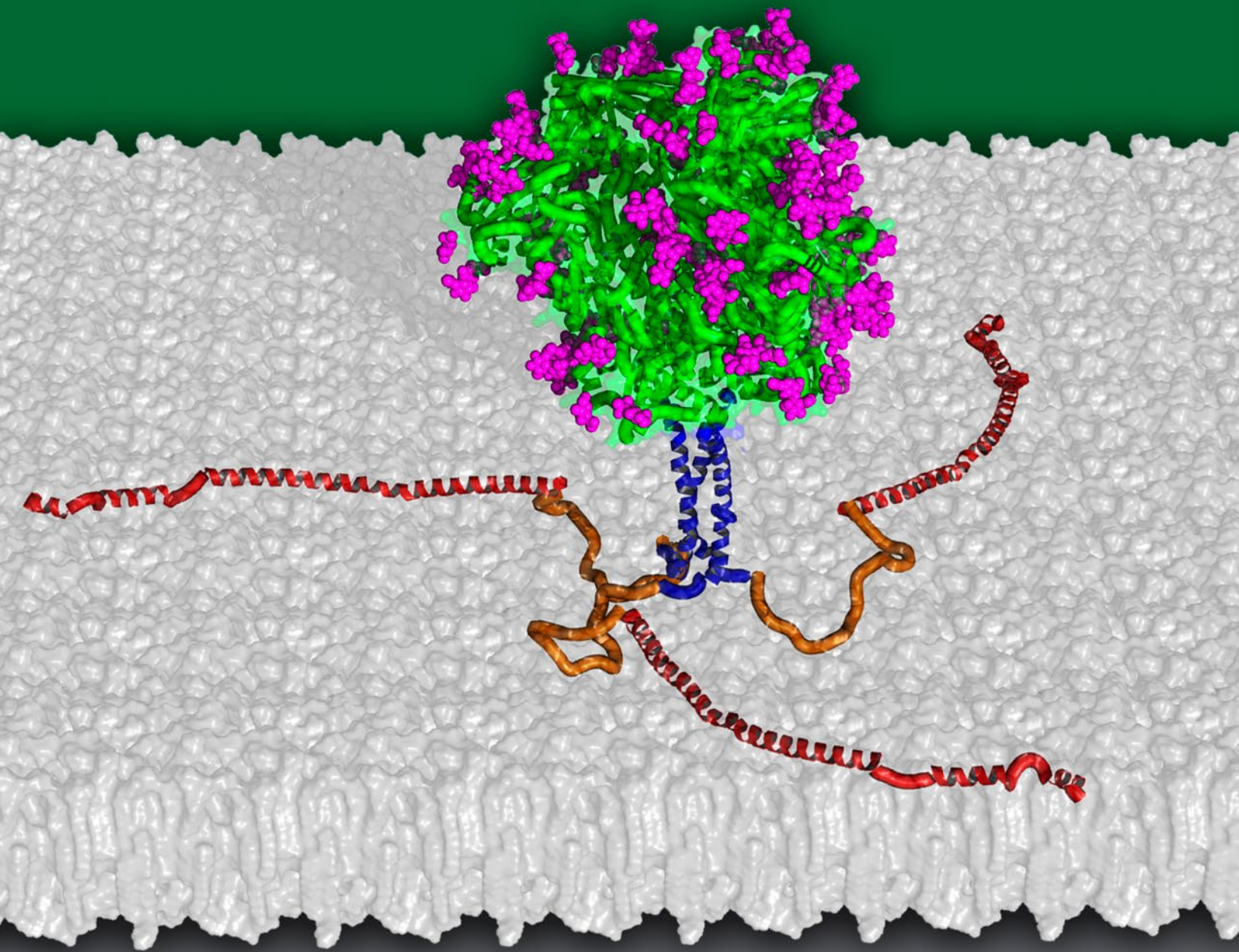
National Institutes of Health

NIH Strategic Plan for HIV and HIV-Related Research

FY 2019/2020



Prepared by the Office of AIDS Research
Maureen M. Goodenow, Ph.D.
NIH Associate Director for AIDS Research and
Director, Office of AIDS Research

Front Cover

Image Description: The structures of three membrane-associated cytoplasmic tails of gp41 are shown in red and orange in this illustration of the trimeric spike structure. The rest of this HIV-1 envelope protein, which is docked on a gray membrane, includes the structures of gp120 and gp41 (green), the transmembrane segment (blue), and glycan residues (magenta).

Source: Jamil Saad, Ph.D., and his team at the University of Alabama at Birmingham has solved the last unknown protein structure of HIV-1, the retrovirus that can cause AIDS.

A Tribute to
Dr. Bonnie Mathieson
1945-2018

This NIH Strategic Plan for HIV and HIV-Related Research is dedicated to the memory of Dr. Bonnie Mathieson at the National Institutes of Health (NIH) Office of AIDS Research (OAR).

Dr. Mathieson will be fondly remembered for her unwavering dedication and efforts toward finding a vaccine to end HIV/AIDS. Losing her is not only a great loss for the NIH, but for the entire HIV/AIDS community.

Dr. Mathieson had a long and distinguished NIH career spanning 43 years of service. After completing a postdoctoral fellowship at the National Institute of Allergy and Infectious Diseases (NIAID), she became a Senior Staff Fellow in that Institute's Laboratory of Microbial Immunity and later worked at the National Cancer Institute (NCI). Dr. Mathieson was one of the first people to use laser-based flow cytometry technology to analyze the physical and chemical characteristics of cells. She became an expert in cell phenotyping and basic immunology, and later made seminal contributions to the field of basic T cell immunology. Yearning to make a greater impact on the HIV/AIDS field, Dr. Mathieson moved to the NIAID Division of AIDS, where her immunology expertise was vital to the NIH's mission of developing an HIV vaccine.

Dr. Mathieson most recently served as a Health Scientist Administrator in the NIH OAR. During her 22-year tenure as the OAR lead for HIV vaccine research, she was instrumental in advancing the NIH HIV vaccine program in countless ways. Dr. Mathieson lent her expertise, wisdom, advice, and support to numerous vaccine trials and helped develop a scholars program to train the next generation of HIV vaccine research scientists. Her dedication to scientific endeavor is demonstrated by her prolific publication record as an author on more than 127 peer-reviewed papers.

