Title: Living with COVID-19 and preparing for future pandemics: revisiting lessons from the HIV pandemic

Authors: Judith D. Auerbach, Andrew D. Forsyth, Calum Davey, James R. Hargreaves, the Group for revisiting lessons for COVID-19 from pandemic HIV *

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Corresponding Author: Calum Davey, Ph.D., London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London, WC1H 9SH UK calum.davey@lshtm.ac.uk.

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*See supplement for a list of all Group members/co-authors

Summary

In April 2020, just months into the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, an international group of public health researchers published three lessons learned from pandemic HIV for the response to coronavirus disease 2019 (COVID-19), which were to: 1) anticipate health inequalities; 2) create an enabling environment to support behaviour change, and 3) engage a multidisciplinary effort.[1] We revisit these lessons in light of over two years' experience with the COVID-19 pandemic. With specific examples, we detail how inequalities have played out within and between countries, highlight factors that support or impede creation of enabling environments, and note ongoing issues with the lack of integrated science and health system approaches. We argue that to better apply lessons learned as the COVID-19 pandemic matures and other infectious disease outbreaks emerge, it will be imperative to create dialogue among polarised perspectives, identify shared priorities, and draw on multi-disciplinary evidence.

Introduction

In April 2020, just months into the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, an international group of public health researchers published three lessons learned from pandemic HIV for the response to coronavirus disease 2019 (COVID-19), which were to: 1) anticipate health inequalities; 2) create an enabling environment to support behaviour change, and 3) engage a multidisciplinary effort.[1] As the COVID-19 pandemic continues into a third year, we consider how these lessons resonate with what has happened, draw new lessons from HIV for the ongoing response, and consider what can be learned to help the world prepare for emerging and future pandemics.

The context has changed radically since the original piece was published. In April 2020, there was little access to SARS-Cov-2 testing and limited experience of treating COVID-19. No vaccines or drugs specifically for COVID-19 had been developed. The disease appeared to threaten all countries. Information about the viral, environmental, and immunologic factors driving infections was insufficient to accurately inform the deployment of non-pharmaceutical interventions.[2] There were many unknowns about asymptomatic infections, aerosol transmission, predictors of severe illness, test sensitivity and specificity, and the emergence of viral variants.[3]

Two years later, there are antibody and antigen tests (including rapid tests that can be administered at home), highly effective mRNA and viral vector vaccines that prevent severe disease and, to some extent, transmission,[4] and effective therapies that reduce symptoms and prevent deaths. This is in great contrast to the long trajectory of the development of effective

HIV diagnostics, medications, and prevention technologies, Yet, these biomedical advances for SARS-CoV-2 have not halted the pandemic. By May 2022, there had been over 6 million deaths globally, with excess mortality estimated to be two to four times higher.[5,6] The virus has mutated, with the Alpha, Beta, Delta, and Omicron variants and subvariants associated with successive waves of the pandemic. A recent Lancet Commission underscored the needless tragedy resulting from a global response best defined as cautious, uncoordinated, inequitable, and underfunded.[7] It is in this context that we revisit our three lessons from the HIV pandemic.

LESSON 1. Anticipate Inequalities

We advised in 2020 that the global response to COVID-19 should anticipate and reduce the unequal burden of infection, severity of disease, and death rate borne by vulnerable groups, including people living in lower- and middle-income countries (LMICs). Indeed, LMICs accounted for 85% of the estimated 15 million excess deaths between January 2020 and December 2021.[6] The true extent of these disparities is unknown as variability in the speed and completeness of mortality data introduced stark differences in reported and estimated deaths within WHO regions, as evidenced in Asia (e.g., China, India and Pakistan), Africa (e.g., Egypt, Nigeria, South Africa), and the Americas (e.g., Brazil, Columbia, and Mexico).[6]

