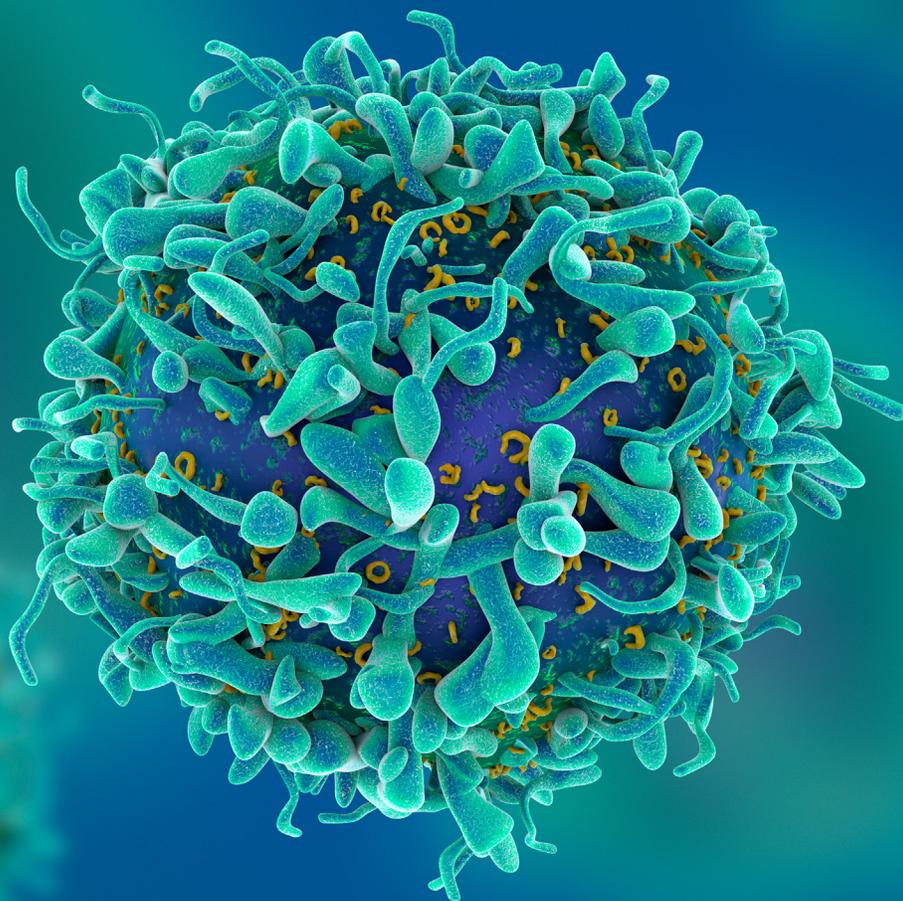


FY 2018

National Institutes of Health
**TRANS-NIH STRATEGIC PLAN FOR
HIV AND HIV-RELATED RESEARCH**



Prepared by the Office of AIDS Research
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FOREWORD

I am pleased to present the fiscal year (FY) 2018 Trans-NIH Plan for HIV-Related Research. This past year has seen important changes in prioritizing HIV/AIDS research at the National Institutes of Health (NIH). Highest priority research includes reducing HIV incidence, developing next-generation therapeutics, continuing research toward a cure, and targeting comorbid conditions and complications of HIV infection (<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-137.html>). Combating HIV/AIDS will require a combination of strategies, partnerships, and investments.

The Office of AIDS Research (OAR) develops an annual Trans-NIH Plan for HIV-Related Research (Strategic Plan) to serve as the framework for developing the annual NIH HIV/AIDS research budget and to ensure that research dollars are invested in the highest priority areas of scientific opportunity. The Plan also serves as a resource to inform the public, the scientific community, Congress, and HIV/AIDS-affected communities about the NIH HIV/AIDS research agenda.

- Legislative Mandate Section 2353 of the Public Health Service Act requires that the Director of OAR (1) establish a comprehensive Plan for the conduct and support of all HIV/AIDS activities of the agencies of the NIH; (2) ensure that the Plan establishes priorities among the HIV/AIDS activities that such agencies are authorized to carry out; (3) ensure that the Plan establishes objectives regarding such activities; (4) ensure that all amounts appropriate for such activities are expended in accordance with the Plan; (5) review the Plan not less than annually, and revise the Plan as appropriate; and (6) ensure that the Plan serves as a broad, binding statement of policies regarding AIDS activities of the agencies, but does not remove the responsibility of the heads of the agencies for the approval of specific programs or projects, or for other details of the daily administration of such activities, in accordance with the Plan. In accordance with the law, the NIH OAR, a component of the NIH Office of the Director in the Division of Program Coordination, Planning, and Strategic Initiatives, has developed this Strategic Plan.

