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.

Serological assays for delayed SARS-CoV-2 case identification

Author's reply

We read with interest the insightful comments put forward by Kay Weng Choy, raising important considerations for clinicians planning to use point-of-care serological assays for delayed case identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in response to those presented in our Article.[1]

We agree that along with evaluating assays for cross-reactivity of IgM and IgG with common infectious diseases, further benefit could be derived by assessing the potential of assay performance in those with autoimmune disease and immunodeficiency. Indeed, previously reported work in SARS-CoV-1 would suggest the potential for cross-reactivity of autoantibodies for SARS-CoV-2 IgG.[2] Similarly, consideration has also been given to how age could affect viral load and the subsequent development of SARS-CoV-2 IgG antibodies,[3] which is a focus of our ongoing work.

Our study was designed specifically to evaluate the use of point-of-care assays for frontline health-care workers directly involved in the clinical care of patients with SARS-CoV-2 infection; therefore, it was not possible to evaluate any difference in detection of SARS-CoV-2 IgG in young or older people. At a strategic level, health-care workers with autoimmune disease or known immunodeficiency were required to be actively shielding during the study period and so were unable to take part.[4] An evaluation of the potential effect of immunodeficiency on assay performance was beyond the scope of our study; however, we strongly agree that this is an important issue for future studies where consideration can be given to testing in different populations.

Additionally, Kay Weng Choy correctly highlights that whole blood is likely to be the primary sample type at point-of-care and, therefore, evaluation of diagnostic performance is warranted for whole blood and serum samples. Further research involving our group has been reported in August, 2020, comparing not only serum with whole blood samples in the laboratory, but also with finger-prick testing across a number of different point-of-care assays.[5] Observed test sensitivity was broadly similar; however, the reported variation in assay performance across these three methods highlights the need for robust evaluation of individual kits (as they become available) in specific populations. This variation is particularly relevant if consideration is being given to use with finger-prick blood. In our study, individuals were recruited on a single occasion and no repeat testing was considered in the performance evaluation.

Finally, Kay Weng Choy highlights the value of orthogonal testing algorithms, advocating for a second test, each with unique assay design characteristics with the aim of improving the positive predictive value. Indeed, within our own institutions we have developed a testing algorithm that uses an anti-nucleocapsid and anti-spike protein immunoassay. This algorithm has potential to increase diagnostic yield but it is worth noting that insufficient antibody target data provided by a considerable number of manufacturers could provide additional challenges to the design of similar testing programmes.[6]

LSPM has consulted for bioMerieux (2013–20), DNAelectronics (2015–18), Dairy Crest (2017–18), Umovis Lab (2020), and Pfizer (2018–20), received speaker fees from Profile Pharma (2018), received research grants from the National Institute for Health Research (2013–20), CW+ Charity (2018–19), and Leo Pharma (2016), and received educational support from Eumedica (2016–18). NM has received speaker fees from Beyer (2016) and Pfizer (2019) and received educational support from Eumedica (2016) and Baxter (2017). RJ has received honoraria, speaker fees, travel support and research grant funding from Gilead, ViiV Healthcare, BMS, AbbVie, Janssen and Merck. SJCP has received a research grant from the Scientific Exploration Society with support from the Viscount Gough. EC has received speaker fees from bioMerieux (2019). All other authors declare no competing interests.

*Scott J C Pallett, Michael Rayment, Aatish Patel, Esmita Charani, Sarah J Denny, Sophia A M Fitzgerald-Smith, Nabeela Mughal, Rachael Jones, Gary W Davies, Luke S P Moore
scott.pallett@nhs.net

Centre of Defence Pathology, Royal Centre for Defence Medicine, Queen Elizabeth Hospital Birmingham, Birmingham B15 2WB, UK (SJCP); Chelsea and Westminster Hospital NHS Foundation Trust, London, UK (SJCP, MR, AP, SJD, SAMF-S, NM, RJ, GWD, LSPM); NIHR Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance, Imperial College London, London, UK (EC, LSPM); and North West London Pathology, London, UK (NM, LSPM)

1 Pallett SJC, Rayment M, Patel A, et al. Point-of-care serological assays for delayed SARS-CoV-2 case identification among health-care workers in the UK: a prospective multicentre cohort study. *Lancet Respir Med* 2020; **8:** 885–94.

2 Wang YS, Shen H, Sun SH, et al. Analysis of false-positive associated with antibody tests for SARS-CoV in SLE patients. *Shi Yan Sheng Wu Xue Bao* 2003; **36:** 314–17 (in Chinese).

3 Y Chen, L Li. SARS-CoV-2: virus dynamics and host response. *Lancet Infect Dis* 2020; **20:** 515–16.

4 Public Health England. Guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19. August 18, 2020. https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19 (accessed on Aug 26, 2020).

5 B Flower, JC Brown, B Simmons, et al. Clinical and laboratory evaluation of SARS-CoV-2 lateral flow assays for use in a national COVID-19 seroprevalence survey. *Thorax* 2020; published online Aug 12. https://doi.org/10.1136/thoraxjnl-2020-215732.

6 Pallett SJ, Jones R, Pallett MA, et al. Characterising differential antibody response is integral to future SARS-CoV-2 serostudies. *J Infect* 2020; published online July 31. http://doi.org/10.1016/j.jinf.2020.07.029.

Published **Online** September 14, 2020 https://doi.org/10.1016/S2213-2600(20)30406-9