FY 2012 Trans-NIH AIDS Research By-Pass Budget Estimate

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FY 2012 Trans-NIH AIDS Research By-Pass Budget Estimate

Legislative Mandate

AUTHORIZING LEGISLATION

Section 2353 of the Public Health Service Act requires that "the Director of the Office of AIDS Research establish a comprehensive plan for the conduct and support of all AIDS activities of the agencies of the National Institutes of Health." It also requires that the Director "shall prepare and submit directly to the President, for review and transmittal to the Congress, a budget estimate for carrying out the Plan for the fiscal year...." That budget "shall estimate the amounts necessary for the agencies of the National Institutes of Health to carry out all AIDS activities determined by the Director of the Office to be appropriate, without regard to the probability that such amounts will be appropriated."

APPROPRIATIONS LANGUAGE

The FY 2010 House Appropriations Committee report stated, "The Committee believes that NIH continues to be the world's leader in research to respond to the critical needs of the AIDS pandemic, both in the U.S. and around the world. The Committee commends NIH for supporting the NIH AIDS and non-AIDS funding allocation at the current relative rate and endorses the continuation of this policy. The Committee continues to endorse the importance of OAR, including its critical trans-NIH budget authority and its status as a unique 'institute without walls.' The Committee commends the Office for its leadership in setting trans-NIH AIDS research priorities, including important new basic science initiatives in the area of genomics, and its ongoing support for innovative research and community outreach to address the complex issues of AIDS in racial and ethnic minority populations in the U.S."

Introduction

In accordance with the law, the National Institutes of Health (NIH) Office of AIDS Research (OAR) has developed this *Fiscal Year (FY) 2012 Trans-NIH AIDS Research By-Pass (Professional Judgment) Budget Estimate* to carry out the scientific priorities established in the *FY 2012 Trans-NIH Plan for HIV-Related Research*. OAR, a component of the Office of the Director, is the only NIH office that is legislatively mandated to develop an annual Presidential by-pass budget estimate. Only the National Cancer Institute has a similar authority.

The by-pass budget estimate is based solely on the current scientific opportunities and the commitment and urgent need to support the highest quality research. This by-pass budget estimate:

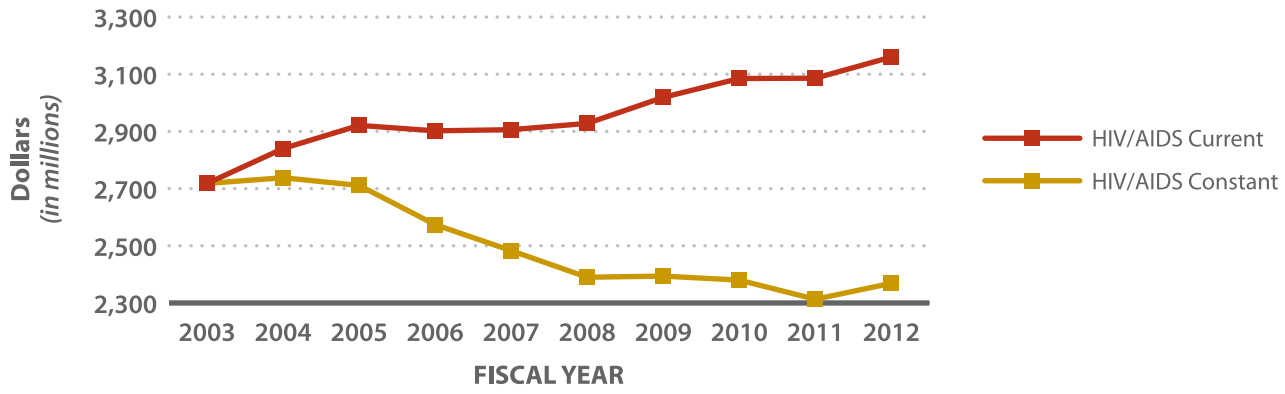
- Addresses critical scientific needs
- Addresses gaps in our understanding through a renewed emphasis on basic science
- Capitalizes on emerging scientific opportunities by providing additional funds for new, exciting areas of investigation
- Restores vital resources that have been drained by the dual effects of inflation and a flat budget
- Establishes the biomedical and behavioral research foundation necessary to implement the major goals of the President's National HIV/AIDS Strategy
- Addresses the key themes of the NIH Director.

This by-pass budget request establishes the critical priorities for trans-NIH AIDS research. These include:

- Prevention research, including biomedical and behavioral research focused on the domestic AIDS epidemic, particularly in racial and ethnic populations of the United States
- Research to build on important advances in prevention research gained in the past year in the areas of microbicides, vaccines, and treatment as prevention
- Research to prevent and treat HIV-associated comorbidities, malignancies, and clinical complications
- Research to address the issues around AIDS and aging
- Research to better understand the issues of adolescents and AIDS
- Basic and therapeutic research focused on elimination of viral reservoirs, leading to a cure
- Genetic studies to delineate the genetic basis for immune responses to HIV and to sequence HIV-associated tumors
- Research on the feasibility, effectiveness, and sustainability required for the scale-up and implementation of interventions in communities at risk.

The FY 2012 by-pass budget request for NIH AIDS research is $3.546 billion, which represents a 15 percent increase over the FY 2011 estimate. At the time of this writing, the final FY 2011 appropriation had not been determined, and the estimate represents the level of the Continuing Resolution.

Impact of Inflation on NIH HIV/AIDS Research Dollars (Current and Constant)



This level includes the total trans-NIH support for intramural and extramural research; research management support; research centers; training; and basic, clinical, behavioral, social science, and translational research on HIV/AIDS and the wide spectrum of AIDS-associated malignancies, opportunistic infections, coinfections, and clinical complications.

This increase represents an investment—a down payment—that must be maintained and enhanced to take advantage of critical emerging scientific advances, and to restore lost opportunity. This amount also is essential to address the impact of the erosion of buying power on critical research programs. The total AIDS research budget at the FY 2011 estimate level was approximately equivalent in constant dollars to the FY 2001 appropriation. Further, there was a 25 percent loss in buying power for NIH AIDS research between FY 2003 and FY 2011.

HIV/AIDS Pandemic

Nearly 30 years since the recognition of AIDS and the identification of HIV as its causative agent, the HIV/AIDS pandemic remains a global scourge that affects people in nearly every country worldwide. UNAIDS reports that in 2009, more than 33 million people were estimated to be living with HIV/AIDS, 2.6 million were newly infected, and 1.8 million people died of AIDS-related illnesses.[1]

1 UNAIDS. *Report on the Global AIDS Epidemic 2010.* Available at *http://www.unaids.org/globalreport/Global_report.htm.*

In the United States, more than 1.1 million people are estimated to be HIV-infected, and someone is infected with HIV every 9 ½ minutes. HIV/AIDS remains an unrelenting public health crisis, disproportionately affecting racial and ethnic populations, women of color, young adults, and men who have sex with men (MSM). The Centers for Disease Control and Prevention (CDC) estimates approximately 56,300 new infections per year, and the incidence of new infections has not declined for more than a decade. Since the beginning of the AIDS epidemic, there have been more than 617,000 cumulative AIDS deaths.[2]

According to CDC statistics, gay and bisexual men of all races and ethnicities and African American men and women are the most affected groups in the United States. Fifty-three percent of all new infections in 2006 occurred in gay and bisexual men. In 2006, blacks accounted for 45 percent of all new infections, even though they comprise only

2 Centers for Disease Control and Prevention. *HIV Surveillance Report: Diagnoses of HIV Infection and AIDS in the United States and Dependent Areas, 2009.* Available at *http://www.cdc.gov/hiv/surveillance/resources/reports/2009report/.*

GLOBAL EPIDEMIC

More than 7,000 new HIV infections a day in 2009:

About 97 percent are in low- and middle-income countries

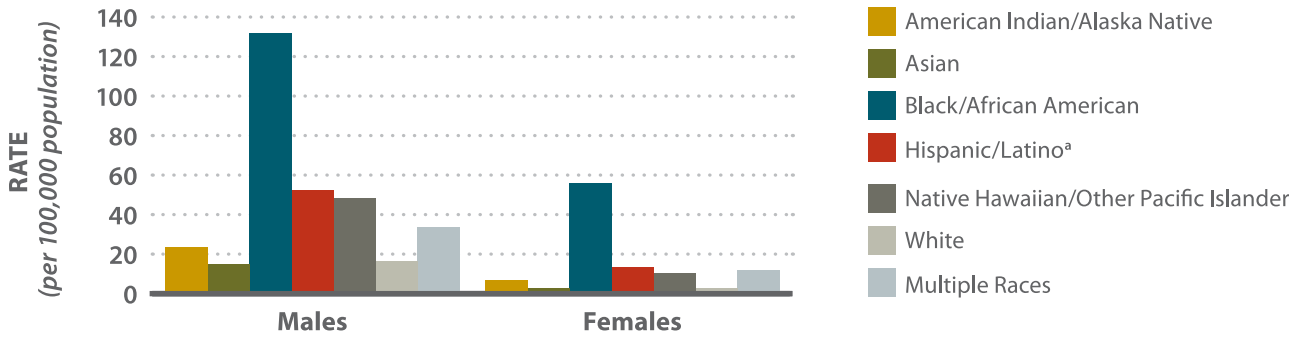
About 1,000 are in children under 15 years of age

About 6,000 are in adults aged 15 years and older, of whom:

- almost 51 percent are among women
- about 41 percent are among young people (aged 15–24)

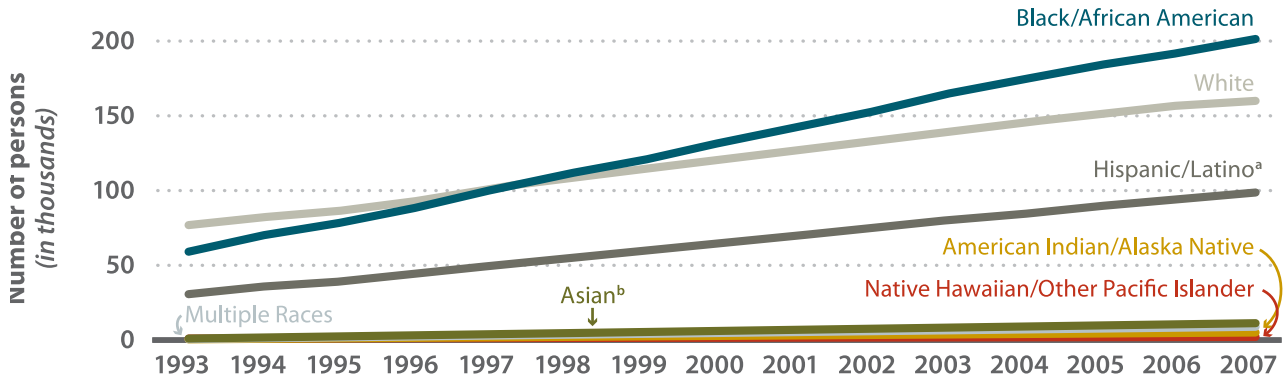
SOURCE: UNAIDS. *Core Slides: Report on the Global AIDS Epidemic 2010.* Available at *http://www.unaids.org/global-report/Epi_slides.htm.*

Rates of Diagnoses of HIV Infection Among Adults and Adolescents, by Sex and Race/Ethnicity, 2008—37 States



NOTES. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis.
Data from 37 states with confidential name-based HIV infection reporting since at least January 2005.
All displayed data have been estimated. Estimated numbers resulted from statistical adjustment that accounted for reporting delays, but not for incomplete reporting.
[a] Hispanics/Latinos can be of any race.
SOURCE: Centers for Disease Control and Prevention. *HIV Surveillance Report, 2008;* vol. 20. Published June 2010.

Persons Living with an AIDS Diagnosis, by Race/Ethnicity, 1993–2007—United States and Dependent Areas



NOTES. All displayed data have been estimated. Estimated numbers resulted from statistical adjustment that accounted for reporting delays, but not for incomplete reporting.
[a] Hispanics/Latinos can be of any race.
[b] Includes Asian/Pacific Islander legacy cases.
SOURCE: Centers for Disease Control and Prevention. *HIV Surveillance Report, 2008;* vol. 20. Published June 2010.

12.6 percent of the total U.S. population.[3] Moreover, the overall prevalence of HIV/AIDS was more than 7 times higher for blacks than for whites.

Further, the populations affected by AIDS continue to shift. HIV/AIDS began its deadly course in the United States mostly as a disease of young men, but today the epidemic touches people of all ages, including adults aged 50 and older. With the advent of potent, multi-drug therapy against HIV in the mid-1990s, many HIV-infected Americans are living into their fifties and well beyond. Although the majority of new HIV infections are in younger Americans, the number of persons aged 50 years and older living with HIV/AIDS has been increasing. In 2005, an estimated 29 percent of HIV-infected adults in the United States were at least 50 years old, and individuals aged 50 and older accounted for approximately 15 percent of all new HIV/AIDS diagnoses.[4] As a consequence of these trends, it has been estimated that by 2015, 50 percent of HIV-infected individuals in the United States may be 50 or older.

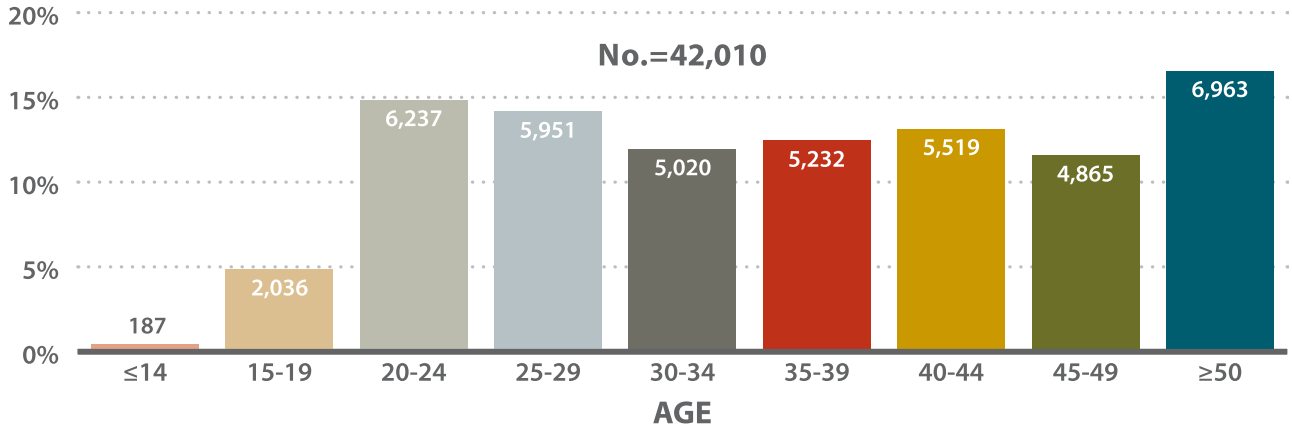
Older adults with long-term or new HIV infection experience complex interactions with HIV, antiretroviral therapy, age-related changes to the body, and, often, treatment for illnesses associated with aging. The research agenda addresses the medical implications of aging with HIV and continues developing more sophisticated treatment strategies so these older adults can live longer, healthier lives. In addition, HIV disease itself appears to cause premature aging. The NIH-sponsored Multicenter AIDS Cohort Study has shown that HIV disease accelerates the development of chronic diseases.

The maturing U.S. epidemic has the potential to generate concentric mini-epidemics of liver disease, tuberculosis (TB), cardiovascular disease, and other HIV-associated comorbidities, foreshadowing an epidemic of greater complexity in the coming years. The HIV/AIDS pandemic will remain the most serious public health crisis of our time until better, more effective, and affordable prevention and treatment regimens are developed and made universally available.

