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benefit patients who are admitted to hospital and, outside hospitals, they should be used only in the context of clinical trials. However, on the basis of our current understanding of the evolution of COVID-19 (appendix), this broad generalisation from the treatment of severely ill patients who have been admitted to hospital to patients with uncomplicated COVID-19 in the community is not supported by current evidence. COVID-19 reflects a changing pathological process. Viral burden peaks early, around the time of first symptoms. This timepoint is when antiviral drugs are likely to be most beneficial. Thereafter, viral burden declines and inflammatory processes dominate in those patients who deteriorate and require admission to hospital, and ultimately respiratory support. Immune modulators and anti-inflammatories are more likely to be of benefit at this later stage but might be harmful if used earlier (ie, by enhancing viral replication).² Evidence reviews² and the guidelines that they generate¹ should recognise that, although SARS-CoV-2 is one virus, both the COVID-19 disease process and access to health care vary widely. The WHO Global Development Group “prioritized outcomes taking a patient perspective”.² They decided that mortality would be most important to patients, followed by need for and duration of mechanical ventilation. We argue that prevention of hospital admission is the therapeutic priority for low-resource settings, which usually have few facilities for intensive care. Efficacy assessments in prevention and in uncomplicated COVID-19 should not be pooled with results from severely ill patients who have been admitted to hospital.

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- 1 WHO. Therapeutics and COVID-19: living guideline. Dec 17, 2020. <https://www.who.int/publications/i/item/therapeutics-and-covid-19-living-guideline> (accessed Feb 14, 2021).
- 2 Siemieniuk R, Rochwerg B, Agoritsas T, et al. A living WHO guideline on drugs for COVID-19. *BMJ* 2020; **371**: m4475.
- 3 The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with COVID-19—preliminary report. *N Engl J Med* 2020; published online July 17. <https://doi.org/10.1056/NEJMoa2021436>.

Vaccines and SARS-CoV-2 variants: the urgent need for a correlate of protection

Immune-escape variants have raised concerns about the effectiveness of vaccines as the world scales up SARS-CoV-2 immunisation. COVID-19 vaccines have shown up to 95% efficacy¹ in preventing clinical cases and up to 100% efficacy² in preventing severe disease or admission to hospital in settings with pre-existing variants. New variants, especially 501Y.V2 (B.1.351), which escape natural-induced and vaccine-induced immunity, have created uncertainty on whether the vaccines are effective in preventing both mild and severe COVID-19.

Preliminary reports show that the 501Y.V2 variant has complete immune-escape in South African convalescent serum samples,³ and reductions in neutralising activity in vaccinee serum samples for all four vaccines tested.⁴⁻⁷ Although these reductions were small for the BBIBP-CorV,⁴ BNT162b2,⁵ and mRNA-1273⁶ vaccines, preliminary data suggest they were substantial, including with a complete immune escape for the AZD1222 vaccine.⁷ Concerningly, the clinical trial efficacy of AZD1222 was 70% in the UK and Brazil,⁸ but 22% according to preliminary data from South Africa.⁷ For NVX-CoV237 the efficacy was 89% in the UK but

49% in South Africa,⁹ whereas for Ad26.COVS-5 the efficacy was 72% in the USA but 57% in South Africa.¹⁰ Extrapolating vaccine efficacy against pre-existing variants to new variants could be seriously misleading.

Adequate genomic surveillance, standardised variant nomenclature, and a repository of variants and vaccine serum samples¹¹ are needed to deal with the challenges of repeatedly emerging new SARS-CoV-2 variants, but there is a particularly pressing need to establish a correlate of protection so that vaccine efficacy results obtained with pre-existing variants can be translated to newly emerging variants because it is impractical and time consuming to repeat clinical trials with each new immune-escape variant. Furthermore, repeating clinical trials for each variant might take so long that even newer variants could emerge while these clinical trials are underway.

Because the immune responses required to prevent mild disease might be different to severe disease, correlates of protection might need to be stratified on the basis of disease severity. There are four key requirements to achieve this aim. First, all SARS-CoV-2 vaccine developers with existing or completed efficacy trials should commit to transparency and open data sharing. Second, an expert committee (preferably under WHO) should be appointed to review existing and planned analyses to identify correlates of protection for each efficacious vaccine. Third, studies with multiple vaccines to fast-track the identification of an animal model, assay, or marker as a correlate of protection should be initiated to address gaps in the correlate research plans. Finally, a central database should be created to collate data for each of the efficacious vaccines, thereby providing larger sample sizes to assess multiple variables as correlates of protection and to test if a correlate identified in one trial is valid in other trials.

The identification of a correlate of protection is too important and urgent

See Online for appendix



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to be left to uncoordinated separate studies by individual investigators or vaccine developers. South Africa, at the forefront of dealing with the challenge of its vaccine roll-out during the spread of a predominant 501Y.V2 variant, has to make vaccine decisions without adequate efficacy data. A correlate of protection for mild and severe SARS-CoV-2 infection will go a long way to providing an evidence base for these decisions and overcome the obstacles that new variants are placing on the vision of global SARS-CoV-2 control with the widespread implementation of effective immunisation.



SSAK is the co-chair of the South African Ministerial Advisory Committee for COVID-19.

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Gender, race, and health workers in the COVID-19 pandemic

The Editors¹ correctly highlighted the situation the health workforce is in, and how it is facing “serious harms to their physical and mental wellbeing while trying to deliver quality care” during the COVID-19 pandemic. Considering the health workforce as a homogeneous group misses the reality of who is affected within this group and the necessary solutions.

70% of the global health workforce are women, a number that increases to 90% with social care workers. Sex-aggregated case data collated by the UN show that more than 70% of COVID-19 infections in health-care workers in the USA, Italy, and Spain are in women. In our work on health professionals’ gender and race at the front line of the COVID-19 pandemic, we found that this rate is partly because of the absence of necessary resources provided to these health-care workers: women, and Black women in particular, have less access to personal protective equipment (PPE) and training. Female health-care workers worldwide are also facing the downstream effects of their work, including mental health issues,² increased physical violence, alternative arrangements for their families so as to not expose them to risk, and physical exhaustion.

Gender-neutral policy making inherently neglects the needs of women.³ Thus, it is imperative to ensure that all considerations of health-care workers are disaggregated by gender and race to understand the differential effect between different members of the workforce. In doing so, targeted interventions can ensure that PPE is distributed fairly, that proper mental health programmes are created, and that these efforts are gender mainstreamed to ensure that they reach those most vulnerable to suffering these effects.

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Lokugamage AU, Wong SHM, Robinson NMA, Pathberiya SDC. Transformational learning to decolonise global health. *Lancet* 2021; **397**: 968–69—In this Correspondence, the published work the authors refer to in their first sentence has been corrected to a Comment. This correction has been made to the online version as of April 1, 2021.

For UN sex-aggregated case data see <https://data.unwomen.org/resources/covid-19-emerging-gender-data-and-why-it-matters>

For more on gender and race on the front line see <https://www.genderandcovid-19.org/resources/covid-19-pandemic-and-health-professionals-gender-and-race-on-the-front-line/>