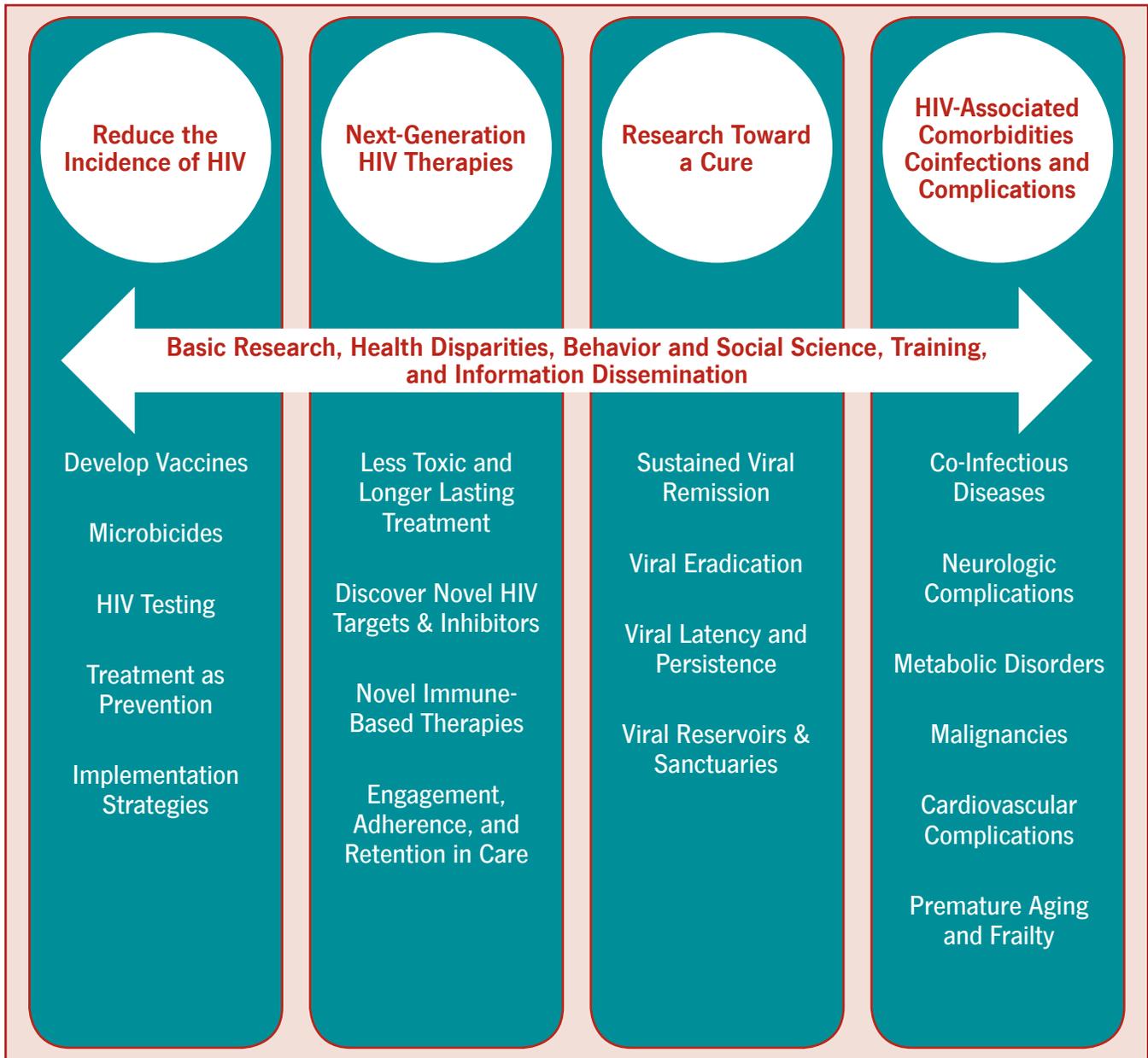
An important change implemented in the development of this FY 2018 Strategic Plan was the adoption of a Request for Information (RFI) (NOT-OD-16-089), the goal of which was to catalyze feedback and comments from a broad array of perspectives, including individuals in academia and industry, health care professionals, patient advocates and health advocacy organizations, scientific and professional organizations, Federal agencies, other interested constituents, and the broader community. The comments received have been carefully considered in the establishment of this FY18 Plan.

