Fiscal Year 2024 NIH HIV/AIDS Professional Judgment Budget

Advancing Science and Enhancing Partnerships

National Institutes of Health
Office of AIDS Research

Cover Photo: A human T cell (blue) is under attack by HIV (yellow), the virus that causes AIDS. The virus specifically targets T cells, which play a critical role in the body's immune response against invaders like bacteria and viruses.
Credit: Seth Pincus, Elizabeth Fischer and Austin Athman, National Institute of Allergy and Infectious Diseases/NIH.

Table of Contents

Director's Message

Maureen M. Goodenow, Ph.D.
Associate Director for AIDS Research and Director, Office of AIDS Research
National Institutes of Health

Global health emergencies underscore how public investment in basic, clinical, behavioral, social, and implementation research protects and promotes human health. Over 40 years ago, the discovery of human immunodeficiency virus (HIV) challenged scientists and policymakers to work together on acquired immunodeficiency syndrome (AIDS), which was then an untreatable, fatal disease. Thanks to the concerted effort of people from every sector of society and sustained support from the U.S. government, the development and implementation of evidence-based therapeutic, clinical, and behavioral strategies have turned HIV infection and AIDS into a manageable chronic condition with near-normal life expectancy for people who can take advantage of HIV treatment and health services.

The HIV/AIDS research enterprise has consistently recognized the importance of scientific collaborations around the world, actively developing innovative partnerships with U.S. government agencies, academia, civil society organizations, and others in the effort to end the HIV/AIDS pandemic. Recently, the COVID-19 pandemic has further demonstrated the substantial return on investment in National Institutes of Health (NIH) HIV/AIDS research and its supported clinical trials networks. When SARS-CoV-2 spread across the globe in 2020, discoveries and infrastructure from NIH HIV/AIDS research enabled the rapid development and testing of new vaccines, diagnostics, and therapies to combat COVID-19 morbidity and mortality.[1] These efforts saved an estimated 20 million lives between December 2020 and December 2021.[2]

The Consolidated Appropriations Act of 2022 provided NIH with $3.194 billion, an increase of $104 million for HIV and HIV-related research.[3] This increase, the largest since FY 2014, highlighted the success of the NIH HIV/AIDS research enterprise. In consultation with the NIH Director, the Office of AIDS Research (OAR) allocated this funding to the NIH Institutes, Centers, and Offices (ICOs) to support focused investments in areas aligned with the goals of the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research*,[4] the objectives of the *National HIV/AIDS Strategy* (NHAS)[5] and the accompanying *NHAS Federal Implementation Plan*,[6] as well as the *Ending the HIV Epidemic in the U.S.* (EHE) initiative.[7] This FY 2024 NIH HIV/AIDS Professional Judgment Budget requests $3.673 billion, an increase of $479 million, or 15 percent, over the FY 2022 enacted budget of $3.194 billion for NIH HIV/AIDS research. The additional funds are necessary to advance HIV/AIDS science, enhance partnerships, and address critical research and implementation opportunities to end the HIV/AIDS pandemic.

1 National Institutes of Health. How Lessons from HIV Research Informed COVID-19 Vaccine Trials. May 12, 2022. Accessed October 17, 2022. covid19.nih.gov/news-and-stories/how-lessons-hiv-research-informed-covid-19-vaccine-trials

2 Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. *Lancet Infect Dis.* 2022;22(9):1293-1302. doi:10.1016/S1473-3099(22)00320-6. pubmed.ncbi.nlm.nih.gov/35753318

3 Consolidated Appropriations Act, 2022. HR 2471. 117th Cong (2022). Accessed October 17, 2022. www.congress.gov/bill/117th-congress/house-bill/2471

4 National Institutes of Health Office of AIDS Research. FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research. 2020. Accessed October 14, 2022. oar.nih.gov/sites/default/files/NIH_StrategicPlan_FY2021-2025.pdf

5 The White House. National HIV/AIDS Strategy for the United States 2022–2025. December 2021. Accessed October 14, 2022. www.whitehouse.gov/wp-content/uploads/2021/11/National-HIV-AIDS-Strategy.pdf

6 The White House. National HIV/AIDS Strategy Federal Implementation Plan. August 2022. Accessed October 14, 2022. files.hiv.gov/s3fs-public/2022-09/NHAS_Federal_Implementation_Plan.pdf

7 What is *Ending the HIV Epidemic in the U.S.?* HIV.gov. Updated July 1, 2022. Accessed October 14, 2022. www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview

Since its establishment by Congressional legislation in 1988, OAR has worked with governmental, academic, industry, and civil society partners to advance research to end the HIV/AIDS pandemic and improve health outcomes for people with HIV. Guided by the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research*, OAR has promoted the NIH HIV/AIDS research contribution to *National HIV/AIDS Strategy* (NHAS) for 2022–2025 released in 2021, its associated Federal Implementation Plan launched in 2022, and the *Ending the HIV Epidemic in the U.S.* (EHE) announced in 2019, which aim to halt new HIV transmissions and improve the lives of people with and affected by HIV in the United States and globally.

Introduction

The latest HIV global statistics from the Joint United Nations Programme on HIV/AIDS (UNAIDS) were published in the 2022 report, entitled *In Danger*. This report describes significant setbacks in the HIV/AIDS response during the COVID-19 pandemic, including the drastic reduction in HIV resources that further exacerbate inequalities in health service access.[8] Indeed, international investments in the HIV/AIDS response have remained relatively flat in recent years; there are disturbing indications that the world's financial commitment to this cause is waning. Allowing the HIV/AIDS pandemic to rebound would be catastrophic not just for the communities affected by HIV, but for the state of global health in the 21st century.[9]

In 2021, an estimated 38.4 million persons across the globe were living with HIV, including 5.9 million who were unaware of their positive HIV status. More than half of those living with HIV were women and girls. Approximately 1.5 million persons became newly infected with HIV in 2021, and approximately 650,000 people died from HIV-related illnesses globally.[10]

