

# FY 2022 NIH HIV/AIDS Professional Judgment Budget

**Optimizing the Investment in HIV Research:  
*Pandemics, Pipelines, and Partnerships***



National Institutes of Health  
Office of AIDS Research



## **OAR Mission**

Ensure that NIH HIV/AIDS research funding is directed at the highest priority research areas and facilitate maximal return on the investment.

## **OAR Vision**

Advance research to end the HIV pandemic and improve health outcomes for people with HIV.

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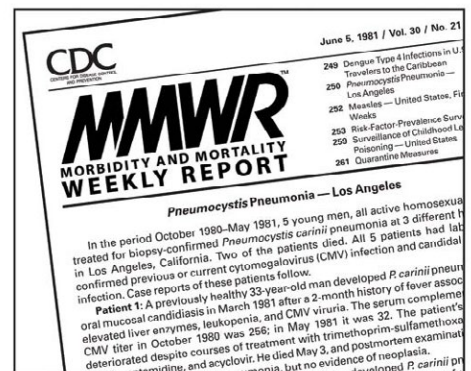
The NIH investment in HIV and AIDS research over the decades has positioned scientists and public health officials to meet the challenges of other infectious diseases, such as the current SARS-CoV-2/COVID-19 pandemic.

At the same time, the impact of the scale and scope of the COVID-19 pandemic on the HIV research enterprise is important to assess in order to safeguard the historical investment to ensure continued progress toward and successfully achieving an end of the HIV pandemic in this country and worldwide.



# Optimizing the Investment in HIV Research: Pandemics, Pipelines, and Partnerships

On June 5, 1981, the Centers for Disease Control and Prevention (CDC) *Morbidity and Mortality Weekly Report* (MMWR) described cases of rare lung infections in five previously healthy, young gay men in Los Angeles, California.<sup>1</sup> We did not know at the time exactly what the observations meant, nor that the HIV/AIDS pandemic was underway. In retrospect, the concerted response by science leaders across disciplines and sectors, in partnership with public health officials and community leaders, was visionary and a testament to what we can achieve together. Now in 2021, the 40th anniversary of



Source: CDC

this historic moment provides an opportunity to reflect on what has been achieved and what more needs to be done in the continuing struggle against a global pandemic that has claimed more than 34 million lives. Forty years later, about 1.5 million people still acquire HIV annually and nearly 700,000 people die.

An important lens on this reflection is how the National Institutes of Health (NIH) investment in HIV and AIDS research over the decades has positioned scientists and public health officials to meet the challenges of other infectious diseases, such as the current SARS-CoV-2/COVID-19 pandemic. At the same time, the effect of the scale and scope of the COVID-19 pandemic on the HIV research enterprise is important to assess in order to safeguard the historical investment to ensure continued progress toward and successfully achieving an end of the HIV pandemic in this country and worldwide.

The NIH Office of AIDS Research (OAR) works collaboratively with local, state, and federal agencies, as well as community and public health partners, to leverage scientific discovery to prevent, treat, and eventually cure HIV. NIH investments in HIV and AIDS research over more than four decades have produced groundbreaking advances in understanding the basic virology, immunology, and pathogenesis of HIV. Research discoveries led to the development and implementation of safe, effective antiretroviral therapy (ART) to extend the lifespan of people with HIV to a near normal life expectancy and to prevent HIV transmission and acquisition. Yet in the United States and globally, rates of new HIV infections continue to increase in some populations and remain unchanged in others, reflecting inequalities and health disparities by race, ethnicity, sex, gender, age, socioeconomic status, and geography—inequalities and disparities that are now shaping the outcomes of the SARS-CoV-2 pandemic.

Understanding and addressing inequalities and health disparities are key to optimize the outcomes of decades of HIV and AIDS research and to achieve the primary goal of [Ending the HIV Epidemic in the U.S.](#) (EHE) to reduce new HIV infections in the United States by at least 90 percent by 2030. At the NIH level, a new effort to end structural racism and racial inequities in biomedical research was launched through an initiative called [UNITE](#). In the words of NIH Director Dr. Francis Collins, “NIH is committed to instituting new ways to support diversity, equity, and inclusion, and identifying and dismantling any policies and practices that may harm our workforce and our science.”<sup>2</sup>

The [NIH Revitalization Act of 1993](#) authorized OAR to plan, coordinate, and evaluate HIV/AIDS research conducted or supported across the NIH. A key component of this authorization is the development of the annual HIV/AIDS Professional Judgment Budget, which highlights accomplishments in HIV research during the prior year and estimates the investment needed to advance progress in priority areas of science “without regard to the probability that such amounts will be appropriated.” The Professional Judgment Budget is guided by the [NIH Strategic Plan for HIV and HIV-Related Research](#) and builds on the [justification to Congress for the President’s Budget](#). For fiscal year (FY) 2022, the NIH HIV/AIDS Professional Judgment Budget requests \$775 million in additional funds, a 25-percent increase in the HIV/AIDS research investment. Funding at this level will expedite NIH efforts to pursue emerging discoveries in focused areas of HIV **pandemic** research, enhance the **pipelines** of novel HIV prevention and treatment products, ensure a diverse pool of HIV investigators, and expand **partnerships** with stakeholders inside and outside of government to make greater inroads into mitigating inequalities and ending the HIV epidemic in the United States and globally.



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Understanding and addressing inequalities and health disparities are key to optimize the outcomes of decades of HIV and AIDS research.



# Snapshot of the HIV Pandemic

## Global

HIV continues to be one of the world's most serious health and development challenges. From 1981, when the first cases of AIDS were reported, to the end of 2020, approximately 78 million people became infected with HIV globally and more than 34 million died.<sup>3,4</sup> Currently approximately 38 million people are living with HIV, including 16 percent (or more than 6 million) who are unaware of their HIV status. Although new HIV infections have diminished by 23 percent overall since 2010, approximately 1.5 million people became infected across the globe in 2020.<sup>5</sup>

HIV prevalence and incidence are not distributed equally around the world. Although some regions, countries, and population groups have declining incidence, others have unchanging or increasing rates of new HIV infections. Continued HIV transmission underscores the growing, still unmet need for HIV prevention, treatment, and care services that are appropriate for the persons and communities most affected in different regions.

