Technologies to advance COVID-19 vaccine equity

Poor countries need vaccine formats with low barriers to manufacture, distribution and administration.

The COVID-19 pandemic is likely to ricochet around the world for years to come. One year after the first SARS-CoV-2 vaccines received Emergency Use Authorization (EUA), ~54% of the world's population and only ~6% of people in low-income countries have received at least one dose. Solving the problem of unequal access to vaccines means addressing its diverse causes, from vaccine hoarding by wealthier countries, to intellectual property and distribution logjams, to antivax disinformation and vaccine hesitancy. But part of the solution may also lie in the vaccines themselves, as new versions with useful features come online. Properties such as temperature stability, needle-free delivery, and simplicity of manufacture promise to galvanize vaccination campaigns in low- and middle-income countries (LMICs) and should be prioritized for investment and scale-up.

Although the first COVID-19 vaccines showed high efficacy against the first waves of the disease, they were not well suited to the extraordinary challenge of immunizing the world's population, particularly the more than two billion people living in poor, rural, or remote communities. These vaccines require a cold chain, injections (and thus syringes, sterile administration, and qualified healthcare workers), and high-tech manufacturing capacity, all of which have limited the geographic reach of vaccination efforts. Logistical hurdles drive up costs and are serious impediments to carrying out life-saving immunization programs in LMICs.

Insufficient vaccination in LMICs and high-income countries alike not only allows the disease to spread but also increases the likelihood that new viral variants of concern like Omicron will emerge. The variants of concern seen to date have been more contagious, more virulent, or more resistant to vaccine-induced immune responses and antibody drugs than the ancestral strains identified early in the pandemic. Delta is much more contagious and has a shorter incubation period than all previous strains, and Delta and particularly Beta are less susceptible to neutralization by vaccine-induced antibodies. The added burden of disease from existing or future variants underscores the urgency of rapid global immunization.

As of late November, the COVID-19 vaccine tracker of the WHO's R&D Blueprint listed 132 vaccines in clinical development and 194 in preclinical development. Many of these candidates are variations of three COVID-19 vaccine types in wide use: modified mRNA in lipid nanoparticles (Pfizer/BioNTech and Moderna), non-replicating adenoviral vectors (AstraZeneca and Johnson & Johnson), and inactivated virus (Sinovac and Sinopharm). But a substantial number rely on alternative approaches that have not yet been as widely tested for COVID-19, including proteins (recent EUAs in Indonesia and the Philippines), DNA (recent EUA in India), virus-like particles, self-amplifying RNA, and live attenuated virus. Many of these programs are evaluating formats that are more temperature-stable than current mRNA vaccines; others are looking beyond the intramuscular delivery route used by current vaccines to intradermal, intranasal or oral routes.

The rigors of vaccine economics and open questions about efficacy and safety suggest that many of the 326 vaccine candidates now in development will not reach the market. But there is still plenty of room for new COVID-19 vaccine formats that better serve the needs of LMICs.

Needle-free administration would allow vaccines to be given by anyone in communities that lack healthcare workers. The ZyCoV-D COVID-19 DNA vaccine uses a high-pressure injector rather than a needle. Microneedle patch vaccines in development for COVID-19 may be another way of avoiding traditional needles, and thermostable versions could dispense with a cold chain. Needle-free delivery of vaccines into the skin, a highly immunoactive organ, may also be more immunogenic than intramuscular injection, potentially sparing scarce vaccine supplies.

Until mRNA vaccine production becomes established in LMICs though initiatives like the WHO's manufacturing hubs, a practical priority for vaccine equity is local manufacturing of vaccines with widely used, non-proprietary, low-cost methods. Protein vaccines, a tried and tested platform for other diseases, make up more than a third of COVID-19 vaccines in development; one was announced as costing just $1.50 per dose, and several are poised for regulatory approval. Strategies to protect against multiple variants using multivalent vaccines or vaccines that target conserved viral regions may also have an important role in LMICs.

The massive global effort over the past two years to develop, make, and administer vaccines against a novel, fast-spreading pathogen is unprecedented in the history of vaccines. The results are still unfolding and will have much to teach us about both the immunology of viral infection and the strengths and weaknesses of emerging COVID-19 vaccine technologies. With international cooperation and open data sharing, they may shed light on some of the most intractable problems in vaccinology: how best to make mucosal vaccines, how to induce robust immunity in the immunocompromised or aged people with immunosenescence, how best to increase the longevity of protection, and how to elicit broadly neutralizing antibodies against diverse viral lineages or a rapidly mutating virus.

The knowledge gained could lead to more-effective COVID-19 vaccines. Current vaccines greatly diminish the risks of infection, transmission, serious illness, and death but do not entirely prevent them, with immunocompromised and elderly people the most vulnerable. Efficacy wanes in a matter of months (in the age cohorts for which data are available — 16 and up). Improvements that can be envisaged include intranasal or oral vaccines for stronger mucosal immunity to reduce infection and transmission, and pan-sarbecovirus vaccines to protect against all SARS coronavirus strains.

No single vaccine will be best for every country and every pandemic condition. But we need to ensure that all people, including those in poor, rural, or remote communities, have access to highly effective and safe COVID-19 vaccines. Vaccine technologies that are validated for COVID-19 may also aid the development of vaccines for other infectious diseases, such as tuberculosis, pandemic influenza, malaria, and respiratory syncytial virus infection, and strengthen our preparedness to fight future pathogens. ❐

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