
- Chronic lung disease (CLD) was not significantly associated with more frequent pathogen detection.
- Our findings suggest that molecular techniques can identify many more bacteria than conventional culture and so may lead to more targeted use of antibiotics, even outside of pandemic conditions.

WHAT DID THE STUDY INVOLVE?

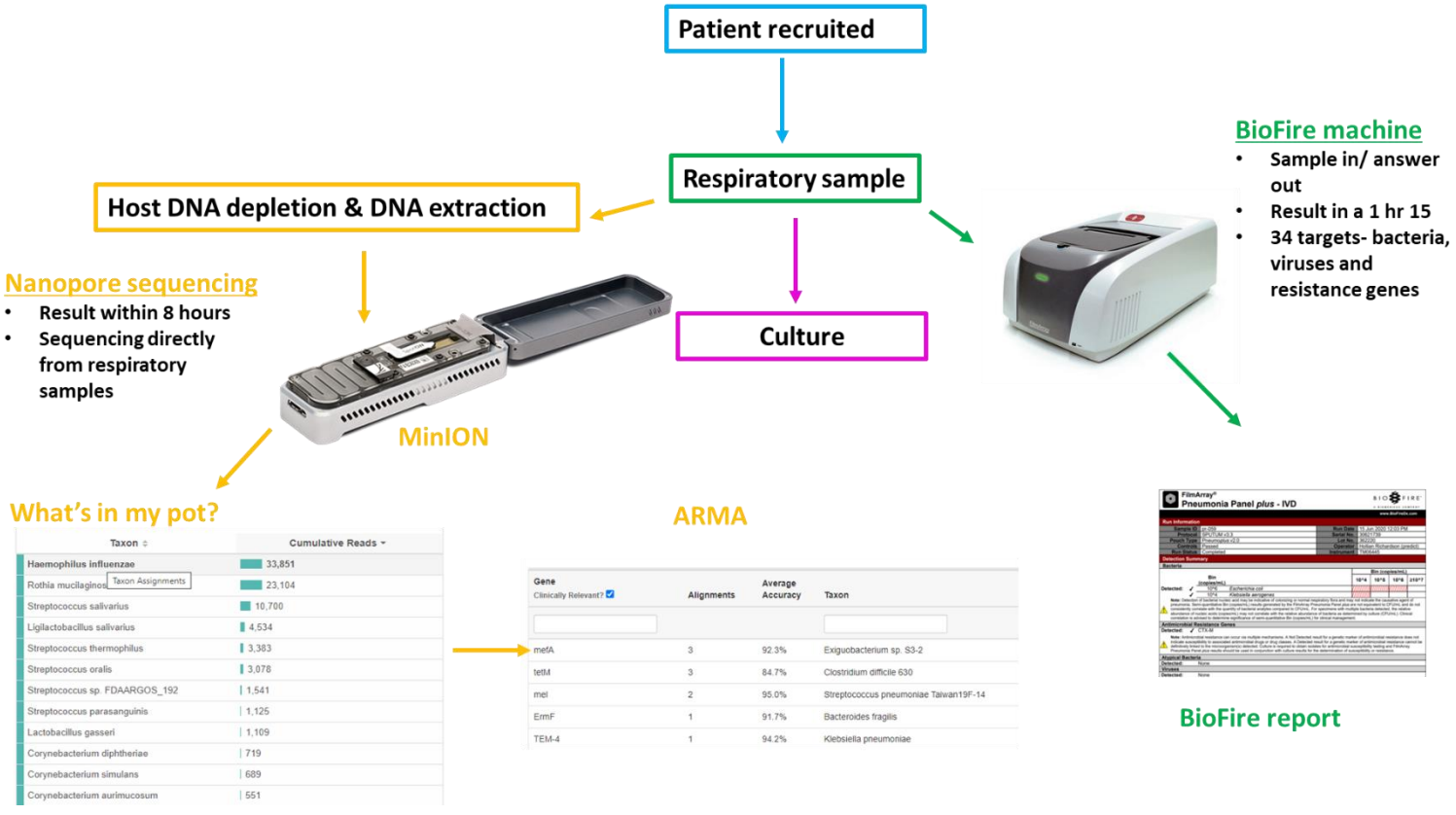
During the SARS-CoV-2 pandemic there was limited research into bacterial co-infections in patients with COVID-19. Bacterial co-infection has been strongly implicated in mortality from COVID-19. The current method for identifying pathogens is culture which involves growing up bacteria on agar and can take >48 hours. Molecular methods can rapidly detect pathogens and may be more sensitive than culture. Molecular methods such as the BioFire (BioMérieux) and nanopore sequencing (Oxford Nanopore Technologies) target the DNA of pathogens.

In this observational study we used culture, BioFire, and nanopore sequencing to investigate bacterial co-infection in SARS-CoV-2 positive patients. Figure 1 shows the methodology used in this study. Patients at Ninewells Hospital (Dundee) with SARS-CoV-2 were enrolled within 96 hours of hospital admission. When it was clinically appropriate, respiratory samples were collected from patient enrolled in this study.

Respiratory samples were tested for pathogens using culture and the BioFire® FilmArray® Pneumonia Panel. The BioFire is a PCR which targets several common lung pathogens and resistance genes. Nanopore sequencing is performed on the MinION, which is a portable USB sequencer. This approach is non-targeted and can detect a range of microbes.