Our concern about inequalities was based on the experience from HIV that pandemics expose societal fault lines. Social and economic disadvantages work synergistically with pre-existing chronic conditions to magnify health inequalities within and between countries.[8] In the case of HIV, the interplay between the virus and social determinants of health has long been understood to elevate rates of co-morbid conditions and worsen health outcomes for

disempowered groups and marginalised communities.[9] Further, interventions and policies introduced to respond to pandemics can inadvertently increase health inequalities, as those better able to access new technologies (e.g. vaccines, tests, drugs) or to adopt new behaviours (e.g. working from home, physical distancing, self-isolating following exposure) benefit more than do those less so.[10] For example, early in the spread of SARS-CoV-2, inequalities in Zambia emerged as its wealthy weathered the pandemic at home with their families and by shopping in lower density venues, while the country's less privileged crowded into higher density neighbourhoods and markets.[11]

The COVID-19 pandemic has led to disproportionate rates of infection, hospitalisation, and death in more marginalised racial and ethnic groups, people with disabilities, socio-economically disadvantaged communities, and persons with higher clinical risk factors that increase COVID-19 severity and associated mortality.[12-14] For example, in the United States, inequalities in morbidity and mortality have been attributed in part to socioeconomic status, race, and ethnicity. Excess deaths among Californians 18 - 65 years old between May and November 2020 were 31-39 percent higher for lower wage, transportation, and agricultural workers than for non-essential workers. Similarly, Black and Latine Californians had the highest excess mortality of all racial or ethnic groups at 28 and 37 percent, respectively, due to employment conditions that require close proximity to others.[15]

In addition to direct health effects of infection, when countries restricted economic and social activity in response to the COVID-19 pandemic, the impacts fell hardest on those worse off at the start of the pandemic. A World Bank study on the unequal impact of the COVID-19

pandemic on income, employment, and food security, as defined by national income levels and select sociodemographic variables, found that social and economic restrictions in 59 countries produced larger and more durable losses of income and employment and greater food insecurity, in lower-income countries than other countries, and these effects were most pronounced for women, young people, and those with lower education levels.[16] Further, a review of empirical studies on the impact of school closures showed that although learning loss was less severe than predicted, the pandemic increased learning inequality and curtailed the educational trajectories in older students.[17] Greater learning loss and higher dropout rates also were observed in rural communities and among students with lower socioeconomic status, particularly adolescent girls and young women, who additionally experienced worsened sexual and reproductive health outcomes that include an expected increase in child marriages in the coming years.[18-20]

COVID-19 inequalities between nations did not take long to manifest. One of the starkest examples was the competition among high-income countries (HIC) to secure safe and effective coronavirus vaccines to protect their populations through bilateral purchase agreements with manufacturers that monopolised vaccines and supplies, causing delays in vaccine acquisition and rollout for many LMICs.[21] A similar scenario is playing out with the announcement of a new WHO vaccine-sharing mechanism that will distribute scarce monkeypox vaccines to countries that can afford them rather than to African nations that have endured outbreaks for decades.[22] With COVID-19, some LMICs were forced to deploy lower-cost and lower-efficacy COVID-19 vaccines and incur inflated health care costs and adverse social and economic outcomes attributable to prolonged efforts to curb transmission.[23] Many countries in Africa paused or scaled back their vaccination programs due to concerns in Europe and North America about the

effectiveness or safety of the lower-cost Oxford-AstraZeneca vaccine that aggravated vaccination hesitancy, mistrust, and disrupted other vaccination and essential health services.[24]

Inequities in access to the tools to fight COVID-19 facilitate the emergence of new viral variants capable of evading both vaccine-induced and naturally acquired host immunity.[25] Although the COVID-19 Vaccine Global Access Facility (COVAX) was intended to ensure equitable access to vaccines through coordinated financing and procurement mechanisms,[26] wealthy countries undermined international cooperation that may have kept prices affordable, shared intellectual property, globalised manufacturing capacity, and accelerated a return to pre-pandemic life.[27] At the time of writing, many LMICs have not acquired a single vaccine dose per capita, implicating supply challenges.[28] The intersecting COVID-19 and HIV pandemics in southern Africa, home to the world's largest number of immunocompromised people, shows the risks of inequitable access to health-preserving, life-extending diagnostics, treatments, vaccines, and essential health services.[29]

Lesson 2: Create an Enabling Environment

Experience with HIV led us to anticipate the importance of addressing the social structures that constrain or enable health-related behaviours. Informed by a social ecological model,[30] we suggested in 2020 that, for clear public health messaging to be effective in the control of COVD-19, there would need to be strong political leadership, meaningful community engagement, and avoidance of stigmatisation and marginalisation.

