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## Operational Research to Improve HIV Prevention in the United States

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### Abstract

The HIV/AIDS epidemic in the United States continues despite several recent noteworthy advances in HIV prevention. Contemporary approaches to HIV prevention involve implementing combinations of biomedical, behavioral, and structural interventions in novel ways to achieve high levels of impact on the epidemic. Methods are needed to develop optimal combinations of approaches for improving efficiency, effectiveness, and scalability. This article argues that operational research offers promise as a valuable tool for addressing these issues. We define operational research relative to domestic HIV prevention, identify and illustrate how operational research can improve HIV prevention, and pose a series of questions to guide future operational research. Operational research can help achieve national HIV prevention goals of reducing new infections, improving access to care and optimization of health outcomes of people living with HIV, and reducing HIV-related health disparities.

### Keywords

combination prevention; HIV/AIDS prevention; operational research; treatment as prevention

## INTRODUCTION

Recent advances have increased the number and kinds of interventions that have demonstrated efficacy for preventing HIV infection. New biomedical interventions—including early antiretroviral therapy (ART) for serodiscordant heterosexual couples,<sup>1</sup> oral ART as pre-exposure prophylaxis (PrEP) for HIV-negative men who have sex with men (MSM),<sup>2</sup> ART in a vaginal microbicide for use by HIV-negative women as topical PrEP,<sup>3</sup> and oral ART as PrEP for heterosexual couples<sup>4,5</sup>—when combined with efficacious behavioral and structural interventions can potentially turn the tide against the domestic HIV epidemic.<sup>6</sup> The increasing focus on using ART treatment as prevention and using different

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kinds of interventions together are “game changers” for HIV prevention.<sup>7–10</sup> Although we have new HIV prevention tools, many organizations face growing operational, technical, and fiscal impediments to realizing the full potential of existing and new prevention strategies. This underscores an urgent need to identify optimal combinations of approaches for addressing HIV prevention at the individual and other levels.<sup>9,11</sup>

This article argues that operational research (OR; also referred to as operations research) offers promise as a valuable tool for addressing challenges of enhancing planning and implementation of comprehensive HIV prevention programs and the corresponding prevention opportunities they create. We define OR, identify and illustrate areas where OR can make important contributions to HIV prevention, and pose a series of questions for future research on the implementation of behavioral and structural interventions, HIV testing, linkage to and retention in medical care, and ART for treatment and prevention.

## THE HIV/AIDS EPIDEMIC IN THE UNITED STATES

The annual number of new HIV infections in the United States has remained relatively stable at about 50,000 Americans each year.<sup>12,13</sup> An estimated 1.2 million Americans are living with HIV infection, and this number is expected to increase.<sup>14</sup> HIV is among the top 10 leading causes of death for certain age groups and races/ethnicities, particularly African Americans and Latinos aged 15–54 years,<sup>15</sup> and specific populations (ie, MSM, injection drug users, and transgender persons) continue to be disproportionately affected.<sup>16</sup>

To heighten awareness of, and systematically address, the HIV epidemic, the Office of National AIDS Policy in the White House released the National HIV/AIDS Strategy (NHAS) in 2010.<sup>17</sup> NHAS calls for increased cooperation and coordination among federal agencies and state and local partners to achieve the following goals by 2015: reduce the number of people infected with HIV, increase access to care and optimize health outcomes of people living with HIV, and reduce HIV-related health disparities.<sup>11,12</sup> To help the nation meet these goals, the Centers for Disease Control and Prevention (CDC) has adopted a “high-impact HIV prevention” approach that emphasizes delivering combinations of scientifically proven, cost-effective, and scalable interventions to the highest risk populations and geographical areas.<sup>18</sup> For this approach to be maximally successful; however, methods are needed to understand the factors that impact program effectiveness, efficiency, scalability, and sustainability over time; and identify strategies needed to enhance and improve program implementation and optimize program value.<sup>18–20</sup>

