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Responding to the National HIV/AIDS Strategy – Setting the Research Agenda

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The National HIV/AIDS Strategy (NHAS) has three goals: (1) reduce the number of people who become infected with HIV, (2) increase access to care and improve health outcomes of people living with HIV, and (3) reduce HIV-related health disparities. [1] In addition the plan and its implementation strategy call for achieving more coordination of HIV programs across the Federal government and between federal agencies and state, and local governments. [2] Accompanying the Strategy is an Implementation Plan that identifies the steps to be taken by Federal agencies as well as all parts of society to support the priorities outlined in the Strategy and sets target for the three goals to be achieved by 2015 (e.g. lowering the number of new HIV infections by 25%). [3] Herein we lay out a role for the National Institutes of Health in facilitating research that supports and informs the goals of the National HIV/AIDS Strategy.

Though the potential benefits of the National HIV Strategy for HIV-infected persons and the broader society are substantial, three important challenges must be addressed to effectively bring the strategy to scale in the United States. First, although virtually everyone who is HIV-infected is eventually identified, diagnosis often occurs too late in the disease to provide optimal benefit to the individual. In addition, until persons know they are infected, they are more likely to transmit their infection to others. Thus, it is critical to detect HIV-infected individuals earlier in their disease. Second, once HIV-infected individuals are identified, it is crucial that they quickly receive and then remain in care. Third, if the individual and society are to benefit from antiretroviral therapy, infected persons must receive and be adherent to treatment in order to maintain long-term virologic suppression to achieve better health outcomes and reduce HIV transmission rates.

While an emphasis on testing and treatment sounds primarily biomedical, the three challenges depend on behavioral, social, systems, and structural factors important to address

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in implementation of the NHAS. Early identification of HIV infection, especially for populations with greatest disease incidence, requires community- and provider-level interventions to make frequent HIV testing normative, easy to obtain, and free of stigma. Engaging and maintaining HIV-infected persons in care requires the development and implementation of practical interventions—at health care system, community, and individual levels—targeted toward those marginalized patient groups least likely to enter and remain without disruption in care. Well-maintained HIV virologic suppression, a cornerstone of treatment-as-prevention approaches, can be achieved only when patients likely to be nonadherent are identified and receive behavioral and social interventions to improve their long-term medication adherence.

Much is known about individual interventions that can achieve some of these goals, but we know much less about how to combine multiple approaches to have the greatest impact on a wide scale. Consensus among researchers is emerging on the need for “combination prevention,” by which we mean multilevel interventions that combine evidence-based individual social, behavioral, and biomedical approaches to produce a community-level impact on the HIV/AIDS epidemic. [4, 5] It is time to move beyond studying social, behavioral, and biomedical HIV prevention interventions in isolation and instead evaluate the impact of comprehensive, integrated, multilevel approaches implemented on a wide scale.

In this editorial, we will describe some current barriers to implementation of the National HIV/AIDS Strategy, present strategies to address them, and outline research needs relevant to the successful implementation of the Strategy.

Improving the Identification of Undiagnosed HIV Infection

The strategy has set as a target to increase the percentage of individuals who are aware of their HIV-infection from 79% to 90% by 2015. [3] To accomplish this target, social marketing campaigns designed to make knowledge of one's HIV status normative, such as Washington, DC's “Ask for the Test” campaign [6] and New York City's “Bronx Knows” campaign [7], have shown promise in decreasing the number of individuals unaware of their HIV infection. Research shows that community mobilization approaches have the potential to reach subpopulations at highest risk for HIV. [8] In addition, the CDC has recommended routine HIV testing in emergency departments, STD clinics, and other publicly funded settings for all patients where the patient population has an estimated HIV prevalence of 0.1% or greater. [9]

