Office of AIDS Research

CONGRESSIONAL JUSTIFICATION

FY 2022

Department of Health and Human Services

National Institutes of Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research (OAR)

FY 2022 Budget Table of Contents Page No.

NIH, Office of the Director, Office of AIDS Research (OAR)

Located within the NIH Office of the Director, OAR is authorized to:

- Oversee, coordinate, and manage all NIH HIV-related research;
- Establish research priorities and develop the strategic plan for HIV research;
- Ensure that funds are invested in the areas of highest scientific priority; and
- Address emerging opportunities.

Mission

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

Director's Overview

Maureen M. Goodenow, Ph.D.

Associate Director for AIDS Research and
Director, Office of AIDS Research
National Institutes of Health

NIH investments in HIV and AIDS research over more than three 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 treatments to extend the lifespan of people with HIV and innovative interventions to prevent HIV transmission and acquisition. Nonetheless, globally and in the United States, new infections continue at rates that are increasing or remain unchanged, reflecting inequalities by race, ethnicity, sex, gender, age, socioeconomic status, and geography. While the HIV pandemic will continue to affect virtually every nation in the world well into the next century, the NIH will continue to lead the investment in basic, clinical, and translational research to discover cutting-edge solutions for the ongoing challenges of the HIV pandemic.

To provide leadership in setting the national and global HIV research agenda, the NIH Office of AIDS Research (OAR) was established in 1988 through Section 2353 of the Public Health Service Act.

OAR operationalizes its authorities through activities related to the four Strategic Goals outlined in the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research*[260]:

[260] www.oar.nih.gov/hiv-policy-and-research/strategic-plan

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: OAR works to catalyze multidisciplinary and novel approaches in HIV prevention, treatment, cure, co-morbidities research; and to support research to address and mitigate underlying HIV-associated medical and social inequalities.

Ensure that the NIH HIV research program remains flexible and responsive to emerging scientific opportunities and discoveries: Examples from the past six years (2016 to 2021) include: the rapid focus on potential effects of the drug dolutegravir on fetal neural tube development; reconstruction of the Puerto Rico non-human primate facilities destroyed by Hurricane Maria; and the continued response to the emergent SARS-CoV-2/COVID-19 pandemic by elucidation and application of lessons learned from HIV science; development of clinical guidelines; and mitigating the effects of the COVID-19 experience on the conduct and recovery of HIV research.

Promote dissemination and implementation of research discoveries for public health impact across agencies, departments, and stakeholders within the U.S. Government and globally: OAR continued its collaboration with the HIV Antiretroviral and Opportunistic Infections Guidelines Working Groups of OARAC which recently issued *Interim Guidance for COVID-19 and Persons with HIV*. The AIDS*info*.nih.gov and *info*SIDA.nih.gov websites moved from the National Library of Medicine to OAR and their content was shifted to HIVinfo.nih.gov and Clinicalinfo.hiv.gov. OAR expanded its program of Listening Sessions and Community Conversations held in multiple sites across the country; and continued support for international HIV-related conferences to ensure broad access to the latest scientific knowledge.

Strengthen human resource and infrastructure capacity to enhance sustainability of HIV research discovery and the implementation of findings by a diverse and multi-disciplinary workforce: OAR is committed to work with the NIH Institutes, Centers, and Offices (ICOs) to ensure that the HIV research program and mechanisms of funding focus on under-represented communities and populations, and to consider novel ways to conduct research that are cost-saving, culturally and ethically appropriate, and attentive to the needs of early career investigators.

The Strategic Goals provide the framework for how OAR promotes the NIH Director's theme of *Science in Service to Society*.

Answering the Call: OAR works to address HIV and related public health needs with urgency and flexibility to ensure that science is in service to all of society. We continue to advance the basic biomedical, behavioral, and social science that is foundational to HIV prevention, treatment, and cure; ensure that discoveries are translated and disseminated widely; and place focus on addressing and strengthening capacity among populations most affected by HIV and related health issues to conduct and apply research. Key initiatives in this regard are:

- ***Implement NIH discoveries in the Ending the HIV Epidemic in the U.S. (EHE) initiative:*** OAR catalyzes research to expand discovery of new modes of prevention and treatment. These include effective vaccines and antibody mediated strategies; diversity of formulations and methods of delivery (oral, injectable, ring) of pre-exposure prophylaxis (PrEP); new antiretroviral therapies that are less toxic and easier to use; and long-acting injectable products for prevention or treatment. We also support efforts to build and leverage across NIH frameworks, such as the Centers for AIDS Research (CFAR), AIDS Research Centers (ARC), Research Centers in Minority Institutions (RCMI), to enhance academic-community-public health collaborations to accelerate the translation and implementation of basic research discoveries.

- ***Contribute knowledge from HIV science to address other, emergent infectious disease epidemics:*** Many of the lessons already learned and the clinical trials infrastructure built through the NIH HIV research program can and are being employed to respond to other epidemics that threaten our nation and the world. For example, when SARS CoV-2/ COVID-19 emerged, OAR: worked with partners inside and outside NIH on the rapid development and dissemination of clinical guidelines for COVID-19 and HIV; appointed an OAR COVID-19 and HIV Task Force to monitor the implications of the COVID-19 pandemic on the HIV pandemic and the HIV research program and to provide guidance on HIV research recovery efforts; and leveraged the HIV/AIDS Trials Networks to support clinical trials of promising COVID-19 prevention and treatment strategies.

- ***Apply the latest technological advances to HIV research:*** OAR stimulates research to advance the development and deployment of promising tools, such as: 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; and genetics. We also support research on the use of digital and social media in designing effective HIV prevention and treatment interventions that focus on end users as well as health care providers.

Closing the gap in health disparities: OAR works with its partners and stakeholders to effect progress in redressing HIV and associated health inequalities experienced by populations characterized by race, ethnicity, age, gender, sexual orientation, or other demographic or social features. We support research, infrastructure, and capacity strengthening focused on under-represented and disenfranchised populations. Priorities include:

- ***Reduce disparities in HIV prevention and treatment:*** OAR supports efforts to engage and retain key populations in HIV prevention and treatment research, and to diversify and expand the research workforce to ensure creative and diverse thinking about discovery, translation, and implementation of HIV prevention, treatment, and care strategies.

