

Near-patient SARS-CoV-2 molecular platforms: new-old tools for new-old problems.

Author:

Luke S.P. Moore, PhD, ORCID 0000-0001-7095-7922

Affiliations:

1. Chelsea and Westminster NHS Foundation Trust, 369 Fulham Road, London, SW10 9NH. UK.

2. North West London Pathology, Imperial College Healthcare NHS Trust, Fulham Palace Road.
London. W6 8RF. UK.

3. National Institute for Health Research Health Protection Research Unit in Healthcare Associated
Infections and Antimicrobial Resistance, Imperial College London, Hammersmith Campus, Du Cane
Road, London. W12 0NN. UK

Correspondence

Dr Luke Moore, Chelsea and Westminster NHS Foundation Trust, 369 Fulham Road, London, SW10
9NH. UK. Email: luke.moore@nhs.net Telephone: 02033155100

Running title

COVID19 molecular POCT implementation

Key words

COVID-19

Point-of-care

Polymerase chain reaction

Respiratory virus

Commentary

Testing for SARS-CoV-2 remains a global issue of capacity, accuracy, and access. In their prospective, interventional, non-randomised, controlled trial published in the Lancet Respiratory Medicine Brendish, Poole, Naidu et al¹ move COVID-19 diagnostics forward both by expanding the repertoire of in-situ evaluated molecular platforms, but also methodologically with a diagnostic controlled trial using clinical impact as a primary outcome measure, analogous to their previous work on other respiratory viruses.² As healthcare providers and public health organisations continue to struggle with COVID-19 case-finding, repurposing existing molecular platforms for this new pathogen, and revising historic laboratory centralisation towards point-of-care syndromic testing may provide some solutions.

In terms of test performance characteristics, Brendish and colleagues¹ find the point-of-care QIAstat-Dx SARS-CoV-2 platform functions well. Across 1054 patients in their UK single centre study, half (499) were tested using the point-of-care system, placed in an acute medicine unit, with the remainder (555) tested at an on-site Public Health England laboratory. This enabled derivation of sensitivity of 99.4% (95%CI 96.9 to 100) and a specificity of 98.6% (95%CI 96.5 to 99.6), albeit against a reference standard the authors describe as 'very poor'.¹ Still, this is an attractive accuracy in the context of the recently published, yet perhaps already outdated, Cochrane review³ of early to market rapid, point-of-care molecular tests for SARS-CoV-2 looking at 13 evaluations of four platforms finding a mean sensitivity of 95.2% (95% CI 86.7 to 98.3) with specificity 98.9% (95% CI 97.3 to 99.5). More recent additions, including the SAMBA⁴ (sensitivity 96.9% (95% CI 83.8 to 99.9), specificity 99.1% (95.3 to 99.9)), bioFire⁵ (sensitivity 93.0% (95% CI 85.4 to 97.4), specificity 100.0 (95% CI 89.7–100.0)), and dnaNudge⁶ (sensitivity 94% (95% CI 86 to 98), specificity 100% (95% CI 99 to 100)) broaden the number of available platforms still further. It must be stressed however that these used a variety of 'gold' standards and reporting of result concordance may be more appropriate than sensitivity and specificity. Furthermore these platforms vary in the degree of hands on time and operator skill needed, and some are perhaps only borderline appropriate for deployment at point-of-care.

Brendish and colleagues'¹ focus on clinical outcomes find that the QIAstat-Dx SARS-CoV-2 turnaround time leads to shorter time to patient placement in an appropriate care area, fewer bed moves, and faster time to enrolment into other COVID-19 clinical trials - all significant advantages. However as we consider how to best leverage this and other platforms, we should be cognizant of the lessons learnt with deployment of point-of-care/near-patient assays in other emergent

infectious diseases settings,⁷ and for other respiratory viruses.² Unless point-of-care infrastructure is developed to underpin point-of-care molecular platforms, including sample adequacy controls, robust internal and external quality assurance, information technology connectivity, training, and use-governance, then widespread deployment may be compromised. Finally, as highlighted in a perspective from Shuren & Stenzel from the US Food and Drug administration,⁸ in learning lessons around diagnostics from this pandemic, beyond ensuring the technical aspects of molecular assays, we must improve clinicians' and policy makers' understanding of test selection, performance, and how results should be interpreted and integrated into care pathways.

Globally, the COVID-19 pandemic has graphically exposed inequitable diagnostic capacity, a key issue being reviewed by the Lancet Commission formed a year ago explicitly to look at equitable access to diagnostics.⁹ It would therefore behove the global response to the pandemic if the development and evaluation of molecular tests enabled deployment in a variety of settings, including those without robust laboratory infrastructure. Whether the platform evaluated by Brendish and colleagues¹ or indeed any of the rapid near-patient SARS-CoV-2 platforms might fit this bill, remains to be seen. Developing clear reporting criteria for rapid point-of-care diagnostic trials which can be compared across different healthcare infrastructure settings and between platforms would seem appropriate, and the metrics used by Brendish and colleagues¹ are certainly among those which should be considered.

