Lessons from the structural innovations catalysed by COVID-19 for the HIV response

A report from IAS – the International AIDS Society

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Introduction

Over the past half-century, the world has mobilized to respond to two pandemics: HIV and COVID-19. Substantial attention has focused on how HIV investments and approaches have contributed to the response to COVID-19. This includes HIV research that provided the foundation for effective COVID-19 vaccines and monoclonal antibody treatments for COVID-19, as well as the early warnings regarding the Omicron variant from surveillance systems in southern Africa, built in part with HIV funding. Where the response to COVID-19 has fallen short, some have argued, it is because of the world’s failure to prioritize equitable access to essential prevention, diagnostic and treatment tools. This reflects a broader failure by the COVID-19 response to heed the lessons of the ongoing HIV response and fully leverage the strategies that have proven to be effective in addressing HIV.

To respond to COVID-19, diverse stakeholders adopted new ways of doing business, in some cases by rapidly implementing innovations that had long been proposed but seldom scaled up. The remarkably short time between identification of SARS-CoV-2 and development of highly effective preventive vaccines is merely one indicator of the spirit of urgency and innovation galvanized by the COVID-19 pandemic.

This report by IAS – the International AIDS Society – examines some of the structural innovations catalysed by COVID-19 to assess possible lessons for the HIV response. In reviewing and analysing these COVID-19-related innovations, the IAS conducted an extensive desk review of peer-reviewed and grey scientific literature, as well as coverage of innovative approaches in the popular media. The IAS supplemented its literature review with a series of key informant interviews with HIV experts and health professionals who engaged with the global architecture that emerged in response to COVID-19.

Openness to innovation has long defined the global response to HIV. This review finds that applicability of COVID-19-related innovations to the future HIV response is mixed, in part due to important differences between HIV and COVID-19 and the historical context in which global responses to these diseases emerged. However, some innovative approaches used to address COVID-19 have clear relevance and potential value to the HIV response and warrant continuation and/or adaptation to accelerate progress towards ending the AIDS epidemic as a threat to public health. At the same time, other COVID-19-related innovations appear less pertinent to HIV, with some arguably offering lessons for what the HIV response ought not to do.
Innovative approaches used to address COVID-19 with clear relevance and potential value to the HIV response

Accelerated product development and roll out

Before COVID-19, the fastest time from the laboratory to roll out of a new vaccine was four years. During the COVID-19 pandemic, clinical development of the earliest vaccines took a mere seven months.¹⁰,¹¹

There are many reasons why COVID-19 vaccines emerged so quickly. This includes years of basic science research on both HIV and coronaviruses, which yielded various vaccine development platforms on which developers could build, as well as innovative clinical trial design and the rapid mobilization of regulatory agencies. But an important impetus for speed was provided by the unprecedented investments that governments made in both “push” and “pull” mechanisms to drive innovation.

“Push” mechanisms involve direct investments in applied research and development. “Pull” mechanisms (typically in the form of advance market commitments) aim to minimize delays associated with perceived financial risks to the vaccine maker. Health advocates have long argued for the combination of push and pull mechanisms to catalyse innovation and speed in the development of global health innovations.¹³,¹⁴ Advance market commitments played an important role in accelerating the roll out of pneumococcal vaccines,¹⁵ which are now being used in more than 60 countries to prevent deaths in young children.¹⁶,¹⁷

Operation Warp Speed, the United States Government’s programme to support COVID-19 vaccines, as well as its predecessor initiative, renamed COVID-19 Countermeasures Acceleration Group in 2021 by incoming US President Joe Biden, yielded multiple effective vaccines at a cost of USD 29.8 billion, including direct investments in research and development and advance purchase commitments.¹⁸,¹⁹,²⁰

(Although Operation Warp Speed made the largest direct investment in COVID-19 vaccine development, numerous other governments, including Australia, France, Germany and the United Kingdom, also made considerable investments in COVID-19 vaccine research and development.)