Dr. Mathieson was a tireless advocate for young people, women, and early-career investigators. Her colleagues knew her as an international leader in the HIV vaccine field and a devout supporter of research to prevent HIV and improve the health and outcomes of persons with HIV.

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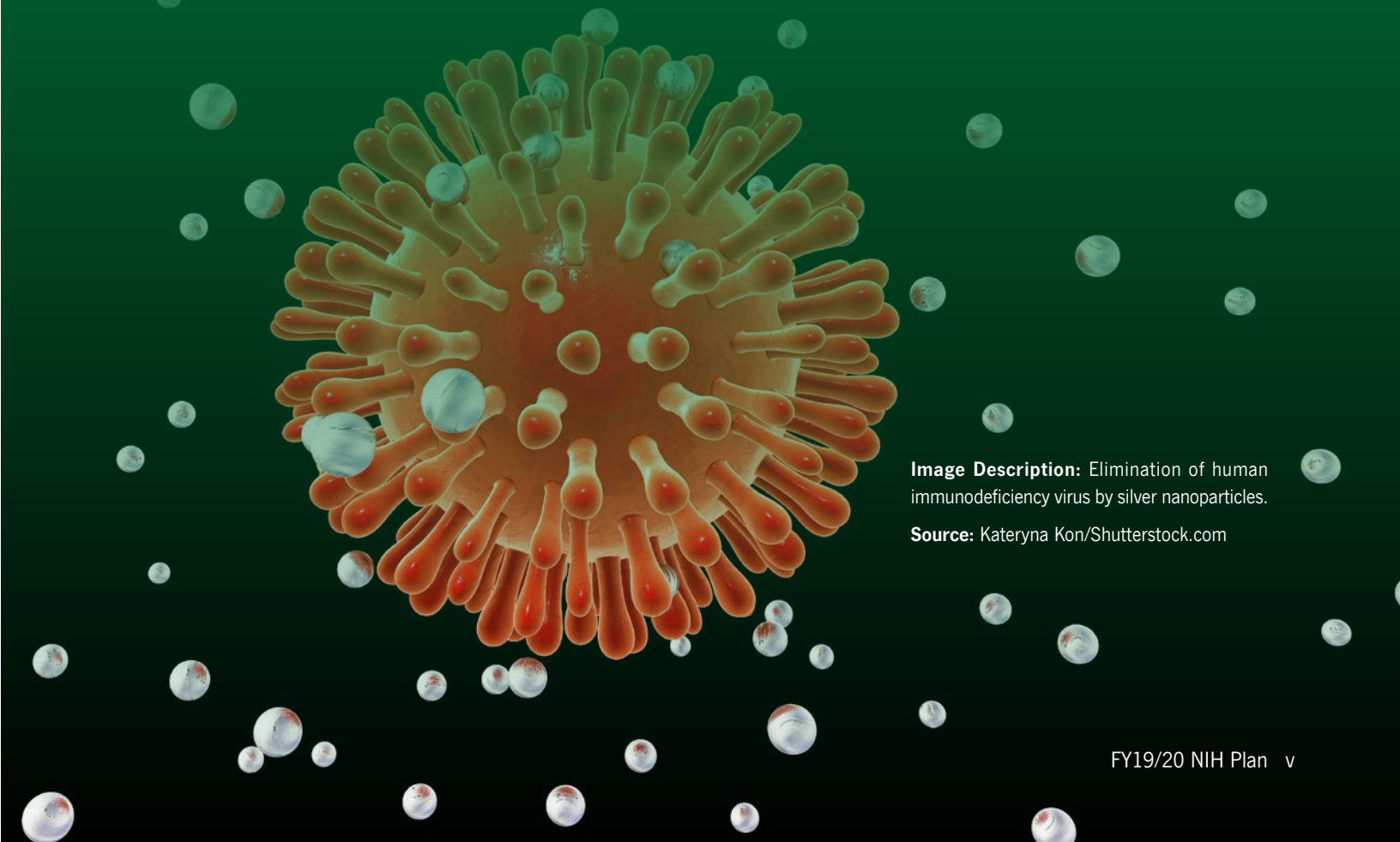


Image Description: Elimination of human immunodeficiency virus by silver nanoparticles.

Source: Kateryna Kon/Shutterstock.com

Acronyms/Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ARVs	Antiretrovirals
ART	Antiretroviral Therapy
BSSR	Behavioral and Social Sciences Research
cART	Combination Antiretroviral Therapy
CCCs	Comorbidities, Coinfections, and Complications
CNS	Central Nervous System
FY	Fiscal Year
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
ICOs	Institutes, Centers, and Offices
IS	Implementation Science
MPTs	Multipurpose Prevention Technologies
NIH	National Institutes of Health
OAR	Office of AIDS Research
PWH	Persons with HIV
PrEP	Pre-exposure Prophylaxis
RFI	Request for Information
STIs	Sexually Transmitted Infections
The Plan	NIH Strategic Plan for HIV and HIV-Related Research
TasP	Treatment as Prevention
TICB	Training, Infrastructure, and Capacity Building
TB	Tuberculosis
U=U	Undetectable Equals Untransmittable
UNAIDS	Joint United Nations Programme on HIV and AIDS
USG	U.S. Government

Letter from the Director

The Office of AIDS Research (OAR), in the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) in the National Institutes of Health (NIH), presents the *NIH Strategic Plan for HIV and HIV-Related Research* (the Plan) for fiscal years (FY) 2019/2020. In accordance with the Legislative Mandate Section 2353 of the Public Health Service Act, the OAR coordinates the scientific, budgetary, legislative, and policy elements for the NIH HIV research portfolio. The OAR allocates funds to the NIH Institutes, Centers, and Offices (ICOs) to advance the NIH-wide HIV research agenda and ensures that funds are aligned with the HIV research priorities outlined in NOT-OD-15-137: reduce the incidence of new HIV infections; develop next-generation HIV therapies; research toward an HIV cure; address HIV-associated comorbidities, coinfections, and complications (CCCs); and advance the critical framework of cross-cutting areas to end the HIV/AIDS pandemic.

In less than 40 years, HIV/AIDS has been transformed from a fatal disease to a manageable chronic illness. This unprecedented progress is due in large part to the significant NIH investments in research, which have produced groundbreaking advances in our understanding of basic virology, human immunology, HIV pathogenesis, the development of safe and effective antiretroviral (ARV) medications, and effective interventions to prevent HIV acquisition and transmission.

