

National Institutes of Health AIDS research priorities and funding

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The exploding global HIV and AIDS pandemic

| Group | People newly infected in 2000 | People living with HIV/AIDS | AIDS deaths in 2000 | Total AIDS deaths as of December 2000 |
|----------|-------------------------------|-----------------------------|---------------------|---------------------------------------|
| Adults | 4.7 million | 34.7 million | 2.5 million | 17.5 million |
| Women | 2.2 million | 16.4 million | 1.3 million | 9.0 million |
| Children | 600,000 | 1.4 million | 500,000 | 4.3 million |
| Total | 5.3 million | 36.1 million | 3.0 million | 21.8 million |

Source: [UNAIDS](#)

By every definition, AIDS is the great plague of the 20th century and the dawn of the 21st century. HIV has infected more than 50 million people around the world, and AIDS has already killed 22 million people, surpassing tuberculosis and malaria as the leading infectious cause of death worldwide ([1](#), [2](#))

AIDS is the greatest international challenge of our generation. If the global spread of HIV/AIDS continues unchecked, South Asia, Southeast Asia, and perhaps China will follow the disastrous course of sub-Saharan Africa. Rapid increases in HIV infection also are occurring in Eastern Europe and Central Asia, and AIDS represents a serious threat in Latin America and the Caribbean.

The coexistence of other endemic diseases widely prevalent in developing countries, such as respiratory and gastrointestinal infections, complicates treatment and poses additional problems for medical personnel caring for HIV-infected individuals. Of particular note is the parallel epidemic of tuberculosis in the developing world. Attitudes, beliefs, and taboos surrounding sex, the status of women and children, and the source and etiology of HIV can complicate attempts to control transmission and provide appropriate prevention and treatment.

The HIV/AIDS epidemic in the United States continues to evolve. The incidence of new AIDS cases has declined, due largely to expanded use of new antiretroviral therapies that delay

progression of HIV infection to AIDS. However, the decline in death rates observed in the late 1990s has now leveled off and, more disturbingly, the rate of new HIV infections has not changed since 1990 and remains constant at about 40,000 each year, according to Centers for Disease Control and Prevention (CDC) estimates. This means that the overall epidemic is continuing to expand (3-5). In fact, HIV infection rates are continuing to climb in a number of subpopulation groups, including women, racial and ethnic minorities, young homosexual men, individuals with addictive disorders, and people over 50 years of age (3, 6). The appearance of multidrug-resistant strains of HIV presents an additional serious public health concern (7-11). These data forebode an epidemic of even greater magnitude in the coming years.

HIV/AIDS research program

To respond to this pandemic, the U.S. National Institutes of Health (NIH) has developed a comprehensive biomedical and behavioral research program to better understand the basic biology of HIV, develop effective therapies to treat and control HIV disease, and design interventions to prevent new infections from occurring. The NIH supports AIDS research both in NIH intramural laboratories and at academic and medical institutions in the United States and internationally. The Office of AIDS Research (OAR) is mandated by public law to plan and coordinate the research programs sponsored by all of the NIH institutes and centers (Table 1). The OAR develops an annual comprehensive AIDS research plan called the "[NIH Plan for HIV-Related Research](#)," which is based on the most compelling scientific priorities that will lead to better therapies and prevention strategies for HIV infection and AIDS. The OAR has established an effective model for developing a consensus on the scientific priorities of the plan. Planning groups for each of the areas of the plan, composed of NIH scientists, experts from academia and industry, and representatives from the AIDS community meet in workshops to develop each section. A list of participants in the fiscal year 2002 planning process can be found in [Appendix D](#) of the plan. The plan is also reviewed by the [OAR Advisory Council](#), which provides advice and guidance to the director of the OAR. This chartered advisory council includes world-renowned experts from academia, industry, community constituency groups, ex-officio members from several NIH institute advisory councils, and representatives from other federal government agencies, including the CDC, Veterans Administration, and Department of Defense.