Compared by some to the US mobilization during the Second World War,²¹ Operation Warp Speed focused diverse experts and constituencies on a single goal, performed critical tasks in parallel (as opposed to sequentially), and distributed responsibilities and risks between the US Government and the private sector.²² As of March 2021, Operation Warp Speed had purchased 1.2 billion vaccine doses from six companies.²³ The US Government purchased hundreds of millions of additional doses for domestic and international distribution after the end of Operation Warp Speed.

The innovative public-private partnership model of Operation Warp Speed is likely to have little immediate application in the HIV field, in part due to the fact that no HIV vaccine appropriate for broad scale up is likely for the foreseeable future. However, given the increasing excitement in the HIV vaccine field, in part due to the potential...
application of mRNA technologies, the combination of push and pull mechanisms could become useful once early-phase clinical research points towards an approach to HIV vaccine that is likely to be effective. In particular, advance market commitments for a promising vaccine could encourage makers to manufacture sufficient quantities to begin roll out as soon as an HIV vaccine receives regulatory approval. An HIV vaccine is unlikely to generate the extraordinary upfront investments in push and pull mechanisms made in the case of COVID-19. However, the successful acceleration of the manufacture and roll out of pneumococcal vaccines suggests that application of this combination to a future HIV vaccine would be feasible and beneficial.

While Operation Warp Speed was highly successful at catalysing the development of vaccines, the US proved less successful than many other countries in rolling out vaccines 24. This underscores the need to pay as much attention to distribution, delivery and demand creation as to research, development and procurement 25. Delays in rolling out approved vaccines and persistent global inequities in vaccination uptake serve as a reminder that when trying to bring a global health emergency to an end, the goal is immunization, not products 26.

Innovative approaches to clinical trials

COVID-19 demonstrated that clinical trials of novel vaccines and therapeutics can be conducted much faster than in the past. According to a comprehensive analysis of COVID-19 vaccine trials, operational efficiencies in these trials shaved off at least 70% of the time that would have been required to yield trial results had pre-COVID research approaches been followed 27.

Concurrency – or the ability to combine Phases I, II and III or to run them in parallel – accounts for more than half of the time saved in testing COVID-19 vaccine candidates 28. Concurrent administration of clinical trial phases avoids the typical and often considerable delay between the end of one trial phase and the beginning of the next.

Other operational efficiencies also accelerated the research and development process for COVID-19 vaccines. A review by the IQVIA Institute for Human Data Science identified 20 different efficiency-enhancing actions taken during COVID-19-related clinical research, including contracting efficiencies, accelerated trial enrolment, decentralized trial structure, digital client support, real-time data processing,
comprehensive organizational alignment of the research team, and changes in behavioural and business norms (such as new approaches to multi-stakeholder partnerships)\textsuperscript{39}. Adaptive trial designs, including the pooling of the placebo group and use of a master protocol for researchers testing different compounds, as well as virtual recruiting and monitoring, have also contributed to clinical trial efficiencies of both vaccines and treatments in the context of COVID-19\textsuperscript{30,31,32}. In addition to enhancing the efficiency of clinical trials, many of these innovations have reduced burdens on trial participants\textsuperscript{31}. Reductions in regulatory approval timelines also accelerated the actual roll out of COVID-19 vaccines.

Some of these innovations, especially those that derived from the willingness of professionals to work 20-hour days for months on end in response to a global crisis, may not be fully replicable in the context of future HIV clinical research. Similarly, the massive investments required to collapse trial phases may be feasible in the case of HIV only when there is early clinical evidence that one or more HIV vaccine candidates are highly likely to have very high efficacy and cost effectiveness. However, many of the structural, organizational and business adaptations used for COVID-19 trials may warrant mainstreaming across HIV and other biomedical trials more generally\textsuperscript{34}.

**Dissemination of breaking medical information**

At the same time that clinical trials have become faster during COVID-19, the pace at which news about biomedical developments reaches the public quickened, at least for COVID-19-related developments. A review of information about COVID-19 published in medical journals found a 49\% decrease in the time between submission and publication of articles, although no reduction was seen in the time required for publication of non-COVID-19-related articles. A reduction in the time required for peer review was cited as the primary factor in speedier publication of scientific news\textsuperscript{36}.

