

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

Trans-NIH AIDS Research Budget

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

Institute / Center	FY 2012 Actual	FY 2013 CR	FY 2014 President's Budget	FY 2014 +/- FY 2012
NCI	\$271,692	\$273,355	\$278,101	\$6,409
NHLBI	67,995	68,431	60,982	(7,013)
NIDCR	20,061	20,301	17,130	(2,931)
NIDDK	30,951	31,140	30,136	(815)
NINDS	46,857	47,144	47,229	372
NIAID	1,572,973	1,583,052	1,631,577	58,604
NIGMS	65,202	65,601	69,597	4,395
NICHD	144,924	146,189	152,923	7,999
NEI	8,902	8,956	-	(8,902)
NIEHS	5,338	5,371	5,122	(216)
NIA	5,632	5,666	5,888	256
NIAMS	4,925	4,955	5,455	530
NIDCD	1,877	1,888	1,888	11
NIMH	190,387	191,733	163,264	(27,123)
NIDA	319,292	321,347	332,286	12,994
NIAAA	28,380	28,554	29,378	998
NINR	12,642	12,719	12,809	167
NHGRI	7,130	7,174	7,120	(10)
NIBIB	3,699	3,722	1,287	(2,412)
NIMHD	20,446	20,571	21,331	885
NCCAM	1,610	1,620	1,610	0
NCATS	68,328	68,766	66,417	(1,911)
FIC	24,241	24,389	27,017	2,776
NLM	7,665	7,712	8,412	747
OD				
OAR	63,802	64,192	64,392	590
ORIP	79,844	80,333	80,365	521
Subtotal, OD	143,646	144,525	144,757	1,111
TOTAL, NIH	\$3,074,795	\$3,094,881	\$3,121,716	\$46,921

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

MECHANISM	FY 2012 Actual		FY 2013 CR		FY 2014 President's Budget		Change	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants:								
<u>Research Projects:</u>								
Noncompeting	1,774	\$1,339,694	1,664	\$1,265,302	1,660	\$988,601	-114	-\$351,093
Administrative Supplements ¹	<i>(107)</i>	<i>16,879</i>	<i>(88)</i>	<i>11,702</i>	<i>(84)</i>	<i>10,562</i>	<i>-(23)</i>	<i>-6,317</i>
Competing	549	281,093	743	370,323	778	682,001	229	400,908
Subtotal, RPGs	2,323	\$1,637,666	2,407	\$1,647,327	2,438	\$1,681,164	115	\$43,498
SBIR/STTR	79	38,750	79	39,831	77	40,401	-2	1,651
Research Project Grants	2,402	\$1,676,416	2,486	\$1,687,158	2,515	\$1,721,565	113	\$45,149
<u>Research Centers:</u>								
Specialized/Comprehensive	65	\$142,665	72	\$138,812	71	\$140,152	6	-\$2,513
Clinical Research	1	58,356	1	58,052	1	58,052	0	-304
Biotechnology	0	1,139	0	1,146	0	1,137	0	-2
Comparative Medicine	11	57,728	11	58,216	10	57,957	-1	229
Research Centers in Minority Institutions	14	14,455	14	14,562	11	14,564	-3	109
Research Centers	91	\$274,343	98	\$270,788	93	\$271,862	2	-\$2,481
<u>Other Research:</u>								
Research Careers	250	\$42,895	247	\$42,514	237	\$41,528	-13	-\$1,367
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	12	18,765	9	11,924	9	11,924	-3	-6,841
Biomedical Research Support	0	2,809	0	2,809	0	2,809	0	0
Minority Biomedical Research Support	2	399	2	399	2	399	0	0
Other	126	60,489	142	60,527	150	62,860	24	2,371
Other Research	390	\$125,357	400	\$118,173	398	\$119,520	8	-\$5,837
Total Research Grants	2,883	\$2,076,116	2,984	\$2,076,119	3,006	\$2,112,947	123	\$36,831
<u>Ruth L. Kirschstein Training Awards</u>	<u>FTTPs</u>		<u>FTTPs</u>		<u>FTTPs</u>			
Individual Awards	97	\$4,101	90	\$3,785	89	\$3,807	-8	-\$294
Institutional Awards	656	33,055	655	32,808	650	33,148	-6	93
Total Research Training	753	\$37,156	745	\$36,593	739	\$36,955	-14	-\$201
<u>Research & Development Contracts</u> <i>(SBIR/STTR)</i>	122 <i>(2)</i>	\$438,395 <i>(1,088)</i>	106 <i>(2)</i>	\$458,274 <i>(1,438)</i>	103 <i>(2)</i>	\$447,605 <i>(1,702)</i>	-19 <i>(0)</i>	\$9,210 <i>(614)</i>
<u>Intramural Research</u>		\$339,071		\$339,346		\$340,016		\$945
<u>Research Management and Support</u>		\$120,255		\$120,357		\$119,801		-\$454
<u>Office of the Director - Appropriation ¹</u>		<i>(143,646)</i>		<i>(144,525)</i>		<i>(144,757)</i>		<i>(1,111)</i>
<u>Office of the Director - Other ²</u>		63,802		64,192		64,392		590
<u>ORIP & SEPA ²</u>		<i>(79,844)</i>		<i>(80,333)</i>		<i>(80,365)</i>		<i>(521)</i>
Total, NIH Discretionary B.A.		\$3,074,795		\$3,094,881		\$3,121,716		\$46,921

¹ All numbers in italics and brackets are non-add.