Table 1. HIV/AIDS funding by institute and center, National Institutes of Health (in millions of dollars).

| Institute or center | Fiscal year¹ | | |
|--|--------------------------------|----------------------|----------------------------------|
| | Actual 2000 | Estimate 2001 | Estimate 2002² |
| National Institute of Allergy and Infectious Diseases | \$928.695 | \$1,062.592 | \$1,192.855 |
| National Institute on Drug Abuse | 217.898 | 244.902 | 284.741 |
| National Cancer Institute | 230.474 | 237.860 | 251.200 |
| National Institute of Mental Health | 128.562 | 145.051 | 161.417 |

| | | | |
|--|-------------|-------------|------------------|
| National Center for Research Resources | 105.788 | 117.410 | 129.112 |
| National Institute of Child Health and Human Development | 89.540 | 101.666 | 114.496 |
| National Heart, Lung, and Blood Institute | 65.527 | 68.008 | 71.717 |
| Office of the Director | 44.653 | 48.234 | 53.540 |
| National Institute of General Medical Sciences | 37.128 | 43.298 | 47.891 |
| National Institute of Neurological Disorders and Stroke | 33.621 | 37.674 | 42.264 |
| National Institute of Diabetes and Digestive and Kidney Diseases | 21.983 | 24.562 | 27.360 |
| National Institute on Alcohol Abuse and Alcoholism | 19.218 | 21.195 | 24.402 |
| National Institute of Dental and Craniofacial Research | 20.193 | 21.862 | 22.937 |
| John E. Fogarty International Center | 14.404 | 16.152 | 18.096 |
| National Eye Institute | 10.890 | 11.555 | 12.730 |
| National Institute of Nursing Research | 7.501 | 9.663 | 10.978 |
| National Institute of Environmental Health Sciences | 7.541 | 7.769 | 8.166 |
| National Library of Medicine | 5.063 | 5.525 | 6.677 |
| National Institute of Arthritis and Musculoskeletal and Skin Diseases | 5.022 | 5.629 | 6.404 |
| National Human Genome Research Institute | 4.188 | 5.750 | 6.158 |
| National Institute on Aging | 3.919 | 4.386 | 4.985 |
| National Center for Complementary and Alternative Medicine | 1.030 | 1.030 | 1.630 |
| National Institute on Deafness and Other Communications Disorders | 1.590 | 1.592 | 1.596 |
| National Institute of Biomedical Imaging and Bioengineering | --- | --- | --- ³ |
| National Center on Minority Health and Health Disparities | --- | --- | --- ³ |
| Total budget authority | \$2,004,428 | \$2,243,365 | \$2,501,352 |

¹ 1 October to 30 September

² [President's budget request for NIH HIV/AIDS Research](#)

³ Newly established center or institute

The plan is divided into scientific areas, including natural history and epidemiology, etiology and pathogenesis, therapeutics, vaccines, and behavioral and social science. The plan further

addresses a number of important areas that cut across all of the scientific areas: racial and ethnic minorities; international research; training, infrastructure, and capacity building; and information dissemination ([Table 2](#)). The OAR is currently preparing the fiscal year 2003 Plan, which will include three new important sections: microbicides, prevention science, and women and girls.

Table 2. HIV/AIDS research spending by scientific areas of the [NIH Plan for HIV-Related Research](#) (in millions of dollars).

| Research area | Fiscal year ¹ | | | Change between 2001 and 2002 |
|---|--------------------------|---------------|----------------------------|------------------------------|
| | Actual 2000 | Estimate 2001 | Estimate 2002 ² | |
| Etiology and pathogenesis | \$582.682 | \$642,270 | \$701,318 | \$59.048 |
| Therapeutics | 570.401 | 629.211 | 673.324 | 44.113 |
| Behavioral and social science | 275.185 | 310.673 | 357.105 | 46.432 |
| Vaccines | 232.107 | 281.734 | 356.589 | 74.855 |
| Natural history and epidemiology | 238.604 | 262.135 | 282.974 | 20.839 |
| Training and infrastructure | 76.463 | 84.999 | 95.097 | 10.098 |
| Information dissemination | 28.986 | 32.343 | 34.945 | 2.602 |
| Total, budget authority | \$2,004.428 | \$2,243.365 | \$2,501.352 | \$257.987 |

¹ 1 October to 30 September

² [President's budget request for NIH HIV/AIDS research](#)

The [NIH Plan for HIV-Related Research](#) also serves as the framework for developing the annual NIH AIDS budget, for determining the use of NIH AIDS-designated dollars, for tracking and monitoring expenditures, and for informing the scientific community, the public, and the HIV/AIDS-affected community about NIH research priorities. In collaboration with the director of NIH, the OAR determines the total annual AIDS research budget. Within that total, the OAR establishes the AIDS research budgets for each NIH institute and center. The institutes and centers use these funds to support their research portfolios in accordance with the plan and their own research missions in both intramural programs (on the NIH campus) and extramural grants and contracts awarded to research institutions in the United States and around the world ([Table 1](#)).

