

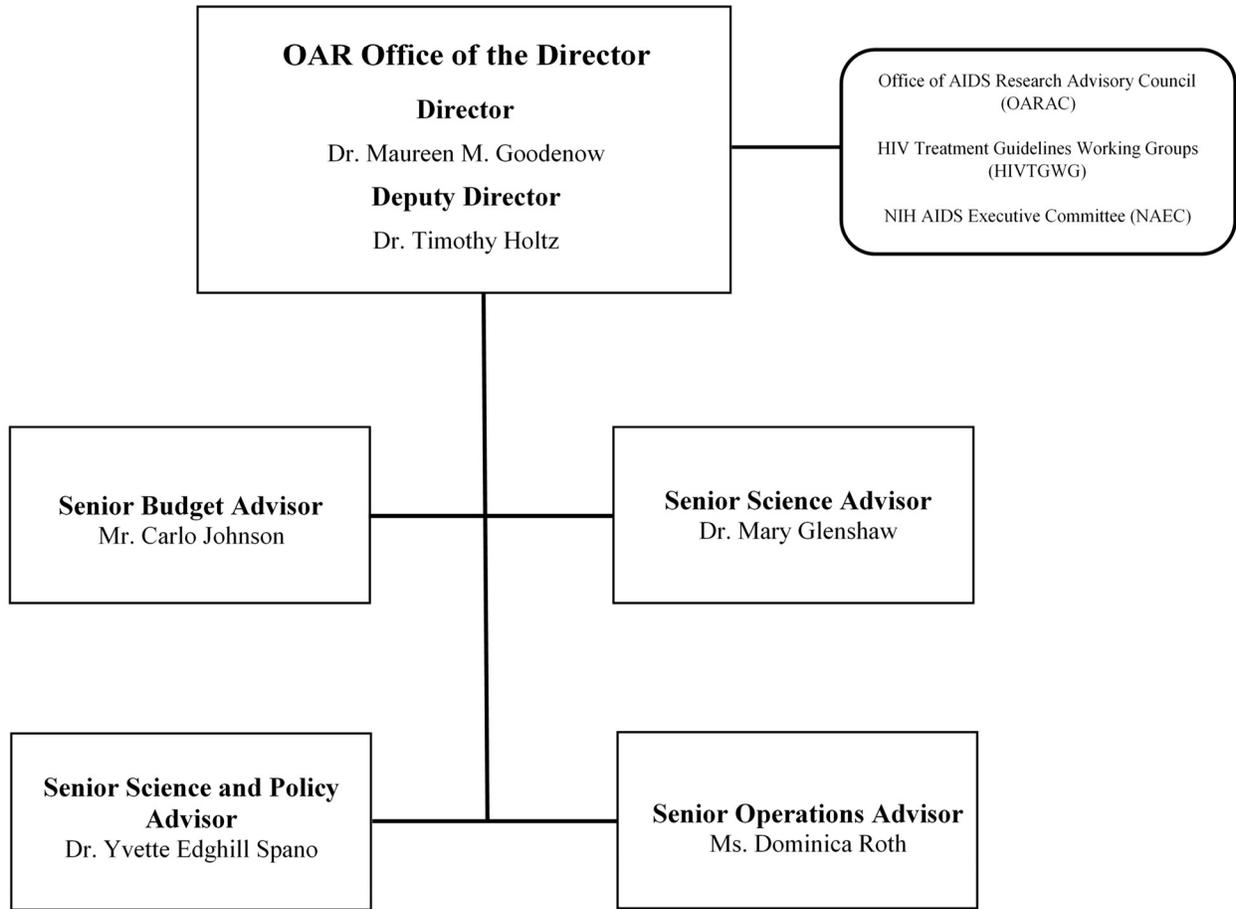
NIH HIV/AIDS RESEARCH BUDGET

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NOTE: Program discussion and amounts do not include HIV/AIDS activities of the Agency for Healthcare Research and Quality, which is proposed for consolidation into NIH in FY 2021 as the National Institute for Research on Safety and Quality (NIRSQ).

ORGANIZATION CHART

**NATIONAL INSTITUTES OF HEALTH
OFFICE OF AIDS RESEARCH**



BUDGET AUTHORITY BY INSTITUTE AND CENTER

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Institute, Center, and Office
(Dollars in Thousands)

