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Investment in HIV Research Profoundly Benefits the COVID-19 Response

Pandemic Disrupts Efforts to Advance HIV Science and End the Epidemic

COVID-19, HIV SCIENCE, AND ENDING THE EPIDEMIC(S)

December 2020 will mark one year since the novel coronavirus (SARS-CoV-2) first appeared in humans. The disease caused by SARS-CoV-2, COVID-19, has since claimed more than one million lives globally¹ and transformed nearly every aspect of daily life. As of October 16, 2020, the United States has seen more cases and deaths than any other country (over 8 million cases and 217,000 deaths).² Yet despite the devastation caused by COVID-19 and the historical underinvestment in public health, the U.S. has catalyzed a robust scientific response in vaccines and therapeutics research. This rapid, multisectoral scientific response would not have been possible without the foundation laid by decades of HIV science, research, and related community engagement investments and infrastructures.

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Current and historical U.S. government investment in HIV research has profoundly benefited the COVID-19 response—and, with adequate funding, can continue to do so. Continued financial support for HIV science can **both** ensure progress on COVID-19 **and** avoid losing ground—and lives—in the fight to end the HIV epidemic. After flatlining for several years around \$3 billion, federal funding for HIV research at the National Institute for Health (NIH)—primarily NIH’s National Institute for Allergy and Infectious Diseases (NIAID) and Office for AIDS Research

(OAR)—saw increases in the last two fiscal years to \$3.070 billion in FY2020 and \$3.045 billion in FY2019.

While notable, these funding increases remain far short of what will be needed to end the HIV epidemic in the U.S. Important research priori-

COVID-19 in People Living with HIV

The extent of any increased risk of COVID-19 to people living with HIV (PLWHIV) is not yet fully known. Life expectancies for people with well-controlled HIV are similar to those of people without HIV, and the U.S. Department of Health and Human Service’s Interim Guidance for COVID-19 and Persons with HIV are explicit that “limited data currently available do not indicate that the disease course of COVID-19 in persons with HIV differs from that in persons without HIV.”²⁷ Yet, in the U.S., more than half of PLWHIV are over 50 and many have comorbidities known to increase the severity of COVID-19 (e.g., cardiovascular disease, hypertension). There are some studies, from the UK and South Africa, that have suggested the possibility of a slightly increased risk of COVID-19 mortality in people with HIV.^{28,29} Further, an estimated 14% of PLWHIV in the U.S. are unaware of their status, meaning their HIV is not well-controlled.³⁰ In keeping with a long history of altruistic research participation, advocates have successfully lobbied for COVID-19 vaccine efficacy trials to be open to people with HIV on stable treatment.³¹

ties include therapies and prevention interventions that require less frequent dosing—particularly HIV vaccines, which infectious disease experts consider essential for eliminating virus transmission.³ Although HIV research advances and infrastructures have been leveraged for the COVID-19 response, it is imperative to bolster federal support for the HIV response to minimize disruptions and avoid losing ground in the fight to end HIV.

COVID-19'S DAMAGE TO THE HIV RESPONSE

Decades of U.S. investment in HIV research has resulted in countless scientific discoveries and improved public health, changing the course of the global HIV epidemic. As the public health impact of COVID-19 became clearer, HIV research infrastructure was quickly redirected to the COVID-19 response in an unprecedented mobilization of resources. For example, the NIAID-funded AIDS Clinical Trials Group (ACTG) research network enrolled the first participants in a remdesivir trial in February 2020—when there were only 14 known cases of COVID-19 in the U.S.⁴ COVID-19 research would not have moved this quickly without the well-established, well-known, and well-regarded HIV researchers and research infrastructure.

However, HIV research is paying the price. The four federally funded HIV research networks have interrupted, paused, and halted existing and planned research, risking the loss of years of preparatory scientific and community engagement work. Study screenings and enrollments were paused, participant follow up went remote, and study development was put on hold. Although the blanket pauses have been lifted, a number of important studies were temporarily closed due to COVID-19, including the HIV Vaccine Trials Network's (HVTN) international vaccine efficacy study (Mosaico), which had

just opened to enrollment before the COVID-19 pandemic.^{5,6,7} Mosaico is testing Johnson & Johnson's adenovirus serotype 26 (Ad26) vaccine platform, which has also entered an efficacy trial for COVID-19.

The short-term costs of temporary study pauses include the expense (in dollars and in personnel time) of restarting interrupted recruitment efforts, updating and/or redesigning outreach materials, and retraining study staff. Local- and country-level lockdowns, institutional policies, and other regulatory elements can add additional costs.

The long-term damage of COVID-related interruptions to HIV research is not yet fully clear, although it is safe to assume that the robust treatment, vaccine, and prevention pipelines will be delayed by at least a few years. Indeed, after extended pauses, large-scale international studies—particularly those that paused early in enrollment—likely won't be able to “hit the ground running” when the enrollment restarts. Given the longer time horizons for HIV research, increases in HIV funding that are desperately needed *now* will need to be maintained for the next several years to offset these future costs.