CDC recommendations call for persons at high risk—men who have sex with men (MSM), injection drug users and their sexual partners, sex workers, sexual partners of HIV-positive individuals, and heterosexuals with multiple partners—to be screened at least annually and for all people being treated for TB or STDs to receive HIV testing. More intensive routine screening programs are likely to be cost-effective only when focused on higher-risk populations, such as black MSM who represent 25% of the HIV epidemic, or in higher-risk settings. [10, 11] However, implementation of routine testing recommendations has proven challenging. In a recent study of six southeastern US community health centers that adopted routine point-of-care rapid testing, only 28% of patients were offered HIV tests, and fewer than 70% of those offered chose to have an HIV test. [12] Integrating appropriate HIV testing into private health-care settings is a crucial element to identifying undiagnosed HIV infections, yet very little research has been conducted in this area. Potential strategies for investigation in the private setting include interventions to increase provider HIV awareness and the use of HIV testing prompts within electronic medical record systems.

Identifying Individuals Earlier in Their Infection

In 2008 about one-third (32%) of individuals with an HIV diagnosis reported to CDC received an AIDS diagnosis within one year of their initial diagnosis. [13] Current approaches often identify HIV for the first time only late in the patient's HIV disease course. [13] This pattern is especially pronounced among marginalized populations and ethnic minorities, and leads to significant HIV health outcome disparities. Identifying individuals earlier in their HIV infection requires encouraging persons at high risk to test frequently. Research is needed to identify effective community mobilization strategies to facilitate frequent HIV testing, make regular testing normative, and decrease stigma associated with HIV and testing, especially for high-risk populations and under-tested minorities.

Specific interventions for low-income persons might include text messaging and low-value cash incentives to promote regular HIV testing. Making rapid HIV tests available to consumers in local pharmacies at a low cost is a strategy that could allow persons in high-risk groups to test their HIV status repeatedly over time, potentially increasing the identification of persons earlier in their course of disease. MSM at high risk for HIV increasingly use the Internet to meet new partners. A promising research intervention for these men is establishing the norm to include in personal profiles the date of last HIV testing; site banners that recommend HIV testing every three months for those at risk could be employed as well.

A second goal related to early HIV detection is to identify persons very soon after HIV infection, during the acute phase, a period characterized by high risk of HIV transmission to uninfected partners. [14] Identifying acutely HIV-infected persons could be aided by the use of newer HIV testing technologies (e.g., fourth-generation ELISA testing, combination antibody and antigen testing, or targeted nucleic acid testing of antibody-negative specimens). Research is needed to develop and evaluate acute HIV infection–awareness campaigns for the community and providers, emphasizing symptoms that often accompany primary infection and the increased infectiousness of acute HIV infection. [15] Research with a small sample of acutely HIV-infected persons has shown a reduction in transmission risk acts following notification of acute infection status, highlighting the potential to reduce onward HIV transmissions if acutely infected persons are made aware of their status and of their increased infectiousness. [16]

Unfortunately, policy does not always translate directly into action. Coordinated public health responses to acute/early HIV infection involving linkage to HIV care and facilitated partner counseling and referral services have been insufficiently studied. [17] A recent Institute of Medicine report identified many of the practical, policy, and regulatory barriers to the implementation of coordinated responses following the diagnosis of acute HIV infection. [18] Researchers must assess the most effective and efficient ways to overcome these barriers.

Linking and Retaining HIV-Infected Individuals in Care

The Strategy has established a target of increasing the proportion of newly diagnosed individuals who are linked to clinical within 3 months of their HIV diagnosis from 65% to 85%. In addition to linkage to routine care, it is important to respond to the distinct and separate challenge of retention in care. [19] Differing definitions and methods make measuring linkage to and retention in care difficult; however, we do know an estimated 30% to 50% of newly diagnosed HIV-infected individuals in the US fail to establish HIV care within six months. [20, 21] In addition, missed appointments are reported among 25% to 35% of HIV patients in care [22–24], and estimates of retention in care (as measured by at least one visit every six months over a two-year period) range from 18% to 61%. [25–27]

Engagement in care is vital for the treatment success of individual patients and for prevention at population levels. Care engagement is known to be worse in marginalized populations, resulting in significant health disparities. As with HIV detection and early identification goals, social marketing and community mobilization strategies aimed at making HIV treatment engagement normative need to be researched.