The momentum and continued investments, however, are necessary to sustain these accomplishments and to secure future advances. The integrated strategic approaches outlined in the Plan will lead to new, innovative research efforts and a pipeline for discovery that will move us closer to the NIH/OAR vision of ending the HIV/AIDS pandemic and meeting the needs of persons living with, at risk for, and affected by the virus.

The Plan is the result of consultations with a broad network of HIV research stakeholders, including NIH scientific and extramural experts, advisory committee members, community representatives, and persons with HIV (PWH). The priorities reflect the pipeline of scientific endeavor from basic discovery through translational research, to clinical and implementation science research. The Plan outlines research opportunities for new and sustained investments and research partnerships designed to encourage the development of new strategies, to improve existing efforts, and to accelerate discovery.

I am honored to partner with you, the dedicated and diverse stakeholders, in the efforts to end the HIV/AIDS pandemic and improve the health of PWH.

With sincere appreciation,

Maureen M. Goodenow, Ph.D.
Associate Director for AIDS Research
Director, OAR
National Institutes of Health

Introduction

The Global HIV/AIDS Pandemic

HIV/AIDS persists as the world's most serious global health and development challenge. New infections continue to devastate communities and destabilize crucial socioeconomic infrastructure around the world. The Joint United Nations Programme on HIV and AIDS (UNAIDS) reports that in 2016, 36.7 million people worldwide were living with HIV, up from 33.2 million in 2010. The continued expansion of the pandemic results from new infections, people living longer with HIV, and general population growth. For example, about 1.8 million new infections, or approximately 5,000 new infections per day, occurred in 2016, with nearly two-thirds in sub-Saharan Africa. Although HIV testing capacity is increasing, about three in 10 PWH worldwide are still unaware of their status.[1]

HIV primarily affects individuals in their most productive years; one-third of new infections worldwide occur among young people between the ages of 15 and 24. Today, women comprise about half of all adults living with the virus, and HIV/AIDS is the leading cause of death among women of reproductive age. Globally, most HIV infections are transmitted heterosexually, but injection drug use remains a major route of transmission in some parts of the world. HIV risk factors and incidence vary by region and may be reinforced by contributing factors such as stigma and discrimination among key populations most affected by the epidemic. In some regions, men who have sex with men, injecting drug users, sex workers, transgender women, and prisoners are disproportionately affected by HIV and experience disparities along the entire HIV care continuum.

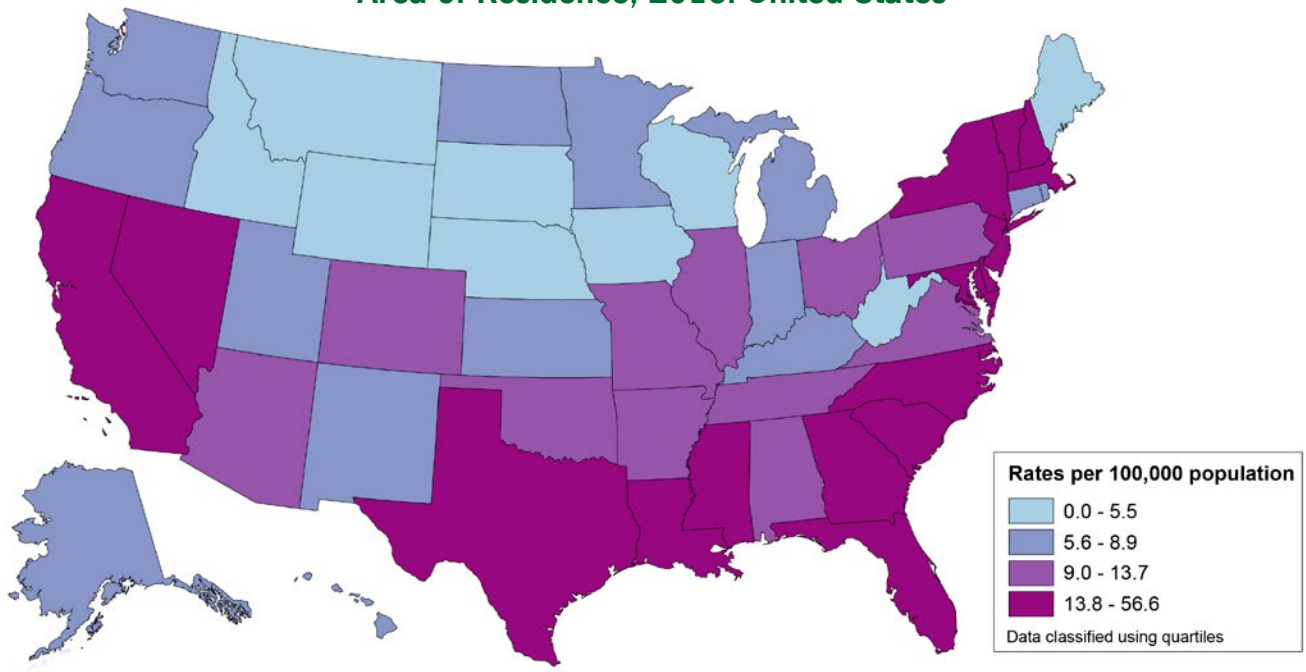
Although some regions and countries have declining or stabilizing incidence rates, the global pandemic remains volatile, with local "hot spots" of new infections that can significantly differ from national averages. The continued transmission and growing, unmet needs for HIV prevention, treatment, and care in concentrated demographic areas underscore the need for research and interventions that target communities most at risk for, or affected by, HIV.

Despite these challenges, global efforts to address the pandemic are making progress. In 2016, deaths from HIV/AIDS declined by 48 percent since peaking in 2005. More than 50 percent of PWH were receiving antiretroviral treatment as of June 2017. The number of persons newly infected by HIV decreased by 48 percent between 2005 and 2016, while new HIV infections among infants and children declined by 47 percent from 2010. Yet, the pace of decline in new infections is too slow to reach the global "90-90-90" targets and eliminate the gaps in coverage that still exist.