- ***Examine and address intersectional stigma related to HIV:*** OAR supports HIV-related research that investigates how overlapping experiences of stigma related to race, gender, sexual orientation, and other psycho-social characteristics affect HIV prevention, treatment, and care among individuals and groups.

- ***Continue Listening Sessions and Community Conversations:*** OAR continues to convene diverse stakeholders from academic, community, and public health organizations to better understand the complexities of HIV-associated health disparities and inequalities at the community and regional level, and to identify priority research questions and mechanisms to address them.

Capitalizing on foundational investments and beyond: The dedicated investment in NIH's basic HIV research program over more than three decades resulted in the transition of HIV from a fatal disease to a chronic and manageable condition, allowing millions of people world to live long and productive lives. With ever-more sophisticated technologies, diversity of thinking, and continued investment, the potential for further advances—including an HIV cure—is extraordinary. OAR works with the ICOs to build on this foundation in a number of ways to:

- ***Expand basic science discoveries in virology, cell biology, and human immunology:*** OAR supports and augments research funded through the ICOs to understand how the virus replicates within cells and perturbs complex cellular interactions, and the complexities of immune responses needed for novel vaccine, treatment, and cure strategies.

- ***Transform NIH practices to facilitate interdisciplinary collaboration and discovery:*** OAR continues to promote interdisciplinary research in high priority areas, particularly in support of the HIV clinical trials networks and cores, shared facilities, infrastructure and capacity building for multipurpose research at academic institutions, including minority-serving institutions through the RCMI Program and to institutions in states historically receiving low levels of support from NIH through the Institutional Development Award Program.

- ***Augment the NIH commitment to the development of the next generation of HIV researchers:*** To enhance the pipeline of HIV researchers in multiple disciplines, OAR has launched an initiative to expand support for early-stage investigators (ESI), with particular attention to women and underrepresented populations from institutions within the United States and globally. To reverse a trend in declining ESI HIV R01-equivalent awards, OAR is working with the ICs to increase opportunities to promote and support ESI applications.

- ***Leverage the NIH HIV research framework, outcomes, and products:*** OAR works with partners inside and outside the NIH to: provide the evidence base for EHE; contribute to SARS-CoV-2/COVID-19 treatment and vaccine research, including cost-sharing with ICs; and apply research findings on factors influencing health behaviors, disparities, and stigma to COVID-19 and other emerging epidemics.

- ***Address the prevalence of co-morbidities, co-infections, and complications with the greatest effects on people living with HIV:*** OAR encourages research that combines epidemiological, clinical, behavioral and social, and implementation science to better address conditions coexisting with HIV, such as tuberculosis, cancer, substance use disorders, cognitive decline, among others.

National Institutes of Health
Office of AIDS Research

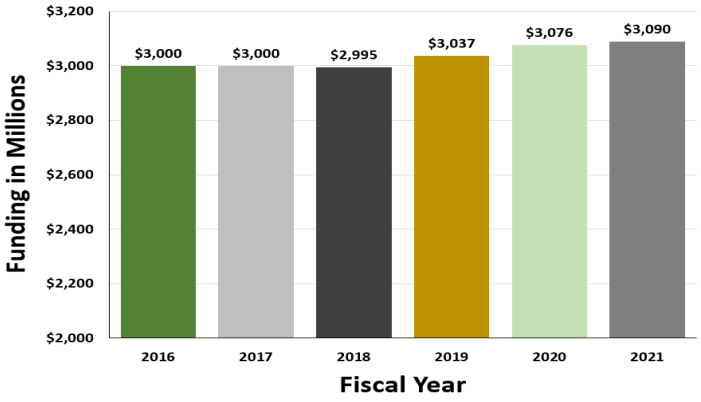
In 1988, the U.S. Congress authorized the establishment of the Office of AIDS Research (OAR) to oversee, coordinate, and manage NIH HIV/AIDS-related research. Located within the Office of the NIH Director, specifically within the Division of Program Coordination, Planning, and Strategic Initiatives, OAR:

- Establishes NIH HIV/AIDS research priorities,
- Allocates research funds in line with scientific priorities,
- Manages HIV/AIDS research across the NIH, and
- Collaborates across the U.S. government and with groups and organizations globally.

OAR Vision: ***Advance research to end the HIV pandemic and improve health outcomes for people with HIV.***

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

NIH HIV/AIDS Funding History FY 2016–2021



The FY 2022 President's Budget Level for the NIH-wide HIV/AIDS research agenda is $3,100.0 million, an increase of $10.0 million or 0.3 percent compared to the FY 2021 Enacted Level.

Research Highlights

- Long-acting injectables show exciting promise—the recent HPTN 083 study demonstrated the superiority of the long-acting form of cabotegravir for the prevention of HIV.
- Studies on an intravaginal ring with the microbicide dapivirine suggest a reduced risk of acquiring HIV infection.
- NIH-supported studies are using an interdisciplinary approach combining epidemiology, statistics, operations research, and decision science by studying three interlocking epidemics—opioid use disorder, HIV, and hepatitis C virus—among people who use drugs.

Maureen M. Goodenow, Ph.D.

Associate Director for AIDS Research and Director, Office of AIDS Research

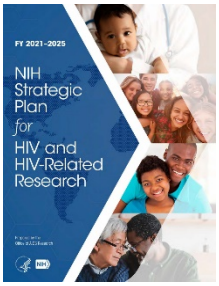
OAR Facts

- With 27 FTEs, OAR coordinates the largest public investment (~$3 B annually) in HIV/AIDS research globally.
- OAR supports HIV/AIDS-related research in more than 24 of the NIH ICOs.
- The NIH Revitalization Act of 1993 authorized OAR to plan, coordinate, and evaluate HIV/AIDS research; set scientific priorities for the NIH research agenda; and determine budgets for all NIH HIV/AIDS research.
- The NIH AIDS Executive Committee (NAEC) facilitates communication between OAR and all ICOs that use HIV/AIDS funding.
- The OAR Advisory Council (OARAC) provides advice to the OAR Director on the planning, coordination, and evaluation of research and other HIV/AIDS activities conducted or supported by NIH.
- Previous OAR Directors include Drs. Anthony Fauci, William Paul, Neal Nathanson, Jack Whitescarver, and Robert Eisinger (Acting).