There have been examples of good practice at the beginning of the pandemic, such as in Zimbabwe. Prior to the pandemic, the country had faced significant economic and climate shocks, including a severe drought and cyclone, that exacerbated the pandemic and produced a recession in 2019 that took a significant toll on the health system. When COVID-19 emerged, the Zimbabwe government unveiled a robust stimulus package to improve health systems, address the constraints faced by small-scale industries, and reduce poverty and hardships in vulnerable groups. Resources for the procurement of COVID-19 vaccines were obtained from governmental and private sector contributions.[31] Finally, a Cabinet Inter-Ministerial Task Force and a Chief Coordinator in the Office of the President and Cabinet were put in place for a whole of government and society response, coordination, and oversight.[32]

However, some political leaders in other countries engaged in withholding information, denialism, and misinformation about COVID-19,[33] which affected initial pandemic response, vaccination uptake, infections, and deaths.[34] In China, state officials delayed releasing important information to the WHO about the SARS-CoV-2 genome and about patients and cases.[35] In the United States and Brazil, two of the hardest-hit countries early in the pandemic, Presidents Trump and Bolsonaro, downplayed, neglected, and actively denied the virus and the illness it caused.[36,37] Trump mocked social distancing, pushed conspiracy theories, and promoted therapies for COVID-19 that were unproven and considered dangerous.[38] As a result, he became the single largest driver of COVID-19 misinformation by early 2020.[39] In Tanzania, the denialism promoted by President Magufuli, including his declaration that Tanzania was `COVID-19 free', delayed the implementation of prevention measures and access to vaccines.[40] Globally, research

has shown that right-wing political ideology and level of national identity were strongly related to resistance to established public health measures.[41]

At the community level, there are numerous examples of engagement that led to improved uptake of COVID-19 information and services, including among some of the most vulnerable populations. For example, a coordinated, community-centred partnership among organizations providing healthcare to homeless persons in Northwest London, United Kingdom, resulted in more than 70 percent of people experiencing homelessness there to be offered their first COVID-19 vaccine and almost 1,500 people being vaccinated by mid-March of 2021.[42]

At the same time, the experience of engaging communities in the control of COVID-19 has been marked in many contexts by misinformation, which in turn has proven to be one of the most important dynamics of the COVID-19 pandemic.[43] Greater understanding of the mechanisms and impact of misinformation—including the role of social media—in different settings is essential for mitigating future pandemics.[44,45] "Infodemics" have been global phenomena, driven by social structures. Survey research among English-speaking respondents in southern Africa found moderate levels of agreement with four common false statements related to COVID-19 (e.g., drinking hot water flushes down the virus; COVID-19 has little effect on Black people compared with White people). Agreement with false statements was associated with older age, being female, having less education, being unemployed, and residing in East Africa.[46] An analysis of rural areas in a number of African countries, where a proactive approach to combat COVID-19 was taken by governments and public health officials, found misinformation and a lack of accurate health information were fuelled by such factors as poor

living conditions, poor health literacy, the influence of culture and religion, and political instability.[47]

Misinformation was not the only impediment to universal understanding of the risks of COVID-19 and to taking preventive action. The pandemic has also been marked by high levels of uncertainty, challenging health promotion efforts.[48] Ever-changing public health recommendations and policies—based on a constantly evolving pandemic—appeared to cause confusion and anxiety, exacerbated by social media, and enabled mistrust of government, scientists, and public health officials to flourish.[49] Misinformation, and mistrust, also contributed to heterogeneity in vaccine uptake across countries. For example, vaccine hesitancy and low uptake in Zambia was affected by myths and misinformation about COVID-19 and related vaccines, fear of adverse side effects, and concern about vaccine efficacy.[50] In Uganda, beliefs that the non-pharmacological measures were a part of the president's election campaign strategy led to refusals to comply.[51] In France, resistance to the requirement to hold a COVID-19 "health pass" was connected to concerns about curtailed civil liberties and to conspiracy theories.