² Number of grants and dollars for the Common Fund, ORIP and SEPA components of OD are distributed by mechanism and are noted here as a non-add. The Office of the Director - Appropriations also is noted as a non-add since these funds are accounted for under OD - Other.

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

Area of Emphasis	FY 2010 Actual	FY 2011 Actual	FY 2012 Actual	FY 2013 CR	FY 2014 President's Budget	FY 2014 +/- FY 2012
HIV Microbicides	\$143,162	\$120,982	\$129,919	\$134,627	\$133,800	\$3,881
Vaccines	534,972	548,834	556,613	560,962	574,966	18,353
Behavioral and Social Science	429,313	412,163	420,084	421,684	430,209	10,125
Etiology and Pathogenesis	744,649	730,978	668,244	674,697	693,851	25,607
Therapeutics						
<i>Therapeutics as Prevention</i>	67,734	65,064	56,561	58,126	66,026	9,465
<i>Drug Discovery, Development, and Treatment</i>	<u>617,257</u>	<u>615,475</u>	<u>650,059</u>	<u>659,261</u>	<u>651,168</u>	<u>1,109</u>
Total, Therapeutics	684,991	680,539	706,620	717,387	717,194	10,574
Natural History and Epidemiology	275,098	278,998	257,973	253,342	247,385	(10,588)
Training, Infrastructure, and Capacity Building	216,329	232,624	280,775	281,474	272,062	(8,713)
Information Dissemination	56,832	54,159	54,567	50,708	52,249	(2,318)
Total	\$3,085,346	\$3,059,277	\$3,074,795	\$3,094,881	\$3,121,716	\$46,921

THE GLOBAL AIDS EPIDEMIC

- The AIDS pandemic has devastating consequences around the world in virtually every sector of society.
- In 2011, 2.5 million [2.2 million–2.8 million] people were newly infected with HIV, a reduction of 20 percent since 2001.
- Around 330,000 [280,000–380,000] children were newly infected with HIV in 2011, a reduction of 24 percent in just two years—from 2009–2011.
- In 2011, more than 8 million people had access to antiretroviral therapy, an increase of 20 percent in just one year from 2010 to 2011.
- Approximately 1.7 million people [1.6 million–1.9 million] died from AIDS-related causes in 2011, a decline of 24 percent since the peak in 2005.
- There were 34.2 million [31.8 million–35.9 million] people living with HIV in 2011, more than ever before due to the life prolonging effects of antiretroviral therapy.
- TB remains the leading cause of death among people living with HIV.
- Young people aged between 15–24 years account for 40 percent of all new adult (15+) HIV infections.
- HIV is the leading cause of death of women of reproductive age:
 - An estimated 1.2 million [1.1 million–2.8 million] women and girls were newly infected with HIV in 2011.
 - Some 63 percent of all young people (15–24) living with HIV are young women.
 - Globally, young women 15–24 years old are most vulnerable to HIV infection, with infection rates twice as high as among men of the same age.
- In the U.S., CDC estimates that approximately 1.2 million people are HIV-infected, with approximately 50,000 new infections occurring each year.
- One in four people living with HIV infection in the U.S. is female. Two-thirds of HIV-infected women in the U.S. are African American; 15 percent are Hispanic/Latina.
- AIDS disproportionately affects racial and ethnic populations, women of color, young adults, and men who have sex with men.

Sources: CDC; UNAIDS Fact Sheet:

http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/201207_FactSheet_Global_en.pdf

Justification of Budget Request

Office Of AIDS Research Trans-NIH AIDS Research Budget Justification

Budget Authority (BA):

	FY 2012 Actual	FY 2013 CR	FY 2014 President's Budget	FY 2014+/- FY 2012
BA	\$3,074,795,000	\$3,094,881,000	\$3,121,716,000	+\$46,921,000

Director's Overview

Extraordinary NIH AIDS Research Accomplishments: In the three decades since AIDS was first reported, NIH has been the global leader in research to understand, prevent, diagnose, and treat HIV and its many related conditions. From the development of the first blood test for HIV infection and the discovery and clinical testing of the first effective therapies, through today's research to determine whether a vaccine, microbicide, or eventual cure for AIDS will one day be possible, NIH research has transformed HIV from a mysterious and uniformly fatal infection into one that can be accurately diagnosed and effectively managed with appropriate treatment. A recent study estimated that 14.4 million life years have been gained since 1995 by the use of AIDS therapies developed as a result of NIH-funded research. Recent scientific advances resulting from NIH-funded research represent a turning point for AIDS research. New avenues for discovery have been identified, providing possibilities for the development of new strategies to prevent, treat, and potentially cure HIV. NIH is leading global research efforts to capitalize on those advances, move science forward, and begin to turn the tide against this pandemic. Recent discoveries include:

- Development of new treatments for many HIV-associated coinfections, comorbidities, malignancies, and clinical manifestations;
- Development of new strategies for the prevention of mother-to-child transmission (MTCT), which have resulted in dramatic decreases in perinatal HIV in the U.S., where now fewer than 100 babies a year are born with HIV infection;
- Demonstration of the first proof of concept that a vaccine can prevent HIV infection and identification of potential immune markers for protection;
- Discovery of more than 20 potent human antibodies that can stop up to 95 percent of known global HIV strains from infecting human cells in the laboratory;
- Demonstration of the first proof-of-concept that a microbicide gel can prevent HIV transmission;
- Demonstration that the use of antiretroviral therapy by infected individuals can reduce HIV transmission to an uninfected partner dramatically;
- Demonstration of the feasibility of pre-exposure prophylaxis (PrEP), the use of antiretroviral treatment regimens by uninfected individuals to reduce their risk of HIV acquisition;

- Discovery that genetic variants may play a role in enabling some individuals, known as “elite controllers,” to control HIV infection without therapy;
- Critical basic science discoveries that continue to provide the foundation for novel research; and
- Advances in basic and treatment research aimed at eliminating viral reservoirs in the body that for the first time are leading scientists to design and conduct research aimed at a cure for HIV/AIDS.

Mission: The NIH AIDS research program that produced these critical accomplishments is coordinated and managed by the Office of AIDS Research (OAR), which functions as an “institute without walls” with responsibility for AIDS-related research supported by every NIH Institute and Center (IC). OAR coordinates the scientific, budgetary, and policy

The NIH Office of AIDS Research establishes a unified NIH AIDS research agenda through:

- An annual trans-NIH strategic planning process that identifies the highest scientific priorities and opportunities to address the changing epidemic
- Development of an annual trans-NIH budget, based on the Strategic Plan
- Ongoing trans-NIH coordination and management
- Facilitation and implementation of domestic and international AIDS research collaborations.

elements of the trans-NIH research program on AIDS and its wide spectrum of associated malignancies, co-infections, and clinical complications. Through its unique trans-NIH processes, OAR identifies the highest priority areas of scientific opportunity, enhances collaboration, minimizes duplication, and ensures that precious research dollars are invested effectively. The OAR identifies trans-NIH AIDS research program priorities and shifts resources across ICs and areas of science as needed to meet the changing epidemic and scientific opportunities.

Extraordinary Opportunities for FY 2014: The advances made by NIH investigators have opened doors for new and exciting research opportunities to answer key scientific questions that remain in the search for strategies to prevent and treat HIV infection both in the U.S. and around the world. These advances also represent the building blocks for the development of this Trans-NIH AIDS research budget. OAR will target and protect funding on research priorities including:

- **Today’s Basic Science for Tomorrow’s Breakthroughs:** Basic research that will underpin further development of critically needed *vaccines and microbicides*.
- **Encouraging New Investigators and New Ideas:** Innovative multi-disciplinary research and international collaborations to develop novel approaches and strategies to eliminate viral reservoirs that could lead toward *a cure for HIV*.
- **New Strategies for Disease Prevention:** Critical studies in the area of *therapeutics as a method to prevent infection*, including treatment to prevent HIV transmission; PrEP; a potential prevention strategy, known as “test and treat,” to determine whether a community-wide testing program with treatment can decrease the overall rate of new HIV infections; and improved strategies to prevent mother-to-child transmission. A key priority is to evaluate prevention interventions that can be used in combination in different populations, including adolescents and older individuals.
- **Improving Disease Outcomes:** Research to develop better, less toxic treatments and to investigate how genetic determinants, sex, gender, race, age, nutritional status, treatment

during pregnancy, and other factors interact to affect treatment success or failure and/or disease progression. Studies will address the increased incidence of malignancies, cardiovascular and metabolic complications, and premature aging associated with long-term HIV disease and antiretroviral treatment (ART).

- **Translational Sciences:** Research on the feasibility, effectiveness, and sustainability required to scale-up interventions from a structured behavioral or clinical study to a broader "real world" setting.