Many nations are losing ground in the fight against the HIV/AIDS pandemic, jeopardizing the ability to achieve the 2030 HIV targets within the World Health Organization's Sustainable Development Goals.[11] Overall, HIV diagnoses have decreased in 40 of 50 countries, a result of reductions in service delivery, not in HIV transmissions. In sub-Saharan Africa, significantly fewer HIV tests were conducted during the height of the COVID-19 pandemic in 2020 and 2021, compared to 2019. While antiretroviral therapy (ART) is highly effective in improving the quality of life and life expectancy for people with HIV, not everyone has access to these resources. The number of persons on ART increased by only 1.5 million in 2021, compared to more than 2 million in previous years in the same region.[12] Harm-reduction services for persons who use drugs were disrupted in 23 of 130 countries. Reduced access to tuberculosis (TB) diagnosis and treatment resulted in increased TB deaths among persons with HIV.[13]

Despite the persistence of HIV transmission, morbidity, and mortality, 20 nations across three continents in 2021 either reached or came close to achieving the President's Emergency Plan for AIDS Relief (PEPFAR)

8 UNAIDS. In Danger: UNAIDS Global AIDS Update 2022. July 27, 2022. Accessed October 14, 2022. www.unaids.org/en/resources/documents/2022/in-danger-global-aids-update

9 Bekker LG, Alleyne G, Baral S, et al. Advancing global health and strengthening the HIV response in the era of the Sustainable Development Goals: the International AIDS Society-Lancet Commission. *Lancet*. 2018;392(10144):312-358. doi:10.1016/S0140-6736(18)31070-5. pubmed.ncbi.nlm.nih.gov/30032975

10 UNAIDS. Global HIV & Aids Statistics. Accessed October 17, 2022. www.unaids.org/en/resources/fact-sheet

11 UNAIDS. 2025 AIDS Targets. Accessed October 17, 2022. aidstargets2025.unaids.org

12 UNAIDS. In Danger: UNAIDS Global AIDS Update 2022. July 27, 2022. Accessed October 14, 2022. www.unaids.org/en/resources/documents/2022/in-danger-global-aids-update

13 UNAIDS-Fact Sheet-World Tuberculosis Day 2022. www.unaids.org/sites/default/files/media_asset/20220324_TB_FactSheet_en.pdf

definition of epidemic control; that is, when new HIV infections fall below deaths among persons with HIV.[14] Unfortunately, the United States is not among these 20 nations. In 2020, 30,635 persons were diagnosed with HIV infection in the United States, a 17 percent decrease from 2019; however, more than 18,400 people with HIV died (due to any cause).[15] In 2020, an estimated 1.1 million persons in the United States and six dependent areas were living with HIV; approximately 87 percent were aware of their positive HIV status. In 2020, 74 percent of persons with HIV received some HIV-related care, 51 percent were retained in care, but only 65 percent attained viral suppression.[16] The U.S. Centers for Disease Control and Prevention (CDC) advises cautious interpretation of 2020 statistics due to the impact of the COVID-19 pandemic on access to HIV testing, care-related services, and case surveillance activities.

There are stark disparities in HIV incidence and prevalence that reflect the demographic and geographic diversity of the United States. Black/African American and Hispanic/Latino communities are disproportionately affected by HIV compared to other racial and ethnic groups. In 2020, Black/African American persons represented 13.6 percent of the U.S. population, but accounted for 42 percent of people with HIV. Hispanic/Latino persons represented 18.9 percent of the U.S. population, but accounted for 27 percent of people with HIV.[17,18] In 2020, only 25 percent of persons eligible for pre-exposure prophylaxis (PrEP) received a prescription. In addition, there are clear racial inequalities in access to PrEP. While 66 percent of eligible White persons received a PrEP prescription, only 9 percent of eligible Black/African American persons and 16 percent of eligible Hispanic/Latino persons received one.[19] Despite advances in HIV treatment and prevention, HIV transmission among gay, bisexual, and men who have sex with men (MSM) continues, in part because of stigma and barriers to accessing prevention and treatment services.[20] Disparities are particularly concerning at the intersection of race and ethnicity with sexual orientation. For example, the majority of new HIV infections occur in gay and bisexual men who are Black or Latino. In addition, access to HIV-related health services is limited by socioeconomic status and geographical location, causing a significant burden of infection in rural areas.[21] Interventions and services may be most effective when issues of intersectionality are considered in the design and implementation of interventions.

HIV basic, translational, and clinical research, suspended for months during the COVID-19 pandemic, has not fully returned to pre-pandemic levels. This continues to delay critical research progress, as well as disrupt training and career advancement opportunities for the new generation of HIV/AIDS investigators. Recruitment

14 Moss K, Rouw A, Kates, J. PEPFAR and Sustained Epidemic Control. Kaiser Family Foundation. August 5, 2022. Accessed October 17, 2022. www.kff.org/global-health-policy/issue-brief/pepfar-and-sustained-epidemic-control

15 Centers for Disease Control and Prevention. HIV Surveillance Report, 2020; vol. 33. May 2022. Accessed October 14, 2022. www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2020-updated-vol-33.pdf

16 Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2020. HIV Surveillance Supplemental Report 2022; 27(3). Revised August 2022. Accessed October 17, 2022. www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-27-3.pdf

17 Centers for Disease Control and Prevention. HIV Surveillance Report, 2020; vol. 33. May 2022. Accessed October 14, 2022. www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2020-updated-vol-33.pdf

18 U.S. Census Bureau. U.S. Population Data by Race From U.S. Census Bureau. *Quick Facts*. 2020. Accessed October 14, 2022. www.census.gov/quickfacts/fact/table/US/RHI125221

19 Centers for Disease Control and Prevention. PrEP for HIV Prevention in the U.S. Reviewed November 23, 2021. Accessed October 17, 2022. www.cdc.gov/nchhstp/newsroom/fact-sheets/hiv/PrEP-for-hiv-prevention-in-the-US-factsheet.html

20 Centers for Disease Control and Prevention. Clusters of Rapid HIV Transmission Among Gay, Bisexual, and Other Men Who Have Sex with Men – United States, 2018-2021. Morbidity and Mortality Weekly Report (MMWR). 71(38); 1201-1206. September 2022. Accessed November 20, 2022. www.cdc.gov/mmwr/volumes/71/wr/mm7138a1.htm

21 NIH HIV/AIDS Executive Committee. FY 2019 EHE in the U.S. Report. October 2021. Accessed October 17, 2022. www.oar.nih.gov/sites/default/files/OAR-NAEC-EHE-WG-508.pdf

and staffing for HIV clinical trials also were affected by social distancing, travel restrictions, and stay-home measures.[22]

While additional research is needed to halt the continued spread of HIV transmission and mitigate HIV-associated illnesses, the emergence of innovative scientific and technological tools shows promise. Recently developed, exciting new therapeutic candidates have multiuse potential, such as long-acting ART formulations developed for HIV treatment that also provide effective PrEP strategies for HIV prevention. Vaccine candidates that produce broadly neutralizing antibodies (bNAbs), which combat a wide range of genetic variants of HIV hidden within the body, also can help drive research toward both prevention and a potential cure.