HIV/AIDS research priorities

The overarching themes of the fiscal year 2002 research agenda are research to prevent and reduce HIV transmission; research to develop therapies for those who are already infected; international research, particularly in developing countries; and biomedical and behavioral research targeting the disproportionate impact of AIDS on minority populations in the United States. These efforts all require a strong foundation of basic science.

It is imperative that the United States help address HIV and AIDS prevention and treatment needs worldwide. The transmissibility of HIV--between individuals and across borders and populations--defines the global pandemic and provides the potential for unlimited global spread. The development of appropriate biomedical and behavioral interventions will provide the opportunity for dramatic reductions in the rates of new infections and ultimate control of the pandemic.

Prevention research

The approach that NIH takes to HIV-prevention research includes contributions from the biomedical, behavioral, and social sciences and emphasizes interventions to reduce HIV transmission for both infected and uninfected at-risk individuals. Our biomedical prevention research priorities include the development of vaccines and topical microbicides, strategies to prevent perinatal transmission (including a better understanding of the risks associated with breast-feeding), and management of sexually transmitted diseases. Behavioral research strategies include interventions related to drug and alcohol use and risky sexual behaviors. This research must be appropriate for different populations and subepidemics in the United States and around the world.

Vaccine research

A safe and effective HIV-preventive vaccine is essential for the global control of the AIDS pandemic. The NIH's funding for HIV vaccine research increased by more than 170% between fiscal years 1997 and 2002 ([Figure 1](#)) and resulted in the award of new grants for novel vaccine design and development, invigoration and reorganization of the NIH HIV-vaccine clinical trials effort, and establishment of the new intramural Vaccine Research Center. In February 1999, NIH-supported investigators initiated the first AIDS vaccine trial in Africa ([see press release](#)).

Behavioral and social science research

Prevention programs based on results of behavioral and social science research have altered sexual and drug-using behaviors and have reduced the risk of transmission in many communities and subgroups both in the United States and globally. The NIH conducts and supports research to further our understanding of how to change behaviors that lead to HIV transmission--including preventing their initiation--and how to maintain protective behaviors once they are adopted in all populations at risk. The NIH also supports research on preventing and mitigating the psychosocial consequences of HIV infection

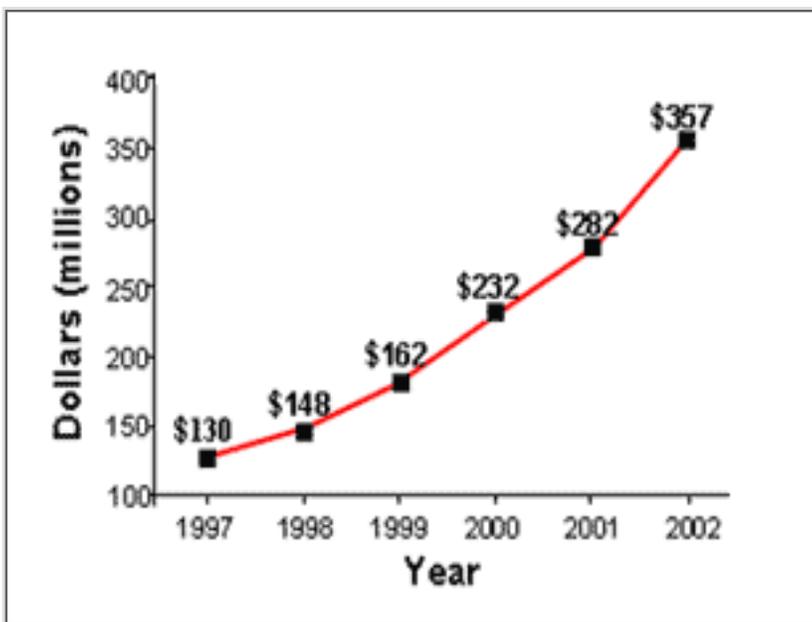


Figure 1. National Institutes of Health funding for HIV/AIDS vaccine research (source: [NIH](#)).

and AIDS on individuals and communities.