NIH-funded basic and pre-clinical research has led to groundbreaking advances in strategies to prevent HIV acquisition and transmission, the development of safe and effective antiretroviral (ARV) drugs and combination drug regimens for treating HIV/AIDS, and understanding basic HIV virology and pathogenesis. Despite these achievements, additional research focused on key issues must be undertaken to end the HIV/AIDS pandemic. Therefore, the NIH will continue to support high-priority research on HIV prevention strategies, improving HIV treatment, and research towards a cure using novel therapeutic approaches to decrease viral reservoirs, comorbidities, co-occurring illnesses, and relevant crosscutting areas of science.

As the Director for OAR, I want to recognize the extraordinary contributions by Acting Director Dr. Robert Eisinger, the OAR staff, the Directors and staff across NIH Institutes and Centers, and all stakeholders for implementing the transition. The entire OAR staff joins me in looking forward to your continued partnership.

With sincere appreciation,
Maureen M. Goodenow, Ph.D.
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OVERARCHING HIV/AIDS RESEARCH PRIORITIES







Overarching HIV/AIDS Research Priorities for AIDS Funding

- **Reduce the incidence of HIV/AIDS, including—**develop and test promising vaccine, microbicide, and pre-exposure prophylaxis (PrEP) candidates combined with novel methods of delivery with potential to reduce adherence issues; develop, test, and define new strategies and their implementation to improve prevention and care across the continuum, from HIV testing to care linkage to sustained viral suppression.
 - **Develop and test next-generation HIV therapies with improved safety and ease of use, including—**identifying HIV treatments that are less toxic, longer acting, with improved tissue penetration, fewer side effects and complications, and more likely to result in adherence; developing and evaluating novel immune-based therapies; conducting implementation research to better understand how to initiate treatment as soon as an HIV diagnosis is made; improving adherence, engagement, and retention in treatment and care; and achieving and maintaining optimal prevention and treatment responses.
 - **Achieve sustained viral remission, with the long-term goal of an HIV cure, including—**research on viral latency, persistence, and reservoir formation and maintenance; development of innovative strategies to induce sustained viral remission without a need for antiretroviral therapy (ART), or in the long-term, viral eradication that is safe, simple, scalable, and sustainable.
 - **Address HIV-associated coinfections, comorbidities, and complications, including—**the effect across the lifespan of HIV-associated comorbidities or coinfections, such as tuberculosis, malignancies, cardiovascular, neurological, metabolic, and other end organ complications; and accentuated aging associated with long-term HIV disease and ART use.
- **Support the crosscutting areas of basic research, health disparities, behavior and social science research, training, and information dissemination, including—**
 - Basic research to understand the mechanisms of HIV transmission and pathogenesis; innate and adaptive dysfunction and chronic inflammation; host and/or viral genetics, epigenetics, and gene expression and host microbiome that affect susceptibility to infection and disease outcomes.
 - Creative research partnerships to determine mechanisms and treatments for comorbidities, complications, and coinfections.
 - State-of-the-art behavior and social sciences research that underpins the development of high-priority HIV prevention, cure, and treatment strategies.
 - Research to reduce health disparities in the incidence of new HIV infections or in treatment outcomes of those living with HIV/AIDS.
 - Training of the research workforce required to conduct high-priority HIV/AIDS or HIV/AIDS-related research, implementation, and information dissemination research to develop new health informatics to achieve effective circulation of discoveries to the community.



Reducing the Incidence of HIV/AIDS

To bring an end to the HIV/AIDS pandemic, new infections must be prevented. The NIH will continue to support a comprehensive balanced HIV/AIDS research portfolio supporting vaccine, microbicide, and PrEP development and clinical testing, funding both “big science” consortia and single-investigator grants to drive in-depth, innovative science. Prevention research will entail multiple approaches, including effective HIV vaccines; prevention of mother to child transmission, treatment is prevention; multi-purpose prevention technologies (MPTs), PrEP; and voluntary medical male circumcision.

The HIV prevention research portfolios encompass basic, pre-clinical, and clinical research, including studies to identify and better understand protective immune responses in HIV-infected individuals and studies of improved animal models for the pre-clinical evaluation of prevention candidates. Because most HIV infections occur at mucosal surfaces, enhanced understanding of mucosal immune functions and properties, including the role of the microbiome, will aid in the discovery, development, and testing of new agents to prevent transmission and infection. In addition, behavioral and social sciences research to advance understanding of the factors that support or prevent HIV risk, transmission, and acquisition and that influence demand for and adherence to effective prevention and treatment strategies is critical.