## OR: CHARACTERISTICS, DEFINITION, AND SCOPE

OR has a strong problem-solving focus that emphasizes the identification, implementation, and assessment of strategies to improve program operations in real-world settings.<sup>20–22</sup> OR uses a range of methods (eg, descriptive and analytical studies and mathematical modeling),<sup>19</sup> but its aim is to increase systematic uptake of research findings and other evidence-based practices into routine service delivery to improve health-related services and outcomes.<sup>23</sup> OR has been defined as research that focuses on the implementation of day-to-day activities or operations of specific agencies/organizations, whereas research focusing on widespread dissemination of programs has been designated as implementation research.<sup>20</sup>

Although the distinctions between OR and implementation research can help articulate the focus and purpose of specific research projects, these 2 areas of research frequently overlap and the terms may be used synonymously.<sup>20</sup> For simplicity, we use the term OR to encompass both areas of research. Our framework for OR presented in Figure 1 begins with the identification of problems encountered during program implementation. Part of this process involves the formulation of research questions to guide OR efforts. Once the problem is articulated, a solution is proposed and tested. If the solution is determined to be effective, efficient, and sustainable, it is then disseminated more broadly.<sup>21,22</sup>

Most OR studies in HIV prevention, treatment, and care have been conducted in developing countries due to a pressing need to determine how best to allocate scarce resources among different interventions along the continuum of prevention and care.<sup>22,24–27</sup> In contrast, OR-related activities for domestic HIV prevention have chiefly focused on “moving research into practice” and studying the implementation of evidence-based interventions by service providers.<sup>28–30</sup> However, as constraints on domestic HIV prevention resources have grown, OR’s potential to maximize the effectiveness of prevention programs has garnered increasing interest and attention.<sup>17,18,31</sup>

## OR AND COMPONENTS OF HIGH-IMPACT HIV PREVENTION

The criteria used by CDC to identify and define the components of a high-impact HIV prevention approach provides context for our discussion of how OR can strengthen the planning and implementation of biomedical, behavioral, and structural HIV prevention interventions. Specifically, OR should be used to assess and improve upon the cost-effectiveness, scalability, target population coverage, interactions, and synergies among and prioritization of interventions.<sup>18</sup> The continuum of HIV prevention services spans from prevention with HIV-negative persons through care and treatment for HIV-positive persons. Thus, the ensuing discussion examines how OR can be used to achieve high-impact prevention within and across continuum elements including behavioral and structural interventions and activities in the testing and treatment cascade (ie, HIV testing, linkage to and retention in medical care, and ART for treatment and prevention).<sup>32,33</sup> Key OR questions are provided (Table 1) for improving capacity to deliver prevention programs with the greatest overall potential to reduce HIV infections.

### Behavioral and Structural Interventions

Behavioral and structural interventions to reduce HIV-related risk behaviors continue to be important components in the domestic portfolio of HIV prevention programs.<sup>18</sup> Efficacious individual-level, group-level, and community-level interventions have been shown to significantly reduce risk behaviors associated with HIV acquisition among uninfected persons and transmission among people living with HIV.<sup>34</sup> In addition, structural interventions, such as condom distribution and syringe services programs, have led to changes in social norms concerning sex and drug injection behaviors and changes in the behaviors themselves.<sup>35,36</sup> Although the efficacy of these interventions has been demonstrated, significant questions remain about their relative scalability, efficiency, and cost-effectiveness. New OR strategies are needed to identify the most appropriate venues for intervention activities to reach the highest risk populations and determine the impact and

sustainability of intervention efforts when implemented in local jurisdictions (Table 1). OR also needs to focus on developing interventions essential to the success of high-impact prevention (eg, promoting linkage to care, overcoming barriers to retention and adherence to medical treatment of HIV-infected persons).

