DEPARTMENT of HEALTH and HUMAN SERVICES

FISCAL YEAR 2020

NATIONAL INSTITUTES OF HEALTH—Volume 1

TAB: OFFICE OF AIDS RESEARCH

Justification of Estimates for Appropriations Committees

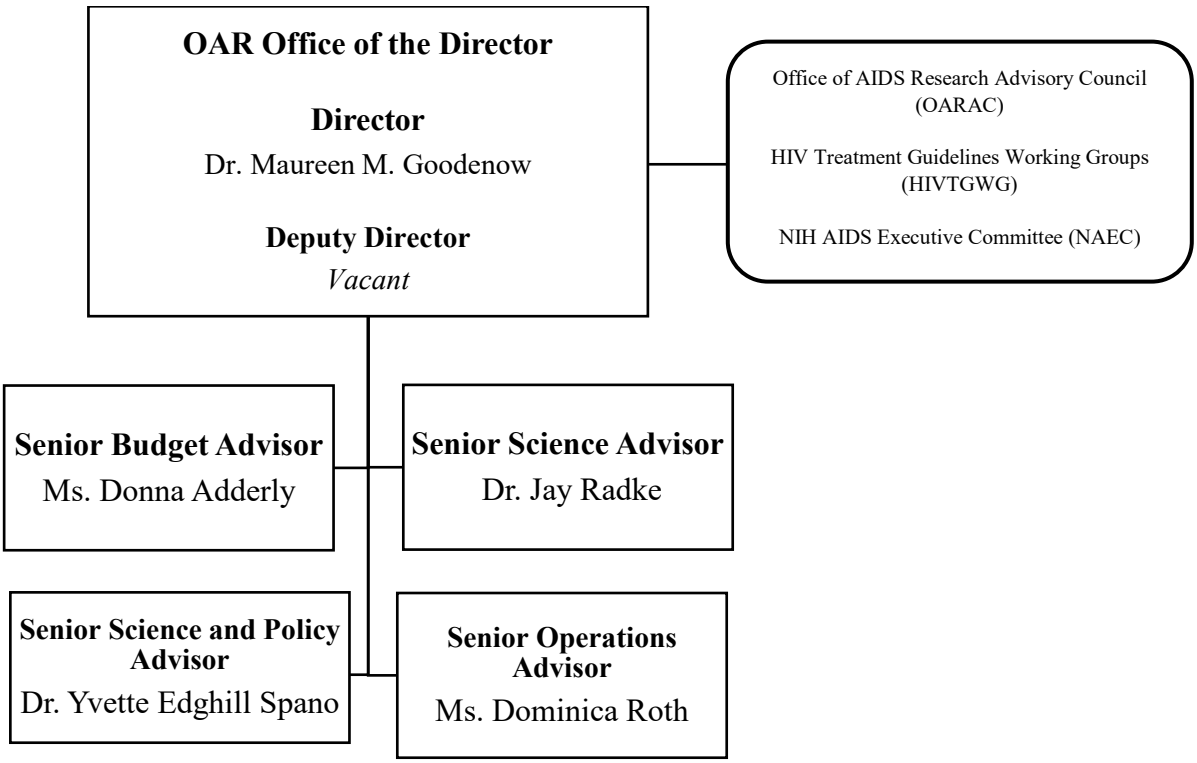
NIH HIV/AIDS RESEARCH BUDGET

FY 2020 Budget — Page No.

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 2020 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 and Center
(Dollars in Thousands)