There is precedent for using linkage support services as core elements in medical care, especially for poor, ethnic-minority patients with cancer, [28] diabetes, [29] and other chronic diseases including HIV. [30] Early research showed the benefits of case management for linking HIV patients into care. [31, 32] More recently, patient navigator interventions have been found to reduce barriers in accessing care and to improve health outcomes for individuals with HIV in the US. [28–30, 33] Navigators, who can be professionals or peers, assist HIV-infected individuals to make use of available resources and develop effective communication with providers, provide practical and emotional support (such as transportation or child care), escort patients, and help them understand the demands of HIV treatment. Patient navigators can be assigned to emergency departments and other health care settings including testing sites to facilitate linkage to care of HIV-infected persons, with the goal of ensuring initial care visits quickly after HIV detection.

Although navigator interventions have shown promise, there is considerable room for improvement in their implementation and in measuring their success. NHAS goals may be better served by defining “linkage success” as receiving an HIV care visit within one month of initial HIV diagnosis, rather than within three months as has been typical in research studies.

Retaining HIV-infected persons in care presents a significant challenge. Missed visits in the first year of care are associated with the risk of death and risk of mortality increases with the number of visits missed. [34] A study of HIV-infected persons in San Francisco showed an almost doubling of mean HIV viral load among those not engaged in care as compared to those in care. [35] Given its obvious importance, it is surprising that no randomized, controlled trials of interventions to retain HIV-infected persons in care have been conducted; and there is no consistent definition of what is meant by “in care” with respect to frequency or content of visits. In clinical trials testing drugs, cohort retention for study visits is a high priority, yet the strategies used to meet retention targets in trials have not been systematically applied to the challenge of keeping HIV patients in care. As with linkage to care, patient navigators could be used to track and assist patients—particularly those patients identified as being at high risk for attrition—to stay in care. Research attention to the development and testing of care retention interventions will benefit patients and benefit the field.

Maintaining Viral Suppression and Improving Health Outcomes

Treatment guidelines have gradually shifted toward beginning treatment at higher CD4 cell counts, with the goal of total HIV viral suppression. Recently, many clinicians have concluded that treatment should be recommended for all HIV-infected individuals, regardless of clinical status, at the time of diagnosis in order to improve long-term health outcomes. [36]

The NHAS aligns well with what the research community has described as a “test-and-treat” approach, which refers to the early identification of HIV and linking and retaining individuals in care with the goal of maintaining viral suppression. The test-and-treat strategy has the potential both to improve the health of HIV-infected individuals and to reduce new infections by reducing HIV-positive individuals' infectivity. [37] In contrast to the virtual eradication of HIV predicted by modeling of test-and-treat approaches in South Africa,

modeling of the US epidemic suggests varying reductions in new HIV infections depending on the extent to which treatment and viral suppression are achieved in the community. [38] The goal of the NHAS is a 25% reduction in new infections in 5 years, which is within the range of modeled effects of increased testing and treatment in selected high-prevalence cities in the U.S. [35, 39–45]

Improvement of health outcomes depends on behavioral factors associated with adherence to both treatment and care. Adherence interventions often involve practical tools such as pillboxes, reminders, and calendars. [46] When warranted, more intensive interventions to improve adherence include cognitive-behavioral approaches, social support, contingency management, home visits, and directly observed therapy. [47–50]

Care for mental health and substance abuse plays a central role in improving health outcomes. Research has shown that substance abuse and depression are prevalent among HIV patients in care. [51, 52] Promising areas of research include short, computer-based screening for these conditions as well as adherence counseling in clinic waiting rooms. Through the use of electronic medical records systems, assessments could be used to generate prompts for clinicians to direct attention to issues of adherence, mental health, and substance use. Clinic-based screening procedures could also include an assessment of HIV transmission risk acts and readiness for behavior change. [53, 54] These assessments could lead to provider-based prevention messages tailored to the stages of change model, [55, 56] previously shown to be both effective [53] and cost-effective for HIV prevention in clinic settings. [57]

Assessing the Impact of Multilevel Interventions

Given the nature of the multilevel interventions needed to implement the NHAS, we must develop and realign our existing research and funding frameworks to evaluate the epidemic impact of these new interventions. Prior HIV/AIDS prevention research has most often examined either theoretically informed, individual-level interventions to promote behavior change or biomedical prevention approaches, usually in isolation from one another. [53, 54] The synergistic effects of multilevel HIV/AIDS prevention approach, combining both behavioral and biomedical methods, need to be evaluated at the community level.