Overall Budget Policy: To address critical AIDS research priorities, the OAR FY 2014 President's Budget estimate for the trans-NIH AIDS research program is \$3,121.716 million, an increase of \$46.921 million and 1.5 percent above the FY 2012 Actual level. This FY 2014 request reflects several shifts of funds across ICs to address the many new and exciting scientific opportunities in AIDS research. These shifts reflect the scientific priorities identified in the annual trans-NIH strategic planning and budget process and address the evolving clinical profile of the epidemic, changing demographics, and most recent scientific advances. This amount includes the total trans-NIH support for intramural and extramural research for basic, clinical, behavioral, social science, and translational research on HIV/AIDS and the wide spectrum of AIDS-associated malignancies, opportunistic infections, co-infections, and clinical complications; as well as research management support; research centers; and training. In this budget request, OAR has provided increases to high priority basic research (etiology and pathogenesis) that provides the underlying foundation for all HIV research; development of vaccines and microbicides; and new and innovative approaches for research toward a cure. In order to provide those increases, OAR has reduced and redirected funds from natural history and epidemiology, therapeutic clinical trials, and training and infrastructure support.

Program Descriptions and Accomplishments

Trans-NIH Strategic Plan and Budget: The OAR trans-NIH planning process, involving both government and non-government experts, and representatives from community constituency groups results in the identification of overarching AIDS-research priorities and specific research objectives and strategies. OAR develops each IC's AIDS allocation based not on a formula, but on the scientific priorities and objectives of the annual Trans-NIH AIDS research strategic plan, taking into account the current scientific opportunities and the IC's capacity to absorb and expend resources for the most meritorious science. This process reduces redundancy, promotes harmonization, and assures cross-Institute collaboration to conduct and support research in domestic and international settings. Specific programmatic areas include:

HIV MICROBICIDES

A safe and effective microbicide will be an important asset to the HIV prevention tool kit. Microbicides are antimicrobial agents, including antiretroviral drugs and other products that could be applied topically or injected to prevent transmission of HIV and other sexually transmitted infections. Microbicides could be used alone or in combination with other

prevention strategies. NIH supports a comprehensive and innovative microbicide research program that includes the screening, discovery, development, preclinical testing, and clinical evaluation of microbicide candidates. NIH supports basic science aimed at understanding how HIV crosses mucosal membranes and infects cells. In addition, NIH supports behavioral and social science research on adherence to, acceptability of, and use of microbicides among different populations. These projects include the safety of microbicide use during pregnancy and menopause; studies in adolescents and in men who have sex with men; and implementation research to better understand how to integrate a potential product into community prevention practices. Basic science and clinical studies have shown promise for the use of antiretroviral (ARV)-based microbicides as HIV prevention strategies. Follow-up studies are underway or being developed to test different ARV- and non-ARV-based products, microbicides combined with a contraceptive for multipurpose prevention, and microbicides combined with antimicrobial agents to prevent HIV and other sexually transmitted infections (STIs). Microbicide formulations that enhance adherence, such as injectable products, films, suppositories, and intravaginal rings also are being developed and studied.

Budget Policy: The FY 2014 President's Budget estimate for Microbicides is \$133.8 million, an increase of \$3.881 million and 3.0 percent above the FY 2012 Actual level for this high priority area of research. In FY 2014, NIH will continue to support the discovery, design, development, formulation, and evaluation of microbicide candidates. Key ongoing activities include support for the microbicide clinical trials network and the necessary infrastructure to conduct microbicide clinical trials. Research activities will be designed to build on recent research advances; develop innovative, novel, and high risk-high reward approaches for the discovery, development, formulation, and testing of microbicide candidates, microbicide delivery systems, and multi-purpose products that prevent HIV or other STIs; the continued study of animal models designed to enhance understanding of the mechanisms of HIV infection and assist safety and efficacy evaluations of candidate microbicides; develop criteria for selecting candidates to be advanced through the different phases of preclinical and clinical studies including clinical effectiveness studies; and research on ethics, adherence, and other behavioral and social science issues that can impact clinical trials and microbicide use. Through a number of trans-governmental working groups and non-governmental expert consultations, OAR will continue to foster coordination and collaboration in innovative microbicide research leading to the development and testing of novel potential candidates that can prevent HIV transmission and acquisition.

VACCINES

The best long-term hope for controlling the AIDS pandemic is the development of safe, effective, and affordable AIDS vaccines that may be used in combination with other prevention strategies. NIH supports a broad AIDS vaccine research portfolio encompassing basic, preclinical, 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 preclinical evaluation of vaccine candidates. Information gained from these studies is being used to inform the design and development of novel vaccine strategies. Since the

announcement of the results of the RV144 trial in Thailand, NIH has supported an unprecedented collaborative effort with investigators around the world to identify clues about the immune responses required to protect against HIV acquisition. To build on the knowledge gained from these studies, clinical trials in other populations and in other parts of the world with new and potentially improved products have been designed. The recent release of data from several phase I and II vaccine clinical studies presents new scientific opportunities for the development of improved HIV vaccine candidates.