National Institutes of Health
Office of AIDS Research

Recent Accomplishments

- Development and release of the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research*, which includes four strategic goals:
  (1) advance rigorous and innovative research,
  (2) ensure flexibility and responsiveness,
  (3) promote dissemination and implementation of research discoveries, and
  (4) build human resource and infrastructure capacity.



- Collaboration with the HIV Antiretroviral and Opportunistic Infections Guidelines Working Groups of OARAC, which are responsible for updating the HHS HIV/AIDS Treatment Guidelines, and recently issued Interim Guidance for COVID-19 and Persons with HIV.
- Transition of the AIDS*info*.nih.gov and *info*SIDA.nih.gov websites from the National Library of Medicine to OAR. As part of this transition, the content has been rebranded and shifted to HIVinfo.nih.gov and Clinicalinfo.hiv.gov.

Current Activities

- Exploring opportunities to leverage NIH-supported HIV research platforms and the clinical trial networks to tackle unanticipated research questions related to other emerging HIV epidemics, such as COVID-19.
- Working with ICs on an initiative to enhance support for early stage investigators—with particular attention to women and those from underrepresented populations and institutions within the U.S. and globally—to enhance the pipeline of HIV researchers through mentoring by NIH program staff and external senior and mid-career investigators.
- Leading NIH's support of the Administration's Ending the HIV Epidemic in the U.S. initiative (EHE).

Ending the HIV Epidemic

- Continuing OAR's series of listening sessions and community engagement meetings in geographically defined locations to bring local and regional focus to discussions of NIH HIV research priorities, translation and dissemination efforts, and capacity-building activities.

Future Initiatives

- Effective HIV vaccines and antibody mediated protection strategies.
- Innovative technology approaches including 3-D printing, artificial intelligence (including machine learning), advanced bioinformatics, genetics, big data mining, and geospatial modeling for advanced discovery.
- New methods and delivery of pre-exposure and post-exposure prophylaxis, multi-purpose prevention technologies, and community-level behavioral and social-structural interventions.
- Novel diagnostics and treatment strategies for viral suppression and sustained ART-free viral remission for a cure for HIV.
- Prevalent HIV-associated coinfections, chronic conditions, and syndemics.
- Complications from virus exposure, long-term HIV disease, immune dysfunction, and/or ART for treatment or prevention across the lifespan: from development in infants, children and youth to aging.
- Strategies for mitigating HIV-associated stigma and discrimination.
- Efforts to increase the number and diversity of early stage investigators in the HIV research pipeline.
- Implementation strategies to improve systematic uptake of evidence-based prevention, care, and treatment interventions in diverse settings and populations.

Budget Policy Statement

The FY 2022 President's Budget request for the NIH-wide HIV/AIDS research program is $3,100.0 million, an increase of $10.0 million or 0.3 percent compared to the FY 2021 Enacted level. 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.

The NIH will continue a multipronged strategy to develop and advance the most promising HIV vaccine candidates. In particular, the NIH will continue to support the 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. The NIH continues to support a broad HIV/AIDS vaccine research portfolio encompassing basic, pre-clinical, and clinical research, including studies to identify and better understand potentially protective immune responses in HIV-infected individuals and studies of improved animal models for the pre-clinical evaluation of vaccine candidates.

The NIH will also continue to support research related to HIV across the lifespan. Although there has been progress in the reduction of the number of HIV-infected infants through expansion of programs for perinatal prevention of mother-to-child transmission (PMTCT), pediatric infection by breast-feeding continues as a challenge. Because the number of HIV-exposed but uninfected (HEU) infants is increasing worldwide, studies to compare rates of pre-term delivery, mortality, growth, and other outcomes are critical to better understand how HIV exposure impacts the health and well-being of a child, long after exposure to both HIV and antiretroviral therapy (ART) has ended. At the other end of the spectrum, as the number of older people living with HIV increases, chronic HIV infection, extended exposure to ART, and aging may all interact to increase risk of neurological impairment, other comorbid conditions, and mortality. Therefore, basic science, epidemiological, clinical, and translational research studies, focused on HIV in aging populations and utilizing multi-disciplinary research teams, are critically necessary.

HIV-related stigma is an underlying feature of health inequalities and is a pervasive challenge to efforts to achieve successful HIV prevention, treatment, and care. The impact of stigma on HIV-related health outcomes is well documented; more research is needed 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 best mitigate the effects of stigma on people affected by HIV.

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

Budget Authority by Institute, Center, and Office
(Dollars in Thousands)

Institute, Center, and Office	FY 2020 Final	FY 2021 Enacted [1]	FY 2022 President's Budget	FY 2022 +/- FY 2021
NCI	$241,975	$241,238	$241,238	$0
NHLBI	84,715	84,715	84,715	0
NIDCR	18,984	18,984	18,984	0
NIDDK	34,135	34,135	34,135	0
NINDS	41,082	38,655	38,655	0
NIAID	1,779,113	1,788,843	1,798,843	10,000
NICHD	144,895	147,716	147,716	0
NEI	388	195	195	0
NIEHS	5,342	5,342	5,342	0
NIA	22,622	23,350	23,350	0
NIAMS	4,587	4,587	4,587	0
NIDCD	2,128	2,128	2,128	0
NIMH	183,991	186,421	186,421	0
NIDA	261,140	262,123	262,123	0
NIAAA	31,879	31,879	31,879	0
NINR	16,350	16,350	16,350	0
NHGRI	3,302	3,538	3,538	0
NIBIB	1,839	1,839	1,839	0
NIMHD	22,780	23,530	23,530	0
NCCIH	748	666	666	0
FIC	24,389	24,389	24,389	0
NLM	9,322	7,685	7,685	0
OD	140,355	141,692	141,692	0
OAR	62,256	63,593	63,593	0
ORIP	78,099	78,099	78,099	0
Subtotal, OD	140,355	141,692	141,692	0
TOTAL, NIH	**$3,076,061**	**$3,090,000**	**$3,100,000**	**$10,000**