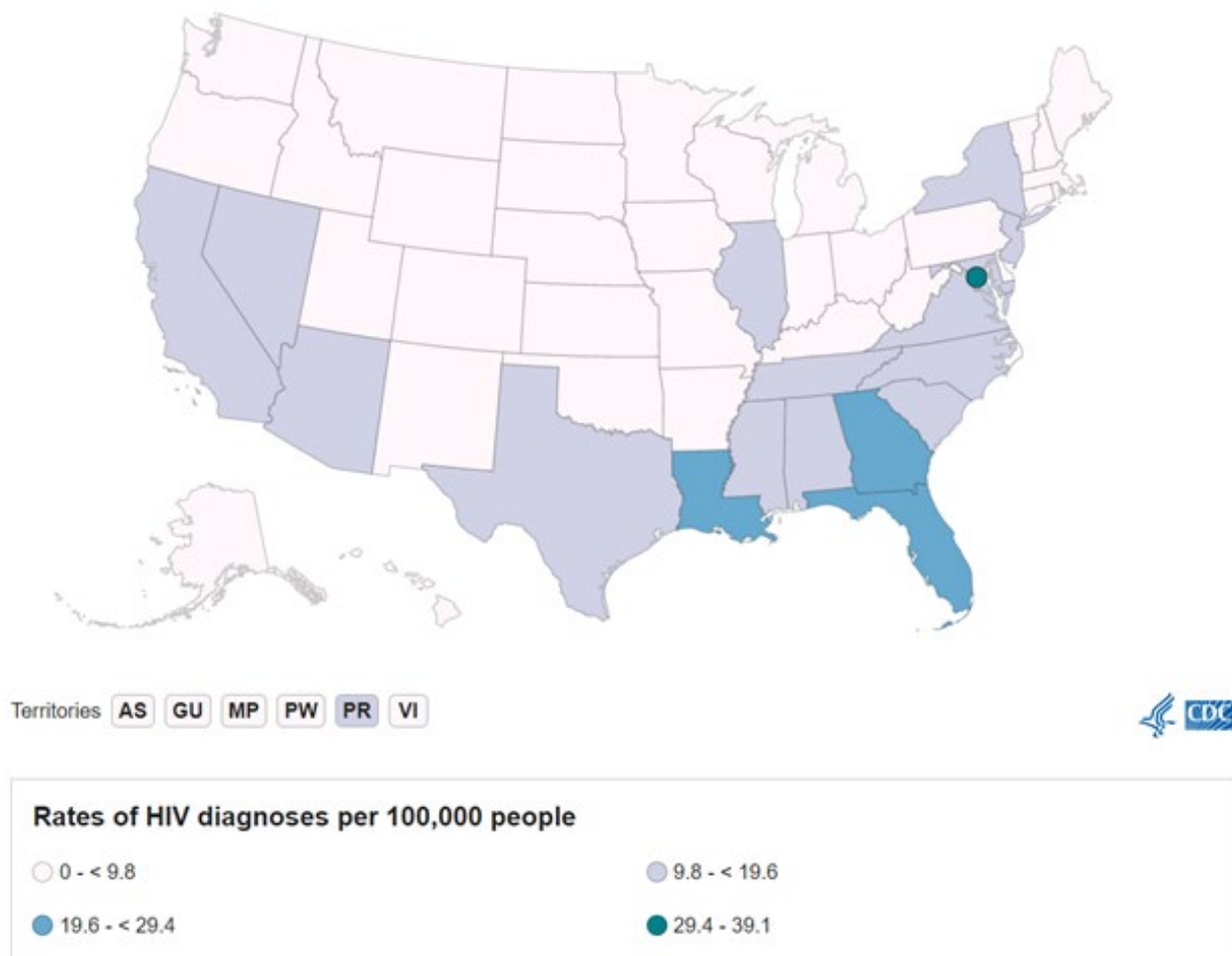
- In sub-Saharan Africa, five in six new infections among adolescents occur in girls; and young women aged 15 to 24 years are twice as likely to be living with HIV than young men.
- Young gay men and other men who have sex with men (aged 15 to 24 years) are at particular risk in high-income countries of Western and Central Europe and North America, accounting for 36 percent of infections in those regions in 2019.
- In Eastern Europe and Central Asia, new HIV infections rose by 72 percent between 2010 and 2019, chiefly driven by high rates of injection drug use.
- In the Middle East and North Africa, there is a significant testing gap, as almost 50% of people with HIV are unaware of their HIV status.
- Globally, there is suboptimal HIV treatment coverage across all ages of persons with HIV; HIV treatment coverage among children with HIV aged 0 to 14 years (53 percent coverage) is significantly lower than among adults (68 percent coverage).

## Domestic

HIV continues to be a public health challenge in the United States. At the end of 2019, an estimated 1.2 million Americans were living with HIV, including almost 160,000 individuals who were unaware of their infection. Of all adults and adolescents with HIV, 66 percent received some HIV care; 50 percent were retained in care; and 57 percent achieved viral suppression.<sup>6</sup> This coverage is far lower than the UNAIDS 2020 targets needed to end the HIV epidemic. HIV incidence has decreased by 73 percent from its peak years in 1984 and 1985, but during 2019, an estimated 34,800 people became newly infected with HIV. Moreover, the distribution of new HIV infections in the United States reveals ongoing disparities related to race, ethnicity, sex, gender, age, and region. For 2019—<sup>7,8</sup>

- Of the 34,800 new HIV infections, 70 percent were among gay and bisexual men and other men who have sex with men (MSM), including those who inject drugs; 22 percent were among heterosexuals (men and women); and 7 percent were among people who inject drugs.
- The number of new HIV diagnoses was highest among people aged 25 to 34 years.
- Among gay and bisexual men and other MSM, new HIV diagnoses remain disproportionately higher among Black/African American and Hispanic/Latino men than among White men.
- The rate of new HIV infections for Black/African American females was 11 times that of White females and 4 times that of Hispanic/Latino females.
- Across regions in the United States, the rate of new HIV infections was highest in the South (17.6 percent), followed by the West (10.9 percent), the Northeast (9.8 percent), and the Midwest (7.9 percent).

