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SARS-CoV-2 variants offer a second chance to fix vaccine inequities

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Global COVID-19 vaccine equity remains aspirational for much of the world. But the emergence of rapidly evolving SARS-CoV-2 variants provides new opportunities to correct past public policies, support local vaccine production and combat rising anti-vaccine aggression.

The fact that almost 70% of the global population has received at least a single COVID-19 vaccination[1] has little relevance for the world's low- and middle-income countries (LMICs), where the percentage of those vaccinated is far lower. In two of Africa's most populous nations, Nigeria and Democratic Republic of Congo, only 24% and 6.4% have received a single vaccine dose, respectively[1]. In addition, we face a new reality that a single COVID-19 immunization, and in some cases even two immunizations, unless these primary immunizations are accompanied by a booster, affords only modest protective immunity against the emerging Omicron subvariants[2]. Across the world's LMICs in Africa, as well as many other large nations such as Pakistan and Papua New Guinea, the percentage of the population that have received boosters is typically in the single digits[1].

The failures to both fully vaccinate and boost could create a dire situation in 2023 as the Omicron subvariants continue mutating into an alphabet soup of variants with unprecedented growth and immune escape advantages. Already, the predominant BA.5 subvariant requires a specific booster, but now newer variants such as XBB, BQ.1.1 and others are emerging with convergent Omicron receptor-binding domain (RBD) mutations[3]. In Singapore, XBB is fueling a surge in cases, and now BQ.1.1 is beginning to spread rapidly in the United Kingdom and the rest of Europe. Although we do not know which (if any) of these new variants might become dominant globally, the fact that many evade most of the available monoclonal antibodies or convalescent plasma[3], as well as plasma from those immunized with vaccines derived from the original lineage first reported in China, could spell further troubles ahead for the LMICs.

The overriding concern is that LMIC populations already remain profoundly under vaccinated because they still lack access to boosters — those based on the original lineage first reported in China would still provide some level of protection against the currently dominant BA.5 subvariant. Soon, even these might not be sufficient. If a new XBB, BQ.1.1 or related convergent Omicron RBD-escape subvariant gains a global foothold, we are practically starting over in terms of ensuring next-generation booster access.

A staggering 15 million people have lost their lives from COVID-19, with more than one-half of those deaths occurring in LMICs led by India, Brazil, Pakistan and Indonesia. Now, with the rise of the convergent Omicron RBD-escape subvariants, will the death rate increase further? The key to prevent this from happening is to look at lessons learned during the first years of the pandemic, when LMICs were denied access to mRNA vaccines in adequate amounts. The countries could not afford them, and vaccine donations came too little, too late. Beyond the tragic losses in life that ensued, this situation bred resentment among LMIC populations[4]. Anti-vaccine activists from the United States and elsewhere also piled on to promote widespread vaccine hesitancy and refusal[5].

This time around, we cannot afford to repeat the missteps of 2020–2022. We must ensure a rapid turnaround of next generation boosters that target the convergent Omicron RBD-escape subvariants. These might include either BA.5-specific boosters, or one corresponding to an emerging escape variant.

A two-pronged approach is essential. Financial support to purchase Omicron- and variant-specific mRNA boosters from Pfizer and Moderna will help, but simultaneously we must empower LMIC vaccine producers to produce effective boosters using locally derived technologies. Although there is now some nascent capacity building for mRNA vaccine technology in LMICs in Africa and elsewhere — and this should continue to be supported and fostered — we must recognize how India (Corbevax), Indonesia (IndoVac), Taiwan (Medigen), and Cuba (Soberana 02 and Abdala) each made their own low-cost domestic recombinant protein vaccines reaching (in some cases) large populations[6]. In the case of Corbevax and IndoVac, the early prototype for these vaccine technologies was developed at the non-profit Texas Children's Hospital Center for Vaccine Development before transfer (without patents) to the LMIC producer. Ultimately, the LMIC vaccine makers (Biological E in India and BioFarma in Indonesia) each produced their own COVID-19 vaccine at large-scale, working out with their respective national regulatory authorities a plan for clinical testing and immunological bridging studies before emergency-use authorization[7].