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

Budget Mechanism – AIDS [1]
(Dollars in Thousands)

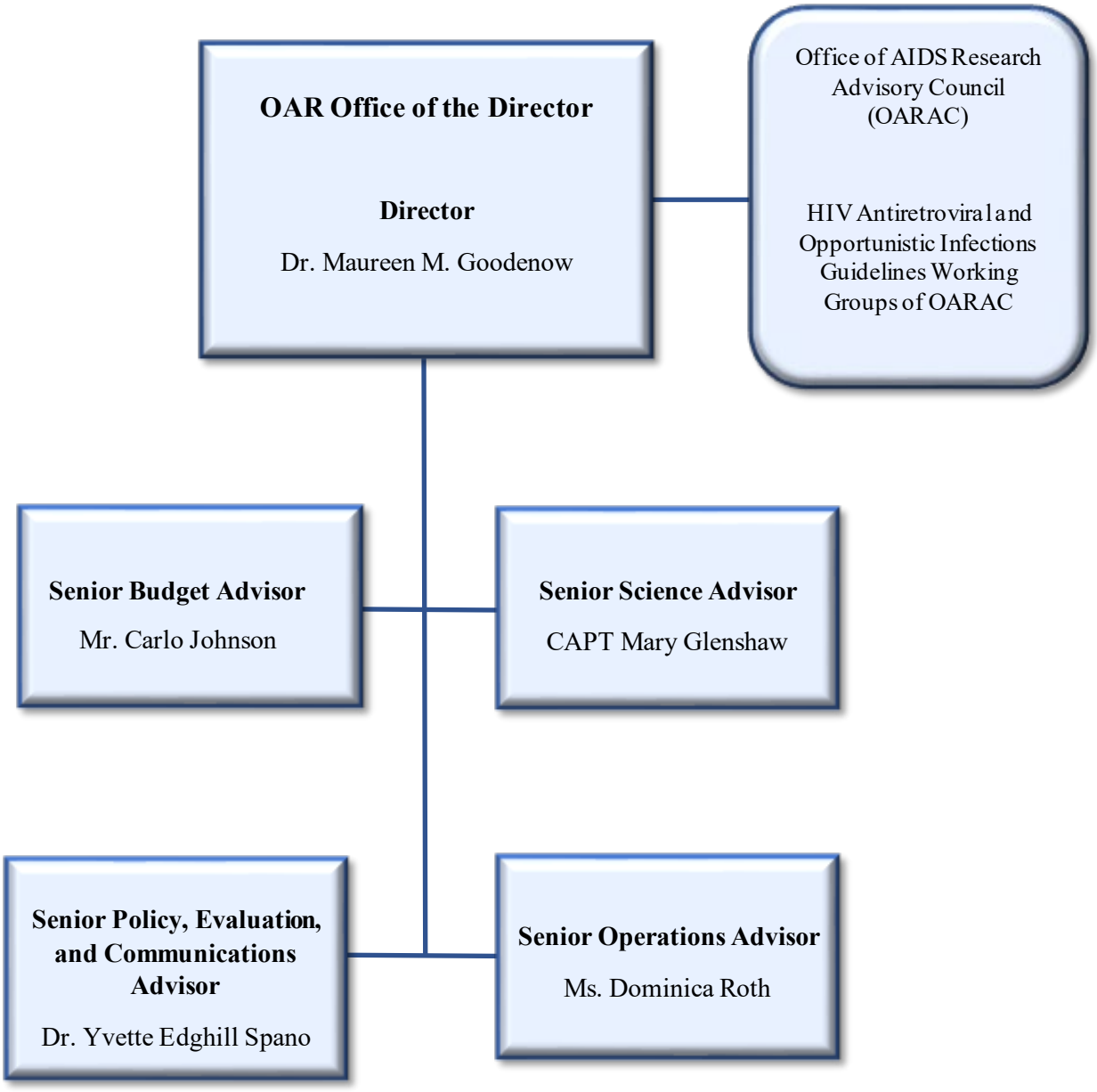
Mechanism	FY 2020 Final		FY 2021 Enacted		FY 2022 President's Budget		FY 2022 +/- FY 2021	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,388	$1,399,826	1,541	$1,080,998	1,456	$1,405,045	-85	$324,047
Administrative Supplements	*(102)*	21,304	*(58)*	17,234	*(50)*	6,699	*(8)*	-10,535
Competing	515	352,038	523	646,265	600	363,836	77	-282,429
Subtotal, RPGs	1,903	$1,773,168	2,064	$1,744,497	2,056	$1,775,580	-8	$31,083
SBIR/STTR	30	15,798	31	17,850	29	17,145	-2	-705
Research Project Grants	1,933	$1,788,966	2,095	$1,762,347	2,085	$1,792,725	-10	$30,378
Research Centers:								
Specialized/Comprehensive	51	$132,976	59	$139,969	56	$151,562	-3	$11,593
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	17	72,680	19	72,298	19	71,427	0	-871
Research Centers in Minority Institutions	0	0	0	1,143	0	1,143	0	0
Research Centers	68	$205,656	78	$213,410	75	$224,132	-3	$10,722
Other Research:								
Research Careers	257	$45,798	260	$45,554	254	$44,182	-6	-$1,372
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	2	1,999	0	3,114	11	4,495	11	1,381
Biomedical Research Support	1	1,628	29	1,600	31	2,000	2	400
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	116	64,796	100	61,131	110	59,930	10	-1,201
Other Research	376	$114,221	389	$111,399	406	$110,607	17	-$792
Total Research Grants	2,377	$2,108,843	2,562	$2,087,156	2,566	$2,127,464	4	$40,308
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	68	$3,114	78	$3,609	80	$3,748	2	$139
Institutional Awards	241	14,619	236	15,075	225	15,276	-11	201
Total Research Training	309	$17,733	314	$18,684	305	$19,024	-9	$340
Research & Develop. Contracts	108	$370,739	75	$402,086	89	$361,945	14	-$40,141
(SBIR/STTR) (non-add)	*(8)*	*(6,551)*	*(9)*	*(6,744)*	*(9)*	*(5,744)*	*(0)*	*(1,000)*
Intramural Research		$354,815		$352,328		$354,902		$2,574
Res. Management and Support		161,675		166,153		173,072		6,919
Res. Management & Support (SBIR Admin) (non-add)		*0*		*0*		*0*		*0*
Office of the Director - Appropriation [2]		*140,355*		*141,692*		*141,692*		*0*
Office of the Director - Other		62,256		63,593		63,593		0
ORIP (non-add) [2]		*78,099*		*78,099*		*78,099*		*0*
Total, NIH Discretionary B.A.		**$3,076,061**		**$3,090,000**		**$3,100,000**		**$10,000**