Uncovering new links among chronic diseases across the lifespan of people with HIV will lead to a better understanding of how HIV impacts physiological processes. The interaction of HIV with persistent coinfections, such as TB and hepatitis B and C viruses, requires expanded basic, clinical, behavioral, and social science research. At the same time, emerging infectious disease outbreaks, such as the current mpox (formerly monkeypox) virus public health crisis, can disproportionately burden persons with or at risk of HIV infection.[23]

The U.S. government is well positioned to leverage the bidirectional lessons learned from national and global efforts during the decades-long response to the HIV/AIDS pandemic and the recent response to the COVID-19 pandemic. For example, PEPFAR changed the global trajectory of the HIV/AIDS pandemic by fostering the deployment of highly effective ART to more than 50 countries worldwide, saving over 20 million lives. The national HIV response must now capitalize on lessons learned in global health to reach the ambitious domestic goals of the EHE initiative, which include achieving a 75 percent reduction in new HIV infections by 2025 and at least 90 percent reduction by 2030.

In the United States, the COVID-19 pandemic disproportionately impacted Black, Indigenous, and people of color (BIPOC). To ensure that COVID-19 vaccine candidates were safe and effective among those most affected, clinical trial volunteers needed to represent the diversity of the population. The NIH HIV/AIDS Clinical Trials Networks, which have built strong linkages with communities affected by HIV, provided a critical foundation for the networks to pivot their focus to the much-needed COVID-19 prevention and treatment efforts.[24] Also, the technology developed for responding to the HIV/AIDS pandemic was rapidly mobilized to combat the COVID-19 pandemic; this has, in turn, spurred clinical trials for three messenger RNA (mRNA)-based HIV vaccine candidates.[25,26]

22 National Institutes of Health Office of AIDS Research. Second HIV Stakeholder Outreach and Engagement Report: September 2020 – July 2021. July 2022. Accessed October 17, 2022. www.oar.nih.gov/sites/default/files/OAR-Phase2-Stakeholders-Report-2021-508.pdf

23 Curran KG, Eberly K, Russell OO, et al. HIV and Sexually Transmitted Infections Among Persons with Monkeypox — Eight U.S. Jurisdictions, May 17–July 22, 2022. *MMWR Morb Mortal Wkly Rep.* 2022;71:1141–1147. doi: dx.doi.org/10.15585/mmwr.mm7136a1

24 National Institutes of Health. How Lessons from HIV Research Informed COVID-19 Vaccine Trials. May 12, 2022. Accessed October 17, 2022. covid19.nih.gov/news-and-stories/how-lessons-hiv-research-informed-covid-19-vaccine-trials

25 NIH launches clinical trial of three mRNA HIV vaccines. News release. National Institutes of Health. March 14, 2022. www.nih.gov/news-events/news-releases/nih-launches-clinical-trial-three-mrna-hiv-vaccines

26 A Clinical Trial to Evaluate the Safety and Immunogenicity of BG505 MD39.3, BG505 MD39.3 gp151, and BG505 MD39.3 gp151 CD4KO HIV Trimer mRNA Vaccines in Healthy, HIV-uninfected Adult Participants. ClinicalTrials.gov identifier: NCT05217641. Updated October 3, 2022. Accessed October 17, 2022. clinicaltrials.gov/ct2/show/NCT05217641

OAR strives to optimize the NIH investment in HIV/AIDS research for the greatest impact on public health. Therefore, all HIV/AIDS research funding initiatives proposed for FY 2024 align with the NIH HIV/AIDS research priorities, as outlined in the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research*, and provide the framework for a robust NIH research agenda in HIV prevention, treatment, and cure that extends across the lifespan and is inclusive of all persons with, or at risk for, HIV infection.[27,28]

Figure 1: Strategic Goals in the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research*

The NIH HIV/AIDS research priorities also align with the updated NHAS, launched by the White House Office of National AIDS Policy (ONAP) in December 2021. The NHAS goals are to prevent new HIV infections, improve HIV-related health outcomes of people with HIV, reduce HIV-related stigma and discrimination, and achieve integrated and coordinated efforts that address the HIV/AIDS epidemic among all partners and interested parties.

NIH is recognized worldwide for its steadfast support of the HIV/AIDS research enterprise. This FY 2024 NIH HIV/AIDS Professional Judgment Budget outlines the level of support needed to accelerate critical, high-priority research and strategies to fill crucial implementation gaps, seize emerging scientific opportunities, and enable cutting-edge scientific discoveries that will have a population-level impact.

27 National Institutes of Health. NOT-OD-20-018. UPDATE: NIH HIV/AIDS Research Priorities and Guidelines for Determining HIV/AIDS Funding. December 31, 2019. Accessed October 17, 2022. grants.nih.gov/grants/guide/notice-files/NOT-OD-20-018.html

28 National Institutes of Health Office of AIDS Research. Research Priorities. Reviewed September 20, 2022. Accessed October 17, 2022. www.oar.nih.gov/hiv-policy-and-research/research-priorities

FY 2024 Professional Judgment Budget Priority Research Areas

Additional resources requested through the FY 2024 NIH HIV/AIDS Professional Judgment Budget would allow NIH to expand important HIV science in the following areas of research:

Basic biomedical and behavioral research to develop effective HIV prevention interventions, treatment, care, and cure:

- Advance the HIV discoveries in immunology and virology, including new therapeutic and prevention product pipelines.
- Evaluate novel HIV vaccine candidates utilizing mRNA and self-amplifying RNA (saRNA) delivery technologies.
- Assess antibody-mediated approaches for HIV prevention.
- Elucidate barriers to curing HIV at the molecular, cellular, and tissue levels, including mechanisms that maintain HIV latency or that otherwise promote the persistence of HIV-infected cells throughout the body.
- Accelerate the development of drug combinations, dosing regimens, and innovative delivery strategies to target viral reservoirs at key anatomic sites.
- Advance the rollout and uptake of long-acting PrEP and investigate the physiological consequences of long-term use of PrEP.