Topical microbicides research

Women's vulnerability to acquiring HIV infection demands the development of safe, effective, and acceptable female-controlled chemical and physical barrier methods, such as topical microbicides, to reduce HIV transmission. To enhance research in this critical area, the OAR co-sponsored the first international conference devoted to all aspects of microbicide research and development ([12](#)), and another international conference will be held in 2002 (see [Web site](#)). The NIH is supporting phase I, phase II, and phase III clinical trials of various topical microbicides and supports behavioral and social research on the acceptability and use of microbicides by different populations. Additional efforts are essential to accelerate microbicide research and to ensure a comprehensive program for screening, discovery, development, preclinical testing, and clinical evaluation of potential spermicidal and nonspermicidal topical agents and other barrier methods. To that end, the OAR has prepared a strategic plan for microbicide research that recently was submitted to Congress.

Mother-to-child transmission

In the United States, regimens of antiretroviral drugs resulting from NIH-supported research have dramatically reduced transmission of HIV from infected mothers to their infants. However, the complexity of administration and high cost continue to make this option impractical for much of the developing world. Research on low-cost alternatives is essential as are better methods for reducing HIV transmission through breast-feeding.

Treatment research

Today, many HIV-infected people are living with the benefits of NIH-supported research. The NIH collaborates with agencies in the Department of Health and Human Services and with nongovernment organizations to develop guidelines for treatment regimens based on current clinical research findings (see [guidelines](#)). The NIH efforts include drug discovery, development, and clinical trials programs for agents against HIV and its associated opportunistic infections and malignancies. Combination regimens, including protease inhibitors, have extended the length and quality of life for many HIV-infected individuals in the United States and Western Europe. Unfortunately, however, highly active antiretroviral therapy (HAART) has failed to eradicate HIV, and a growing proportion of patients receiving therapy experience treatment failure ([6](#), [13-15](#)). Some patients find it difficult or impossible to comply with arduous treatment regimens, develop toxicities and side effects, or cannot afford the high cost of the medications ([16-18](#)). Others fail to obtain a satisfactory reduction in viral load even while adhering to treatment regimens ([19](#), [20](#)). In addition, metabolic complications, including insulin resistance, and body composition changes, such as deforming deposits of abdominal adipose tissue, have emerged in individuals who have been on long-term antiretroviral regimens ([21-23](#)). Finally, an increasing number of treatment failures are linked to the emergence of drug-resistant and cross-resistant HIV and other mechanisms, such as bioavailability of drugs ([24-26](#)).

The need for simpler, less toxic, and cheaper drugs and drug regimens to treat HIV infection and its associated opportunistic infections, malignancies, and other complications continues to be a high priority. This includes the discovery and development of the next generations of antiviral drugs directed against new cellular and viral targets. Clinical trials will help to better define when to begin and/or when to switch drugs within a regimen and identify regimens for treatment-experienced individuals who no longer respond to these anti-HIV drugs.

Regimens of antiretroviral treatment and prophylaxis of opportunistic infections are becoming increasingly complex with respect to drug-drug interactions and adherence. Protease inhibitors, in particular, interact with each other and many other medications commonly used by HIV-infected individuals. Additional research is either planned or ongoing to find ways of minimizing viral replication and delaying disease progression, drug resistance, and development of manifestations such as metabolic complications and body-composition changes.

Basic research

Of paramount importance in our fight against HIV infection and AIDS is maintaining a strong commitment to basic research. Tremendous progress has been made in understanding the fundamental steps in the life cycle of HIV, the host-virus relationship, and the clinical manifestations of HIV infection and AIDS. Groundbreaking research on basic HIV biology and pathogenesis has revolutionized the design of drugs, methodologies for diagnosis, and the monitoring for safety and efficacy of antiviral therapies.

