INTRODUCTION

The First National Scientific Meeting of the Social and Behavioral Science Research Network

Michael B. Blank, PhD,*† David S. Metzger, PhD,*† Gina M. Wingood, ScD, MPH,‡§ and Ralph J. DiClemente, PhD‡§

In November 2005, a small group of behavioral and social sciences investigators from the University of Pennsylvania and Emory University began planning for the establishment of a network between scientists involved in HIV prevention and treatment research. The purpose of this network was 3-fold. First, it was intended to foster multisite collaborations between behavioral and social scientists. Second, it was intended to share strategies on how behavioral and social scientists could be better partners with more basic and clinical scientists and how the basic and clinical sciences could be better used to inform behavioral and social science research. Finally, the Social and Behavioral Science Research Network (SBSRN) was explicitly intended to provide a forum for the exchange of the most recent information in the behavioral sciences regarding HIV/AIDS and to mentor the next generation of scientists engaged in social and behavioral science surrounding HIV prevention and treatment. By combining the intellectual capital and synergies among the community of scientists engaged in this work, it is hoped to invigorate state-of-the-art science in this area. In the National Institutes of Health (NIH) roadmap, the “research teams of the future” are described as problem-oriented multidisciplinary and interdisciplinary teams. We believe the SBSRN provides the foundation on which these teams can be built and directed toward HIV research.

The SBSRN planning meeting was held in Atlanta, March 27–28, 2006. The meeting was hosted by the Emory University Center for AIDS Research (CFAR) and jointly supported by the University of Pennsylvania and Emory University CFARs. Representatives from 14 CFARs attended this 2-day meeting that focused on the development of consensus on the importance of the SBSRN and its mission. The following mission statement was adopted: “To articulate a national research agenda for the Social and Behavioral Science Research Network across CFARs and to stimulate cross-CFAR sharing of resources and future collaborative research.” This meeting also established the network’s research priorities and the development of an outline of the structure of the first national scientific meeting of the SBSRN. An Executive Committee was elected (Dr. DiClemente and Dr. Wingood from the Emory University CFAR and Dr. Metzger and Dr. Blank from the University of Pennsylvania CFAR) and given the responsibility to begin planning for a larger national meeting of the SBSRN. It was agreed that this first national scientific meeting of the SBSRN would be held in Philadelphia in the fall of 2006. The group also identified a number of potential shared resources that could be developed to support the efforts of individual CFAR cores and investigators. These included Web-based tools useful in the preparation of interdisciplinary research applications, a common database for tracking service delivery in social and behavioral sciences, a national directory, and a cross-CFAR list-serve to speed communication and enhance collaborations. The group thought that the value added by the SBSRN to each CFAR had the potential to encourage all sites to include support for this effort in their respective competitive renewal applications and that

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the SBSRN serves as an exemplar for how cross-site collaborations can be intentionally engineered.

At the Atlanta meeting, it was agreed that the scientific portion of the national SBSRN meeting would be structured around the top 3 research priorities developed by the group: (1) effectiveness and cost-effectiveness of primary and secondary HIV prevention research, (2) mental health and substance abuse comorbidity—prevention and treatment, and (3) racial and ethnic disparities in HIV prevention and treatment. The conference eventually expanded to include in the top 6 priorities (4) global perspective of the HIV pandemic, (5) effectiveness/translational studies of prevention and treatment models, and (6) future directions of the science. It was further agreed that this meeting would be designed to facilitate innovative research applications and result in a series of policy papers. The audience for the national meeting was expanded from social and behavioral scientists within CFARs to include other social and behavioral scientists who have a focus on HIV/AIDS and NIH program staff, representatives from clinical and basic sciences, and community representatives.

A supplement from the National Institute of Allergy and Infectious Diseases (NIAID) to the University of Pennsylvania CFAR (Principal Investigator: James Hoxie) allowed the first national SBSRN conference to be held in Philadelphia, October 10–13, 2006. Before the meeting, the SBSRN solicited concept plans from identified speakers for research within specified priority areas that reflect its mission and maximize the resources of the CFAR program. Concept plans that involved multiple CFARs and other social and behavioral scientists who were unaffiliated with CFARs and used multiple core resources were selected for presentation and discussion with a focus on protocol development. Each research area session began with a nationally prominent invited speaker who provided an overview of the current state of science within that area. These overview talks were followed by breakout groups that focused on selected research concept plans that were submitted by participants before the meeting. Each concept was critiqued and fully discussed by the attendees. Our goal for these sessions was to provide the investigators with feedback on design, measurement, specific ideas for collaboration, and guidance on the most appropriate funding mechanism. The series of articles presented here are an outgrowth of these efforts.

The first day of the meeting was structured around mentoring and identified 4 main goals: (1) to provide a team mentoring, supportive, and collegial atmosphere, where early career and transitional social and behavioral science investigators can meet and discuss common challenges they confront in establishing interdisciplinary HIV research careers; (2) to assist in addressing this gap by identifying promising early career and transitional investigators around the country, providing a day-long orientation, and facilitating early career and transitional investigator linkages with senior scientists; (3) to expose early career and transitional investigators seminars specifically tailored to their needs, including crafting a successful NIH grant, mechanisms for support for early career and transitional investigators, HIV research priorities, and a brief review of HIV prevention research among (a) adolescents, (b) substance users, (c) mental health aspects of HIV, (d) women, and (e) international HIV prevention research; and (4) to provide the opportunity to meet with senior-level researchers and prosper from their experiences (successes and failures).

The second and third days of the meeting were structured around the 6 research priorities identified at the Atlanta organizing meeting: (1) cost-effectiveness studies of prevention and treatment models, (2) racial disparities in HIV prevalence and incidence, (3) the role of mental health and substance abuse in HIV prevention and treatment, (4) global perspective of the HIV pandemic, (5) effectiveness of translational studies of prevention and treatment models, and (6) future directions of the science. It is important to note that these research priorities overlap significantly with those of the Office of AIDS Research (OAR). Overall, the mentoring and scientific meeting days were well attended by a plethora of participants from various backgrounds (see Table 1).

The SBSRN Planning Committee convened on the fourth and final day of the conference to define organizational and operational issues for the SBSRN further and to plan for future activities. It was determined that an application would be submitted to the NIH to support a series of 3 additional meetings. The University of Alabama at Birmingham volunteered to host the next meeting in 2007, and the University of Washington volunteered to host the meeting in 2008, followed by a consortium between Harvard and Brown Universities in 2009. An important area of consensus emerging from the First National Scientific Conference was the need to continue to develop a strategy to mentor early career social and behavioral scientists interested in establishing research careers that merge AIDS-related social and behavioral science research with other scientific disciplines. The group also recognized the importance of efforts designed to engage social and behavioral scientists who have established programs of research that have not focused on AIDS-related research. These transitional investigators represent an important potential resource to the research agenda of the NIH, and to HIV research generally. The guiding theme is to facilitate

| TABLE 1. Characteristics of Participants at the 1st SBSRN Scientific Meeting |
|-------------------------------|-----------------|-----------------|
|                               | Mentoring Day   | Scientific Conference |
| PhD                           | 56%             | 54%              |
| MD                            | 25%             | 13%              |
| MPH                           | 19%             | 10%              |
| RN/MSN                        | 0.06%           | 0.2%             |
| Students                      | 0               | 7%               |
| MSW/LCSW                      | 0.06%           | 0.2%             |
| PsyD                          | 0.06%           | 0.008%           |
| DrPh                          | 0.06%           | 0                |
| ScD                           | 0               | 0.008%           |
| Female                        | 67%             | 42%              |
| Male                          | 33%             | 58%              |
| Racial/ethnic minority        | 33%             | Unknown          |
| CFARs represented             | 9               | 17               |
| Non-CFARs represented         | 9               | 15               |
| Total attendees               | 16              | 120              |
integration of social, behavioral, and biomedical research on HIV. The SBSRN can contribute to the development of the “research teams of the future,” which should be problem focused and utilize science and methods from many diverse and complementary disciplines.

We are pleased to be able to present the proceedings of the First National SBSRN Scientific Conference in this supplement entitled “Research Lessons: Setting the Social and Behavioral Sciences Agenda for Future HIV/AIDS Research.”

In the first article, James Kahn, Christine D. Des Jarlais, Loren Dobkin, Sarah French Barrs, and Ruth M. Greenblatt present “Mentoring the Next Generation of HIV Prevention Researchers: A Model Mentoring Program at the University of California San Francisco and Gladstone Institute of Immunology and Virology Center for AIDS Research.” Here, they note that mentoring is absolutely critical to develop and nurture early-career investigators and is especially important for investigators focused on HIV research because of the demands of high-impact multidisciplinary collaboration. They describe the highly successful mentoring program they developed targeting postdoctoral scholars and early career faculty. To date, more than 50 mentors and mentees have participated, and the article presents the results of the evaluation of that innovation. Activities that were particularly well received included networking among mentees, in addition to the networking between mentors and mentees, and workshops that focused on grant applications and first academic appointments and promotions. They conclude that a multidisciplinary mentoring program for postdoctoral fellows and early career investigators is useful and that umbrella organizations like the SBSRN are particularly well situated to provide these types of mentoring experiences. The University of California San Francisco mentoring program provides a model that we would encourage others to adopt and tailor for use in their own settings and for the needs of their own faculties.

In the next article, Steven D. Pinkerton, Cynthia R. Pearson, Susan R. Eachus, Karina M. Berg, and Richard M. Grimes present a “Proposal for the Development of a Standardized Protocol for Assessing the Economic Costs of HIV Prevention Interventions.” Here, they discuss the basic elements of a standardized cost data collection and analysis and further propose a standardized computer-based approach that could be used across sites. They argue that the development of such a protocol would foster increased dialogue and collaboration among HIV behavioral and social science researchers, cost-effectiveness analysts, community collaborators, public health decision makers, and funding agencies. This contribution is in keeping with the spirit and intent of the SBSRN, because it provides a primer for multisite efforts that ultimately are likely to be useful to policy makers and health and mental health authorities in allocation of resources to mitigate the impact of the epidemic.

In the next article in this series, James Walkup, Michael B. Blank, Jeffrey S. Gonzalez, Steven Safren, Rebecca Schwartz, Larry Brown, Ira Wilson, Amy Knowlton, Frank Lombard, Cynthia Grossman, Karen Lyda, and Joseph E. Schwumacher present their contribution on “The Impact of Mental Health and Substance Abuse Factors on HIV Prevention and Treatment.” It is becoming increasingly apparent that mental illness and substance abuse interact synergistically to affect HIV prevention and treatment; not only are persons with mental illnesses at increased risk for seroconversion, but HIV/AIDS has profound effects on subsequent mental health and substance use.

In “Examining Racial Disparities in HIV: Lessons From Sexually Transmitted Infections Research,” Julie Kraut-Becher, Marlene Eisenberg, Chelsea Voytek, Tiffany Brown, David S. Metzger, and Sevgi Aral examine 15 factors that have been shown to relate to racial and ethnic disparities in rates of sexually transmitted infections. This comprehensive and timely review concludes that observation of individual-level behaviors and individual factors to the exclusion of analyses of ecologic, contextual, and community-level factors is inadequate to explain these disparities and that interventions not addressing sexually transmitted infections at multiple levels are inadequate to address the problem.

In the next article, Jeffrey A. Kelly, Freya Spielberg, and Timothy L. McAuliffe present “Defining, Designing, Implementing, and Evaluating Phase 4 HIV Prevention Effectiveness Trials for Vulnerable Populations.” These authors argue that we have a number of behavioral HIV prevention interventions with proven effectiveness in clinical phase 3 randomized controlled trials but that little is known about the effectiveness of these same interventions when delivered by community-based providers to their own clients. These authors argue for phase 4 effectiveness trials that have been found efficacious in the research arena in the community and raise a number of design and methodologic issues associated with the conduct of such trials.

Susan Cassels, Samuel J. Clark, and Martina Morris next present an article entitled “Mathematical Models for HIV Transmission Dynamics: Tools for Social and Behavioral Science Research.” In this article, the authors note that HIV researchers need to understand the social and behavioral determinants of HIV-related risk behavior and that mathematic modeling can help us to understand how individual behaviors affect HIV on the population level. They argue that methods for studying this are largely of traditional social science or epidemiology training programs and that mathematic modeling provides an approach to examine biologic and behavioral determinants of HIV transmission dynamics.

In the next article, “The ADAPT-ITT Model: A Novel Method of Adapting Evidence-Based HIV Interventions,” Gina M. Wingood and Ralph J. DíClemente present their work on dissemination of evidence-based interventions (EBIs) in different settings. The ADAPT-ITT model consists of 8 sequential phases that inform HIV prevention providers and researchers of a prescriptive method for adapting EBIs. The ADAPT-ITT model has evolved over repeated applications from adaptations of several of the authors’ Centers for Disease Control and Prevention (CDC)-defined EBIs. The article cautions against transferring public health strategies and interventions from one setting to another or with diverse target populations without attention to social, ecologic, and contextual factors. The authors emphasize the need to use methodologically appropriate tools that are empirically supported and, at the same time, culturally congruent and include input from the target population. The article offers an approach to
adapting EBIs, and implementation of the ADAPT-ITT model provides an efficient mechanism of designing culturally competent and effective prevention programs.

Finally, in the conclusion “Future Directions for HIV Prevention Research: Charting a Prevention Science Research Agenda” Ralph J. DiClemente, Gina M. Wingood, Michael B. Blank, and David S. Metzger outline a vision for the continuation and expansion of the SBSRN. This includes an emphasis on integration of social and behavioral sciences with basic and clinical science to forward research and interventions for HIV prevention and treatment and a vision for how multisite and cross-disciplinary collaborations can help to forward our combined mission for the SBSRN.

It has been a distinct pleasure for us to interact with the esteemed scientists who have contributed to the success of the SBSRN. We believe that a scientific collaborative such as this, which provides a vehicle for scientists from multiple disciplines to interact and exchange findings, ideas, and methodology, indeed represents the scientific teams of the future, not only for HIV but for improving generally the public health of our communities, nations, and world.
Mentoring the Next Generation of HIV Prevention Researchers

A Model Mentoring Program at the University of California San Francisco and Gladstone Institute of Immunology and Virology Center for AIDS Research

James Kahn, MD,*† Christine D. Des Jarlais, EdD,‡ Loren Dobkin, MPH,§ Sarah French Barrs, MPH,† and Ruth M. Greenblatt, MD,††

Purpose: Mentoring is critical to develop and nurture early career investigators, helping them to succeed in building networks of colleagues, and is especially important for investigators focused on HIV research. We piloted a multidisciplinary mentoring program targeting postdoctoral scholars and early career faculty concentrating on HIV/AIDS research.

Method: The pilot mentoring program was conducted at the Center for AIDS Research (CFAR) at the University of California San Francisco and the Gladstone Institute of Virology and Immunology. Mentees were self-referred postdoctoral scholars and early career faculty. Mentors were drawn from the senior faculty. Early career mentees were matched with senior investigators for individual meetings, a monthly workshop on topics directed by the mentees, and single-day mentoring seminars.

Results: More than 30 mentees and 20 mentors have participated in the pilot project. Most mentees reported that the 1-on-1 mentoring was a satisfying experience. The most highly valued activities were those that facilitated networking among mentees, networking between mentors and mentees, and workshops that focused on grant applications and first academic appointments and promotions.

Conclusions: A multidisciplinary mentoring program for postdoctoral scholars and early career faculty focused on HIV/AIDS research is valuable. Umbrella organizations, such as the CFAR, are well suited to create and provide highly valued mentoring experiences.

Key Words: HIV, mentoring, program development

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mentoring is a central activity; yet, the specific strategies and methodologies for providing this are not well documented, and the outcome of these experiences are largely dependent on lucky pairings of well-suited mentors and mentees. To fill this gap and to promote the advancement of and the commitment to the next generation of HIV investigators, the San Francisco CFAR developed a mentoring model to augment the existing mentoring activities for individuals beginning careers focused on HIV research.

**METHODS**

The University of California San Francisco (UCSF)–Gladstone Institute of Virology and Immunology (GIVI) CFAR Mentoring Program is modeled on local and national consensus panels and statements that elucidate the essential methodologic components of optimal mentoring. The programs of highest value included the following: Advisor Teacher Mentor Friend. On Being a Mentor to Students in Science and Technology,15 The UCSF Postdoc Mentoring Program: Guidelines for Faculty Mentors,16 The UCSF Graduate Student Mentoring Program: Guidelines for Faculty Mentors,17 the Gladstone Institute’s Postdoctoral Fellows Program Mentoring Standards,18 A Guide to Training and Mentoring at the Intramural Research Program,19 and The Climate for Faculty Report of the Chancellor’s Task Force on the Climate for Faculty.20

Several points were considered, including who would be mentored, who would serve as mentors, the matching method between mentors and mentees, the voluntary nature of the program, and the evaluation methods. Three primary activities were identified as the cornerstones of the project: individual meetings between matched mentee and mentors, a monthly workshop series for mentees that would also be open to the campus, and a mentee orientation to the UCSF-GIVI CFAR enterprise.

The following definitions are used in the mentoring program model:

**Mentor:** a senior faculty member engaged in the development of a set of knowledge and skills whose professional satisfaction would benefit from a relationship with a senior faculty member at the institution

**Mentee:** an individual engaged in the development of a set of knowledge and skills who takes an interest in helping another person to develop into a successful professional

**Mentoring:** a process supported by the CFAR to encourage the sharing of intellectual, experiential, and life experience resources to facilitate individual development and professional satisfaction for mentees and mentors

**Identification of Mentees**

Mentees were identified by self-referral and by faculty referrals. E-mail solicitations were sent by means of a large CFAR list to increase awareness of the pilot program and encourage participation.

**Identification of Mentors**

Mentors were chosen from the CFAR senior faculty with proven records of academic accomplishments and with an interest in participating in a pilot mentoring project.

**Matching Mentees and Mentors**

In the first year of the program, the mentoring codirectors (JK and RG) paired each mentee with 2 mentors using the following guidelines: (1) mentors must not be current members of the mentee’s research unit, (2) at least 1 female mentor for each female mentee, and (3) at least 1 mentor from outside the mentee’s main field of research. In the second year of the program, using feedback from the first year’s mentees, a different approach was taken to matching. At the onset of the second year of the mentoring program, mentees were invited to review the CFAR mentor Web site and the mentors’ profiles and then to rank 3 mentors in preferential order. Mentees’ preferences were reviewed, and pairings were assigned based on the following priorities: (1) retaining the prior year’s pairing for continuing mentees, (2) matching the mentee with his or her highest ranked mentor, (3) matching a female mentee with a female mentor, and (4) matching a mentee with a mentor who would augment his or her mentoring experience. The entire program and each workshop were evaluated using a multiple-choice questionnaire designed by 2 of the authors (LD and SFB) with optional fill-ins, framed according to previously published guidelines.21

**RESULTS**

In the first year of the UCSF-GIVI CFAR Mentoring Program, 12 mentees were matched in a 1-to-1 ratio with a total of 21 different mentors (Table 1). In the second year of the program, 20 mentees (14 new and 6 continuing mentees) were matched in a 1-to-1 ratio with 22 mentors (2 mentees were each paired with 2 mentors). In the first year of the program, there were more female mentees (N = 7) than male mentees (N = 5). In the second year, there were again more female mentees (N = 12) than male mentees (N = 8). In the first year of the program, most mentees had an MD degree (N = 10), whereas in the second year of the mentoring program, the numbers of mentees with PhD degrees increased substantially (N = 10). In both years of the program, the mentees were at beginning stages of their career, usually at the postdoctoral scholar level (45% and 35% in years 1 and 2, respectively) or assistant professor level (45% and 55% in years 1 and 2, respectively). The same mentors participated in the first and second years of the program, with the addition of 1 man in clinical science and 1 woman in behavioral science. One mentor from the first year decided not to participate in the second year, citing commitments to other projects. Among the 22 mentors in the second year of the program, 11 are women and 11 are men. More than two thirds of the mentors are professors at UCSF.