| Institute, Center, and Office | FY 2019 Final ¹ | FY 2020 Enacted Level ² | FY 2021 President's Budget | FY 2021 +/- FY 2020 |
|--|---------------------------------------|---|---|------------------------------------|
| NCI | \$241,979 | \$241,975 | \$220,132 | -\$21,843 |
| NHLBI | 83,715 | 84,715 | 77,068 | -7,647 |
| NIDCR | 18,734 | 18,984 | 17,270 | -1,714 |
| NIDDK | 33,203 | 34,135 | 31,054 | -3,081 |
| NINDS | 39,192 | 41,082 | 37,374 | -3,708 |
| NIAID | 1,743,221 | 1,779,113 | 1,632,583 | -146,530 |
| NIGMS | 8,300 | - | - | - |
| NICHHD | 144,367 | 144,895 | 131,815 | -13,080 |
| NEI | 1,153 | 388 | 353 | -35 |
| NIEHS | 5,342 | 5,342 | 4,860 | -482 |
| NIA | 20,426 | 22,622 | 20,580 | -2,042 |
| NIAMS | 4,571 | 4,587 | 4,173 | -414 |
| NIDCD | 2,128 | 2,128 | 1,936 | -192 |
| NIMH | 178,899 | 183,991 | 167,382 | -16,609 |
| NIDA | 264,814 | 261,140 | 237,567 | -23,573 |
| NIAAA | 30,556 | 31,879 | 29,001 | -2,878 |
| NINR | 13,100 | 16,350 | 14,874 | -1,476 |
| NHGRI | 5,533 | 3,302 | 3,538 | 236 |
| NIBIB | 839 | 1,839 | 1,673 | -166 |
| NIMHD | 22,701 | 22,780 | 20,724 | -2,056 |
| NCCIH | 611 | 748 | 680 | -68 |
| FIC | 24,239 | 24,389 | 22,187 | -2,202 |
| NLM | 9,322 | 9,322 | 8,480 | -842 |
| OD | | | | |
| OAR | 62,256 | 62,256 | 56,636 | -5,620 |
| ORIP | 78,099 | 78,099 | 71,049 | -7,050 |
| Subtotal, OD | 140,355 | 140,355 | 127,685 | -12,670 |
| TOTAL, NIH | \$3,037,300 | \$3,076,061 | \$2,812,989 | -\$263,072 |

¹ Reflects effects of Secretary's transfer² Includes effects of FY 2020 HIV/AIDS transfers

BUDGET AUTHORITY BY MECHANISM

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Mechanism - AIDS ¹
(Dollars in Thousands)

| MECHANISM | FY 2019 Final ² | | FY 2020 Enacted Level | | FY 2021 President's Budget | | FY 2021 +/- FY 2020 | |
|--|----------------------------|----------------------|--------------------------|-----------------------|-------------------------------|----------------------|---------------------------|-------------------|
| | No. | Amount | No. | Amount | No. | Amount | No. | Amount |
| Research Projects: | | | | | | | | |
| Noncompeting | 1,520 | \$1,404,709 | 1,458 | \$1,361,479 | 1,341 | \$955,066 | -117 | -\$406,413 |
| Administrative Supplements | (60) | 24,263 | (38) | 10,347 | (25) | 7,336 | -13 | -3,011 |
| Competing | 452 | 330,860 | 518 | 383,342 | 540 | 633,483 | 22 | 250,141 |
| Subtotal, RPGs | 1,972 | \$1,759,832 | 1,976 | \$1,755,168 | 1,881 | \$1,595,885 | -95 | -\$159,283 |
| SBIR/STTR | 30 | 17,361 | 29 | 18,601 | 28 | 17,013 | -1 | -1,588 |
| Research Project Grants | 2,002 | \$1,777,193 | 2,005 | \$1,773,769 | 1,909 | \$1,612,898 | -96 | -\$160,871 |
| Research Centers: | | | | | | | | |
| Specialized/Comprehensive | 57 | \$116,811 | 58 | \$130,828 | 58 | \$124,009 | 0 | -\$6,819 |
| Clinical Research | 0 | 0 | 2 | 986 | 2 | 986 | 0 | 0 |
| Biotechnology | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Comparative Medicine | 18 | 69,990 | 20 | 71,361 | 18 | 64,939 | -2 | -6,422 |
| Research Centers in Minority Institutions | 0 | 96 | 0 | 1,270 | 0 | 1,143 | 0 | -127 |
| Research Centers | 75 | \$186,897 | 80 | \$204,445 | 78 | \$191,077 | -2 | -\$13,368 |
| Other Research: | | | | | | | | |
| Research Careers | 253 | \$44,514 | 260 | \$45,118 | 248 | \$41,880 | -12 | -\$3,238 |
| Cancer Education | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cooperative Clinical Research | 0 | 5,149 | 0 | 5,150 | 0 | 4,790 | 0 | -360 |
| Biomedical Research Support | 31 | 2,249 | 31 | 1,600 | 29 | 1,456 | -2 | -144 |
| Minority Biomedical Research Support | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Other | 128 | 56,096 | 121 | 52,799 | 110 | 48,083 | -11 | -4,716 |
| Other Research | 412 | \$108,008 | 412 | \$104,667 | 387 | \$96,209 | -25 | -\$8,458 |
| Total Research Grants | 2,489 | \$2,072,098 | 2,497 | \$2,082,881 | 2,374 | \$1,900,184 | -123 | -\$182,697 |
| Ruth L. Kirschstein Training Awards: | FTTPs | | FTTPs | | FTTPs | | | |
| Individual Awards | 77 | \$3,284 | 81 | \$3,227 | 81 | \$3,136 | 0 | -\$91 |
| Institutional Awards | 258 | 14,904 | 257 | 15,020 | 251 | 14,374 | -6 | -646 |
| Total Research Training | 335 | \$18,188 | 338 | \$18,247 | 332 | \$17,510 | -6 | -\$737 |
| Research & Develop. Contracts (SBIR/STTR) (non-add) | 88 (10) | \$363,884 (7,792) | 76 (9) | \$387,439 (10,105) | 76 (9) | \$340,731 (9,285) | 0 0 | -\$46,708 -820 |
| Intramural Research | | \$359,724 | | \$356,814 | | \$336,695 | | -\$20,119 |
| Res. Management and Support | | 161,150 | | 168,424 | | 161,233 | | -7,191 |
| Res. Management & Support (SBIR Admin) (non-add) | | | | | | | | |
| Office of the Director - Appropriation ³ | | 140,355 | | 140,355 | | 127,685 | | -12,670 |
| Office of the Director - Other | | 62,256 | | 62,256 | | 56,636 | | -5,620 |
| ORIP (non-add) ³ | | 78,099 | | 78,099 | | 71,049 | | -7,050 |
| Total, NIH Discretionary B.A. | | \$3,037,300 | | \$3,076,061 | | \$2,812,989 | | -263,072 |