The risk of COVID-19-related stigma was also recognized early in the pandemic. Racism and discrimination directed toward people from East Asia emerged quickly.[52] The term "China virus" propagated through social media and catalysed acts of racism.[53] Early in the epidemic, race and wealth were blamed in sub-Saharan Africa for bringing the virus to Africa.[54] Additionally, COVID-19 revealed ageism linked to the more severe effects among older individuals.[55] Meanwhile, the removal of blanket restrictions in many countries marked a transfer of responsibility for epidemic control from the state to the individual, with the potential to

catalyse fear, blame, and judgement within and between populations.[56] Concerns about stigma similarly are being raised as monkeypox emerges as a potential pandemic with initial cases primarily identified in gay and other men who have sex with men.[57] We have learned from these experiences the importance of communicating risk to particularly vulnerable populations and to the overall population without further stigmatizing specific, often already marginalised groups.

LESSON 3: A Multidisciplinary Approach is Essential

In early 2020, we noted that an important lesson from the decades-long HIV pandemic was the need for a multidisciplinary and integrated approach to fight COVID-19, addressing the complex interactions between viral pathogen, human behaviour, emerging protective tools and technologies, and social context. We argued that a multidisciplinary response would address an inherent challenge for epidemiological modelling in predicting infectious disease dynamics dependent on human interactions and behaviours that evolve over time.[58] We noted that as national policies were drafted, they should be guided by a theory of change for population-level coverage of safe practices, integrate understanding from a range of disciplines, and incorporate monitoring and evaluation of implementation strategies seeking to affect behaviour at the population-level impact. The case we made for an integrated scientific response to the pandemic was based in an understanding of the myriad factors influencing the spread of infection.[59] Specifically, we anticipated that limited access to safe and effective vaccines, quality diagnostic testing, and efficacious treatments early in the pandemic would place a premium on uptake and adherence to non-pharmaceutical interventions, as recommended by public health authorities in LMICs and beyond. Input from behavioural and social scientists with expertise in these areas,

along with perspectives from community members representing the eventual beneficiaries of prevention and care services, would complement that from biomedical scientists focused on vaccine and therapeutic development.

But in practice, many national COVID-19 scientific advisory councils were comprised of persons with biomedical competencies essential to understanding a novel respiratory virus — e.g., virology, immunology, pulmonology, epidemiology, mathematical modelling —who then were expected to provide guidance on topics for which they had little expertise. For example, Italy's *Comitato Tecnico Scientifico* (CTS) tasked its biomedical experts to provide guidance related to child psychology, education, and neuropsychiatry.[60] Belgium's *Group of Experts on Exit Strategy* (GEES) included experts in biomedicine and economics but none to address the task of anticipating the social and behavioural implications of exiting from national lockdowns.[61] In the United States, the Biden Administration's transitional COVID-19 Response Team included biomedical, public health, and health policy expertise but lacked other scientific perspectives pertinent to managing infectious disease outbreaks, including risk communication, decision-making in the face of uncertainty, misinformation and disinformation campaigns, and adherence to public health guidelines.[62] Even in France[63] and the United Kingdom,[64] which consulted experts in anthropology, sociology, information technology, behavioural science, and education, governmental advisory committees relied disproportionately on biomedical and allied sciences perspectives that marginalised or ignored views from other disciplines.[65]

We also highlighted the need to strengthen health systems, particularly in LMIC settings, and devise tailored, context-specific responses to COVID-19.[66] For example, deploying

ventilators within a healthcare system unable to house or maintain the equipment, and in a setting with erratic electricity supply, was not an appropriate strategy. Additionally, we cautioned against taking a verticalized response to COVID-19—one of the failings of the response to HIV – to avoid undoing gains made in HIV, TB and malaria.[67] But this did not occur; pivoting focus and funding singularly to the COVID-19 effort resulted in reductions in people accessing TB treatment and declines in global spending on diagnostic, treatment and prevention services in 2020.[68] Once again, opportunities were missed to build more robust integrated services across multiple sectors critical to addressing the long term consequences—including other infectious diseases, mental health conditions, chronic conditions, and non-communicable diseases—exacerbated by the COVID-19 pandemic.