### **HIV Testing in Clinical and Nonclinical Settings**

HIV testing, linkage to medical care, and initiation of ART are the 3 components of a “test and treat” paradigm for reducing HIV transmission.<sup>37</sup> Learning one’s HIV serostatus through testing is critical for the subsequent uptake of prevention and treatment services, and HIV testing has been shown to be cost-effective in clinical and nonclinical settings.<sup>38,39</sup> A resource allocation model of CDC funds suggested that targeted HIV screening programs are essential to HIV incidence reduction efforts.<sup>40</sup> Although 16–22 million Americans test for HIV annually, more than one-fifth of infected persons are unaware of their HIV serostatus,<sup>41</sup> and more than one-third of those identified as HIV positive for the first time are diagnosed with AIDS within 1 year of their HIV test.<sup>42</sup> Late testing and delayed diagnosis are particularly common among racial/ethnic minority populations.<sup>43,44</sup>

In an effort to expand access to HIV testing in the United States, CDC funded demonstration projects to determine the feasibility and effectiveness of using conventional and rapid HIV tests in various clinical and nonclinical settings.<sup>45</sup> Challenges to expanding the scope of HIV testing included competing priorities for limited resources within clinical settings; logistical difficulties testing large numbers of people in clinical and correctional settings; delivering preliminary positive test results in community-based venues and confirmatory results to transient, homeless and other hard-to-reach populations; and linking persons with HIV infection to care in nonclinical settings.<sup>45</sup>

Many of the implementation challenges highlighted by these demonstration projects and other published studies examining various HIV testing strategies readily lend themselves to OR.<sup>46,47</sup> At a minimum, OR must identify optimal strategies for reaching high-risk persons to increase early detection, receipt of test results, and linkage to medical care. Effective strategies must be developed and disseminated to ensure that persons who receive preliminary test results also receive confirmatory results, to enhance partner services programs to identify new HIV-positive persons, and to strengthen the implementation of self-testing. Moreover, strategies must be developed for improving HIV testing programs at the agency and system levels, including the identification of internal agency structures that improve testing programs. Finally, OR should inform the development of models for allocating testing resources in ways that reinforce and support programs. Table 1 lists OR questions to address these and other issues.

### **Linkage to and Retention in Continuous Medical Care**

Linkage to and retention in care ensures that HIV-infected persons receive life-saving treatment, which also reduces their risk of transmitting HIV to others. A meta-analysis of US-based studies for improving linkage to care found that 69% of HIV-diagnosed persons entered HIV medical care, and of these persons, 72% entered care within 4 months of their diagnosis.<sup>48</sup> With regard to retention in care, the same meta-analysis found 59% of persons

had multiple HIV medical care visits (follow-up periods ranged from 6 months to 3–5 years), retention in care was lower at 26% over longer follow-up periods, and up to 40% of HIV-positive persons were not retained in life-long medical care.<sup>48</sup> A mathematical modeling study suggests early entry into and retention in medical care has the potential of reducing viral load levels in the community, thus potentially lowering the HIV transmission rate at the population level.<sup>49,50</sup>

Despite the personal and public health benefits of early entry into and retention in care, a significant number of HIV-positive persons delay entering or re-entering medical care. Approaches to strengthen both linkage and retention in care include cognitive behavioral approaches, proactive case management, and delivery of services in general health care settings.<sup>51,52</sup> OR studies are needed to determine the optimal mix of structural and behavioral approaches to link newly diagnosed persons into care, identify innovative strategies that reward providers' retention efforts (eg, reimbursement models), and improve infrastructure and systems for tracking linkage to identify persons out of care at multiple levels (eg, individual, agency, and community; Table 1).<sup>32,53</sup>

### **ART for Treatment and Prevention**

HIV-infected persons who receive ART experience positive health outcomes and reduced mortality. ART as a prevention strategy had been established since the advent of antiretrovirals,<sup>8</sup> with prevention of mother-to-child transmission as a major accomplishment.<sup>54</sup> Several clinical trials have demonstrated the prophylactic efficacy of ART to prevent HIV acquisition by uninfected persons. The Preexposure Prophylaxis Initiative trial of high-risk uninfected MSM reported an overall 44% reduction in incident HIV infection, with reductions varying from 21% to 73% depending on adherence level,<sup>2</sup> the CAPRISA004 study of ART PrEP as a microbicide in women reported a 39% reduced rate of HIV acquisition,<sup>3</sup> and 2 studies of ART PrEP use in heterosexual serodiscordant couples reported preliminary findings of efficacy in preventing new HIV infections.<sup>4,5</sup> However, 2 PrEP studies failed, possibly due to implementation challenges. Meanwhile, the HPTN052 clinical trial of 1763 serodiscordant heterosexual couples has unequivocally demonstrated that treating HIV-infected persons early in their infection resulted in a 96% reduction in the sexual transmission rate of the virus to their uninfected partners.<sup>1</sup>