Institute / Center	FY 2018 Actual [1]	FY 2019 Enacted Level	FY 2020 President's Budget	FY 2020 +/- FY 2019
NCI	$241,234	$244,853	$210,769	-$34,084
NHLBI	76,543	77,691	66,876	-10,815
NIDCR	18,015	18,285	15,740	-2,545
NIDDK	30,119	30,643	26,378	-4,265
NINDS	42,888	43,541	37,480	-6,061
NIAID	1,684,054	1,713,305	1,474,813	-238,492
NIGMS	52,484	53,271	45,856	-7,415
NICHD	142,421	144,897	124,727	-20,170
NEI	1,153	1,170	1,007	-163
NIEHS	5,342	5,422	4,667	-755
NIA	12,973	13,168	11,335	-1,833
NIAMS	4,576	4,656	4,008	-648
NIDCD	1,878	1,906	1,641	-265
NIMH	170,132	173,009	148,926	-24,083
NIDA	269,765	273,811	235,697	-38,114
NIAAA	28,597	29,026	24,986	-4,040
NINR	12,180	12,363	10,642	-1,721
NHGRI	3,693	3,748	3,226	-522
NIBIB	837	852	733	-119
NIMHD	22,825	23,167	19,942	-3,225
NCCIH	611	620	534	-86
FIC	23,884	24,242	20,868	-3,374
NLM	8,822	8,954	7,708	-1,246
OD				
OAR	62,256	63,190	54,394	-8,796
ORIP	78,099	79,271	68,236	-11,035
Subtotal, OD	140,355	142,461	122,630	-19,831
TOTAL, NIH	**$2,995,381**	**$3,045,061**	**$2,621,189**	**-$423,872**

[1] Reflects effects of Secretary's transfer.

Budget Authority by Mechanism

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

MECHANISM	FY 2018 Actual [2]		FY 2019 Enacted Level		FY 2020 President's Budget		FY 2020 +/- FY 2019	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,487	$1,466,571	1,546	$1,424,857	1,514	$1,262,979	-32	-$161,878
Administrative Supplements	*(94)*	45,765	*(48)*	5,768	*(40)*	4,092	*-8*	-1,676
Competing	472	240,604	435	317,830	361	221,729	-74	-96,101
Subtotal, RPGs	1,959	$1,752,940	1,981	$1,748,455	1,875	$1,488,800	-106	-$259,655
SBIR/STTR	37	20,165	29	20,800	29	17,890	0	-2,910
Research Project Grants	1,996	$1,773,105	2,010	$1,769,255	1,904	$1,506,690	-106	-$262,565
Research Centers:								
Specialized/Comprehensive	57	$114,936	69	$112,647	55	$102,525	-14	-$10,122
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	21	69,860	21	70,940	19	62,725	-2	-8,215
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	78	$184,796	90	$183,587	74	$165,250	-16	-$18,337
Other Research:								
Research Careers	265	$44,881	271	$46,158	221	$38,955	-50	-$7,203
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	6	10,722	0	5,275	0	3,000	0	-2,275
Biomedical Research Support	11	615	11	627	10	600	-1	-27
Minority Biomedical Research Support	1	375	0	0	0	0	0	0
Other	133	53,678	135	56,097	121	49,527	-14	-6,570
Other Research	416	$110,271	417	$108,157	352	$92,082	-65	-$16,075
Total Research Grants	2,490	$2,068,172	2,517	$2,060,999	2,330	$1,764,022	-187	-$296,977
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	85	$3,781	74	$3,390	66	$2,950	-8	-$440
Institutional Awards	277	15,736	246	14,685	217	12,836	-29	-1,849
Total Research Training	362	$19,517	320	$18,075	283	$15,786	-37	-$2,289
Research & Develop. Contracts	71	$334,807	91	$379,506	89	$327,802	-2	-$51,704
(SBIR/STTR) (non-add)	*(7)*	*(5,773)*	*(9)*	*(9,767)*	*(8)*	*(8,607)*	*-1*	*-1,160*
Intramural Research		$357,024		$364,115		$315,290		-$48,825
Res. Management and Support		153,605		159,176		143,895		-15,281
Res. Management & Support (SBIR Admin) (non-add)								
Office of the Director - Appropriation [3]		*140,355*		*141,289*		*122,630*		*-18,659*
Office of the Director - Other		62,256		63,190		54,394		-8,796
ORIP (non-add) [3]		*78,099*		*78,099*		*68,236*		*-9,863*
Total, NIH Discretionary B.A.		**$2,995,381**		**$3,045,061**		**$2,621,189**		**-423,872**

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

[2] Reflects effects of Secretary's transfer.