DISCUSSION: Emerging lessons for living with COVID-19 and pandemic preparedness

Our 2020 commentary was perhaps the first but not the last to consider lessons from pandemic HIV for the COVID-19 response. Since it was published, several other commentaries have offered a range of perspectives, including the Lancet's,[7] many of which overlap with ours in the areas of looking out for the most vulnerable groups and taking a harm reduction approach, exerting scientific and political leadership, ensuring community engagement, and mitigating stigma.[69-73] A number of authors also focused on the need for an intersectoral and multidisciplinary approach, many specifically highlighting insights from HIV-related behavioural and social research.[74,75]

We recognize that our analogy with HIV is useful to a point. We never could have imagined the magnitude of the epochal global changes resulting from the COVID-19 pandemic,

the speed and scale of which were unprecedented. In the first case, COVID-19 has played out more quickly than HIV. It is unclear if we are near the beginning or approaching the end of this pandemic. A much higher proportion of the world's population has been exposed to SARS-CoV2 and likely has some immunity, either through natural infection, vaccination, or both. Yet, the epidemic to date has shown that we must be watchful; viral mutations leading to greater transmissibility, vaccine escape, and perhaps worse clinical outcomes remain a clear and present threat. Our predictions two years ago, while not perfect, resonate and lead us to ask: what lessons might we now seek to draw from our perspective for the next phase of this pandemic, and to inform a growing policy interest in pandemic preparedness?

Our initial lessons remain relevant for the next phase, with adaptation. The focus on inequalities is perhaps more relevant now than ever, given the importance of efficacious technologies and tools in the pandemic response. Like HIV, the early phase of the COVID-19 pandemic was driven by mobile populations, often from higher socioeconomic groups in higher-income countries. It is in the longer, later phases of a pandemic that socioeconomic disadvantages come into play most heavily, driven in part by differential access to new technologies, tools and nonpharmaceutical interventions among individuals, groups, and countries. To mitigate these disadvantages and broader inequalities, it is essential for LMIC to take the lead in crafting and implementing pandemic responses in their settings through strengthened, indigenous infrastructure and governance entities, such as Africa CDC and the African Union.

Fostering an enabling environment for health promoting and health-seeking behaviours remains relevant to the later stage of the pandemic, particularly as "fatigue" with mitigation strategies and the funding thereof sets in. There have been long-standing concerns about donor fatigue in investing in the HIV response that might spill over to COVID-19. The global public health response community will have to face these concerns as new pandemics emerge and further tax public patience and public (and private) coffers.

Our third lesson, in combination with the other two, is particularly resonant for ongoing pandemic preparedness efforts, which need to be more multidisciplinary and integrative than they currently are. The Coalition for Epidemic Preparedness Innovations (CEPI) is perhaps the highest profile global initiative, with a mission to accelerate the development of vaccines and other biologic countermeasures against epidemic and pandemic threats so they can be accessible to all people in need. Its focus is on proof of concept and safety testing of new vaccines, accelerating manufacturing and development, and improving country responses, with an emphasis on regulatory science. The United Kingdom government launched a pandemic preparedness group in 2021 in support of CEPI and will likely revise its pandemic preparedness plans following the public enquiry planned for 2022-2023. Its current pandemic preparedness policy paper—last updated in November 2020 and based on planning for an influenza pandemic—emphasises surveillance, modelling, infection prevention and control practices, stockpiling and authorising antivirals, advance purchase agreements for vaccines, vaccination and surge planning. These approaches reflect the dominant view that rapid technological innovation represents the greatest hope for avoiding or limiting the impact of another global pandemic. While these efforts are necessary, they are insufficient. All the modelling and the

stockpiling of drugs, vaccines, and other technologies will be of little use in countries where health systems are weak and individuals are unable to follow public health guidance because of their socioeconomic circumstances. Moreover, we have learned over and over again in HIV that there is no "magic bullet"—no single technology or approach—that will change the course of a pandemic; but combination, integrated approaches might.

