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# Focusing National Institutes of Health HIV/AIDS Research for Maximum Population Impact

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**Progress in advancing research on the pathophysiology, prevention, treatment, and impact of human immunodeficiency virus (HIV) is threatened by the decaying purchasing power of National Institutes of Health (NIH) dollars. A working group of the NIH Office of AIDS Research Advisory Council was charged by the NIH Director with developing a focused and concise blueprint to guide the use of limited funding over the next few years. Science priorities outlined by the working group and reported here are intended to maximally address individuals, groups, and settings most affected by the epidemic, and to redress shortcomings in realizing population-level HIV prevention, treatment, and eradication goals. Optimizing these priorities requires that traditional silos—defined by topic focus and by scientific discipline—be dissolved and that structural issues affecting the pipeline of new investigators and the ability of the Office of AIDS Research to fulfill its role of steward of the NIH HIV/AIDS research program be directly addressed.**

**Keywords.** HIV; AIDS; research; National Institutes of Health (NIH).

Over the last decade, the US National Institutes of Health (NIH) has experienced a steep decline in the buying power of investments in biomedical research overall and, parallel to it, for human immunodeficiency virus (HIV)-related research specifically. Despite a modest but apparent increase in the NIH (and HIV/AIDS) budget, analysis in inflation-adjusted dollars demonstrates a 20% decrease in purchasing power for HIV/AIDS research (Figure 1) [1]. In the context of increasing budget constraints and the need to focus resources, the Director of the NIH recently charged the NIH Office of AIDS Research Advisory Council

(OARAC), a group of nongovernmental experts, with the development of a brief blueprint outlining top priorities for NIH HIV/AIDS research over the next 3–5 years. A Working Group comprised of several OARAC members and additional scientific and community experts was formed to undertake this charge, and its final report was presented at a public meeting of the Advisory Committee to the Director in June 2014 [2]. Following are highlights from the Working Group's report.

## GUIDING PRINCIPLE

Despite great progress in ebbing the tide of the pandemic, HIV/AIDS remains a public health challenge. In 2012, there were 2.3 million new infections, 1.6 million AIDS-related deaths, and 35.3 million people living with HIV [3]. Globally, the greatest burden of incidence and prevalence lies in sub-Saharan Africa. Even in this region, some groups—particularly young women and young gay and other men who have sex with men (G/MSM)—are disproportionately affected. In Eastern

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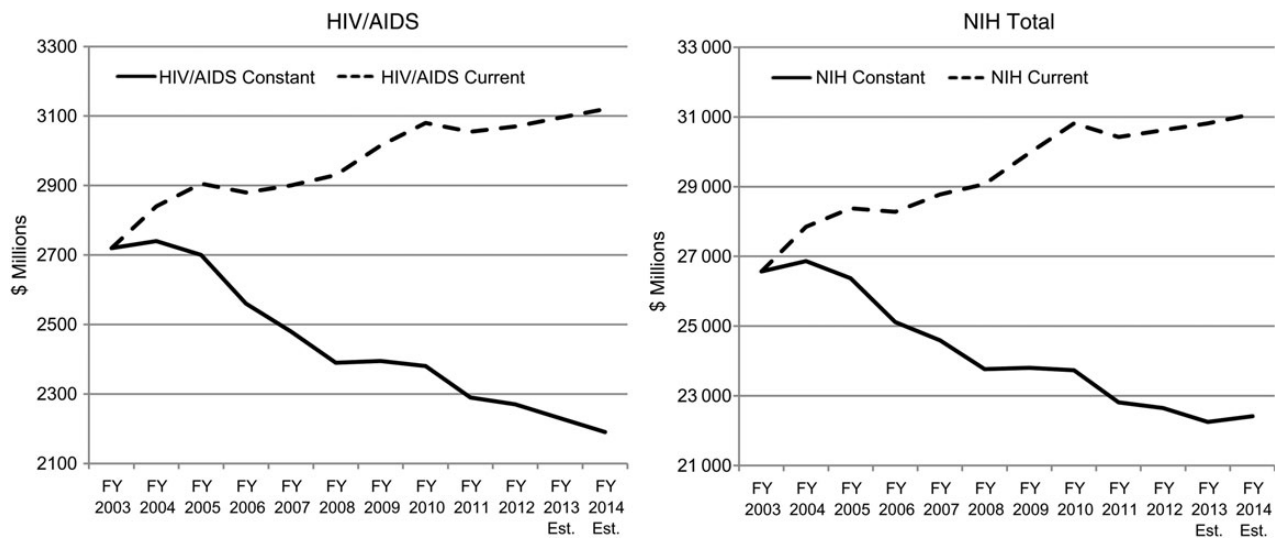
<sup>a</sup>Members and their affiliations of the OARAC Working Group are provided in the Acknowledgement section; each has approved this submission.