3 U.S. Census Bureau. 2010 Census. Available at *http://2010.census.gov/2010census/data.*

4 Centers for Disease Control and Prevention. HIV/AIDS Statistics and Surveillance. *HIV/AIDS among Persons Aged 50 and Older.* Available at *http://www.cdc.gov/hiv/topics/over50/resources/factsheets/over50.htm.*

Estimated Number of Diagnoses of HIV Infection,* By Age—2009



* in the 40 states with confidential name-based HIV infection reporting.

SOURCE: Centers for Disease Control and Prevention. *HIV Surveillance Report: Diagnoses of HIV Infection and AIDS in the United States and Dependent Areas, 2009.* Available at *http://www.cdc.gov/hiv/topics/surveillance/basic.htm.*

NIH AIDS Research Program

To address this pandemic, the NIH supports and conducts a comprehensive program of basic, clinical, translational, and behavioral research on HIV infection and its associated coinfections, opportunistic infections, malignancies, and other complications. AIDS research is carried out by all of the NIH Institutes and Centers (ICs) in accordance with their mission, in both intramural and extramural programs.

NIH-funded research has led to:

- Critical discovery of antiretroviral therapies and regimens that have resulted in improved life expectancy for those with access to and who can tolerate these drugs
- Development of treatments for many HIV-associated coinfections, comorbidities, malignancies, neurologic complications, TB, and other clinical manifestations
- Advances in HIV prevention, including groundbreaking strategies for the prevention of mother-to-child transmission, safety of the blood supply, and effectiveness of medically supervised circumcision of adult men in reducing the risk of heterosexual HIV acquisition
- Critical basic science discoveries that continue to provide the foundation for novel research. Research on basic HIV biology and AIDS pathogenesis also has revolutionized the design of drugs, methodologies for diagnosis, and monitoring of the safety and effectiveness of antiviral therapies.

Despite these important advances, the epidemic continues to expand, and improved prevention strategies and therapeutic regimens are critically necessary. The AIDS pandemic will continue to wreak devastating consequences in the United States and around the world for decades to come. The pandemic affects the future of families, communities, military preparedness, national security, political stability, national economic growth, agriculture, business, health care, child development, and education in countries around the globe.

NIH AIDS RESEARCH PROGRAM

Represents the largest public investment in AIDS research in the world

Encompasses all NIH Institutes and Centers

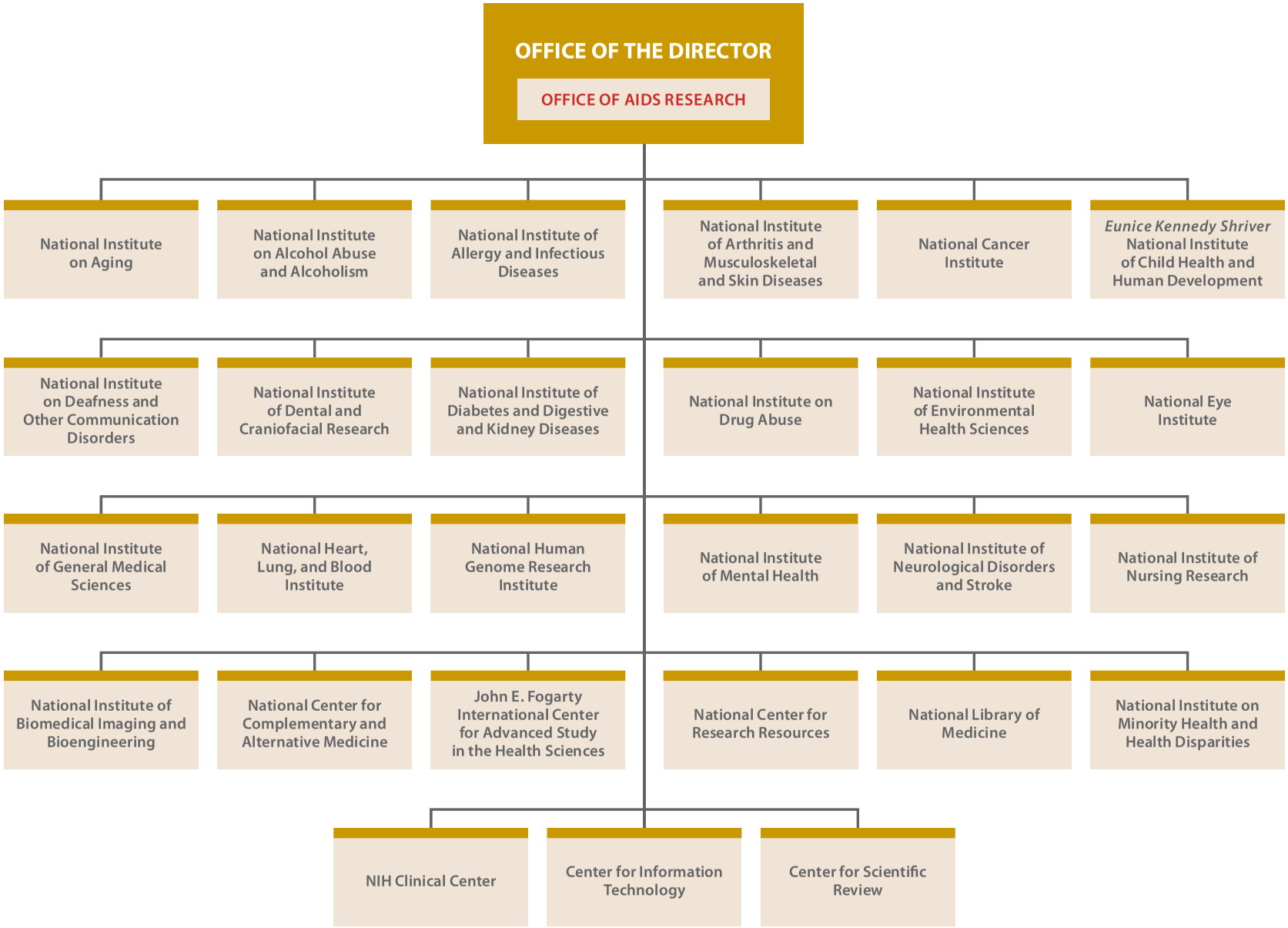
Transcends every area of clinical medicine and basic scientific investigation

Comprises a comprehensive program of basic, clinical, translational, and behavioral research on HIV infection, its associated coinfections, opportunistic infections, malignancies, and other complications

Includes research or training projects in more than 100 countries

Requires unprecedented trans-NIH scientific coordination and management of research funds

NATIONAL INSTITUTES OF HEALTH



NIH Office of AIDS Research

OAR *(http://www.oar.nih.gov/)*, established in 1988, has unique legislative authorities unlike any other NIH entity to plan, coordinate, evaluate, and budget the entire $3 billion NIH AIDS research program, which represents approximately 10 percent of the total NIH budget—the largest and most significant public investment in AIDS research in the world. OAR serves as the principal liaison with the U.S. Department of Health and Human Services, other Federal agencies, and domestic and international governmental and nongovernmental organizations on behalf of NIH AIDS-related research.

OAR serves as a model of trans-NIH planning and management, operating as an "institute without walls," vested with primary responsibility for overseeing all NIH AIDS-related research, and thus allowing the NIH to pursue a united research front against the global AIDS epidemic.

Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation, crossing the boundaries of every IC. This diverse research portfolio demands an unprecedented level of trans-NIH scientific coordination and management of research funds. OAR coordinates the scientific, budgetary, legislative, and policy elements of the NIH AIDS research portfolio and sets the trans-NIH scientific priorities for this large and diverse program. Utilizing its legislative authorities, OAR has established comprehensive trans-NIH planning, budgeting, and portfolio analysis processes to identify the highest priority areas of scientific opportunity, to enhance collaboration, to minimize duplication, and to ensure that precious research dollars are invested effectively and efficiently.