COVID-19 prompted a massive increase in medical publishing generally, and specifically in the use of preprints (preliminary data reports that have not been subjected to peer review). One study found that only 5.7\% of preprints were ultimately published in a peer-reviewed journal and that the citation rate was significantly higher for preprints that were published than for those that were not\textsuperscript{37}.

Numerous leading medical journals removed their paywalls for COVID-19-related articles to facilitate access to medical information during the COVID-19 pandemic. This step built on momentum in medical publishing over the past two decades, which has seen an increase in open-access medical journals (for example, PLOS), as well as online subscription journals (for example, the *Journal of Medical Internet Research*).

The increasing swiftness and ease of access with which medical information is becoming available offers both opportunities and risks. More rapid online access to research developments responds to the increasing desire of many in the medical and public health fields to work this way\textsuperscript{38}. However, truncation of the time for peer review, as well as the publication through preprints of research that may lack the ability to withstand peer review, runs the risk of diminishing the confidence that practitioners can have in the increasingly voluminous amount of scientific information available.
Diagnostic innovations

Early testing approaches for COVID-19 relied on health facilities. This is consistent with historic practice in the HIV response, which long prioritized standalone HIV testing programmes and provider-initiated testing and counselling.

Increasingly, however, COVID-19 testing is being performed at home through rapid antigen tests. When results are positive, these rapid COVID-19 tests are highly accurate, indicating that the person tested has a current infection and should self-isolate and inform their close contacts. A negative test result does not foreclose the possibility of infection, although multiple negative tests over 24-48 hours can increase the confidence one can have in a negative result.

COVID-19 home testing responds to the needs and preferences of many people, providing immediate and useful health information and avoiding the need to wait (in some settings, for several days) to receive facility-based results. The increased use of COVID-19 testing in countries where home tests are available does, however, decrease the surveillance utility of lab-reported COVID-19 test results; as home testing accounts for an increasing share of COVID-19 tests, lab-based reporting covers a decreasing share of testing, making results less generalizable across populations.

There has been considerable innovation over the past several years with respect to HIV diagnostics. The World Health Organization (WHO) now recommends HIV self-testing. Numerous countries have endorsed self-testing, which proved especially useful during the COVID-19 pandemic when many testing programmes either shut down or had difficulty attracting clients. In addition, rapid point-of-care diagnostics are now available for early infant HIV diagnosis and viral load monitoring.

However, these HIV testing tools, while increasingly available, have yet to be brought fully to scale as standard practice. While the number of people accessing HIV self-testing in countries supported by the US President’s Emergency Plan for AIDS Relief (PEPFAR) in the first quarter of 2021 (slightly more than 1 million) represented a nearly three-fold increase over the first quarter of 2019, these numbers still represent a small proportion of people needing HIV testing services in these countries. In 2020, one in three infants exposed to HIV received no virologic testing within the first two months of life, highlighting coverage challenges for both point-of-care and facility-based early infant diagnostic testing.

The popularity and utility of at-home testing for COVID-19 highlights the need for further actions to incentivize and rapidly bring to scale additional HIV diagnostic innovations. For innovations that are already recommended, immediate efforts are needed to catalyse expeditious uptake, including through community-centred programmes to build demand for these rapid diagnostic tools. Recent experience indicates that public sector resources can aid in the roll out of at-home diagnostic tests, reaching individuals most vulnerable to HIV who are otherwise not reached by facility-based testing programmes.

Initiatives to encourage more robust uptake of at-home HIV testing will need to take into account the specific motivations for taking an HIV test as the implications of testing positive for HIV are markedly different than testing positive for COVID-19.

Further efforts are needed to develop additional diagnostic tools for HIV. For example, an at-home HIV viral load monitoring test would contribute greatly to self-care (much in the way personal monitoring aids in self-care for diabetes or hypertension) and help decongest overburdened clinics and laboratories. At-home viral load monitoring could prove pivotal in our ability to conduct clinical trials for experimental HIV cures, reducing the resources required for monitoring of trial participants and lessening the burdens associated with trial participation.
Innovative use of real-time data

Although the growing emphasis in global health on evidence-based medicine and public health approaches acknowledges the central importance of data for sound, timely health decision making, the reality is that health systems lag behind the private sector and other disciplines in the sophisticated and strategic collection and use of data. Indeed, the typical months- and years-long delays in cleaning, analysing and disseminating health data have been cited as an important contributor to missteps by some high-income countries in the early response to COVID-19.