[3] 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)

Overarching Priorities	FY 2016 Actual	FY 2017 Actual	FY 2018 Actual [1]	FY 2019 Enacted Level	FY 2020 President's Budget	FY 2020 +/- FY 2019
Reducing Incidence of HIV/AIDS	$732,003	$687,495	$714,553	$741,203	$634,517	-$106,686
Next Generation HIV Therapies	360,085	362,820	364,484	369,680	322,611	-$47,069
Research Toward a Cure [2]	108,337	170,375	175,757	190,735	159,384	-$31,351
HIV-associated Comorbidities, Coinfections, and Complications	614,090	556,608	517,884	537,435	469,998	-$67,437
Crosscutting	1,185,546	1,222,763	1,222,703	1,206,008	1,034,679	-$171,329
Total	**$3,000,061**	**$3,000,061**	**$2,995,381**	**$3,045,061**	**$2,621,189**	**-$423,872**

[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. The FY 2016 amount is a comparable budget figure.

Justification of Budget Request

Office of AIDS Research
NIH AIDS Research Budget Justification
(see also: OAR section in Office of the Director/DPCPSI)

Budget Authority (BA):

FY 2018 Actual	FY 2019 Enacted Level	FY 2020 President's Budget	FY 2020+/- FY 2019
$2,995,381,000	$3,045,061,000	$2,621,189,000	-$423,872,000

DIRECTOR'S OVERVIEW

HIV crosses nearly every area of medicine, public health, and scientific investigation; thus, the National Institutes of Health's (NIH) response to the HIV pandemic requires a comprehensive, multidisciplinary, and integrative global research program that traverses the boundaries of nearly every Institute, Center, and Office (ICO). 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.** OAR coordinates the scientific, budgetary, legislative, and policy components of NIH HIV/AIDS research.
- **Establish research priorities.** OAR works across the NIH and with the scientific and HIV communities to establish the scientific research priorities for the global fight against HIV.
- **Develop the strategic plan for HIV research.** OAR produces the *NIH Strategic Plan for HIV and HIV-Related Research,* which identifies research priorities for NIH-funded intramural and extramural research.
- **Ensure that funds are invested in the areas of highest scientific priority.** Based on the strategic plan, OAR plans and evaluates the NIH-wide research portfolio. OAR identifies opportunities and addresses gaps to guide the HIV research agenda.
- **Address emerging needs.** OAR convenes stakeholders, encourages collaboration, and catalyzes innovation to address emerging scientific and public health challenges.

Groundbreaking Accomplishments with Unprecedented Scientific Opportunities

The NIH-wide HIV research program has achieved unprecedented progress against the global HIV pandemic. Since HIV/AIDS was discovered more than three decades ago, HIV has been transformed from a fatal condition to a manageable chronic illness. Such a remarkable achievement is due in large part to NIH's significant investments in scientific research, which continue to produce groundbreaking discoveries and advances in our understanding of basic virology, human immunology, HIV pathogenesis, and socio-behavioral dynamics. The advances

have led to the development of safe and effective antiretroviral therapies (ART), improved systems of wellness and care, and novel intervention strategies to prevent HIV acquisition and transmission.

Coordinated NIH-wide HIV Research Program and Priority Setting Review

Although significant progress has been made, the HIV pandemic continues to spread, representing a serious global public health threat across the lifespan. To date, 35 million people have died because of HIV. Currently, there are 1.1 million people with HIV (PWH) in the United States and 37 million PWH globally.[1, 2] In 2017, 1.8 million people worldwide became newly infected with HIV.[2] Continued investment in the NIH-wide HIV research program is essential to sustain the accomplishments already made and secure future advances to prevent the spread of HIV; improve health outcomes for persons with, at risk for, or affected by HIV; and ultimately to find a cure for HIV.

The Budget is proposing a once-in-a-generation opportunity to eliminate new HIV infections in our nation. *Ending the HIV Epidemic: A Plan for America* will work to reduce new infections by 75 percent in the next five years and by 90 percent in the next ten years, averting more than 250,000 HIV infections in that span. The multi-year program will infuse 48 counties, Washington, D.C., San Juan, Puerto Rico, as well as 7 states that have a substantial rural HIV burden with the additional expertise, technology, and resources needed to end the HIV epidemic in the United States. HHS's four strategies – diagnose, treat, protect, and respond – will be implemented across the entire U.S. within 10 years. Without this new intervention, new infections will continue and could increase, costing more lives and the U.S. government more than $200 billion in direct lifetime medical costs for HIV prevention and medication.