OFFICE OF AIDS RESEARCH MISSION

Establish a unified NIH research agenda to address the AIDS pandemic through:

An annual trans-NIH strategic planning process to identify highest scientific priorities and opportunities to address the changing epidemic

An annual trans-NIH budget based on the Strategic Plan

Trans-NIH coordination, management, and evaluation

Facilitation and implementation of domestic and international collaborative AIDS research agreements

OAR identifies emerging scientific opportunities and public health challenges that require focused attention; manages and facilitates multi-Institute and trans-Institute activities to address those needs; fosters research by designating funds and supplements to jump-start or pilot program areas; sponsors reviews or evaluations of research program areas; and facilitates international AIDS research and training. OAR's unique budget authorities also allow it to transfer funds across ICs and across scientific areas.

OAR supports a number of initiatives to enhance dissemination of research findings to researchers, physicians, institutions, communities, constituency groups, and patients. OAR also has placed high priority on research and community outreach initiatives to address the disproportionate impact of the epidemic on racial and ethnic minority communities in the United States.

Trans-NIH Strategic Plan

Each year, OAR develops the *Trans-NIH Plan for HIV-Related Research (http://www.oar.nih.gov/strategicplan/)*. This Strategic Plan (see second tab in this document) is developed in collaboration with scientists from the NIH ICs, other Government agencies, and nongovernmental organizations, as well as community representatives. During the planning process, the state of the science is reviewed, newly emerged and critical public health needs are assessed, and scientific opportunities are identified. The annual process culminates with the identification of the highest strategic priorities and critical research needs in each of the following scientific areas: Etiology and Pathogenesis; Vaccines; Microbicides; Behavioral and Social Science; Treatment as Prevention; Drug Discovery, Development, and Treatment; Training, Infrastructure, and Capacity Building; Natural History and Epidemiology; and Information Dissemination. The Plan also addresses research in special populations, including: Racial and Ethnic Populations; Women and Girls; and Research in International Settings.

OAR requires ICs to report all AIDS-related expenditures, including extramural, intramural, and research management and support, on a quarterly basis, to the OAR trans-NIH AIDS Research Information System database. All expenditures must be coded to the appropriate objective(s) of the Plan. This database also serves as the primary resource for AIDS research information in the new Research Conditions and Diseases Categorization process, which permits OAR to review, monitor, and analyze the total intramural and extramural AIDS research program.

THE STRATEGIC PLAN IS A UNIQUE AND CRITICAL DOCUMENT THAT SERVES AS THE FRAMEWORK FOR:

Developing the annual AIDS research budget for each IC

Determining the use of AIDS-designated dollars

Developing the annual Presidential by-pass budget estimate

Tracking and monitoring all NIH AIDS research expenditures.

OAR Planning Process Participants

- Trans-NIH Coordinating Committees
- NIH ICs
- Other Government entities with research responsibilities (CDC, FDA, USAID, VA, DoD)*
- Nongovernment experts from academia, foundations, and industry
- Office of AIDS Research Advisory Council

* These Federal Government agencies are the Centers for Disease Control and Prevention, Food and Drug Administration, U.S. Agency for International Development, Department of Veterans Affairs, and Department of Defense, respectively.

OAR Budget Development Process

OAR is mandated to develop the annual trans-NIH AIDS research budget in partnership with the ICs and explicitly tied to the objectives of the Strategic Plan. The law provides that OAR "shall receive directly from the President and Director of the OMB all funds available for AIDS activities of the NIH" for allocation to the ICs in accordance with the Plan. Subsequently, however, an agreement with Congress established the tradition that rather than receiving a separate, single appropriation, OAR would determine each IC's AIDS research allocation to be included within the IC total appropriation. It also was agreed that AIDS and non-AIDS appropriations would grow at approximately the same rate; that is, as an "institute without walls," AIDS research, as determined by OAR, would receive the same increase as the other ICs. Thus, AIDS research has historically represented approximately 10 percent of the total NIH budget.

For all appropriated funds, the OAR Director and NIH Director determine the total amount to be allocated for AIDS-related research within the overall NIH budget. Within that total, OAR develops each IC's allocation. The ICs submit their AIDS-related research budget requests to OAR, presenting proposed new, expanded, or recompeting program initiatives, coded to specific Plan objective(s). OAR reviews the IC initiatives in relation to the Plan, to its priorities, and to other IC submissions to eliminate redundancy and/or to ensure cross-Institute collaboration. The unique budget authorities allow OAR to build each IC budget from the commitment base, rather than from the previous year's appropriation.

OAR BUDGET DEVELOPMENT PROCESS

1. ICs develop new or expanded program initiatives with budget requests for each scientific area.
2. OAR reviews IC initiatives in relation to the Plan and OAR priorities.
3. Consultations occur between the ICs and OAR throughout the process.
4. The budget is developed in consultation between the OAR Director and the NIH Director.
5. OAR allocates budget levels to each IC.

The careful determination of the balance of the research budget—among Institutes, across areas of science, between intramural and extramural research programs, between basic and clinical research, and between investigator-initiated and targeted research—requires a comprehensive knowledge of the science and of the ICs' portfolios. Dollars are allocated to the ICs based on the priorities of the Plan, scientific opportunities, and the ICs' capacity to absorb and expend resources for the most meritorious science, and not according to a formula. This process reduces redundancy, promotes harmonization, and ensures cross-IC collaboration. At the time of the appropriation, OAR informs each IC of its AIDS-related budget allocation, specifying amounts for each approved initiative.

OAR also has a 3 percent transfer authority to move dollars across ICs during the fiscal year.

OAR budget authority also requires the development of this by-pass budget, based solely on scientific opportunity.

National and International Impact and Need

The role of the NIH is to conduct research that will provide the science base and the necessary tools to facilitate the implementation of the President's National HIV/AIDS Strategy.

GLOBAL IMPACT OF NIH AIDS RESEARCH:

In addition to addressing the U.S. epidemic, NIH research to address the global pandemic is essential. Since the early days of the epidemic, the NIH has supported research efforts in countries affected by AIDS. Beginning in 1983 with a research project in Haiti, the NIH has maintained a strong international AIDS research portfolio that now includes projects in approximately 100 countries around the world. AIDS research represents the largest component of the total NIH global research investment. NIH AIDS research studies are designed so that the results are relevant for both the host nation and the United States. Implementation studies are critical to translating clinical trial research results into community-based interventions that can be operational in international settings. The development of research infrastructure, including training of scientists and health care providers, is an essential component of these research programs. 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.

THE PRESIDENT'S NATIONAL HIV/AIDS STRATEGY

The critical priorities of this by-pass budget estimate are aligned and in concert with the major goals of the President's National HIV/AIDS Strategy.

The goals of the Strategy are:

Reducing HIV incidence

Increasing access to care and optimizing health outcomes

Reducing HIV-related health disparities

New Scientific Advances and Opportunities

The past year has been a significant one for AIDS research. The NIH investment in the priority areas of HIV prevention research and in basic science over the past several years has reaped rewards resulting in important progress in critical areas of the NIH AIDS research program. Recent research advances by NIH intramural and extramural investigators have opened doors for new and exciting research opportunities in the search for strategies to prevent, treat, and ultimately cure HIV infection.

All of these important advances, while preliminary and incremental, provide the groundwork for further scientific investigation and the building blocks for the development of this by-pass budget request.

ANTIBODY DISCOVERIES PROPEL HIV VACCINE RESEARCH: A team of scientists led by researchers at the National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center discovered two potent human antibodies that can stop more than 90 percent of known global HIV strains from infecting human cells in the laboratory and determined the structural analysis of how they work. The novel techniques used in this research may accelerate HIV vaccine research, as well as the development of vaccines for other infectious diseases.

PROOF-OF-CONCEPT OF MICROBICIDES: For the first time in nearly 15 years of research, scientists discovered a vaginal microbicide gel that gives women a level of protection against HIV infection. Conducted by the Centre for the AIDS Programme of Research in South Africa (CAPRISA), and sponsored by USAID, the CAPRISA 004 study showed that the use of a microbicide gel containing a 1 percent concentration of the antiretroviral drug tenofovir resulted in 39 percent fewer HIV infections compared with a placebo gel. The NIH provided substantial support and resources to establish the infrastructure and training for CAPRISA. Ongoing and future clinical trials will build on these study results with the goal of bringing a safe and effective microbicide to the general public.