When considering each new SARS-CoV-2 diagnostic evaluation, we should consider that while the gene targets for the SARS-CoV-2 molecular platforms are new, the technologies we are adapting to seek these targets are on the whole well established. While the need to rapidly identify patients with COVID-19 is a huge and new stressor on healthcare provision and public health measures, the need to safely manage clinical care yet minimise communicable disease transmission potential is an age old problem. Whilst independent, prospective, controlled, in-situ evaluations of respiratory virus diagnostics such as that by Brendish and colleagues¹ are essential, we need to push even further for clear analyses of implementation and impact, to best understand and leverage the value added from point-of-care platforms during this pandemic and beyond.

References

1. Brendish NJ, Stephen Poole S, Naidu VV, Mansbridge CT, Norton NJ, Wheeler H, Presland L, Kidd S, Cortes NJ, Borca F, Phan H, Babbage G, Visseaux B, Ewings S, Clark TW. Clinical impact of molecular point-of-care testing for suspected COVID-19 in hospital: A prospective, interventional, non-randomised, controlled study (COV-19POC). *Lancet Resp Med*. 2020;[epub ahead of print].
2. Brendish NJ, Malachira AK, Armstrong L, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. *Lancet Resp Med*. 2017;5(5):401-411.
3. Dinnes J, Deeks JJ, Adriano A, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database Syst Rev*. 2020;8:CD013705.
4. Collier DA, Assennato SM, Warne B, Sithole N, Sharrocks K, Ritchie A, Ravji P, Routledge M, Sparkes D, Skittrall J, Smielewska A, Ramsey I, Goel N, Curran M, Enoch D, Tassell R, Lineham M, Vaghela D, Leong C, Mok HP, Bradley J, Smith KGC, Mendoza V, Demiris N, Besser M, Dougan G, Lehner PJ, Siedner MJ, Zhang H, Waddington CS, Lee H, Gupta RK; CITIID-NIHR COVID BioResource Collaboration. Point of Care Nucleic Acid Testing for SARS-CoV-2 in Hospitalized Patients: A Clinical Validation Trial and Implementation Study. *Cell Reports Medicine* 2020;100062.
5. Liotti FM, Menchinelli G, Marchetti S, Morandotti GA, Sanguinetti M, Posteraro B, Cattani P. Evaluating the newly developed BioFire COVID-19 test for SARS-CoV-2 molecular detection. *Clin Microbiol Infect*. 2020;[epub ahead of print].
6. Gibani MM, Toumazou C, Sohbaty M, Sahoo R, Icely C, Karvela M, Hon TK, De Mateo Lopez S, Leung F, Barnett J, Orbeladze A, Luan S, Pournias S, Sun J, Flower B, Bedzo-Nutakor J, Amran M, Skolimowska K, Klaber R, Davies G, Muir D, Randell P, Crook D, Taylor GP, Barclay W, Mughal N, Moore LSP, Jeffery K, Cooke GS. Covid Nudge: diagnostic accuracy of a novel lab-free point-of-care diagnostic for SARS-CoV-2. *Lancet Microbe*. 2020;[epub ahead of print].
7. Pollock NR, Wonderly B. Evaluating Novel Diagnostics in an Outbreak Setting: Lessons Learned from Ebola. *J Clin Microbiol*. 2017;55(5):1255-1261.
8. Shuren J, Stenzel T. Covid-19 Molecular Diagnostic Testing - Lessons Learned. *N Engl J Med*. 2020 Sep 9;[epub ahead of print]. doi: 10.1056/NEJMp2023830.
9. Wilson ML, Atun R, DeStigter K, Flanigan J, Fleming KA, Horton S, Kleinert S, Sayed S; Commissioners of The Lancet Commission on diagnostics. The Lancet Commission on diagnostics: advancing equitable access to diagnostics. *Lancet*. 2019;393(10185):2018-2020.

Declarations

Acknowledgements

LSPM acknowledges academic support from the National Institute of Health Research (NIHR) Imperial Biomedical Research Centre (BRC) and the National Institute for Health Research Health Protection Research Unit (HPRU) in Healthcare Associated Infection and Antimicrobial Resistance at Imperial College London in partnership with Public Health England. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, or the UK Department of Health.

Competing interests

LSPM has consulted for bioMerieux (2013-2020), DNAAelectronics (2015), Dairy Crest (2017–2018), Pfizer (2018-2020), and Umovis Lab (2020), received speaker fees from Profile Pharma (2018), and received research grants from the National Institute for Health Research (2013–2019) and CW+ Charity (2018-2020)