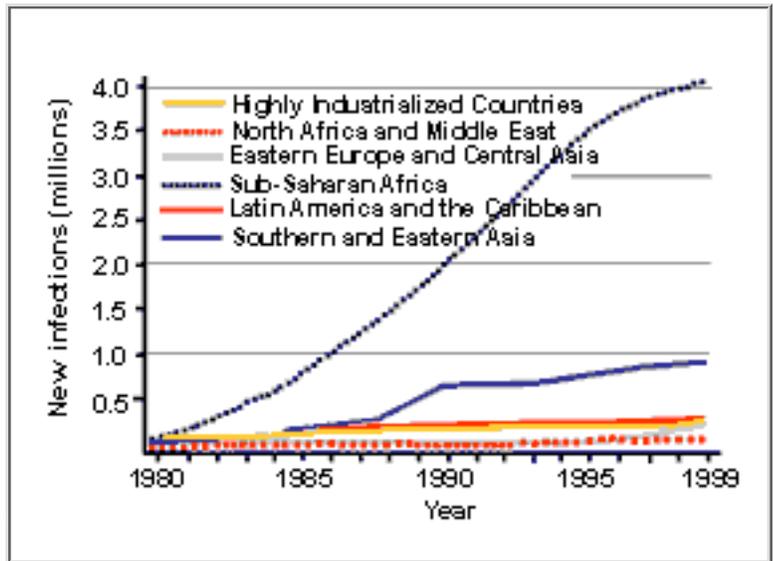
In spite of these achievements, we still do not have a clear understanding of major aspects of the virus interaction with the infected individual, the nature of the immune response to the virus, how the virus establishes infection and spreads throughout the body, and the mechanisms of HIV pathogenesis. This basic knowledge is critical for our efforts to prevent, treat, and control HIV infection and disease progression. Basic behavioral and social science studies are also needed to provide further information on risk factors and behaviors, the identification of populations at risk, and the development of successful interventions that are culturally and ethnically sensitive and appropriate. Thus, a substantial portion of NIH-sponsored, AIDS-related research will continue to be devoted to fundamental biomedical, behavioral, and social science research.

International research priorities

The NIH supports a growing portfolio of research conducted in collaboration with investigators in developing countries. Results of this research benefit people in the country where the research is conducted and people affected by HIV/AIDS worldwide ([Figure 2](#)). The NIH collaborates with the Joint United Nations Programme on HIV/AIDS (UNAIDS), the World Health Organization, host-country governments, and in-country scientists on vaccine development and preparations for efficacy trials. The NIH sponsors research in Africa, Asia, and Latin America on factors related to HIV transmission and the pathogenic mechanisms associated with HIV-disease progression. The success of international studies requires that foreign scientists be full and equal partners in the design and conduct of collaborative studies and that they have full responsibility for the conduct of studies in their country. To that end, NIH supports international training programs and initiatives to build research infrastructure,

including trained personnel and research facilities, and laboratory capacity in developing countries where the research is conducted.

To address the increasing urgency of the global AIDS pandemic, the OAR has established a new initiative and strategic plan for global research on HIV/AIDS to slow the disaster and reverse its destruction of communities, economies, and nations worldwide. The [Global AIDS Research Initiative and Strategic Plan](#) reaffirms NIH's long-standing commitment to international AIDS research and to significantly increase research efforts in the coming year to benefit nations with limited resources. The NIH plans to increase its investment in international AIDS research from an estimated \$133 million in fiscal year 2001 to about \$154 million in fiscal year 2002.