COVID-19 has transformed the use of health data for impact. In the place of long delays in the release of health data, COVID-19 gave rise to easy-to-understand dashboards that provided real-time data on new COVID-19 cases, hospitalizations, deaths and demographics for municipalities, states/provinces, countries and the world as a whole. Ongoing tracking of hospital and intensive care capacity has proven pivotal to health system planning during the COVID-19 pandemic; surveillance of wastewater often offered the earliest evidence of localized increases in SARS-CoV-2 incidence, as well as the emergence of new viral variants; and tracking of mobile phone data provided evidence of the effectiveness of COVID-19 lockdowns.

In sub-Saharan Africa, data systems built over time, including through HIV investments and further resourcing during the COVID-19 pandemic, have been cited as an important reason why African countries responded so quickly and effectively to the pandemic. Molecular epidemiology, which has played a key role in informing public health decision making during the COVID-19 pandemic, will likely become even more important as the world focuses on identifying novel variants and phenotypic characteristics that might affect a variant’s virulence or capacity for immune escape.

The HIV response has served as an incubator for data innovation. Sophisticated modelling has provided reliable HIV epidemiological estimates in settings where health information systems are weak and underfunded. Monitoring of outcomes across the HIV testing and treatment cascade has aided national and sub-national programmes in identifying and addressing service gaps or bottlenecks. Sub-national data systems are being used to inform strategic planning and programme monitoring at local, district and provincial levels. And innovative data visualization tools, such as the country-tailored data dashboards used in HIV and health situation rooms in eight countries, support evidence-based decision making for health policies and programmes. A global network of laboratories has monitored HIV drug resistance since 2004.

Where HIV and broader health systems lag in comparison with COVID-19 is in the collection, dissemination and effective use of real-time data. As COVID-19 has demonstrated, real-time data strengthens the adaptability and strategic impact of public health efforts. While the need for speedy access to data is more pressing for COVID-19 than for HIV, accelerating the availability of HIV-related strategic information could still have important benefits, enabling more rapid identification of gaps and bottlenecks and swifter adaptation of policy and programmatic approaches. The ability to collect real-time data for public health impact requires an integrated system built on electronic record-keeping and data dissemination. In countries such as the United Kingdom, integrated, centralized data systems proved to be the “lifeblood” of the national health system during COVID-19, with data triangulation used to monitor system capacity and improve health services.
Integrated, real-time data systems could enable more sophisticated, high-impact data collection and analysis for the HIV response. For example, integrated data systems could theoretically track PrEP efficacy in real time by linking data on PrEP utilization with reported cases of new HIV diagnosis. For all use of data, robust, meaningful, enforceable regulations must be in place to protect the privacy and confidentiality of personal medical information.\textsuperscript{55}

Similarly, real-time molecular epidemiology has the potential to accelerate the identification and response to HIV transmission clusters and outbreaks.\textsuperscript{56} However, given that HIV is transmitted primarily through behaviours that are intimate and often criminalized – and that HIV is concentrated among groups that are often marginalized and socially excluded – use of molecular epidemiology in the context of HIV involves important ethical issues that must be addressed.\textsuperscript{57}
COVID-19-related innovations that offer important lessons but may be less pertinent to the HIV response

It is less clear that certain other structural approaches adopted to respond to COVID-19 offer new lessons for the HIV response. Although these structural innovations are unlikely to serve as models for the HIV response, the challenges confronted by some of these COVID-19-related structural interventions flag potential issues of concern that the HIV field will want to take into account.

Joint, multi-stakeholder problem solving

In the face of a complex, dynamic and rapidly expanding pandemic, global health agencies joined together to launch the Access to COVID-19 Tools (ACT) Accelerator. Focused on four pillars of work – diagnostics, treatments, vaccines and health systems strengthening – the ACT-Accelerator has brought together governments, global health initiatives, civil society and the private sector for planning, problem solving, innovation, advocacy and resource mobilization.