[1] All items in italics and brackets are non-add entries.

[2] Number of grants and dollars for the ORIP component of OD are distributed by mechanism and are noted here as a non-add. Office of the Director - Appropriation is the non-add total of these amounts and the funds accounted for under OD - Other.

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

ORGANIZATION CHART



NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

Budget Authority by Activity
(Dollars in Thousands)

Overarching Priorities	FY 2018 Actual [1]	FY 2019 Actual [1]	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
Reduce the Incidence of HIV	$714,553	$741,401	$719,217	$706,497	$691,639	-$14,858
Develop Next-Generation HIV Therapies	364,484	368,912	345,378	350,198	351,466	$1,268
Research Toward a Cure for HIV	175,757	187,777	209,133	210,025	211,730	$1,705
Address HIV-Associated Comorbidities, Coinfections, and Complications	517,884	531,440	554,452	559,382	552,747	-$6,635
Cross-Cutting Areas	1,222,703	1,207,770	1,247,881	1,263,898	1,292,418	$28,520
Total	**$2,995,381**	**$3,037,300**	**$3,076,061**	**$3,090,000**	**$3,100,000**	**$10,000**

[1] Reflects effects of Secretary's transfer.

JUSTIFICATION OF BUDGET REQUEST

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

Budget Authority (BA)

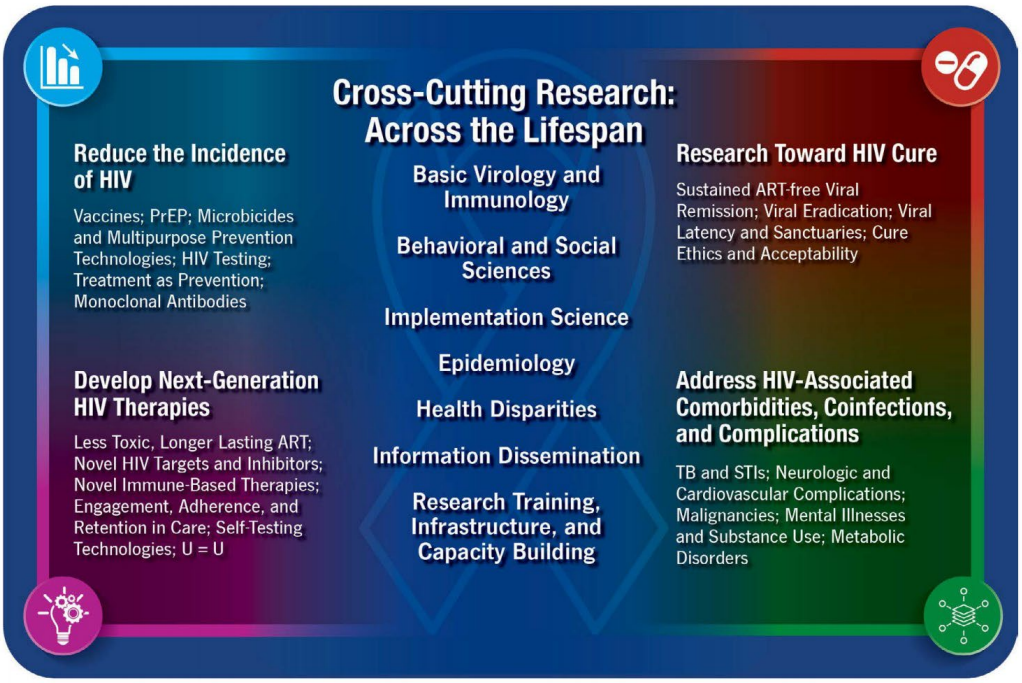
FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
$3,076,061,000	$3,090,000,000	$3,100,000,000	$10,000,000

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

PROGRAM DESCRIPTIONS, ACCOMPLISHMENTS, AND FUTURE DIRECTIONS

The following selected programs and activities focus on the highest HIV research priorities as they further the NIH Director's theme of *Science in Service to Society*.

NIH Priorities for HIV and HIV-related Research



Reduce the Incidence of HIV

Given persistent high rates of new HIV infections globally, developing an effective preventive vaccine against HIV remains a critical research goal, although it has proven to be a formidable challenge. In 2009 a key milestone was reached with results from the RV144 vaccine trial, supported by the U.S. Department of Defense, NIH, and the government of Thailand, which showed partial efficacy (31 percent) in a large-scale field trial of an experimental vaccine regimen. However, the follow-on study, HVTN 702, carried out in South African populations, was halted because the vaccine strategy failed to prevent HIV infection.

One of the lessons learned from these and other HIV vaccine studies is the value of forming multidisciplinary teams of researchers across different fields of basic and translational science and incorporating behavioral and social science early in the development process. The scientific complexity and cost of these endeavors has led to the establishment of public/private partnerships to advance the evaluation of vaccine candidates. NIH currently is partnering with pharmaceutical companies in two large-scale, multi-national trials—Imbokodo (HVTN 705) and Mosaico (HPTN 706) that are testing a novel mosaic vaccine regimen.