High-priority research opportunities focused on reducing the incidence of HIV/AIDS include:

- Conducting clinical trials for vaccines, microbicides, MPTs, PrEP, and other biomedical prevention modalities in various at-risk populations.
- Evaluating the role of immunity to HIV (including, but not limited to T cells, B cells, antigen-presenting cells, innate responses, and host factors), particularly at mucosal sites, for protection in the context of studies on vaccines, microbicides, and long-acting ARV agents.
- Examining the relationship between the genital/lower GI tract microenvironment, host factors, immune function, microbiome, and HIV risk, transmission, and acquisition.
- Developing novel epidemiological tools to track HIV incidence in communities, including geospatial and phylogenetic approaches, as well as geostatistical methodologies to identify HIV transmission hotspots and accelerate the testing of interventions to reduce the spread of HIV in key populations.
- Developing and testing standardized assays to better understand the mechanisms of infection and transmission that inform vaccine, microbicides, and PrEP efficacy in various at-risk populations.
- Developing approaches and models to study the contributions and interactions of behavioral, social, structural, and environmental factors in at-risk communities, as well as approaches and models for community engagement to reduce HIV/AIDS in different populations and cultural settings.
- Identifying strategies and clinical guidelines (standards of care) to overcome barriers to the rapid adoption, adaptation, integration, scale-up, and sustainability of evidence-based interventions and tools, while accounting for racial, ethnic, cultural, gender, sex, and age differences in diverse settings.



Next-Generation Therapies for HIV/AIDS

NIH-sponsored research leading to critical advances in the development and clinical testing of ART. ART results in immune recovery in HIV-infected individuals who are able to adhere to prescribed HIV treatment regimens and tolerate the side effects and toxicities. With the expansion of the classes of antiretroviral drugs, simplified daily regimens, and an array of combination treatments, sustained viral suppression is achievable. Consistent use of ART not only prevents the progression of HIV infection to AIDS, but also has been effective at maintaining viral suppression and improved immune function, with the accompanying benefit of delayed development of viral resistance. However, new drugs and delivery technologies are needed to improve treatment and adherence. The NIH will continue to support a comprehensive HIV/AIDS therapeutics research portfolio that includes drug discovery, preclinical drug development, clinical testing of new drugs and multidrug therapeutic regimens with improved safety, and identification of new and novel targets to allow durable remission of viral activity.

High-priority research opportunities focused on next-generation therapies for HIV/AIDS include the following:

- Elucidating the mechanisms of HIV persistence in persons on maximally suppressive ART as well as developing and testing strategies to eliminate viral reservoirs and latency infected cells.
- Accelerating the discovery and validation of novel agents and strategies aimed at new and existing viral and cellular targets to develop safe, tolerable, low-cost, and maximally long-term suppressive antiviral activity.
- Developing and testing existing and novel agents that can be used alone or in combination with behavioral and other strategies to maximize viral suppression and adherence to ARV drug regimens to treat and prevent the transmission of HIV disease.



Research Toward a Cure

The mechanisms by which HIV persists in a latent state and in reservoirs within the body are not well understood and represent the major barrier to sustained viral remission (also called a functional cure) without ART and to the longer term goal of viral eradication (also called a sterilizing, or classic, cure). Additional basic research on viral latency, persistence, and reservoir formation/elimination is needed to increase understanding and overcome this barrier. Continuing priorities include the development and validation of biomarkers predictive of viral remission or viral reactivation/rebound viremia. The NIH will continue to support preclinical basic and animal model research that might translate to clinical studies of innovative and sustainable cure strategies. These strategies will be evaluated for use in diverse populations accounting for age, gender, race/ethnicity, and coinfections, comorbidities, and other complications. The final goal is for an intervention(s) inducing sustained viral remission, or viral eradication in the longer term, that are at least as safe as ART, simple (implemented in community or primary care setting), and scalable to enable timely and widespread availability for use.

High-priority research opportunities focused on research toward a cure include:

- Understanding viral and host mechanisms—including differential tissue and cellular distribution—that direct HIV persistence, latency, and reservoir formation.
- Developing and testing novel interventions, including immune-based therapies, to control or eliminate latent and/or persistent reservoirs of HIV in the presence of effective ART.
- Identifying and validating novel biomarkers, assays, and imaging techniques to advance research toward a cure.