A key aspect of the mentoring program is the expectation that each mentee would meet with his or her mentor at least once every 2 months. Because there were 2 mentors for each mentee, it was anticipated that each mentee would have a monthly meeting with a mentor. This did not happen. Only 4 mentee-mentor pairs met monthly; the other pairings met less frequently, and 6 pairs met only every 6 months. Interestingly, the most common cited explanations for infrequent meetings were mentee preference and that the mentee was too busy with other activities. Few mentees...
identified a lack of administrative support or a lack of mentor responsiveness as a factor that prevented frequent meetings with their assigned mentors. Meetings were evenly divided between the office or laboratory and off-site venues. In general, most mentees were satisfied with the selection of their mentors, and most found it beneficial to have a nonsupervising mentor. Some mentees also highly rated the benefit of having a mentor from their field, however; perhaps reflecting a shortcoming in their primary research setting or a personal preference for more focus. Considering this, in the second year of the program, mentors were assigned based on the mentees’ preferences for mentors. As a result, 12 mentees received their first choice, 5 received their second choice, 2 received their third choice, and 2 received an alternative choice for their mentor.

At the start of the second year of the mentoring program, the mentees were asked to rank the mentoring workshops they believed to be of greatest value. The ranking confirmed that mentees were mostly interested in a program that would help them to network and expand their collaborations (Table 2). The mentees placed high value on activities associated with understanding National Institutes of Health (NIH) funding, grant submission, and first academic appointments. Interestingly, and somewhat unexpectedly, workshops focusing on life and work balance issues were not identified as of high value to the mentees. When asked how the first year’s workshop series provided benefit, the mentees gave the highest values to “Provided career-related skill-building tips,” “Increased my interaction with colleagues,” and “Revealed sources of institutional support.”

### DISCUSSION

This program was unique in several respects. First, to our knowledge, it is the first programmatic approach directed to postdoctoral scholars and early career faculty seeking to establish a career in HIV/AIDS research. Second, this program involves mentees and mentors who were organized around the general theme of HIV/AIDS research but specifically focused on 3 major academic areas: basic, clinical, and behavior research. The intersections of basic, clinical, and behavioral research represent key areas for this CFAR. Third, the program facilitated networking by matching mentees with senior faculty mentors who were not their direct supervisor but who could augment the junior investigators’ professional experiences. Finally, this program utilized frequent workshops with themes that the mentees identified as important. Evaluation results demonstrated that, overall, the program was rated valuable to the mentees, which led to the decision to continue

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**TABLE 1.** Demographics of the UCSF-GIVI CFAR Mentees

<table>
<thead>
<tr>
<th></th>
<th>2004 to 2005</th>
<th>2005 to 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>N = 12</td>
<td>N = 20</td>
</tr>
<tr>
<td>Gender (female/male ratio)</td>
<td>7:5</td>
<td>12:8</td>
</tr>
<tr>
<td>Age (y)</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Doctoral degree(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PhD</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>MD</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>MD, PhD</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pharm D</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Academic position at UCSF-GIVI CFAR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postdoctoral scholars</td>
<td>6 (50%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Assistant professors</td>
<td>5 (42%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Assistant adjunct professors</td>
<td>0 (0%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Resident scientists</td>
<td>1 (8%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Clinical instructor</td>
<td>0</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Primary work site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCSF or San Francisco General Hospital</td>
<td>6 (50%)</td>
<td>15 (75%)</td>
</tr>
<tr>
<td>GIVI</td>
<td>4 (33%)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>San Francisco Department of Public Health</td>
<td>2 (17%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Primary area of academic activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic science or basic/clinical interface</td>
<td>4 (33%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Clinical/clinical or behavioral interface</td>
<td>6 (50%)</td>
<td>12 (60%)</td>
</tr>
<tr>
<td>Behavioral science</td>
<td>2 (17%)</td>
<td>2 (10%)</td>
</tr>
</tbody>
</table>

**TABLE 2.** Areas of Interest Leading to Mentee-Directed Workshops at the UCSF-GIVI CFAR

<table>
<thead>
<tr>
<th>Workshops</th>
<th>Extremely or Very Useful</th>
<th>Neutral</th>
<th>Not as or Not Useful</th>
<th>Not Ranked</th>
</tr>
</thead>
<tbody>
<tr>
<td>Networking and expanding collaborations</td>
<td>80%</td>
<td>10%</td>
<td>0</td>
<td>10%</td>
</tr>
<tr>
<td>NIH funding and peer review</td>
<td>75%</td>
<td>5%</td>
<td>5%</td>
<td>15%</td>
</tr>
<tr>
<td>Embarking on international research</td>
<td>55%</td>
<td>20%</td>
<td>0</td>
<td>25%</td>
</tr>
<tr>
<td>First appointments and promotions</td>
<td>55%</td>
<td>25%</td>
<td>5%</td>
<td>15%</td>
</tr>
<tr>
<td>Submitting your first R01</td>
<td>50%</td>
<td>15%</td>
<td>10%</td>
<td>25%</td>
</tr>
<tr>
<td>Ethics of HIV research</td>
<td>45%</td>
<td>30%</td>
<td>5%</td>
<td>20%</td>
</tr>
<tr>
<td>Managing a laboratory or program</td>
<td>45%</td>
<td>30%</td>
<td>0</td>
<td>25%</td>
</tr>
<tr>
<td>Resolving academic conflicts</td>
<td>45%</td>
<td>25%</td>
<td>5%</td>
<td>25%</td>
</tr>
<tr>
<td>Industry and academic research careers</td>
<td>40%</td>
<td>15%</td>
<td>15%</td>
<td>30%</td>
</tr>
<tr>
<td>Review process for journals</td>
<td>40%</td>
<td>20%</td>
<td>15%</td>
<td>25%</td>
</tr>
<tr>
<td>Submitting a first UCSF grant</td>
<td>40%</td>
<td>15%</td>
<td>20%</td>
<td>25%</td>
</tr>
<tr>
<td>Life and work balance issues</td>
<td>35%</td>
<td>20%</td>
<td>20%</td>
<td>25%</td>
</tr>
<tr>
<td>Human subjects research</td>
<td>25%</td>
<td>40%</td>
<td>10%</td>
<td>25%</td>
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the program with some modifications. Programmatic changes between the first and second years were aimed at reducing perceived burdens among the mentees and mentors (excessive meetings were eliminated), and mentees were encouraged to rank their choice of mentors to influence the assignment of mentor-mentee pairings.

The mentoring program was presented to prospective mentees and to the mentors as a pilot program. Key to the effort was the recognition that this new program was not designed to replace the ongoing traditional mentoring that is part of the culture at UCSF and GIVI. The CFAR program was designed to enhance existing informal mentoring by providing a structured opportunity for senior and junior investigators, who typically would not interact, to establish personal connections. It was hoped that the nonsupervising mentor would provide an avenue for the mentee to explore issues not easily raised with a direct supervisor. Although the individual 1-on-1 meetings did not occur as often as initially designed, the networking that developed was perceived as satisfying and filled a need for the mentees.

The pilot mentoring program was developed to provide added value to the mentees through mentee-mentor meetings, workshops, and the general orientation to the research enterprise at the CFAR. The program directors worked closely with the mentees and mentors to identify challenges and engage in problem solving with mentees and mentors. The mentees and mentors were paired to maximize the range of experiences for both, to facilitate new collaborative work, and to reduce the potential risk of perceived conflict that might develop between mentees’ direct supervisors and the CFAR mentors. Despite these attempts, 5 mentees left the program after the first year. Two mentees left for reasons not associated with the program: 1 because she recognized that she was not interested in a career focused on HIV research and the other because she successfully competed for a career development award overseas. In fact, both of these cases may represent success of the mentoring program in that it helped a mentee to identify a career path with higher level of personal satisfaction and it helped another mentee to obtain a career award in HIV research at another center. The 3 mentees who chose not to continue in the program because of insufficient time probably failed to obtain value from the pilot program, however.

The addition of 15 new mentees in the second year of the program surprised us. Although the first year of the program was highly rated, we considered that persons eligible to participate in the second year might be disinclined to sign up and participate because of a lack of time or perceived lack of value. The increase in the number of new mentees may reflect that first-year mentees who received the greatest value may have been more likely to inform their peers of the program than were persons who opted to discontinue the program. The option of selecting mentors may also have helped to draw in new mentees. In addition, the second year may have benefited from better outreach or better targeting of persons eligible to participate. Another reason for the increase in the number of mentees in the second year is that mentees were allowed to participate in the selection of their mentors. This greater “buy-in” may have contributed to a greater sense of value to the new mentees. In addition, coinciding with the second year of the program, the CFAR’s new focus on international clinical research may have attracted more persons focused on international research, an area for intense mentoring. Finally, the mentees are geographically dispersed, working at more than 6 major sites in San Francisco. The geographic dispersion is a key issue that contributes to being disconnected from the diverse research enterprise in San Francisco and results in networking obstacles for early career faculty and postdoctoral scholars. The opportunity to establish unique connections with researchers and to overcome the problems associated with geographic dispersion may represent the greatest value of this pilot program and explain why 15 new mentees decided to participate in this project.

It is interesting to note that mentees perceived their own schedules as the limiting factor for meeting with mentors. It is surprising that mentees would fail to prioritize a meeting with a senior faculty member outside the mentee’s area of expertise. This may indicate that the mentees were simply not engaged in the mentoring relationship or that they did not receive any added value to the relationship with a senior nonsupervising faculty member. It was this possibility that led us to change the second year’s mentoring activity so that mentees could participate in the selection of their mentor; hence, giving them an added stake in the program and the resulting mentoring relationship. At the end of the second year, we plan to analyze whether the mentees who received their highest ranked mentors found the greatest value in the mentoring relationship.

It is important to note that all but 1 of the mentors from the first year of the program continued in the second year. Although we did not include them in the evaluation of the pilot project, it was gratifying that virtually all the mentors remained in the program in the second year. The mentors’ sustained commitment suggests that mentoring is relevant and rewarding for the senior faculty. In the second year, we plan to develop and analyze the program from the mentors’ perspective.

Defining the outcomes for successful mentoring is difficult. Such tangible outcomes as publications, peer-reviewed grants, and faculty promotions take years to achieve. Definitive assessment of the effect of any mentoring intervention on career outcome is technically problematic; randomization, even to a usual care program compared with an experimental program, is likely to be poorly accepted. In addition, there are multiple factors that influence the distal outcomes, thus making such impractical. The long incubation period needed to assess mentoring success and the difficulty with assigning specific attribution to mentoring activities may discourage the establishment of mentoring programs. In addition, mentoring is expensive. Not only are there costs associated with program development and maintenance but there are costs associated with the time and effort for the mentors and the mentees. Structured programmatic mentoring is still relatively new, and compensatory funding for mentoring activities is rare. Nevertheless, mentoring is perceived and reported by many successful investigators to be a valuable activity and crucial for academic advancement. The CFAR, a bridging resource to support HIV/AIDS research, represents an ideal mechanism to support an HIV/AIDS-specific mentoring program.
Mentoring is a cornerstone activity among medical scientists throughout their careers. The formal mentoring between a laboratory or clinic director and an early career faculty member or postdoctoral scholar is often the difference between career success and satisfaction or career disruption and dissatisfaction for the junior member. The task of sustaining progress in understanding the AIDS epidemic and HIV disease pathogenesis, and the basic biology of HIV, is soon going to fall to the next generation of scientists. The development and testing of specific mentoring methods and structured mentor program components should contribute to the growth of new investigators and prevent the potentially enormous costs of failed research careers. When the costs of attrition, suboptimal productivity, and problematic interactions are considered, a mentoring program with proven methods may be the most cost-effective intervention to create and sustain the next generation of HIV/AIDS scientists.

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Summary: Maximizing our economic investment in HIV prevention requires balancing the costs of candidate interventions against their effects and selecting the most cost-effective interventions for implementation. However, many HIV prevention intervention trials do not collect cost information, and those that do use a variety of cost data collection methods and analysis techniques. Standardized cost data collection procedures, instrumentation, and analysis techniques are needed to facilitate the task of assessing intervention costs and to ensure comparability across intervention trials. This article describes the basic elements of a standardized cost data collection and analysis protocol and outlines a computer-based approach to implementing this protocol. Ultimately, the development of such a protocol would require contributions and “buy-in” from a diverse range of stakeholders, including HIV prevention researchers, cost-effectiveness analysts, community collaborators, public health decision makers, and funding agencies.

Key Words: cost, cost-effectiveness, HIV prevention, intervention trial

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Nearly 40 million people worldwide are infected with HIV, the virus that causes AIDS.1 The scale of this epidemic and the required response are unprecedented in world history. Because economic resources are limited, decision makers at local, national, and international levels face difficult choices between competing needs for treatment and prevention and choices among alternative programs within the treatment and prevention arenas. This article focuses on HIV prevention interventions, but similar considerations also apply to HIV treatment programs.

HIV prevention decision makers must consider myriad factors when selecting interventions for deployment, including but not limited to the appropriateness and acceptability of candidate interventions for the target community, intervention costs, and potential intervention effects.2 Because HIV prevention budgets are universally constrained, funding a particular intervention imposes an “opportunity cost” in that the economic resources devoted to that intervention are no longer available to fund alternative interventions. Maximizing the investment in HIV prevention requires balancing the costs of candidate interventions against their effects and selecting the most cost-effective interventions for implementation.3

Determining intervention costs is a necessary first step toward assessing overall cost-effectiveness. HIV prevention intervention trials are a potentially important source of cost estimates for “state of the science” HIV prevention approaches. Many HIV prevention intervention trials do not collect cost information, however, and those that do use a variety of cost data collection methods and analysis techniques. These 2 issues likely are related. HIV prevention intervention trials are complex enterprises, and intervention researchers may be reluctant to devote the additional time, energy, and money required to design their own cost data collection methods and develop their own instruments.

If “off the shelf” data collection methods and instruments were available and were packaged together with user-friendly cost data analysis software, more intervention researchers likely would incorporate cost data collection and analyses into their overall study designs. This argues for the need to develop standardized cost data collection procedures, instrumentation, and analysis techniques. The need for standardization is further underscored by the intended use of intervention cost information; namely, to assist HIV prevention decision makers in the difficult task of comparing one intervention with the next. The current lack of standardization creates “apples” and “oranges” that cannot be directly compared.

A similar need for standardization is evident with regard to the often difficult question of quantifying the impact of an HIV prevention intervention, which is the second element (along with costs) needed to assess the cost-effectiveness of an...
intervention. Because of space limitations, the present article focuses exclusively on the cost side of the equation. With or without corresponding effectiveness estimates, cost information can provide valuable guidance to decision makers, whose first question often is “Can we afford it?”

This article describes the basic elements of a standardized cost data collection and analysis protocol and outlines a computer-based approach to implementing this protocol. Ultimately, the development of such a protocol would require contributions and “buy-in” from a diverse range of stakeholders, including HIV prevention researchers, cost-effectiveness analysts, community collaborators, public health decision makers, and funding agencies. It is beyond the restricted scope of the present article to describe potential consensus development procedures or to propose concrete recommendations for the protocol itself. Rather, the present article is exploratory in nature. It is meant to provoke thought, outline the terrain, and suggest possible approaches for developing a standardized cost data protocol for use in HIV prevention intervention trials.

STANDARDIZING HIV PREVENTION INTERVENTION COST DATA COLLECTION AND ANALYSIS

There are 3 main steps involved in assessing the cost of an HIV prevention intervention: (1) identification of specific resource items utilized in the intervention, (2) development of appropriate procedures and instruments for collecting cost information about the items identified in the first step, and (3) combining and summarizing the information from the second step to estimate the costs of intervention-related activities and the overall cost of the intervention. The standardized protocol envisioned here would consist of a series of “best practice” recommendations with respect to each of these 3 steps (see the next section for examples of best practice recommendations).

These recommendations could be promulgated through the usual channels (eg, conference presentations, journal articles, possibly a monograph) to reach the target audience of HIV prevention intervention researchers. Adoption of a standardized protocol would enhance the quality and the comparability of HIV prevention intervention cost analyses. By itself, however, the existence of a standardized protocol is unlikely to increase the number of investigators who integrate cost data collection and analyses into their intervention trials.

Designing a cost study and conducting cost data analyses are complex tasks that require a modicum of specific expertise that may or may not be optimally represented on a particular study team. It takes time and effort to identify the intervention-related costs that should be included in the “cost inventory,” to develop cost data collection procedures and to design the associated forms or other instrumentation, to conduct the analyses themselves, and to compile and format summary reports. The guidance provided by a standardized protocol that included best practice recommendations on cost study design, data collection and instrumentation, cost analysis techniques, and ways to summarize and report study findings would reduce the burden on investigators and, presumably, increase the number of studies that collect intervention cost information.

To reduce the burden on study investigators further, an integrated software package could be developed that would assist the study team with the myriad tasks associated with conducting an economic evaluation. The proposed software package would incorporate expert knowledge related to the conduct of HIV prevention intervention cost studies and would codify elements of the standardized protocol (best practices). It would significantly simplify the process of designing and implementing a cost study, which could help to increase the number of investigators who collect and analyze intervention-related cost data.

HIV prevention intervention strategies range from behavioral approaches, such as mass media campaigns or risk reduction counseling, to mainly biomedical approaches, such as male circumcision or sexually transmitted infection (STI) detection and treatment. To accommodate the diverse range of HIV prevention strategies evaluated in current and future intervention trials, the proposed software package should be modular in design and should guide investigators through the selection of individual modules applicable to their particular study designs. A flow chart–based algorithm in the software program would allow investigators to customize the standardized protocol to their particular intervention applications. Decision points might include, for example, “Will participants be provided with behavioral counseling?” A “yes” answer to this question would trigger the behavioral counseling module of the program, which would solicit further information regarding the number and length of counseling sessions; the number and types of staff who conduct the sessions; where the sessions are conducted and associated facility costs; and materials, supplies, and equipment needed in the counseling sessions. The software would be expected to anticipate and suggest resource costs that might potentially be associated with the behavioral counseling component of the intervention and would “work” with the investigator to ensure that the resultant cost inventory is comprehensive, appropriate for the target intervention, and consistent with the standardized protocol.

Despite the wide diversity of possible HIV prevention approaches, the types of resources utilized in HIV prevention interventions generally can be classified as belonging to one of several broad categories, such as personnel costs, materials and supplies, equipment, and facilities. Refining these categories and compiling a comprehensive list of the items that fall into each category is a necessary first step toward standardizing HIV prevention intervention cost analyses. The development of a standardized list of potential elements to be included in intervention cost inventories would allow development of structured data collection methods, forms, and analysis techniques.

Based on the cost inventory, the software would help the investigator to identify procedures to collect the necessary cost information (eg, using time diaries to record staff time spent in various intervention-related activities) and would provide detailed instructions about the implementation of these procedures. The program would generate the necessary cost data collection forms customized to the specific requirements of the intervention study (eg, time diary forms could be broken down by activity, with different activities listed for staff with
different responsibilities). Forms could be paper based or computer based. Use of computer-based forms would obviate the necessity to enter the cost data at a later time but might be impractical for gathering certain types of cost information or might not feasible in certain settings. In short, the automated protocol would encourage the use of similar methods and instruments for collecting intervention cost information, which, in turn, would enhance cross-intervention comparability.

The final component of the software package would perform basic analyses of the cost data collected in the intervention trial. For example, it would combine information about the time spent by staff in a particular intervention activity (eg, behavioral counseling) with staff compensation information (salary or hourly wage rate plus fringe benefits) to determine the total personnel costs associated with that activity. This information would then be combined with other costs related to the particular activity (eg, materials and supplies, facility costs) to determine the overall cost of the activity. The total cost of the intervention would then be calculated by summing across intervention activities. Total cost by category (eg, personnel costs, equipment costs) across activities also would be calculated. To increase cross-study comparability, the software would generate cost analysis summaries, tables, and figures in standardized formats suitable for publication.

BEST PRACTICE GUIDELINES

The standardized protocol would include best practice recommendations similar to those advanced by the Panel on Cost-Effectiveness in Health and Medicine but tailored to the specific challenges associated with conducting HIV prevention cost studies. Here, we provide initial thoughts on some of the main issues that would need to be addressed by the standardized protocol.