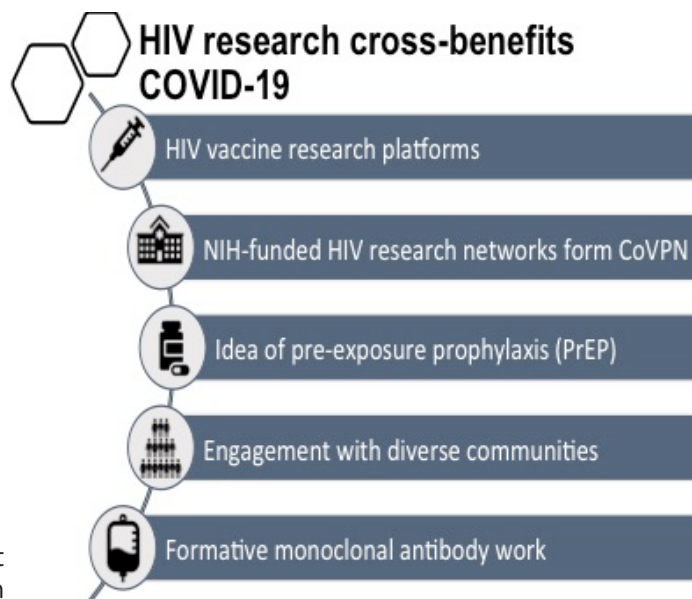
HIV cure-related research has also been uniquely challenged by the COVID-19 pandemic. Cure-related studies often involve frequent study visits, invasive procedures (e.g., biopsies, lumbar punctures, high volume blood draws), or analytic treatment interruptions (ATIs)—procedures that complicate a study's transition to remote follow up or telehealth. Emerging guidance for reopening cure studies that include ATIs outline a number of adaptations that may be considered to safely restart cure studies during the COVID-19 pandemic, including providing participants with transportation funds, masks, and home phlebotomy visits when desired and feasible.⁸ Implementing these recommendations may depend on the availability of supplemental funding.

“Decades of research on HIV have taught scientists an enormous amount about the immune system, honed vaccine technologies now being repurposed against the coronavirus and created a worldwide infrastructure of clinical trial networks that can be pivoted from HIV to the pathogen that causes the disease covid-19.”⁹

HIV RESEARCH BENEFITS COVID-19 RESPONSE, AND THE CASE FOR INCREASED INVESTMENT IN HIV RESEARCH

Existing HIV research infrastructures—from basic science to community engagement mechanisms—can be leveraged to benefit the COVID-19 response. Insights and technologies from HIV vaccine, treatment, and prevention research have already proven invaluable in the COVID-19 response. Some of the earliest COVID-19 treatment research investigated the possibility of repurposing HIV medications (including lopinavir, ritonavir, darunavir, and bicitgravir) for use in COVID-19.¹⁰

Vaccine platforms developed for HIV were quickly repurposed to investigate for use against COVID-19. Increased and sustained investment in established HIV research frameworks will continue to facilitate **efficient and effective scale-up of COVID-19 diagnostics, treatments, vaccines, and prevention**. For example, challenges in implementing HIV pre-exposure prophylaxis (PrEP) demonstrated the importance of leadership from key populations as part of any effective scale up—a hard-learned lesson that can inform the current effort to enroll diverse participants in COVID-19 vaccine studies.¹¹ The U.S. Food and



Drug Administration’s (FDA) fast track and compassionate use programs were borne from HIV advocacy in the 1980s. Continued investment in HIV research, coupled with strategic application of lessons learned from HIV advocacy, will allow the U.S. to continue progress toward ending the HIV epidemic while also promoting the scientific and public health breakthroughs in COVID-19 that we need.

Table 1: HIV research cross-benefits COVID-19

Vaccine technology	<p>An effective vaccine for COVID-19 is widely recognized as essential for a return to pre-pandemic normalcy. In a comprehensive summary of COVID-19 vaccine efforts to date, advocacy organization AVAC notes that successes in COVID-19 vaccine research “will be due to the research knowledge, vaccine platforms, trial networks, and community engagement models created through HIV vaccine research.”¹² Examples of HIV vaccine research cross-benefits to COVID include:</p> <ul style="list-style-type: none"> <i>Platform technologies:</i> Many of the vaccine candidates in development draw on advances from the HIV response. Adenovirus vectors (used in the vaccine candidates from Johnson & Johnson, Oxford University, and CanSino Biologics) have been widely studied in HIV, as have DNA vaccine platforms (repurposed for COVID-19 by Inovio) and antigen design. <i>Research centers:</i> The NIH Vaccine Research Center (VRC) played a key role in the development of Moderna’s vaccine candidate; the VRC was founded by President Clinton to pursue HIV vaccine research.
Research infrastructure	<p>Four NIH-funded research networks merged to form the COVID-19 Prevention Trials Network (CoVPN), including the HIV Vaccine Trials Network, the HIV Prevention Trials Network, the AIDS Clinical Trials Group, and the Infectious Diseases Clinical Research Consortium.¹³ CoVPN, which supports Operation Warp Speed, connects vast research networks into a centralized and unified structure for NIH’s COVID-19 prevention research. NIH-funded COVID-19 research has been able to move at a historic pace in part due to decades of engagement and operational and scientific expertise honed in the HIV research networks.</p>