NIH-funded research has supported development of the science and tools that make the ambitious goals of this initiative possible. NIH will inform HHS partners in this initiative on best practices, based on state-of-the-art biomedical research findings, and by collecting data on the effectiveness of approaches used in this initiative.

To ensure that essential research dollars are invested strategically and effectively, OAR has established comprehensive planning, budgeting, and portfolio analysis processes to identify the highest priority areas of scientific research necessary to end the HIV pandemic and to facilitate maximum return on NIH's investment.

The strategic planning and budget process coordinated by OAR allocates NIH research funds for:

- NIH-wide HIV research agenda aligned with the highest HIV research priorities;
- Initiatives that address HIV research gaps and emerging scientific opportunities that require focused attention;
- Cross-Institute activities and collaborations to catalyze integrative scientific research, enhance discovery, leverage resources, and minimize duplication; and

[1] "Basic Statistics," Centers for Disease Control and Prevention, accessed October 17, 2018, www.cdc.gov/hiv/basics/statistics.html.
[2] "Global HIV & AIDS statistics — 2018 fact sheet," UNAIDS, accessed October 17, 2018, www.unaids.org/en/resources/fact-sheet.

- Basic science to accelerate scientific discoveries into the next frontier of clinical and public health applications.

Overall Budget Policy: The FY 2020 President's Budget request for the NIH-wide HIV/AIDS research program is $2,621.2 million, a decrease of $423.9 million or 13.9 percent compared to the FY 2019 Enacted level. The FY 2020 budget includes $6 million for NIH to support the President's Ending the HIV Epidemic Initiative to end HIV transmission in the United States by 2030. This will be accomplished by geographic concentration of efforts and utilizing significant recent research developments focused at reducing new infections, including pre-exposure prophylaxis (PrEP) and treatment as prevention. NIH-sponsored Centers for AIDS Research (CFARs) will inform HHS partners on evidence-based best practices to expand existing prevention and treatment resources and evaluate the effectiveness of approaches used in this initiative. In the long term, development of a safe, effective, practical, and affordable HIV/AIDS vaccine is our best hope to end the HIV pandemic. 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.

Program Descriptions

OAR manages the NIH-wide HIV program and allocates funds to the ICOs to advance the HIV research agenda, ensuring that funds are aligned with the highest priorities of HIV research to:

- Reduce the incidence of HIV.
- Develop next-generation HIV therapies.
- Promote research toward an HIV cure.
- Address HIV-associated comorbidities, coinfections, and complications.
- Advance the critical framework of crosscutting research areas to combat the HIV pandemic.

The overarching research priorities identified within the NIH-wide budget, as well as selected programs that reflect the NIH Director's key themes, are described below.

Reduce the incidence of HIV. Preventing new infections is crucial to ending the HIV pandemic. An effective HIV vaccine would be a groundbreaking advancement essential to preventing new infections and controlling the pandemic. Several major HIV vaccine efficacy studies are testing different vaccine candidates, with results anticipated by 2022. Candidate vaccines are built on the scientific advances of the past 10 years and showed promise in small, early phase clinical trials. Currently, there is a robust pipeline of products in assessment for immunogenicity in humans, with more than 30 clinical studies in various phases of testing.

In parallel with vaccine-based prevention strategies, antibody-mediated protection (AMP) studies are testing a new alternative for prevention in HIV-negative individuals with studies to determine whether periodic infusions or injections of certain broadly neutralizing antibodies (bNAbs) can prevent HIV acquisition in approximately 5,000 PWH in multiple countries. Although the studies represent advances toward treatment and prevention of HIV, further research is needed to expand upon these results by extending the half-life of the antibodies, developing more potent antibodies and vector-based bNAbs for HIV prevention, and identifying bNAb combinations that can suppress HIV long-term in people whose HIV sensitivity to bNAbs is unknown.

Basic, clinical, and translational research to evaluate the human immune response to vaccines remains a high priority. Advances in imaging technologies have led to the development of vaccine candidates that more closely mimic HIV structural components and could be the foundation of improved vaccines to induce protective immunity. In preparation for clinical trials, NIH has strategically invested in expanding manufacturing capabilities, such as enhancing automation processes, to meet current and future research demands.