These issues include general questions related to the framing of the cost analysis, such as the study’s perspective and the time frame over which cost data are collected. With regard to the study perspective, the panel recommends that all studies include a “reference case” analysis conducted from the “societal perspective.” This perspective differs from the “provider prospective” in that it includes all costs, regardless of who incurs them, rather than only costs borne by the intervention provider. For example, costs associated with intervention participants’ lost work time, transportation costs, and other expenses related to their participation in the intervention would be included in an analysis conducted from the societal perspective but excluded from a provider perspective analysis. To maximize the usefulness of HIV prevention intervention cost analyses, we recommend that studies collect and report those costs needed to support analyses from both perspectives.

With regard to the time frame of the analysis, in some cases, it may be sufficient to collect a “snapshot” of intervention costs, for example, by collecting costs over a restricted period once the intervention is fully operational. For others, it may be desirable to collect costs over an extended period to capture potential seasonal or other temporal variability. Recommendations would be developed to identify the circumstances under which one approach or the other might be required.

Given the international application of HIV prevention interventions, the generalizability of cost study findings must be carefully considered. Differing wage rates and the costs of other goods and services make it difficult to apply the results found in one country to programs that are designed for another country. This becomes even more complicated when one has to adjust for currency differences. Preliminary recommendations related to these issues include the following. First, intervention personnel should be identified by job title or professional classification (eg, project manager, physician). Titles that are idiosyncratic to the location of the study (eg, civil service level 14) should be avoided. The applicable wage rate for that job category in the local market should be used to calculate personnel costs and should be included in the cost analysis summary so that others who are utilizing the results can convert the results to their settings. Reporting universally understood job titles would allow decision makers to apply the results to their circumstances by using local pay scales.

To make comparisons more viable, it also is important that costs be broken down to basic levels so that they can be easily converted for use in other settings. For example, cost analyses should report not only the total intervention cost but the cost of each main intervention activity (eg, disaggregate the costs of HIV testing from the costs of counseling in a voluntary counseling and testing [VCT] intervention). Further, personnel costs should be reported as “X minutes of nursing time per patient” rather than as “Y dollars of personnel costs per patient,” because these broad categories may not be transferable to other settings.

Similarly, it is important to disaggregate supply costs, including purchased services (eg, laboratory services), so that others can apply local costs when adapting study results to local circumstances. An excellent example of this is the cost of antiretroviral drugs, which varies greatly across settings. Because countries have negotiated different prices with drug companies, an intervention that involves antiretroviral medications may be cost-effective in one country but not in another.

Cross-study comparability requires the use of a common stable currency. Local currency can be used to perform the original calculations but should be converted to a stable currency that is regularly used in international transactions (eg, US dollars, Euros) at the exchange rates that are in place at the end of the study.

Clearly, there are many more issues that need to be addressed in the standardized protocol, including questions related to startup costs, training, and program evaluation. To enhance the likelihood that the standardized protocol is widely adopted in HIV prevention trials, consensus among HIV prevention economists, investigators, and other stakeholders is necessary with respect to the best practice recommendations advanced in the protocol.

A MAJOR CHALLENGE

Perhaps the most significant challenge to the development and implementation of a standardized cost data
collection and analysis protocol for HIV prevention interventions is the potential discrepancy between the intervention costs observed in the context of research trials and the costs of implementing interventions under “real-world” conditions. The main rationale for conducting a cost analysis is to provide public health decision makers with the information they need to prioritize HIV prevention and other health-related intervention efforts. Therefore, the closer the fit between the study intervention and its (eventual) real-world counterpart, the greater is the policy relevance of the cost analysis results. The discrepancy issue is not unique to the question of intervention costs but applies to the effectiveness side of the equation as well, perhaps more so.

With regard to intervention costs, the discrepancy can be minimized by carefully distinguishing between research-related costs and true intervention costs. “Intervention costs” are costs that would be incurred if the intervention were conducted in the real world rather than in a research setting. Only intervention costs should be included in the cost analyses; costs associated with the research objectives of the intervention trial should be excluded. For instance, costs associated with tracking participants for follow-up purposes, data collection and analyses, and assessing the effectiveness of the intervention generally are research related rather than truly intervention related and should not be included in intervention cost analyses.

Transferability of research trial findings to a real-world setting could be enhanced further if, as recommended previously, costs were disaggregated and reported at meaningful levels; for example, minutes of staff time required to perform a particular intervention-related task, together with the staff person’s job classification. This would allow decision makers to substitute relevant local wage rates and other costs for the costs observed in the intervention trial and reported in the cost analysis summary. Importantly, the substitution of real-world costs for the costs obtained in the intervention trial requires the principled development of a model of how the intervention would be implemented in the real world and how this implementation might differ, if at all, from the intervention trial protocol.

SUMMARY AND DISCUSSION

The primary goals of developing a standardized cost data collection and analysis protocol are 3-fold: first, to encourage investigators to collect information about intervention costs; second, to make it simpler for investigators to integrate cost data collection and analyses into their studies; and third, to increase the comparability of cost estimates across intervention studies. Although the development of a standardized protocol is largely independent of its possible implementation in the form of an integrated software package, we believe that success in achieving these 3 objectives would be greatly enhanced if such a computer package were available. Specifically, investigators should be responsive to a user-friendly automated system that incorporates expert knowledge related to the costs of HIV prevention interventions, provides guidance on cost data collection, generates customized forms to facilitate the collection of cost information, and automatically summarizes this information. This would make it easier and less expensive for investigators to integrate cost data collection and analyses into their intervention trial study designs. Acceptance of this system would enhance cross-study comparability through the standardization of cost inventories; cost data collection procedures; and generation of cost analysis summaries, tables, and figures, all in standardized formats.

The development and implementation of a standardized cost data collection and analysis protocol for HIV prevention intervention trials face several significant but surmountable challenges. First, the breadth of possible intervention approaches makes standardization difficult. Standardized cost protocols have been developed for more limited ranges of intervention strategies, however.9,10 The proposed protocol, which would span behavioral, biomedical, and mixed approaches to HIV prevention, is a bit more ambitious than previous standardization efforts but does not differ qualitatively from these efforts.

Second, the software package envisioned here would need to be highly interactive and flexible enough to allow investigators to substitute their own judgment for the program’s “artificial intelligence.” It also would need to be extendable to accommodate the needs of future researchers, advances in the science of HIV prevention, novel intervention strategies, and revisions to the standardized cost analysis protocol. Finally, it would need to be user-friendly and simple to navigate to encourage its widespread adoption by HIV prevention researchers across a range of disciplines.

Third, the development of a standardized cost protocol, and especially the automation of this protocol, would require a substantial financial investment. It also would require the time and effort of a variety of stakeholders and a commitment to the goal of establishing best practice recommendations through a consensus-building process. Additional commitment on the part of study investigators and funding agencies would be needed to ensure the ultimate success of this undertaking. At present, there is little incentive for investigators to incorporate cost studies into their intervention study designs. The standardized protocol would significantly ease the burden on investigators; however, without explicit encouragement from funding agencies, many investigators likely would be reluctant to increase their study budgets to accommodate the additional costs associated with conducting an economic evaluation of proposed interventions.

Once developed, the cost analysis software could be offered under an open-source license to allow and encourage collaboration in maintaining the software and keeping it up to date; for example, by extending it to handle novel types of interventions. A Web site could be developed to support the software and assist in the dissemination of the software program, updates, and information about the standardized protocol. Through such a site, researchers could download software and documentation, share their experiences, and get answers to their questions regarding how best to apply the standardized protocol. Intervention investigators would be encouraged to upload the results of their cost analyses, which then could be integrated into an intervention cost database. These detailed
and standardized data would be invaluable for comparing costs across interventions and conducting meta-analyses of the economic costs of HIV prevention interventions. This Web site would be an important resource not only for intervention researchers but for policy planners interested in projecting the costs of future HIV prevention programs.

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The Impact of Mental Health and Substance Abuse Factors on HIV Prevention and Treatment

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Summary: The convergence of HIV, substance abuse (SA), and mental illness (MI) represents a distinctive challenge to health care providers, policy makers, and researchers. Previous research with the mentally ill and substance-abusing populations has demonstrated high rates of psychiatric and general medical comorbidity. Additionally, persons living with HIV/AIDS have dramatically elevated rates of MI and other physical comorbidities. This pattern of co-occurring conditions has been described as a syndemic. Syndemic health problems occur when linked health problems involving 2 or more afflictions interact synergistically and contribute to the excess burden of disease in a population. Evidence for syndemics arises when health-related problems cluster by person, place, or time. This article describes a research agenda for beginning to understand the complex relations among MI, SA, and HIV and outlines a research agenda for the Social and Behavioral Science Research Network in these areas.

Key Words: addiction, depression, health services, mental illness, substance abuse

HIV/AIDS, MENTAL HEALTH, AND SUBSTANCE ABUSE: STATE OF AFFAIRS

When asked to comment on the system of care for patients whose HIV/AIDS is complicated by mental illness (MI) or substance abuse (SA), it is tempting to recall the reply attributed to Gandhi when asked to comment on Western Civilization. He said he thought it would be a good idea. Certainly, we believe a system of care for these patients with HIV, MI, and SA would be a good idea and should be given a try. We are far from having one of the literature on persons with HIV, MI, or SA. We lack the space, and other reviews are available on serious mental illness (SMI) and HIV, on SMI and SA, and on all 3. Instead, this report continues work commenced at the meeting of the Social and Behavioral Science Research Network (SBSRN) of the Centers for AIDS Research (CFARs) intended to maximize the yield of behavioral and social science research through efforts to improve integration with basic and clinical sciences, share new information, and develop cross-site collaborations. Accordingly, we focus on unmet needs, institutional barriers or gaps in knowledge that interfere with meeting those needs, and strategies for breaching those barriers or filling those gaps. We call attention to high payoff areas where significantly improved clinical care can be produced by definable investments in research or system change. We also highlight topics where the evidence does not accord with currently prevailing assumptions, because old knowledge has been made obsolete by changes in the course over the epidemic. Simplified somewhat, 3 overlapping lines of development can be seen. First, early work

RESEARCH ON HIV AND PSYCHIATRIC AND SUBSTANCE USE DISORDERS

Research related to psychiatric and SA problems among people living with HIV/AIDS (PLWHA) has expanded in scope over the course of the epidemic. Simplified somewhat, 3 overlapping lines of development can be seen. First, early work
by consultation services tended to focus on psychiatric symptoms as complicating comorbidities of HIV/AIDS; later attention expanded to the possible role of psychiatric conditions in increasing the likelihood a person might become infected or put others at risk through risk behavior or, more recently, through the impact of poor antiretroviral (ARV) adherence on infectivity. Second, early attention tended to focus on less severe disorders, such as depression or anxiety; later attention expanded to include concern with sexual risks among injection drug users (IDUs) and non-IDUs. Throughout, there has been an increasing recognition of multiple comorbidities of MI, SA, and HIV/AIDS. In what follows, we cover topics related to these areas and consider some special issues raised by HIV among youth.

**Depression and Anxiety**

Many studies have found elevated rates of depression and anxiety in PLWHA. For example, the HIV Cost and Services Utilization Study (HCSUS) used a national probability sample of PLWHA in medical care and found that almost half (48%) of the sample reported significant recent symptoms of depression, anxiety, or panic, whereas nearly 40% reported illicit drug use (other than marijuana) and 12% screened positive for drug dependence. Rates of diagnosable disorders were elevated as well: 36% screened positive for major depression, 16% for generalized anxiety disorder, and 11% for panic attack. A full 61% used mental health or SA services in the prior 6 months, but evidence from a subset of patients in the HCSUS suggests depression may be routinely under-diagnosed among patients under care for HIV.

Depression and anxiety can have important impacts on the health and behavior of PLWHA. A number of studies have documented a relation between depression and increased mortality in PLWHA. Dozens of studies have examined the relation between depression and ARV adherence, with most reporting a significant negative relation. Anxiety symptoms are less frequently assessed but have also been related to poor ARV adherence. Thus, poor adherence with ARV and other medications is a plausible pathway through which depression and anxiety can negatively affect the health of PLWHA.

Although it seems plausible that negative affective states, such as depressive symptoms, anxiety, and anger, also might be linked to sexual risk behavior, a 2001 meta-analysis of 34 studies found insufficient evidence to support a relation. Developing research suggests more complex patterns of causation in subgroups, however. Longitudinal studies have reported that depressive symptoms predict sexual risk in some subgroups, such as African-American adolescents and IDUs. Also, in studies linking childhood sexual abuse to sexual risk behaviors, various negative affect components may mediate different aspects of the linkage or make an additive contribution to sexual risk (along with other factors). Increasingly, there is evidence of high rates of exposure to trauma, including but not limited to sexual abuse, among men and women with HIV/AIDS and elevated rates of posttraumatic stress disorder.

Given the elevated rates of mood and anxiety disorders among PLWHA, and evidence for their negative impact on medical adherence and risk behaviors, the SBSRN collaboration could contribute in at least 2 areas. First, to counter underdiagnosis of depression, screening must be made a high priority for already busy clinicians, and it must be closely linked to adequate depression care. Multisite multisector initiatives can lay a foundation for improved performance. Second, screening/linkage studies could be integrated with treatment trials that can help to target and tailor care strategies. Although it is natural to anticipate that successful treatment of depression would result in improved adherence or less risk behavior, compelling evidence for this inference does not yet exist. The SBSRN could provide the scaffolding needed for adequately powered controlled trials to address this gap. Symptoms of depression/anxiety may influence behavior through a variety of mechanisms, and interventions may need to target symptoms and behaviors. Combining treatment of psychiatric symptoms with health behavior change interventions has shown promise and should be explored.

**Severe Mental Illness**

The prospect that HIV might spread to groups defined by SMI was largely ignored until seroprevalence reports from institutional settings in US disease epicenters began to be seen in the 1980s. Rates ranged from 4% to 23%. Studies using administrative data found lower but still elevated rates in population-based studies and community-dwelling populations and overrepresentation of SMI among those with HIV. Indirect evidence also came from the risk profiles of people with SMI. Despite progress in this area, answers to some basic epidemiologic questions are still needed. A new level of epidemiologic sophistication requires that we consider that we likely face not a single nation-wide epidemic but multiple epidemics with distinctive dynamic properties and trajectories. Although high rates of anxiety and mood disorder comorbidity have been found in nonmetropolitan settings, scattered reports indicate HIV may be less common among people with SMI living outside cities. To date, most of what we know about SMI/HIV is limited to the cities of the East Coast or West Coast of the United States, with many of them being disease epicenters. Finally, existing studies are snapshots at moments in time that can help to estimate point prevalence, but they can say nothing about trends in incidence or prevalence. We need to know how these rates vary across time, locale, and setting.

Recent data from a treated Veterans Administration (VA) population suggests that once proper controls are used for the influence of comorbid SA, rates of HIV are lower for patients with schizophrenia than for others rather than higher. Although this pattern may not generalize to SMI populations outside the VA system, it underlines the potential role of SA in viral transmission. Specifically, what is the intersection of the spread of HIV among people with SMI with local and regional infection patterns among IDUs, their sex partners, and other substance-abusing populations? What are the social network overlaps and points of contact between the SMI and IDU populations, and how do variations in overlap affect rates of infection? When IDU/HIV incident infections drop as a result
of regional drug markets, syringe availability, or behavior change, how (if at all) are incident infections affected among subgroups with SMI?

Assessing and improving SA and HIV identification in psychiatric settings can clarify patterns of infection, improve care, and promote prevention. Although far from perfect, assessment and identification of SA in psychiatric settings is now standard practice. Efforts to promote HIV testing in some psychiatric settings have had an impact, but inpatient psychiatric settings pose particular challenges. Staff members may be reluctant to test on admission, when patients may be acutely ill, or near discharge, when distress may cause delays. Emergency department (ED) testing has been used in general medical populations, and, with appropriate procedures and adaptation, routine voluntary testing could hold promise with psychiatric patients in the ED who are able to give informed consent.

The SBSRN collaborative can provide the institutional structure needed to make headway in this domain. Working with institutional review boards (IRBs), procedures similar to those developed by Turner et al might be adapted. They intercepted waste blood from inpatient admissions for anonymous testing. Rates from such testing could provide epidemiologic estimates across geographic settings. Additionally, these rates could be compared with aggregate rates of identified HIV based on unit records, allowing institutions to assess the number of missed cases of infection and to adjust clinical strategies to minimize them. Just which strategies can bring down rates of missed HIV cases in a given institution may best be developed in the context of the broader service environment. Hospitals could be required (or given incentives) to experiment with protocols to meet performance standards.

Research on HIV/AIDS care for patients with SMI has yielded some surprises. Early studies gave reason for concern that ARV initiation might be delayed for IDUs or patients with psychiatric diagnoses. Evidence for delays in ARV medications based on psychiatric status suggests that they may be limited in scope, however, especially after psychiatric treatment is initiated. Neither recent data on physician decisions regarding case vignettes nor filled prescriptions from pre-highly active antiretroviral therapy (HAART) and HAART eras provide evidence of reluctance to prescribe to patients with schizophrenia.

Substance Abuse

Much has been learned about the impact of SA on HIV risk and treatment and how best to limit it. The common sense assumption that a given individual is more likely to take risks when drinking or using drugs has required more than simple correlations to demonstrate. Some people may be drawn to substance use and to risk taking, without the first actually influencing the second. New work on men who have sex with men uses designs that allow for the event level analyses needed to suggest that a person’s substance use contributes to his or her risk behavior, however. Research has also informed our picture of widely observed connections; for example, that current drug use undermines viral suppression among IDUs on HAART. One way it does so is by harming the supportive functioning of their network ties.

Intervention work is based on a straightforward, and indeed obvious, foundation. Because when drug use leads to risky behavior, whether through needle sharing or unprotected sex with high-risk partners, the probability of HIV exposure increases, interventions should target drug use and risk behavior. Reductions in HIV transmission have, in fact, been achieved by targeting drug use with drug treatment (particularly methadone treatment) and by targeting needle-based risk with syringe exchange programs.

As discussed previously, the relations between negative affect and risk behavior suggest other avenues for intervention, such as combined treatments that target mood states and risk behaviors.

Given these successes, the challenge lies in connecting efficacious treatments to those who need them. One study found the chief entry points for SA services to be primary care and criminal justice settings. Waiting lists for specialty care are often long. SA clinic location exerts an influence on access, utilization, and acceptability, as do broadly defined ancillary medical and social services.

Children and Youth

Claude Ann Mells recently challenged existing research agendas on adherence with a talk entitled “Where are the Children?” The question could be made more general by noting that children, particularly adolescents, face many of the same SA and MI challenges discussed so far, plus many that are distinctive yet seldom researched (eg, the impact on children of parental SA, MI, and HIV). Without empiric development of the ecologically sensitive models of care needed for this group, combined with attention to training and financing issues, infected youth are at risk of becoming “orphaned” by a well-meaning but fragmented series of medical and social welfare agencies. CFAR initiatives with associated HIV pediatric clinics and other agencies can provide the documentation needed to build support for more need-sensitive reimbursement and can create a platform for research on the implementation and empiric validation of integrated care models for HIV-positive youth with mental health and SA disorders.

High rates of multiple risk behaviors are found in youth in alternative care settings. Compared with peers, those in the juvenile justice system more frequently have SA and mental health disorders, coupled with sexual risk behaviors. Large-scale reorientation from punitive and social control frameworks toward therapeutic and preventive approaches would be difficult, but smaller changes might be practical, such as use of low-cost brief strategies that could be introduced into various settings (eg, interactive computer-based interventions).

Voluntary counseling and testing (VCT) for at-risk adolescents presents another opportunity for CFARs to contribute. Medical providers may meet difficulties in targeting at-risk community youth, particularly those alienated by general mistrust of the medical system felt by marginalized and minority youth. Community-based organizations (CBOs) are an underutilized but potentially highly effective resource for at-risk youth and may provide partnerships for CFAR outreach programs. CFARs can provide support for VCT with medical information, speedy access to medical care for
HIV-infected youth, and resources and skills needed to document program efficacy.