90-90-90

The Fast Track strategy, launched by UNAIDS in 2014[2], provides a roadmap and lays the groundwork for ending the HIV/AIDS epidemic by 2030, including interim 90-90-90 targets by 2020[3]: 90 percent of all PWH will know their HIV status, 90 percent of persons with diagnosed HIV will receive antiretroviral therapy (ART), and 90 percent of all people on HIV treatment will achieve viral suppression.

Rates of Diagnoses of HIV Infection Among Adults and Adolescents by Area of Residence, 2016: United States



Source: *CDC 2015.*

The HIV Epidemic in the United States

At the end of 2015, approximately 1.1 million adults and adolescents were living with HIV in the United States. An estimated 15 percent were not aware of their infection and therefore not accessing the care and treatment they need to stay healthy and reduce the likelihood of transmitting the virus to their partners. Just 62 percent of PWH were engaged in care, 48 percent were retained in care, and 49 percent achieved viral suppression.[4]

Although HIV infection rates have decreased in the United States, new infections continue in every U.S. state, with 38,000 new infections, or more than 100 per day, occurring in 2016. HIV diagnoses are not equally distributed among the U.S. population and vary by region and across the lifespan. African Americans and Hispanics or Latinos are disproportionately affected by HIV compared to other races and ethnicities, and account for 44 percent and 25 percent of HIV diagnoses, respectively. New HIV infection rates are highest among people who inject drugs, gay and bisexual men, and communities in the U.S. South, a large proportion of which are rural. Although the Southern region represents 38 percent of the U.S. population, in 2016 more than half of new HIV diagnoses in the United States occurred in the Southeast.[5-7]

Young people ages 13-24 are especially affected by HIV, comprising 21 percent of all new HIV diagnoses in the United States. Youth with HIV are the most likely of any age group to be unaware of their infection status, and the least likely to be linked to care in a timely manner and to achieve a suppressed viral load. Within this population, 44 percent were living with undiagnosed HIV at the end of 2015. Among young PWH, only 41 percent were engaged in care, 31 percent were retained in care, and 27 percent were virally suppressed.[5,8,9]

As a result of better treatments, PWH are living longer and healthier lives. People aged 50 and older now account for an estimated 45 percent of Americans living with diagnosed HIV. Although people in this age group may have the same HIV risk factors as younger people, they are more likely to receive a diagnosis of HIV infection later in the course of their disease.[10]

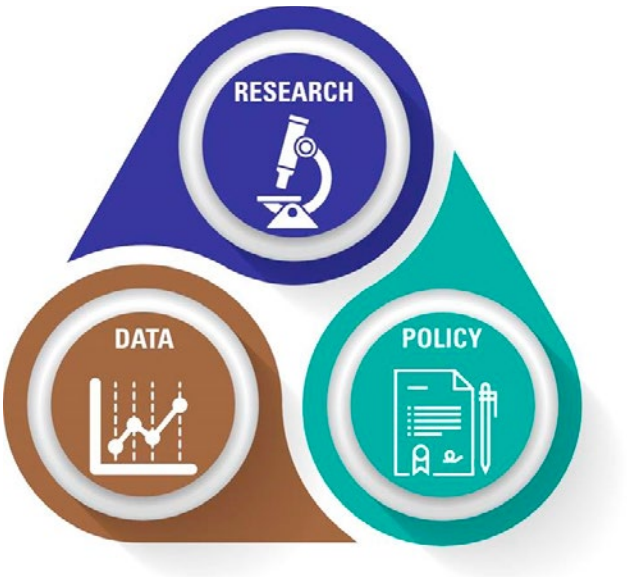
> "In 2016, more than 100 new infections occurred each day across the United States."

The Role of NIH in the HIV/AIDS Pandemic

The NIH supports a comprehensive HIV research program that crosses the boundaries of nearly every ICO. This program encompasses basic, clinical, behavioral, and social sciences; translational and implementation science research on HIV infection, prevention, treatment, and cure; and research on HIV-associated coinfections, comorbidities, and complications. The NIH expenditure (approximately $3 billion in FY 2017) is the largest public investment in HIV/AIDS research globally.

In 1988, Section 2353 of the Public Health Service Act established the NIH OAR (http://www.oar.nih.gov/) in the Office of the NIH Director to coordinate the scientific, budgetary, and policy elements of a diverse HIV research program across the NIH.

To ensure a comprehensive, multidisciplinary, and global research response to the pandemic, the OAR provides the NIH-wide scientific coordination and management of HIV research funds; conducts periodic evaluations of the field for scientific accomplishments and emerging opportunities; develops the *NIH Strategic Plan for HIV and HIV-Related Research*; and performs an annual review and analysis of the NIH-wide HIV research portfolio. The OAR's role is implemented in partnership with the ICO Directors, who oversee specific programs or projects in accordance with the Plan. The Plan outlines a research agenda applicable across the lifespan and inclusive of research on women, racial and gender minorities, and other groups experiencing health disparities, such as those in rural and underserved areas.



The scope of the Plan includes the mandate of the 21st Century Cures Act (signed into law on December 13, 2016), which provides the NIH with critical tools and resources to advance biomedical research across the spectrum, from foundational basic research studies to advanced clinical trials of promising new therapies.

NIH HIV Research Goals

To end the HIV/AIDS pandemic and improve health outcomes for persons with, or at risk for and affected by, HIV.

OAR Mission

To ensure that NIH HIV research funding is directed at the highest priority research areas and to facilitate maximum return on this investment.

Development of the NIH Strategic Plan for HIV and HIV-Related Research

The *NIH Strategic Plan for HIV and HIV-Related Research* provides information about the NIH HIV research agenda to the general public, scientific community, Congress, and HIV-affected communities. Development of the Plan involves a comprehensive and unique process that begins with the formulation of overarching research priorities, first delineated in the NOT-OD-15-137, followed by solicitation of input from HIV and related scientific experts across the NIH to further refine key priorities for the next 3- to 5-year period. NIH scientific input for the Plan is provided through OAR-established Coordinating Committees for the overarching priorities, consisting of representatives from the NIH ICOs that invest in HIV research. During the planning process, critical public health needs are assessed, and new scientific opportunities are identified.

