

Discuss testing strategies for managing COVID-19

by Maeve McLaughlin

'Our key message is: test, test, test'.

This was the broadcasted message from Tetros Adhanom Ghebreyesus, head of the World Health Organisation in April 2020, to healthcare systems across the world as we began to tackle the deadly virus starting to spill over the globe. Whilst previous messages had highlighted the importance of handwashing and social distancing, this message was clear. Testing is essential to gain control of this rapidly spreading virus and he reiterated, 'It is not possible to fight a fire blindfolded'¹. One year on, we look at the different methods of testing for the SARS-CoV-2 virus and the impact it has globally on social distancing restrictions.

Polymerase chain reaction (PCR) testing is the most accurate test for current infection, using nasal or throat swabs to test for virus RNA, providing the swabs have been taken correctly. Current recommendation is that a nasopharyngeal specimen should be obtained first. In severe cases requiring intubation, lower specimen samples can be taken from aspirate from endotracheal tube or bronchoscopy. However as this is an aerosol generating procedure, risks need to be taken into consideration and determining if a positive result will change management. Whilst difficult to measure the true sensitivity and specificity, data has shown the false-positive rate is less than 0.005%, making it the current gold standard for testing².

Lateral flow testing (LFT) is being expanded on a daily basis; any resident in the UK can order a kit from the UK government website and test themselves twice weekly. From March 2021, up to 1.5million LFTs were conducted in the UK according to Health Secretary Matt Hancock, this compares to the data from last year when the Government was struggling to reach a target of 100,000 PCR tests a day. Advice from Public Health England emphasises LFT should only be used in asymptomatic individuals and are used to help identify the suspected one-third of patients who have COVID-19 without showing any symptoms. As rapid antigen testing becomes more accessible, there were concerns that this can give a false sense of security and reduce the need to socially distance.

An NHS asymptomatic staff pilot study evaluated Loop-mediated Isothermal Amplification (LAMP) molecular testing technologies in 22,941 swab samples with RNA extraction showed a sensitivity of 99.57% and specificity of 99.40%, showing equivalent sensitivity and specificity to the Gold Standard RT-qPCR³. LAMP testing is conducted at a constant temperature rather than using a series of temperature changes to produce copies of viral

DNA. LAMP testing, therefore, provides a cheaper and quicker method of testing for SARS-CoV-2 compared with RT-qPCR without compromising on specificity⁴. Whilst not yet approved for use in the UK, as we approach winter and the likelihood of new variants and further waves of infection it is essential to continue frontline testing to detect outbreaks.

As mass testing becomes more available, pooled sample testing can be used. This is usually in areas where the results are expected to be negative. This allows large volumes of tests to be processed and is a quick way of excluding an active COVID-19 infection within that pool. However, if the result is positive, each member of the pool will need to be retested to identify which members are positive. This testing strategy was rolled out by the University of Nottingham and the University of Cambridge in September 2020 to prevent massive outbreaks⁵, and allowing campuses to stay open, as at the time lateral flow testing was not as readily available. Sewage analysis is also a helpful tool to detect outbreaks in particular areas, RNA extraction and detection can be taken from wastewater samples to provide real-time monitoring of the presence of SAR-CoV-2 infection in the community. Waste-based epidemiology is widely recognised and has been used previously for detecting conditions such as Polio and Zika virus in affected countries. Viral shedding occurs in stool even if the individual is asymptomatic; whilst different individuals will shed different amounts of the virus, it can provide a Snapchat of the combined viral prevalence in an area⁶.

A quick online search will result in multiple websites offering 'antibody tests', this raised concerns, especially before the international vaccine roll out as the link between antigens and acquired immunity was not well investigated. They were sold at high prices to a population that was panicked and wanted to know their immunity status. Most of these antibody tests look at binding antibodies, developed in response to past infection with SARS-CoV-2. Binding antibodies flag a pathogen to the immune system whereas a neutralising antibody stops the pathogen in its track. A study including 113 COVID-19 patients found that the most severe cases were associated with increased inflammatory markers and high anti-receptor binding domain (RBD) antibody levels⁷. Quantitation of neutraliser potency revealed high potency was a predictor of survival. Measuring neutralising antibodies is not widely performed but may have a role in predicting disease severity and survival in the most unwell patients infected with SARS-CoV-2.

Variants of concern are continuing to spread globally, with the WHO reporting in June 2021 the delta variant first identified in India has been detected in 62 countries and has overtaken the alpha variant to be the UK's dominant strain⁸. The U.S Food and Drug Administration has warned healthcare leaders to be aware of the possibility of false negatives with molecular tests, as mutations of the part of the virus' genome that is tested could lead to a negative test result. They recommend using multiple genetic targets to determine a final result as the prevalence of genetic variants rises⁹.

Developing accurate, cost-effective, and timely testing is essential as we try to catch outbreaks and prevent further lockdowns. Social distancing measures are the safest way to prevent the spread of disease however businesses, healthcare and personal lives can have detrimental effects from these lockdowns. Mass testing, alongside global vaccination programmes, are essential to gain control of the spread of the virus, and ultimately save lives as winter approaches.

References

1. World Health Organisation. WHO - Press Conference. 2020 [cited 20 April 2021]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>
2. Coronavirus (COVID-19) Infection Survey, UK - Office for National Statistics. Ons.gov.uk. 2021 [cited 20 April 2021]. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveyspilot/latest#test-sensitivity-and-specificity>
3. Department of Health and Social Care. Clinical evaluation confirms accuracy of LAMP test. Gov.UK; 2020.
4. MacDonald A. LAMP-Based Testing for COVID-19 [Internet]. Diagnostics from Technology Networks. 2020 [cited 20 April 2021]. Available from: <https://www.technologynetworks.com/diagnostics/blog/lamp-based-testing-for-covid-19-340508>
5. Mahase E. Covid-19: Universities roll out pooled testing of students in bid to keep campuses open. BMJ. 2020;.
6. Michael-Kordatou I, Karaolia P, Fatta-Kassinou D. Sewage analysis as a tool for the COVID-19 pandemic response and management: the urgent need for optimised protocols for SARS-CoV-2 detection and quantification. Journal of Environmental Chemical Engineering. 2020;8(5):104306
7. Garcia-Beltran W, Lam E, Astudillo M, Yang D, Miller T, Feldman J et al. COVID-19 Neutralizing Antibodies Predict Disease Severity and Survival. SSRN Electronic Journal. 2020.
8. Tracking SARS-CoV-2 variants [Internet]. Who.int. 2021 [cited 11 June 2021]. Available from: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants>
9. U.S Food & Drug Administration. Genetic Variants of SARS-CoV-2 May Lead to False Negative Results with Molecular Tests for Detection of SARS-CoV-2 - Letter to Clinical Laboratory Staff and Health Care Providers. FDA; 2021.