CONCLUSIONS

Efforts to provide services to people with HIV/SA/MI, or even to study them, must do so in an environment complicated by a legacy of service fragmentation resulting from institutions designed to treat psychiatric illness, SA, or HIV but not real-world combinations of all 3. Nevertheless, experience shows that, despite the difficulties, patient engagement with the service system can produce encouraging outcomes. Seropositive drug users who use medical care have lower risk behaviors than their counterparts who do not.47 In a clinic with integrated care, HAART-naive psychiatric patients were 50% more likely to initiate HAART and twice as likely to continue it for 6 months compared with their counterparts without psychiatric illness.48 Research that finds delays in HAART initiation for patients with untreated depression reported no delays for patients with treated depression.49 ARV adherence by patients with schizophrenia correlates with mental health appointments.50 Among patients with SMI from publicly funded mental health clinics in Los Angeles, most were on HAART and their CD4 cell counts and viral load levels were closely followed.51 Most were insured, received case management, and reported high levels of satisfaction with HIV and mental health care.52 Systemic integration of care for doubly and triply diagnosed patients has long been advocated but seems unlikely to be achieved soon. SA-, MI-, and HIV-related organizations are accountable to different licensing and regulatory bodies, draw from different budgets, commonly develop quite different professional cultures, and seek different sources of legitimacy. Full integration can threaten the autonomy of specialty services, and the strong incentives to overcome obstacles are rare. Instead, the existing regulatory bodies, draw from different budgets, commonly develop quite different professional cultures, and seek different sources of legitimacy. Full integration can threaten the autonomy of specialty services, and the strong incentives to overcome obstacles are rare. Instead, the existing fragmentation is increasingly overlaid with multiple local strategies to counteract it, such as case management, service integration or colocation, and creation of specialized treatment settings. We know little about when and where these develop, what factors predict success and for whom, and what processes may be essential to achievement of effects.

Cites and states do not differ only in how they fund and organize care delivery and the strategies they use to overcome fragmentation. Disease dynamics are sure to be affected by policies in neighboring domains, such as housing and criminal justice, for example. Residential segregation of people with SMI in high-prevalence areas, exposure of people with MI and SA to HIV in jails and prisons, and the impact on IDUs’ risk of periodic police crackdowns all need to be considered in devising effective strategies. Comparisons across multiple sites and settings are needed to understand how the identified mechanisms may operate in various contexts, and the SBSRN can provide an organizational structure well suited to pursue these issues.

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Examining Racial Disparities in HIV
Lessons From Sexually Transmitted Infections Research

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Summary: Racial differences in the prevalence and incidence of HIV infection and AIDS diagnoses in the United States are striking. These differences have been recognized for nearly 20 years, yet they are not well investigated. In this article, we examine 15 factors identified in the sexually transmitted infection (STI) literature to explain the presence of racial/ethnic disparities in STIs. We review findings from these studies and offer suggestions for future research, with the goal of further understanding and reducing disparities in HIV. In general, the STI literature shows that an evaluation of individual behavior is necessary but insufficient on its own to account for racial/ethnic disparities in STIs. Population parameters should be included within models that traditionally include individual-level factors. The 15 factors can be categorized into 3 broad overarching themes: behavioral, prevention participation, and biologic explanations of differentials in STI transmission and infection. Future research that focuses on only 1 of the 15 factors discussed in this review, to the exclusion of others, is likely to yield poor outcomes. Conversely, an emphasis on the interactions of several factors is more likely to produce effective public health interventions and reductions in HIV transmission.

Key Words: health disparities, HIV, race

In the United States, racial differences in the prevalence and incidence of HIV infection and AIDS diagnoses are dramatic. In the most recent reports from the Centers for Disease Control and Prevention (CDC), African-American (AA) adults and adolescents were 9 times more likely to be diagnosed with AIDS than whites and almost 3 times more likely than Hispanics. The rate of AIDS diagnoses for AA men was 7 times the rate for white men, and AA women were diagnosed with AIDS at a rate 21 times that of white women.1 These differences are large, have been recognized for nearly 20 years, and are as yet not well investigated.

The cause of racial disparity is inadequately understood but is widely recognized as a multifaceted phenomenon that is long standing and prevalent, with a complexity that has made it resistant to intervention.2 Understanding the causal factors underlying the dramatic disparities in HIV infections and AIDS diagnoses that exist between AA, whites, and Latinos is an urgent priority with significant implications for the conceptualization and implementation of prevention services.

Few studies have been designed specifically to test hypotheses that might explain the racial disparities in HIV incidence and prevalence. Most past research has examined selected risk factors in isolation from other factors known to increase the likelihood of viral exposure and susceptibility to infection. In this article, we examine 15 factors identified in the sexually transmitted infection (STI) literature to explain the presence of racial/ethnic disparities in STIs. We review findings from these studies and offer suggestions for future research, with the goal of further understanding and reducing disparities in HIV.

Socioeconomic Factors

The social epidemiology of racial/ethnic disparities considers socioeconomic differentials across racial/ethnic groups that get reflected in a wide range of health outcomes (eg, STIs). To examine the ways in which socioeconomic differentials across racial/ethnic groups affect STIs and HIV, it is necessary to work through not only the sexual and health behaviors of individuals but through the behaviors of the providers administering care to those who are affected.

Sexual and general health behaviors of individuals are influenced by individuals’ resources and beliefs. In addition, personal management of health is affected by physical, cultural, and economic aspects of individuals’ communities. For example, individuals in socioeconomically disadvantaged neighborhoods are more likely to be overweight and engage in less healthy behaviors, such as smoking and eating high-fat diets. These differences persist even after controlling for race and ethnicity.3,6

Racial stereotypes, such as poor patient adherence and poor social support, held by physicians may contribute to differential treatment by providers.7 In terms of sexual health, racial/ethnic minorities are more likely than whites to use public sources for health care seeking. Thus, minority populations often lack the benefits that result from an ongoing

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relationship with a specific provider. Less privacy is a resulting feature borne out by evidence of higher reporting of STI diagnoses to state and local health departments by public sources of care (eg, STI clinics or family planning clinics) than by private providers. This reporting bias may be partly responsible for why STI surveillance data show higher rates of STIs among minority racial/ethnic groups than among whites.4

Racial differences in health status decrease substantially when racial/ethnic groups are compared at similar levels of socioeconomic status (SES), but health is affected not only by current SES but by exposure to social and economic adversity over the life course. Personal experience of discrimination and institutional racism is an added pathogenic factor that can affect the health of minority group members in multiple ways.5,10

DEMOGRAPHIC FACTORS

Differences in demographic characteristics of racial/ethnic groups in terms of age and gender composition may result in racial/ethnic disparities in health outcomes, especially STIs. AAs tend to be younger than whites in the United States, and Hispanics tend to be even younger than AAs. Populations characterized by young age pyramids have higher STIs than populations characterized by old age pyramids. Not only do differences in age composition result in higher STIs in certain groups, but the ratio of men to women (ie, gender ratio) varies across groups, which may affect STI rates in different subgroups. The scarcity of men in subpopulations is associated strongly with STIs. The impact of the gender ratio happens not only through the intermediary variable of the number of partners (ie, scarcity of men increases the number of partners) but through influencing the sex network characteristics in subpopulations.11–13 Gender ratios are affected by natural demographic causes, such as birth and death rates, and also by political factors. AAs, particularly AA men, have higher death rates at young and middle ages than whites. Political factors, such as incarceration rates, affect gender ratios at any point in time. Incarcerations are highest among AA and young adult men; these are ages with a high prevalence of STIs, including HIV.

POLITICAL FACTORS

Political factors have been examined as means of creating and reinforcing disparities. Placement within a jail or prison constitutes yet another risk factor for HIV transmission, because one quarter of all HIV-infected Americans pass through the correctional system annually14 and the inmate population is at least 5 times as likely to be infected with HIV than is the general population.15 At the same time, 47% of the prison population is AA, even though they comprise only 13% of the overall US population.16–18 In fact, a male AA has a >1 in 4 chance of going to prison compared with a 1 in 23 chance for a male white,19 with almost 60% of AA high-school dropouts predicted to be incarcerated at some point in their life20 and 28% incarcerated at any single point in time.21

Jail crowding, and its accompanying high-risk behavior, increases transmission of infectious diseases, resulting in the finding that HIV-infected inmates constitute from 12% to 18% of all HIV-infected individuals within the United States.22 This may be attributable to the high concentration of people with infectious diseases, which amplifies the effects of risky sex and drug use behaviors because of the lack of access to condoms and sterile injection equipment.23–27 It may also be attributable to the endurance of core network relationships created and sustained within the prison environment.

The impact of incarceration on STI transmission extends beyond the jail. As noted previously, high rates of incarceration for AA men cause a skewed ratio of available men to women in the community. Fewer AA men in the community results in multiple simultaneous sexual partnerships, which further serves to maintain the closed networks that propagate infection so efficiently.28 In addition, on release, individuals may bring any added exposure to STIs or HIV during prison with them as they re-enter the community.29–31

SOCIAL NETWORKS

Studies of sexual networks have made several contributions to explaining health disparities. Social networks play a critical role in understanding an individual’s risk of STI and HIV infection. Recent theoretic and empiric STI and HIV research has shifted from focusing on individual-level attributes and behaviors to describe the risk of STI and HIV acquisition to using population-level parameters to predict STI and HIV transmission and its prevention.1,2,23 This paradigm shift includes an emphasis on the interdependence of health outcomes between persons (ie, one cannot acquire an STI or HIV unless one’s sex partner is infected with that sexually transmitted pathogen); infected individuals and their role in STI or HIV spread (eg, “source” and “spread” cases); characteristics of sex partners and partner selection processes; and collection of data that include not only infected cases but uninfected cases.

Population-level parameters shown to be important determinants of STI rates include the extent to which members of a population have sexual connections with members of other populations (assortative/dissortative mixing); composition and mixing patterns within a population;23,24 the extent to which members of a population have concurrent, or overlapping, partnerships; and the absolute and relative (to the size of the general population) sizes of the “core” group, small proportions of individuals who are often infected with STIs and HIV and have large numbers of sex contacts;22,37–41 the average level of risk of those who constitute the core group; the extent to which members of the core group have sex contacts outside of the core group; and the amount of sexual interaction between subpopulations (“bridges”), especially between core groups of different subpopulations and between core group members of a single population and members of the general population.28,35,42–44

It has also been observed that mixing patterns between individuals in different sex activity classes (ie, different rates of partner change) vary according to race/ethnicity.45 In the United States, AAs with low-risk sex behavior are more likely than whites to have partners with high-risk sex behavior. Laumann and Youm28 describe sexual network patterns of a nationally representative sample to explain differentials in STI rates across racial/ethnic groups in the United States. They...
categorize the population into 3 groups: a core population (lots of partners, sex, and mixing), an intermediary population, and a peripheral population (couples practicing lifetime monogamy). Their network data analysis results show that sex mixing between core and periphery subpopulations is much higher among AAs than whites. Higher rates of sexual contact between “core” AAs and “peripheral” AAs facilitates spread of infection through the AA population. This finding may automatically be a result of being a minority (sheer numbers); however, there is no definitive answer in the empirical literature. Similarly, in a study of heterosexual STI clinic attendees in Seattle, Aral et al. find dissortative mixing between low-prevalence and high-prevalence subpopulations associated with gonorrhea and assortative mixing within low-prevalence subpopulations associated with chlamydia. Dissortative mixing was highest among AA men and their low-prevalence white female partners.

In the United States, AAs report much higher concurrency rates than whites. This has been shown in different regions, locales, and national data. Age mixing patterns vary only slightly across racial/ethnic groups; thus, they likely do not contribute much to health disparities.

SEXUALLY TRANSMITTED INFECTION RATES

A number of studies have shown the presence of an interrelation between HIV infection and other STIs. Studies that examine the role of STIs in sexual transmission of HIV find that ulcerative (eg, syphilis, chancroid) and nonulcerative (eg, gonorrhea, chlamydia, trichomoniasis) STIs increase HIV risk from 2 to 5 times. Although less evidence exists, the relation also works in the opposite direction. HIV may affect STIs by increasing or lengthening the infectiousness period of an individual. Thus, an “epidemiologic synergy” exists: whereas HIV prolongs the infectiousness period of STIs, STIs that have facilitative effects on HIV transmission have more time to increase spread of HIV. Therefore, this 2-way relation may lead to many serious and costly sequelae in society.

Cross-national comparisons of HIV rates highlight the STI cofactor effect. For example, Oster et al. shows that differences in HIV prevalence rates between the United States and sub-Saharan Africa can be explained by differences in HIV transmission rates. The differences in HIV transmission rates are likely attributable to differences in untreated STIs, because treatment levels for STIs are much lower in sub-Saharan Africa than in the United States and survey data show that sex behaviors do not differ much between the United States and sub-Saharan Africa.

To quantify the effect of STIs on HIV transmission, Chesson and Pinkerton applied a mathematical model to estimate the number of STI-attributable HIV infections in 1996. In total, they estimated that 5052 new cases of HIV were attributable to 4 STIs: chlamydia (3249 cases), syphilis (1002 cases), gonorrhea (430 cases), and genital herpes (371 cases). These STI-attributable HIV infections were estimated to total approximately $985 million dollars (in 1996 dollars) in direct HIV treatment costs.

STIs are disproportionately experienced by racial and ethnic minorities, as evidenced by ecologic, geographic, cross-sectional, and longitudinal studies of surveillance reports, STI clinic attendees, and other subgroups, which show higher rates of bacterial STIs among minority populations than among whites. This is true across sexually transmitted pathogens and over time. Genital herpes (herpes simplex virus-2 [HSV-2]), gonorrhea, chlamydia, syphilis, and other STIs, such as bacterial vaginosis and chancroid, are much higher in minority populations than in majority populations. For example, in 2005, rates of chlamydia and gonorrhea were substantially higher among AAs and Hispanics than among whites. This was true even across genders. The chlamydia rate per 100,000 population was 1729 for female AAs and 733.2 for female Hispanics compared with 237.2 for female whites, and it was 717.8 for male AAs and 201.4 for male Hispanics compared with 63.6 for male whites. The gonorrhea rate per 100,000 population was 590.4 for female AAs and 82.7 for female Hispanics compared with 42.5 for female whites, and it was 666 for male AAs and 67.5 for male Hispanics compared with 27.7 for male whites.

HOST BIOLOGIES

Differences in host biologies are another factor that might explain the presence of racial/ethnic disparities in STIs and HIV. On almost every health index, AAs suffer in relation to white Americans. They die younger (69 vs. 75 years for whites), they have a 30% higher rate of mortality, and AA infants are more than twice as likely as white infants to die within the first year of life. Research into the biologic expression of life experiences, including discrimination, racism, and inequality, can be useful for understanding health disparities; however, much caution should be exercised around genetic arguments that attempt to account for ethnic and racial disparities in HIV prevalence and incidence. Some people interpret racial differences in disease as being linked to genes, whereas others view racial differences as a consequence of the classification of individuals into races, or “racing,” and racism. Attempts to classify human variability into genetically defined continental groups or populations, to assign individuals to such fixed categories, and to use these categories in genetic research of disease causation can reify human difference and racialize health disparities. All humans share 99.9% of our DNA, and there is much greater within-group variation among people classified in any particular “race” than there is between “racial” groups. Race is a social concept rather than a scientific one, and race and ethnicity in the United States are risk markers that are associated with other more fundamental determinants of health status, such as poverty, access to quality health care, and living in communities with high prevalence of infectious diseases (eg, STIs).

ACCESS TO HEALTH CARE AND QUALITY OF HEALTH CARE

Racial ethnic minorities make up 33% of the nonelderly population, yet they comprise 52% of the uninsured, who are less likely to have a regular doctor or receive routine care and more likely to be hospitalized for routine preventable conditions. AAs often live in underserved neighborhoods.
without adequate access to health care services: 22% of AAs and 28% of Latinos report having little or no choice in where to seek health care compared with 15% of whites.65 These neighborhoods are often characterized by insufficient transportation, few local providers, and prohibitively priced services.67 For example, AAs are less likely to be in substance abuse treatment than whites; this may be because, when compared with whites, AAs are more likely to have no access to treatment for substance abuse or for mental health care (25.4% vs. 12.5%).68 Disparities in access to quality health care services have implications for STI and HIV transmission. The extent to which STIs (eg, HSV-2, HIV) are suppressed in the population is expected to contribute to the extent of transmission. This factor also influences other STIs and the prevalence of STIs and HIV in partner pools.

When health care is obtained, the quality of care provided is often not as desirable as that found in white neighborhoods and AAs are less likely to receive even routine medical procedures than their white counterparts.7,69 For example, even for those with insurance coverage, AAs received lower quality care for pneumonia65 and those with managed care also received fewer services than their white peers.70 This may be because the providers who are available within AA neighborhoods are less well clinically trained, have access to fewer clinical resources, and self-report having difficulty in providing quality care.45

This lower quality of care translates into lower satisfaction with the patient-provider dyad, as expressed by reports of poor treatment at doctors’ offices and general poor communication.71,72 Research on patient-provider racial discordance may help to explain some of these findings, because racial/ethnic concordance may influence diagnostic decisions73 and patient satisfaction with care and continuation of care.74 The behavioral manifestation of low patient satisfaction is the early termination of care and more missed appointments.75

It is tempting to explain disparities in service utilization with differences in income or medical coverage; however, the data are not that orderly or predictable. Uninsured blacks and Latinos are poorer than uninsured whites; three quarters of uninsured blacks and Latinos have incomes below 200% of the federal poverty level compared with 56% of uninsured whites.66 Other studies have identified racial disparities in access and service utilization of preventive care attributable to SES; insurance coverage does not confer blanket access if the individual is unable to pay copayments and deductibles.76,77 Comparisons of service utilization and health outcomes within income groups have found reductions in observed racial disparities. For example, Shapiro et al78 found that higher HIV death rates were more likely related to lower income, less education, and less accumulated wealth rather than to race. In a study of preventive care services, racial disparities were not observed for the number of services received, number of well-care visits, or number of chronic illnesses.79 The authors postulate that the absence of disparity may be related to the nature of the care offered; that is, preventive care is usually the type of care that engenders a longer term relationship between the provider and patient, thus avoiding issues of trust and discrimination that may occur for acute care needs or for conditions that are more serious when unfamiliar providers are involved.

An underlying theme linking many of the inconsistent service utilization findings is a fundamental distrust of the medical system, provider/patient cultural differences, and perceived institutional racism.10,80–86 This is clearly borne out by a recent study of New York City inmates who were educated about HIV and risk reduction. Even after completion of the training program, nearly half of the inmates continued to believe that HIV was a manmade virus and two thirds believed in a government conspiracy.87

COUPLE DYNAMICS

Dynamics within a relationship are an important determinant for STI and HIV acquisition and transmission. Gender power inequality, often present in relationships between young women and older male partners, affects practice of safer sex.88–90 This notion may be different in minority subpopulations compared with majority populations.91

INDIVIDUAL BEHAVIOR

Many observers of the differential prevalence and incidence of STIs, HIV infections, and AIDS diagnoses in the United States have concluded that these disparities exist because prevention messages, supplies, and/or interventions do not effectively reach those at greatest risk of infection. In essence, such interpretations would suggest that blacks and Hispanics are more risky than whites. There is much empiric data to suggest that this is not true, however.92,93 In fact, when risk behaviors are examined by race, whites have repeatedly been found to report much higher rates of risk behaviors. For example, in a representative sample of young adults in the United States, Hallfors et al92 classified black and white survey respondents into 15 sex and alcohol, tobacco, and other drug (ATOD) use patterns and found that more than one third (37.6%) of blacks were in the most normative behavior pattern of “few partners and low ATOD use.” In this study, whites were more likely to be infected with HIV or other STIs if they engaged in high-risk drug and sex behaviors, but young black adults had a higher STI prevalence even when they engaged in normative behaviors.

