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.

Therefore, whether increased PVR directly affected the risk of mortality or only represented an indirect marker of severity for underlying comorbid conditions remains unknown. Consistently, it should be emphasised that if some disease entities are based almost exclusively on a single parameter, a PVR value used in isolation cannot characterise a clinical condition and does not define the pathological process per se. Therefore, although mildly elevated PVR might favour detection of early pulmonary hypertension, the risk of overdiagnosis and overtreatment is substantial, as recognised by the authors. This is especially of concern for patients with mild pulmonary hypertension due to left heart disease and chronic lung diseases for whom current vasoactive therapies have been most commonly shown to be ineffective or even deleterious, resulting in strong recommendations against their routine use.[7,8]

All in all, Maron and colleagues should be congratulated on providing solid evidence that PVR values as low as 2·2 Wood units can identify a subgroup of people at increased risk of morbidity and mortality. Hopefully, this finding will foster further explorations to delineate the diverse mechanisms responsible for this association, as well as the optimal management of patients.

SP reports grants from Actelion, AstraZeneca, and Resverlogix, outside the submitted work. SB reports personal fees from Actelion and resverlogix and grants and personal fees from Janssen and Morphic, outside the submitted work. All other authors declare no competing interests.

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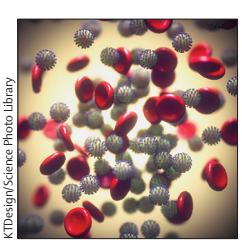
The time to do serosurveys for COVID-19 is now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Published **Online** July 24, 2020 https://doi.org/10.1016/S2213-2600(20)30313-1

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In their study in *The Lancet Respiratory Medicine*, Scott Pallett and colleagues[1] assessed the performance of lateral flow serological assays and estimated the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection to be 10·6% (95% CI 7·6–13·6) in asymptomatic health-care workers and 44·7% (42·0–47·4) in symptomatic health-care workers at two hospitals in London, UK. This work raises important issues in the design of seroprevalence surveys, how they should be done, and, importantly, how to interpret and act on the results.

Seroprevalence studies, serosurveys for short, are important for determining the true extent of an outbreak, map its distribution, and identify hotspots and at-risk groups, such as health-care workers and older people. For serosurveys to inform public health measures and control strategies, they must have high sensitivity and specificity. Of these attributes in a serology test, high specificity is crucial, to avoid misclassifying people as having been infected when they have not (ie, false-positive results). This would give a false sense of security to individuals and governments, misleading public health interventions by overestimating the level of immunity in the population, and prematurely easing restrictions. Therefore, establishing the accuracy of lateral flow serological assays before doing a serosurvey is crucial to generate confidence in the results. Relatively small variations in test specificity and the prevalence of SARS-CoV-2 infection can heavily influence results.

Two lateral flow serological assays were evaluated in this study: the Encode SARS-CoV-2 IgM/IgG One Step Rapid Test Device (Zhuhai Encode Medical Engineering, Zhuhai, China) and the Onsite CTK Biotech COVID-19 split IgG/IgM Rapid Test (CTK Bitotech, Poway, CA, USA). The Encode assay had a sensitivity (compared with PCR-confirmed cases of SARS-CoV-2 infection) of

93·4% (95% CI 87·8–96·9) and a specificity of 99·0% (94·6–100·0), whereas the Onsite assay had a sensitivity of 88·2% (81·6–93·1) and a specificity of 94·0% (87·4–97·8). Having established which test to use, the next questions are identifying the study population and estimating an adequate sample size for the results to be generalisable. Pallet and colleagues focused on health-care workers, an essential resource in a pandemic response, and a group that is at particular risk when caring for patients, especially when personal protective equipment might be in short supply. Infection rates in this group are expected to be higher than in the general population. At a seroprevalence of 10·6%, a test with 99·0% specificity would have a positive predictive value (PPV) of 91·7%, meaning around 8% of the results might be false positives. However, if the authors had used the test with 94·0% specificity to do the serosurvey, the PPV would be 63·6%, meaning approximately a third of the results would be false positives, leading to an overestimate of prevalence in health-care workers by almost a third. If these tests were used to do serosurveys in the general population (estimated prevalence 2·7%), then the Encode assay would have a PPV of 72·2% and the Onsite assay 29·0%, leading to unacceptably high rates of false-positive results.

So far, 58 serological tests of varying performance have received emergency use approval from the US Food and Drug Administration.[2] How could serosurveys be carried out in the general population? In a study of COVID-19 in households in Geneva,[3] cumulative seroprevalence increased from 4·8% in week 1 to 10·8% by week 5. The authors mitigated against the effect of false-positive results by confirming all positive and indeterminate results with another assay.

Moving forward, research on better tests for serosurveys should include non-invasive sampling and assays measuring protective immunity. Large-scale studies can be efficiently done on high-throughput immunoassay systems, but the drawback is that they need serum or plasma, requiring phlebotomists to collect blood samples and processing in the laboratory. Immunoassays on non-invasive samples, such as oral fluids, would be a game-changer.