External advice for the Plan is sought through a Public Notice Request for Information (RFI) designed to solicit input from other Government agencies, nongovernment experts, the community, and other stakeholders. The RFI for the current Plan received more than 300 responses from a wide range of HIV research and community stakeholders. Although the annual review of the Plan will continue, the new OAR process

replaces the development of an annual Plan with a 3- to 5-year Plan to encompass a longer term vision and better address the natural progress of research.

The Plan Informs NIH HIV Budget Development

The Plan provides the framework for developing, in partnership with the ICOs, the annual HIV research budget for the NIH. Each ICO submits requests to the OAR for proposed new, expanded, or recompeting HIV-related research program initiatives that support the specific priorities of the Plan. The OAR allocates funding to each ICO, based on scientific opportunities and the ICO's capacity to support and manage the most meritorious HIV science. This process reduces unnecessary duplication, promotes harmonization of effort, and ensures cross-ICO collaborations. At the time of the HIV funding appropriation, the OAR informs each ICO of its HIV-related budget allocation, specifying amounts for each approved initiative. The ICOs develop the funding announcements, facilitate peer review, and award funds for each project determined by OAR to be aligned with high-priority HIV research.

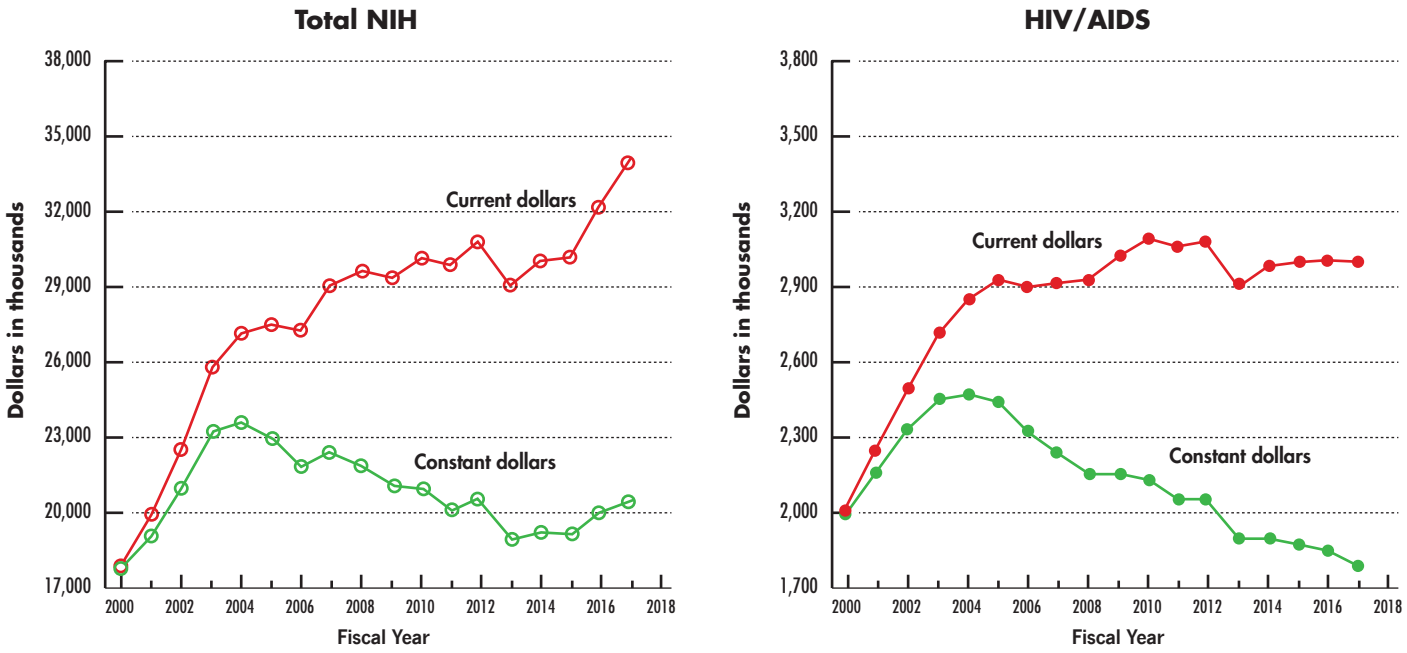
Review and Analysis of the HIV Portfolio

A critical element of the planning process is the annual review of the NIH-wide portfolio of intramural and extramural HIV research grants and contracts that are eligible for renewal in the coming fiscal year. Each project is reviewed by a team of OAR and ICO staff to ensure alignment with current HIV research priorities. This review ensures that the NIH HIV research budget is allocated with consideration for the rapidly changing clinical and scientific profile of the HIV/AIDS pandemic, the need to address emerging scientific opportunities, and the highest priorities for HIV research.

The OAR recently instituted an analysis of the NIH-wide HIV portfolio to determine the level of investment relative to topical areas across the ICOs. This analysis provides a picture of the distribution of research topics across the NIH to ensure that overall investment is balanced and aligned with the highest priority research to identify opportunities for collaboration and cost-sharing across the NIH.

These reviews and analyses together are integral components of the strategic planning and budget-development processes.