Budget Policy:

The FY 2014 President's Budget estimate for Vaccines is \$574.966 million, an increase of \$18.353 million and 3.3 percent above the FY 2012 Actual level. Basic research studies, particularly those using samples from ongoing clinical trials, are critically needed on the virus and host immune responses that can inform the development of new and innovative vaccine concepts; as well as the development of improved animal models to conduct pre-clinical evaluations of vaccine candidates. In FY 2014, NIH will fund additional basic research in these areas, as well as the design and development of new vaccine concepts and the pre-clinical/clinical development of vaccine candidates in the pipeline. Resources will be directed toward the development and testing of improved vaccine candidates in additional clinical studies, both in the U.S. and abroad, building on the early protection observed in the recent Phase III vaccine trial in Thailand. This also includes support for new initiatives to integrate systems biology with HIV vaccine discovery and for additional research involving new models for vaccine challenge studies in non-human primates. These initiatives will develop new test systems to measure immune responses to the vaccine that will more closely integrate preclinical animal and human clinical studies. To ensure that these new opportunities can be pursued, a realignment of resources will be needed. This budget request reflects OAR's redirection of funds from other scientific areas to support critical vaccine research opportunities.

BEHAVIORAL AND SOCIAL SCIENCE

NIH supports research to better understand the risk behaviors and social contexts that lead to HIV infection and disease progression, how to change those behaviors and social contexts, and how to maintain protection once it is achieved. Scientists are developing and evaluating interventions targeting substance abuse, sexual behaviors, and key factors associated with HIV transmission. Research is ongoing to better understand social and environmental factors associated with infection and disease outcomes, including stigma, housing, employment, health care access, and interpersonal networks. Research on care settings and behaviors of providers is suggesting ways to improve strategies to test HIV-infected persons, link them to care, promote adherence to antiretroviral therapy, and reduce stigma affecting care. Studies have shown that modifying care settings can promote early access to medical care, reduce costs, extend life expectancy, and improve quality of life. NIH also supports research to improve methodologies for the conduct of behavioral and social science studies, as well as clinical investigations,

including strategies to improve recruitment into trials; enhance statistical analysis of behaviors, such as alcohol use, that can affect medication studies; and characterize behavioral traits relevant to genetic or genomic studies.

Budget Policy:

The FY 2014 President's Budget estimate for Behavioral and Social Science is \$430.209 million, an increase of \$10.125 million and 2.4 percent above the FY 2012 Actual level. NIH will continue to fund research to reduce HIV-related risk behaviors and to better understand social factors contributing to HIV transmission, with an emphasis on racial and ethnic communities most affected by HIV. Resources will be directed toward several new prevention initiatives, addressing the challenges of integrating behavioral and social science methods with biomedical prevention strategies, community-based approaches to engaging and retaining persons in care, and the impact of improved care on reducing HIV transmission. NIH will support initiatives to better understand the multiple factors related to adherence, utilizing novel ways to ensure that patients take their medications and use prevention strategies appropriately. Genetic and genomic factors related to behavioral issues in prevention and disease progression will continue to receive attention.

ETIOLOGY AND PATHOGENESIS

NIH supports a comprehensive portfolio of research focused on the transmission, acquisition, establishment, and maintenance of HIV infection and the causes of its associated profound immune deficiency and severe clinical complications. Research on basic HIV biology and AIDS pathogenesis has revolutionized the design of drugs, methodologies for diagnosis of HIV infection, and tools for monitoring disease progression and the safety and effectiveness of antiviral therapies. Ground-breaking strides have been made towards understanding the fundamental steps in the life-cycle of HIV, the host-virus interactions, and the clinical manifestations associated with HIV infection and AIDS. Additional research is needed to further the understanding of the virus and how it causes disease, including studies to delineate how sex, gender, age, ethnicity, race, pregnancy, nutritional status, and other factors interact to influence vulnerability to infection and disease progression; determine the role of immune dysfunction and chronic inflammation in HIV pathogenesis; and further the understanding of the development of HIV-associated co-morbidities, such as cardiovascular, neurological, and other clinical complications, malignancies, and co-infections (including TB and hepatitis C). Research examining the genetic determinants associated with HIV susceptibility, disease progression, and treatment response is also needed. These studies may lead to the development of customized therapeutic and preventive regimens formulated for an individual patient based on his or her genetic sequence. A gene sequence associated with adverse reactions to the drug abacavir and genes associated with susceptibility to HIV infection in a small subset of individuals already have been identified. NIH also prioritizes research examining the mechanisms by which HIV establishes and reactivates latent reservoirs of infection and studies that further the understanding of factors that are associated with the ability of the host to restrict HIV infection and/or mitigate

HIV disease progression. A better understanding of these processes could help identify key targets for the development of new therapeutic strategies to prevent or control HIV infection and possibly lead to a cure for HIV disease.

