



Perspective

Covid-19, Ebola, and HIV — Leveraging Lessons to Maximize Impact

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As researchers who have long experience with HIV/AIDS prevention, vaccines, and therapies, some of whom also have experience with Ebola, we believe it is critical to build the

response to the Covid-19 pandemic on lessons from the HIV pandemic and recent Ebola outbreaks.

First and foremost, those epidemics have taught us that interventions must be based on sound science. As in the early days of AIDS, we face many uncertainties about the epidemiology, clinical presentation, and natural history of a new virus. SARS-CoV-2 science is therefore evolving quickly, which adds to the complexity of decision making, communication, and development and sustainability of public trust. Yet Covid-19 presents an important opportunity for smart deployment of our hard-won knowledge.

HIV/AIDS has taught us the

value and imperative of involving affected communities in planning and implementation of research and care. And both HIV and Ebola have shown that accurate and timely local information are required to enable and guide tailored interventions; public health and medical experts should heed the slogan “Know your epidemic” and target interventions accordingly.

Of course, Covid-19 presents new challenges: the epidemiology of a pandemic respiratory virus changes rapidly, and responses must be nimble. Given that everyone is susceptible to this novel coronavirus for which we lack effective biologic interventions, the response has required large-scale

behavior change, including social distancing and public masking, which were proposed rapidly under emergency circumstances. These measures could have had greater impact, however, if they had been adopted earlier and more widely — rapid action that requires community trust and buy-in. There are examples of public health successes against Covid-19; for instance, Hong Kong, which has a much higher population density than New York City, had fewer than 100 Covid-related deaths, thanks in part to swift and widespread uptake of masking, augmented by easily accessible testing. Germany introduced large-scale Covid-19 testing combined with locally led responses and strong national leadership. Globally, individual and community-level responses required substantial sacrifices that had major economic effects. The U.S. response, how-

ever, has been hampered by denial, missteps, delays in scaling up testing, inconsistent messaging, and politicization of public health responses; consequently, community transmission increased in many parts of the United States.

But this pandemic presents an opportunity to build bridges between scientists and the public. Trust must be earned. Experience with HIV/AIDS demonstrated that scientist–community collaboration was feasible and improved the scientific process. AIDS advocates pressured scientists to act more quickly, to be more transparent, and to communicate clearly about scientific rationale and methods. The result was shorter timelines for scientific investigation, regulatory review, and implementation of effective interventions. Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, provided an outstanding model for building bridges with the public; his willingness to listen to advocates' concerns about AIDS research was instrumental in making clinical research on HIV/AIDS consultative and collaborative.

In facing Ebola, the Partnership for Research on Ebola Vaccines in Liberia (PREVAIL) trial demonstrated that substantial investment and adaptive approaches to community education and social mobilization could address myths about Ebola, motivate participation, and achieve high retention in vaccine trials — despite the widespread mistrust of government, low literacy, stigma associated with Ebola, and poor clinical infrastructure in the affected communities.

With Covid-19, community engagement must be on an even larger scale and must be adaptive and led by trusted scientists and

public health experts. In the United States, Fauci has again led the way, confidently and authoritatively providing clear, fact-based communication about Covid-19. His voice must continue to be heard, especially since the U.S. pandemic response has become so politicized.

As scientists and public health professionals, we must convey the critical need for well-designed research, surveillance, and rigorously implemented clinical trials to identify safe, effective interventions, including preexposure and postexposure prophylaxis (PrEP and PEP), treatments, and vaccines. Objective markers of response are needed to assess efficacy, including SARS-CoV-2 shedding as a measure of infectivity in addition to clinical end points. Given the plethora of treatment and vaccine trials, many tens of thousands of study participants are needed. Recruiting Black and Latinx participants is essential, in light of the higher rates of Covid-19 acquisition and worse clinical outcomes in these groups.¹ Community engagement is needed to address mistrust of research and reluctance to participate in clinical trials; health care providers, scientists, community leaders, and policymakers can all work to encourage participation.

With Covid-19, we have the public's attention; now we need to earn their trust by doing the best science possible, as efficiently as we can, and by clearly communicating our rationale, methods, and results. We have very limited preclinical data on SARS-CoV-2 to guide drug development and immunologic strategies. It is our duty as scientists to avoid supporting unproven interventions, conflating opinion with evidence, or making strong proclamations

based on preliminary data from small studies, which are then picked up by the media.

More specifically, the fight against HIV demonstrated the need for a combination of interventions to reduce new infections and revealed the false dichotomy between treatment and prevention. HIV treatment has the powerful secondary benefit of preventing transmission by means of viral suppression, and some HIV medications have high efficacy for primary prevention. Initial efforts to prevent HIV infection focused on behavioral interventions, even as the biomedical pipeline was being developed. Eventually, we saw treatment breakthroughs, and now we have more than 30 antiretroviral drugs; neither this portfolio nor HIV PrEP would exist if we had stopped after the initial studies. Investment in HIV drugs has led to major reductions in new infections, better quality of life for people with HIV, and lower mortality, despite the lack of a vaccine.

HIV has also taught us that the timing of an intervention during the disease course may be critical to its therapeutic impact; delaying treatment because of the magnitude of immunocompromise led to unnecessary illness and deaths. This principle is key in addressing Covid-19, given the potential contribution of a hyper-immune response to the severity and duration of illness. Early intervention is needed to prevent acquisition of Covid-19 or disease progression before multiorgan involvement occurs.

We need multiple strategies for preventing and treating Covid-19, including PrEP, PEP, and vaccines, since it's highly unlikely that we'll hit a home run on the first trial of any intervention. Like HIV,

Covid-19 will continue to require nonpharmacologic public health strategies, even after a partially effective drug or vaccine is identified.² The rationale for testing repurposed drugs needs to be clearly articulated and based on their potential activity against SARS-CoV-2 and on available safety data. For example, remdesivir was evaluated for Ebola and has shown partial efficacy for moderate-to-severe Covid-19 infection.³ Data from in vitro studies led hydroxychloroquine and chloroquine to be selected as candidates for PEP, PrEP, and treatment for Covid-19, with subsequent political support, media attention, and heightened expectations and misconceptions. The first trials, however, were small and poorly controlled, and the results received disproportionate media attention. The problem was compounded by the publication and subsequent retraction of a study showing potential harm or lack of benefit from hydroxychloroquine,^{4,5} which led to further confusion and undermining of trust in science.

Thus, the scientific community's priority, as past experienc-

es suggest, should be to pursue hypothesis-based and data-driven strategies with sufficient imagination and resources to test new approaches for Covid-19 prevention and treatment. Clinical trials should be coordinated and implemented well, and the results should be scrutinized and interpreted clearly and objectively. We need to prepare the public for a discovery process that is iterative and seldom linear.

Interventions should not be siloed into biomedical and behavioral categories, since decisions about testing, masking, quarantine, and use of preventive or therapeutic interventions all have social and behavioral components. Scientific and public health efforts therefore require multidisciplinary teams.

But Covid-19 presents opportunities commensurate with its challenges, including the chance to build on our collective experience with high-priority, high-impact, high-quality science conducted in an efficient and coordinated manner. Throughout the process, we must build and sustain public trust by communicating clearly about

our evolving understanding of this life-threatening disease.

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