

A new rapid molecular test for pathogen detection in pneumonia: first insights into potential antibiotic savings

S. Poole¹, K.R. Beard¹, C. Chan¹, S. Mills¹, T.W. Clark¹

¹NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust Southampton, UK

BACKGROUND

- Lower respiratory tract infections (pneumonia) are mainly caused by bacteria. They are the third most common cause of death worldwide, accounting for an estimated 2.7 million deaths annually¹.
- Administration of appropriate antibiotics within hours of diagnosis is critical for treatment of patients with pneumonia.
- Current diagnostics do not allow us to work out which bacteria have caused the infection within these first few hours. As a result '**broad spectrum**' antibiotics are prescribed as a best guess, which kill a lot of different species of bacteria.
- The use of **these antibiotics drives antimicrobial resistance** and can lead to other serious complications like *Clostridium difficile* infection (CDI).
- The current standard diagnostic tests **only detect an organism in 23-40%** of patients with clinically diagnosed pneumonia². This process takes 72 hours minimum therefore often the patient remains on broad spectrum antibiotics even if an organism is eventually detected.

NIHR | Southampton Biomedical Research Centre

NHS
National Institute for Health Research

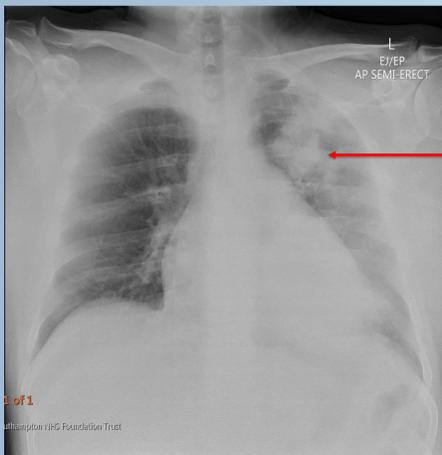


MATERIALS AND METHODS

- The BioFire Filmarray is a multiplexed PCR platform (picture top right). A pneumonia panel was recently licensed for in-vitro diagnostic use on sputum samples. It rapidly detects 33 respiratory pathogens and antibiotic resistance genes with a **turn-around time of 80 minutes**.
- It detects pathogens **in 71% more specimens than routine culture** and is **highly concordant with organisms detected in culture**³.
- We retrospectively tested 3 sputum samples from patients with pneumonia to see whether a change in antibiotics (e.g. narrowing of spectrum, quicker targeting of antibiotics) could have been facilitated. **In 2 out of 3 cases, antibiotic change could be supported.**

CASE 1 – November 2017

- A 63 year old woman with a background of chronic obstructive pulmonary disease (COPD) was admitted to intensive care with pneumonia. She was empirically treated with co-amoxiclav and azithromycin- a broad spectrum of antibiotic cover.
- Culture results were negative after 72 hours so no change was made in antibiotic therapy.
- The Filmarray detected Haemophilus influenzae. The absence of detection of some atypical organisms **would have facilitated stopping azithromycin, saving 7 antibiotic days.**



CASE 2 – February 2018

- A 47 year male diabetic was admitted with breathlessness and diarrhoea. He was diagnosed with pneumonia (his chest x-ray is shown picture left: arrow to patch of pneumonia)
- He was empirically managed with co-amoxiclav and azithromycin. No sputum culture was performed. On day 3 of his admission blood cultures were positive with **Streptococcus pneumoniae**. Stool sample on admission to ICU was **positive for Clostridium difficile toxin** so additional **metronidazole was started** and isolation precautions put in place.
- The Filmarray detected Streptococcus pneumoniae, Staphylococcus aureus, Escherichia coli and rhinovirus. These results again **would have facilitated stopping azithromycin, saving 7 antibiotic days**. Arguably the result could also have led to **earlier targeted therapy** against S. pneumoniae.

CONCLUSION

- Rapid molecular tests do have the potential to improve antibiotic usage in pneumonia, which is an area of huge consumption globally.
- Our group has recently gained ethical approval for a pragmatic RCT to investigate this impact.

REFERENCES

1. Wang Haidong, Naghavi Mohsen, Allen Christine, Barber Ryan M, Bhutta Zulfiqar A, Carter Austin, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016;388(10053):1459–544. Doi: 10.1016/S0140-6736(16)31012-1.
2. Jain Seema, Self Wesley H., Wunderink Richard G., Fakhran Sherene, Balk Robert, Bramley Anna M., et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. N Engl J Med 2015;373(5):415–27.
3. Buchan B, Windham S, Faron M, Balada-Llasat J, Relich R, Humphries R, et al. Clinical Evaluation and Potential Impact of a Semi-Quantitative Multiplex Molecular Assay for the Identification of Pathogenic Bacteria and Viruses in Lower Respiratory Specimens. ATS. 2018.