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women*

QA Karim, SS Karim et al.

- Double-blind, randomized controlled trial (*n*=889) in sexually active, HIV-uninfected 18- to 40-year-old women in South Africa
- 1% tenofovir vaginal gel reduced HIV incidence by 54% with high adherence (>80 percent)
- No serious adverse events

* From *Science* Vol. 329, No. 5996, 3 September 2010. Reprinted with permission from AAAS. Published online 19 July 2010. *http://www.sciencemag.org/content/329/5996/1168.abstract.* [DOI:10.1126/science.1193748].

EFFECTIVENESS OF PRE-EXPOSURE PROPHYLAXIS (PrEP): A large international NIH clinical trial provided strong evidence that the use of pre-exposure prophylaxis—that is, the use of antiretroviral treatment before exposure to prevent infection—can reduce risk of HIV acquisition in MSM. Additional and continued research is needed to determine whether PrEP will be similarly effective at preventing HIV infection in other at-risk populations.

RESEARCH TOWARD A CURE: Progress in both basic science and treatment research aimed at eliminating viral reservoirs has resulted in the establishment of an international alliance to plan and conduct research that could lead to a cure.

ADVANCES IN HIV GENETICS: NIH-sponsored researchers made an important discovery related to the genetics of an individual's immune system. These genes appear to be involved in the control of disease progression among a group of individuals considered "elite controllers," who have been exposed to HIV over an extended period, but whose immune systems have controlled the infection without therapy and without symptoms.

FURTHER ADVANCES IN PREVENTION OF MOTHER-TO-CHILD TRANSMISSION: Two recent studies have demonstrated the effectiveness of new multi-drug antiretroviral regimens for the prevention of mother-to-child-transmission of HIV during pregnancy and breastfeeding.

Preliminary Results of RV144 Announced

> **"For First Time, AIDS Vaccine Shows Some Success"**
>
> *The New York Times,* September 24, 2009*

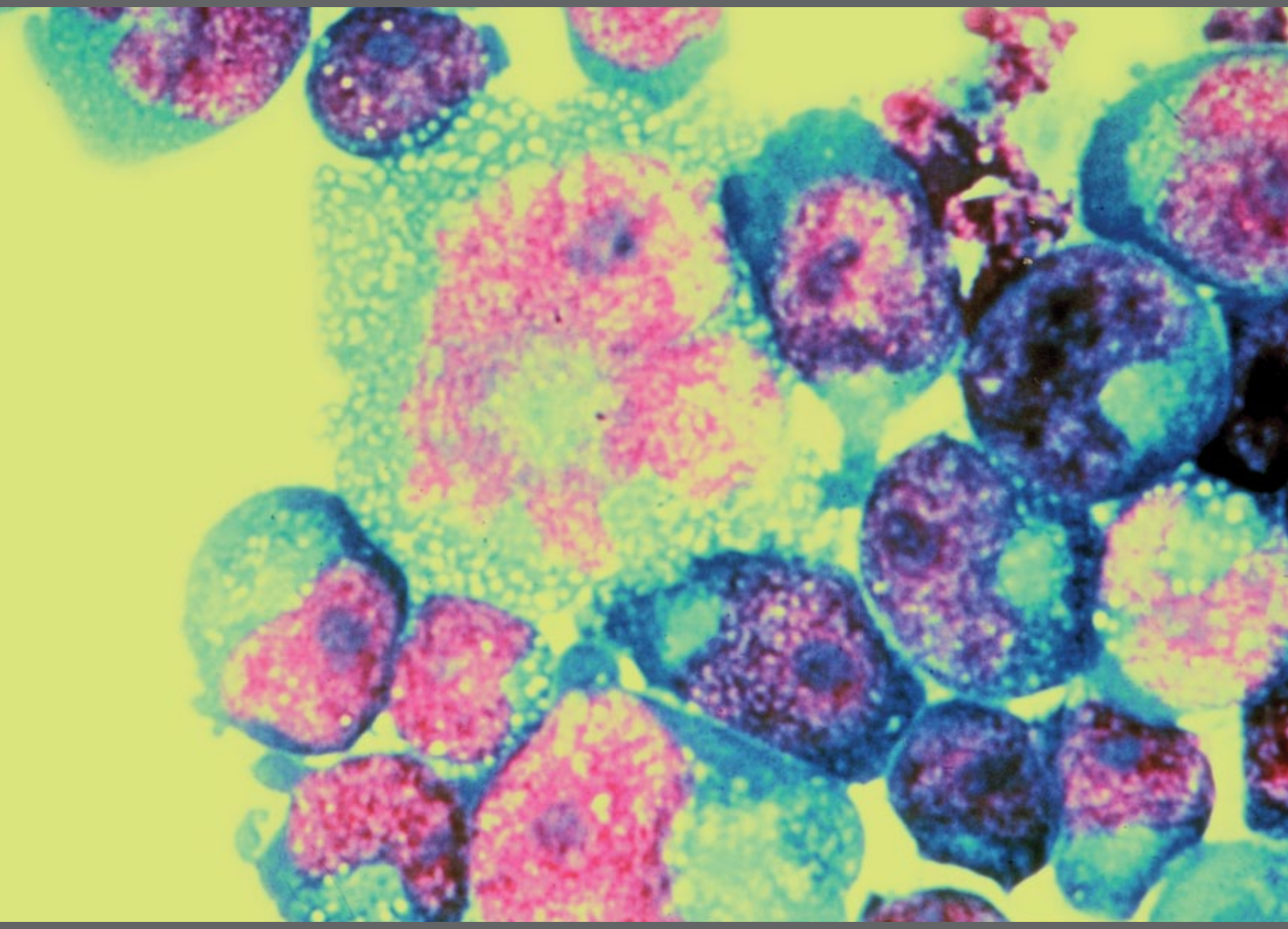
* Available at *http://www.nytimes.com/2009/09/25/health/research/25aids.html.*

HIV VACCINE PROOF-OF-CONCEPT: An HIV vaccine clinical trial conducted in Thailand by the NIH and the Department of Defense demonstrated the first indication of a modest but positive effect in preventing HIV infection. The trial marked the first step in proving the concept that a vaccine to prevent HIV infection is feasible.

NEW HOPE FOR PEOPLE COINFECTED WITH HIV AND TB: A Cambodia-based study co-funded by NIAID and the French National Agency for Research on AIDS and Viral Hepatitis demonstrated that the survival of untreated, HIV-infected adults with very weak immune systems and newly diagnosed TB can be prolonged by starting antiretroviral therapy 2 weeks after beginning TB treatment, rather than waiting 8 weeks, as had been standard.

IMPROVED THERAPY FOR AIDS-RELATED LYMPHOMA: The development of new lymphoma regimens and the tailoring of these regimens to specific tumor types have markedly improved the therapeutic outcome and survival of patients with AIDS-related lymphoma. In a recent study, 95 percent of patients with germinal center B-cell lymphoma were progression-free at 5 years.

PREVENTION OF CANCER IN HIV-INFECTED INDIVIDUALS: The human papillomavirus (HPV) vaccine, which was developed in the National Cancer Institute and licensed to Merck & Co. and to GlaxoSmithKline, has been shown to prevent anal intraepithelial neoplasm or anal cancer by preventing infection with oncogenic strains of HPV. In addition, this vaccine has been demonstrated to be safe and immunogenic in HIV-infected individuals. The incidence of anal cancer is rising very rapidly in the HIV-infected population.



FY 2012 Trans-NIH AIDS Research Priorities

To capitalize and build on these important scientific advances, the research priorities of the *FY 2012 Trans-NIH Plan for HIV-Related Research* and this trans-NIH AIDS research by-pass budget request represent the most critical and promising areas of research to address the continuing pandemic.