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**Figure 1.** The declining buying power of biomedical research funding (fiscal year [FY] 2003–2014). Funding for human immunodeficiency virus (HIV)/AIDS and overall National Institutes of Health (NIH) biomedical research, FY2003–FY2014 (estimated), in current and constant (inflation-adjusted) dollars. The solid lines show funding in constant 2003 dollars, and demonstrate a progressive loss in purchasing power for HIV/AIDS and overall biomedical research financing. This figure has been reproduced from the Office of AIDS Research, NIH; with permission from the Foundation for AIDS Research and the Treatment Action Group [1]. © amFAR, The Foundation for AIDS Research.

Europe and Central Asia, people who inject drugs harbor the greatest HIV burden; in the United States, black/African American G/MSM and black/African American women are most at risk. A core principle of the Working Group was that NIH HIV/AIDS research should emphasize prevention, care, and treatment approaches that focus on the most affected people and settings and that address the disease throughout the life course, to maximize population-level impact and resource efficiency.

## PREVENTION

Stable and increasing HIV incidence rates observed in numerous settings reflect lack of universal access to and uptake of effective prevention methods [4]. NIH-supported research should focus on developing novel methods, in addition to optimizing implementation of those already available. Among newer strategies, antiretroviral-based methods, including preexposure prophylaxis (PrEP) and microbicides, offer considerable promise. Studies assessing efficacy and effectiveness at a population level of these methods, alone and in combination, should be supported. This includes research that addresses the social and structural issues that encourage (or discourage) access to, adoption of, and adherence to prevention methods both in the context of and independent of clinical trials.

Continued attention must also be paid to pursuit of an HIV vaccine, which will ultimately provide the greatest and broadest-scale HIV prevention benefit. Priorities in vaccine research include new strategies to improve immunogen design, alternative

approaches for targeting germ lines, and novel animal models for testing of vaccine candidates.

## TREATMENT

HIV treatment today includes 28 approved antiretroviral drugs and 7 preferred first-line regimens and has contributed to virologic suppression rates of approximately 85% [5]. But to optimize health outcomes and quality of life for people living with HIV, it is imperative to develop drugs and regimens that are even more potent; convenient and adherence-promoting; less toxic and more likely to avert comorbidities; and increasingly able to achieve greater immunologic reconstitution.

## PREVENTION/CARE CONTINUUM

Antiretroviral therapy (ART) serves not only to improve health outcomes for HIV-infected individuals, but also to prevent HIV transmission [6]. The population-level impact of ART has remained unrealized, largely due to significant drop-offs in each step of the so-called “treatment cascade”—from HIV testing to engagement in care to suppression of virus [7]. Indeed, only 28% (United States) and 24% (sub-Saharan Africa) of HIV-infected patients have suppressed viral load [8, 9]. Research is necessary to develop, test, and implement strategies that address clinical, behavioral, and social issues attendant with improving outcomes throughout the cascade around the world.

## **CURE**

Currently, HIV treatment is lifelong (incurring toxicities and expense), HIV persistence results in immune dysregulation and resultant end-organ damage, and HIV transmission continues. Recent cases suggest that HIV cure obviating these realities may be possible, but not easily achieved [10].

NIH must maintain a steadfast commitment to research on cure strategies, including therapeutic vaccines, biologic response modifiers, gene therapy, and broadly neutralizing antibodies. Critical to the cure agenda is further understanding of HIV latency and reservoirs and development of animal models to understand pathogenesis and test novel strategies. Individuals' willingness to participate in cure research (which might include analytic treatment interruptions) must also be explored.