Budget Policy:

The FY 2014 President’s Budget estimate for Etiology and Pathogenesis is \$693.851 million, an increase of \$25.607 million and 3.8 percent above the FY 2012 Actual level. The results from recent microbicide, vaccine, PrEP, and cure-related clinical studies have revealed gaps in knowledge and understanding of HIV etiology and pathogenesis, particularly with regard to host immune responses, how HIV interacts with and crosses host target surfaces, and the establishment and maintenance of latent viral reservoirs in the body (HIV persistence). NIH will provide increased resources for research on the biology of HIV transmission and pathogenesis studies including research on immune system activation and inflammation. NIH will support studies of complications such as research on HIV-associated co-infections, malignancies, premature aging, cardiovascular disease, neurological and metabolic disorders. An important area will focus on research related to the potential for a cure or lifelong remission of HIV infection, including studies on viral persistence, latency, and reactivation. In addition, funds will be provided for research to better understand the differences in HIV transmission, treatment, and progression in women compared to men as well as the unique clinical manifestations of HIV disease in women.

Program Portrait: Eradication of Viral Reservoirs: Toward a Cure

FY 2012 level: \$60 million

FY 2014 level: \$65 million

Change: \$ +5 million

NIH research focused on this area includes:

- **Pathogenesis studies:** Basic research on viral reservoirs, viral latency, and viral persistence, including studies on genetic factors associated with reactivation of the virus, and other barriers to HIV eradication.
- **Animal models:** Identification and testing of various animal and cellular models to mimic the establishment and maintenance of viral reservoirs. These studies are critical for testing novel or unique strategies for HIV reactivation and eradication.
- **Drug development and preclinical testing:** Programs to develop and preclinically test new and better antiretroviral compounds capable of entering viral reservoirs, including the central nervous system.
- **Clinical trials:** Studies to evaluate lead compounds, drug regimens, and immune-based strategies capable of a sustained response to HIV, including clinical studies of drugs and novel approaches capable of eradicating HIV-infected cells and tissues.
- **Therapeutic vaccines:** Design and testing of vaccines that would be capable of suppressing viral replication and preventing disease progression.
- **Adherence/compliance:** Development and testing of strategies to maintain adherence/compliance to treatment, in order to improve treatment outcomes and reduce the risk of developing HIV drug resistance.

THERAPEUTICS

Therapeutics as Prevention: A critical new area of prevention research is the study of treatment strategies as a method to prevent new HIV infections. This approach builds on NIH-sponsored landmark clinical trials that demonstrated that treatment of HIV-infected pregnant women could significantly reduce transmission of HIV from mother to child. Recent groundbreaking studies have demonstrated the successful use of antiretrovirals to prevent transmission of HIV in specific populations. Clinical results from a large NIH-sponsored international clinical trial (HPTN 052) showed that early initiation of antiretroviral treatment of HIV-infected heterosexual individuals resulted in a 96 percent reduction in sexual transmission of HIV to their uninfected partner. Another major NIH-sponsored clinical trial (iPrEx) demonstrated that daily use of an antiretroviral drug by some high-risk uninfected men could reduce their risk of acquiring HIV. The findings from this study showed proof of concept and the effectiveness of a novel HIV prevention strategy known as PrEP. Studies are ongoing to determine if these findings can be replicated in women. NIH supports ongoing basic, clinical, and implementation research to develop antiretroviral drugs that can be used in potential new PrEP strategies; test PrEP in high-risk uninfected women and adolescents; evaluate post-exposure prophylaxis, the use of treatment to prevent HIV infection after accidental exposure, including in a healthcare setting; develop improved regimens to prevent mother-to-child transmission; and evaluate a potential innovative prevention strategy known as “test and treat” to determine the impact of increased testing with immediate referral to treatment at the community level.

Drug Discovery, Development and Treatment: Antiretroviral treatment (ART) has resulted in improved immune function in patients who are able to adhere to the treatment regimens and tolerate the toxicities and side effects associated with antiretroviral drugs. ART has also delayed the progression of HIV disease to the development of AIDS. Unfortunately, the treatment is beginning to fail in an increasing number of patients who have been on antiretroviral therapy. These patients are experiencing serious drug toxicities and developing drug resistance. Recent epidemiologic studies have shown that the incidence of co-infections, co-morbidities, AIDS-defining and non-AIDS defining malignancies, and complications associated with long-term HIV disease and ART are increasing. These include tuberculosis, Hepatitis C, metabolic disorders, cardiovascular disease, conditions associated with aging, and neurologic and neurocognitive disorders. NIH supports a comprehensive therapeutics research program to design, develop, and test drugs and drug regimens. Under development are drugs to maintain undetectable viral load,

Improved Therapies for Long-Term Survival

NIH researchers are working to:

- Develop innovative therapies and novel cell- and immune-based approaches to control and eradicate HIV infection;
- Identify new drug targets based on the structure of HIV/host complexes;
- Delineate the interaction of aging and AIDS, including neurological, cardiovascular, and metabolic complications, as well as issues of frailty;
- Discover and develop improved therapies for AIDS-defining and non-AIDS-defining malignancies; and
- Discover the next generation of drugs that may be used in potential “therapeutics as prevention” strategies.

to overcome drug resistance and treatment failure, and to prevent and treat HIV-associated co-infections, co-morbidities and other complications. The program is also focused on developing drugs and other strategies that can target and eradicate persistent viral reservoirs in various cells, tissues, and organ systems, including the central nervous system that may lead to a functional cure for HIV disease.