¹ All items in italics and brackets are non-add entries.² Reflects effects of Secretary's transfer³ 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.

BUDGET AUTHORITY BY ACTIVITY

**NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Activity
(Dollars in Thousands)**

| | FY 2017 Actual | FY 2018 Actual ¹ | FY 2019 Final ¹ | FY 2020 Enacted Level | FY 2021 President's Budget | FY 2021 +/- FY 2020 |
|--|---------------------------|--|---------------------------------------|----------------------------------|---|------------------------------------|
| Overarching Priorities | | | | | | |
| Reduce the Incidence of HIV | \$687,495 | \$714,553 | \$741,401 | \$737,348 | \$660,231 | -\$77,117 |
| Develop Next-Generation HIV Therapies | 362,820 | 364,484 | 368,912 | 365,526 | 313,066 | -\$52,460 |
| Research Toward a Cure for HIV ² | 170,375 | 175,757 | 187,777 | 197,637 | 180,794 | -\$16,843 |
| Address HIV-Associated Comorbidities, Coinfections, and Complications | 556,608 | 517,884 | 531,440 | 543,531 | 501,591 | -\$41,940 |
| Cross-Cutting Areas | 1,222,763 | 1,222,703 | 1,207,770 | 1,232,019 | 1,157,307 | -\$74,712 |
| Total | \$3,000,061 | \$2,995,381 | \$3,037,300 | \$3,076,061 | \$2,812,989 | -\$263,072 |

¹ Reflects effects of Secretary's transfer

² Beginning in FY 2017, Research Toward a Cure for HIV/AIDS became a separate activity. Dollars for Research Toward a Cure for HIV/AIDS were previously included within other science areas, such as Next Generation Therapies, Crosscutting--Basic Research, and Reducing Incidence of HIV/AIDS.

JUSTIFICATION OF BUDGET REQUEST

**Office of AIDS Research
NIH AIDS Research Budget Justification**

Budget Authority (BA):

| FY 2019 Final | FY 2020 Enacted Level | FY 2021 President's Budget | FY 2021+/- FY 2020 |
|------------------|-----------------------------|----------------------------------|-----------------------|
| \$3,037,300,000 | \$3,076,061,000 | \$2,812,989,000 | -\$263,072,000 |

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

Mission Statement

To ensure NIH HIV research funding aligns with high-priority research areas and to facilitate the maximum return on investment.

DIRECTOR'S OVERVIEW/PROGRAM NARRATIVES

Director's Overview

NIH's investments in Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) research have, over more than three decades, produced groundbreaking advances in understanding the basic virology, immunology, and pathogenesis of HIV. Research discoveries enabled the development of safe, effective antiretroviral medications that can extend the lifespan of people with HIV and the design and implementation of effective strategies to prevent HIV transmission and acquisition. Nonetheless, globally including the United States, new infections continue at alarming rates in some locations while remaining unchanged in others, reflecting inequalities by race, ethnicity, sex, gender, age, socioeconomic status, and geography. NIH will continue to lead basic, clinical, behavioral, and translational research to develop cutting-edge solutions to address the ongoing challenges of the HIV pandemic.

There is little doubt that the HIV pandemic will continue to affect virtually every nation in the world well into the next century. It is important to broaden our understanding of the affected populations to more effectively tailor prevention and treatment strategies. To accomplish these objectives, a major advance in moving NIH's research efforts forward is the 21st Century Cures Act, passed in 2016. This act amends the Public Health Service Act to charge researchers with gathering inclusive clinical research data to improve the health of women, members of minority groups, and relevant age categories. Individuals from minority groups – including racial and ethnic minorities and sexual and gender minorities – historically have been underrepresented in biomedical research. NIH has implemented efforts to address inclusion and exclusion of

pediatric and older adult populations relating to research studies, which will increase the knowledge of how to improve and support health across the lifespan.

