Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

factors? As our knowledge about the pathophysiology of COVID-19 increases, we will be better able to elucidate whether differences in the prevalence of important underlying comorbidities is a cause of this variability, and thus refine the approach to calculating the relative risk of mortality presented by Lewer and colleagues. In countries where access to health care is a key issue, the implications of long-term health issues from COVID-19 among people experiencing homelessness are all the greater and ought to be considered.

According to the evidence provided by Lewer and colleagues, measures in England to protect people experiencing homelessness during the COVID-19 pandemic have been effective to date and might remain so.[8] Celebrating the success of such measures not only involves their protection as the pandemic continues, but also consideration of how they could be expanded to further promote inclusion health by enhancing access to additional components of health care.

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*Mary Flook, Steph Grohmann, *Helen R Stagg*
helen.stagg@ed.ac.uk

Usher Institute (MF, HRS) and Centre for Homelessness and Inclusion Health (SG), University of Edinburgh, Edinburgh EH8 9DX, UK

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

Testing for severe acute respiratory syndrome coronavirus 2 (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*, Nathan Brendish and colleagues[1] move COVID-19 diagnostics forward, both by expanding the repertoire of in-situ evaluated molecular platforms, and 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 health-care providers and public health organisations continue to struggle with COVID-19 case finding, repurposing existing molecular platforms for this new pathogen, and revising historical laboratory centralisation towards point-of-care syndromic testing could provide some solutions.

In terms of test performance characteristics, Brendish and colleagues[1] show that the point-of-care QIAstat-Dx Respiratory SARS-CoV-2 Panel functions well. In their UK-based single-centre study, 499 patients were tested with the point-of-care system, placed in an acute medicine unit, while 555 patients (control group) were tested by PCR done an on-site Public Health England laboratory. Time to results, the primary outcome, was considerably faster in the point-of-care testing group (median 1·7 h [IQR 1·6–1·9]) than in the control group (21·3 h [16·0–27·9]; difference 19·6 h [95% CI 19·0–20·3], p<0·0001), with a hazard ratio of 4023 (95% CI 545–29 696) after controlling for age, sex, time of presentation, and severity of illness. The QIAstat-Dx Respiratory SARS-CoV-2 Panel also had high accuracy, with sensitivity of 99·4% (95% CI 96·9–100) and specificity of 98·6% (96·5–99·6), albeit evaluated against


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a reference standard that the authors describe as very poor.[1] Nevertheless, this level of accuracy is attractive in the context of the recently published (yet perhaps already outdated) Cochrane review[3] of early-to-market, rapid, point-of-care molecular tests for SARS-CoV-2, which looked at 13 evaluations of four platforms, finding a mean sensitivity of 95·2% (86·7–98·3) with a specificity of 98·9% (97·3–99·5). More recent additions, including the SAMBA2[4] (sensitivity 96·9% [83·8–99·9], specificity 99·1% [95·3–99·9]), bioFire[5] (sensitivity 93·0% [85·4–97·4], specificity 100·0% 89·7–100·0]), and dnaNudge[6] (sensitivity 94% [86–98], specificity 100% [99–100]) broaden the number of available platforms further. It must be emphasised, however, that these platforms used a variety of gold standards, and reporting of result concordance might 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 the point of care.

Brendish and colleagues also showed that the fast turnaround time of the QIAstat-Dx Respiratory SARS-CoV-2 Panel decreased the time taken for patients to be placed in an appropriate care area, and led to 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 cognisant of the lessons learnt through the deployment of point-of-care or 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 might be compromised. Finally, as highlighted in a perspective from Shuren and 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 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 colleagues,[1] 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 that can be compared across different health-care infrastructure settings and between platforms would seem appropriate, and the metrics used by Brendish and colleagues[1] are certainly among those which should be considered.