Figure 1. Rates of New HIV Diagnoses in the U.S. and Dependent Areas, 2018



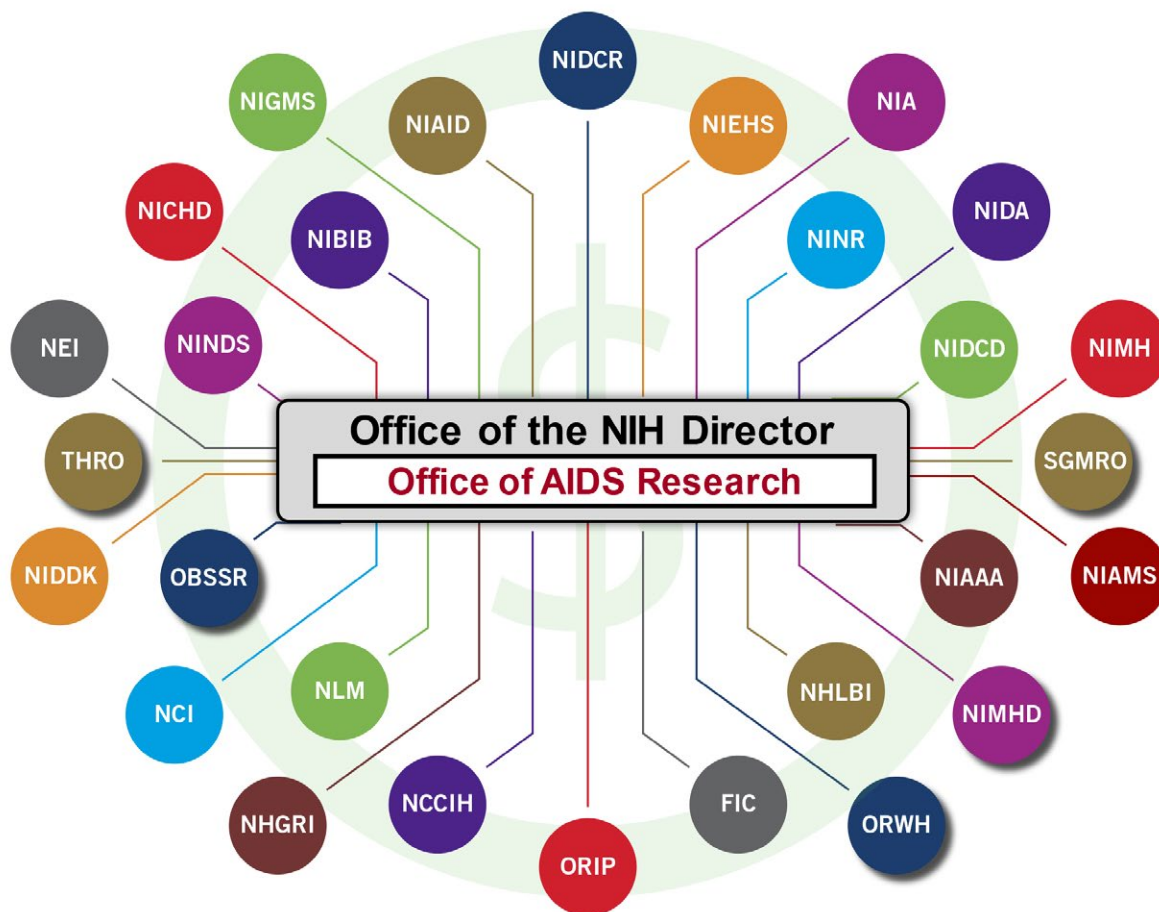
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# NIH Priorities and Strategic Goals for HIV and HIV-Related Research

The OAR develops, coordinates, and manages NIH HIV-related research and ensures that research funds are invested in the areas of highest scientific priority. Priorities are established by OAR in collaboration with entities across the NIH, as well as with partners and stakeholders from the scientific community, people with HIV, and nongovernmental groups. The priorities outline a broad HIV research agenda, guide decision-making processes related to HIV funding, and inform the development of the *NIH Strategic Plan for HIV and HIV-Related Research* (the NIH Plan).

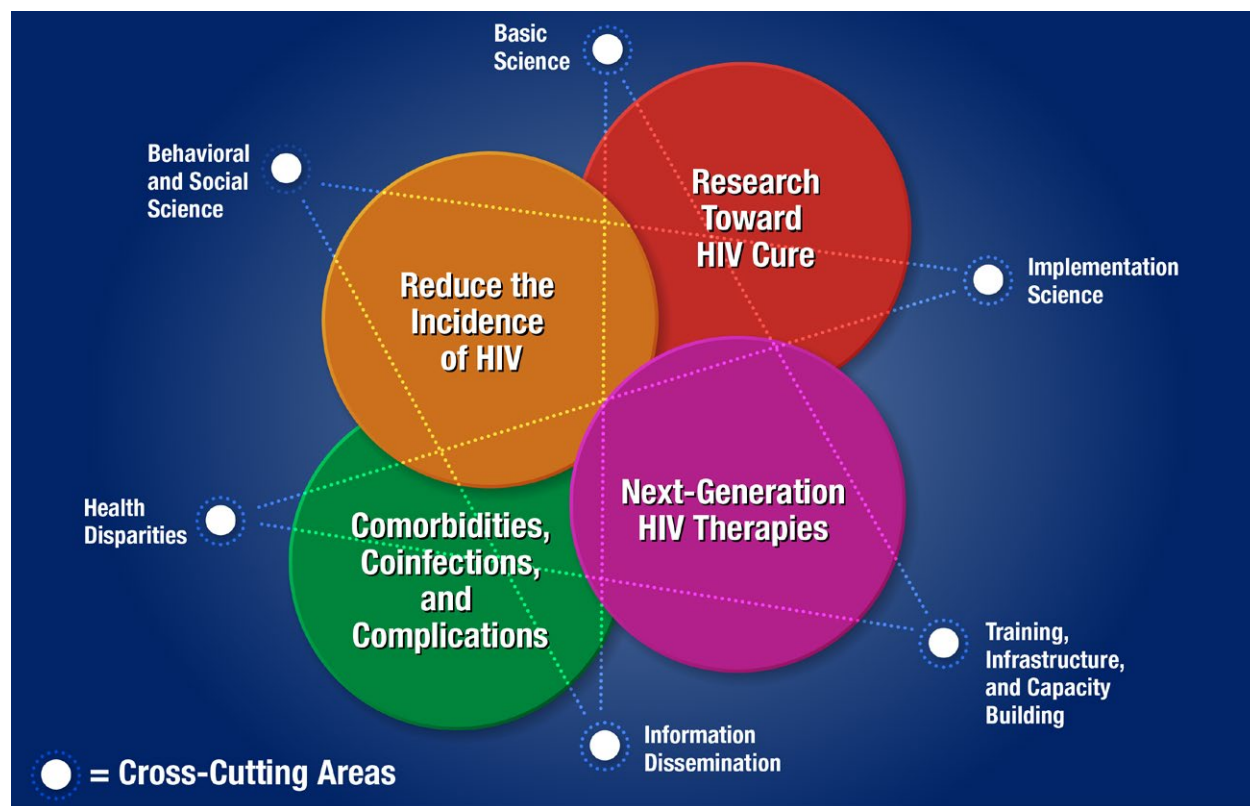
Figure 2. OAR develops, coordinates, and manages NIH HIV-related research



OAR works with NIH Institutes, Centers, and Offices (ICO) and external stakeholders to:

- Establish HIV research priorities
- Ensure HIV funds are invested in highest priority areas
- Address emerging needs
- Develop the NIH Strategic Plan for HIV and HIV-Related Research

Figure 3. NIH Priorities for HIV and HIV-Related Research



- **Reduce the Incidence of HIV** (orange) includes vaccines; pre-exposure prophylaxis (PrEP); microbicides and multipurpose prevention technologies; HIV testing; treatment as prevention; monoclonal antibodies.
- **Next-Generation HIV Therapies** (purple) includes less toxic, longer-lasting ART; novel HIV targets and inhibitors; novel immune-based therapies; engagement, adherence, and retention in care; self-testing technologies; U=U (undetectable = untransmittable).
- **Research Toward HIV Cure** (red) includes sustained ART-free viral remission; viral eradication; viral latency and sanctuaries; cure ethics and acceptability.
- **Comorbidities, Coinfections, and Complications** (green) includes tuberculosis and sexually transmitted infections; neurologic and cardiovascular complications; malignancies; mental illnesses and substance use; metabolic disorders.
- **Cross-Cutting Research** (white circles) includes health disparities; behavioral and social science; basic science; implementation science; epidemiology; training, infrastructure, and capacity building; information dissemination.