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. Located within the NIH Office of the Director, Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), OAR is authorized to:

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

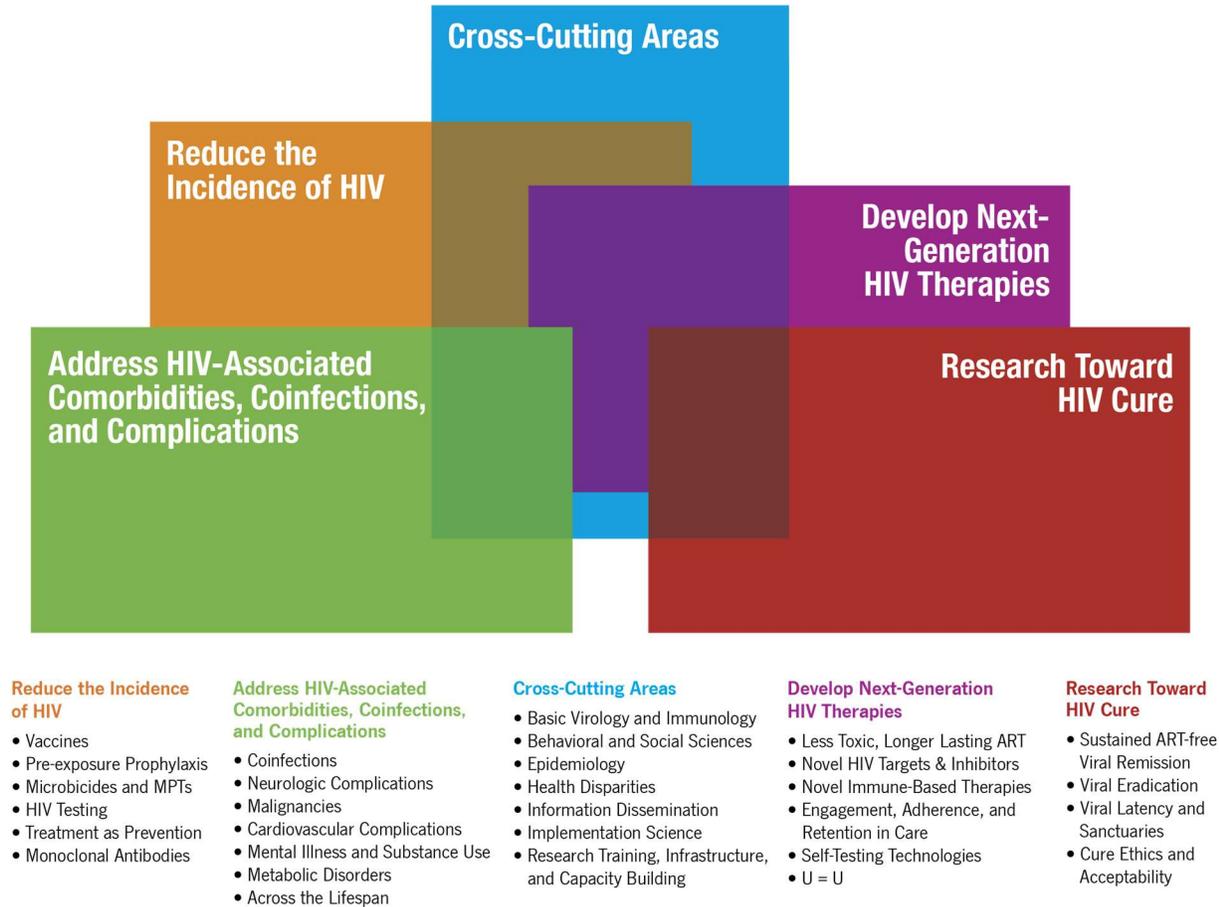
Coordination & Management: OAR coordinates the scientific, budgetary, legislative, and policy components of the NIH HIV/AIDS research program by leading the NIH-wide HIV research strategic planning, priority-setting, and resource allocation to:

- Promote, coordinate, and implement cost-sharing between Institutions, Centers, and Offices (ICOs) and OAR;
- Accelerate discovery, enhance collaboration, and minimize duplication; and
- Translate basic research discoveries into clinical practice and public health implementation.

Priority-setting: OAR partners with stakeholders across the NIH, governmental agencies, research organizations, and communities to establish HIV research priorities (Figure 1) in the global fight against HIV to:

- Reduce the incidence of new HIV infections;
- Develop next-generation HIV therapies;
- Research toward HIV Cure;
- Address HIV-associated comorbidities, coinfections, and complications (CCCs); and
- Support a broad array of cross-cutting research areas to combat the HIV pandemic.