While developing vaccine strategies, the HIV prevention field has had considerable success in developing novel, global nonvaccine prevention strategies. NIH-sponsored studies led to the development of treatments and strategies to prevent the acquisition and transmission of HIV, including pre-exposure prophylaxis (PrEP), which can reduce the risk of sexual transmission of HIV by as much as 92 percent, and post-exposure prophylaxis (PEP), which can protect individuals who have had a one-time exposure to HIV. Research discoveries found that treatment as prevention (TasP) with ART significantly reduces transmission of HIV during pregnancy and breast-feeding and enables PWH to achieve undetectable viral loads, thereby improving their health and effectively reducing the risk of HIV transmission to zero.

One long-standing NIH goal is to develop multipurpose prevention technologies (MPTs), including microbicides and intravaginal rings, to protect women and men from acquiring HIV through sex. Such methods will offer particular advantages for women who may not have other options for protection. Several clinical trials are currently underway to test the effectiveness of a variety of MPTs.

Budget Policy: The FY 2020 President's Budget request to reduce the incidence of HIV is $634.5 million, a decrease of $106.7 million or 14.4 percent compared to the FY 2019 Enacted level.

Develop next-generation HIV therapies. NIH-sponsored research has led to the development of combination antiretroviral therapy (cART), which has significantly improved the health outcomes of PWH. Consistent use of cART reduces damage to the immune system of PWH by

suppressing viral replication, delaying the development of viral resistance, and leading to undetectable viral loads, thus preventing sexual transmission of HIV to an uninfected partner. However, even with simplified daily one-pill treatment regimens capable of suppressing HIV only 22 million of the approximately 37 million PWH worldwide currently receive treatment.[3] Barriers to receiving and adhering to cART include treatment availability, the high cost, the need for daily treatment, the possibility of 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 PWH across race, ethnicity, sex and gender, age, and socioeconomic status.

NIH has allocated funding for the development of new long-acting medications with fewer side effects and complications, including monthly injections of continuously released cART, anti-HIV antibody infusions, and a 6-month cART implant. Simpler treatment schedules compared to current daily medication regimens are expected to improve adherence. Parallel research is focusing on development of novel delivery and testing technologies, including sensitive, rapid point-of-care or self-administered viral load testing, to provide increased ease of monitoring for enhanced prevention of HIV transmission and improved treatment adherence leading to viral suppression. An estimated 10 percent of people receiving cART worldwide are resistant to at least one drug.[4] Immune-based treatments may reverse the weakening of the immune system that occurs even when the virus is suppressed.

Budget Policy: The FY 2020 President's Budget request to develop next-generation HIV therapies is $322.6 million, a decrease of $47.1 million or 12.7 percent compared to the FY 2019 Enacted level.

Promote research toward a HIV cure. Latent HIV reservoirs, DNA coding for HIV that persists in PWH despite the use of cART, present a significant challenge to finding a cure for HIV. 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 either sustained, ART-free viral remission, also known as a functional cure, or viral eradication, and leading to 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. The ultimate goal is to permanently eradicate HIV with cure interventions and

[3] "Global HIV & AIDS statistics — 2018 fact sheet," UNAIDS, accessed October 17, 2018, www.unaids.org/en/resources/fact-sheet.
[4] World Health Organization. 2017. *HIV Drug Resistance Report 2017.* Available at apps.who.int/iris/bitstream/handle/10665/255896/9789241512831-eng.pdf;jsessionid=3A32877D555CB649B1A56DF89DD72C99?sequence=1.

treatments that are at least as safe, effective, and available for widespread use as current cART regimens.

Budget Policy: The FY 2020 President's Budget request to promote research toward a HIV cure is $159.4 million, a decrease of $31.4 million or 16.4 percent compared to the FY 2019 Enacted level.