The NIH Plan provides a framework for addressing the priorities by focusing investments and partnerships in novel ways to stimulate scientific discovery to develop more effective strategies, enhance existing approaches, and accelerate innovation for prevention and treatment. The framework includes four Strategic Goals:



**Strategic Goal 1:** Advance rigorous and innovative research to end the HIV pandemic and improve the health of people with, at risk for, or affected by HIV across the lifespan.



**Strategic Goal 2:** Ensure that the NIH HIV research portfolio remains flexible and responsive to emerging scientific opportunities and discoveries.



**Strategic Goal 3:** Promote dissemination and implementation of research discoveries for public health impact across agencies, departments, and stakeholders within the U.S. government and globally.



**Strategic Goal 4:** Build human resource and infrastructure capacity to enhance sustainability of HIV research discovery and the implementation of findings by a diverse and multidisciplinary workforce.

**FY 2021–2025**

NIH Strategic Plan *for* HIV  
and HIV-Related Research





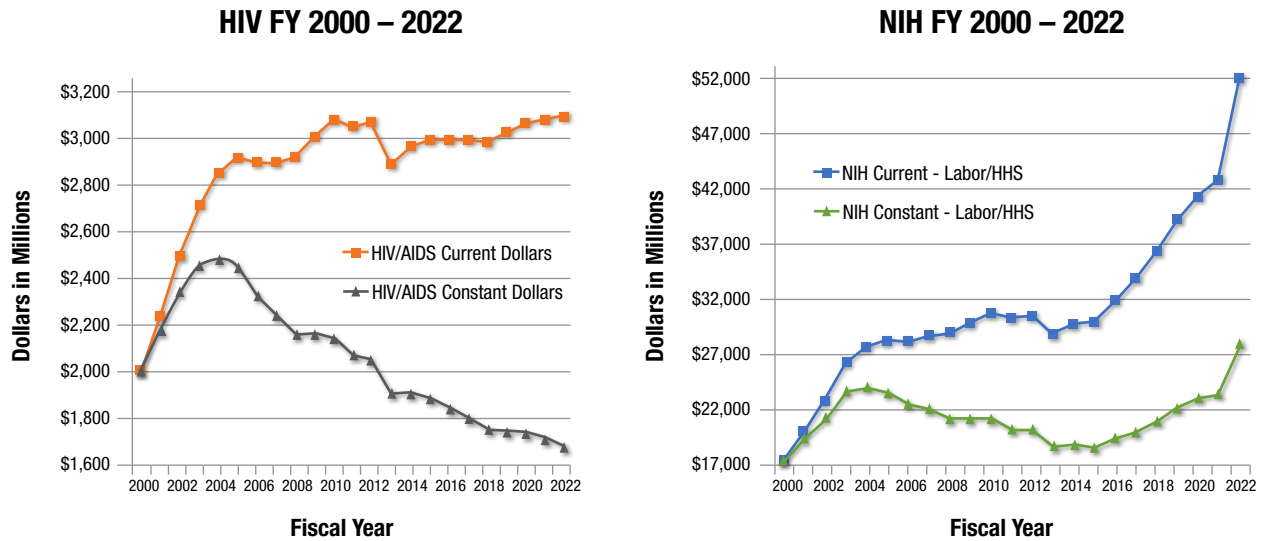
## Professional Judgment Budget

Over the past four decades meaningful NIH investment in HIV and AIDS research across priority areas has yielded crucial understanding of the basic virology and immunology of infectious diseases, as well as the development of effective strategies for HIV diagnosis, prevention, treatment, and cure. Building on this cumulative knowledge, recent scientific discoveries point to exciting new directions in HIV research that provide even greater promise for ending the HIV epidemic and would benefit from additional resources. The experience of the COVID-19 pandemic has taught us that with concerted investment and strong partnerships among stakeholders, it is possible to create new, faster, and more effective ways to advance discovery and translate outcomes to public health implementation. Now is the time to capitalize on lessons learned and achieve the commitment to end the HIV pandemic.

NIH HIV research funding has increased only modestly over the past 10 years and has lagged behind the increases in costs associated with conducting this critical research. As people with HIV are living longer to a near normal life expectancy and are experiencing more comorbidities associated with HIV and antiretroviral treatment (ART), the overall cost of HIV health care management is projected to continue to increase.<sup>9</sup> Strengthening the HIV/AIDS research investment now to end the HIV pandemic will reap the benefit of controlling health care costs in the future.



**Figure 4. Effect of Inflation on Research Purchasing Power**



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

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

Within this context, the proposed FY 2022 Professional Judgment budget for the NIH-wide HIV research program is \$3.875 billion, an increase of \$775 million, or 25 percent, over the FY 2022 Estimate (see [Table 1](#)). This budget estimates the resources needed to optimize recent and exciting discoveries in HIV prevention and treatment to significantly reduce the incidence of HIV, reduce HIV-associated health disparities, improve the health and well-being of all people with HIV, and ensure a robust pipeline of diverse HIV investigators, as well as correct some of the increased loss of spending power. The Professional Judgment budget proposal is displayed in accordance with the overarching NIH HIV research priorities described in the NIH Plan. One of the unique features of the OAR is its mandate to allocate and manage the NIH HIV research budget, in collaboration with the NIH Institutes, Centers, and Offices (ICOs), who carry out and manage the HIV research programs, in alignment with the Plan’s priorities.