Figure 1. NIH HIV Research Priorities



Strategic Planning: OAR develops the *NIH Strategic Plan for HIV and HIV-Related Research (The Plan)*,¹⁵¹ which identifies research priorities for NIH-funded intramural and extramural research. The Plan informs the general public, scientific community, Congress and policy-makers, and communities impacted by HIV about the NIH HIV research agenda. NIH is transitioning from annual or biennial Plans to a five-year strategic plan for FY 2021 to 2025 to encompass a longer-term vision for the research agenda.

The five-year Plan outlines an integrated approach for the NIH HIV/AIDS research program that leverages partnerships to develop new and innovative strategic research efforts to effectively end the HIV pandemic and improve health outcomes of all persons with or at risk for HIV. The strategic goals of the Plan closely align with the goals of the current *National HIV/AIDS Strategy for the United States: Updated to 2020* (NHAS)¹⁵² and the National Viral Hepatitis Action Plan (NVHAP) 2017-2020.¹⁵³

¹⁵¹ www.oar.nih.gov/hiv-policy-and-research/strategic-plan

¹⁵² www.hiv.gov/federal-response/national-hiv-aids-strategy/nhas-update

¹⁵³ www.hhs.gov/sites/default/files/National%20Viral%20Hepatitis%20Action%20Plan%202017-2020.pdf

The Plan provides a framework for NIH efforts in support of the *Ending the HIV Epidemic: A Plan for America* (EHE) – a once-in-a-generation opportunity to eliminate new HIV infections in our nation. EHE is working to reduce new infections by 75 percent in the next 5 years and by 90 percent in the next 10 years, averting more than 250,000 new HIV infections in that span.¹⁵⁴

Budgeting: OAR continues to manage the allocation of NIH HIV research funds to the ICOs to advance HIV science and ensure that funds are aligned with the highest research priorities. Based on the Plan and priorities, OAR evaluates the NIH-wide research portfolio and, in consultation with the ICOs, allocates resources to addresses emerging research opportunities.

Stakeholder Engagement: OAR convenes stakeholders, encourages collaboration, and catalyzes innovation to address emerging scientific and public health challenges. To ensure that the NIH HIV research agenda addresses the most important scientific questions associated with the pressing needs of HIV-affected communities over the next five years, OAR is conducting a series of Listening Sessions across the country to gather input from scientists, advocates, health care providers, public health implementers, community representatives, and other stakeholders. These sessions provide a platform for the OAR Director and staff to hear stakeholder perspectives on key scientific questions, research methodologies, and capacity issues of local and regional importance. Outcomes from the sessions will inform OAR planning and budgeting recommendations to the NIH Director.

Program Descriptions, Accomplishments, and Future Directions

The following selected programs and activities focus on the highest HIV research priorities to illustrate the NIH Director’s theme of *Science with an Eye to the Future: The Long Arc of Research*.

The research response to the HIV/AIDS pandemic has had an impactful and transformative arc on biomedical research spanning more than three decades (Table 1). From identification of the first cases of AIDS and delineation of HIV as the causative agent in the early 1980s to the groundbreaking initiative to end the HIV epidemic in the United States by 2030 through enhancing implementation of effective evidence-based prevention and care strategies in the hardest-hit jurisdictions, HIV research at NIH produces life-saving changes for people with HIV (PWH), catalyzes paradigm-changing approaches to research infrastructure, methodologies, and strategies that extend across research fields, and raises the future feasibility of an HIV vaccine and a cure.

¹⁵⁴ www.hhs.gov/sites/default/files/ending-the-hiv-epidemic-fact-sheet.pdf

Table 1. Highlights of discovery from NIH HIV/AIDS supported research from 1981–2019.

| Year | Event |
|-----------|--|
| 1981 | CDC published the first <i>Morbidity and Mortality Weekly Report</i> (MMWR) about a disease later named the Acquired Immune Deficiency Syndrome (AIDS). |
| 1982 | The National Institutes of Health (NIH) provided the first HIV/AIDS funding. |
| 1983 | Congress passed the first bill with funding for AIDS research and treatment. The NIH and the Pasteur Institute announced the viral causative agent. |
| 1985–1987 | NIH researchers discovered that zidovudine (ZDV); also known as azidothymidine (AZT) suppressed viral replication becoming the first antiretroviral approved by the FDA. |
| 1988 | Congress established the Office of AIDS Research (OAR) to coordinate HIV/AIDS research across NIH. |
| 1996–1997 | Combining antiretroviral drugs led to the development of highly active antiretroviral therapy (HAART), which became the new standard of HIV care. NIH funded PACTG 076 clinical trial showed ZDV treatment of pregnant women with HIV and their infants reduced perinatal infection by 67 percent. |
| 1998 | The CDC issued the first national treatment guidelines for the use of antiretroviral therapy in adults and adolescents with HIV. |
| 2003 | President Bush established the U.S. President’s Emergency Plan for AIDS (PEPFAR) to provide antiretroviral therapy (ART) to resource-limited countries. |
| 2006 | A new fixed-dose combination of three widely used antiretroviral drugs is developed that can be taken in a single tablet once a day, alone or in combination with other antiretroviral products for treatment in adults. |
| 2013 | The FDA approved a second-generation integrase inhibitor dolutegravir that could be widely used by PWH. |
| 2016–2017 | The U=U slogan was launched by the Prevention Access Campaign. The CDC officially backed the science behind the campaign and was endorsed by HIV organizations around the world. |
| 2019 | <i>Ending the HIV Epidemic: A Plan for America</i> is announced, with the goal of reducing the number of new HIV infections in the United States by 75 percent within five years, and then by at least 90 percent within 10 years. |