Address HIV-associated comorbidities, coinfections, and complications (CCCs). HIV is associated with complex health issues and although the use of cART results in significant improvement in PWH, HIV-associated CCCs continue to challenge the clinical management of disease conditions across the lifespan. NIH invests in basic, translational, and clinical research to understand how the mechanisms underlying HIV infection, such as immune dysfunction and inflammation, may increase the risk for cardiovascular disease, certain cancers, neurologic and cognitive disorders, mental illness, substance use disorders, metabolic and bone abnormalities, accelerated aging, and increased mortality. Adherence to cART regimens not only slows the progression to AIDS, but also reduces HIV-related concomitant conditions or comorbidities, such as cardiovascular disease, kidney disease, and cancer, as well as infections and other complications, in PWH.

Research is needed to differentiate between complications related to aging, immune dysfunction, long-term antiretroviral use, and HIV-associated disease and/or co-occurring chronic illnesses, such as diabetes or hypertension. To that end, it is necessary to understand interactions between antiretroviral treatment and medications that are used to treat comorbidities and to develop novel therapies for HIV and CCCs that minimize side effects and toxicities. For example, neuroimaging is being developed to detect and measure changes in the brain more accurately. Advances in brain imaging promise powerful ways to noninvasively assess the status of the brain over time in PWH and may enable the use of observed changes in the brain as endpoints for clinical trials.[5] The development and testing of low-cost, rapid techniques that require minimal infrastructure to prevent, diagnose, and monitor HIV-associated CCCs is a particular need in resource-limited settings.

Due to the integrative nature of such diseases, research to address CCCs is not only important for PWH but promises to inform research strategies for other key public health challenges that affect the general population, such as cancer, heart disease, and neurologic disorders.

Budget Policy: The FY 2020 President's Budget request to address HIV-associated comorbidities, coinfections, and complications (CCCs) is $470.0 million, a decrease of $67.4 million or 12.5 percent compared to the FY 2019 Enacted level.

Advance the critical framework of crosscutting areas of research to end the HIV pandemic. A significant proportion of HIV research has relevance to not just one, but all five overarching NIH HIV priority research areas. The crosscutting research areas contribute to fundamental knowledge that advances HIV research.

[5] Clifford, D.B. "HIV Associated Neurocognitive Disorder," *Current Opinion in Infectious Diseases* 30, no. 1 (February 2017): 117–122. Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC5382956.

- **Basic science research** provides the underlying foundation for all HIV research areas and includes studies on HIV virology, transmission, susceptibility, and investigations of HIV-related immunology and host-viral interactions. Research on the viral, cellular, molecular, genetic, and immune mechanisms of pathogenesis is essential to better understand HIV acquisition, prevention, and disease progression; the mechanisms leading to the pathogenesis of HIV-associated CCCs; and a potential cure. Efforts must be made to ensure linkages to NIH-supported HIV cohorts, biorepositories, and databases and to integrate animal studies, particularly studies using nonhuman primates, into the discovery pipeline. For example, characterizing similarities and differences in the immune response by using animal models to develop cross-reactive antibodies between species may provide promising new treatment options.

  NIH partners with industry, academia, and other research organizations to support a broad array of basic and clinical research to develop cutting-edge diagnostic technologies that will quickly identify infection, measure treatment efficacy, and determine drug resistance. NIH focuses on behavioral social science and implementation research to develop innovative strategies to increase treatment uptake and engage PWH in their own care to prevent transmission, achieve viral suppression, and improve health.

- **Epidemiology research** and epidemiologic methods provide accurate, real-time information to understand the changing demographics of the HIV pandemic. NIH invests in research on the epidemiology of HIV drug resistance to inform treatment strategies and disease outcomes. Understanding the causes, patterns, and social phenomena that have led to higher rates of HIV infection in the southern and midwestern United States is key to rapidly identifying and preventing HIV outbreaks, and with a surging opioid epidemic, methodologies to detect infection clusters early and prevent future outbreaks is a priority. The use of big-data science, machine learning, modeling, registries, phylodynamics, and other epidemiologic approaches will determine where research should be conducted, inform prevention and treatment approaches, and contribute to early detection and improved outcomes across the HIV prevention and care continuum.