Research on co-occurring and underlying biological, behavioral, and social conditions that are associated with suboptimal HIV health outcomes across the lifespan and among populations disproportionately affected by HIV:

- Launch interdisciplinary studies on the biological and psychosocial mechanisms of chronic HIV-associated coinfections and comorbidities.
- Implement new technologies and methodologies, such as telemedicine, specific HIV-related applications to be used in portable devices, and self-testing, to improve HIV prevention and treatment and increase uptake by persons with or at risk for HIV.
- Promote implementation strategies to adopt and integrate evidence-based interventions in community, clinical, and other settings to improve the uptake and outcomes of HIV services at the national and global levels.
- Develop and launch health communication strategies that are culturally appropriate and include community input.

Programs to expand the HIV/AIDS research workforce and strengthen the capacity of institutions conducting HIV/AIDS research:

- Expand the pool of diverse early career HIV/AIDS investigators, including individuals with varying expertise, such as physicians, dentists, veterinarians, or registered nurses.
- Enhance support for improving and upgrading infrastructure and equipment at institutions and facilities conducting HIV/AIDS research, particularly those with limited resources.

OAR will increase collaborations with NIH and U.S. Department of Health and Human Services (HHS) partners to advance the EHE goals. Importantly, OAR will continue working with the White House ONAP in the implementation of the research objectives of the NHAS goals.

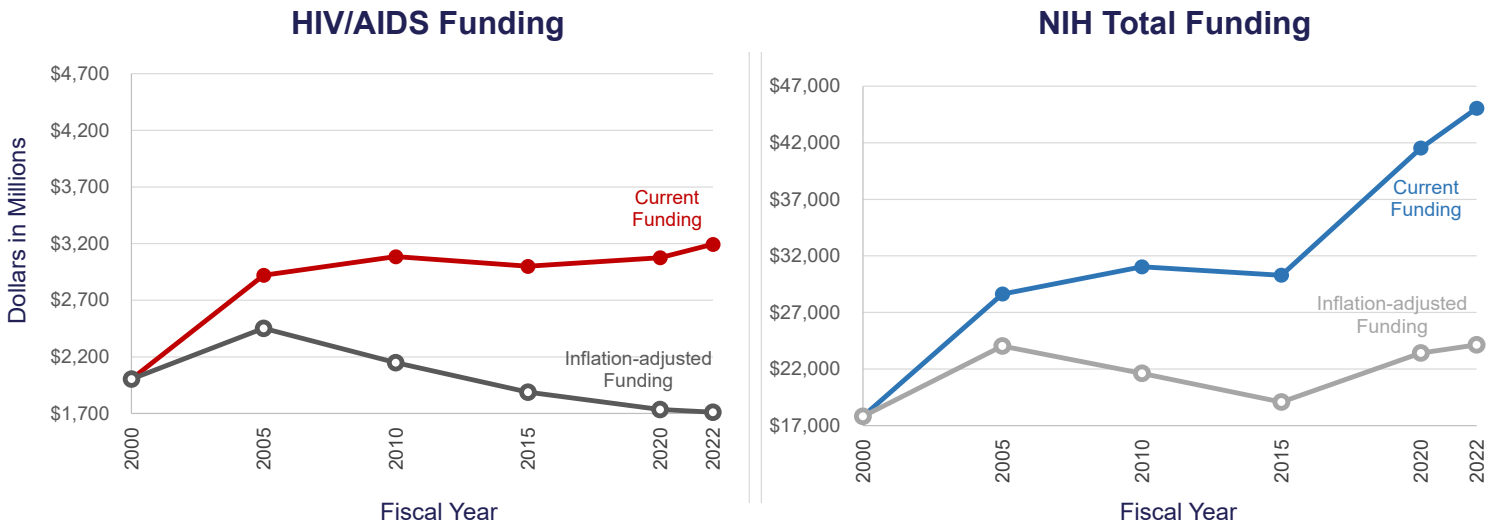
Budgets, Funding, and Resources Needed

OAR was authorized initially by the Health Omnibus Programs Extension (HOPE) Act of 1988, PL 100-607, a U.S. statute amending the Public Health Service Act 42 U.S.C. This legislation mandated the appropriation of federal funding for HIV/AIDS education, prevention, testing, and research. Subsequently, the NIH Revitalization Act of 1993, PL 103-43, authorized OAR to plan, coordinate, and evaluate HIV/AIDS research conducted or supported across NIH, enhance HIV research collaboration, minimize duplication, and ensure that research funds are invested effectively and efficiently across the ICOs conducting HIV/AIDS research. In this unique role, OAR coordinates the scientific, budgetary, legislative, and policy elements of the NIH HIV/AIDS research program to develop new tools in the national and international fight against the HIV/AIDS pandemic.

For 35 years, OAR has aimed to catalyze, coordinate, and communicate HIV/AIDS research across the NIH, HHS, other government agencies, academia, community, and non-governmental organizations. The annual NIH HIV/AIDS Professional Judgment Budget highlights accomplishments in HIV/AIDS research during the prior year and estimates the funds needed to fully pursue scientific priority areas of science "without regard to the probability that such amounts will be appropriated." The NIH HIV/AIDS Professional Judgment Budget builds on the justification to Congress for the President's Budget.

After several years of flat funding from FY 2015 to FY 2018, the NIH HIV/AIDS research budget increased from FY 2019 to FY 2021. Throughout the entire period, the HIV budget lagged behind increased costs of conducting critical HIV/AIDS research (**Figure 2**).

Figure 2: Effect of Inflation on Research Purchasing Power



Note: NIH funding does not include COVID-19 appropriations.

Source: Biomedical Research and Development Price Index (BRDPI).