Different partners lead work under each of the four ACT-Accelerator pillars. Given the emergency nature of the COVID-19 challenge, the ACT-Accelerator opted for an agile, informal approach rather than a rigid governance model. Working groups under each pillar meet regularly, and the ACT-Accelerator issues quarterly reports that describe the state of the COVID-19 pandemic and detail activities and progress in each area of work.

As of April 2022, the ACT-Accelerator had delivered 1.4 billion COVID-19 vaccine doses, 150 million COVID-19 tests, USD 187 million worth of oxygen supplies, USD 7.9 million in therapeutic medicines and USD 463 million in personal protective equipment. An independent evaluation of the first year of the ACT-Accelerator concluded that the collaborative initiative "played an additive and important role in accelerating the development and delivery of critical tools and has responded to country needs".

The ACT-Accelerator is an interesting vehicle for collaboration, but its value as a model for the HIV response is unclear. The HIV response already has in place its own mechanisms to undertake many of the roles played by the ACT-Accelerator, such as negotiations for optimized commodity pricing, procurement and supply management, and interventions to accelerate service uptake (including through market-shaping approaches by Unitaid, the Clinton Health Access Initiative and other actors). The Global Fund and PEPFAR each invest at least USD 1 billion annually in health system strengthening.

The HIV response has given rise to multidisciplinary working approaches that are similar to, although not at the scale of, the ACT-Accelerator. For example, the Global HIV Vaccine Enterprise, hosted by the IAS, serves as a neutral convenor of research agencies, development agencies, private industry, philanthropic foundations, UN agencies and civil society to focus on key aspects of the HIV vaccine agenda. This includes strengthening and advancing the HIV vaccine pipeline, expanding and diversifying engagement and resources for HIV vaccine research,
and mobilizing knowledge to accelerate product development. For several years, international agencies and programme implementers working to eliminate new HIV acquisitions among children have organized their efforts in collaborative working groups focused on diverse elements of this agenda, including prevention of vertical HIV transmission, early infant diagnosis and paediatric HIV treatment optimization.

As a Geneva-driven enterprise, the ACT-Accelerator has received criticism (including in its independent evaluation) for the inadequacy of its engagement of low- and middle-income countries, civil society and affected communities. For example, civil society is not represented on the ACT-Accelerator Facilitation Council, which provides guidance and advice to the Enterprise, although civil society is invited to attend Facilitation Council meetings. Civil society participates in ACT-Accelerator working groups.

An aspect of the ACT-Accelerator that has greater, if uncomfortable, resonance for the HIV response is its struggle with mobilizing sufficient resources to fulfil its mission. As of April 2022, the ACT-Accelerator was USD 14 billion short of the amounts needed to implement its work plan for 2022, having mobilized only USD 1.96 billion. The HIV response is experiencing similar struggles. The approximately USD 20 billion available in 2020 for HIV programmes in low- and middle-income countries was nearly one-third lower than the annual spending of USD 29 billion that Joint United Nations Programme on HIV/AIDS (UNAIDS) projects will be needed to get the HIV response on track to end the AIDS epidemic by 2030.

Especially concerning for the future of the HIV response is the trend in spending as resources available for HIV programmes have declined for the past three years. Funding for research and development for HIV vaccines and other new prevention technologies is also on the decline.

The global community’s failure to mobilize the resources needed to respond to COVID-19 is deeply concerning for the future of the HIV response. As the world pivots to investments for pandemic preparedness and response – and as the price tag to address the growing and inequitable toll of climate change becomes clearer – there is a risk that donor fatigue could further diminish essential support for HIV investments. More effectively making the case for the value of HIV investments, identifying new sources of financing and galvanizing investments whose benefits extend beyond individual health siloes are key priorities for the HIV response.

HIV advocates should also work to ensure that investments for pandemic preparedness yield benefits that improve responses to all health challenges, including HIV. These broad-based benefits can include strengthened surveillance, recruitment and training of health workers, stronger and more resilient supply management systems and strengthened community systems.
A new mechanism for vaccine roll out

The most prominent and well-known component of the ACT-Accelerator is the COVID-19 Vaccines Global Access (COVAX) initiative. Co-led by WHO, Gavi and the Coalition for Epidemic Preparedness Innovations (CEPI), COVAX was designed as a global procurement mechanism for COVID-19 vaccines, ostensibly available for use by countries of all income levels. COVAX aimed to use donor-financed advance market commitments to drive vaccination purchase and uptake in low- and middle-income countries.