**Table 1. FY 2022 AIDS Professional Judgment Budget Request (Dollars in Thousands)**

Overarching Research Priority	FY 2022 Estimates	Requested Increase	FY 2022 Professional Judgment Total
Reduce the Incidence of HIV	\$719,220	\$705,205	\$949,330
Develop Next-Generation Therapies	345,219	348,382	504,157
Research Toward a Cure	209,134	210,025	266,600
Address HIV-Associated Comorbidities, Coinfections, and Complications	554,450	564,252	689,027
Cross-Cutting Areas*	1,247,862	1,262,136	1,465,886
<b>TOTAL</b>	<b>\$3,075,885</b>	<b>\$3,090,000</b>	<b>\$3,875,000</b>

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

**Note:** The proposed \$775 million increase includes a 10% inflation factor.

Within the overarching categories of research, increased resources are proposed specifically for focused efforts to stimulate research to:

### **Reduce the Incidence of HIV**

- Accelerate testing of promising HIV vaccines approaches utilizing mRNA and self-amplifying RNA (saRNA) delivery technologies and structure-based designer antigens
- Extend the repertoire of long-acting formulations for pre-exposure prophylaxis (PrEP) and for antibody-mediated approaches for HIV prevention

### **Next Generation Therapies**

- Capitalize on advanced imaging and computer modeling to identify new therapeutic targets to constrict emergence of drug-resistant HIV variants
- Enhance assessment of the acceptability and effectiveness of new technologies, such as long-acting injectables, implants, microarray patches, and vaginal rings, to diversify delivery options for HIV therapeutic interventions

## **Research Toward a Cure**

- Develop and implement technology for novel testing strategies to measure effectiveness of treatments to sustain viral suppression, and eradicate viral replication in all cellular reservoirs

## **Comorbidities, Coinfections, and Complications**

- Delineate the factors associated with the neurological complications of HIV across the lifespan and develop strategies to ameliorate these conditions
- Address the interplay of HIV and SARS-CoV-2 coinfection on HIV pathogenesis

## **Cross-Cutting Areas**

- *Basic Science*: Expand understanding of the virus lifecycle by imaging and modeling to inform development of next generation HIV therapies with new targets
- *Behavioral, Social, and Implementation Science*: Develop effective behavioral and social-structural interventions to mitigate HIV-associated health disparities and stigma
- *Training, Capacity-Building, and Infrastructure*: Expand the pool of heterogeneous early stage HIV investigators to meet the challenges of 21st Century HIV research



# Focusing New Resources to Advance HIV Research

Since HIV/AIDS was first reported 40 years ago, NIH research discoveries have transformed HIV infection from causing a rapidly fatal disease to a manageable chronic condition. Such a remarkable achievement is due in large part to the significant NIH investment in focused research in the basic, clinical, epidemiological, behavioral, social, and implementation sciences that has produced highly safe and effective HIV prevention and treatment interventions. The investment also has produced a wealth of discoveries, knowledge, and infrastructure leveraged to address other pandemics, such as the current COVID-19 pandemic. NIH is poised to optimize this investment by focusing additional resources in specific high priority areas, as outlined above and detailed below.

## Reduce the Incidence of HIV

### Vaccines

mRNA vaccines are nucleic acid vaccines that have certain advantages over other types of vaccines, including speed and ease of manufacture and amplified immune response. Approaches using the mRNA platform to develop vaccines for HIV prevention<sup>10,11</sup> quickly were applied to respond to the COVID-19 pandemic and resulted in the rapid development of two safe and effective COVID-19 vaccines currently being rolled out globally (Pfizer BioNTech's BNT162 and Moderna's mRNA-1273). A key difference between SARS-CoV-2 (a coronavirus) and HIV (a lentivirus) is





that the body mounts an effective immune response to natural infection by coronavirus, but not lentiviruses, accounting in part for the challenges of developing an HIV vaccine. The success of the mRNA strategy for COVID-19 vaccines, however, has reinvigorated implementation of the mRNA platform for the development of new HIV vaccine candidates.

Another innovative vaccine approach involves bioinformatically optimized bivalent mosaic antigens as immunogens for protection against HIV infection. Two NIH-supported clinical trials involving approximately 6,400 participants in Africa, South America, North America, and Europe are in progress with results from IMBOKODO-HVTN 705 (Phase 2) anticipated in the fall of 2022, and from MOSAICO-HVTN 706 (Phase 3) expected in the first quarter of 2024.

**Future Directions:** In view of the approximately 1.5 million new HIV infections each year globally, development of a safe and effective preventive vaccine against HIV remains a critical research goal. The NIH promotes a multipronged strategy to develop and advance the most promising HIV vaccine candidates. To build on basic and clinical research findings and to meet future research needs for vaccine efficacy clinical trials using mRNA-based technologies, NIH will need to expand production capabilities for candidates to test in vaccine trials. In particular, the NIH will support the accelerated development of promising mRNA-based HIV vaccine approaches, building on the success of the COVID-19 mRNA-based vaccines that establish the utility of the mRNA platform in vaccine development and showcase the advantages of the approach.

### **Pre-Exposure Prophylaxis (PrEP)**

Results from the HPTN 083 and HPTN 084 studies demonstrated that a long-acting injectable PrEP strategy containing cabotegravir (CAB-LA), administered once every 8 weeks, is safe and effective for preventing HIV acquisition in men who have sex with men, trans women, and cis women and, in fact, is superior to a daily oral PrEP pill with tenofovir/emtricitabine (Truvada®).<sup>12,13,14</sup> These results underscore that CAB-LA is an important addition to HIV prevention options.

Data from Microbicide Trial Network (MTN) 036/International Partnership for Medicines (IPM) 047—a Phase 1 pharmacokinetics (PK), safety, and acceptability study in Alabama and San Francisco—showed that dapivirine vaginal rings with extended 3-month duration were well tolerated and achieved higher drug concentration than monthly rings with moderate efficacy.<sup>15,16</sup>



**Future Directions:** Having PrEP options with more adherence-friendly schedules increases choice and, potentially, improves acceptability of this important HIV prevention strategy among populations most at risk of HIV in the United States and globally. In an effort to increase strategies that optimize adherence to and expand the range of choices for prevention, NIH will support basic, clinical, behavioral, and

implementation research on the safety, efficacy, acceptability, and feasibility of additional long-acting formulations for PrEP, including research on broadly neutralizing antibodies (bNAbs) and long-acting small molecules as antiretroviral agents, delivered in various ways. These findings provide an opportunity for the NIH to capitalize on behavioral and implementation research models that improve PrEP adherence and uptake in diverse communities and hasten the impact of EHE and similar strategies globally.

## **Antibody-Mediated Prevention Approaches**

Antibody-mediated prevention (AMP) studies, conducted jointly by the NIH HIV Vaccine Trials Network (HVTN) and the HIV Prevention Trials Network (HPTN), evaluated the feasibility of developing bNAbs as a prevention tool. Recent results from the AMP clinical trials showed that infusions of the NIH Vaccine Research Center (VRC) VRC01 bNAb were effective in preventing HIV infection from viral strains that were sensitive to the antibody, although bNAbs offer no protection against resistant strains. Results from another VRC AAV8-VRC07 bNAb study, delivered using the adeno-associated virus (AAV) gene vector, showed durable expression of HIV specific antibodies. Taken together, the results provide important proof of concept that combinations of bNAbs can be used for HIV prevention<sup>17</sup> and that antibodies have the potential to provide cost-effective HIV treatment.<sup>18</sup> Several Phase 1 trials evaluating safety and efficacy of more potent antibodies or immunogens with different modes of delivery are ongoing and will report out within the next 2 years.