The Consolidated Appropriations Act of 2022 provided NIH with "no less than $3,194,000,000 for HIV/AIDS research across NIH," an increase of $104 million (3.4 percent) over the FY 2021 enacted budget level.[29] The increase represented the equivalent of 13.4 percent of the $775 million requested in the FY 2022 NIH HIV/AIDS Professional Judgment Budget. This was the largest increase for the NIH HIV/AIDS research program since 2014, providing funding to build on new opportunities to end the HIV/AIDS pandemic globally and in the United States.

The proposed FY 2024 NIH HIV/AIDS Professional Judgment Budget for the NIH HIV/AIDS research program is $3.673 billion, an increase of $479 million, or 15 percent, over the FY 2022 enacted budget (see **Table 1**). The budget addresses the goals of the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research* and estimates the resources needed to optimize recent and exciting discoveries in HIV/AIDS research, ensure a robust pipeline of diverse HIV/AIDS investigators, and address some of the accumulated decreased spending power.

Table 1: FY 2024 NIH HIV/AIDS Professional Judgment Budget (Dollars in Millions)

FY 2022 Enacted Budget	**$3,194**		
FY 2024 Proposed Increase by Overarching Research Priority	**$479**	$115	Reduce the Incidence of HIV
		$48	Develop Next-Generation Therapies
		$48	Research Toward a Cure
		$86	Address HIV-associated Comorbidities, Coinfections, and Complications
		$182	Cross-Cutting Areas
FY 2024 Total Proposed Budget	**$3,673**		

Note: Projected distribution of proposed increase across research priorities.

Cross-cutting areas include basic science, behavioral and social science, epidemiology, health disparities, implementation science, information dissemination, and research training.

29 Consolidated Appropriations Act, 2022. HR 2471. 117th Cong (2022). Accessed October 17, 2022. www.congress.gov/bill/117th-congress/house-bill/2471

Scientific Advances and Opportunities

NIH-funded HIV/AIDS research has produced significant scientific discoveries, innovative programmatic approaches, and cross-disciplinary outcomes that have improved the lives of persons with and at risk for HIV and society at large. Additional resources are essential to capitalize on these advances and stimulate further innovation to:

- Expand basic biomedical, behavioral, and social sciences research.
- Understand the effects of HIV across the lifespan.
- Develop transformative tools and strategies.
- Strengthen the capacity and diversity of the HIV research workforce.

Basic Biomedical Research

HIV targets cells that play a critical role in the body's immune response. The unique characteristics of the HIV structure, life cycle, and persistence present unprecedented challenges for developing effective HIV vaccine and cure strategies.

The pool of HIV-infected cells in people receiving ART includes cells that harbor the viral genome. These cells, known as the latent HIV reservoir, are infected with HIV but are not producing new virus. HIV reactivation from such latent reservoirs may allow ongoing virus replication and disease progression upon interruption of ART, even after decades of effective viral suppression. The discovery of new ways to target and destroy latent reservoirs is a major challenge in the search for effective HIV cure strategies.[30,31,32]

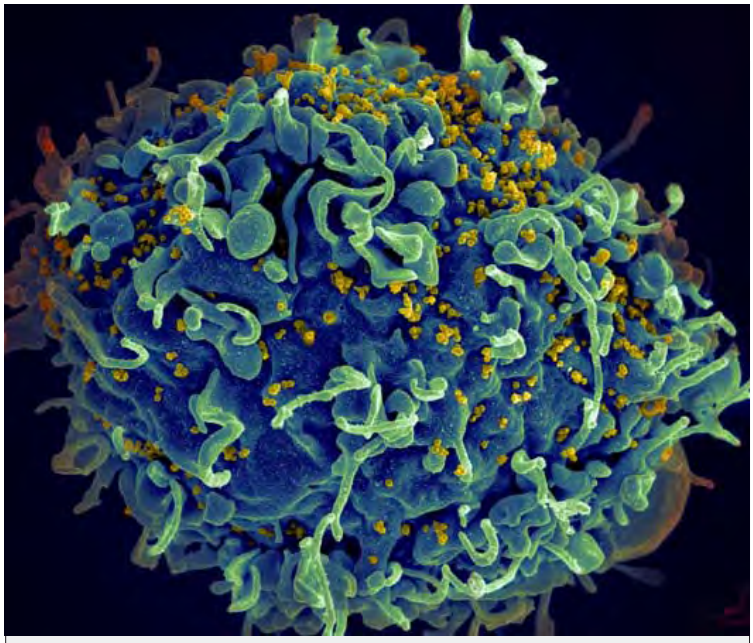


Figure 3: This human T cell (blue) is under attack by HIV (yellow), the virus that causes AIDS. The virus specifically targets T cells, which play a critical role in the body's immune response against invaders like bacteria and viruses.

Credit: Seth Pincus, Elizabeth Fischer, and Austin Athman
National Institute of Allergy and Infectious Diseases/NIH

Advanced technologies can be used for both innovative prevention and cure strategies. Next-generation sequencing and single cell studies, which capture multiple intracellular processes, may help identify the factors that allow HIV to persist in different

30 Boritz EA, Clark IC, Mudvari P, et al. Transcriptional programs of HIV silencing and cell survival in HIV-infected memory CD4 T cells under antiretroviral therapy. Abstract presented at: 24th International AIDS Conference; July 29, 2022; Montreal, Canada, and virtual. programme.aids2022.org/Abstract/Abstract/?abstractid=12900

31 New Insights into HIV Latent Cells Yield Potent Cure Targets. News release. National Institute of Allergy and Infectious Diseases. July 27, 2022. www.niaid.nih.gov/news-events/new-insights-hiv-latent-cells-yield-potential-cure-targets

32 Corley MJ, Farhadian SF. Emerging Single-cell Approaches to Understand HIV in the Central Nervous System. *Curr HIV/AIDS Rep*. 2022;19(1):113-120. doi:10.1007/s11904-021-00586-7. pubmed.ncbi.nlm.nih.gov/34822063

genomic locations.[33,34] The development of an HIV vaccine has been, and continues to be, a high priority for NIH. However, progress has been slow, often hindered by the complexity and high mutation rates of HIV. A Phase 1 clinical trial was recently launched to assess three experimental HIV vaccines that utilize mRNA technology similar to the vaccine platform for COVID-19.[35] If successful, this approach will be an example of bidirectional utilization of publicly funded scientific discoveries. Another potential prevention or cure strategy may involve generating broadly neutralizing HIV-1 antibodies (bNAbs), which can recognize a range of viral mutations and have been shown to target many types of HIV variants hiding within the body. Current trials using mRNA technology aim to stimulate the immune response to produce bNAbs at a level that is protective against several strains of HIV. Additional resources are needed to broaden our understanding of basic HIV virology; immunology; systems biology, which evaluates multiple factors simultaneously to understand the complex interactions between HIV and the human host; and to develop and evaluate novel strategies leading to safe and effective HIV vaccines and improved treatment modalities.