Finally, to better apply lessons learned as the COVID-19 pandemic matures, it will be imperative to bring currently polarised perspectives together in national (and global) discussions involving structured considerations of priorities and trade-offs and using multi-disciplinary evidence from all stakeholder groups. Without such dialogue, we are destined to repeat mistakes and be ill-prepared to respond effectively to the next pandemic that is sure to come along.

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Supplement: Co-authors and Members of the Group for revisiting lessons for COVID-19 from pandemic HIV

First	Last (degree)	Affiliation	Country
Prof. Judith D.	Auerbach PhD	School of Medicine, University of California San Francisco, San Francisco, CA	US
Andrew D.	Forsyth PhD	Independent Consultant, Berkeley California	US
Calum	Davey PhD	Department of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London	UK
Prof. James R.	Hargreave PhD	Department of Epidemiology and Evaluation, London School of Hygiene & Tropical Medicine, London	UK
Prof. James	Blanchard, MD	Max Rady College of Medicine, University of Manitoba, Winnipeg	CA

First	Last (degree)	Affiliation	Country
Prof. Virginia	Bond PhD	Department of Global Health and Development, London School of Hygiene & Tropical Medicine, London; Zambart House, Lusaka	ZM
Prof. Chris	Bonell PhD	Department of Public Health, Environments, and Society, London School of Hygiene & Tropical Medicine, London	UK
Rochelle A.	Burgess PhD	Institute for Global Health, University College London, London	UK
Prof. Tim	Colbourn PhD	Institute for Global Health, University College London, London	UK
Prof. Frances M.	Cowan MD	Liverpool School of Tropical Medicine, Liverpool & Centre for Sexual Health and HIV/AIDS Research Zimbabwe, Harare	UK/ZW
Aoife M.	Doyle PhD	Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London & The Health Research Unit Zimbabwe, Biomedical Research Training Institute, Harare	ZW
Prof. Mina C.	Hosseinipour MD	Department of Medicine, University of North Carolina Chapel Hill; UNC Project Tidziwe Centre, Lilongwe	MW/US

First	Last (degree)	Affiliation	Country
Leesa	Lin PhD	London School of Hygiene & Tropical Medicine, London; and Laboratory of Data Discovery for Health (D24H), Hong Kong	UK/HK
Agnes	Mahomva MBChB	Office of the President & Cabinet, Harare	ZW
Nyasha	Masuk MBChB	Independent Consultant, Harare	ZW
Webster	Mavhu PhD	Liverpool School of Tropical Medicine, Liverpool; Center for Sexual Health & HIV/AIDS Research, Harare	ZW
Owen	Mugurungi MD	AIDS & TB Programme, Ministry of Health & Child Care, Harare	ZW
Solomon Huruva	Mukungunugwa MPH	US Agency for International Development, Harare	ZW
Prof. Melissa	Parker DPhil	Department of Global Health and Development London School of Hygiene & Tropical Medicine, London	UK
Prof. Lucy	Platt PhD	Centre for Research on Drugs and Health Behaviour, London School of Hygiene & Tropical Medicine, London	UK
Prof. Audrey	Prost PhD	Institute for Global Health, University College London, London	UK

First	Last (degree)	Affiliation	Country
Eugene	Ruzagira PhD	Medical Research College/Uganda Virus Research Institute, Entebbe; London School of Hygiene & Tropical Medicine, London	UG/UK
Prof. Janet	Seeley PhD	Department of Global Health and Development, London School of Hygiene & Tropical Medicine, London	UK
Isaac	Taramusi MPH	National AIDS Council Zimbabwe, Harare	ZW
Raymond	Yekeye BA	National AIDS Council Zimbabwe, Harare	ZW