Models of community engagement from the HIV response, such as the Denver Principles and Good Participatory Practice, teach us that in community engagement for public health, one size rarely fits all.

Pre-exposure prophylaxis (PrEP)	The 2012 approval of Truvada (a drug used for HIV treatment) for HIV prevention (a concept called pre-exposure prophylaxis, or PrEP) represented a paradigm shift in HIV prevention. Increased access to and uptake of PrEP is a cornerstone of the U.S. effort to end the HIV epidemic. Anecdotal case reports early in the COVID-19 pandemic indicated that Truvada might also protect against COVID-19; although initial data do not seem to support that hypothesis, ¹⁴ Truvada is being tested for use as PrEP in frontline healthcare workers at high risk for COVID-19. ¹⁵
Community engagement models	Stark racial disparities in COVID-19 incidence and outcomes illustrate the health effects of structural racism in the U.S. High levels of vaccine reluctance and mistrust underscore the importance of engaging diverse communities in all stages of COVID research. Models of community engagement from the HIV response, such as the Denver Principles ¹⁶ and Good Participatory Practice, ¹⁷ teach us that in community engagement for public health, one size rarely fits all. Implementing the widely accepted best practices for community engagement that were developed and validated in HIV will ensure the COVID-19 response considers the experiences and autonomy of all communities impacted by the disease.
Monoclonal antibody knowledge	Monoclonal antibodies (mAb) are a biologic therapy that have been widely used to treat a range of diseases and conditions. HIV researchers pioneered ¹⁸ new approaches that have allowed for the rapid identification of mAb that potently inhibit SARS-CoV-2. ¹⁹ IAVI, an organization founded to pursue the development of an HIV vaccine, is leading a timely effort to reduce the costs of mAb therapies and enhance global access. ²⁰
HIV/AIDS cohort studies	Samples from the Amsterdam Cohort Studies on HIV-1 infection and AIDS, which have been collected on an ongoing basis since the 1980s, have provided a critical source of insight into the duration of protective immunity against seasonal coronaviruses. The findings have important implications for immunity against SARS-CoV-2. ²¹

RECOMMENDATIONS FOR CONGRESS AND POLICYMAKERS

Significant federal support must be allocated to the HIV response in order to minimize disruptions to HIV research and avoid losing ground in the fight to end HIV. Additionally, key investments and policy changes can continue to solidify a robust scientific strategy to address the COVID-19 pandemic by leveraging HIV research and can also strengthen health security against future pandemics. We urge policymakers to:

1. Increase funding for HIV research through regular and future appropriations as well as stimulus bills to (a) ensure continuation of current studies and (b) leverage HIV research networks for COVID-19 research and development. In-line increases to meet, or exceed, NIH OAR's latest professional judgement budget recommendation for a level of \$3.845 billion in FY21 will ensure progress on current research and support critical future HIV studies.²² Appropriators should strive to reach OAR's annual professional judgement budget recommendations for HIV/AIDS research every year.
2. Increase financial support for Global Fund/PEPFAR and domestic HIV prevention efforts.
3. Develop policies to reward innovation, creativity, and adaptability in HIV research, such as efforts to maintain studies during and following the COVID-19 pandemic. Dedicated funding can ensure that innovation and adaptation are prioritized across sectors.
4. Repeal the de facto ban on the use of fetal tissue in federally funded biomedical research. The onerous restrictions on the use of fetal tissue limit the scientific tools at the disposal of researchers to make critical gains on both HIV and COVID-19 research. Humanized mouse models that rely on fetal tissue could profoundly benefit COVID-19 research, potentially accelerating the development of therapeutics and facilitating investigations

into critical questions such as whether immune responses induced by seasonal coronaviruses can inhibit SARS-CoV-2 infection.²⁵ Notably, a cell line originally derived from aborted fetal tissue was used in the testing Regeneron’s antibody cocktail for COVID-19, which was recently administered to the U.S. president.²⁶

5. Require open licensing requirements, data sharing, and other access provisions for all federally funded COVID-19 R&D. Data must be open and accessible to affected communities in all stages of the research pipeline. Ensuring transparency and access will lay a strong foundation that will facilitate future translational science.

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