Behavioral and Social Sciences Research

Investment in HIV-related basic behavioral and social sciences research has advanced the understanding of many concurrent determinants of health, including psychological and structural factors that contribute to HIV infection acquisition, as well as HIV prevention and treatment uptake and adherence. For example, social determinants of health influence sexual activity and substance use, behavioral risk factors that may affect HIV acquisition. Intersectional stigma and discrimination based on multiple factors, like race, gender identity, and sexual orientation, can increase risk of HIV acquisition; in turn, stigma and discrimination are associated with social isolation and marginalization, perpetuating a detrimental cycle in which individuals may face severe consequences. Ongoing stigma related to HIV and its treatment, as well as medical mistrust and distrust, can contribute to hesitancy to seek health services and support. In addition, social, economic, and health disparities increase vulnerability to emerging public health emergencies, as seen with the COVID-19 pandemic and the global mpox outbreak.

Figure 4: Intersectional stigma and discrimination make persons more vulnerable to HIV.

Credit: Kwame Amo/Shutterstock.com

NIH supports research that explores HIV transmission/acquisition and its intersection with behavioral health, mental illness, sexual risk behaviors, and substance use disorders in persons with HIV at all ages and in all

33 Novel insights into the nature of the HIV reservoir and mechanisms of persistence. Symposium at: 24th International AIDS Conference; July 29, 2022; Montreal, Canada, and virtual. programme.aids2022.org/Programme/Session/24

34 Chen S, Lake BB, Zhang K. High-throughput sequencing of the transcriptome and chromatin accessibility in the same cell. *Nat Biotechnol.* 2019;37(12):1452-1457. doi:10.1038/s41587-019-0290-0. pubmed.ncbi.nlm.nih.gov/31611697

35 NIH launches clinical trial of three mRNA HIV vaccines. News release. National Institutes of Health. March 14, 2022. www.nih.gov/news-events/news-releases/nih-launches-clinical-trial-three-mrna-hiv-vaccines

social groups.[36,37,38,39] Additional investment in behavioral and social sciences research is needed to inform appropriate strategies to reduce HIV-related intersectional stigma and discrimination. Addressing these challenges can enable increased engagement and retention in prevention and care services, both for HIV and for co-occurring conditions across the lifespan. This investment is essential for all populations affected by HIV, particularly those in communities and settings with limited access to quality healthcare services and support, and in populations with existing health disparities.[40]

Health communication strategies need to be reframed to combat misinformation and disinformation campaigns that promote the inaccurate rejection of public health research and evidence-based medical advice. A key priority is to inform and support the acceptance and uptake of a future vaccine against HIV and other prevention strategies among those at risk. Implementation approaches are critical to strengthen our current national and global HIV response and capitalize on the latest and future scientific advances in the field of HIV/AIDS research. In addition, enhancing partnerships across sectors and nations will ensure the equitable application of advances resulting from over four decades of NIH investment in HIV/AIDS research.

Increased NIH investment in basic biomedical, behavioral, and social sciences research is needed to better understand the nuanced molecular mechanisms of HIV infection and to develop effective, community-appropriate, and person-centered interventions to prevent and manage HIV infection.

HIV Across the Lifespan

Comorbidities, coinfections, and complications can affect the health and well-being of persons with HIV of all ages. Multiple co-occurring conditions can significantly jeopardize the quality of life of persons with HIV.

There has been considerable progress in preventing perinatal HIV transmission in the United States and globally, thanks to routine HIV screening of pregnant persons, use of ART for treatment and prevention, avoidance of breastfeeding when advised, and use of elective cesarean delivery when appropriate. With these interventions, rates of HIV transmission from pregnant persons with HIV to their infants during pregnancy, labor, or delivery are now less than 2 percent.[41]

Adolescents and young adults represent a large percentage of new HIV infections and have unique needs for HIV testing and counseling, mental health, and treatment. In the United States in 2020, persons ages

36 Aronson ID, Zhang J, Rajan S, et al. Mobile Augmented Screening to Increase HIV Testing Among Emergency Department Patients as Young as 13 Years. *Cureus*. 2021;13(6):e15829. Published 2021 Jun 22. doi:10.7759/cureus.15829. pubmed.ncbi.nlm.nih.gov/34327070

37 Aronson ID, Zhang J, Rajan S, et al. Automated Substance Use/Sexual Risk Reporting and HIV Test Acceptance Among Emergency Department Patients Aged 13-24 Years. *AIDS Behav.* 2022;26(5):1544-1551. doi:10.1007/s10461-021-03507-2. pubmed.ncbi.nlm.nih.gov/34705152

38 Safren SA, O'Cleirigh C, Andersen LS, et al. Treating depression and improving adherence in HIV care with task-shared cognitive behavioural therapy in Khayelitsha, South Africa: a randomized controlled trial. *J Int AIDS Soc.* 2021;24(10):e25823. doi:10.1002/jia2.25823. pubmed.ncbi.nlm.nih.gov/34708929

39 *Eunice Kenney Shriver* National Institute of Child Health and Human Development. Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN). Reviewed August 27, 2021. Accessed October 17, 2022. www.nichd.nih.gov/research/supported/atn

40 National Institutes of Health Office of AIDS Research, National Institute of Mental Health Division of AIDS Research. HIV-Related Intersectional Stigma Research Advances and Opportunities Workshop. July – September 2020. Accessed October 17, 2022. www.nimh.nih.gov/sites/default/files/documents/nih_oar_and_nimh_hiv-related_intersectional_stigma_final_workshop_summary_final_508.pdf