For reasons described below, COVAX is unlikely to serve as a meaningful model for the future finance, purchase and distribution of HIV-related vaccines or other commodities. However, the COVAX experience nevertheless provides useful insights for the HIV response, including the enduring value of HIV-related innovations that have not always been fully leveraged in responding to COVID-19.

COVAX has recorded important achievements. As a result of the work of COVAX, COVID-19 vaccines reached low- and middle-income countries quicker than is typical for newly approved vaccines, and the pace of COVAX-supported vaccine procurement and distribution has accelerated in 2022. As of April 2022, COVAX and its ACT-Accelerator partners had supplied 82% of all vaccine doses in low-income countries and 67% of vaccine doses in Africa.

However, COVAX has fallen short of its targets. Having aspired to deliver 2 billion COVID-19 vaccine doses by the end of 2021, COVAX delivered its one billionth dose in January 2022. As of April 2022, COVAX had delivered 1.4 billion doses. The world is unlikely to reach the WHO target of 70% vaccination by September 2022 due to persistently slow vaccine supply, and consequently uptake, in low-income countries and especially in sub-Saharan Africa. As of May 2022, only 22% of people living in Africa and 16% of people in low-income countries had received at least one vaccine dose.

In the historic scale up of antiretroviral therapy for the treatment of HIV, roll out occurred sequentially – first primarily in high-income countries, where health systems often paid “full freight” for originator prices of medicines, and then in most low- and middle-income countries, where prices for generic antiretrovirals were much lower. In the case of COVID-19 vaccination, by contrast, roll out occurred simultaneously in all parts of the world.

This dynamic had devastating consequences for the ability of COVAX to meet its early targets. Instead of the international solidarity that characterized the eventual roll out of antiretroviral therapy in resource-limited settings, vaccine nationalism emerged in response to COVID-19, with high-income countries scooping up vaccine doses for their own populations. This meant that COVAX was effectively competing with the same donor countries on which it was relying to finance advance market commitments to low- and middle-income countries. Donors failed to contribute the sums that COVAX estimated it needed to reach its vaccination targets.
Especially in the early stages of scale up, challenges in vaccine delivery systems in many low- and middle-income countries delayed uptake of vaccines delivered by COVAX \(^7^7\). In some countries, this led to wastage of vaccine doses. Gavi, the legal entity behind COVAX, has world-renowned expertise in purchasing and distributing vaccines for children, but the populations first targeted for COVID-19 vaccination were adults.

COVAX is unlikely to serve as a fruitful model for the procurement and delivery of HIV vaccines, long-acting injectable antiretrovirals or other HIV commodities. In part, this is due to the fact that the HIV response has already developed commodity procurement and supply management mechanisms, as well as facilities and community systems to reach the adolescents and adults who will likely be targeted by early HIV vaccination campaigns or further HIV treatment innovations. Moreover, while the creation of COVAX arguably made sense in the context of COVID-19, where urgent clinical trials achieved rapid recruitment and swift data on endpoints, HIV drug and vaccine trials typically take much longer, as does regulatory review of data from HIV clinical trials.

However, COVAX’s challenges highlight key priorities for the future HIV response, including the importance of reinforcing international solidarity and mobilizing sufficient resources for rapid uptake. A focus on commodity procurement for future HIV technologies must be accompanied by equally intensive efforts to identify and address potential delivery bottlenecks. Low- and middle-income countries, as well as civil society and affected communities, will have to be engaged from the very beginning as full and essential partners in future efforts to roll out HIV-related innovations \(^7^8\). The emergence of vaccine hesitancy as a barrier to rapid vaccine scale up in the case of COVID-19 \(^7^9\) could well be repeated once an HIV vaccine emerges, further underscoring the need to engage and capacitate communities to build demand for vaccines.