Overall Budget Policy: The FY 2021 President’s Budget request for the NIH-wide HIV/AIDS research agenda is \$2,813.0 million, a decrease of \$263.1 million or 8.6 percent compared to the FY 2020 Enacted Level. The FY 2021 budget request reflects the ambitious but achievable goal to end the HIV epidemic in the United States by 2030, as well as achieve HIV pandemic control globally. NIH HIV research investments focus on the expansion of innovative basic science discoveries in virology, human immunology, and biotechnology to accelerate HIV vaccine efforts through the research pipeline from basic discovery and preclinical studies to the impending outcomes from landmark clinical trials in diverse settings around the world. The NIH HIV research portfolio includes innovative interventions and new implementation strategies for pre-exposure prophylaxis to significantly reduce the number of new HIV infections, and new

long-acting therapies to improve viral load suppression among people with HIV to levels that prevent transmission. Novel technologies will expand point-of-care and self-testing modalities for monitoring HIV viral load suppression, while gene therapy strategies are in development for delivery of an HIV cure. The FY 2021 President’s Budget request supports research to address the health and quality of life of persons with HIV, including comorbidities, co-infections, and complications resulting from the near-normal lifespan now afforded by simplified, potent antiretroviral therapies. The health effects of HIV infection and treatment often intersect social health determinants, including racial, ethnic, gender, geographic disparities, poverty, stigma, and socioeconomic disenfranchisement. NIH HIV research strategies employ approaches that include high quality, multidisciplinary, community-engaged research and implementation science to best understand the most effective interventions. Training and building capacity of new and early stage investigators is an enhanced priority to build the skills and scope of current and future generations of HIV researchers who can address 21st century challenges with 21st century solutions.

Reduce the incidence of HIV

Developing an effective preventive vaccine against HIV remains a critical research goal. In 2009 a key milestone was reached with results from the RV144 vaccine trial, supported by the 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.¹⁵⁵ NIH is currently supporting additional large-scale efficacy trials of candidate HIV vaccine regimens with new products developed since RV144. In January 2020, vaccine administration was discontinued in the HVTN 702 trial, led by the Pox-Protein-Public-Private Partnership (P5), as results indicated that the regimen did not prevent HIV, although there were no safety concerns for study participants.^{156,157} Two other HIV vaccine trials using different vaccines, HVTN705/HPX2008 (Imbokodo) and HPX3002/HVTN 706 (Mosaico), are ongoing in multiple international sites with initial results anticipated in 2021. In addition, a robust pipeline of candidate vaccine products includes multiple clinical studies in various stages of testing in humans.

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. The Division of AIDS, Vaccine Research Program, Translational Research Branch, in the National Institute of Allergy and Infectious Disease, works closely with academic institutions, biotech, pharmaceutical companies, non-profit organizations, vaccine trial networks, contract manufacturing and contract research organizations to advance clinical HIV vaccine development.¹⁵⁸

¹⁵⁵ www.hivresearch.org/rv144-trial

¹⁵⁶ www.niaid.nih.gov/diseases-conditions/empirical-approach

¹⁵⁷ www.nih.gov/news-events/news-releases/experimental-hiv-vaccine-regimen-ineffective-preventing-hiv

¹⁵⁸ www.niaid.nih.gov/research/daims-translational-research-program

In parallel with vaccine-based prevention strategies, antibody-mediated protection (AMP) 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 of at-risk individuals. While the studies represent significant advances toward prevention of HIV, further research is essential to extend the half-life of the antibodies, develop more potent antibodies and vector-based bNAbs for HIV prevention, and identify bNAb combinations that can suppress HIV long-term.

In addition to vaccine strategies, NIH will continue to pursue the development of other HIV prevention approaches, such as pre-exposure prophylaxis (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 in the United States and globally, 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. The goal is to develop PrEP options that require weeks or months between doses, rather than everyday dosing. In addition to product development, behavioral, social, and implementation sciences research is being supported to better understand how adherence to prevention interventions such as PrEP may be optimized for different populations.

PrEP is only administered to HIV-negative individuals. To determine HIV status in ways that are acceptable to people at risk of HIV infection, NIH is continuing to partner with organizations to develop new HIV testing technologies, in particular self-testing methods. Internal to NIH, this is being done in alignment with the priorities of the NIH Point-of-Care Technologies Research Network (POCTRN), housed within the National Institute of Biomedical Imaging and Bioengineering (NIBIB). OAR and a host of NIH ICOs support POCTRN activities, which aim to develop diagnostic technologies that are rapid, sensitive, specific, easy to use, and cost effective.