Total NIH and HIV/AIDS Research Funding

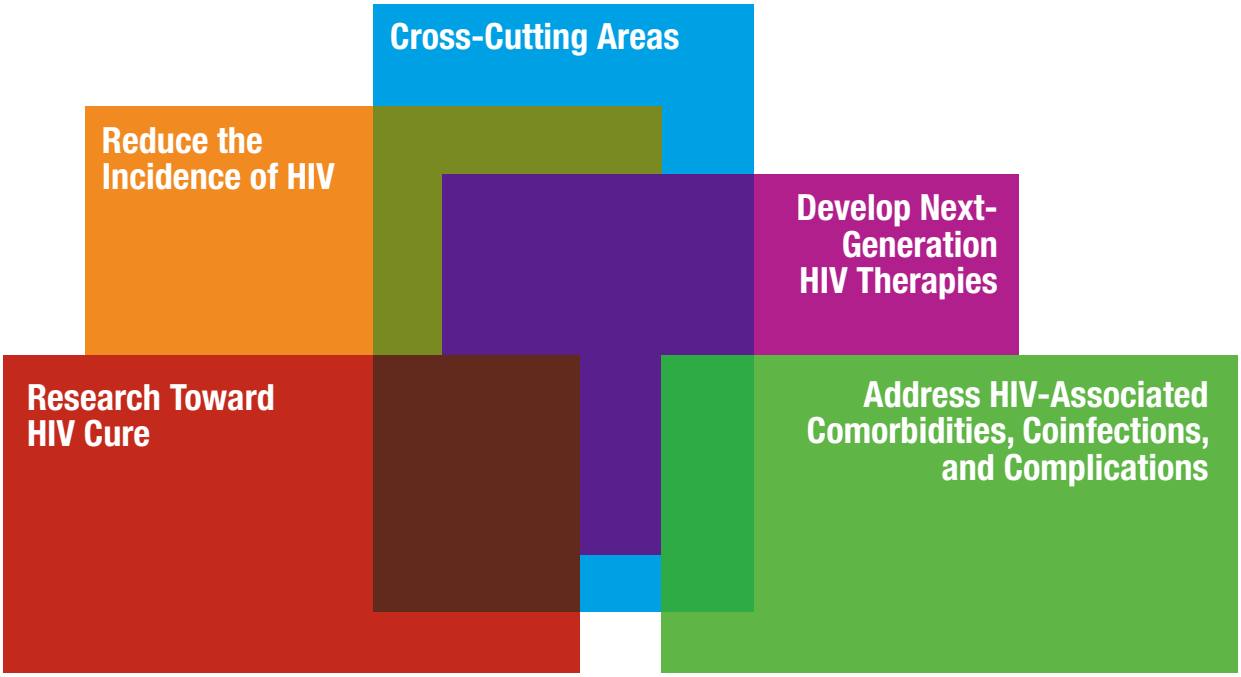


Source: NIH Office of the Director, Office of Budget, Congressional Justification, Biomedical Research and Development Price Indexes, 2018.
Notes: The funding level (Current dollars in red) is compared to the funding level with inflationary increases considered (Constant dollars in green) for the total NIH (left panel) and HIV/AIDS (right panel) research dollars from FY 2000–FY 2017. [https://officeofbudget.od.nih.gov/gbiPriceIndexes.html]

Priorities for the NIH Strategic Plan for HIV and HIV-Related Research

The priorities developed for the Plan, as outlined in NOT-OD-15-137, establish a focus for the research pipeline from basic discovery through translational, clinical, and implementation research for FY 2019 and 2020. These priorities capitalize on scientific opportunity, efficiently leverage resources, and apply to research across the lifespan, to all races and ethnicities, and to all sex and gender identities. The research must address populations most affected by the epidemic and underserved regions across the globe, such as rural and non-urban areas in the United States. Emphasis is placed on opportunities that will lead us closer to the goals of ending the HIV/AIDS pandemic and improving the lives of individuals living with the virus. Understanding how to effectively implement biomedical, behavioral, social, and structural interventions is key to reaching these goals. Sustaining global and trans-governmental partnerships and developing collaborations with community, academic, and privately funded institutions will be necessary to ensure success.

NIH Priorities for HIV and HIV-Related Research



Reduce the Incidence of HIV

- Vaccines
- Pre-exposure Prophylaxis
- Microbicides and MPTs
- HIV Testing
- Treatment as Prevention
- Monoclonal Antibodies

Research Toward HIV Cure

- Sustained ART-free Viral Remission
- Viral Eradication
- Viral Latency and Sanctuaries
- Cure Ethics and Acceptability

Cross-Cutting Areas

- Basic Virology and Immunology
- Behavioral and Social Sciences
- Epidemiology
- Health Disparities
- Information Dissemination
- Implementation Science
- Research Training, Infrastructure, and Capacity Building

Develop Next-Generation HIV Therapies

- Less Toxic and Longer Lasting ART
- Novel HIV Targets & Inhibitors
- Novel Immune-Based Therapies
- Engagement, Adherence, and Retention in Care

Address HIV-Associated Comorbidities, Coinfections, and Complications

- Coinfections
- Neurologic Complications
- Malignancies
- Cardiovascular Complications
- Mental Illness and Substance Use
- Metabolic Disorders
- Across the Lifespan

Reduce the Incidence of HIV

Preventing new infections is crucial to ending the HIV/AIDS pandemic. The NIH HIV research agenda addresses prevention through vaccine, non-vaccine biomedical, and behavioral and social sciences research. Integrated approaches, such as the development of safe, effective, and affordable biomedical interventions, used in combination with behavioral and social science-based prevention approaches, remain a high priority for the NIH.

The NIH is committed to ensuring a robust pipeline for vaccine and other innovative biomedical prevention candidates that prevent HIV, other sexually transmitted infections (STIs), and/or pregnancy. To develop viable vaccine approaches, exploring immunologic correlates of protection against HIV and novel approaches to modulate immune responses, including vaccine adjuvants, remains important. At the same time, it is critical to build on the advances in research and development related to non-vaccine prevention, such as oral pre-exposure prophylaxis (PrEP), while improving strategies to enhance uptake and adherence, expand product delivery options, and implement effective HIV prevention packages. New developments in non-vaccine prevention that are under study include the use of broadly neutralizing monoclonal antibodies to block infection. Other scientific opportunities include understanding the impact of mucosal and microbiome environments on transmission dynamics and the effectiveness of HIV prevention interventions, as well as improved approaches for early diagnosis of infection, such as low-cost self or home testing to promote early initiation into care.

Opportunities to develop effective behavioral and social science-based HIV prevention interventions at individual and population levels include research on cultural norms, stigma dynamics, cost-benefit analyses, and other socio-behavioral factors. The NIH will continue to support a broad research portfolio encompassing basic, preclinical, clinical, behavioral and social sciences, and applied research to prevent HIV infection. Supporting community-based partnerships for the development and successful implementation of interventions remains a critical strategy for HIV prevention research.

Develop Next-Generation HIV Therapies

NIH-sponsored research has led to critical advances in the development and clinical testing of ARVs. Combination drug antiretroviral treatment (cART) results in immune recovery in PWH who adhere to prescribed HIV treatment regimens and tolerate the side effects and related toxicities. Consistent use of ART not only hinders disease progression to AIDS, but also is effective for decreasing cardiovascular, renal, and other end-organ dysfunction associated with HIV infection. cART is associated with delaying the development of viral resistance and achieving an undetectable viral load, thus preventing sexual transmission of the HIV virus to an uninfected partner (known as Treatment as Prevention, or TasP, and Undetectable = Untransmittable, or U=U). With the expansion of antiretroviral drug classes, simplified daily regimens, and an array of combination treatments, sustained viral suppression is now achievable. However, new long-acting medications with fewer side effects, and novel delivery and testing technologies—including sensitive, rapid, point-of-care, or self-administered viral load testing—are needed to improve efficacy of and adherence to treatment, assure continuous undetectable viral load, and ultimately, prevent HIV transmission.