## **COMORBIDITIES, COINFECTIONS, COMPLICATIONS**

Because HIV infection increases the risk of developing other chronic noninfectious comorbidities, including cardiovascular disease, cancer, bone fractures, and osteoporosis, ongoing research should provide insight into the role of chronic inflammation and immune activation related to these comorbidities [11–13]. Investigation should similarly continue at the intersection of biological, clinical, behavioral, and social issues attendant with neurological complications from HIV and aging with HIV.

HIV overlaps with numerous other infectious epidemics, especially hepatitis C virus (United States) and tuberculosis (internationally), among others (eg, hepatitis B, cryptococcosis, malaria). Progress must be made in diagnostics, treatment, and prevention strategies for these co-occurring infections, and in further delineating their impact on people with HIV, as well as the reciprocal effects of HIV on these coinfections.

## **CROSS-CUTTING AREAS**

Cutting across the topics mentioned above are several areas that the Working Group believed were essential to an effective NIH HIV/AIDS research program:

### **Basic Science**

Advances in basic science laid the framework for understanding HIV virology and pathogenesis and established treatment targets that have resulted in the success of current HIV therapy. However, significant gaps in understanding the interplay between the virus and the host remain. Future priorities should focus on the host response to HIV, on alternative mechanisms for drug delivery, and on novel animal models for vaccine and cure.

### **Behavioral and Social Science**

The success of any advances in HIV prevention, care, treatment, and cure depends on the actions of individuals and groups. Thus, it remains important for NIH to focus resources on social and behavioral research that develops and tests novel interventions using innovative methods (eg, adaptive intervention designs and social media strategies), including, but not limited to, those attendant with new “biomedical” technologies (eg, vaccines, PrEP, and microbicides). Additionally, mathematical modeling analyses demonstrating economic value, budgetary impact, and return on investment are needed to guide decision makers toward embracing new scientific advances.

### **Implementation Science**

Given the diversity of US and international populations and settings in which scale-up of effective HIV prevention, care, and treatment strategies is needed, NIH must support implementation science that concentrates on methods to promote the integration of research findings into healthcare policy and practice. The implementation science program should emphasize combinations of interventions and strategies that can best address obstacles in access to, uptake of, and engagement in HIV services.

## **TRAINING AND INFRASTRUCTURE**

Innovative HIV-related research in the areas outlined above relies on a continued influx of fresh, properly trained, and supported scientists. Unfortunately, since the early 2000s, the NIH funding pipeline has seen a stark reduction in young investigators across disciplines [14]. In 2013, >40% of all US-based infectious disease fellowship programs did not fill their available positions; these fellowships provide the physician-based supply for key basic and clinical HIV-related research. Given the tenuous pipeline of future researchers, attention must be paid to the types, levels of support, and distribution of training early career and mentorship awards for both US and international scholars.

## **CRITICAL STRUCTURAL REQUIREMENTS FOR HIGH-IMPACT HIV/AIDS RESEARCH AT NIH**

While deliberating scientific priorities, the Working Group also identified several issues that affect the NIH's ability to ensure effectiveness and efficiency in its HIV/AIDS program. The group recommended that the Office of AIDS Research play an increasingly proactive role in approval of funding announcements, grant assignments to Institutes/Centers, configuration of HIV-related study sections, and development of a trans-NIH policy regarding full and proportional funding of grants and portfolios with dedicated AIDS dollars.

## CONCLUSIONS

Unprecedented progress has been made in HIV/AIDS research in the last 30 years—progress that also has catapulted many other fields [15]. The approximately 25% of HIV-infected patients successfully engaged in care with suppressed viral load globally can anticipate a survival similar to their HIV-uninfected counterparts. However, the other approximately 75% remain disengaged from care, are unwittingly contributing to continued HIV transmission, and are losing potential life expectancy. Current research suggests that an HIV cure and an HIV vaccine are, for the first time, viable. Budget constraints, although a potential obstacle, provide an opportunity to maximally focus on the highest priorities with the greatest potential for population-level impact and sustainability if control and elimination of this epidemic are to be our collective research legacy.

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