PRIORITY:
Expanding Basic Discovery Research

The NIH will continue its strong commitment to basic science, which is fundamental to the mission of the NIH and essential to enable innovation, to address critical gaps, and to capitalize on emerging scientific opportunities. Progress in basic science provides the building blocks to progress across all other scientific areas to ultimately achieve the goals of the President's National HIV/AIDS Strategy. Research is needed to better understand the virus and how it causes disease, including studies to delineate how gender, age, ethnicity, and race influence vulnerability to infection and HIV disease progression. OAR will increase support for genetic studies and breakthroughs in sequencing the human genome, and for new opportunities to apply these valuable tools to the search for new HIV prevention and therapeutics strategies. OAR also will increase research on eliminating viral reservoirs toward identifying a cure.

ETIOLOGY AND PATHOGENESIS

The NIH supports a comprehensive portfolio of research focused on gaining a better understanding of how HIV infection is established and maintained and what causes the 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, and monitoring of the safety and effectiveness of antiviral therapies. Groundbreaking strides have been made toward 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 affect treatment success or failure and influence vulnerability to infection and HIV-disease progression, including the development of HIV-associated comorbidities, malignancies, and coinfections. Additional studies of the genetic determinants associated with HIV susceptibility, disease progression, and treatment response 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 already has been identified. This finding led the Food and Drug Administration to recommend that doctors conduct genetic screening before prescribing abacavir to patients.

Research Toward a Cure

Research examining the mechanisms by which HIV establishes and reactivates latent reservoirs of infection is a high priority for the NIH. A better understanding of these processes could lead to the development of therapies that eradicate persistent viral reservoirs. Some have speculated that the eradication of these reservoirs might provide a cure for HIV disease. This represents an important priority for AIDS research and this by-pass budget request.

The FY 2012 by-pass budget request for this area is $862 million, which is an increase of 16 percent over the FY 2011 estimate. This includes increased funding for new, exciting areas of investigation, including studies on the application of genetics, genomics, epigenetics, proteomics, systems biology, and other related technologies to better understand HIV/AIDS

and the host immune response. The NIH will increase support for genomics studies and breakthroughs in sequencing the human genome, and will provide new opportunities to apply these valuable tools to the search for new HIV prevention and therapeutics strategies. The results from recent microbicide and vaccine 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 transverses mucosal surfaces, and the establishment and maintenance of latent viral reservoirs. The amount requested includes funding for research on the biology of HIV transmission and pathogenesis, including studies on coinfections, malignancies, premature aging, and other complications.

PRIORITY:
Reducing New Infections

Prevention of new HIV infections remains a top priority for NIH research. A vaccine that prevents the acquisition of HIV is our best hope for ending the HIV pandemic, but we also must work with and improve the many HIV prevention tools currently available, and add new ones to the toolbox. A varied set of available HIV prevention tools is imperative, because reducing HIV incidence inevitably will require a combination of various biomedical, behavioral, and structural interventions, and not just a single "silver bullet." For example, an HIV vaccine, a microbicide, and/or pre-exposure prophylaxis with antiretroviral drugs—even if only partially effective—used in combination with behavioral interventions could prove highly effective in preventing new infections. Biomedical and behavioral interventions are urgently needed to reach individuals at risk, particularly in racial and ethnic populations in the United States, in international settings, among women, and among MSM.

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. AIDS vaccine research remains a high priority to ensure that new and innovative concepts continue to be tested. The 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. The recent release of data from several vaccine clinical studies presents new scientific opportunities for investigation that will require realignment of resources.

The FY 2012 by-pass budget request for this activity is $625 million, an increase of 17 percent over the FY 2011 estimate. Basic research studies, particularly those using samples from the 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 on the development of improved animal models to conduct preclinical evaluations of vaccine candidates.

Advances in Basic and Clinical Vaccine Research Provide New Scientific Opportunities

In FY 2012, the NIH will capitalize on the important incremental findings from the NIH-supported vaccine clinical trial conducted in Thailand that demonstrated for the first time that a vaccine candidate could have a protective effect. With by-pass funding, the NIH will support:

- Additional basic research on HIV and host immune responses
- Design and development of new vaccine concepts
- Preclinical development and testing, including research involving nonhuman primates
- Evaluation of vaccine candidates in the pipeline
- New initiatives to integrate systems biology with HIV vaccine discovery.

MICROBICIDES

Microbicides are antimicrobial and other products that can be applied topically or orally as pre-exposure prophylaxis (oral PrEP), alone or in combination with other strategies, for the potential prevention of HIV and other sexually transmitted infections. These products may represent promising primary prevention interventions. The NIH supports a comprehensive and innovative microbicide research program that includes the screening, discovery, development, preclinical testing, and clinical evaluation of microbicide candidates; basic science aimed at understanding how HIV transverses mucosal membranes and infects cells; behavioral and social science research on adherence to and acceptability and use of microbicides among different populations; studies of the safety of microbicide use during pregnancy; and implementation research to better understand how to integrate a potential product into community prevention practices.

The FY 2012 by-pass budget request for this area is $169 million, which represents an increase of 18 percent over the FY 2011 estimate for this high-priority area of research. In FY 2012, the NIH will continue to support the discovery, design, development, and evaluation of microbicide candidates.

Research to Build on Important Microbicide Advances

Microbicide research is a high priority in this by-pass budget estimate to continue the momentum of science in this area. Key activities include:

- Support for the microbicide clinical trials network and the necessary infrastructure to conduct microbicide trials and oral PrEP trials—especially to build on recent research advances of a clinical trial, known as CAPRISA 004, conducted in South Africa and supported primarily by USAID
- Development of innovative, novel, high-risk, high-reward approaches for the development and testing of microbicide candidates
- Development of criteria for selecting potential products to be evaluated in clinical trials and for advancing them through the different phases of preclinical and clinical studies
- Research to define and analyze normal and abnormal male and female genital tract and anal/rectal immune function and their impact on HIV risk and acquisition
- Research on ethical, adherence, and other behavioral and social science research issues that can affect these clinical trials.

BEHAVIORAL AND SOCIAL SCIENCE

The NIH supports research to better understand how to change the risk behaviors that lead to HIV infection and disease progression, as well as how to maintain protective behaviors once they are adopted. This research includes studies to develop and evaluate interventions that directly target the substance abuse and sexual behaviors associated with HIV transmission. Other research aims toward better understanding the environmental, social, and cultural factors associated with HIV infection and disease outcomes, including stigma. Determining effective strategies to test HIV-infected persons, to link them to care, and to promote adherence to antiretroviral therapy is another important area of research. Comprehensive approaches that integrate biomedical and behavioral science perspectives are necessary to develop the needed range of preventive and therapeutic strategies. The NIH also supports research to improve behavioral methodologies, including ways to improve recruitment into clinical

trials, to enhance statistical analysis of behaviors such as alcohol use that can affect medication studies, or to characterize behavioral traits relevant to genetic or genomic studies.

The FY 2012 by-pass budget request for this area is $494 million, which is an increase of 15 percent over the FY 2011 estimate. The NIH will continue to fund research to develop and evaluate effective interventions to prevent HIV transmission and acquisition by reducing HIV-related risk behaviors and increasing protective behaviors.

Development of Combination Strategies

The long-term goal of prevention research is the development of combination strategies. No one prevention strategy alone will be sufficient. This by-pass budget request includes critical resources that will be directed toward several new prevention initiatives, including studies 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. Strategies are particularly needed to address specific high-risk populations, including MSM, older individuals, and adolescents, particularly among racial and ethnic populations.

TREATMENT 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 successfully demonstrated that treatment of HIV-infected pregnant women could significantly reduce transmission of HIV from mother to child. During the past year, NIH-supported researchers reported a landmark finding that the use of antiretroviral treatment in high-risk, uninfected MSM can reduce risk of infection.