**Future Directions:** In parallel with vaccine-based prevention strategies, AMP studies will develop biological interventions as alternative prevention strategies in uninfected individuals. Although these studies represent significant advances toward HIV prevention, further research is essential to extend the half-life of the antibodies and to develop more potent antibodies and vector-based bNAbs for HIV prevention. In parallel,

social and behavioral research on acceptance and hesitancy in the use of vaccine and AMP approaches is essential if these novel approaches are to be implemented successfully.

## Develop Next-Generation Therapies

### Long-Acting Treatment (and Prevention)

Interim results from a Phase 2/3 clinical trial of lenacapavir (LEN)—an investigational, long-acting first-in-class HIV capsid inhibitor—showed that addition of LEN to a failing antiretroviral regimen in heavily treatment-experienced people with multidrug resistant HIV was safe, well tolerated, and maintained viral suppression. In addition, data from an animal model study provided proof of concept for further



exploration of the use of LEN for HIV prevention.<sup>19</sup> These results exemplify opportunities for development of dual-purpose therapeutics for treatment and prevention.

Data also have emerged from early studies of Islatravir (ISL), the first nucleoside reverse transcriptase translocation inhibitor, in development for HIV treatment and prevention. A Phase 1 study found that prototype ISL subdermal implants were generally well tolerated,<sup>20</sup> and *in vitro* assessments support continued development of ISL implants as potential once-yearly PrEP options.<sup>21</sup>

Based on fundamental science conducted and supported by the NIH, the first long-acting injectable HIV treatment was developed by industry and approved by the U.S. Food and Drug Administration (FDA) in February 2021.<sup>22</sup> Called CABENUVA, this treatment involves a combination of two injectable medications (CAB and rilpivirine) administered monthly by a health care provider. Similar to the advantages long-acting injectable PrEP offers for people at risk of acquiring HIV, long-acting injectable treatment offers people with HIV more options to achieve and maintain viral suppression than taking a pill every day.

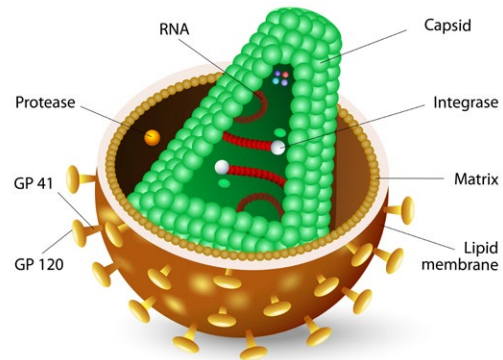
**Future Directions:** The NIH will support research to accelerate development of new therapies that target specific stages of viral replication, employ various routes of administration, and are safe and effective against multidrug resistant HIV. This includes expanded support for basic research on the virus lifecycle, including virus–host

interactions, to point to promising targets. The NIH will support research assessing the acceptability, effectiveness, and programmatic implementation of new technologies for delivery of therapeutic interventions, such as long-acting injectables, implants, microarray patches, and vaginal rings.

## Research Toward an HIV Cure

Development of novel strategies that can induce long-term, drug-free remission of HIV infection is a high priority in research toward an HIV cure. Remission has been naturally

observed in a small number of people with HIV, referred to as “elite controllers.” These individuals maintain undetectable levels of HIV replication and show no evidence of clinical disease progression in the absence of ART. Recent studies suggest that some of these “elite controllers” have viral DNA that is integrated and limited to untranslated regions of the host DNA, effectively keeping the virus in a state of deep latency.<sup>23</sup> This discovery implies that a functional cure for HIV may be possible by developing strategies that inhibit or help eliminate cells with HIV integrated in transcriptionally active genome regions.



**Future Directions:** The NIH will increase support for fundamental virology, cell biology and clinical research that uses novel technologies to understand genomic and epigenetic features of HIV integration sites; characterize, quantify, eliminate, or control the viral reservoirs in different anatomical sites and cell types; and discover the mechanisms of viral control in elite controllers, who appear to have a combination of characteristics, including defective HIV, a hypervigilant and specific immune response to HIV, and cells that are unusually resistant to infection. The overarching aim is to understand the mechanisms of virus–host cell interactions that will lead to rational design of innovative 21st century strategies for extended viral suppression and, ultimately, viral elimination.





## **Address HIV-associated Comorbidities, Coinfections, and Complications**

### **Neurological Complications**

Effective ART has ushered in a new era for the HIV epidemic. People with HIV now can achieve nearly normal lifespans, but are more likely to suffer from multiple, chronic comorbidities, coinfections, and complications (CCCs) resulting from HIV exposure, long-term HIV disease, immune dysfunction, and/or ART for HIV treatment or prevention, which can severely affect their quality of life.

Key among these CCCs are neurological complications. HIV-associated neurological and cognitive complications can occur across the lifespan, even when HIV is well controlled with ART. This is likely due to the fact the virus establishes a reservoir in the central nervous system (CNS) early in infection and most antiretroviral drugs are not able to cross the blood–brain barrier. The presence of a viral reservoir within the CNS has potential relevance for research to finding a cure for HIV.

**Future Directions:** The NIH will support neuroAIDS research across the lifespan to accelerate understanding the multi-faceted mechanisms of HIV neuropathogenesis and to identify targets to inform development of safe and effective therapies to ameliorate HIV-induced CNS dysfunction. Additionally, the NIH will support research to define HIV reservoirs within the CNS and their clinical relevance for the development of ART-free remission strategies.

### **HIV and SARS CoV-2 Coinfection**

Over the past year since the emergence of SARS-CoV-2, NIH-supported HIV research platforms, resources, and clinical trials networks were rapidly leveraged to tackle important research questions related to SARS-CoV-2 and COVID-19. The strategy proved essential to successful development and preclinical and clinical testing of the safety and efficacy of various vaccine and therapeutic candidates to address the emergent pandemic.