White American women report having the largest number of sex partners, especially when examining distributions (ie, tails) rather than means and medians.93,94 In terms of rates of pelvic inflammatory disease (PID), it has been shown that the same incremental difference in sex behavior (eg, an increase in partners from 1 to 2) across racial/ethnic groups is associated with an incremental difference in STI risk95 that differs across groups. These behavioral data suggest that whites should have higher STI rates. In fact, we observe the opposite: whites have lower STI rates than minority populations. The inconsistency between risky sex behavior and STI rates by race/ethnicity suggests that it is not just behavior that matters.

Among men who have sex with men (MSM) surveyed in 7 US cities, sex and drug risk behaviors were reported most frequently by whites and least frequently by blacks; however, HIV prevalence was 16% for black and multiethnic black participants, 6.9% among Latinos, and 3.3% among whites.96

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CIRCUMCISION

Male circumcision is being investigated as a protective intervention for STIs and HIV, because the area underneath the foreskin provides a warm moist location where pathogens might replicate. Langerhans' cells concentrated in the prepuce of the uncircumcised penis could be a target for HIV; therefore, removal or reduction of the foreskin would decrease the number of immunologic cells through which HIV could potentially enter the body. It has also been suggested that the foreskin is prone to tearing during sexual intercourse, which would provide additional entry and exit points through which HIV transmission could occur.

In a national probability sample of men aged 18 to 59 years in 1992, whites (81%) were more likely to be circumcised than blacks (65%) or Hispanics (54%). Lack of circumcision has been linked to various STIs. For example, Diekstra et al suggest that lack of circumcision may be related to increased risk for gonorrhea and syphilis but not for chlamydia, and Weiss et al suggest that circumcision is associated with lower risk for ulcerative STIs, particularly syphilis and chancroid, but not for HSV-2. Despite inconsistent findings regarding the role of male circumcision in vulnerability to particular STIs, circumcision is a major current topic in the literature on male circumcision in vulnerability to particular STIs. 

circumcision is a major current topic in the literature on HIV/AIDS prevention. In Africa, cross-country differences in circumcision rates have been cited to explain cross-country differentials in HIV rates. HIV transmission may be made more likely in uncircumcised men through genital ulcers as an entry/exit point or through microulcerations occurring after trauma during sex, which may be caused or exacerbated by poor penile hygiene. Therefore, some researchers are investigating the role of penile hygiene in HIV transmission and the potential effect that penile washing could have on HIV transmission could occur.

Recent randomized controlled trials have shown reductions in HIV acquisition among men who have been medically circumcised. More information is needed about the potential risks and benefits of male circumcision, however, including its subsequent effect on HIV transmission among women, and a number of ethical, cultural, and practical issues must be addressed before rolling out this procedure as an HIV prevention intervention.

AGE OF SEXUAL DEBUT

Blacks initiate sexual intercourse at younger ages than do whites, and early sexual debut is associated with current STI and a history of STI. The association diminishes with age among young adults, however. Therefore, difference in age at sexual debut likely does not account for much of the observed disparities.

SEX WORK

Differences in prevalence of sex work in interaction with socioeconomic differentials have been considered as a factor to explain racial/ethnic disparities in STIs. The thesis is that a larger percentage of minority subpopulations engage in sex work than in the majority population. Differentials are disappearing in terms of prevalence of sex work, however. These differentials may have been relevant in the past, but essentially no differences are expected in the near future. Therefore, differentials in sex work likely do not explain racial/ethnic disparities in STIs.

OTHER FACTORS

Several other related factors have been identified in the STI literature to explain the existence of racial/ethnic disparities in STIs, including HIV. One factor is exposure to a particular pathogen. Exposure to STIs and HIV is determined by prevalence in partner pools, and prevalence may vary by race/ethnicity. Prevalence is determined by social networks, individual health behaviors, quality and access to health care, and provider behavior, especially when dealing with STIs and now HIV. Another factor concerns the characteristics of particular pathogens. Different subpopulations are marked by different subtypes or strains of STI pathogens. Few studies have dealt with this fine level of differentiation. The evidence is not clear, but future studies need to consider this distinction. A final factor relates to the duration of a particular pathogen's existence, more specifically, the phase of the epidemic. Whether HIV was introduced into a specific population 10, 20, or 30 years ago has a tremendous impact on the extent of disparity today in those populations. The STI cofactor effect must consider the phase of the HIV epidemic and also the phase of a specific STI epidemic that may be feeding trends in the HIV epidemic.

DISCUSSION

This article has reported on 15 factors identified in the STI literature to explain the presence of racial/ethnic disparities in STIs, including HIV. Previous research has proposed various explanations for differential STI (including HIV) rates across subpopulations that span countries and continents. For example, differences in the number of partners and differences in sexual mixing patterns have been presented as explanations for disparities in HIV rates across subpopulations. Disparities in HIV rates have also been attributed to differences in the incidence of STIs, which translate into differences in HIV transmission rates.

An evaluation of individual behavior is necessary but insufficient on its own to account for the racial/ethnic disparities observed in STIs. Population parameters should be included within models that traditionally include individual-level factors, such as HIV viral load, stage of HIV infection, HIV treatment status, circumcision status, infection with STIs, individual sexual behavior, and sociodemographic factors. As an area of growing research interest and concern, social network analysis has become prominent within the arsenal of strategies used to identify and clarify the most potent patterns of disease transmission.

The focus of future research needs to be on minority status as a problem definition rather than a focus on racial categories as meaningful entities. We believe that something sociologically important happens when any characteristic defines a minority population. Given that we cannot change context in the short run and that we run interventions with immediate impact in consideration of the seriousness of the
condition we study, we need to focus on interventions that neutralize effects of context. Racializing the problem of health disparities can severely divert attention from the ways in which political, economic, and social factors affect life experience and produce different health outcomes among different groups. Instead, research should focus on the effects of particular health outcomes, including conditions (which become “preexisting conditions”) that can lower immunity and increase susceptibility to additional diseases, in the way that previous STIs can increase the likelihood of repeat infection with STIs or HIV infection. Therefore, decreasing STI prevalence may help to decrease HIV incidence.

In summary, the studies reviewed here can most properly be categorized into broad overarching themes, such as providing behavioral, prevention participation, and biologic explanations of the differentials in STI (including HIV) transmission and infection. For example, “behavioral” studies include consideration of the characteristics of sex and drug-using partners, “biologic” studies the prevalence of HIV and STIs known to increase susceptibility to infection, and “prevention participation” studies examine individuals’ use of health care and prevention service involvement. A focus on only 1 of the 15 factors discussed within this review, to the exclusion of others, is likely to yield poor outcomes, however. Conversely, an emphasis on their interactions may produce effective public health interventions and reductions in HIV transmission.

Many theories have been proposed that may help in gaining a better understanding of the persistence of racial disparities in STIs and HIV, with most accepting the problem as multifaceted and deeply embedded within a variety of domains found in our common culture; thus, it is also important to consider the context within which we are working carefully. In addition, most theorists suggest the concurrent consideration of important mediating variables, such as the quality of services offered, perceived value and efficacy of services offered, and patient adherence. Perhaps most importantly, individual behaviors must be considered within a broad social and ecologic perspective that includes community level and structural characteristics, with a special emphasis placed on the social context within which individual risk behaviors occur, because HIV transmission is, by definition, a socially transmitted disease.

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Defining, Designing, Implementing, and Evaluating Phase 4 HIV Prevention Effectiveness Trials for Vulnerable Populations

Jeffrey A. Kelly, PhD,* Freya Spielberg, MD, MPH,† and Timothy L. McAuliffe, PhD*

Summary: The efficacy of behavioral HIV prevention interventions has been convincingly demonstrated in a large number of randomized controlled phase 3 research outcome trials. Little research attention has been directed toward studying the effectiveness of the same interventions when delivered by providers to their own clients or community members, however. This article argues for the need to conduct phase 4 effectiveness trials of HIV prevention interventions that have been found efficacious in the research arena. Such trials can provide important information concerning the impact of interventions when applied in heterogeneous “real-world” circumstances. This article raises design issues and methodologic questions that need to be addressed in the conduct of phase 4 trials of behavioral interventions. These issues include the selection and training of service providers engaged in such trials, maintenance of fidelity to intervention protocols in provider-delivered interventions, determination of intervention core elements versus aspects that require tailoring, selection of relevant phase 4 study outcomes, interpretation of findings indicative of field effectiveness, sustainability, and other aspects of phase 4 trial design.

Key Words: effectiveness trial, HIV prevention, phase 4 trial, methodology

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Behavioral HIV primary prevention interventions have been shown to reduce risk behaviors in a wide range of community populations, including men who have sex with men (MSM), injection drug users (IDUs), women, adolescents, patients treated for sexually transmitted diseases (STDs) or seen in health clinics, and persons with other risk issues. Often utilizing randomized controlled trial (RCT) designs, a large body of research literature has established the efficacy of culturally tailored behavioral interventions—derived from several theoretic frameworks and using different delivery modalities—directed toward individuals, couples, small groups, social networks, and even subsets of entire community populations. Several meta-analyses, reviews, and compendia have summarized evidence-based HIV prevention behavioral intervention research that met high standards for study design and produced interventions deemed ready for use by service providers. One of the most noteworthy achievements in the entire history of the behavioral and psychologic sciences is how rapidly applied efforts were mobilized to develop and evaluate rigorously interventions designed to protect persons from HIV/AIDS.

For advances in our scientific understanding of HIV prevention interventions to contribute to public health goals of curtailing the disease, at least 2 additional steps must now be taken. The first is evaluating optimal strategies for disseminating evidence-based HIV prevention interventions, after they are found efficacious, from the research arena to the frontline service providers who carry out applied programs in their own communities. Although publication of intervention outcome findings in journals is a traditional academic end product, the true audience for HIV prevention intervention research is service providers whose applied programs can benefit if informed by results of HIV behavioral research. Advances have been made in identifying training delivery modalities that can be used to help AIDS service organizations to adopt evidence-based HIV prevention intervention models. Much remains to be learned about how best to transfer interventions developed and tested in the research arena to meet the needs of the service providers who are hoped to use them eventually, however.

A second step necessary for translating research advances made in HIV prevention science to their public health application is determining the effects that are produced when evidence-based interventions are implemented by service providers in the field as opposed to researchers in carefully controlled research trials.

WHAT ARE PHASE 4 EFFECTIVENESS TRIALS OF BEHAVIORAL INTERVENTIONS?

Research in the medical therapeutics arena—often involving medications—has traditionally been conceptualized in terms of study phases that range from initial basic science discovery research through studies that are meant to test...
mechanisms of action, dose/response relations, and safety (phase 1); to preliminary studies of efficacy (phase 2); to definitive studies of efficacy using larger samples and well-controlled outcome evaluation research designs (phase 3); and, finally, to wide-scale intervention application in the field under diverse, heterogeneous, real-world conditions beyond the confines of a highly controlled phase 3 trial (phase 4). Medical therapeutics are usually taken through all these study phases, with phase 4 findings—the “effectiveness” of the intervention when applied by real providers in the real world—considered the final test of an approach that had been found “efficacious” in the well-controlled phase 3 research trials. Phase 4 trials are an essential culmination of the intervention development and deployment picture. It is, after all, an intervention’s performance when used by providers in the field that determines its true public health benefit.

Although there has been a long and intensive history of research evaluating the effects of HIV prevention behavioral interventions, few of these evaluations have been carried beyond phase 3 studies that examine intervention effects in highly controlled studies. Our knowledge concerning the impact of HIV prevention interventions is generally derived from studies that delivered interventions following carefully specified protocols that employed highly trained research staff (or counselors trained to function as research staff surrogates), who were taught and were closely monitored to deliver the intervention with fidelity, that enrolled study volunteers motivated and willing to complete intervention and assessment protocols, and that used participation and intervention supports (eg, incentive payments, high-quality delivery support resources) common in the research arena but rare in the service provision sector. Further, participants enrolled in phase 3 trials of HIV prevention interventions are usually persons who are carefully screened for study eligibility, and who therefore represent a select subsample of all persons for whom the intervention is ultimately likely to be offered in real-life service provision settings. For these reasons, we now know more about the impact of HIV prevention interventions in the context of phase 3 efficacy trials than their effectiveness when offered by providers under more genuine and diverse circumstances.

Although there is general consensus that phase 4 trials should involve implementation of an intervention with larger samples and under conditions more heterogeneous and realistic than those conditions that characterize a highly controlled phase 3 experimental trial, there is little precedent in the field for determining the methodologies and designs needed to carry out field effectiveness studies of behavioral interventions. For the field to advance to the point of determining the field effectiveness of evidence-based HIV prevention interventions that were found efficacious in the phase 3 research arena, several critical design and methodological issues need to be resolved.

To conduct phase 4 trials of behavioral HIV prevention interventions, dissemination and design frameworks are needed for engaging and training service providers in how to deliver to their own clients an intervention whose efficacy has already been established. Effectiveness trials require that the intervention being tested is offered by applied providers to their own clients or to community populations in real-world field settings. In an HIV prevention effectiveness trial, providers are likely to be AIDS service organizations, nongovernmental organizations (NGOs), public health departments, schools, clinics, or other agencies that carry out programs serving populations for whom the intervention is believed to be useful. Initial considerations when planning a phase 4 trial of an HIV prevention intervention include determining the types of providers who are going to implement the intervention; assessing provider capacity, resources, skills, and motivation for systematic intervention implementation and outcome measure data collection; and determining the appropriateness of the providers’ client populations as recipients of the intervention that is to be delivered.

To what extent should providers who deliver an HIV prevention intervention in a phase 4 effectiveness trial be monitored for delivery adherence and to what extent should quality control (QC) procedures be used to detect and correct any provider “drift” from protocol in intervention delivery? Even brief HIV prevention behavioral interventions involve considerable presentation of information; active interaction between a client and the deliverer of the intervention; and, often, staged exercises intended to influence the client’s risk reduction skills, attitudes, motivations, beliefs, and intentions. Behavioral interventions are sufficiently complex that the facilitators who deliver intervention in phase 3 trials are usually intensively trained in all content and procedures, follow manuzaled guides, are frequently monitored to measure their adherence to the intervention’s protocol and methods, and are retrained whenever deviations from protocol (sometimes called drift) are observed. These procedures serve to maintain high levels of fidelity in intervention delivery in phase 3 trials. If the same oversight was attempted in a phase 4 trial, one could argue that the intervention under evaluation is not being tested in real-world circumstances and that the trial remains in phase 3 with overly tight controls imposed on intervention delivery. Conversely, the absence of oversight QC monitoring and periodic provider retraining could lead to a circumstance in which the delivered intervention is fundamentally different—perhaps in unknown ways—from the one that was intended. Thus, it would not be possible to specify accurately what intervention was being delivered. Planners of phase 4 behavioral trials are confronted with the need to maintain oversight of intervention delivery sufficient to ensure that the approach being implemented is the one that was planned, whereas, at the same time, allowing for realistic adaptation and tailoring by providers. Presumably, a phase 4 trial of an HIV prevention behavioral intervention would begin by carefully training providers in how to implement the model correctly with their own clients. The question that needs to be conceptualized is how closely to monitor and correct any subsequent drift in providers’ intervention delivery to ensure that the intended intervention is really being offered while not violating the conceptual underpinnings of a phase 4 (as opposed to phase 2) trial. The collection of ongoing intervention delivery process data permits one to characterize how well an intervention adhered to a protocol or how it may have been changed.

The accomplishment of successful phase 4 interventions depends on the design and structure of the preceding phases.
Table 1 describes key components of design, goals, considerations, phase-dependent outcomes, and potential funding mechanisms for each study phase. In each research phase, we suggest working with the same populations and in the same settings in which the program is ultimately going to be disseminated. In phase 1, an iterative design process and qualitative evaluation allows a theory-driven model to be refined and operationalized in a manner consistent with end-user priorities. The goal in phase 2 is to estimate potential effect size and to gather further information on intervention acceptability and feasibility. With the effect size estimated, phase 3 and 4 trials can be designed to determine the impact of an HIV intervention on individual (phase 3) and population (phase 4) levels.

Phase 4 research seeks to determine the impact of an intervention when disseminated by service providers in real-world settings. In phase 3, individuals are typically randomized to an intervention or control condition and incentives are generally provided to ensure intervention participation and longitudinal follow-up. The use of consents and incentives may lead to a different population participating in the study than would accept services in the absence of a research study. In phase 4 trials, one way to allow accurate collection of process, outcomes, and cost data is by randomizing to intervention or standard-of-care services based on a discrete time period such as day, week, or month. Using incentives to increase initial acceptance of intervention services or the provision of additional staff is discouraged in phase 4 designs unless they are part of the usual standard of care or are only for follow-up data collection.

If an intervention that is being tested in a phase 3 trial cannot be conducted without extensive training, or if it is too costly, the likelihood of successful scale-up and dissemination in a sustainable way is low. Thus, when choosing interventions for phase 3 and phase 4 trials, we suggest ensuring that the ultimate target populations have been included in all phases of the research; that the intervention is grounded in qualitative data from clients in real-world settings; that a training system has been developed with high potential for efficient and consistent replication; that the intervention has expected higher effectiveness or lower cost than existing effective models; and that plans for scaling, dissemination, and ongoing funding are well thought out. There may also be circumstances when proceeding directly from phase 2 to phase 4 may provide the most relevant data at the least cost. This is particularly the case for interventions based on proven theories that are being adapted for new populations, disseminated through new technologies, tested in new settings, or simply targeting different risk groups.

In designing phase 4 trials, it is critical to distinguish between essential “core elements” of an intervention that cannot be changed versus other intervention characteristics.

| TABLE 1. Structure and Design of Behavioral Intervention Research and Evaluation |
|---------------------------------|-----------------|-----------------|-----------------|
| **Research Phase**             | **Design**      | **Goal**        | **Approximate Sample Size** |
| Phase 1 research               | Qualitative iterative design process | To design and pilot a theory-based HIV prevention intervention | 20 per setting and iterative design |
| Phase 2 research               | Longitudinal quantitative pilot     | To determine potential effect sizes for a new HIV prevention intervention | 150 per arm per setting |
| Phase 3 research               | Longitudinal randomized controlled trial (individuals are randomized) | To test the efficacy of a new behavioral intervention | Required sample size to define significant differences is determined based on results of phase 2. Larger sample sizes to allow the measurement of biologic outcomes should be funded whenever possible |
| Phase 4 evaluation             | Longitudinal randomized controlled trial by time frame (d, wk, y) | To test the effectiveness and cost of a new behavioral intervention when scaled up in real-world settings | Sample size calculations take into account phase 3 results and cluster correlation |
| Postmarketing evaluation       | Postmarketing surveillance          | To evaluate sustainable dissemination of effective interventions | Market dependent |

<table>
<thead>
<tr>
<th><strong>Outcomes</strong></th>
<th><strong>Potential Funding Mechanism</strong></th>
</tr>
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<tbody>
<tr>
<td>Acceptability and usability/feasibility among potential clients and service providers</td>
<td>NIH R21, R38, SBIR CDC RFA, SBIR Foundation</td>
</tr>
<tr>
<td>Behavioral (unprotected vaginal or anal sex or needle sharing with a partner of unknown or discordant status) and biologic outcomes (HIV or STDs) to define prevalence and potential effect size</td>
<td>NIH R38, R01 CDC RFA, SBIR Foundation</td>
</tr>
<tr>
<td>Comparison of behavioral and biologic outcomes between intervention and control groups</td>
<td>NIH R01, U10 CDC RFA Foundation</td>
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NIH indicates National Institutes of Health, RFA, request for applications; SBIR, small business innovation research.
that can (or must) be tailored. One way to resolve the tension between intervention delivery consistency versus variation is by identifying core elements that must be present for a delivered intervention to constitute what it is meant to be. Core elements may involve critical content, intensity or duration, procedures used, or other aspects of the model that, if changed, would also fundamentally change the intervention from that which had been shown efficacious in prior phase 3 trials. The determination of an intervention’s core elements could be based on empiric component analysis to determine its “active ingredients,” theoretic principles underlying the intervention, core elements that were always present in past evaluations of the intervention that have been found efficacious, or cumulative past practical experience with the intervention. The core elements may then be differentiated from other characteristics of intervention delivery that can be tailored to meet provider needs and to ensure intervention relevance across client populations more diverse than those studied in earlier and efficacy outcome studies.