Expanding Basic, Clinical, and Applied Knowledge About Treatment as Prevention

At the by-pass budget level, the NIH will increase and expand research in this new and emerging area to further advance knowledge about the uses of potential strategies, including:

- PrEP, the long-term use of treatment regimens for high-risk uninfected populations to prevent HIV acquisition
- Postexposure prophylaxis, the use of treatment to prevent HIV infection after accidental exposure, including in a health care environment
- Improved prevention of mother-to-child transmission, including prevention of transmission through breast milk
- A potential innovative prevention strategy known as “test and treat” to determine whether a community-wide HIV testing and counseling program with immediate treatment for HIV-infected individuals can decrease the overall rate of new HIV infections in that community.

PRIORITY:
Improving Disease Outcomes for HIV-Infected Individuals

Antiretroviral therapy (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; consequently, ART has delayed the progression of HIV disease to the development of AIDS. However, a growing proportion of patients receiving long-term ART are demonstrating treatment failure, experiencing serious drug toxicities and side effects, and developing drug resistance. Recent epidemiologic studies continue to show an increasing incidence of coinfections, comorbidities, AIDS-defining and non-AIDS-defining malignancies, and complications associated with long-term HIV disease and ART, including TB, hepatitis C, metabolic disorders, cardiovascular disease, conditions associated with aging, and neurologic and neurocognitive disorders. There is a need 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.

DRUG DISCOVERY, DEVELOPMENT, AND TREATMENT

The NIH supports a comprehensive therapeutics research program to design, develop, and test drugs and drug regimens to maintain long-term undetectable viral load, overcome drug resistance and treatment failure, prevent and treat HIV-associated comorbidities and complications, and eradicate persistent viral reservoirs that may lead to a potential or functional cure for HIV disease.

The FY 2012 by-pass budget request for this area is $692 million, which represents an increase of 12 percent over the FY 2011 estimate. Improved therapeutic regimens for the treatment of HIV and its associated coinfections and comorbidities are urgently needed, especially regimens that can be implemented in resource-limited settings. Over the past several years, the highest priority has been placed on prevention research within constrained budgets. However, expanding research in this area is critical to address new findings regarding complications and side effects of long-term disease and treatment.

Improved Therapies for Long-Term Survival

This by-pass budget provides critical support for:

- New and/or expanded initiatives for developing innovative therapies to control and eradicate HIV infection that may lead to a cure
- Identification of new drug targets based on the structure of HIV/host complexes
- Delineation of the interaction of aging and AIDS—including neurological, cardiovascular, and metabolic complications, and issues of frailty
- Discovery and development of improved therapies for AIDS-defining and non-AIDS-defining malignancies
- Discovery of the next generation of drugs that may be used in potential "treatment as prevention" strategies.

PRIORITY:
Reducing HIV-Related Disparities

Research is needed to better understand the causes of HIV-related health disparities, their role in disease transmission and acquisition, and their impact on treatment access and effectiveness. These include disparities among racial and ethnic populations in the United States, between developed and resource-constrained nations, between men and women, between youth and older individuals, and disparities based on sexual identity. The NIH will support research training for new investigators from racial and ethnic communities, development of research infrastructure, community outreach, information dissemination, and research collaborations to help reduce these disparities.

TRAINING, INFRASTRUCTURE, AND CAPACITY BUILDING

The NIH supports the training of domestic and international biomedical and behavioral AIDS researchers, and provides support for the equipment necessary for the conduct of AIDS-related research and clinical studies. The expansion of NIH-funded HIV research globally has necessitated the development of research infrastructure in many locations, including resource-limited settings in Africa, the Caribbean, India, and Asia. Numerous NIH-funded programs have increased the number of training positions for AIDS-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 United States.

The FY 2012 by-pass budget request for this area is $251 million, which represents an increase of 16 percent above the FY 2011 estimate. The NIH will continue to support ongoing efforts to increase the supply of nonhuman primates, particularly rhesus macaques, for AIDS research and other areas of biomedical research in both the United States and abroad. The NIH also will support training programs for U.S. and international researchers to build the critical capacity to conduct AIDS research in both racial and ethnic communities in the United States and in developing countries. 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 the NIH.

PRIORITY:
Translating Research From Bench to Bedside to Community

Research will focus on analyses of the feasibility, effectiveness, and sustainability required for the scale-up and implementation of interventions from a structured behavioral or clinical study to a broader "real world" setting. These research activities include critical epidemiologic and natural history studies, collaborative networks, and specimen repositories to evaluate various operational strategies that can be employed to scale up and evaluate treatment programs and successful prevention interventions in communities at risk.

NATURAL HISTORY AND EPIDEMIOLOGY

Natural history and epidemiologic research is essential for monitoring epidemic trends, developing and evaluating prevention modalities, following the changing clinical manifestations of HIV disease in different populations, and measuring the effects of treatment regimens. The NIH supports research in domestic and international settings to examine HIV transmission, HIV disease progression (including the occurrence of coinfections and opportunistic infections; malignancies; and metabolic, cardiovascular, neurological, and other complications), development of other HIV-related conditions, and improved methodologies to support this research. Epidemiologic research is instrumental in identifying and describing AIDS-related comorbidities, and in disentangling effects related to treatment from those related to HIV disease itself.

The FY 2012 by-pass budget request for this area is $308 million, which represents an increase of 12 percent above the FY 2011 estimate. As the AIDS epidemic continues to evolve, there is a crucial need to continue to conduct epidemiologic studies in both domestic and international settings. These studies have delineated the significant health disparities that are critical factors in the epidemic. The NIH will continue to place high priority on understanding the causes of HIV-related health disparities, in both the United States and around the world, their role in disease transmission and acquisition, and their impact on treatment access and effectiveness.

Addressing Critical Populations

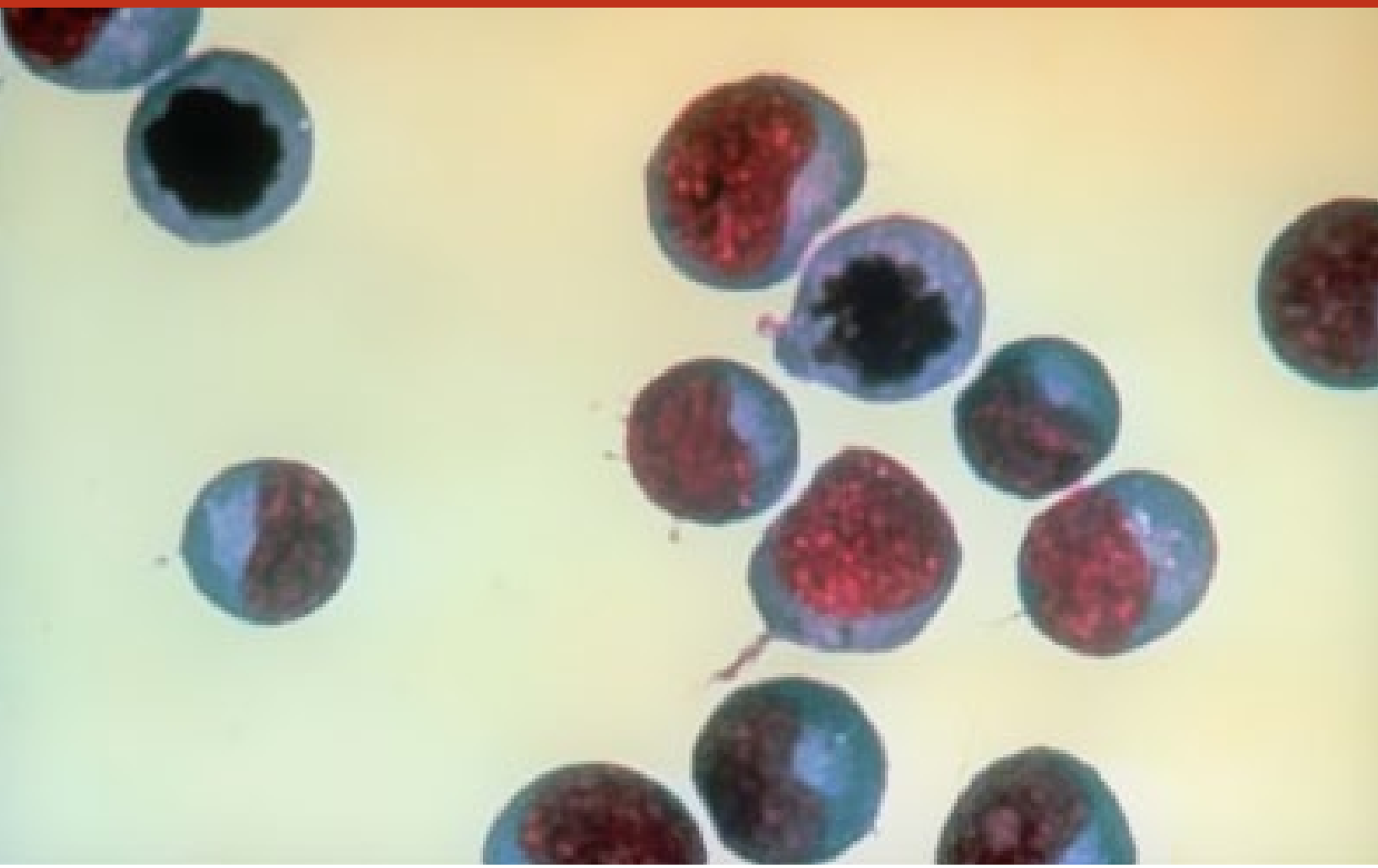
The by-pass budget level will allow the NIH to provide adequate support for high-priority epidemiology studies of groups and populations affected by HIV and at high risk for infection in the United States and around the world, including individuals aged 50 and older, MSM, substance users, women, and adolescents, especially African American and Hispanic adolescents. The NIH also will increase support for studies on:

- Mechanisms of disease progression
- Role of race and gender
- Effects of increased HIV testing and linkage to care
- Implementation/operational science, including the evaluation of strategies to scale up efficacious and cost-effective interventions to the community level.

INFORMATION DISSEMINATION

Effective information dissemination approaches are integral to HIV prevention and treatment efforts and critical in light of the continuing 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 incidence of HIV infection in specific population groups in the United States, such as racial and ethnic populations, MSM, and women, underscore the need to disseminate HIV research findings and other related information to communities at risk. The flow of information among researchers, health care providers, and the affected communities represents new opportunities to rapidly translate research results into practice and to shape future research directions. The NIH supports initiatives to enhance dissemination of research findings; develop and distribute state-of-the art treatment guidelines; and enhance recruitment and retention of participants in clinical studies, including women, adolescents, and racial and ethnic populations.

The FY 2012 by-pass budget request for this area is $64 million, which represents an increase of 12 percent above the FY 2011 estimate. As the number and complexity of clinical studies increase, 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 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 to health care providers and patients through the AIDSinfo Web site *(www.aidsinfo.nih.gov)*.



Benefits to Other Areas of Research

Because of the unique nature of HIV—the way the virus enters a cell, causes infection, affects every organ system, and unleashes a myriad of opportunistic infections, comorbidities, cancers, and other complications—and the pace at which the knowledge base has been expanded, AIDS research also is helping to unravel the mysteries surrounding many other infectious, malignant, neurologic, autoimmune, and metabolic diseases, as well as complex issues of aging and dementia. Basic knowledge of the biology of HIV infection and the processes by which it causes disease benefits other areas of basic research, including immunology, virology, microbiology, molecular biology, and genetics. AIDS research has provided an entirely new paradigm for drug design, drug development, and clinical trials to treat viral infections and to address the special recruitment requirements of women, minorities, and other underserved and at-risk populations. Drugs developed to prevent and treat AIDS-associated opportunistic infections also now benefit patients undergoing cancer chemotherapy or receiving anti-transplant-rejection therapy. Thus AIDS research is providing a new understanding of the relationship between viruses and cancer.

Conclusion

The scientific advances of the past year represent a turning point for AIDS research, opening new avenues for discovery and demonstrating the possibility of new strategies to prevent, treat, and potentially cure HIV. This by-pass budget estimate provides the resources necessary to capitalize on those advances to move science forward. OAR has shifted AIDS research program priorities and resources to meet the changing epidemic and scientific opportunities. This investment in AIDS research has produced groundbreaking scientific advances. However, serious challenges lie ahead. The AIDS pandemic will continue to wreak devastating consequences around the world for decades to come for virtually every sector of society. This by-pass budget request represents the collective professional judgment of scientific experts from around the country and the world on the highest priority areas of scientific opportunity and investment of our precious research dollars to move us forward from this important moment in science, to find new tools in the fight against AIDS—the deadliest epidemic of our generation.

Budget Tables

TABLE 1: NIH AIDS Research Funding by Scientific Area of Emphasis (Dollars in Millions)

AREA OF EMPHASIS	FY 2010 Actual Budget Authority	FY 2011 Estimate	FY 2012 By-Pass Estimate	Percent Change FY 2011 to FY 2012
Etiology and Pathogenesis	$745	$745	$862	16.0%
Vaccines	535	535	625	17.0
Microbicides	143	143	169	18.0
Behavioral and Social Science	429	430	494	15.0
Treatment as Prevention	68	69	81	17.0
Drug Discovery, Development, and Treatment	617	616	692	12.0
Total Therapeutics	685	685	773	13.0
Training, Infrastructure, and Capacity Building	216	216	251	16.0
Natural History and Epidemiology	275	275	308	12.0
Information Dissemination	57	57	64	12.0
TOTAL	$3,085	$3,086	$3,546	15.0%

TABLE 2: NIH AIDS Research Funding by Mechanism (Dollars in Millions)

	FY 2010 Actual Budget Authority		FY 2011 Estimate		FY 2012 By-Pass Estimate		Percent Change FY 2011 to FY 2012
	NO.	AMT.	NO.	AMT.	NO.	AMT.	
RESEARCH PROJECTS							
Noncompeting	1,751	1,345	1,729	1,275	1,800	1,448	14.0
Administrative supplements	(114)	18	(114)	15	(125)	25	67.0
Competing	583	295	687	361	750	433	20.0
Subtotal, RPGs	2,334	1,658	2,416	1,651	2,550	1,906	15.0
SBIR/STTR	67	29	79	36	100	45	25.0
Total, RPGs	2,401	1,687	2,495	1,687	2,650	1,951	16.0
RESEARCH CENTERS							
Specialized/comprehensive	66	143	69	133	69	145	9.0
Clinical research	—	55	1	55	—	67	22.0
Biotechnology	—	5	1	5	—	6	20.0
Comparative medicine	14	56	18	57	15	72	26.0
Research centers in minority institutions	1	14	2	14	1	14	0.0
Subtotal, Centers	81	273	91	264	85	304	15.0
OTHER RESEARCH							
Research careers	248	43	237	41	259	55	34.0
Cancer education	—	—	—	—	—	—	—
Cooperative clinical research	13	21	12	18	17	34	89.0
Biomedical research support	—	2	1	2	1	2	0.0
Minority biomedical research support	—	—	1	—	—	—	—
Other	142	60	122	61	170	73	20.0
Subtotal, Other Research	403	126	373	122	447	164	34.0
Total, Research Grants	2,885	2,086	2,959	2,073	3,182	2,419	17.0
TRAINING	**FTTPs**		**FTTPs**		**FTTPs**		
Individual	86	4	86	4	86	4	0.0
Institutional	649	31	649	31	701	40	29.0
Total, Training	735	35	735	35	787	44	26.0
Research and development contracts	145	461	145	474	155	520	10.0
(SBIR/STTR)	(2)	(1)	(2)	(1)	(2)	(2)	100.0
Intramural research	—	313	—	314	—	355	13.0
Research management and support	—	126	—	126	—	140	11.1
Construction	—	—	—	—	—	—	—
Office of the Director	—	64	—	64	—	68	6.0
Buildings and facilities	—	—	—	—	—	—	—
TOTAL, Budget Authority	**—**	**$3,085**	**—**	**$3,086**	**—**	**$3,546**	**15.0%**