The NIH will continue to support a comprehensive HIV therapeutics research portfolio that includes basic sciences research, drug discovery, and preclinical drug development. Clinical testing of new drugs that focus on new druggable targets that prevent viral assembly or virus-host interactions, and multi-drug therapeutic regimens with improved safety and ease of use, remain top NIH priorities. It is important to study the mechanisms of adverse multi-drug interactions, while simultaneously developing methods to reduce or eliminate side effects such as immune reconstitution inflammatory syndrome. Other research opportunities include developing new, effective biomarkers and identifying novel viral targets that support durable viral suppression and counter drug resistance. Research on treatment acceptability, sustainability, accessibility, and effectiveness from both individual and population perspectives is a critical, ongoing aspect of developing and implementing effective HIV therapies. Clinical studies and resulting interventions need to be designed to include participants who reflect the epidemic's demographic burden.

Source: *cigdem/Shutterstock.com.*

Research Toward HIV Cure

The NIH is the major sponsor of research toward a cure for HIV. Such research has revealed that HIV persists in anatomic sanctuary sites that protect the virus from immune response and cART, even when the virus is undetectable in the circulation. These stable latent reservoirs are a major barrier to sustained ART-free viral remission (or functional cure) and/or viral eradication (sterilizing, or classic, cure). Because the mechanisms that underlie reservoir dynamics are not well understood, further basic research on viral latency and persistence in host cells targeted by HIV is essential. The development and validation of biomarkers, and appropriate animal and other surrogate models, which predict viral remission or reactivation/rebound of latent virus, are important priorities for cure research. An improved understanding of the dynamics of the HIV reservoir will inform the expansion of new therapeutic interventions for sustained ART-free viral remission and eradication. Novel technologies with the potential to enable reliable and valid self-administered testing for viral replication will be explored.

The NIH will continue to support innovative, evidence-based preclinical, translational, and clinical studies of cure interventions. Key scientific opportunities include gene modification/gene silencing, small-molecule agents, immunotherapeutic agents and their derivatives, cell modification-based interventions, and other novel approaches to ART-free viral remission or even eradication, including targeting reservoirs in the central nervous system (CNS) and other sanctuary sites. The ultimate goal is an intervention that is simple, safe, sustainable, and scalable. Studies to better understand ethical considerations and the acceptability of cure research across the lifespan and in diverse populations are vital to the HIV cure research agenda.

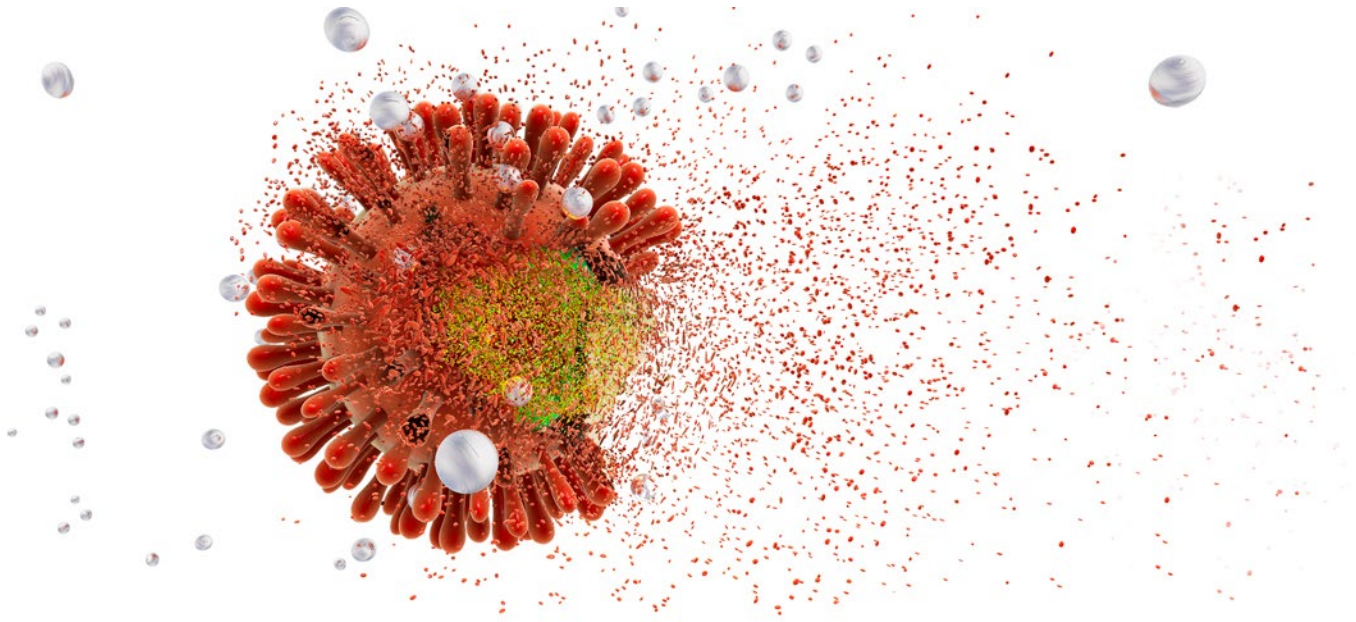


Image Description: Elimination of human immunodeficiency virus by silver nanoparticles.

Source: Kateryna Kon/Shutterstock.com

Address HIV-Associated Comorbidities, Coinfections, and Complications

HIV is associated with a complex array of coinfections and comorbid conditions, including end-organ dysfunction. Although the use of cART results in significant improvement in many HIV-associated comorbidities, coinfections, and complications (CCCs), challenges in the clinical management of concurrent HIV-associated CCCs across the lifespan continue. Advances in basic, clinical, and behavioral and social sciences research have revealed the close interrelationship between HIV, HIV treatment, and other infections such as tuberculosis (TB), hepatitis B and C, human papillomavirus (HPV), and sexually transmitted infections (STIs). Further study is needed to better understand the association between HIV and other comorbidities and the complex mechanisms involved in their pathogenesis that will lead to improved treatment and prevention of these related disorders.