- **Behavioral and Social Sciences Research (BSSR)** ranges from basic to applied research, with an emphasis on behavioral interventions. Research systematically examines the behavioral, social, cultural, environmental, and organizational factors, as well as individual and interpersonal dynamics and community beliefs, to provide essential insights to factors that influence the transmission, prevention, treatment, and management of HIV. Results are essential to understand the most effective strategies to engage individuals in treatments or products to prevent transmission or maximize treatment effectiveness. NIH-supported studies have helped to reduce HIV-related stigma, improve medication adherence, increase retention in the HIV prevention and care continuums, and develop innovative HIV prevention/treatment technologies. For example, a recent study designed to facilitate treatment for HIV and substance abuse was associated with a 50 percent reduction in mortality when PWH who also inject illicit drugs adhered to an intervention consisting of psychosocial counseling and guidance in navigating the health care system. Other studies are improving the application of social network analyses, leading to the creation of socioculturally-specific interventions, and testing other key elements and integrative approaches to prevent and treat HIV infection.

- **Implementation science research** is needed to develop approaches to support the uptake of interventions developed within the five overarching priorities and to identify factors that are barriers to or can help facilitate effective treatment, as well as health care programming and policy development. NIH has an increasing focus on studying and integrating evidence-based health interventions and strategies into clinical and community settings to improve patient outcomes and public health. Further research is needed to define approaches and models for scaling up comprehensive, integrated interventions for expanding testing, prevention, and treatments that optimize adherence, retention, and health outcomes in real-world settings.

- **Health disparities research** is essential to better understand and address how complex biological, behavioral, structural, and sociocultural factors that may be linked to race/ethnicity, sex and gender, age, and geography lead to disparities in HIV prevention, incidence, treatment, and health outcomes. NIH seeks to define and address the factors that contribute to health disparities and worsen health outcomes among key populations disproportionately affected by the pandemic and to develop effective interventions to eliminate disparities.

- **Training, infrastructure, and capacity building (TICB)** are crucial to the development of the next generation of HIV researchers, both in the United States and globally. TICB includes building laboratories, developing education systems, and designing novel multidisciplinary approaches to mentoring and training a broad and diverse scientific workforce. Fundamental HIV-related research training will provide support to the field in general and to achieving the specific research priorities to end the HIV pandemic and improve the health of PWH. NIH supports opportunities for early exposure to and increased awareness of careers in the biomedical, behavioral, and social sciences, including HIV research, particularly for students from underrepresented communities and disadvantaged backgrounds.

- **Information dissemination** of research findings to diverse communities and stakeholders, including patients, clinicians, researchers, and the public, remains a critical component of NIH-supported HIV research and is essential to the prevention and treatment of HIV. The creation and incorporation of new communication strategies and state-of-the-art technologies to improve access to hard-to-reach, underserved, and underrepresented populations within diverse settings and to strengthen the broad dissemination of HIV research findings is a priority. Because social media use has become deeply entrenched in most industrialized societies and among all populations, the development of HIV-preventive interventions on social media platforms to reach such populations as adolescents and young adults, men who have sex with men, and transgender populations would be a valuable tool in curbing the rates of new infections.

Budget Policy: The FY 2020 President's Budget request to advance the critical framework of crosscutting areas of research to end the HIV pandemic is $1,034.7 million, a decrease of $171.3 million or 14.2 percent compared to the FY 2019 Enacted level.

Programs and Activities to Support NIH's Highest Scientific Priorities

In addition to the five overarching HIV research priorities, OAR allocates funds to support select forward-thinking initiatives and innovations that advance the NIH-wide HIV research agenda. The following activities reinforce the key themes established by the NIH Director to speed the pace of research and improve the translation of scientific discovery into new treatment approaches:

- **Invest in transformational tools and technologies.** OAR invests in innovative information technology tools to perform analyses of the NIH-wide HIV research portfolio to identify research gaps and emerging opportunities, as well as facilitate budget projection. OAR has integrated new innovative data systems and tools, such as the AIDS Budget System and AIDS Portfolio Review System, to enhance the effectiveness of the budget development and review process.