Investments in research, development and manufacturing capacity in low- and middle-income countries

The COVID-19 pandemic has given renewed urgency to efforts to build biomedical manufacturing capacity in low- and middle-income countries. Ten years ago, the African Union developed a business plan to implement its vision for robust manufacturing capacity within the region \(^8^0\). HIV advocates have endorsed this aim, urging investments and other actions to increase local pharmaceutical production in Africa \(^8^1\).
The HIV response has an important stake in efforts to increase manufacturing capacity in low- and middle-income countries and especially in sub-Saharan Africa. The global HIV response has long depended heavily on the generics industry of a single country – India – for the vast majority of its HIV medicines. Supply chain disruptions associated with COVID-19 caused anxieties regarding the security of antiretroviral medicine supplies. In addition, India’s decision during COVID-19 to temporarily halt exports of its COVID-19 vaccine in order to focus on vaccinating its own people in response to skyrocketing cases at home served as a reminder that robust, sustainable supplies of future HIV vaccines will ideally draw on a multiplicity of manufacturing options.

The HIV response pioneered a critical vehicle for facilitating the decentralized manufacture of priority health commodities at affordable prices – the voluntary licencing mechanism of the Medicines Patent Pool (MPP). Under voluntary licences negotiated by MPP with the makers of breakthrough biomedical tools, 22 generic manufacturers were working with MPP in 2022 to supply 18 affordable, quality-assured medical products to more than 100 low- and middle-income countries. The world’s failure to use this scheme in the case of COVID-19 vaccines – yet another example of how lessons from the HIV response have not always been heeded in the response to COVID-19 – is arguably an important reason why vaccination efforts have gone so slowly in Africa and low-income countries generally. While MPP has executed voluntary licences with both private manufacturers and the U.S. National Institutes of Health for various COVID-19 medicines, diagnostics and building blocks for further product development (such as the stabilized SARS-CoV-2 spike proteins), MPP has not reached a licencing agreement for any validated COVID-19 vaccine.

In refusing to enter into voluntary licences, the manufacturers of the mRNA COVID-19 vaccines have asserted that low- and middle-income countries lack the capacity to manufacture these vaccines or to navigate complicated supply chains for raw materials in time to address the COVID-19 emergency. However, several analyses have identified robust, untapped manufacturing capacity in every region of the world that could be rapidly leveraged to manufacture mRNA vaccines. Observers have argued that the transfer of technology and manufacturing know-how, combined with funding to retrofit manufacturing production lines in low- and middle-income countries, could ensure an adequate supply of COVID-19 vaccines, including for future versions designed to address new variants that may emerge.

Several innovations are potentially available to increase the ability of low- and middle-income countries to manufacture COVID-19 vaccines. More than 120 countries endorsed a waiver of patent protections for COVID-19 vaccines to facilitate scaled-up manufacture at affordable prices. Opposition from some European countries blocked early agreement on such a waiver, although a compromise was announced in May 2022 that would allow a narrower temporary waiver.

To facilitate technology transfer for the manufacture of COVID-19 vaccines in low- and middle-income countries, WHO, MPP and ACT-Accelerator established the mRNA vaccine technology transfer hub. With a hub based at Afrigen in South Africa and additional “spokes” in low- and middle-income countries, the programme aims to accelerate the production of mRNA vaccines for COVID-19 and other mRNA technologies in low- and middle-income countries. As of April 2022, Afrigen had begun sharing knowledge relating to mRNA vaccines with the hubs, although it was still awaiting equipment needed to begin manufacture of the vaccines. Also as of April 2022, Afrigen’s ability to realize its mission to catalyse the manufacture of mRNA vaccines was threatened by complicated patent issues, including Moderna’s patents in South Africa on various aspects of mRNA technology.