Basic, clinical, and translational research to evaluate the human immune response to vaccine remains a critical priority. Advances in imaging technologies have led to the development of vaccine candidates that more closely mimic HIV envelope structural components and could provide the foundation for improved vaccines to induce protective immunity. In preparation for an increased number of vaccine efficacy clinical trials, NIH has strategically invested in expanding vaccine product manufacturing capabilities to meet future research demands.
In parallel with vaccine-based prevention strategies, antibody-mediated protection studies are testing biologicals as alternatives for prevention in uninfected individuals. Studies in multiple countries are in progress to determine whether or not periodic infusions or injections of certain broadly neutralizing antibodies (bNAbs) can prevent HIV acquisition in different populations.

Along with vaccine strategies, NIH will continue to pursue the development of other HIV prevention approaches, such PrEP. NIH has supported studies demonstrating that daily, oral antiretroviral therapy (ART)-based PrEP can reduce the risk of HIV acquisition by nearly 100 percent if taken as prescribed. For many people, however, "a pill a day" is not optimal and adherence can be a challenge. Consequently, NIH is expanding research into long-acting formulations for PrEP (as well as for HIV treatment) including research into bNAbs and long-acting small molecules as antiretroviral agents. This research will expand from the NIH-funded study, HPTN 083, which demonstrated that a PrEP regimen containing long-acting cabotegravir injected once every eight weeks was superior to daily oral tenofovir/ emtricitabine for HIV prevention in cisgender men and transgender women who have sex with men. Other long-acting alternatives under development include intra-vaginal rings, implants, transdermal patches and additional injectables.

NIH will continue to support the efforts for the development of multipurpose technologies that use HIV prevention interventions with other sexually transmitted infection (STI) preventives and/or contraceptives. Such methods will offer the advantages of discreet, self-initiated, and

long-acting HIV prevention options for women providing simultaneous protection against multiple health risks.

In concert with product development, NIH will continue to support behavioral, social, and implementation sciences research to better understand how reach, uptake, and adherence to prevention interventions may be optimized for different populations. Primary prevention options, such as PrEP are only administered to people without HIV. To determine HIV status in ways that are acceptable to those at risk of HIV infection, NIH is continuing to partner with organizations to develop new HIV testing technologies, in particular self-testing methods.

Budget Policy: The FY 2022 President's Budget request to reduce the incidence of HIV is $691.6 million, a decrease of $14.9 million or 2.1 percent compared to the FY 2021 Enacted level.

Develop Next-Generation HIV Therapies

NIH-sponsored research has led to the development of combination ART that has significantly improved the health outcomes, including the quality and length of life, of people with HIV. With effective treatment, HIV infection has changed from a rapidly fatal disease to a chronic condition. Consistent use of ART reduces damage to the immune system by suppressing viral replication, delaying the development of viral resistance, and leading to undetectable viral loads, thereby preventing sexual transmission of HIV to an uninfected partner. This has led to the highly effective "Uninfected = Untransmittable" (U=U) campaign. However, even with simplified, effective daily one-pill treatment regimens capable of suppressing HIV, only 23 million (60 percent) of the approximately 38 million people with HIV worldwide currently receive ART.

Barriers to uptake and adherence to ART include treatment unavailability, high cost, the need for daily doses, interactions with other drugs, psychosocial factors, and the potential for drug resistance and/or adverse events. Stigma and disparities in access to ART also adversely affect health outcomes in people with HIV across race, ethnicity, sex, gender, age, socioeconomic status and geographic location.

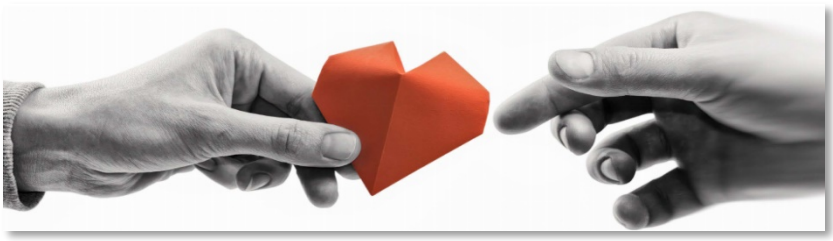
Budget Policy: The FY 2022 President's Budget request to develop next-generation HIV therapies is $351.5 million, an increase of $1.3 million or 0.4 percent compared to the FY 2021 Enacted level.

Research Toward a Cure for HIV

Significant challenges to cure HIV continue because of the persistence of HIV as integrated DNA in latently infected cells and other reservoirs. To date, only three people in the world have been cured of HIV: two individuals achieved long term ART-free suppression of HIV through a complex and costly bone marrow transplant procedure, and one individual cleared HIV through a genetic variation in her immune system that controlled the virus. While these cases provide optimism that cure of HIV is achievable, intensive focus on understanding the dynamics of viral reactivation and the nature of viral reservoirs in achieving long-term HIV suppression is a vital and essential step towards cure. Further fundamental research using novel technologies, such as clustered regularly short palindromic repeats—discovered by NIH-funded and recent Nobel Prize-winning investigators—will be supported to better understand genomic and epigenetic features of integration sites as well as to characterize, quantify, eliminate or control the viral

reservoir in different anatomical sites, cell types and to test the efficacy of novel cure strategies in appropriate animal models and human clinical trials.

NIH will invest in cure strategies with a "back to basics" approach that focuses on fundamental virology and cell biology. The aim is to better understand mechanisms of virus/host cell interactions that will lead to rational design of innovative strategies for extended viral suppression and ultimately viral elimination.



A range of techniques, including single-cell and imaging technologies, are being used to identify and describe the HIV reservoir and discover mechanisms of viral reactivation from latently infected cells. Experimental treatments in development include therapeutic vaccines, genetically engineered immune cells that are resistant to HIV infection, drugs that reactivate latent HIV to make the virus visible to the immune system so that the virus can be cleared, cure-inducing immunotherapies, and interventions to prolong the time between antiretroviral treatments from one day to a few months or longer for an ART-free viral remission.