41 Nesheim SR, FitzHarris LF, Mahle Gray K, Lampe MA. Epidemiology of perinatal HIV transmission in the United States in the era of its elimination. *Pediatr Infect Dis J.* 2019;38(6):611-616. doi:10.1097/INF.0000000000002290. pubmed.ncbi.nlm.nih.gov/30724833

25–34 years had the highest percentage of new HIV diagnoses, accounting for 37 percent of new infections, while young persons ages 13–24 years accounted for 20 percent of HIV diagnoses.[42] Improved HIV testing and counseling has increased the proportion of persons with HIV who are aware of their positive HIV status; however, persons ages 13–24 with HIV are the least likely of all age groups to know their HIV status, according to the CDC.[43] Linkage to care within one month of HIV diagnosis is associated with improved outcomes but remains an elusive goal for young persons.[44] Regulatory approval is slower for novel treatment strategies in adolescents or children. Clinical trial participation for this age group has a higher perceived risk, resulting in limited clinical trial data. In addition to cognitive and developmental changes that influence decision-making behavior during adolescence, adolescents with HIV are at increased risk for mental health conditions. These factors collectively threaten adherence to medication.[45] Adolescents with HIV also face unique challenges during the transition from pediatric to adult health care settings, including interruptions in HIV care, changes in socioeconomic and health insurance status, and stigma and disclosure issues.[46] Young people experiencing homelessness without a guardian may lack access to health care or other social safety nets and face additional challenges related to HIV risk and management, including a lack of access to transportation.[47]

Half of all people with HIV living in the United States are aged 50 or older, and about 17 percent of new infections annually occur in this age group.[48] Research to identify and address the long-term health care service and assistance needs of persons aging with HIV across the care continuum will be necessary to support this increasing population, as well as their informal and formal care providers. The development of safe and effective ART has enabled persons with HIV to have near-normal life expectancies. However, for some older adults, cognitive impairment and other comorbidities may contribute to challenges with medication adherence. Chronic HIV infection and long-term use of ART can also contribute to complications, coinfections, and comorbidities in persons with HIV, particularly as they age. Older adults with HIV often experience multiple comorbidities such as cardiovascular and lung diseases; some neurocognitive, neuropsychiatric, and neurological conditions; some cancers; and bone, muscle, and other end-organ diseases. There also is a growing body of evidence to suggest that women with HIV who are on ART experience menopause at younger ages and have higher rates of severe menopause symptoms compared to women who do not have HIV.[49,50]

HIV-associated coinfections are a significant challenge across the lifespan, including hepatitis, tuberculosis (TB), and sexually transmitted infections (STIs). Hepatitis B and C progress faster and cause higher rates

42 Centers for Disease Control and Prevention. HIV Surveillance Report, 2020; vol. 33. May 2022. Accessed October 14, 2022. www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2020-updated-vol-33.pdf

43 Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2015–2019. HIV Surveillance Supplemental Report 2021;26(1). May 2021. Accessed October 24, 2022. www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-26-1.pdf

44 Miller RL, Chiaramonte D, Strzyzykowski T, Sharma D, Anderson-Carpenter K, Fortenberry JD. Improving Timely Linkage to Care among Newly Diagnosed HIV-Infected Youth: Results of SMILE. *J Urban Health.* 2019;96(6):845-855. doi:10.1007/s11524-019-00391-z. pubmed.ncbi.nlm.nih.gov/31677014

45 Yusuf H, Agwu A. Adolescents and young adults with early acquired HIV infection in the United States: unique challenges in treatment and secondary prevention. *Expert Rev Anti Infect Ther.* 2021;19(4):457-471. doi:10.1080/14787210.2021.1829473. pubmed.ncbi.nlm.nih.gov/32990092

46 Continisio GI, Lo Vecchio A, Basile FW, et al. The Transition of Care From Pediatric to Adult Health-Care Services of Vertically HIV-Infected Adolescents: A Pilot Study. *Front Pediatr.* 2020;8:322. doi:10.3389/fped.2020.00322. pubmed.ncbi.nlm.nih.gov/32714885

47 Chelvakumar G, Ford N, Kapa HM, et al. Healthcare Barriers and Utilization Among Adolescents and Young Adults Accessing Services for Homeless and Runaway Youth. *J Community Health*. 2017;42(3):437-443. doi:10.1007/s10900-016-0274-7. pubmed.ncbi.nlm.nih.gov/27817043

48 Centers for Disease Control and Prevention. HIV Surveillance Report, 2020; vol. 33. May 2022. Accessed October 14, 2022. www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2020-updated-vol-33.pdf

49 Ageing with HIV. Editorial. *Lancet Healthy Longev.* 2022;3(3):e119. doi:10.1016/S2666-7568(22)00041-1. pubmed.ncbi.nlm.nih.gov/36098283

50 Bullington BW, Edmonds A, Ramirez C, et al. Premature and early menopause among US women with or at risk for HIV. *Menopause.* 2022;29(6):741-747. Published 2022 Jun 1. doi:10.1097/GME.0000000000001964. pubmed.ncbi.nlm.nih.gov/35324546

of mortality in persons with HIV than in those who do not have HIV.[51] U.S. Food and Drug Administration (FDA) approved safe and effective vaccines preventing hepatitis B are available, but none are currently FDA approved for hepatitis C prevention. While HIV and hepatitis B and C coinfections are treatable for most people, highly effective treatment can be complex and expensive, particularly for hepatitis C, in low- and middle-income countries.

Tuberculosis is the leading cause of death for persons with HIV worldwide, particularly in resource-limited countries.[52] Among people with latent TB infection, those with HIV coinfection are more likely to develop active TB disease because HIV weakens the immune system needed to combat the bacteria that causes TB.[53]

Sexually transmitted infections significantly increase the risk of HIV acquisition, as viral shedding is higher with ulcerations and inflammation. Some behaviors may increase the risk of HIV transmission, such as having sex with someone who has HIV without using condoms. Certain STIs, including syphilis and herpes simplex virus, have a greater association with HIV transmission.[54] STIs are a considerable health risk to persons with HIV, as HIV infection can increase susceptibility to other sexually transmitted pathogens. For example, there is a reciprocal relationship between HIV and genital herpes (HSV-2) as both conditions can facilitate the acquisition of the other pathogen.[55] Women with HIV are at a higher risk for human papillomavirus (HPV) infection, which can lead to cervical cancer.[56]

Individuals with HIV may require integrated health services delivery to cope with the clinical and sociobehavioral needs of aging populations, such as multiple comorbidities, polypharmacy, frailty, declining physical and cognitive function, alterations in body composition, and social isolation. Research is needed to help identify and optimize best practices for individual health needs across the lifespan.

