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children, this deployment could further threaten childhood immunisation coverage that is already precariously low in several settings.

Finally, because individuals are not equally susceptible and contagious, our current target to vaccinate 65–70% of the population to achieve herd immunity might be an overestimate.¹⁰ If young children are excluded, there will be more vaccines available for the more epidemiologically susceptible subgroups. Initiating efficacy trials in youths aged 12–18 years is a welcome development, but a new strategy might ultimately be required for immunising younger children, should this become necessary.

I declare no competing interests.

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Vaccine development lessons between HIV and COVID-19



The SARS-CoV-2 pandemic has many parallels to the early days of the HIV epidemic. Both began with efforts to identify the causative pathogen, followed by rapid development of diagnostics, animal models, therapeutics, and preventive vaccines. After targeting of the gp120 and gp160 HIV envelope proteins proved ineffective, development of candidate vaccines to prevent HIV expanded to encompass DNA and viral vector vaccines, with the intent of inducing both humoral and cellular immunity. In recent years, mRNA has been harnessed as a newer platform for the development of candidate HIV vaccines.¹ Advancing the evidence from HIV vaccines, research supporting vaccines against other pathogens has also influenced SARS-CoV-2 vaccine design, including structure-based design of stabilised epitope-scaffold proteins for respiratory syncytial virus,² DNA vaccines for MERS-CoV,³ and ongoing global molecular surveillance for the design of influenza vaccines.⁴ Collectively, the knowledge gained through these preclinical, manufacturing, and clinical development experiences has allowed for a rapid pivot to apply these approaches to SARS-CoV-2 vaccine research. The success of several large efficacy trials

of HIV candidate vaccines has been used to advance SARS-CoV-2 vaccine research and development via existing public–private partnerships and networks such as the HIV Vaccine Trials Network and their established connections with local investigators and community advocates.

The most noteworthy difference between responses to SARS-CoV-2 and HIV is the time to authorisation and rollout of effective preventive vaccines. Emergency use authorisation of initial vaccines against COVID-19 was granted by the US Food and Drug Administration and European Medicines Agency less than 1 year after initial publication of the genetic sequence of SARS-CoV-2. By stark contrast, after more than 30 years of research, only six efficacy trials of candidate HIV vaccines have been completed,⁵ of which only one showed partial efficacy in preventing acquisition of new HIV-1 infection (risk lowered by 31%).⁶ Much of this discrepancy is due to inherent biological differences between HIV and coronaviruses, such as HIV's substantially higher mutation rate due to reverse transcription and evasion of immune responses after HIV integration into the host genome. Nonetheless, there is much that can be learned

from SARS-CoV-2 vaccine development to accelerate the current pace of HIV vaccine development.

Because of the urgency to control the global pandemic, development of a vaccine to prevent COVID-19 gained strong, unified support from multiple private and public agencies. Rapid clinical development was facilitated by open and transparent cooperation between government, private, and academic research groups, including sharing of data in real time, public posting of manuscript preprints in advance of peer review, and formation of collaborative working groups. Standardisation of reagents and challenge stocks allowed for comparison of preclinical data between groups. Global coordination, harmonisation of clinical development criteria, and standardisation of reference laboratories allowed for comparable evaluation of vaccine safety, immunogenicity, and efficacy.⁷

A key component to this vaccine development drive was the involvement of multiple industry partners and a proactive and collaborative plan for the purchase of vaccines by governments in advance of manufacturing. Given the greater immunological challenges for efficacy with HIV vaccines versus SARS-CoV-2 vaccines, and the skewed distribution of the HIV epidemic in low-income and middle-income countries, securing similar widespread interest from industry partners was more difficult in advance of proven efficacy. At present, two large HIV vaccine efficacy trials are ongoing, Imbokodo (NCT03060629) and Mosaico (NCT03964415). Both are led by Janssen Pharmaceuticals and use the same adenovirus-based Ad26 platform as the Ad26.COVS.2 SARS-CoV-2 vaccine,⁸ although in the case of HIV, doses are administered as multiple vaccinations in conjunction with a protein boost. The HIV regimens were chosen systematically on the basis of a series of primate challenge studies identifying correlates of protection against challenge studies with simian-human immunodeficiency virus and early phase clinical studies, which showed clinical safety and similar immunogenicity.⁹ Should the strategy with Ad26-based vaccine prove successful, the COVID-19 vaccine experience will provide a helpful blueprint for negotiating global rollout under multiple regulatory agencies and phase 4 safety monitoring.

The concurrent, and possibly competitive, rollout of multiple SARS-CoV-2 vaccines has highlighted

the impact of multiple factors on vaccine uptake and global distribution, such as number of vaccinations, administration schedule, and cold chain requirements. Because the immunological threshold for HIV preventive vaccines remains high, we and others in the field have been willing to support the development of more complex and prolonged regimens to achieve efficacy. Lessons learned from COVID-19 vaccination regarding the practicalities of scalable manufacturing after emergency use authorisation to meet global demand, distribution, and storage with an intact cold chain, public vaccine acceptance, and large-scale safety monitoring are factors that we can consider early in the pipeline of HIV vaccine development to simplify products and regimens as much as possible and standardise safety monitoring for rare events. In addition, although HIV researchers have paved the way for community engagement globally,¹⁰ we can learn from these experiences with SARS-CoV-2 vaccine implementation. Communities should be engaged early in the development process, continued emphasis is needed on the importance of diversity in clinical trial participation, and large centralised participant registries should be used to facilitate the rapid testing and implementation of effective HIV vaccines.

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