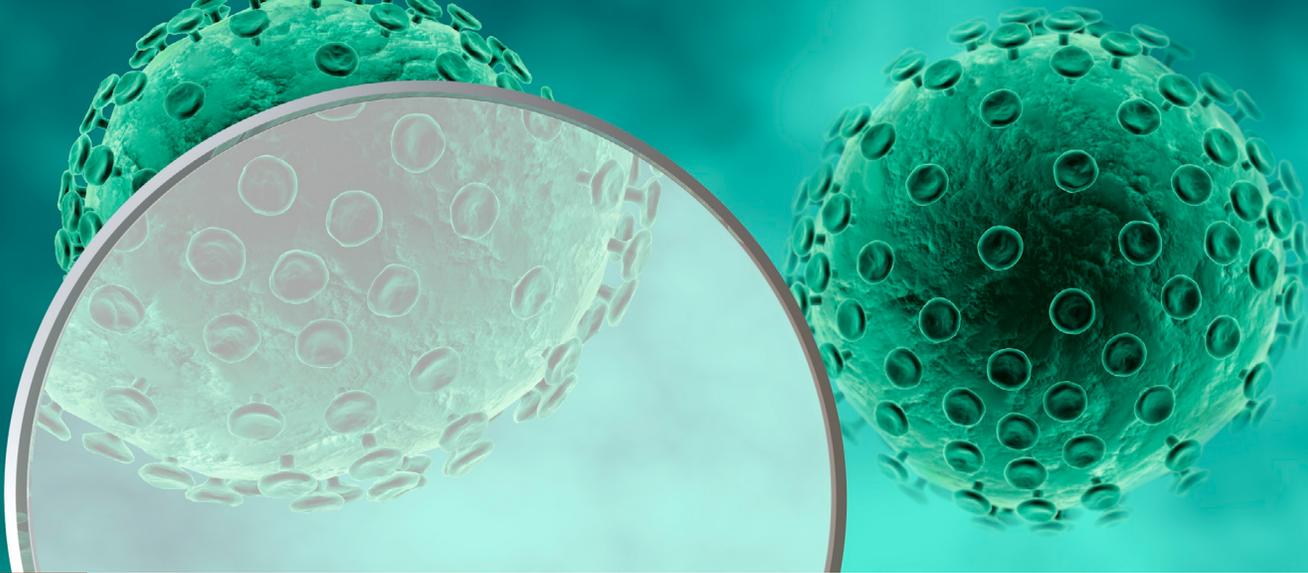


HIV-Associated Coinfections, Comorbidities, and Other Complications

HIV/AIDS is a disease often defined by coinfections and comorbid conditions. HIV infection can be preceded by and co-occur with other health and mental health issues, such as substance use, mental disorders, and malnutrition. With the advent and widespread use of ART, significant changes in the types of HIV-associated coinfections, comorbidities, and complications have developed, but the challenges in HIV clinical management continue. Examples are numerous and include, but are not limited to, tuberculosis, hepatitis B and C, human papillomavirus, and other sexually transmitted infections. Associated comorbidities include cardiovascular disease; metabolic abnormalities and diabetes/insulin resistance; bone and muscle dysfunction; liver and kidney dysfunction; neurological disorders, including cognitive decline; AIDS-defining and non-AIDS defining cancers; and frailty in people aging with HIV. Epidemiologic and observational studies continue to identify new HIV-related comorbidities and help to differentiate effects related to long-term ART use from those related to HIV disease and suboptimal immune function. Development of new agents, alone and in combination, and novel sustained release formulations and delivery systems may affect the prevention and treatment of coinfections, comorbidities, and other long-term HIV-associated complications.

High-priority research opportunities focused on HIV-associated coinfections, comorbidities, and other complications include the following:

- Accelerating the discovery, testing, and validation of strategies and low-cost technologies to effectively diagnose, prevent, and treat HIV-associated comorbidities across the lifespan of HIV-infected individuals, while developing approaches to integrate prevention and care for effective management of HIV infection.
- Elucidating the mechanisms responsible for the pathogenesis of comorbid conditions, including the contribution of the immune system, inflammation, and long-term ART on the development of these comorbidities.
- Defining the mechanisms that increase the risk of acquiring HIV-associated coinfections in diverse populations and evaluating the interaction of coinfecting pathogens on HIV disease progression and vice versa.
- Addressing the behavioral and sociocultural factors and conditions that are associated with HIV-related comorbidities and/or complications.
- Examining comorbid factors—such as substance use, mental health disorders, and malnutrition—within the context of HIV/AIDS.