Further information on the BioFire and MinION used in this study can be found on the website https://www.biofiredx.com/products/filmarray & https://nanoporetech.com

Patient and public involvement was limited as the study started at the beginning of the pandemic, but the results and benefits of the new tests were discussed with a patient group in 2023. Patients viewed the potential to get a faster result of their tests as a major benefit.



WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

- The study conducted compared nanopore sequencing, BioFire FilmArray (PCR based) and culture from May 2020 to June 2021. A total of 196 patients (including SARS-CoV-2 positive patients (n=92) and SARS-CoV-2 negative patients (n=104)) were recruited to the study and from these 196 patients, 215 respiratory samples were tested.
- Chronic lung disease (CLD) was not significantly associated with more frequent pathogen detection as shown in Figure 2.
- The Biofire PCR was significantly more sensitive than culture for both SARS-CoV-2 positive and negative groups. Culture provided a positive result in 23.7% and 37.8% of SARS-CoV-2 positive and negative groups respectively. This compared to >50% using the Biofire. This means that more pathogens were detected using the BioFire and is shown in Figure 3. The study shows the benefits of using molecular methods in rapidly identifying a bacterial pathogen compared to culture.
- Biofire PCR was more sensitive than other methods for pathogen detection. Nanopore sequencing detected a range of bacteria and antibiotic resistance genes but not all of these were clinically relevant as shown in Figure 2.
- The pathogen distribution in *both* SARS-CoV-2 positive and negative individuals was not significantly different. *Staphylococcus aureus* and *Haemophilus influenzae* were the most frequently identified pathogens in both groups. Clinically relevant antibiotic resistance genes were rarely detected in both patient groups.

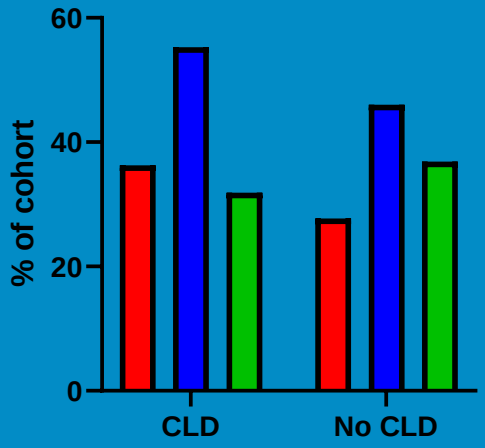


Figure 2. Pathogen detection in chronic lung disease (CLD) and non-CLD using culture, Biofire and nanopore sequencing

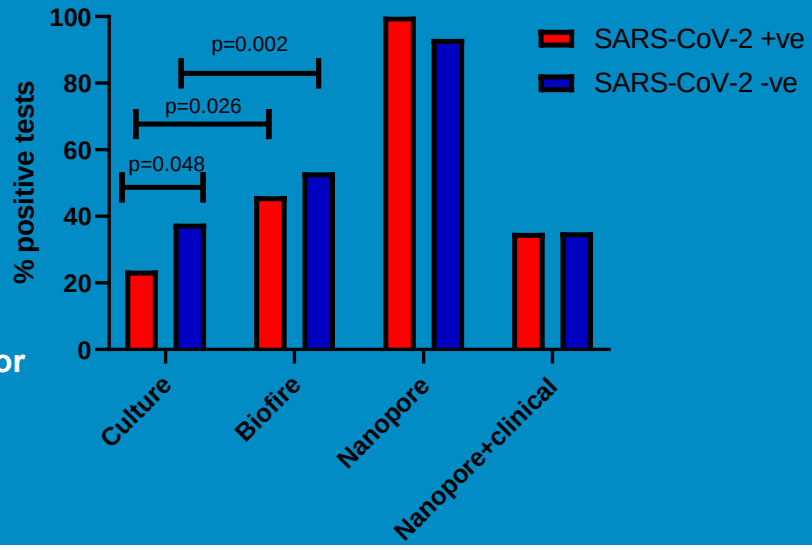


Figure 3. Percentage positive tests for SARS-CoV-2 positive and negative patients using culture, Biofire and nanopore sequencing

WHAT IMPACT COULD THE FINDINGS HAVE?

This study shows the advantage of using molecular methods to rapidly identify pathogens and antibiotic resistance in comparison to culture.

Results from this study can inform Scottish, UK and international antibiotic prescribing guidelines for SARS-CoV-2.

The data show that molecular platforms like the Biofire are likely to increase bacterial detection even outside of pandemic conditions. A cost effectiveness assessment is now needed to understand if this increased detection leads to better outcomes and therefore justifies the costs of testing.

HOW WILL THE OUTCOMES BE DISSEMINATED?

The results will be published in a peer reviewed journal. The data from the study was presented in an oral presentation at the European Respiratory Society International Congress 2021. A further study using the Biofire has been published in July 2024 showing its value in people with lung disease. Results have been discussed with patient groups who have underlying lung conditions (bronchiectasis and COPD).

This study has led to extensive follow-on funding. The BioFire and nanopore sequencing have been implemented in the BRILLIANT study which will investigate the lung microbiome and resistome in bronchiectasis. This method will allow real-time microbiome investigation of respiratory samples from bronchiectasis patients. The BRILLIANT study is externally funded (£1.7m).

CONCLUSION

Bacterial co-infection is more frequently identified in hospitalized patients with SARS-CoV-2 infection using PCR compared with culture. The most frequently identified pathogens in both SARS-CoV-2 positive and SARS-CoV-2 negative individuals were S. aureus and H. influenzae. This study demonstrates the value of molecular methods when used in clinical practice and will lead to the use of these methods beyond COVID-19.

RESEARCH TEAM & CONTACT

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