- **Leverage existing resources to support interdisciplinary collaborations to accelerate research innovations and discoveries.** OAR is pursuing innovative approaches to leverage resources for funding new and existing HIV research. Cost-sharing initiatives between ICOs and OAR maximize the use of NIH's research dollars and promote interdisciplinary and integrative collaborations to accelerate research innovations and discoveries that impact the health outcomes of PWH. Collaborations include the Centers for AIDS Research (CFAR) to support multidisciplinary HIV research at NIH-funded research centers of academic institutions across the United States. The CFAR partnership with the Claude D. Pepper Older American Independence Centers of the National Institute on Aging (NIA) is generating interdisciplinary research on aging with HIV. OAR's commitment to collaboration includes bringing together research on HIV-related and non-HIV-related comorbidities/coinfections through the recent renewal and expansion of two long-standing longitudinal research studies—the Multicenter AIDS Cohort Study (MACS) and the Women's Interagency HIV Study (WIHS)—into one combined study. The combined study, supported through 15 ICOs, places greater emphasis on HIV-associated comorbidities, especially conditions linked to aging, and is an unparalleled opportunity for investigators to study the effects of HIV infection and aging. OAR is partnering with the NIA to further explore HIV-associated neurocognitive disorders, HIV persistence in the central nervous system, and the added impact of aging. Research awards for the OAR/NIA Funding Opportunity Announcement (FOA) on the Pathogenesis of Age-Related HIV Neurodegeneration (RFA-AG-18-023) were announced in September 2018 and will contribute to the development of a cadre of interdisciplinary research.

- **Build on basic science to foster translational and clinical research to improve health.** NIH will continue to invest in basic research to understand the fundamental mechanisms that drive HIV infection and the development of related diseases and conditions. Advances in basic and clinical research have led to a better understanding of the relationship between HIV and associated comorbidities, including AIDS-defining and non-AIDS-defining cancers, and of the potential impact of HIV treatment on such conditions. Clarifying the biological role of HIV and its associated immune dysfunction in the mechanisms that lead to the development of cancers will require continued research efforts. It is critical to investigate the complications of treating cancers in PWH to improve treatment outcomes across the lifespan,

minimize adverse events, and decrease morbidity and mortality in PWH with cancer. Developing improved therapies, including immunotherapy for HIV-associated cancers, continues to be a top scientific priority. NIH will continue funding basic, translational, and clinical research to develop promising vaccine candidates, new diagnostic tools, and new drugs and formulation technologies to address the critical needs of clinicians and public health professionals engaged in the fight against HIV.

- **Support urgent and emerging scientific needs.** OAR supports urgent and/or emerging scientific needs, such as providing supplemental funding to evaluate the short- and long-term effects of dolutegravir (an ART medication) and other integrase inhibitors after recent data suggested a potential relationship between *in utero* exposure and neural tube defects in infants born to mothers on treatment. In addition, OAR supports new high-priority projects with funds recovered from the annual review of the NIH-wide HIV research portfolio.

- **Explore the next frontier.** OAR sets the direction of HIV research through NIH-wide collaborations and strategic partnerships among stakeholders. The Office works in partnership with the ICOs through the NIH AIDS Executive Committee to identify NIH-wide HIV research priorities, scientific gaps and opportunities in emerging areas of research, all of which guide the development of the *NIH Strategic Plan for HIV and HIV-related Research* and the annual NIH HIV budget.

  NIH is undertaking new, complex challenges by enhancing strategic partnerships among stakeholders from the community, academia, and government to advance future HIV research. For example, OAR is collaborating with the National Institute of Biomedical Imaging and Bioengineering (NIBIB) and the National Institute of Allergy and Infectious Diseases (NIAID) to plan for an immuno-bioengineering funding opportunity targeting and integrating cross-disciplinary research involving immunologists, bioengineers, and other investigators to advance HIV vaccine research and development.

NIH will continue to support innovative preclinical, translational, and clinical studies of HIV treatment and cure interventions across the lifespan. Key scientific opportunities include transforming the vaccine field of research with a novel strategy to direct B cells to make antibodies that protect vaccinated individuals from acquiring HIV. Other opportunities include gene modification/gene silencing approaches, immuno-therapeutic agents (including monoclonal antibodies) and their derivatives, and cell modification–based interventions to boost or to direct the immune system against HIV. Novel technologies with the potential to enable accurate self-administered testing for viral replication will be sought as another key enabler of cure clinical trials. The ultimate goal is a cure intervention that is simple, safe, sustainable, and scalable.