- Tools and technologies honed over many years to develop monoclonal antibodies for HIV prevention and treatment were used to identify monoclonal antibodies suitable for treating COVID-19.<sup>24</sup>
- Access to nonhuman primates through the National Primate Research Centers, supported in part with HIV/AIDS funds, is currently prioritized as researchers around the country seek to investigate COVID-19 pathology, potential treatments, and vaccine candidates using animal resources.<sup>24</sup>
- HPTN, HVTN, and the AIDS Clinical Trials Group (ACTG), established and supported by HIV resources, are part of the Accelerating COVID-19 Therapeutic Interventions and Vaccines ([ACTIV](#)) partnership, launched by the NIH and the National Institute of Allergy and Infectious Diseases (NIAID) COVID-19 Prevention Network ([CoVPN](#)). The goal is to maximize clinical trial capacity and effectiveness by leveraging infrastructure and expertise from across NIH networks.
- The International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) infrastructure also is being leveraged for COVID-19 studies. The [IMPAACT 2032](#) clinical trial will evaluate PK and safety of remdesivir for treatment of COVID-19 in pregnant and non-pregnant women in the United States.
- Numerous Multi-Center AIDS Cohort Study /Women's Interagency HIV Study Combined Cohort Study sites are conducting research on mental and physical health outcomes of HIV and COVID-19 coinfection among men and women.



**Future Directions:** The NIH will continue to support focused research that investigates HIV and SARS-CoV-2 coinfection among diverse populations, including the effects of coinfection on immune dysfunction, and vaccine and therapeutic efficacy across the lifespan.

## Cross-cutting Areas

### Basic Science: Better Understanding the Virus Life Cycle

Imaging research related to the HIV-1 structure has produced a significant breakthrough in understanding the viral life cycle within host cells. NIH intramural researchers developed a method to directly label infectious viral complexes with green fluorescent protein and showed that HIV-1 capsids remain intact until minutes before uncoating in the nucleus for viral DNA integration into the host genome.<sup>25</sup> Novel imaging work conducted by scientists at the University of Heidelberg further demonstrated that nuclear pores are larger than previously estimated. HIV-1 capsids can enter the nucleus intact and release the genomic complexes inside the nucleus—not in the cytoplasm, as previously thought.<sup>26</sup>

**Future Directions:** NIH will support basic research to build on this new understanding of the viral lifecycle as the basis for development of next-generation HIV therapies focused on novel targets and different modes of delivery.

### Apply Technological Advances to HIV Research

Remarkable advances have been made in technological tools with potential application to HIV. These include rapid, point-of-care diagnostics and self-administered viral load testing; 3-D printing; artificial intelligence (including machine learning); big data mining; geospatial modeling; advanced bioinformatics; genomic strategies for epigenetic analyses; and use of digital and social media.

**Future Directions:** The NIH will advance multidisciplinary research to accelerate the development and deployment of promising technological tools in HIV prevention and treatment interventions.

### Reduce HIV-Related Disparities and Health Inequalities

HIV continues to affect communities and populations in unequal ways: racial and ethnic minorities, sex and gender minorities, people who use drugs, sex workers, and people experiencing incarceration are at disproportionate risk of HIV transmission and poor physical and mental health outcomes. HIV-related intersectional stigma is an underlying feature of health inequalities and is a pervasive challenge to efforts to achieve successful HIV prevention, treatment, and care.

**Future Directions:** The NIH will advance clinical, behavioral, social, translational, and implementation research to identify innovative approaches to address HIV-associated health disparities and inequalities. Research findings will improve HIV testing, increase



engagement and retention in prevention and care services, and enhance the health and well-being of persons with and at risk for HIV in underserved and marginalized communities. NIH will support research on the intersectional nature of stigma based on multiple aspects of people’s identities, social positions, and health status to develop and successfully implement strategies to optimally mitigate the effects of stigma on people affected by HIV.

### **Training, Infrastructure, and Capacity-building: Enhancing the Pipeline of HIV Researchers**

Novel ideas and innovative discoveries often come from investigators who have varied backgrounds and thinking, are new to the field, or are early in their research careers. OAR is committed to collaborating with the NIH Director and NIH ICOs to ensure the development of the next generation of multidisciplinary HIV researchers, particularly women and those from underrepresented populations and institutions within the United States. To expand the heterogeneous pool of early-stage HIV investigators (ESI) and to respond to recommendations from stakeholders, OAR developed an initiative to increase HIV ESI awards by 20 percent in FY 2020 and by a similar percentage in FY 2021.

In collaboration with NIH ICOs, OAR supports initiatives to strengthen research capacity among underrepresented and under-resourced institutions to facilitate greater diversity in the HIV research workforce at all career stages. For example, in FY 2020 OAR co-funded supplements with the NIH Sexual & Gender Minority Research Office (SGMRO) for four HIV-related extramural research projects and provided supplements to the Research Centers in Minority Institutions (RCMI) Program of the National Institute on Minority Health and Health Disparities (NIMHD) to support research laboratory renovations for HIV-related research activities at two RCMI institutions. In FY 2021, OAR is collaborating with NIMHD and the National Institute of General Medical Sciences (NIGMS) to support an increased number of physical infrastructure projects



at RCMI, Institutional Development Award (IDeA), and Native American Research Centers for Health (NARCH) institutions. Additionally, OAR collaborated with the Office of Research on Women's Health (ORWH), SGMRO, the Tribal Health Research Office (THRO), and Office of Research Infrastructure Programs (ORIP) on [joint blog posts](#) and listening sessions.

**Future Directions:** The NIH recently launched the [UNITE](#) program to address structural racism in the biomedical enterprise, both inside and outside of the agency. In line with this effort, OAR is committed to extending diversity of thinking, strategies, and approaches to HIV research by building capacity among underrepresented individuals (e.g., by enhanced support for ESI) and under-resourced institutions (e.g., by building and strengthening research at RCMI, NARCH, and IDeA states). NIH will support the development of novel programs (e.g., at community colleges) for training technical research staff and allied health workers for roles in research teams at various sites and in diverse communities.





## Expanding Partnerships

OAR sets the direction of NIH HIV research through collaborations and strategic partnerships among diverse stakeholders. Within the NIH, OAR works with the ICOs through the NIH AIDS Executive Committee (NAEC), which includes representatives from all NIH ICOs that support HIV research. Through the NAEC, OAR identifies NIH-wide HIV scientific research priorities, gaps, and opportunities; facilitates information exchange; and supports scientific and funding collaborations among the ICOs.

A key partner for engagement with academic, policy, and community stakeholders is the Congressionally mandated OAR Advisory Council (OARAC), whose members include diverse subject-matter experts from a range of scientific disciplines and representatives of community constituents from across the country. Collaboration and bidirectional dialogue with the OARAC allow OAR to highlight late-breaking science from the HIV field, as well as to hear from external experts regarding potential directions for NIH HIV initiatives.

OAR continues to expand partnerships with community organizations, academic institutions, and public health departments by engaging in a series of listening sessions and community conversations hosted by local institutions to obtain diverse stakeholder input into the NIH HIV research program. These sessions yield important observations and ideas about focusing HIV research priorities, supporting ESI, diversifying the HIV workforce, and



November 2019 OAR Listening Session that included community-based organizations in Oakland, CA.

strengthening academic–community research partnerships. OAR, in collaboration with the NIH ICOs, has begun to address this feedback, as described in the [\*NIH/OAR HIV Stakeholder Outreach and Engagement Report: June 2018–February 2020\*](#). The sessions are continuing and currently include attention to the impact of COVID-19 on HIV research efforts.