Regardless of whether ART is used as treatment or as PrEP, adherence to medication regimens is necessary to achieve beneficial effects. Suboptimal adherence can have myriad negative consequences including treatment failure, viral resistance, and increased community viral load through the transmission of resistant strains to noninfected persons.<sup>55</sup> Interventions have been developed to increase ART adherence, and CDC recently updated its online “Compendium of Evidence-based HIV Prevention Interventions” to include adherence interventions implemented in clinical and nonclinical settings.<sup>56</sup> OR studies are needed to understand and enhance the impact of medical providers on patients' adherence behaviors, to determine the best interventions to address patients' treatment history and prior ART adherence, and to study how organizational factors, such as collaborative relationships with pharmacies or community-based organizations, can extend or supplement how providers serve their patients (Table 1). The use of ART for PrEP has unique challenges. OR

is needed to develop effective combinations of interventions and counseling approaches for high-risk HIV-negative populations for which PrEP works, such as MSM.<sup>57,58</sup> In terms of the allocation of HIV prevention resources for PrEP, a critical issue will involve how to prioritize behavioral counseling and risk reduction for persons using PrEP versus those not using PrEP and how to best allocate resources in support of PrEP.

## CONCLUSION AND FUTURE DIRECTIONS

We have described and illustrated how OR can be useful for clarifying barriers to implementing HIV prevention activities that are likely to have a high level of impact on the HIV/AIDS epidemic in the United States and for identifying strategies to overcome those barriers and improve the effectiveness and efficiency of HIV prevention programs. Sustainable high-impact prevention activities are critical to achieving NHAS goals of reducing new HIV infections, increasing HIV-positive persons' access to care, and reducing health disparities.<sup>17</sup> Our description of how OR can contribute to improved HIV prevention and service delivery are intended to stimulate thinking on ways to improve the effectiveness and efficiency of the continuum of HIV prevention services including behavioral and structural interventions and the cascade of HIV testing and treatment.

Although the opportunities for future research are considerable, particularly important areas for future inquiry include developing appropriate research designs to address specific OR questions; clarifying how OR, monitoring and evaluation, surveillance systems, and quality assurance activities can be used together to improve program performance and impact; and identifying solutions stemming from disparities in HIV-related social determinants, including affordable housing, deteriorated neighborhoods, and insufficient health insurance coverage. OR studies that guide public health policy and inform decision-making at the jurisdiction level concerning the effective allocation of constrained HIV prevention resources are also critical. Although resource allocation models provide idealized scenarios,<sup>40</sup> OR studies can help translate modeled scenarios to real-world settings, provide modelers needed data to produce recommendations that better account for and incorporate real-world constraints, and support iterative improvements on allocation recommendations produced by models.

Resources for HIV prevention programs will likely continue to be limited. These circumstances increase the need for high-impact programs that are evidence-based, cost-effective, scalable, and sustainable for populations at the highest risk of acquiring and transmitting HIV. As needs vary among geographic areas and populations, OR can be used to identify specific combinations of intervention tools, which are optimally tailored to meet localized needs. Our OR framework (ie, identifying problems, developing solutions, testing solutions, and disseminating effective solutions; Fig. 1) can be applied to any HIV prevention-related program including biomedical, behavioral, or structural.<sup>32</sup> As CDC and other federal agencies institutionalize the use of combination approaches that span the HIV prevention continuum, the need for OR will become ever more imperative.<sup>59</sup>