Budget Policy:

The FY 2014 President's Budget estimate for Therapeutics is \$717.194 million, an increase of \$10.574 million and 1.5 percent above the FY 2012 Actual level. The overall funding for therapeutics research will be enhanced to allow for increased funding for HIV prevention science research, including the development and clinical testing of potential microbicides, vaccines, and behavioral and social science interventions. A portion of the funds from expiring grants and contracts for therapeutics research will be reallocated to studies on the treatment and prevention of HIV-associated co-infections and co-morbidities and to support crucial basic research on HIV and genomics studies on the host immune response to HIV. Resources within the area of Therapeutics also will be directed to support: the recompetition of the Leadership Groups and Clinical Trial Units for the NIH Clinical Trials Research Networks; several new and/or expanded multidisciplinary initiatives to develop innovative antiviral therapies and novel cell- and immune-based approaches to control and eradicate HIV infection that may lead to a cure; identifying new drug targets based on the structure of HIV/host complexes; delineating the interaction of aging and neuro-AIDS; developing new strategies to test and treat patients with HIV-coinfections including Hepatitis C virus; and conducting clinical studies on cardiovascular complications of HIV disease and ART. Increased funding will be provided for the area of *Therapeutics as Prevention*, including discovery and testing the next generation of antiretroviral drugs that may be used in potential new strategies for PrEP (therapeutic regimens for uninfected at-risk individuals); treatment of HIV-infected individuals to prevent transmission; post-exposure prevention; and new triple antiretroviral drug regimens to prevent mother-to-child transmission, including transmission through breastfeeding.

NATURAL HISTORY AND EPIDEMIOLOGY

Natural history and epidemiologic research on HIV/AIDS is critical to the monitoring of epidemic trends, evaluation of prevention modalities, characterization of the clinical manifestations of HIV disease, and measurement of the effects of treatment regimens at the population level. Novel methodologies in the area of biostatistics, mathematical modeling, and laboratory technology have provided the basis for new epidemiological approaches in addressing HIV/AIDS. Multi-site epidemiologic studies in the U.S. are identifying new HIV-related co-morbidities and helping to differentiate effects related to antiretroviral treatment from those related to HIV disease. As the AIDS epidemic evolves, there is a crucial need for epidemiologic studies in domestic and international settings. NIH supports a comprehensive research portfolio in both settings to study the epidemiologic characteristics of populations in which HIV is transmitted and the changing spectrum of HIV-related disease (including the occurrence of co-infections, malignancies, metabolic, cardiovascular, neurological, skeletal, and other

complications). These studies have delineated the significant health disparities that are critical factors in the epidemic (e.g., racial and ethnic disparities in the U.S.; between industrialized and resource-constrained nations; between men and women; and health disparities based on sexual identity). Ongoing observational studies are adding focus on at-risk individuals from the rural South, as well as individuals over the age of 50. Research on HIV-related health disparities and their impact on treatment access and effectiveness, as well as HIV prevention, will continue to be an NIH AIDS research priority.

Budget Policy:

The FY 2014 President's Budget estimate for Natural History and Epidemiology is \$247.385 million, a decrease of \$10.588 million and 4.1 percent below the FY 2012 Actual level. NIH will continue to provide support for high-priority epidemiology studies of groups and populations affected by HIV and at high risk of infection, including individuals over fifty years of age, men who have sex with men (MSM), especially MSM of color, women, and adolescents. NIH also will increase support for critical studies of the specific role of race and gender, the effects of increased HIV testing and linkage to care on HIV spread, the impact of therapy in changing the spectrum of HIV disease, and the preventable causes of death. In addition, resources will be provided for studies of HIV in aging populations and for implementation science, including how to implement and evaluate strategies to scale up cost-effective interventions that might accelerate the progress toward an AIDS-free generation.

TRAINING, INFRASTRUCTURE, AND CAPACITY BUILDING

NIH supports the training of domestic and international biomedical and behavioral HIV researchers. NIH also provides infrastructure and capacity building support as integral aspects of its commitment to carrying out scientifically sound and highly productive HIV-related research. The expansion of NIH-funded HIV research globally has necessitated the development of research training and infrastructure and capacity building efforts in many resource-limited settings throughout the world. NIH-funded programs have increased the number of training positions for HIV-related researchers, including programs specifically designed to recruit individuals from underrepresented populations into research careers and to build research infrastructure at minority-serving institutions in the U.S. Equipment, shared instrumentation, and tissue and specimen repositories are examples of the research infrastructure and capacity building support that NIH provides to strengthen the conduct of AIDS-related research, both domestically and internationally.