The outcome of this technology transfer initiative is of potential significance for the future of the HIV response. The search for an HIV vaccine has been energized by the potential of mRNA platforms, and the Afrigen-based technology hub’s vision is to enable production of mRNA vaccines for other diseases in addition to COVID-19, such as Ebola, tuberculosis, viral hepatitis and HIV.
Multi-sectoral collaboration for planning and coordinating pandemic responses

COVID-19 has given rise to far-reaching, inclusive mechanisms for coordinating national responses. COVID-19 coordinating mechanisms have frequently stretched across the whole structure of governments, including extensive leadership and participation by senior HIV decision makers. Although HIV in the future is unlikely to elicit the kinds of whole-of-society and whole-of-government responses that COVID-19 demanded, especially in countries with low HIV prevalence, the mobilization of non-health sectors to address the fallout from COVID-19 offers possible lessons for building stronger working partnerships between health and non-health sectors to reduce HIV vulnerability and facilitate increased service utilization.

National AIDS strategies and coordinating bodies have historically aimed to foster multisectoral engagement and collaboration in the response to HIV. For example, the current strategic AIDS plan for South Africa calls for coordinated action among diverse national departments in addition to health, including departments for social development, correctional affairs, women, justice, basic education, higher education and training, and home affairs. Within this multisectoral effort for HIV, however, the health sector has remained predominant. In South Africa, the national Department of Health accounts for 90% of budgeted amounts devoted to the responses to HIV, TB and STIs.

Given the extensive body of evidence linking HIV vulnerability with poverty and other socioeconomic issues, the HIV response has increasingly emphasized the importance of social protection to reduce HIV-related inequalities. The case for social protection as part of the HIV response is buttressed by studies finding that conditional cash transfers to support girls to stay in school are associated with reductions in girls’ sexual risk behaviours and HIV incidence (although the evidence for unconditional cash transfers is mixed).

In response to the severe effects of COVID-19 on national economies and household livelihoods, COVID-19 generated unprecedented investments by countries of all income levels in cash transfers, food support and other forms of social protection. According to the United Nations, global spending on social protection nearly tripled during COVID-19. Increased donor support enabled much of the increase in social protection spending in low- and middle-income countries.

COVID-19 gave rise to innovations in HIV-sensitive social protection. In response to survey data indicating that half or more of people living with HIV in West and Central Africa were in need of financial or food assistance, the UNAIDS Secretariat and the World Food Programme collaborated with community-based organizations to provide cash transfers to nearly 4,000 people.
members of key populations in four countries. This programme was unique, both in its specific focus on key populations in West and Central Africa (which social protection programmes in the region had not specifically done) and on the engagement of civil society groups to facilitate the cash transfers.

In Belgium, advocacy by sex workers led to the decision by the government to specifically include sex workers in the national COVID-19 relief programme, which in turn contributed to Belgium’s decision in 2022 to decriminalize sex work.

Although some countries faced operational challenges in rapidly scaling up social protection programmes during COVID-19, experience during the pandemic definitively demonstrated the feasibility of cash transfers to reduce economic and health vulnerability. The question now is whether the commitment to social protection will outlast the COVID-19 pandemic.

For the HIV response, one immediate priority is to build the capacity of civil society, including organizations and networks of people living with HIV and key populations, to advocate for and deliver social protection interventions. In October 2021, UNAIDS and the Civil Society Institute for HIV and Health in West and Central Africa convened a workshop (with four half-day sessions) to build civil society capacity on social protection, reaching 80 civil society stakeholders from 10 countries in the region.

Conclusion

Several innovations catalysed by COVID-19 warrant focused attention as innovations to be applied or adapted for the HIV response. These include the combination of push and pull mechanisms to accelerate product development, innovative trial designs coupled with expedited regulatory review, rapid dissemination of and enhanced access to breaking biomedical information, diagnostic innovations, enhanced use of real-time data, and the energetic and innovative engagement of non-health sectors in the pandemic response. Other COVID-19-related innovations appear less clearly applicable to the HIV response moving forward, although their experiences offer useful lessons for the HIV response. Among these experiences are difficulties in mobilizing sufficient resources, engaging low- and middle-income countries and civil society, and overcoming barriers posed by intellectual property rules.

The COVID-19 and HIV responses share a critical characteristic. While both pandemics galvanized global action and achieved important gains, the response to each has been undermined by inadequate attention to persistent inequalities and disparities, including many that stem from the unbalanced distribution of wealth embedded in the international economic order. A shared lesson from pandemic responses over the past half-century is that sustainable success demands attention to equity in access and outcomes in every aspect of the response.
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