HIV-associated coinfections and comorbidities present significant challenges across the lifespan. Additional funds are urgently needed to support research on new strategies to prevent and treat HIV-associated coinfections and comorbidities; expand the current understanding of geroscience, at the intersection between basic aging biology and chronic disease; and improve health outcomes in persons living and aging with HIV.

51 HIV.gov. Hepatitis B & C. Updated September 20, 2022. Accessed October 17, 2022. www.hiv.gov/hiv-basics/staying-in-hiv-care/other-related-health-issues/hepatitis-b-and-c

52 UNAIDS. Tuberculosis. Accessed October 17, 2022. www.unaids.org/en/topic/tuberculosis

53 Centers for Disease Control and Prevention. Tuberculosis: The Connection Between TB and HIV. Reviewed June 21, 2016. Accessed October 17, 2022. www.cdc.gov/tb/publications/pamphlets/tbandhiv_eng.htm

54 Cohen MS, Council OD, Chen JS. Sexually transmitted infections and HIV in the era of antiretroviral treatment and prevention: the biologic basis for epidemiologic synergy. *J Int AIDS Soc.* 2019;22 Suppl 6(Suppl Suppl 6):e25355. doi:10.1002/jia2.25355. pubmed.ncbi.nlm.nih.gov/31468737

55 Kalichman SC, Pellowski J, Turner C. Prevalence of sexually transmitted co-infections in people living with HIV/AIDS: systematic review with implications for using HIV treatments for prevention. *Sex Transm Infect.* 2011;87(3):183-190. doi:10.1136/sti.2010.047514. pubmed.ncbi.nlm.nih.gov/21330572

56 Liu G, Sharma M, Tan N, Barnabas RV. HIV-positive women have higher risk of human papilloma virus infection, precancerous lesions, and cervical cancer. *AIDS. 2018*;32(6):795-808. doi:10.1097/QAD.0000000000001765. pubmed.ncbi.nlm.nih.gov/29369827

Capacity Strengthening

Building the Next Generation of HIV/AIDS Researchers

NIH is committed to developing the next generation of multidisciplinary HIV/AIDS researchers to include expanded participation by women, underrepresented populations, and under-resourced institutions within the United States. OAR prioritizes developing and implementing a long-term plan to support the next generation of HIV/AIDS researchers and improving the diversity of the HIV/AIDS research workforce. The OAR Early Career Investigator (ECI) initiative focuses on ECIs and grantees who were awarded funding within the past two years.[57]

Expanding Diversity in the HIV/AIDS Research Workforce

NIH is engaged in multiple collaborative initiatives to build a more diverse science workforce. In FY 2022, OAR aimed to facilitate greater diversity in the HIV/AIDS research workforce at all career stages. OAR collaborated with NIH ICOs to develop funding opportunities for HIV/AIDS research facilities at institutions serving underrepresented populations or communities with limited resources, or those located in Institutional Development Award (IDeA)-eligible states. IDeA is a congressionally mandated program that builds research capacity in states that historically have had low levels of NIH funding. The program aims to strengthen an institution's ability to support biomedical research, enhance the competitiveness of investigators in securing research funding, and enable clinical and translational research that addresses the needs of medically underserved communities. Furthermore, OAR provided supplements to expand research capacity for laboratory improvements for HIV/AIDS research.

With additional resources, NIH will support the development and expansion of novel programs for training and support of underrepresented minorities and women, as well as expand efforts to strengthen capacity of under-resourced institutions to enhance diversity in the HIV/AIDS research workforce.

Figure 5: As part of an NIH training program, students load proteins onto a gel that will separate them by size.

Credit: Office of Intramural Training & Education, NIH

57 National Institutes of Health Office of AIDS Research. Early Career Investigator Resources. Accessed October 14, 2022. www.oar.nih.gov/trans-nih-hiv-research-program/hiv-early-career-resources

Conclusion

Additional resources, outlined in the FY 2024 NIH HIV/AIDS Professional Judgment Budget, would allow NIH to expand important HIV science in focused areas of research and to ensure that research is a central component of national HIV initiatives. For public investment in research and scientific discovery to be successful, the development and implementation of evidence-based strategies must also be linked to policy and programmatic considerations. OAR collaborates with a broad network of strategic partners across the NIH ICOs, other government agencies, academia, and civil society to advance the science and improve health outcomes for persons with and affected by HIV.

Sustained financial support of the NIH HIV/AIDS research enterprise has saved millions of lives in the past 40 years. Continued investment is critical to prevent a global rebound of the HIV/AIDS pandemic. We must continue to work together in unique ways to translate scientific discovery into action, encourage a holistic response to the HIV/AIDS pandemic, and stimulate innovation. The powerful connections among NIH-funded researchers, front-line health care workers, individuals with and at risk for HIV, advocates, and industry partners show that, together, we can end the HIV/AIDS pandemic.

Acronyms and Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral therapy
CDC	U.S. Centers for Disease Control and Prevention
ECI	Early career investigator
EHE	*Ending the HIV Epidemic in the U.S.* initiative
FDA	U.S. Food and Drug Administration
HHS	U.S. Department of Health and Human Services
HIV	Human Immunodeficiency Virus
ICOs	NIH Institutes, Centers, and Offices
NHAS	*National HIV/AIDS Strategy*
NIH	National Institutes of Health
OAR	Office of AIDS Research
ONAP	White House Office of National AIDS Policy
PEPFAR	United States President's Emergency Plan for AIDS Relief
PrEP	Pre-exposure prophylaxis
STI	Sexually transmitted infection
TB	Tuberculosis

National Institutes of Health
Office of AIDS Research