Budget Policy:

The FY 2014 President's Budget estimate for Training, Infrastructure, and Capacity Building is \$272.062 million, a decrease of \$8.713 million and 3.1 percent below the FY 2012 Actual level. NIH will continue to support both training programs and infrastructure development for U.S. and international researchers to build the critical capacity to conduct AIDS research both in the United States and in developing countries. NIH will continue to support ongoing efforts to

increase the supply of non-human primates and other animal models, particularly rhesus and pigtail macaques, for AIDS research and other areas of biomedical research both in the United States and abroad. Support also will be provided for the NIH AIDS Research Loan Repayment Program and the Intramural AIDS Research Fellowship program that will help ensure an adequate number of trained AIDS researchers at NIH.

INFORMATION DISSEMINATION

NIH supports initiatives to enhance dissemination of research findings; develop and distribute state-of-the-art treatment and prevention guidelines; and enhance recruitment and retention of participants in clinical studies. Effective information dissemination approaches are an integral component of HIV prevention and treatment efforts. These efforts are crucial in light of the advent of new and complex antiretroviral treatment regimens, issues related to adherence to prescribed treatments, and the need to translate behavioral and social prevention approaches into practice. The changing pandemic and the increasing number of new infections in specific population groups in the U.S. underscore the need to disseminate HIV research findings and other related information to communities at risk, such as racial and ethnic populations, women, older individuals, and men who have sex with men. The flow of information among researchers, health care providers, and the affected communities represents new opportunities to use new and emerging technologies to speed the translation of research results into practice and to shape future research directions.

Budget Policy:

The FY 2014 President's Budget estimate for Information Dissemination is \$52.249 million, a decrease of \$2.318 million and 4.2 percent below the FY 2012 Actual level. As the number and complexity of clinical studies increases, resources must be invested in clinical trials-related information dissemination to ensure recruitment of an adequate number of participants, particularly from populations at risk, including women and racial and ethnic populations in the United States. In addition, funding will be provided to ensure that clinical trial information and critical federal guidelines on the use of antiretroviral therapy, as well as guidelines for the management of HIV complications for adults and children, will be updated regularly and disseminated widely to healthcare providers and patients through the *AIDSinfo* website (www.aidsinfo.nih.gov).

Global Impact of NIH HIV/AIDS Research: Research to address the global pandemic is essential. AIDS research represents the largest component of the total NIH global research investment. Since the early days of the epidemic, NIH has maintained a strong international AIDS research portfolio that has grown to include projects in approximately 100 countries around the world. NIH AIDS research studies are designed so that the results are relevant for both the host nation and the U.S. These research programs also enhance research infrastructure and training of in-country scientists and healthcare providers. New collaborations have been designed to improve both medical and nursing education as a mechanism to build a cadre of global health leaders.

Most of these grants and contracts are awarded to U.S.-based investigators to conduct research in collaboration with in-country scientists; some are awarded directly to investigators in international scientific or medical institutions.

AIDS Research Conducted in International Settings
(Dollars in Millions)

FY 2012 Actual	FY 2013 CR	FY 2014 PB
\$ 392.454	\$ 392.052	\$ 399.104

Benefits of AIDS Research to Other Areas: It is essential to point out that AIDS research also pays extensive dividends in many other areas of biomedical research, including in the prevention, diagnosis, and treatment of many other diseases. It deepens our understanding of immunology, virology, microbiology, molecular biology, and genetics. AIDS research is helping to unravel the mysteries surrounding so many other diseases because of the pace of discovery and the unique nature of HIV, i.e., the way the virus enters a cell, causes infection, affects every organ system, and unleashes a myriad of opportunistic infections, co-morbidities, cancers, and other complications. AIDS research continues to make discoveries that can be applied to other infectious, malignant, neurologic, autoimmune, and metabolic diseases, as well as to the complex issues of aging and dementia. AIDS treatment research has led to more effective drugs for multiple bacterial, mycobacterial, and fungal diseases and fostered significant improvements in drug design technologies. AIDS research has led to the development of new models to test treatments for other diseases in faster, more efficient, and more inclusive clinical trials. Drugs developed to prevent and treat AIDS-associated opportunistic infections also now benefit patients undergoing cancer chemotherapy and patients receiving anti-transplant rejection therapy. AIDS research also has advanced understanding of the relationship between viruses and cancer. New investments in AIDS research will continue to fuel biomedical advances and breakthroughs that will have profound benefits far beyond the AIDS pandemic.

Conclusion: While the NIH investment in AIDS research has produced groundbreaking scientific advances, many serious challenges lie ahead. There is little doubt that, despite our progress to date, the AIDS pandemic will continue to impact virtually every sector of society in virtually every nation in the world for decades to come. In light of this reality, the U.S. national commitment to AIDS research remains strong. NIH will continue to build on this important moment in science and to support critical research to find new tools to turn the tide in the fight against AIDS, so that we can all once again live in a world without AIDS.