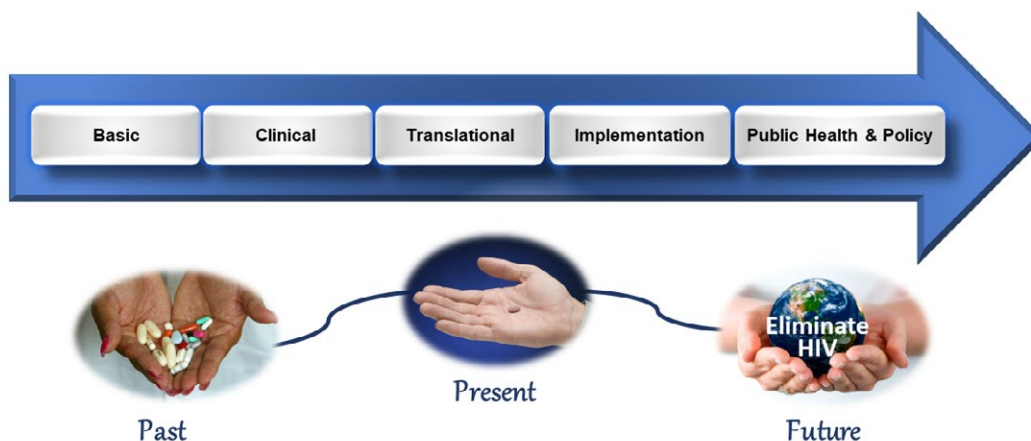
**Future Directions:** The NIH HIV program will leverage new partnerships for collaborative approaches —within the agency and between the NIH and other federal agencies (e.g., through OAR representation of NIH on the Presidential Advisory Council on HIV/AIDS and with the White House Office of National AIDS Policy)—for accelerating research at the intersection of HIV and other health issues, such as infectious diseases (e.g., SARS-CoV-2, hepatitis, sexually transmitted infections) domestically and globally, and behavioral health problems (e.g., substance use disorders, mental illness) across the lifespan. OAR will expand the Stakeholder Outreach and Engagement Program to identify new research and community partners for local and regional collaborations.

# Conclusion

OAR works with its NIH and U.S. Department of Health and Human Services (HHS) partners to continue to advance the goals of the federal [HIV National Strategic Plan \(HIV Plan\)](#) and [EHE](#). The HIV Plan focuses on preventing new HIV transmission; improving health outcomes for people with HIV; reducing HIV-related disparities and health inequities; and better integrating and coordinating efforts that address the HIV epidemic among all partners and stakeholders. EHE aims to end the HIV epidemic in the United States by 2030, specifically to reduce new HIV infections by 75 percent by 2025 and by at least 90 percent by 2030. To support this aim, the NIH issued three funding opportunity announcements (FOAs) in 2021 to support priority HIV research in the areas of [epidemiology](#), [treatment](#), and [prevention](#).

Achieving the goals of both the HIV Plan and EHE and contributing to targets for ending the global HIV pandemic requires optimizing and leveraging critical scientific developments—past, present, and future—along the research discovery pipeline, from basic science to public health and policy implementation. The experiences from the COVID-19 pandemic highlight the ways in which knowledge along this discovery pipeline builds across diseases, conditions, and viruses to lead to improved health for all.

Much needs to be done, but with additional investment combined with the amazing talents and dedication of stakeholders in the NIH HIV research enterprise, including investigators, community partners, advocates, private sector partners, and people with HIV, the goals to end the HIV pandemic globally and in the United States are achievable.





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# Acronyms/Abbreviations

<b>AAV</b>	adeno-associated virus
<b>ACTG</b>	AIDS Clinical Trials Group
<b>ACTIV</b>	Accelerating COVID-19 Therapeutic Interventions and Vaccines partnership
<b>AIDS</b>	acquired immune deficiency syndrome
<b>AMP</b>	antibody mediated prevention
<b>ART</b>	antiretroviral therapy
<b>bNAb</b>	broadly neutralizing antibody
<b>CAB-LA</b>	cabotegravir as a long-acting injectable
<b>CCC</b>	comorbidities, coinfections, and complications
<b>CDC</b>	Centers for Disease Control and Prevention
<b>CNS</b>	central nervous system
<b>COVID-19</b>	coronavirus disease of 2019
<b>CoVPN</b>	NIAID COVID-19 Prevention Network
<b>EHE</b>	<i>Ending the HIV Epidemic in the U.S.</i> initiative
<b>ESI</b>	early-stage investigators
<b>FDA</b>	U.S. Food and Drug Administration
<b>FOA</b>	funding opportunity announcement
<b>FY</b>	fiscal year
<b>HHS</b>	U.S. Department of Health and Human Services
<b>HIV</b>	human immunodeficiency virus
<b>HPTN</b>	HIV Prevention Trials Network
<b>HVTN</b>	HIV Vaccine Trials Network
<b>ICO</b>	NIH Institutes, Centers, and Offices
<b>IDeA</b>	NIH Institutional Development Award
<b>IMPAACT</b>	International Maternal Pediatric Adolescent AIDS Clinical Trials Network
<b>IPM</b>	International Partnership for Medicines
<b>LEN</b>	lenacapavir
<b>MMWR</b>	<i>Morbidity and Mortality Weekly Report</i>
<b>mRNA</b>	messenger ribonucleic acid
<b>MSM</b>	men who have sex with men
<b>MTN</b>	Microbicide Trials Network
<b>NAEC</b>	NIH AIDS Executive Committee
<b>NARCH</b>	NIH Native American Research Centers for Health
<b>NIAID</b>	National Institute of Allergy and Infectious Diseases

- NIGMS** National institute of General Medical Sciences
- NIH** National Institutes of Health
- NIMHD** National Institute on Minority Health and Health Disparities
- OAR** NIH Office of AIDS Research
- OARAC** OAR Advisory Council
- ORIP** NIH Office of Research Infrastructure Programs
- ORWH** NIH Office of Research on Women's Health
- PK** pharmacokinetics
- PrEP** pre-exposure prophylaxis
- RCMI** NIMHD Research Centers in Minority Institutions
- RNA** ribonucleic acid
- saRNA** self-amplifying RNA
- SARS-CoV-2** severe acute respiratory syndrome coronavirus 2
- SGMRO** NIH Sexual & Gender Minority Research Office
- THRO** NIH Tribal Health Research Office
- U = U** undetectable = untransmittable
- VRC** NIH Vaccine Research Center





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