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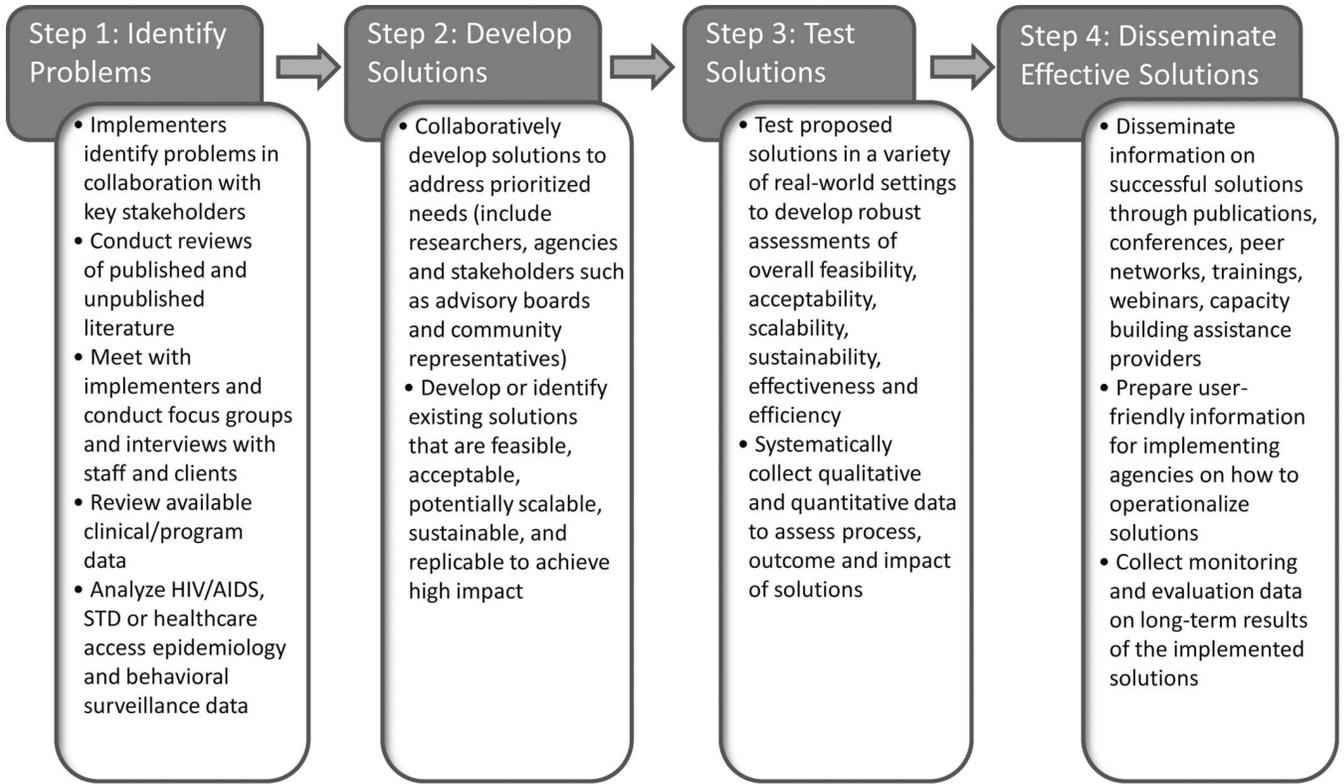
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**FIGURE 1.** Framework of operational research for HIV prevention.