This approach led to the administration of more than 80 million doses to date, possibly reaching 100 million doses by the end of 2022. It provided proof-of-concept that it is possible to decolonize the traditional model that depends on the multinational companies to fully create, mature and deliver vaccines, although in the case of the Oxford–AstraZeneca adenovirus-vectored vaccine or Novavax particle vaccine, the Serum Institute of India successfully reproduced those processes to make these vaccines locally. The bottom line is that the timely production and delivery of Omicron RBD-escape subvariant boosters or possibly next-generation universal sarbecovirus vaccines will demand public and financial support for a balanced vaccine ecosystem inclusive of fully engaged LMIC producers at the outset. This will also require full engagement from the group of 20 (G20) nations.

Such balance in the global vaccine ecosystem would not only benefit the delivery of COVID-19 boosters but also the development of vaccines for other pressing neglected and emerging infections. The University of Oxford has developed a promising new malaria vaccine (R21/Matrix-M, including the saponin-based Matrix-M adjuvant

developed by Novavax) that has been manufactured by the Serum Institute of India and is showing high levels of protective immunity, which exceed World Health Organization target criteria[8]. Similar approaches would also benefit related vaccines for neglected tropical diseases, including schistosomiasis, hookworm infection, leishmaniasis, Chagas disease, leptospirosis, Buruli ulcer and many others[9].

Promoting local vaccine development capacity is essential but not sufficient to ensure vaccine equity. Anti-vaccine activism, much of it now initiated in the United States, expanded during the pandemic to promote widespread COVID-19 vaccine refusal in LMICs[5]. Too often, we portray the 'infodemic' as random misinformation or disinformation popping up on the internet. This is an outdated and discredited mode of thinking, and one that also denies justice for the victims who died because they refused a COVID-19 vaccination. The anti-vaccine movement has evolved into a deliberate, organized and well-financed destructive force. Increasingly, it connects to a political agenda, mostly authoritarian and far-right politics. It kills more people than global terrorism, nuclear proliferation and cyberattacks combined[10]. Yet, we do not treat it as such.

Exactly how we defuse this new-generation anti-science aggression remains uncertain, but a first step is to understand how this has become a lethal force, responsible for the deaths of hundreds of thousands of people who refused a COVID-19 vaccine during the Delta and Omicron waves of 2021 and 2022, respectively.

The new convergent Omicron RBD-escape subvariants are bearing down. Promoting local vaccine production of the Omicron boosters while countering the anti-vaccine activism now influencing LMICs with devastating effect represent the new twin pillars of global vaccine equity. Urgent action to address both forces will help to correct the past mistakes that continue to haunt our COVID-19 pandemic.

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Competing interests

P.J.H. is a co-inventor on non-revenue generating patents for parasitic infections and neglected tropical diseases owned by Baylor College of Medicine (BCM). He is also a co-inventor of a COVID-19 recombinant protein vaccine technology owned by BCM that was recently licensed by Baylor Ventures non-exclusively and with no patent restrictions to several companies committed to advance vaccines for low- and middle-income countries. These include Biological E (India), BioFarma (Indonesia), Incepta (Bangladesh) and ImmunityBio (United States with partnerships in the African Continent including Botswana and South Africa). The co-inventors have no involvement in licence negotiations conducted by BCM. Similar to other research universities, a long-standing BCM policy provides its faculty and staff, who make discoveries that result in a commercial licence, with a share of any royalty income. To date, BCM has not distributed any royalty income to the co-inventors on the COVID-19 recombinant protein vaccine technology. Any such distribution will be undertaken in accordance with BCM policy. In addition, P.J.H. is also the author of several books published by academic presses (ASM–Wiley and Johns Hopkins University Press), and he receives modest royalty income from this activity.