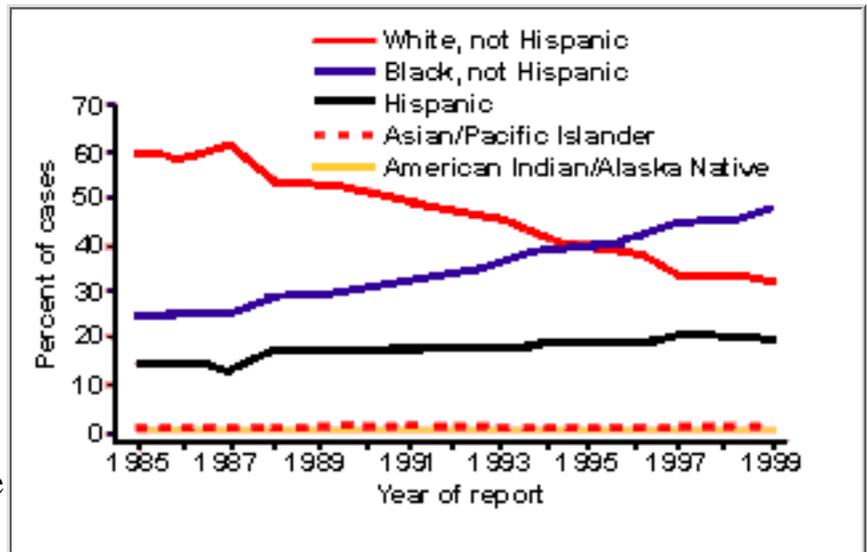


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Figure 2. Estimated annual number of new HIV infections by region, 1980 to 1999 (figure adapted from [UNAIDS](#)).

Racial and ethnic minorities

Recent CDC reports describe the disproportionate increase of AIDS cases among U.S. racial and ethnic minorities, especially blacks and Hispanics ([Figure 3](#)). As of 31 December 2000, 61% of cumulative AIDS cases were black or Hispanic ([3](#)).



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Figure 3. Proportion of AIDS cases, by race/ethnicity and year of report, 1985-1999 (figure adapted from [CDC](#)).

Research to address the impact of the epidemic on minority communities continues to be a high priority (see the [OAR Minority Initiatives](#)). We are directing increased resources toward new community-sensitive interventions, including those that address the co-occurrence of other sexually transmitted diseases, hepatitis, drug abuse, and mental illness, and interventions that consider the role of culture, family, and other social factors in the transmission and prevention of these disorders in minority communities.

The NIH is making significant investments to improve research infrastructure and training

opportunities for minorities, and we will continue to ensure that participation in AIDS clinical trials and natural history, epidemiology, and prevention studies reflects the demographics of the epidemic. The NIH plans to increase its investment in research addressing racial and ethnic minorities from an estimated \$444.7 million in fiscal year 2001 to about \$495 million in fiscal year 2002.

The OAR has provided additional funds to increase the number of minority investigators conducting behavioral and biomedical research; target the links between substance abuse, sexual behaviors, and HIV infection; increase the number of outreach education programs targeting minority physicians and at-risk populations; and expand our portfolio of population-based research.

One of these projects is a series of training and career development workshops for racial and ethnic minority investigators. These workshops provide minority investigators with an opportunity to learn about available NIH-funding mechanisms and to meet and network with senior minority investigators who receive NIH funding.

Conclusion

This investment in AIDS research is unraveling the mysteries surrounding many other infectious, malignant, neurologic, autoimmune, and metabolic diseases. For example, AIDS research has provided an entirely new paradigm for drug design and development to treat viral infections. The drug known as 3TC, developed to treat AIDS, is now the most effective therapy for chronic hepatitis B virus infection. Drugs developed to prevent and treat AIDS-associated opportunistic infections also benefit patients undergoing cancer chemotherapy or receiving antitransplant-rejection therapy.

Dr. Anthony Fauci, director of the [National Institute of Allergy and Infectious Diseases of the NIH](#), has stated that "... the potential for biomedical research to provide the tools for lasting solutions to the major infectious disease killers and indeed all diseases that afflict mankind is enormous. It remains critical that the medical and public health communities continue to argue cogently for adequate attention and sustained research support for all diseases of global health importance. The biomedical research experience with the AIDS epidemic should serve as an important paradigm in the pursuit of this goal" ([27](#)).

The worldwide human and economic toll of this insidious disease is profound, and we will never solve the crisis of HIV/AIDS for our own citizens without controlling the pandemic in the rest of the world. We have made enormous strides in our fight against this horrible disease, but the challenges before us are enormous. AIDS research sponsored by NIH has and will continue to provide scientific insight and basic understanding of HIV, its pathogenic mechanisms, and the immune system, which is crucial for the development of treatments, vaccines, and prevention interventions to halt the further spread of the pandemic and help those already affected by the disease.

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