Critical core elements may also be studied within the context of the phase 4 trial by using a time period randomization methodology or by varying key aspects of the core content and comparing it with the full strategy delivered on random weeks, for example. Likewise, it is possible to utilize methods of an iterative phase 4 design, where services that isolate different core elements are varied during randomized time periods and are evaluated to determine which core elements have the most significant impact on service acceptance, effectiveness, and cost.

The iterative phase 4 design model for effectiveness trials varies time frames for conditions in contrast to historical designs, where individuals are randomized and study arms are compared. Advantages in utilizing an iterative design strategy include feasibility to integrate the design into a functioning service delivery program; potential cost savings between service funders and research funders; reduction of biases if individuals do not receive their hoped for strategy as with individual randomization; and the potential to collect data on service acceptance, program effectiveness among people who are likely to use it, and the real costs of providing such services.

What constitute appropriate study outcomes in a phase 4 behavioral intervention trial, and how can they best be measured? One aim of a phase 4 trial is to determine whether the effectiveness of an intervention when used by providers in the field is comparable to, is better than, or is worse than the same intervention when tested under the controlled circumstances of a phase 3 trial. To address this question in the most direct possible manner, it would seem ideal to use outcome measures, assessment procedures, and follow-up periods in the phase 4 trial that closely match those used in earlier efficacy studies of the same intervention. If providers’ real-world clients are assessed in the same way and with the same measures as were participants in earlier efficacy studies, it should be possible to compare directly the effect sizes produced in the provider-delivered (relative to the earlier researcher-delivered) intervention.

If used alone, this approach fails to take full advantage of the potential scientific contributions of phase 4 effectiveness trials, however, which, we would argue, should also attempt to address broader questions about intervention acceptance, impact, safety, and cost. Interventions taken to the field, especially when using larger sample sizes, can potentially be designed to assess impact on public health outcome indicators broader than self-reported behavior change alone. Reductions in STD and HIV incidence, increased (or decreased) levels of client health service utilization, unwanted or early pregnancy reduction, and similar health outcomes can rarely be directly assessed, except in the largest of phase 3 studies, because of limited statistical power to detect such indicators of impact. As interventions are taken to the field in phase 4 trials, larger client sample sizes may afford increased statistical power to measure such public health effects.

An additional goal of an effectiveness trial is determining the acceptability of the intervention to the clients who receive it and to the providers who deliver it. Assessed outcomes in this domain can involve the measurement of client acceptance rates, client and staff satisfaction and perceived benefit, but also potential unanticipated adverse events that might be of sufficiently low frequency to avoid detection in earlier stage trials. Because phase 4 trials are intended to examine the impact of an intervention on populations more heterogeneous and less rigidly selected than research participants in phase 3 trials, effectiveness studies also afford the opportunity to examine whether different outcomes are achieved among clients with differing demographic, risk, or other background characteristics.

With what should phase 4 trial outcomes be compared to reach conclusions about their effectiveness? If the intent of a phase 4 field trial is to ascertain the effectiveness of an evidence-based intervention when offered by providers to their own clients and in their own communities, a trial design question that arises involves determining with what to compare observed phase 4 intervention outcomes. Phrased differently, providers in a phase 4 trial might administer pre- and postintervention measures to their own clients who receive the intervention being evaluated. With whom or with what are potential changes found on these measures compared to determine whether the tested intervention is, in fact, effective?

Several comparison strategies are available. One is to determine the pre- to postintervention risk reduction effect sizes produced in the provider-delivered intervention and to examine descriptively the magnitude of those effect sizes compared with the effects that were produced by the same intervention in earlier controlled efficacy outcome studies. This approach does not take into account temporal changes that may have an impact on study outcomes. Another strategy is to compare the intervention’s outcomes relative to those produced by other programs (including present standard-of-prevention services) also offered by the provider agency. The latter approach necessitates the systematic collection of outcome data from clients who receive the intervention being tested and also clients who participate in the comparison program. A rigorous application of this approach includes the design described earlier, where standard-of-care and the tested intervention services are randomized by day, week, or month.

This approach provides comparison outcome data that control for temporal changes, allowing accurate collection of process

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outcomes necessary for realistic cost comparisons. Although data collection from a comparison group considerably increases the scope of a phase 4 trial, it also permits one to reach conclusions about the relative effectiveness of the tested intervention compared with other programs in current use.

In addition, to maintain high-quality programs, data collection should be efficiently incorporated into ongoing systems. National efforts are currently underway to require routine data collection, such as in the Program Evaluation and Monitoring System (PEMS) for all organizations receiving HIV funding from the Centers for Disease Control and Prevention (CDC). Most service providers presently lack adequate infrastructure to manage data collection and reporting, however. New systems that allow real-time data collection on tablet personal computers (PCs), cell phones, or personal digital assistants (PDAs) could facilitate data collection, QC, and evaluation reports, minimizing staff time needed for data entry and report preparation. Such new technologies can enhance prospects for phase 4 evaluations of interventions with little negative impact on program delivery.

How large should a phase 4 trial be, and how can phase 4 trials be made feasible in an era of research funding constraints? There is general consensus that phase 4 effectiveness trials should seek to enroll diverse heterogeneous samples larger than those typically enrolled in phase 3 outcome studies. The sample size requirement of an effectiveness trial is determined, as in any other study, by the expected effect size of the intervention on measures of primary interest and by the nature of comparisons to be made with other standards of care. Additional considerations must also be taken into account, however, if an effectiveness trial enrolls participants attending different clinics, accessed in different settings, or seen by different counselors, participant data may not constitute independent observations because clients are nested within clinics, settings, or counselors. In such instances, effectiveness trial statistical power is determined not just by the total number of enrolled clients but by the number of clinic, setting, or counselor units represented. Additionally, sample size determination is influenced by whether there are plans to analyze outcomes in relation to differences in client risk, background, or demographic characteristics. Sufficient sample sizes are needed to support such subanalyses.

What measures should be used to assess sustainability? Collection of real cost and population-based effectiveness outcomes may result in data that allow health care funders to prioritize spending. In addition, it may be worthwhile to consider conducting phase 4 effectiveness studies in collaboration with “social enterprise” businesses—organizations that trade in goods or services and link that trade to a social mission—to ensure sustainable dissemination of effective interventions. Such for-profit or not-for-profit enterprises have clearly defined business models to promote sustainable and scalable services. Some social enterprises use mixed financing models for service delivery; higher cost services are provided to populations with resources to subsidize the care of people without resources. A successful example of this model is David Green’s Project Impact, which aims to make medical technology and health care services (eg, cataract surgery, low-cost hearing aids, other basic medical technology) accessible and affordable to those in the developing world in a self-sustaining manner. Private and sliding-scale delivery models produce adequate profit to allow providers also to offer services to persons without resources. Other social enterprise models pair lucrative businesses with HIV prevention delivery programs, relying on market demand and standard business structures to scale, disseminate, and sustain their programs. Relative to traditional nonprofit organization models that rely solely on grant funding and result in a constant struggle for organizational survival, new social enterprises for sustainable dissemination of effective HIV prevention interventions must be developed.

Finally, AIDS service providers in the United States and abroad are increasingly expected by program funders to use evidence-based interventions in their activities. Given that service providers are often being expected to conduct the same kinds of interventions in their service programs that researchers may seek to study in phase 4 trials, there are excellent prospects for researcher/provider collaboration. Historically, these types of collaborations have been limited by funding streams for service provision that commonly allow only 5% of the budget to be spent on evaluation. To facilitate well-designed effectiveness studies that leverage existing dollars spent on service provision, new collaborations are required between funders of research and funders of services to foster joint applications from researchers and service delivery partners. This type of collaboration can leverage the expertise and dollars of both communities, ultimately resulting in well-designed field effectiveness studies of large-scale HIV prevention interventions.

CONCLUSIONS

Great advances have been made in the development of theory-based culturally tailored behavioral interventions to help persons reduce risk for contracting HIV infection. Interventions that have been shown to be efficacious in well-controlled experimental studies must be disseminated to service providers, and the effectiveness of the interventions studied under diverse “real-world” conditions must be evaluated. The development of approaches, methodologies, and analytic models for designing and implementing phase 4 effectiveness trials should allow the field to reach firm conclusions about the impact and benefits of behavioral HIV prevention interventions when used by service providers.

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The basic routes of HIV transmission between persons are now well understood and widely known, but the determinants of the disparities in HIV prevalence and trends among populations remain an area of debate and intense scientific research. These disparities have roots in the transmission system; thus, understanding that system—its components and its dynamics—is key to understanding the disparities. Mathematical models of HIV transmission dynamics are an important research tool in this endeavor.

The HIV transmission system has biologic and social determinants. Biologic determinants include characteristics of the pathogen, the host, and biomedical interventions. Social determinants include individual-level, pairwise, and community-level processes that affect behavior, and thus the structure and dynamics of the transmission networks. This covers a wide range of factors: knowledge, attitudes, beliefs, power differentials, cultural norms, population mobility and mixing patterns, and the larger social context that gives rise to all these.

HIV researchers have long appreciated the need to understand the social and behavioral determinants of HIV-related risk behavior, but the cumulative impact of individual behaviors on population-level HIV outcomes can be subtle and counterintuitive, however, and the methods for studying this are rarely part of a traditional social science or epidemiology training program. Mathematical models provide a way to examine the potential effects of the proximate biologic and behavioral determinants of HIV transmission dynamics, alone and in combination. The purpose of this article is to show how mathematical modeling studies have contributed to our understanding of the dynamics and disparities in the global spread of HIV. Our aims are to demonstrate the value that these analytic tools have for social and behavioral sciences in HIV prevention research, to identify gaps in the current literature, and to suggest directions for future research.

**Summary:** HIV researchers have long appreciated the need to understand the social and behavioral determinants of HIV-related risk behavior, but the cumulative impact of individual behaviors on population-level HIV outcomes can be subtle and counterintuitive, and the methods for studying this are rarely part of a traditional social science or epidemiology training program. Mathematical models provide a way to examine the potential effects of the proximate biologic and behavioral determinants of HIV transmission dynamics, alone and in combination. The purpose of this article is to show how mathematical modeling studies have contributed to our understanding of the dynamics and disparities in the global spread of HIV.

**Key Words:** AIDS, microsimulation, prevention

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**MATHMATICAL MODELS FOR HIV**

The primary purpose of a mathematical model of HIV transmission is to project population-level outcomes from individual-level inputs. There are many possible outcomes that can be examined with a model, for example, the incidence of infection, the prevalence of infection, or the doubling time of the epidemic. The most basic outcome, however, is simply the likelihood of an epidemic occurring—whether there is sufficient transmission potential for a chain of infection to be sustained. In classic epidemic theory, this outcome is captured by a simple summary statistic: the reproduction number of the infectious process, $R_0$. In a susceptible population, $R_0$ represents the expected number of secondary infections generated by the first infected individual. If $R_0$ is 1 or greater, an epidemic is expected. At an $R_0 < 1$, the infection is expected to die out.

$R_0$ is a function of biologic and behavioral factors. For a simple homogeneous population, it is defined as:

$$R_0 = \beta c D$$

where the terms on the right-hand side are the average probability of transmission per sexual contact ($\beta$), the average number of sexual partnerships formed per unit time ($c$), and the average duration of infectiousness of an infected individual ($D$). If $R_0$ is $>1$, disease transmission typically persists and the magnitude of $R_0$ determines the speed, scale, and spread. Each component of $R_0$, in turn, unfolds into more detailed behavioral and biologic determinants, and the factors that...
influence $R_0$ also influence the other epidemic outcomes of interest. As in a laboratory, mathematical studies often vary one of these components of $R_0$, holding the others constant, to understand its effects. These 3 components thus provide a natural outline for our review of the literature.

Mechanically, there are many different ways to construct a model. There are 2 basic dimensions, however, and these define 4 classes of models with similar strengths and limitations. First, the underlying processes can be represented in a deterministic or stochastic form. The difference is analogous to using the mean as a prediction summary versus using the full probability distribution of outcomes. Second, the dynamics over time can be explored analytically or using computational methods. Analytic, or “closed-form,” solutions isolate the outcome on the left-hand side of an equation, with all the determinants on the right-hand side; thus, it is clear how the outcome depends on the inputs. Not all processes can be represented this way, however. Computational, or “numeric,” solutions must be used if there are nontrivial feedback loops in the process, so that the outcome ends up on both sides of the equation. Models of this sort are said to be “analytically intractable.” This happens quickly as simplifying assumptions are relaxed; thus, most models that attempt to build in realistic heterogeneity need to be solved computationally.

All models divide the population into states (eg, susceptible, infected) and define the process and rate of movement between those states. Deterministic models are usually built on group aggregates or macrolevel states, whereas stochastic simulation models are usually built to reflect the microlevel states occupied by discrete individual persons. The primary difference between deterministic and stochastic models is how they define the movement between states. Deterministic models define the dynamics using the average rate of transition between states. Stochastic models define the dynamics using the probability that an individual makes the transition from one state to another.

Analytic models of both sorts (deterministic and stochastic) are typically regarded as the ideal because they reveal a process in terms of simple cause and effect. Many infectious processes are not simple in that way, however, and the assumptions made to gain tractability often come at the cost of ignoring important parts of the process, and thus failure to project the outcomes of interest properly. As computing power has become more widely available, the need for tractability has declined and computational-deterministic models have become the workhorse of mathematical epidemiology. Their use has led to substantial insight into the population dynamics of HIV and other sexually transmitted infections (STIs) as well as a wide range of other infectious diseases. Increasingly, the limitations of deterministic models are leading to the adoption of computational-stochastic or “microsimulation” methods. These methods are better for representing heterogeneities in the transmission process, behavioral or biologic, and they are the only way to represent accurately something as simple as a person having multiple ongoing (“concurrent”) partnerships. The advantages of microsimulation are discussed in detail by van Imhoff and Post.

The primary disadvantages are that it requires richer inputs and may require significantly more computational capacity.

In the review that follows, we group studies by topic (the component of the process that is the focus of interest) and note the classes of models used.

### $\beta$: Transmission Probability Per Contact

The first component of the basic reproductive number $R_0$ is $\beta$, the probability of transmission per contact. This single parameter actually represents 2 components of transmission: the infectivity of the HIV-positive partner and the susceptibility of the HIV-negative partner. Both components may, in turn, depend on a wide range of demographic, behavioral, and biologic factors. Most of the studies discussed here use computational-deterministic models.

### Demographic Heterogeneity

For many years, it was assumed that the probability of HIV transmission by means of heterosexual sex from the male to female partner was higher than from the female to male partner. The most recent evidence from an empiric study of discordant couples in Uganda, however, suggests that there may be little asymmetry in transmission by gender. Population-level outcomes can differ dramatically given different assumptions of HIV transmission probabilities by gender. The kind of impact can be seen in the modeling study by Goodreau et al in this article: in general, asymmetric transmission lowers the rate of spread through a population, and therefore lowers prevalence. High rates of infection among young women in many countries of sub-Saharan Africa also led to theories that susceptibility might vary with age. Recent empiric work, however, suggests that the pattern of sexual mixing by age rather than by some biologic mechanism may be responsible. Mathematical models of the impact of mixing by age are reviewed in the contact rate section in this article as well.

### Stage of Disease

There is now compelling evidence that for HIV-infected individuals, infectivity is not constant over time but varies by stage of infection and viral load. Most studies agree that the probability of transmission peaks at the early (acute) stage of infection, decreases during the latent stage, and then increases again during the symptomatic stage.

At the population level, however, there are 2 reasons that might explain why individuals in the primary stage of infection contribute the highest proportion of secondary infections: heightened infectiousness during acute infection or a period of higher contact rates that leads to infection and secondary transmission in short succession. Biology and behavior can be confounded here, and they may both contribute.

Jacquez et al were the first to use mathematical models to emphasize the importance of primary stage transmission. Using a computational-deterministic model, they showed that an interval of high contagiousness during primary infection followed by a large decline in infectiousness was consistent with the pattern of epidemic spread seen in cohorts of men who have sex with men (MSM) in the early years of the epidemic. These findings depend on many assumptions: that
people have serially monogamous relationships, that there is random mixing by activity levels, on population prevalence, and on the distribution of persons in each stage of infection. Changes in any of these assumptions would change the findings. A recent modeling study reanalyzed these data and pointed out that the time spent in each stage (the duration component) is an equally important factor in determining the impact of infection stage on transmission. Given the much longer time spent in stages after primary infection, it is argued that the impact of primary stage infection on overall incidence declines dramatically as an epidemic matures.7 Thus, an individual-level effect (higher primary stage infection) may not drive the population-level outcome (incidence).

**Coinfection With Other STIs**

Coinfection with HIV and other pathogens is believed to have strong implications for infectivity and susceptibility. For instance, herpes simplex virus type 2 (HSV-2) is associated with a 2- to 4-fold increased risk of HIV-1 acquisition.8 Mathematical models have been used to estimate the cofactor effect of various STIs on the risk of HIV transmission, and thus population-level prevalence. Blower and Ma9 used a deterministic mathematical model to predict that HSV-2 epidemics can more than double the peak HIV incidence and that biologic heterogeneity in susceptibility and transmission induced by an HSV-2 epidemic can cause HIV incidence to vary nonlinearly. The implication was that STI treatment would be useful for preventing HIV transmission. The empirical findings of a large randomized community trial of STI treatment in Uganda (for bacterial STIs like gonorrhea, syphilis, trichomoniasis, and bacterial vaginosis), unfortunately, showed no effect on HIV incidence.10 Mathematical models were then used to help understand why. These stochastic-computational models suggested that 2 population-level factors, STI prevalence and HIV epidemic maturity, play a determining role. STI management may be an effective HIV prevention strategy in populations with a high prevalence of curable STIs, particularly in an early HIV epidemic, but epidemic maturity reduces the effectiveness of STI treatment.11,12 Work is continuing on the potential impact of treating viral STIs such as HSV-2.

**Circumcision**

Male circumcision recently has been shown to reduce annual susceptibility to infection with HIV by approximately 60%,13-15 The first randomized controlled trial was quickly followed by a mathematical model of the potential impact of male circumcision as a public health intervention.16 The investigators used a deterministic simulation model and found that male circumcision could lower the rate of transmission by nearly 40% after the intervention is in place for at least 10 years but that it was unlikely to bring transmission rates down lower than the reproductive threshold.

**Vaccines**

No HIV vaccine has been successfully produced, and the current candidates are all expected to be less than perfect at preventing infection. Mathematical models can show the population level effects of imperfect vaccines, in what scenarios they might be effective, and what other prevention strategies need to be coupled with imperfect vaccines to reduce transmission to lower than the reproductive threshold.

There are several ways in which a vaccine can work. A “sterilizing” vaccine protects everyone completely against infection, and no current candidates are of this sort. A “leaky” vaccine protects everyone partially, and an “all-or-nothing” vaccine protects a fraction of the population completely.17 A vaccine can also lower infectiousness or lower susceptibility (or both).18 Finally, a “therapeutic vaccine” may increase the symptom-free period, establishing a longer duration in a less infective state. The population-level effects of a vaccine depend entirely on these differences. With any nonsterilizing vaccine, the protective effect could be overwhelmed by an increase in risky behavior, a phenomenon called “behavioral disinhibition,” or by an increase in life expectancy that is proportionally greater than the decrease in infectivity. In general, the effect is determined by the combined impact of the 3 components of secondary transmission: the probability of transmission (presumably lowered by means of infectivity or susceptibility), the rate of contact (which could rise because of behavioral inhibition), and the duration of infection (which would rise under a therapeutic vaccine). Recent models have predicted that eradication of HIV using a vaccine alone is unlikely unless the vaccine is combined with considerable reductions in risk behavior.18-20

C: CONTACT RATE

The component c in the basic reproduction number denotes the average rate of sexual partner change, or the contact rate. This is an area in which social scientists have much to contribute, and the recent progress in modeling the nature and impact of the contact network on HIV transmission has been substantial.21

**Core Group Theory**

This was the first theory to address the heterogeneity in contact rates explicitly. Studies of STI clinic patients in United States in the late 1970s found that 3% to 7% of the infected persons accounted for approximately 30% of the caseload; these were people with high contact rates who would be reinfected quickly after treatment.22-23 Mathematical models then demonstrated that even if the rest of the population had contact rates too low to sustain transmission, a small “core” group like this could have enough partners to keep the disease circulating.24,25 The idea of a core group of transmitters was seen as a driving force behind sustained STI transmission, and therefore a clear target for intervention strategies.