Crosscutting Research for HIV/AIDS

A major proportion of HIV/AIDS research has relevance to not one, but all of the overarching NIH HIV/AIDS priority research areas. This includes basic research, health disparities research, behavior and social sciences research, and training and information dissemination.

Basic Research

Basic research provides the underlying foundation for all HIV/AIDS studies and includes studies to examine virology, transmission, acquisition, susceptibility, and host-viral interactions. Research on the viral, cellular, and molecular mechanisms of HIV-associated clinical complications is critical to better understand the development of HIV-associated comorbidities and the acquisition and pathogenesis of coinfections. Studies that aim to elucidate the genetic and immune mechanisms involved in HIV disease progression and to determine how multiple factors influence disease and treatment are essential.

High-priority research opportunities focused on basic research include the following:

- Furthering the understanding of host-viral interactions, including innate and adaptive immune responses, the role of the microbiome, host restriction, and host and viral genetics to inform the highest priority HIV/AIDS research.
- Developing and improving research models to advance research on HIV transmission, acquisition, acute and chronic infection, latency and persistence, pathogenesis, vaccines, and treatment.
- Developing new tools, standards, biomarkers, systems biology, behavioral-social-contextual factor analytics, and other novel methodologies for the evaluation and design of biomedical and behavioral research interventions.

Health Disparities

Disparities in morbidity and mortality in HIV infection remain despite significant advances in HIV prevention and treatment. Epidemiologic trends underscore the differential in HIV risk and prevalence among key populations in the United States. The reasons for these disparities are many and can be linked to the conditions in which individuals and communities live, work, and make their social connections, best characterized as the social determinants of health. Reconciling the differences in HIV treatment outcomes alone is insufficient; many of these populations have disproportionately high rates of comorbid conditions.

An emerging research need is the creation of evidence-based interventions to close these gaps and improve outcomes in key populations. To achieve these goals, the NIH continues to prioritize the enrollment and retention in clinical trials of individuals who represent the demographics of the epidemic. Research that identifies and utilizes effective strategies to maximize opportunities for early diagnosis and access to services, treatment adherence, thus reducing the gap in treatment outcomes and minimizing HIV-associated comorbidities and mortalities is critical.



High-priority research opportunities focused on HIV-related health disparities include the following:

- Enhancing the understanding of the effect of socioeconomic status, race, ethnicity, sex, gender, culture, migration status, and other social determinants of health on HIV acquisition, prevention, transmission, and diagnosis and on access to state-of-the-art clinical management and treatment.
- Expanding current research methods and developing innovative methodologies to accurately assess the biological, contextual, social, and individual facilitators and barriers to HIV acquisition, transmission, and disease progression in racial, ethnic, and gender across the lifespan.
- Developing HIV diagnostic, prevention, and therapeutic technologies that retain effectiveness across a range of community settings, as well as expanding the implementation science portfolio to determine the impact and cost effectiveness of interventions and strategies, alone and in combination, to improve uptake and scale-up using evidence from diverse settings.
- Creating new communication strategies and incorporating state-of-the-art technology to improve access to hard-to-reach populations and settings.
- Strengthening the broad dissemination of HIV/AIDS research findings to better inform clinical practice in diverse populations and settings; improve recruitment and retention of minority and marginalized participants in clinical studies; and enhance the translation of clinical research to treatment guidance in disproportionately affected communities, studying ways to sustain high fidelity to this translational guidance of enhancing care and eventually HIV care outcomes.

Training and Information Dissemination

The NIH supports the training of a broad-based and diverse research workforce to build the critical capacity and infrastructure to conduct HIV/AIDS research with an increased emphasis on multidisciplinary teams and approaches. Training and capacity to address the many challenges and collaborative opportunities of HIV/AIDS research, including teaching, evaluating, and maintaining the highest bioethical standards in the conduct of HIV research, as well as developing and maintaining collaborations and leadership in HIV/AIDS research and its related sciences are necessary.

High-priority research opportunities focused on training and information dissemination include the following:

- Promoting and supporting training, capacity building, and infrastructure development critical to enhancing HIV/AIDS research.
- Developing and supporting transdisciplinary HIV-related research training programs to strengthen recruitment, retention, and career sustainability of a diverse workforce.
- Applying information dissemination research to develop new health informatics that use state-of-the-art technology and to understand the most effective and efficient way to disseminate recent research discoveries widely, among the research community, internal and external stakeholders, and the general public.



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