In parallel to basic and clinical research, NIH is supporting behavioral and social science research to ascertain what kind of cure strategies will be perceived as feasible and desirable among different groups of people with HIV. A core question under exploration is how the risks and benefits of potential HIV cure strategies (including participation in the associated research) are weighed, particularly in the context of living a healthy life and maintaining viral suppression under currently available, highly effective ART. In the end, the goal of integrated HIV cure research is to develop safe, scalable, and sustainable strategies for cure for the 38 million people with HIV.

Budget Policy: The FY 2022 President's Budget request to promote research toward a HIV cure is $211.7 million, an increase of $1.7 million or 0.8 percent compared to the FY 2021 Enacted level.

Address HIV-Associated Comorbidities, Coinfections and Complications

Effective ART has ushered in a new era for the HIV epidemic. People with HIV can now achieve nearly normal lifespans, but are more likely to suffer from multiple, chronic comorbidities, coinfections, and complications (CCCs) resulting from virus exposure, long-term HIV disease, immune dysfunction, and/or ART for treatment or prevention, which can severely impact their quality of life. These include neurocognitive and cardiovascular complications, malignancies, metabolic and bone disorders, mental health impairments, substance use, and others. HIV interacts with other infectious and non-communicable diseases in significant ways. Among people with HIV globally, tuberculosis is the greatest cause of mortality. Viral hepatitis, and some viral-associated cancers also are challenges for people with HIV. HIV often occurs concomitantly with other STI and/or in association with alcohol, tobacco, and drug misuse, violence and trauma, mental illness, and other behavioral and psychosocial issues. The

overlapping etiologies and consequences of HIV-associated diseases need to be better understood in order to improve the health and well-being of people with HIV across the lifespan.

Budget Policy: The FY 2022 President's Budget request to address HIV-associated comorbidities, coinfections, and complications (CCCs) is $552.7 million, a decrease of $6.6 million or 1.2 percent compared to the FY 2021 Enacted level.

Cross-Cutting Areas

Basic Science: Basic biomedical research has generated fundamental knowledge to improve understanding of HIV virology, immunology and pathogenesis that can inform the development of effective prevention, treatment, and cure strategies. Nonetheless, significant gaps remain in areas that could lead to innovations in vaccine development, better therapies, and cure approaches. NIH will continue to invest in research to enhance understanding of fundamental aspects of innate immunity, B and T cell immunology, virology, and interplay between the virus and host, and basic mechanisms involved in host cellular interactions with HIV. Systems biology approaches to examine HIV risk, immunity, treatment response, and disease progression in diverse populations will provide additional scientific value.

Behavioral and Social Science: Insights about human behavior, social networks, community institutions, and social forces that influence the emergence and spread of HIV epidemics have contributed to the development of important HIV prevention, care, and social-structural interventions. Further research will be supported to better understand and address key individual, relational, community, and social-structural dynamics that fuel or mitigate HIV epidemics in diverse populations and settings. This includes attention to addressing intersectional stigma as a continuing challenge to information about, access to, and uptake of HIV prevention and treatment methods in at-risk communities.

Epidemiology: Epidemiologic methods provide accurate, real-time information to better understand the global HIV/AIDS pandemic and its associated CCCs, inform prevention and treatment approaches, and determine where research should be conducted. The use of surveillance, big data science, machine learning, modeling, registries, phylodynamics, and other epidemiologic approaches will contribute to improved outcomes across the HIV prevention and care continua.

Health Disparities: Research to better understand and address disparities and inequalities based on such things as sex, gender, race, ethnicity, socioeconomic status, age, sexual orientation and behavior, substance use behavior, and geographic location—including through community-based participatory research methods—will be supported to improve HIV testing and engagement and retention in prevention and care services, and to enhance the health and wellbeing of persons living with and at risk for HIV in underserved and marginalized communities.

Implementation Science: To have the greatest impact on domestic and global HIV programs and policies and help move from efficacy to effectiveness, the NIH will support implementation science to promote and improve the systematic uptake of evidence-based HIV prevention, care, and treatment interventions in diverse settings. Further understanding of the processes and factors that influence scale-up and sustainability of effective strategies will help achieve the

goals of the *National HIV/AIDS Strategy for the United States* and *Ending the HIV Epidemic in the U.S.*, and the UNAIDS global *95-95-95* targets.

Information Dissemination: A critical component of the NIH HIV research program is ensuring that research findings are shared with diverse communities and stakeholders, including patients, clinicians, researchers, public health practitioners, policy-makers, and the general public. NIH will utilize emerging technologies and venues to develop accurate, timely, and culturally responsive communication approaches, including social media, that target underserved populations.

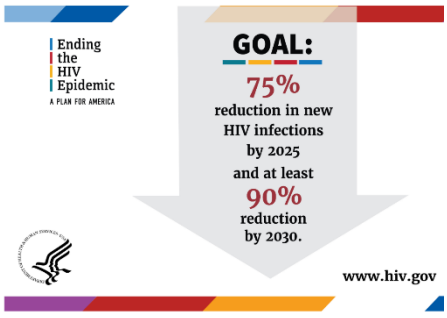
Training, Infrastructure, and Capacity-building: To ensure that the priority areas of HIV science are addressed with novel, innovative, and culturally responsive approaches, the NIH will augment its commitment to the development of the next generation of HIV researchers, particularly those from underrepresented populations and institutions. This includes providing both human resources (e.g., mentoring) and support for infrastructure (e.g., laboratories).