**Selective Mixing**

Early studies of core groups assumed that the members of the core group selected their partners at random (ie, without regard to the activity level of their partners), but researchers soon realized that this assumption might be inappropriate. Mathematical models introduced selective (or heterogeneous) mixing and showed that the degree of mixing between groups had a major influence on the pattern and spread of STIs and HIV. In general, assortative mixing by activity level was shown...
to lead to more rapid but constrained spread, whereas disassortative mixing led to slower but more pervasive spread.26-28 Other simulation studies have shown that these effects can be strong and highly variable29 and that they can bias other model estimates if they are not taken into account.

Social scientists and demographers have approached the question of assortative mixing differently. Starting from the question of how people identify and choose “appropriate” partners, they focus on social attributes that influence the partner selection process. This generates mixing between groups by attributes such as age, race, and sexual preference as well as by “bridge populations” that form links between otherwise unconnected groups. It may also induce assortative mixing by degree if demographic groups vary in their activity levels and mix assortatively.

Assortative mixing by race and ethnicity may help to explain the large disparities in HIV infection rates across races; HIV infection is significantly higher among non-Hispanic blacks than it is among any other young adult racial or ethnic group in the United States.30 Using a range of statistical models to summarize the “local network” mixing structure and drive a dynamic deterministic model for transmission through this structure, researchers have shown that assortative mixing by race, ethnicity, sexual preference, and sexual roles can have large population-level effects on transmission and prevalence disparities.3,29,31

Age mixing is another major behavioral determinant in individual risk of infection.32 In the generalized epidemic in sub-Saharan Africa, it is almost universally the case that women are infected at a younger age (15 to 20 years old) than men. Greseng et al33 find that having an older male partner is a significant determinant of infection in young women in Zimbabwe. This might suggest that we should encourage age-assortative mixing to reduce prevalence among the younger group by protecting them from the higher prevalence older group. A computational-deterministic study based on data from a longitudinal cohort of MSM found that if contact rates are sufficiently higher among the young, however, this could actually amplify the spread of infection.33

In some cases, selective mixing can lead to a complete lack of contact between spatially integrated groups, but indirect exposure may exist if there is a “bridge population” that links the 2 groups. A good example is men who have sex with female commercial sex workers (CSW) and non-CSW partners. Morris et al34 used a simple deterministic-analytic model based on local network data collected in Thailand and showed that this male bridge population would play a key role for the spread of HIV into the general population.

Another mixing example is behavioral role patterns among MSM. Individual men can have the insertive or receptive role. Some men consistently perform one or the other, whereas others perform both. This yields 3 role subgroups of men—insertive, receptive, and versatile—as opposed to the 2-role categories of male and female partners in heterosexual intercourse. The impact on transmission dynamics depends on the prevalence of each role, the patterns of mixing among roles, and the relative transmission probabilities of insertive and receptive sex. In a recent data-driven simulation, Goodreau et al35 show that a population of MSM with identical contact rates but complete role versatility would have had twice the HIV prevalence for the epidemic’s first 3 decades. It also showed that versatility, although raising population prevalence, is not necessarily an individual risk factor; versatile men remain less at risk than receptive-only men. This is not true, however, if versatile men mix assortatively with other versatile men and role-segregated men mix selectively (but disassortatively) with role-segregated men.

In many of these mathematical modeling studies, deterministic-computational models were used. This is because the attribute classifications are few and easily translated into additional group states for the model. Mixing between classifications can then be controlled in an ad hoc fashion (as in the early core group simulations) or by statistical estimates from data (as with the later demographic mixing simulations).

Timing, Sequence, and Concurrency
Another dimension of contact networks is governed by timing: the duration and sequencing of partnerships. One of the main issues explored here is the impact of concurrent (or overlapping) partnerships. Concurrency has a number of effects on a network that all work to amplify the dynamics of transmission.

The earliest studies of partnership timing and sequence focused on monogamy, using deterministic models; long-duration monogamy was shown to slow the rate of disease transmission and raise the number of contacts needed to reach the epidemic threshold.36 The first model that considered the concept of partnership concurrency was a simple deterministic compartmental model, but it allowed for the possibility that an initially uninfected partner of a susceptible individual may become infected over the duration of their partnership.36 This model found that an infection spreads more quickly with a high number of overlapping partnerships.

A handful of mathematical models in the late 1990s began to use stochastic models to examine the impact of concurrency on HIV transmission dynamics better.37 These showed that concurrency can dramatically increase the size of an epidemic, even without increasing the total number of partnerships in the population (ie, keeping the mean contact rate the same). The effect is attributable to 3 things. First, concurrency destroys the protective effect of sequencing that serial monogamy confers; earlier partners in the sequence can now be exposed to infection that an index partner picks up from a subsequent concurrent partner. Second, concurrency reduces the waiting time between infections, because partnerships in which a transmission occurs do not have to end before the next one begins. Finally, small amounts of concurrency can have a dramatic nonlinear effect on the connectivity of a network and the robustness of that connectivity.38,39

There is now growing evidence that concurrency may be part of the explanation for the generalized epidemics in sub-Saharan Africa40,41 and that it may play a role in the racial disparities in HIV in the United States.42 Thus, the prevention message of “1 partner at a time” is as important as promoting fewer partners.41
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Social Influences on Behavior

Societal context can also influence individual behavior and the contact rate (c), and thus population-level outcomes of HIV. For instance, migration and travel, brothels, and bathhouses all structure contact rates. A study of HIV concordance and discordance in migrant couples suggested that migrant men are significantly more likely to be infected from outside their primary relationship than from inside compared with nonmigrant men.43 A deterministic model demonstrated the key role that migration can play at different epidemic stages; early on, it has an impact on the propagation of HIV between communities, and, later on, it can have an impact on the scale of the epidemic.44

The population-level impact of these issues, or the importance for HIV prevention, has not been examined much through the use of mathematical models. The reason may be that the social structuring introduces a multilevel process with additional demands on the data needed for inputs. The growing interest in “venue-based” interventions is likely to lead to more emphasis on this type of modeling.

D: DURATION OF INFECTIOUSNESS

The duration of infectiousness is the last component of the basic reproduction ratio, R0. HIV disease is defined by at least 3 stages that coincide with viral load and CD4 cell counts: primary (or acute) infection, defined by the initial spike in viral load and infectiousness, which can last from a few weeks to 6 months; the asymptomatic (or latent) stage, during which viral load and infectiousness stay low, which lasts approximately 10 years on average; and the symptomatic stage, which includes the onset of AIDS when viral load rises again. Without treatment this final stage lasts an average of 3 years until death,45 but it can vary greatly if an individual receives antiretroviral therapy (ART), which extends the asymptomatic stage and life expectancy, and thus the duration of infection.

The primary focus of models that examine the impact of duration is the role of ART. The population-level effects of ART are similar to those observed with imperfect vaccines.46 ART reduces viral load47 and the probability of transmission by 50%.48 It also reduces mortality and increase the life expectancy of infected individuals, however. These factors work in opposite directions. Increases in transmission-related behavior may occur if ART recipients perceive that treatment reduces their infectiousness or if the general population no longer fears HIV infection.49 Boily et al50 used a computational-deterministic model to examine the potential impact of disinhibition. They suggest that the impact of ART on HIV transmission dynamics depends on treatment coverage and efficacy. Whether or not ART is actually associated with behavioral disinhibition is still unclear.51,52

CONCLUSION AND DISCUSSION

For the behavioral scientist, mathematical models are the equivalent of a laboratory: a way to examine the potential effects of the proximate determinants of HIV transmission dynamics alone and in combination. These methods provide the tools for bridging the micro-macro gap in the study of HIV and STI population dynamics as well as in any complex biobehavioral system. As the models become more sophisticated and better able to capture observed heterogeneities in data, their role begins to change from “what if” scenarios designed to provide basic insights into population dynamics to design optimization for community trials of the range of prevention interventions that are becoming available. Modeling can help to ground the debate about the tradeoffs between treatment and prevention and can give behavioral scientists the tools to demonstrate the population impact of a well-designed social or behavioral intervention.

The key topics for future modeling can be drawn from the global and local disparities in the current burden of HIV infection. Why is there a generalized epidemic in sub-Saharan Africa? How much is behavioral (eg, concurrent partnerships), and how much is biologic (eg, circumcision, cofactor STIs)? Why are there such large racial disparities in HIV prevalence in industrialized countries? How much of this is attributable to simple immigration? How do we make progress in further reducing the epidemic among MSM? Should serosorting (ie, encouraging HIV-positive individuals to partner with other HIV-positive individuals) and other forms of risk network segregation be promoted? In all populations, what mix of imperfect treatment and prevention interventions might together bring transmission down to lower than the reproductive threshold? As more prevention interventions become available, the tools of mathematical modeling will become increasingly important for helping us to understand and maximize the population level impacts these interventions can have.

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The ADAPT-ITT Model
A Novel Method of Adapting Evidence-Based HIV Interventions

Gina M. Wingood, ScD, MPH*† and Ralph J. DiClemente, PhD*†‡

Summary: The Institute of Medicine (IOM) recommends the use of HIV prevention interventions with proven efficacy to avert new infections. Given the time and cost associated with the development, implementation and evaluation of efficacious HIV interventions, adapting existing evidence-based interventions (EBIs) to be appropriate for a myriad of at-risk populations may facilitate the efficient development of new EBIs. Unfortunately, few models of theoretic frameworks exist to guide the adaptation of EBIs. Over the past few years, the authors have systematically developed a framework for adapting HIV-related EBIs, known as the “ADAPT-ITT” model. The ADAPT-ITT model consists of 8 sequential phases that inform HIV prevention providers and researchers of a prescriptive method for adapting EBIs. The current article summarizes key components of the ADAPT-ITT model and illustrates the use of the model in several case studies.

Key Words: adapting, HIV interventions

The Institute of Medicine (IOM) recommends the use of HIV prevention interventions with proven efficacy to avert new infections. In accordance with the IOM recommendations, the Centers for Disease Control and Prevention (CDC) require CDC-funded health departments and community-based agencies to use evidence-based behavioral interventions (EBIs) defined as effective through the CDC’s Synthesis of Interventions published through 2004. Although identification of EBIs is an important public health priority, ultimately, to avert further escalation of the HIV epidemic, it is required that EBIs be “scaled up” for wider dissemination and adoption by a diverse array of HIV prevention providers. Adoption of EBIs often requires agencies to modify existing interventions to facilitate implementation, encourage ownership, and enhance acceptability of the intervention for new target populations. Thus, the CDC has developed a 3-phase process in which EBIs are identified, packaged in a user-friendly format, and disseminated nationally to HIV prevention providers. Although the CDC has identified EBIs for several high-risk populations, there remains an urgent need to develop additional EBIs for other populations at high risk of HIV transmission or acquisition.

Given the time and cost associated with the development, implementation, and evaluation of efficacious HIV interventions, adapting existing EBIs to be appropriate for a myriad of at-risk populations may facilitate the efficient development of new EBIs. The process of modifying an EBI without competing with or contradicting its core elements or internal logic is referred to as “adaptation”. Without attention to the cultural context and HIV-related risks of a new target population, adapted interventions may remain faithful to the underlying theoretic framework and core elements on which they were originally developed but, unfortunately, may lack relevance, sustainability, and acceptability for the target population.

Unfortunately, few models or theoretic frameworks exist to guide the adaptation of EBIs. One study reporting on the replication of several EBIs for adolescents described the processes used to adapt the interventions. Although informative, discussion of the replication and adaptation of the EBIs lacked a coherent model. Other investigators have discussed the importance of ethnography for guiding the adaptation process and the importance of culturally adapting interventions; however, implications for model development were limited. In an article on advancing translation, Solomon et al discussed principles for guiding researchers’ adaptation efforts. In an effort to systematize guidance for adapting EBIs, the CDC has articulated the map of the adaptation process (MAP) of the adaptation process. This approach includes an assessment phase, to assess the new target population’s HIV risk, the appropriateness of the EBI being considered, and the agency’s capacity to implement the EBI. The assessment phase is followed by a preparation phase, during which the agency prepares to adapt the EBI and, finally, an implementation phase, in which the agency implements and pilots the adapted intervention. Throughout these 3 phases, there are specified action steps, feedback loops, and activities associated with...
monitoring and evaluating the adaptation process. Although it is a valuable addition to the adaptation literature, the MAP is quite an involved model, which may limit its utility for some community-based organizations, the primary providers of HIV prevention education in the United States.12

Over the past few years, Drs. Wingood and DiClemente have systematically developed a framework for adapting HIV-related EBIs, known as the “ADAPT-ITT” model. The ADAPT-ITT model consists of 8 sequential phases that inform HIV prevention providers and researchers of a prescriptive method for adapting EBIs. The ADAPT-ITT model has evolved over repeated applications from adaptations of several of the authors’ CDC-defined EBIs.5,13–15 Through this process, each application has informed the evolution and development of successive iterations of the ADAPT-ITT model. Additionally, ADAPT-ITT has been applied with diverse populations of adolescents and adults in domestic and international settings.

Moreover, observing the implementation and national dissemination of these EBIs16 also assisted the authors in developing and refining the ADAPT-ITT model. This iterative and experiential process has resulted in the development of a pragmatic framework for adapting EBIs. The current article summarizes key components of the ADAPT-ITT model and illustrates the use of the model in several case studies.

THE ADAPT-ITT MODEL

Phase 1, Assessment, involves conducting focus groups, elicitation interviews, or needs assessments with the new target population. Several researchers have documented the importance of assessment as part of the adaptation process.6,11,17 Formative evaluations are necessary to assess the HIV-associated behavioral and psychosocial risks of the new target population, their preferences for intervention content and delivery, and their perceived need for HIV prevention. Identification of HIV-associated risks that differentiate the new target population from the population on which the original EBI was developed and evaluated is critical. Obviously, it may not be feasible to adapt an HIV intervention to every risk profile. Identifying risks associated with HIV vulnerability is critical for effective adaptation, however.18 Focus groups or elicitation interviews should also be conducted with agency staff involved in implementing the HIV prevention intervention and key stakeholders. These formative evaluations are conducted to assess the capacity of an agency to adapt and implement an adapted EBI and to assess the availability of potential resources (eg, fiscal, space, staff) that could be provided by the agency and other key community stakeholders. At the end of this phase, the results from the formative evaluations should be analyzed. Thus, the assessment phase informs the next phase of the adaptation process.

Phase 2, Decision, involves: (1) reviewing the HIV interventions defined as EBIs in articles and publications written by the CDC,3–5 (2) deciding which EBI to select for the new target population, and (3) deciding if the EBI should be adopted or adapted. Restricting the selection of interventions to EBIs is consistent with the emphasis on using evidence-based decision making heralded by the IOM and adopted by the CDC.12 Deciding which EBI to select requires examining the “goodness of fit” between the original EBI and the proposed adapted EBI, with respect to the primary outcome targeted (eg, reduction in drug use, increase in condom use), the demographic characteristics of the target populations (eg, age, gender), the riskiness of the population, content, and delivery of the intervention; the agency’s capacity to adapt and implement the EBI; and the resources available from key stakeholders and agency staff to assist in the adaptation process and implementation. Subsequently, the agency decides whether to adopt or adapt the EBI. If the EBI can be utilized without modification, the agency is encouraged to adopt the EBI. If, however, the agency believes that modifications would optimize the efficacy of the intervention, enhance its relevance for the new target population, and facilitate the agency’s ability to implement the EBI, the agency is encouraged to adapt the EBI and proceed to the next phase of the adaptation process.

Phase 3, Adaptation, involves using an innovative pretesting methodology known as theater testing to adapt the EBI. Theater testing is a type of pretesting methodology that is commonly used to test products, such as television advertisements, videos, print advertisements, and public service announcements.19 Using this methodology, participants typical of the intended audience (the new target population) are invited to a central location to respond to a demonstration of a product (ie, the HIV intervention). At the end of the demonstration, participants receive a questionnaire and answer questions designed to gauge their reaction to the product. An important strength of this methodology is the opportunity to obtain reactions to messages, concepts, and visual materials in a relatively short period. Furthermore, this methodology closely resembles what is experienced by the target population; thus, an accurate assessment of their reactions to the product can be obtained.

As part of the adaptation process, we extend the use of the theater pretest methodology to gauge participants’ reactions to an HIV prevention intervention. Approximately 15 members of the new target population are invited to participate in the theater test. During theater testing, facilitator(s) implement modules of the original EBI that capture core elements of the intervention. While the members of the target population serve as “participants” for the intervention modules, key stakeholders and agency staff, seated behind participants, observe the implementation of the intervention modules. At the end of each module, participants, key stakeholders, and agency staff complete brief surveys that contain closed-ended and open-ended questions to elicit their reactions regarding the appropriateness of the elements in the module for the new target population, such as role plays, materials, didactic instruction, and other content. The goal is to collect critiques of the material, content, and delivery of the EBI and to identify additional materials and/or activities not in the EBI that should be included to enhance its relevance and efficacy for the new target population.

Facilitators collect the surveys and then, using these surveys as triggers, engage in a group discussion with the participants regarding the relevance of the module content for the new target population. Subsequently, key stakeholders and agency staff are invited to join the discussion and offer ideas.
TABLE 1. The ADAPT-ITT Model: Phases and Methodology

<table>
<thead>
<tr>
<th>Phase (Answers the Following Question)</th>
<th>Methodology</th>
<th>EBI Draft</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Assessment* (Who is the new target population and why is it at risk of HIV?)</td>
<td>Conduct focus groups/needs assessment with the new target population</td>
<td>N/A</td>
</tr>
<tr>
<td>2. Decision (What EBI is going to be selected and is it going to be adopted or adapted?)</td>
<td>Review HIV interventions defined as EBIs</td>
<td>Original</td>
</tr>
<tr>
<td>3. Administration* (What in the original EBI needs to be adapted, and how should it be adapted?)</td>
<td>Conduct elicitation interviews with the key stakeholders</td>
<td>Draft 1</td>
</tr>
<tr>
<td>4. Production (How do you produce draft 1 and document adaptations to the EBI?)</td>
<td>Conduct editorials involving topical experts</td>
<td>Draft 2</td>
</tr>
<tr>
<td>5. Topical experts (Who can help to adapt the EBI?)</td>
<td>Integrate content from topical experts based on the capacity of the agency, and create draft 2 of the adapted EBI</td>
<td>Draft 3</td>
</tr>
<tr>
<td>6. Integration (What is going to be included in the adapted EBI that is to be piloted?)</td>
<td>Integrate scales that assess new intervention content in the study survey</td>
<td>Draft #3</td>
</tr>
<tr>
<td>7. Training (Who needs to be trained?)</td>
<td>Integrate readability testing of draft 2 of the EBI to create draft 3</td>
<td>Final</td>
</tr>
<tr>
<td>8. Testing* (Was the adaptation successful, and did it enhance short-term outcomes?)</td>
<td>Analyze results of the pilot study and results in the phase 2 study for the EBI</td>
<td>Final</td>
</tr>
</tbody>
</table>

*Target population, key stakeholders, and agency staff are directly involved in these phases of adaptation.

for adaptation of the EBI. Analyses of the surveys are used to summarize common themes that emerge from the theater test. This active pretesting methodology closely resembles what participants may experience when they participate in an EBI; thus, this methodology greatly facilitates the adaptation process. Specifically, theater testing highlights what needs to be adapted and solicits guidance on how the content, delivery style, and/or materials should be adapted to enhance the relevance and efficacy of the EBI for the new target population.