Budget Policy: The FY 2021 President’s Budget request to reduce the incidence of HIV is \$660.2 million, a decrease of \$77.1 million or 10.5 percent compared to the FY 2020 Enacted level.

Develop Next-Generation HIV Therapies

NIH-sponsored research has led to the development of combination ART (cART) that has significantly improved the health outcomes, including the quality and length of life, of people with HIV. HIV infection has changed from a rapidly fatal disease to a chronic condition with treatment. Consistent use of cART 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. 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 treatment. Barriers to uptake and adherence to cART include treatment unavailability, high cost, the need for daily doses, interactions with other drugs, and the potential for drug

resistance and/or adverse events. In addition, stigma and disparities in access to cART adversely impact health outcomes in people with HIV across race, ethnicity, sex, gender, age, socioeconomic status and geographic location.

NIH will continue to support the development of new, long-acting HIV medications with fewer side effects and complications, including monthly injections of continuously released cART, a six-month cART implant, and anti-HIV antibody infusions. Ideally, new long-acting interventions should be highly effective, safe, user-friendly, suitably durable, inexpensive, socially acceptable, and easy to implement.

One major area for development of new therapeutic agents is bNAbs, originally discovered in the search for strategies for an effective vaccine. Over the last 5-10 years, significant advances have been made in isolating bNAbs and understanding how this class of antibodies develops in humans. NIH research is building on these advances by supporting clinical trials to verify the concept of passive bNAb infusions as a modality for HIV prevention, for longer-acting antiretroviral treatment, and for inducing sustained ART-free HIV remission. In parallel, research is supporting biotechnology strategies to engineer more potent and/or longer acting bNAbs, as well as antibodies better able to promote killing of HIV-infected cells as distinct from neutralizing circulating free virus.

An important factor in the development of any new therapeutic target is understanding the life cycle of HIV within the host cell. Currently, there are more than five classes of antiretroviral medications that target different points in the viral life cycle. New therapeutic targets will prevent HIV replication at additional stages in the viral life cycle, such as maturation, egress and necessary host interactions.

Budget Policy: The FY 2021 President’s Budget request to develop next-generation HIV therapies is \$313.1 million, a decrease of \$52.5 million or 14.4 percent compared to the FY 2020 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, one individual has demonstrated long term ART-free suppression of HIV through a complex and costly bone marrow transplant procedure. While the outcome supports the possibility that cure of HIV ultimately may be achievable, focus now is on achieving long-term HIV suppression as a vital and essential step towards cure. Further fundamental research using novel technologies will be supported to characterize, quantify, eliminate or control the viral reservoir in different anatomical sites and 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. Latent HIV reservoirs, DNA coding for HIV that

persists in people with HIV despite the use of cART, present a significant challenge to finding a cure. Reservoirs of HIV can be found in certain “sanctuary” sites in the body, including the brain, allowing the virus to hide and be protected from both the immune system and cART, preventing sustained, ART-free viral remission, viral eradication, and a permanent HIV cure.

Because the mechanisms that underlie reservoir dynamics are not well understood, NIH invests in basic research to identify, characterize, and eradicate HIV or to inhibit viral reactivation through novel approaches and treatments that target HIV reservoirs. 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 cART.

Budget Policy: The FY 2021 President’s Budget request to promote research toward a HIV cure is \$180.8 million, a decrease of \$16.8 million or 8.5 percent compared to the FY 2020 Enacted level.

Address HIV-Associated Comorbidities, Coinfections and Complications

HIV infection affects and is affected by co-occurring infections, conditions, and non-communicable diseases. Among people with HIV, tuberculosis, viral hepatitis, and cancer are among the greatest causes of mortality, and the risk for comorbidities such as cardiovascular disease, some cancers, bone fractures/osteoporosis, liver disease, kidney disease, cognitive decline, and aging-related frailty is higher than among those without HIV. Additionally, treatment of cancer and other comorbidities can be complicated by co-existing HIV infection. Similarly, HIV often occurs concomitantly with other sexually transmitted infections (STI) and/or in association with alcohol, tobacco, and drug misuse, violence and trauma, and mental illness. Further research will be supported to better understand and address all of these co-occurring conditions.

Effective cART has ushered in a new era for the HIV epidemic. PWH can now achieve nearly normal lifespans, but are more likely to suffer from multiple, chronic comorbidities, coinfections, and complications resulting from virus exposure, long-term HIV disease, immune dysfunction, and/or cART 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. The overlapping etiologies and

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

While, traditionally, most ICO initiatives focus on diseases that fall within a specific ICO's mission, OAR will continue to encourage and support opportunities that will engage multiple ICOs to target the interrelationship among multiple comorbidities, co-infections that exacerbate prognosis and burden of disease, and the overall impact of HIV infection.

Budget Policy: The FY 2021 President's Budget request to address HIV-associated comorbidities, coinfections, and complications (CCCs) is \$501.6 million, a decrease of \$41.9 million or 7.7 percent compared to the FY 2020 Enacted level.