When considering each new SARS-CoV-2 diagnostic evaluation, we should consider that, although 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. Additionally, whereas the need to rapidly identify patients with COVID-19 is a huge and new stressor on health-care provision and public health measures, the need to safely manage clinical care while minimising the potential for communicable disease transmission is an old problem. Independent, prospective, controlled, in-situ evaluations of respiratory virus diagnostics, such as that by Brendish and colleagues,[1] are essential. However, 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.

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Luke S P Moore
luke.moore@nhs.net

Chelsea and Westminster NHS Foundation Trust, London SW10 9NH, UK; North West London Pathology, Imperial College Healthcare NHS Trust, London, UK; National Institute for Health Research Health Protection Research Unit in Healthcare-Associated Infections and Antimicrobial Resistance, Imperial College London, London, UK

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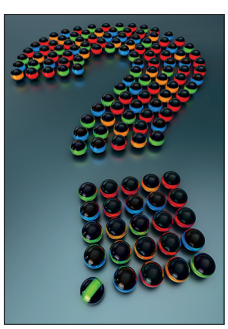
Physiological and biological heterogeneity in COVID-19-associated acute respiratory distress syndrome

One of the most common causes of hospital admission and death in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is acute respiratory distress syndrome (ARDS), a clinical syndrome characterised by acute lung inflammation and increased-permeability pulmonary oedema due to injury to the alveolar capillary barrier. As clinicians care for a surge of patients with ARDS due to COVID-19, two questions arise. First, is COVID-19-associated ARDS intrinsically different from ARDS unrelated to COVID-19? The answer to this question has implications for the use of evidence-based therapies such as lung-protective mechanical ventilation, proning, and conservative fluid management in COVID-19-associated ARDS. Second, is COVID-19-associated ARDS a uniform syndrome, or can phenotypes be identified? Recent clinical studies in so-called classical ARDS (a term used here to refer to ARDS unrelated to COVID-19, the causes and characteristics of which are heterogeneous) using latent class analysis have shown distinct hyperinflammatory and hypoinflammatory biological phenotypes of ARDS,[1] and emerging evidence indicates that these phenotypes respond differently to some clinical interventions.[2,3] Identification of similar, or new, distinct phenotypes within the scope of COVID-19-associated ARDS could shed light on mechanisms of lung injury in COVID-19 and have implications for clinical trial design.

In *The Lancet Respiratory Medicine*, two Articles begin to answer these questions. To address the first question, Giacomo Grasselli and colleagues[4] studied clinical and laboratory characteristics of 301 adults with COVID-19-associated ARDS admitted to intensive care units (ICUs) in seven Italian hospitals over a 2-week period in March, 2020. Lung mechanics were assessed in the first 24 h of ICU admission and compared with findings in historical cohorts of patients with classical ARDS. Similar to classical ARDS, the distribution of values for static compliance of the respiratory system was broad. Although patients with COVID-19-associated ARDS had higher median static compliance (41 mL/cm H_2O [IQR 33–52]) than those with classical ARDS (32 mL/cm H_2O [25–43]), this difference diminished in multivariable models controlling for other clinical characteristics. Furthermore, almost all of those with COVID-19-associated ARDS (280 [94%] of 297 patients) had static compliance values below the 95th percentile of reported values for classical ARDS, and the extent of pulmonary oedema in patients with COVID-19, measured by calculation of total lung weights from lung CT scans, was similar to that of patients with classical ARDS. D-dimers in 261 patients with COVID-19 were associated with ventilatory ratio, which is a surrogate for dead-space ventilation. A subgroup of patients with D-dimer concentrations greater than the median and static compliance equal to or less than the median (high D-dimers, low compliance [HDLC]) had markedly worse 28-day mortality than the others subgroups of high D-dimers, high compliance (HDHC); low D-dimers, low compliance (LDLC); and low D-dimers, high compliance (LDHC). 28-day mortality was 56% (40 of 71 patients) in the HDLC group, 27% (18 of 67 patients) in the LDHC group, 22% (13 of 60 patients) in the LDLC group, and 35% (22 of 63 patients) in



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