Investment in research on the correlates of protection and its duration will enable the development of serology tests that allow those who test positive to safely return to work or school. Striking a balance between public health and economic interests has been notoriously difficult during the pandemic. The World Bank issued a policy brief describing how two tests can contain the COVID-19 pandemic and save the economy.[4] Serosurveys to inform the design of chemoprophylaxis and vaccine trials are also needed to provide reliable estimates of the risk of infection in the target population and calculate the appropriate population sample to detect the desired effect size.

Changing testing strategies as the pandemic unfolds has made it very difficult for countries to estimate the proportion of the population that has been infected. Yet, this information is crucial for developing evidence-based strategies to adapt public health measures and travel restrictions.[5] Furthermore, studies have shown that as much as 44% of COVID-19 transmission can take place when individuals are pre-symptomatic or asymptomatic.[6] As most infections result in individuals developing antibodies against SARS-CoV-2 regardless of symptoms, seroprevalence studies are the most useful means of understanding the true prevalence of the pandemic, monitor trends and geographical distribution over time, identify hotspots and at-risk populations needing special attention, and ultimately allow infection control programmes to assess the effectiveness of interventions. With most of the world still in some form of lockdown, and the prospect of a vaccine more than a year away, governments need a strategy to ease restrictions while ensuring that the country has a healthy workforce for its hospitals and care homes, as well as a means of monitoring safe environments for health-care facilities and other workplaces, schools, and mass gatherings.

The time to do serosurveys is now, but we need to proceed with care.

We declare no competing interests.

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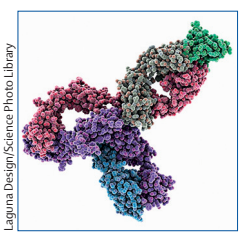
Immunotherapy in lung cancer: effective for patients with poor performance status?



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Published **Online** March 19, 2020 https://doi.org/10.1016/S2213-2600(20)30107-7

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For advanced non-small-cell lung cancer (NSCLC) without targetable genomic alterations, treatment with programmed cell death 1 (PD-1) pathway immune checkpoint inhibitors in the first-line setting has become the standard of care in many parts of the world.[1–3] One key subgroup that has been universally excluded from transformative, randomised, phase 3 NSCLC immunotherapy trials is patients with an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 2 or worse.[1–5] Our understanding of the safety and efficacy of immune checkpoint inhibitors in this population is quite limited. Patients with a poor PS comprise a sizeable proportion of the lung cancer population, with 34–48% of patients having a PS of 2–4 at the time of initial diagnosis.[6] Insufficient information on how these patients respond to immunotherapy represents a major knowledge gap in clinical care. To fill this unmet need, prospective studies have begun to explore clinical outcomes with immune checkpoint inhibitors in patients with a poor PS. The CheckMate 153 and 171 trials of nivolumab in previously treated patients with NSCLC enrolled those with a PS of 0–2 and showed that although treatment was largely safe in the PS2 subgroup, the median overall survival was very short (about 4–5 months),[7,8] drawing attention to the limited efficacy of immune checkpoint inhibitor therapy in this population.

In *The Lancet Respiratory Medicine*, Gary Middleton and colleagues present the results of the PePS2 study, which is the first prospective immunotherapy study that specifically enrolled only patients with NSCLC of PS2.[9] This single-arm trial of 60 patients given the PD-1 inhibitor pembrolizumab, sheds new light on outcomes for this population with a poor prognosis. Determination of a PS can be challenging because of inter-rater discordance, and the physician's tendency to overestimate performance compared with a patient's self-assessment of their own functional status.[6] Although the PePS2 study did not include patient-reported PS self-assessment, the authors took careful measures to ascribe an accurate PS and ensure that patients had a stable PS of 2 at two different timepoints assessed at least 2 weeks apart.

Compared with other trials, this trial also uniquely enrolled both patients who were treatment-naive and those who had received previous chemotherapy. However, with small numbers of patients in each subgroup (n=24 first-line, n=36 subsequent-line), it is difficult to predict if treatment outcomes will differ significantly by line of therapy in larger populations. Furthermore, when available, the authors attempted to correlate treatment responses with the programmed cell death ligand 1 (PD-L1) tumour proportion score (TPS), which is the one clinically available biomarker of immunotherapy efficacy in NSCLC. Although the authors suggest a greater clinical benefit with increasing PD-L1 expression, the small PD-L1 subgroups (n=27 for TPS <1%, n=15 for TPS 1–49%, and n=15 for TPS ≥50%) and overlapping 95% CIs for all clinical efficacy measures in this study limit the ability to conclude at this time that PD-L1 expression behaves similarly as a predictive biomarker of pembrolizumab efficacy in the poor PS population as it does in patients with a better PS.

While the study examined an endpoint not commonly used in other immunotherapy trials (durable clinical benefit at 18 weeks), the inclusion of toxicity as a co-primary endpoint is an important outcome to investigate in a group of patients who might already have difficult cancer-related symptoms. Only 10% of patients discontinued treatment because of drug toxicity, and the proportion of high-grade adverse events was relatively low at 15%. These data are similar to other immunotherapy studies in patients with NSCLC of poor PS, suggesting that immune checkpoint inhibitors are reasonably well tolerated in this population.