Cross-Cutting Areas

HIV epidemics often result from and provide a lens on social inequalities, stigma and discrimination, and health disparities that reflect factors such as sex, gender, race, ethnicity, socioeconomic status, age, sexual orientation and behavior, substance use behavior, and geographic location. NIH will continue to support research to better understand the social determinants of health – to improve HIV testing, engagement, 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.

To maximize efficiencies and investments toward reaching global HIV pandemic control, NIH will support implementation science that includes purposeful blending of known and new methodologies of translational research, clinical effectiveness, and effective scale-up.

To ensure that the priority areas of HIV science are addressed with novel, innovative, and culturally responsive approaches, NIH will augment its commitment to the development of the next generation of HIV researchers, particularly those from underrepresented populations and institutions, by providing support for human resources and infrastructure.

Moving forward, NIH will continue to leverage advances in big data science, combine data sets from multiple cohorts, and utilize novel clinical trial designs to move the field forward across the NIH priorities for HIV and HIV-related research.

Budget Policy: The FY 2021 President's Budget request to address cross-cutting areas is \$1,157.3 million, a decrease of \$74.7 million or 6.1 percent compared to the FY 2020 Enacted level.

Programs and Activities to Support NIH's Highest Scientific Priorities

New NIH-Wide (and HHS-Wide) Initiatives

As stated earlier, the NIH HIV/AIDS Research Program is strategically aligned with the goals and timelines of three closely related domestic plans: NHAS, NVHAP, and EHE. OAR will

collaborate with its partners across NIH and HHS to ensure that the goals of the NIH HIV/AIDS Research Program complement and enhance these activities.

The four goals of the current NHAS are 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.¹⁵⁹ The OAR is actively engaged with the HHS Steering Committee in developing the next five-year (FY 2021–2025) NHAS strategy. Concurrent with the development of the updated NHAS, the NVHAP is being updated for FY 2021–2025 and aligned with the NHAS. The four goals of the current NVHAP are to: (1) prevent new viral hepatitis infections; (2) reduce death and improve the health of people living with viral hepatitis; (3) reduce viral hepatitis health disparities; and (4) coordinate, monitor, and report on implementation of viral hepatitis activities.¹⁶⁰

The EHE initiative, first proposed in the President’s 2020 Budget and announced during the President’s State of the Union address in February 2019, aims to end the domestic HIV epidemic by 2030. To meet the goals of reducing new infections in the United States by 75 percent within five years, and then by 90 percent within 10 years, HHS will leverage critical scientific advances in HIV prevention, diagnosis, treatment, and care by coordinating the highly successful programs, resources, and infrastructure of the Centers for Disease Control and Prevention (CDC), NIH, Health Resources and Services Administration (HRSA), Substance Abuse and Mental Health Services Administration (SAMHSA), and Indian Health Service (IHS). The initiative is focused on geographic and demographic hotspots in 19 states, Washington, DC, and Puerto Rico, as well as in 7 states with a disproportionate occurrence of HIV in rural areas, where the majority of the new HIV cases are reported.¹⁶¹

The multi-year program will increase expertise, technology, and resources needed to end the HIV epidemic in the United States. The initiative has four pillars – (1) diagnose all people with HIV as early as possible after infection; (2) treat the infection rapidly and effectively to achieve sustained viral suppression; (3) protect people at risk for HIV using potent and proven prevention interventions, including pre-exposure prophylaxis (PrEP); and (4) respond rapidly to detect and respond to growing HIV clusters and prevent new infections. Activities related to these will be implemented across the entire United States within 10 years. Without this EHE initiative, new infections will continue to increase, costing more lives and the U.S. government more than \$200 billion in HIV-associated direct lifetime medical costs. NIH’s Centers for AIDS Research are the first step to increase research’s best approaches in different communities to inform HHS partners based on state-of-the-art biomedical research findings, and by collecting and disseminating data on the effectiveness of approaches used. The FY 2021 budget includes an additional \$10 million in funding, for a total of \$16 million, to leverage the CFAR’s pilot data to design and evaluate effective, sustainable systems for the implementation of prevention and treatment interventions, with a focus on implementing strategies at scale that will be the most effective.

Conclusion

¹⁵⁹ www.hiv.gov/federal-response/national-hiv-aids-strategy/nhas-update

¹⁶⁰ www.hhs.gov/hepatitis/viral-hepatitis-action-plan/index.html

¹⁶¹ Fauci, et. al., Ending the HIV Epidemic – A Plan for the United States; JAMA 2019; 321:844-845

The HIV/AIDS research investment from the NIH continues to produce significant groundbreaking scientific advances, unprecedented opportunities, and exciting new challenges. NIH's leadership, commitment and dedication to strategically allocate funds to the highest research priorities are essential to successfully bring an end to the HIV/AIDS pandemic and the continuance to improve the quality of life for PWH. OAR will continue to coordinate HIV/AIDS efforts across all ICOs receiving HIV funding to make the most of NIH's and the public's investments.