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TABLE 1

## Examples of High-Impact HIV Prevention Activities and OR Questions to Improve Implementation

High-Impact HIV Prevention Activity	OR Questions
Behavioral and structural interventions	<p>What agency characteristics are predictive of greater capacity to implement EBIs (eg, budget, “age” of agency, type of agency)?</p> <p>What strategies should be developed to assist agencies to select and adopt appropriate EBIs to meet the prevention needs of specific target populations?</p> <p>What factors are associated with successful and unsuccessful recruitment and retention into EBIs? Do recruitment and retention challenges vary based on intervention and characteristics of the target population?</p> <p>How do implementing agencies adapt EBIs to meet the needs of their target population or local setting?</p> <p>What are the barriers to monitoring and evaluation of EBIs, and what strategies can be used to enhance EBI monitoring and evaluation activities?</p> <p>How can the implementation of condom distribution programs be improved to increase the number of high-risk persons reached?</p> <p>What are ideal venues for distributing condoms to specific high-risk populations, including persons living with HIV?</p> <p>How do agencies use HHS guidance to implement syringe services programs?</p> <p>How can syringe services programs be integrated with HIV testing and other HIV prevention activities to provide an array of needed services for injection drug users?</p>
HIV testing in clinical and nonclinical settings	<p>For HIV testing programs implemented in clinical (eg, hospital emergency rooms, community health centers, and sexually transmitted disease clinics) and nonclinical settings (eg, community-based organizations), what are the most effective strategies for reaching the highest risk persons to yield the greatest HIV seroprevalence (eg, use of new media technology, HIV testing campaigns, mobile vans, testing in new venues such as community colleges and faith-based organizations, self-testing)? Do the most effective strategies vary by risk group or other population/agency characteristics?</p> <p>How should testing be implemented in different clinical settings so that programs can be sustained in the absence of dedicated public health funds?</p> <p>What actions can be taken to increase the number of persons tested with acute infection and decrease the number tested with advanced HIV disease (ie, late testers)?</p> <p>What strategies can agencies employ so persons with preliminary HIV-positive test results return for a confirmatory test?</p> <p>What HIV testing policies at the program-level, agency-level, or jurisdiction-level are barriers and facilitators to effective HIV testing?</p> <p>Given imperfect coverage of routine HIV testing, what types of providers should health departments focus on to encourage and support implementation and uptake?</p> <p>Given a fixed budget for HIV testing, does it make more sense for health departments to directly fund or provide HIV testing or focus on training for clinical providers to implement routine HIV testing?</p>
Linkage to and retention in continuous medical care	<p>How can HIV testing programs effectively track client referrals to ensure successful linkage to care?</p> <p>What is the best mix of structural and behavioral approaches to link into medical care newly diagnosed HIV-positive persons and HIV-positive persons who have not received care?</p> <p>How can effective partnerships be established among HIV testing programs, linkage case managers, and HIV clinicians to increase rates of persons linked to and engaged in medical care?</p> <p>What are the most efficient strategies for linking newly diagnosed clients to medical care (eg, behavioral counseling, cross-training HIV prevention counselors, education and support, and use of case managers and patient navigators)?</p> <p>How can ancillary services (eg, childcare services, mental health, and substance abuse treatment programs) be used to enhance retention in care and how should they be prioritized and allocated to maximize public health impact?</p> <p>How can or should health departments use viral load and surveillance data to (1) identify persons not linked to and retained in care, and (2) support reengagement in care?</p>

High-Impact HIV Prevention Activity	OR Questions
ART for treatment and prevention	<p>Given resource limitations, how should health departments and providers prioritize for outreach and reengagement in care efforts?</p> <p>What are the most effective strategies that result in consent for early ART (eg, peer navigators, streamline HIV testing with linkage to care)?</p> <p>What factors should clinicians or CBOs consider when selecting interventions to improve medication adherence among clients? How can adherence interventions be adapted to address individual patient needs? How often should adherence be assessed?</p> <p>What are the optimal settings (clinical versus nonclinical) and providers (clinicians versus community-based providers/peers) for delivering ART adherence interventions?</p> <p>What models can clinical care teams and community providers work with to synergistically support adherence?</p> <p>What types of risk-reduction messages (eg, promotion of consistent condom use) should be delivered by clinicians to high-risk clients using PrEP to reduce risk behaviors?</p> <p>How should PrEP be integrated within existing evidence-based interventions and other medical or social services to form a comprehensive HIV prevention program?</p> <p>How should health departments and CBOs prioritize support for PrEP users versus high-risk persons and populations without access to or use of PrEP?</p>

ART, antiretroviral therapy; CBO, community-based organization; EBI, evidence-based behavioral intervention; PrEP, preexposure prophylaxis.