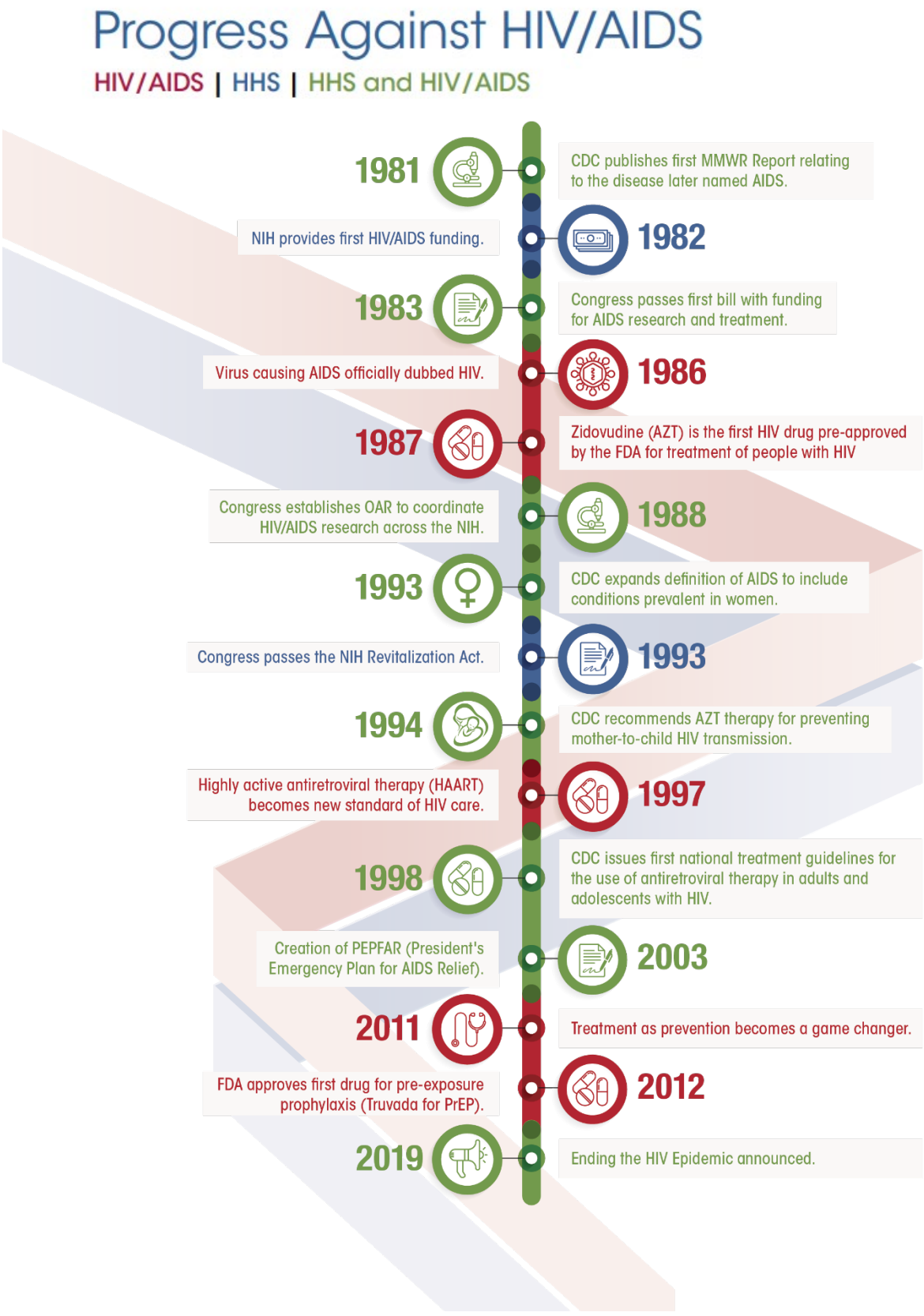
Specifically, NIH is committed to promoting opportunities for new researchers and enhancing training and mentorship programs to encourage successful, independent careers for ESIs in a way that enhances workforce diversity. Over the last several years, NIH has taken numerous steps to balance, strengthen, and stabilize the biomedical research workforce, but increased investments in supporting and expanding ESIs in the HIV field are needed. A priority for developing workforce diversity is to promote research on the engagement of community health workers as integral members of a multidisciplinary health care team to improve HIV care engagement, antiretroviral adherence, viral suppression, and ultimately, health outcomes.

Budget Policy: The FY 2022 President's Budget request to advance the critical framework of crosscutting areas of research to end the HIV pandemic is $1,292.4 million, an increase of $28.5 million or 2.3 percent compared to the FY 2021 Enacted level.

NIH- and HHS-wide Initiative

Ending the HIV Epidemic in the U.S. (EHE): OAR works with its NIH and HHS partners to continue to advance the goals of the EHE to: (1) reduce new HIV infections; (2) increase access to care and improve health outcomes for people with HIV; (3) reduce HIV-related health inequities; and (4) achieve a more coordinated national response to the HIV epidemic. NIH will expand upon its initial support of pilot implementation science projects funded through its CFARs and ARCs to leverage investments in these and other institutions that represent and are located among populations in U.S. states and territories most affected by the HIV epidemic.




Progress Against HIV/AIDS
HIV/AIDS | HHS | HHS and HIV/AIDS
1981
CDC publishes first MMWR Report relating to the disease later named AIDS.
NIH provides first HIV/AIDS funding.
1982
1983
Congress passes first bill with funding for AIDS research and treatment.
Virus causing AIDS officially dubbed HIV.
1986
1987
Zidovudine (AZT) is the first HIV drug pre-approved by the FDA for treatment of people with HIV
Congress establishes OAR to coordinate HIV/AIDS research across the NIH.
1988
1993
CDC expands definition of AIDS to include conditions prevalent in women.
Congress passes the NIH Revitalization Act.
1993
1994
CDC recommends AZT therapy for preventing mother-to-child HIV transmission.
Highly active antiretroviral therapy (HAART) becomes new standard of HIV care.
1997
1998
CDC issues first national treatment guidelines for the use of antiretroviral therapy in adults and adolescents with HIV.
Creation of PEPFAR (President's Emergency Plan for AIDS Relief).
2003
2011
Treatment as prevention becomes a game changer.
FDA approves first drug for pre-exposure prophylaxis (Truvada for PrEP).
2012
2019
Ending the HIV Epidemic announced.