Indeed, there is progress in this direction with multi-level intervention feasibility research being conducted by the HIV Prevention Trials Network (HPTN) in the Bronx, NY, and Washington, DC. [5] In addition, the CDC through its “Enhanced Comprehensive HIV Prevention Planning” program or ECHPP is supporting the implementation of the NHAS in the 12 US cities most affected by the HIV epidemic to assess how multiple interventions can be combined in the most cost effective and efficient manner in real-world settings. [58–62] NIH researchers are involved in this effort, providing technical assistance to local health departments on evidenced-based intervention and community-level evaluation methods.

Recent developments in the use of public health surveillance data give researchers the potential to examine an aggregate biologic measure of HIV-1 viral load for particular geographic locations. [44] Community viral load can serve as a population-level biologic marker of HIV transmission risk and antiretroviral therapy-mediated virologic suppression. [35] This innovation represents a methodological advance for evaluating the success of intervention strategies aimed at achieving goals of the NHAS.

Implementation of multilevel interventions and evaluation of their epidemic impact present challenges to traditional research paradigms. Current methods and research funding emphasize randomized, controlled trials of efficacy over evaluation and effectiveness studies responding to implementation challenges, thereby limiting needed research. A possible

solution would be for the National Institutes of Health to develop mechanisms focusing on the implementation gaps we have identified. Such an approach could strengthen the evidence base needed to achieve the practical goals outlined in the National HIV/AIDS Strategy. The public health and scientific fields will be well served by the integration of biomedical advances in HIV prevention with the behavioral, social, and structural interventions needed for implementation on a large scale.

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Table 1

Intervention Research to Respond to Implementation Gaps and Identified for the National HIV/AIDS Strategy.

Implementation Gap	Research Areas	Outcome Metrics
1 - Identifying Undiagnosed HIV	<ul style="list-style-type: none"> • Social marketing of importance of knowing HIV status • Community-level interventions for making testing normative • Routine testing in emergency departments and other settings • Implement CDC guidance on testing in private sector • Awareness campaigns for providers on screening 	Number of HIV tests performed Number of new HIV cases identified Percentage meeting testing guidelines Percentage tested w/in high risk groups
2 - Identifying Individuals Earlier in Their Infection	<ul style="list-style-type: none"> • Community mobilization and outreach to increase the frequency of testing • Text messaging and incentives for screening at regular intervals • Implementing improved testing technology for acute HIV identification • Acute HIV infection awareness campaign (community & provider) • Tailored counseling on acute/early HIV infectiousness • Rapid response mechanism within public health system 	CD4 at HIV diagnosis Percentage acute HIV of all new HIV
3 – Linking and Retaining Individuals in Care	<ul style="list-style-type: none"> • Patient navigator • Emergency room and HIV testing site linkage programs • Changing community norms on seeking treatment • Retention in care – navigator model 	Percentage linked into care w/in 1 month Percentage in regular HIV care Percentage retained in care
4 –Improving Health Outcomes	<ul style="list-style-type: none"> • Expanded ART start (all HIV-infected offered treatment) • Adherence screening & referral • Substance abuse screening, referral, and care integration • Mental health screening, referral, and care integration • Provider-based prevention with positives 	Percentage virologically suppressed Percentage screened for: Medication Adherence Substance Abuse Depression HIV transmission risk Percentage referred for services Percentage receiving prevention-with-positives messages
5-Assessing Multi-Level Epidemic Impact	<ul style="list-style-type: none"> • Methods • Attribution • Evaluation framework • Quasi experimental designs • Cost-effectiveness evaluation and frameworks 	Community Viral Load HIV incidence Outcome disparities by race/ethnicity risk groups Healthcare expenditures