The NIH is committed to research that will establish the etiology, prevalence, and clinical relevance of HIV-associated CCCs in different settings. Given limited resources, it will be imperative to focus research on the comorbidities for which interventions will have the greatest impact on the health and well-being of PWH. These include prevalent coinfections and opportunistic infections, certain cancers, neurologic and cognitive disorders, cardiovascular disease, mental illness and substance use, metabolic and bone abnormalities, and liver and renal dysfunction. Research is needed to differentiate between complications related to aging, immune dysfunction, long-term ART use and HIV-associated disease, and/or co-occurring chronic illnesses such as diabetes or hypertension. To that end, it will be necessary to study interactions between ART and medications used to treat comorbidities and drugs of abuse and to develop novel multi-use therapies for HIV and CCCs that minimize side effects, such as additive treatment toxicities. The development and testing of low-cost rapid technologies that require minimal infrastructure to prevent, diagnose, and monitor HIV-associated CCCs will be a particular need in resource-limited settings.

Cross-Cutting Areas: Advancing the Critical Framework

Key cross-cutting areas, taken together, represent the NIH's fifth overarching HIV research priority, while supporting the other priorities. These include the basic sciences; epidemiology; behavioral and social sciences research; health disparities; training, infrastructure, and capacity building; implementation science; and information dissemination. While each of these areas cuts across and is included in the other four overarching priorities, the cross-cutting areas stand alone as a single research priority, provide fundamental knowledge that advances the critical framework of HIV research, and serve as a platform for leveraging partnerships across the NIH and other U.S. Government agencies.

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

Epidemiology research and epidemiologic methods provide accurate, real-time information to better understand the global HIV/AIDS pandemic and its associated CCCs, inform prevention and treatment approaches, and determine where research should be conducted. The use of big data science, machine learning, modeling, registries, phylodynamics, and other epidemiologic approaches will contribute to improved outcomes across the HIV prevention and care continua. Systems biology approaches to examine HIV risk, immunity, treatment response, and disease progression in diverse populations will provide additional scientific value.

Behavioral and social sciences research (BSSR) provides essential insights related to individual and interpersonal dynamics, community beliefs and structures, and systemic factors that influence the transmission, prevention, treatment, and management of HIV/AIDS. BSSR is critical to studying behavioral, social, and structural factors that influence HIV risk, HIV testing, linkage to and retention in care, ART adherence, and sustained viral suppression to improve outcomes across the HIV care continuum. Research is needed to identify and minimize structural barriers and the role of internal and external stigma experienced by key populations most affected by the epidemic.

Health disparities research is needed to better understand and address how complex biological, behavioral, structural, and sociocultural factors that may be linked to race/ethnicity, sex and gender, and geography lead to disparities in HIV risk, incidence, and outcomes among individuals and communities. Emphasis must be placed on recruiting individuals of underrepresented groups in clinical research and strengthening community-based participatory research to develop effective interventions and eliminate disparities in HIV incidence and outcomes among key populations disproportionately affected by the pandemic.

Training, infrastructure, and capacity building (TICB) are crucial to the development of the next generation of HIV researchers, both in the United States and globally. TICB includes building laboratories, developing education systems, and designing novel multidisciplinary approaches to mentoring and training a broad and diverse scientific workforce. Fundamental HIV-related research training will provide support to the field in general and to achieving the specific research priorities to end the pandemic and improve the health of PWH.

Implementation Science (IS) research develops approaches to support the uptake of interventions developed within the four overarching priorities and as its own research to determine the community and structural support needed to mitigate the effects of the HIV/AIDS pandemic. Further research, in partnership with other U.S. Government agencies and Departments, is needed to define approaches and models for scaling up comprehensive, integrated interventions for expanding testing, prevention, and treatment that optimize adherence, retention, and health outcomes in real-world settings.

Information dissemination of research findings to diverse communities and stakeholders, including patients, clinicians, researchers, and the public, remains a critical component of NIH-supported HIV research. Efforts must focus on utilizing emerging technologies and venues to develop accurate, timely, and culturally responsive communication approaches that target hard-to-reach populations.

Source: *NIH, Office of Intramural Training and Education (OITE).*

Conclusion

The pace and scope of scientific discoveries resulting from NIH-funded HIV research continue to advance the promise to end the HIV/AIDS pandemic. However, there is little doubt that the pandemic will continue to affect virtually every nation in the world well into the next century. As we work toward overcoming the challenges to develop a vaccine and optimize treatment toward a cure, it is critical to remember:

- Although HIV is treatable, cART can have side effects and toxicities that complicate disease management across the lifespan.
- Despite receiving effective treatment, PWH experience early signs of aging and comorbidities, such as cardiovascular disease and neurologic deterioration, that compromise increasing numbers of PWH.
- Management along the HIV care continuum is limited by complex social and structural barriers that differ by population and locale and need to be better understood and overcome.
- The NIH HIV basic science research investment provides a crucial basis for prevention and treatment and informs other areas of research and disease management beyond HIV.
- Accelerating discovery and utilizing best practices in clinical research networks are crucial to addressing existing gaps and eliminating disparities across the globe, such as the micro-epidemics affecting key populations in the rural United States.
- Community norms and practices influence individuals' behaviors and must be a focus across biomedical, behavioral, and social interventions.
- Developing and sustaining partnerships and cost-sharing models are integral to leverage research resources in transdisciplinary areas, such as the interface between HIV and the opioid crisis, as well as the complex links between HIV and human development across the lifespan.

The Plan is designed to outline critical research to find new tools to continue to turn the tide in the fight against HIV/AIDS. The strong and sustained U.S. commitment to HIV research supports the NIH as the leader in global research efforts to capitalize on recent accomplishments, advance science, and conquer the HIV/AIDS pandemic. New avenues for discovery provide exciting possibilities for the development of novel strategies to prevent, treat, manage, and eventually cure HIV. The NIH, working with partners and stakeholders, will continue to build on the scientific progress and push for discovery and breakthroughs to achieve a nation and a world free of HIV.

"There is little doubt that the pandemic will continue to affect virtually every nation in the world well into the next century."

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