Phase 4, Production, involves producing draft 1 of the adapted EBI. Production of draft 1 of the adapted EBI involves

TABLE 2. Applying the ADAPT-ITT Model to the SiSTA³ Intervention to Create a Faith-Based HIV Intervention for Young Adult African-American Women Attending the Nondenominational Megachurch in Atlanta

<table>
<thead>
<tr>
<th>Phase</th>
<th>Methodology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Assessment</td>
<td>Conducted focus groups and a needs assessment with young adult African-American women attending a nondenominational megachurch in Atlanta</td>
</tr>
<tr>
<td>2. Decision</td>
<td>Conducted elicitation interviews with key stakeholders (eg, pastors, elders, directors of the Health Ministry, the Women’s Ministry, the College Ministry and the Youth Ministry)</td>
</tr>
<tr>
<td>3. Administration</td>
<td>Conducted focus group/elicitation interviews with the key stakeholders</td>
</tr>
<tr>
<td>4. Production</td>
<td>Conducted editorials involving topical experts</td>
</tr>
<tr>
<td>5. Topical Experts</td>
<td>Decided to adapt the SiSTA HIV intervention defined as an EBI by the CDC³</td>
</tr>
<tr>
<td>6. Integration</td>
<td>Administer a brief survey with open-ended and close-ended items to elicit participants’ and stakeholders’ reactions to the theater test</td>
</tr>
<tr>
<td>7. Training</td>
<td>Administer theater test with members of the new target population</td>
</tr>
<tr>
<td>8. Testing</td>
<td>Identify 3 topical experts knowledgeable about HIV prevention for African-American women and the “culture” of the nondenominational megachurch in Atlanta</td>
</tr>
</tbody>
</table>

*Target population, key stakeholders, and agency staff are directly involved in these phases of adaptation.

for adaptation of the EBI. Analyses of the surveys are used to summarize common themes that emerge from the theater test. This active pretesting methodology closely resembles what participants may experience when they participate in an EBI; thus, this methodology greatly facilitates the adaptation process. Specifically, theater testing highlights what needs to be adapted and solicits guidance on how the content, delivery style, and/or materials should be adapted to enhance the relevance and efficacy of the EBI for the new target population.

Phase 4, Production, involves producing draft 1 of the adapted EBI. Production of draft 1 of the adapted EBI involves
balancing the need to maintain fidelity to the core elements, the underlying psychosocial theory, and the internal logic of the original EBI with numerous priorities, including the capacity of the agency to modify and implement the adapted EBI, the resources available from key stakeholders, the results of the theater test, the results of the formative evaluation, and the assistance that could be afforded by consultants (phase 5).

Production of draft 1 of the adapted EBI can be a time- and resource-intensive process. To facilitate documentation of the options considered and decisions made to produce draft 1 of the adapted EBI, it can be useful to create an adaptation plan. This plan outlines (1) the aim of the adaptation, (2) the EBI to be adapted, (3) the CDC publication citing the intervention as an EBI, (4) the new target population or context, (5) the core elements of the original EBI, (6) the aim of the new materials and/or activities for inclusion in the adapted EBI, and (7) the new material and/or activities that may be more appropriate and relevant for the target population. The term core elements, as defined by the CDC, are those components that are critical features of an intervention’s intent and design and are thought to be responsible for its effectiveness. Core elements are derived from the behavioral theory on which the intervention is based and are essential to the implementation of the intervention and cannot be ignored, added to, or changed. Unlike the core elements, the key characteristics of an EBI can be adapted. As defined by the CDC, key characteristics are important but not essential attributes of the original EBI’s recommended activities and delivery method. The key characteristics can

### TABLE 3. Adaptation Plan for Adapting the SISTA Intervention to Young African-American Women Attending the Nondenominational Megachurch in Atlanta

<table>
<thead>
<tr>
<th>Session</th>
<th>Aim of Activity</th>
<th>Examples of Modified Text and/or New Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Address the concept of self-righteous, a value identified by the church</td>
<td>Self-righteous means that no one is perfect—we are all sinners. Exercises were added that addressed this concept by discussing that although participants may have engaged in unhealthy sexual practices, they can &quot;Begin the New Life.&quot; The New Life is conceptualized as a life in which safer sex is the norm.</td>
</tr>
<tr>
<td></td>
<td>Address the concept of destiny, a value identified by the church</td>
<td>Dream of This by Marianne Williamson &quot;Our deepest fear is not that we are inadequate. Our deepest fear is that we are powerful beyond measure. It is our Light, not our darkness that most frightens us. We ask ourselves—Who am I to be brilliant, gorgeous, talented, and fabulous? Actually, who are we not to be? You are a child of God. Your playing small does not serve the world. There is nothing enlightened about shrinking so that other people do not feel insecure around you. We were born to manifest the Glory of God that is within us. It is not just in some of us, it is in everyone. And as we let our light shine, we unconsciously give other people permission to do the same. As we are liberated from our own fears, our presence automatically liberates others.&quot;</td>
</tr>
<tr>
<td>2</td>
<td>Add a role play on refusing unsafe sex to address this practice within the church setting to enhance relevance to the population</td>
<td>Ask SISTA in service: Last Sunday, I met a man during “passing the peace” (welcoming hugs). While we were hugging, he kissed me on my neck and he touched my bottom. When we sat down, he passed me a note asking me to step out in the hall for a minute. He walked me to an unused classroom, and we started kissing; he wanted to have sex, but I didn’t have any condoms. I didn’t want to ruin the moment, so I had sex with him. He says he wants to “hook up again.” What do I say?</td>
</tr>
<tr>
<td></td>
<td>Add examples of excuses that men say to women who go to church and comebacks that women can use to facilitate negotiating safer sex</td>
<td>Excuse: God will understand if we do it just once. He’s the one that put this sexual desire in us in the first place. Comeback: Yes, God put the desire in us, but he also told us when to use the desire. Excuse: The Bible says to be fruitful and multiply. Don’t you want to have my baby? Comeback: Yes, however, the commandment was given to married couples. Excuse: You know you are the one I’m going to marry, so it is okay to start now. Comeback: The man that I marry would not pressure me to be doing something that is against what I stand for.</td>
</tr>
<tr>
<td></td>
<td>Add text on monogamy and abstinence to enhance HIV prevention messages relevant to church values</td>
<td>Added more text discussing the importance of the participant and her partner being monogamous (eg, reducing concurrency) and selecting abstinence as an HIV risk-reduction option.</td>
</tr>
<tr>
<td>Core elements</td>
<td>The core elements of SISTA are to (1) conduct small group sessions to discuss the session objectives, model skills development, role play women’s skills acquisition, and address the challenges and joys of being an African-American woman; (2) utilize skilled facilitators to implement group sessions; (3) utilize cultural- and gender-appropriate materials to acknowledge pride and enhance self-worth; (4) train women in sexual assertion skills so that they can demonstrate care for partners and negotiate safe behaviors; (5) teach women proper condom use and foster positive attitudes and norms toward consistent condom use; (6) discuss cultural and gendered triggers that may make it challenging for women to negotiate safer sex and the importance of partner involvement in safer sex; and (7) emphasize the importance of partner involvement in safer sex.</td>
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</table>
be adapted to fit the risk factors, behavioral determinants, and risk behaviors of the new target population and the specific circumstances of the agency and key stakeholders. Because adaptation can be a complex process, developing an adaptation plan can assist in documentation of the elaborate process of adapting an EBI. Thus, producing an adaptation plan addresses the questions of why the content and/or materials were adapted and what has been adapted. The adaptation plan provides for a transparent and verifiable adaptation process.

Additionally, during this phase, the agency needs to decide whether the goal of adaptation is to produce a successfully adapted EBI for the new target population or to test whether the adapted EBI produces changes in theoretically important HIV prevention mediators and behavioral outcomes. If the goal of adaptation is to assess the effect of the adapted EBI on mediators and behavioral outcomes, the agency should develop quality assurance procedures and process evaluation measures. These measures are used to monitor the quality and assess the fidelity of recruitment efforts, intervention delivery (ie, fidelity), survey administration, and informed consent activities (if required).

Phase 5, Topical Experts, involves identifying consultants who possess significant expertise in substantive content areas, relevant to draft 1 of the adapted EBI, for which the agency perceives a lack of expertise. Prior research on adapting EBIs has found that consultations and technical assistance greatly facilitate the adaptation process. Often, but not always, agencies lack a particular area of expertise that is critical to the adaptation of an existing EBI. For example, if theater testing identified “substance abuse prevention” or “the need to adapt an EBI for a different ethnic group or gender” and the agency does not have this requisite expertise, the agency would attempt to identify experts who could serve as consultants to provide specific content expertise.

Phase 6, Integration, involves integrating content provided by the topical experts into the adapted EBI. The integration of content from the topical experts results in a second draft (draft 2) of the adapted EBI. Integration of intervention content suggested by the topical experts is weighed by prioritizing the capacity of the agency to implement the suggested adaptation and by maintaining fidelity to the core elements and theoretic underpinnings of the original EBI. Additionally, topical experts may provide measures for the study survey that are valid, reliable, and culturally appropriate for the new target population. Finally, readability testing is integrated into the adapted EBI to create a third draft (draft 3) of the adapted EBI. Utilizing the Flesch-Kincaid Readability Test, a computerized formulaic assessment of the grade level of reading skill that would be required to comprehend the adapted EBI session activities can assist in gauging readability of the adapted EBI materials. Tailoring the adapted EBI’s content to a fifth-grade reading level may increase comprehension of the EBI, facilitate its use, and, as a consequence, enhance its efficacy.

Phase 7, Training, involves training personnel, including: (1) facilitators in group management and facilitation skills, (2) recruiters and retention staff in effective recruitment and retention techniques, (3) assessment staff in administering the study assessments, and (4) data management staff in managing the study data. Additionally, topical experts may be actively involved in training facilitators on material they have contributed to the adapted EBI.

Phase 8, Testing, involves 2 discrete steps. The first step involves conducting a pilot test with approximately 20 participants from the new target population of draft 3 of the adapted EBI. The CDC’s adaptation process has also identified pilot testing as a key step in the adaptation process. The pilot test serves as a “dress rehearsal” during which the agency uses trained staff to implement the adapted EBI. At the end of each session, participants complete exit interviews designed to solicit feedback about whether they think the intervention content, materials, and delivery are relevant, useful, and appropriate. At the end of each session, feedback is also solicited from key stakeholders and agency staff who observed the implementation of the adapted EBI. Thus, the first step of the testing phase assesses “adaptation efficacy” by answering the question of how successful the original EBI adapted for the new target population was. Analyzing the data from this step

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**TABLE 4. Applying the ADAPT-ITT Model to Adapt the SiHLE\(^5\) Intervention to Zulu-Speaking Female Adolescents**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Methodology</th>
</tr>
</thead>
</table>
| 1. Assessment  | ● Conducted focus groups with young adult Zulu-speaking women  
|                | ● Conducted focus groups with key stakeholders in a rural primary care clinic in KwaZulu-Natal  
|                | ● Conducted elicitation interviews with key stakeholders who were HIV/AIDS prevention scientists  
|                | ● Analyzed results of formative evaluations  |
| 2. Decision    | ● Decided to adapt the SiHLE HIV intervention defined as an EBI by the CDC\(^5\)  |
| 3. Administration | ● Administered theater test with Zulu adolescents  
|                | ● Analyzed results of the theater test  |
| 4. Production  | ● Produced draft 1 of the adapted EBI and developed process measures  |
| 5. Topical Experts | ● Identified 3 topical experts knowledgeable about HIV prevention and the population of Zulu-speaking adolescents living in KwaZulu-Natal, the target audience for intervention  |
| 6. Integration | ● Integrated content from topical experts and created draft 2 of the adapted EBI  
|                | ● Integrated scales that measure new intervention content in the study survey  
|                | ● Integrated readability testing into draft 2 of the EBI to create draft 3  |
| 7. Training    | ● Trained recruiters, facilitators, assessors and data management staff to implement draft 3 of the adapted EBI  |
| 8. Testing     | ● Pilot study is being planned  |

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Adapting Evidence-Based HIV Interventions

Unique and Salient Features of the ADAPT-ITT Model

Although other adaptation models have been designed and proven valuable, the ADAPT-ITT model has several unique and salient features that should be highlighted. Specifically, throughout the adaptation process, the ADAPT-ITT model (1) directly involves members of the new target population, key stakeholders, and agency staff from the initial phase to the last phase; (2) triangulates diverse measures by using numerous qualitative assessments (ie, formative and process measures) and quantitative assessments (ie, theater tests, pilot study pretest/posttest surveys); (3) uses multiple and novel pretesting methodologies, including didactic (ie, focus group, elicitation interviews), action-oriented (ie, theater testing), and computer-based (ie, readability testing) technology, to indicate what needs to be adapted and how adaptation should proceed; (4) attempts to promote a balance between fidelity and adaptation; (5) uses topical experts to assist in creating the adapted intervention; (6) prescriptively indicates when during the adaptation process a draft of the adapted EBI is to be generated and the number of drafts of the EBI that are to be created; (7) facilitates the documentation necessary for efficient adaptation (eg, the adaptation plan); (8) indicates the sources of data (eg, focus group, theater test, exit interviews, pilot study, phase 2 study) that need to be analyzed, which facilitates data analysis; (9) uses a sequential and systematic process to create an adapted intervention; (10) assess adaptation efficacy of the adapted EBI by means of a pilot study; and (11) assesses short-term outcome efficacy of the adapted EBI by means of a phase 2b study. Table 1 summarizes the ADAPT-ITT model.

CONCLUSIONS

Diversity cautions against transferring public health strategies and interventions from one local to another or from one population to another without attention to the social environment. Using methodologically appropriate tools that

<table>
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<tr>
<th>Session</th>
<th>Aim of Activity</th>
<th>Examples of Modified Text and New Activities</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Modify activity on strong African-American women to enhance ethnic pride in South African female teens</td>
<td>Include strong South African women, such as Albertina Sisulu, Miriam Makeba, and Yvonne Chaka Chaka</td>
</tr>
<tr>
<td>1</td>
<td>Modify study pact to be more reflective of participants’ collective lives</td>
<td>Modified the existing prewriten pact and had participants create their own pact as a group and sign it together on poster paper to reflect their more communal lives</td>
</tr>
<tr>
<td>1</td>
<td>Modify “Values Clarification” activity to be more reflective of the participants’ holistic perspective</td>
<td>Participants developed a “tree of life” that illustrated their personal values, support systems, and goals. This activity began in session 1 and was discussed in all 4 sessions.</td>
</tr>
<tr>
<td>2</td>
<td>Modify myths about HIV to address myths prevalent among Zulu female teens</td>
<td>Discuss availability of free sexually transmitted disease testing and treatment; the availability of free HIV testing and antiretroviral drugs; and the role of traditional healers, nurses, and medical doctors</td>
</tr>
<tr>
<td>3</td>
<td>Add examples of excuses that Zulu boys/men say to female teens and comebacks that teens can use to facilitate negotiating safer sex</td>
<td>Participants demonstrated self-efficacy in condom application and condom negotiation skills through the use of more creative mechanisms, such as skits, singing, and dancing</td>
</tr>
<tr>
<td>4</td>
<td>Add condom use and negotiation role plays that use singing and dancing to reflect creativity of participants’ lives</td>
<td>The core elements of SiHLE are to (1) conduct small group sessions to discuss the session objectives, model skills development, role play women’s skills acquisition, and address the challenges and joys of being an African-American female teen; (2) utilize a skilled adult educator and a peer educator (teen) to implement group sessions; (3) utilize cultural- and gender-appropriate materials to acknowledge pride and enhance self-worth; (4) train teens in sexual assertion skills so that they can demonstrate care for partners and negotiate safe behaviors; (5) teach adolescents proper condom use and foster positive attitudes and norms toward consistent condom use; (6) discuss cultural and gendered triggers that may make it challenging for adolescents to negotiate safer sex and the importance of partner involvement in safer sex; and (7) emphasize the importance of partner involvement in safer sex.</td>
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TABLE 5. Adaptation Plan for Adapting the SiHLE5 Intervention to Zulu-Speaking Female Adolescents

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are based on sound scientific practice, are culturally congruent, and include the target population can be beneficial, however. This article offers an approach to adapting EBIs, and it implementation could provide an efficient mechanism of designing culturally sensitive and efficacious HIV interventions.

REFERENCES


APPENDIX

Case Study 1: Traditionally, African-American faith-based institutions have been instrumental in addressing social issues confronting African Americans. The involvement of faith-based institutions in HIV prevention has the potential to influence an individual’s norms, attitudes, and perceptions supportive of risk-reduction practices. A partnership has been formed between the Emory University Rollins School of Public Health and a nondenominational megachurch and its satellite churches in Atlanta. The goal of this unique partnership is to develop a “faith-based HIV intervention” for young adult African-American women. The 5 counties in which the churches are located have the highest proportion of HIV and AIDS cases relative to the rest of Georgia, thus indicating the population’s vulnerability to HIV. Over a 3-month period, we observed the implementation process and also provided feedback on how to adapt the interventions. While the original EBI was being implemented to participants, key stakeholders observed the implementation process and also provided feedback on how to adapt the intervention. After these activities, biweekly conference calls were initiated to create an adaptation plan (Table 3), to collate the suggestions from the theater test, and to integrate the ideas of the topical experts knowledgeable about HIV prevention for African-American women and the culture of the church. A 3-session adapted curriculum has been developed, and we are in the process of pilot testing the adapted intervention.

Case Study 2: More than 70% of women and girls infected with HIV live in sub-Saharan Africa. Studies of HIV acquisition throughout sub-Saharan Africa show sharply increasing prevalence in women during the teenage years. Des Wingood and DiClemente are collaborating with scientists from the Nelson Mandela School of Medicine to adapt the EBI known as SIHLE for Zulu-speaking female adolescents residing in KwaZulu-Natal, South Africa. With discretionary funds from the HIV Prevention Trials Network (HPTN), a meeting was held focusing on adapting the SIHLE intervention to enhance its relevance for female adolescents in KwaZulu-Natal, South Africa. Over a 4-month period, the adaptation team proceeded to adapt the EBI known as SIHLE using the ADAPT-ITT model (Table 2). In accordance with the ADAPT-ITT model, the adaptation team first conducted focus groups with adolescents and key community stakeholders and elicitation interviews with HIV prevention scientists in KwaZulu-Natal. Subsequently, as part of a theater test, over a 2-day period, the original EBI was administered to 15 African-American women, aged 18 to 29 years, who attend the megachurch. Participants provided feedback on activities that needed to be adapted and direction on how to adapt the activities. While the original EBI was being implemented to participants, key stakeholders observed the implementation process and also provided feedback on how to adapt the intervention. After these activities, biweekly conference calls were initiated to create an adaptation plan (Table 3), to collate the suggestions from the theater test, and to integrate the ideas of the topical experts knowledgeable about HIV prevention for African-American women and the culture of the church. A 3-session adapted curriculum has been developed, and we are in the process of pilot testing the adapted intervention.

CONCLUSION

Future Directions for HIV Prevention Research
Charting a Prevention Science Research Agenda
Ralph J. DiClemente, PhD,*† Gina M. Wingood, ScD, MPH,*† Michael B. Blank, PhD,‡§ and David S. Metzger, PhD‡§

Globally, the HIV epidemic continues to exact a substantial toll on the health and well-being of many, causing considerable morbidity and mortality as well as significant disruption to the social and economic infrastructure of severely impacted countries. The HIV epidemic exploits and amplifies existing social and economic disparities in many parts of the globe, particularly in sub-Saharan Africa.1 Productivity has been adversely affected, and national revenues have and may continue to decline. HIV is undermining human capacity and, through early death and prolonged illness of key segments of the workforce, is incapacitating systems, making attempts at improving governance increasingly challenging. The net effect is institutional fragility and a downward spiral of reduced state capacity, creating an environment that, unfortunately, further exacerbates the HIV epidemic.

The scope of the HIV epidemic is daunting. Since the first cases of AIDS were reported in 1981, infection with HIV has grown to pandemic proportions, resulting in an estimated 65 million infections and 25 million deaths.1 During 2005 alone, an estimated 2.8 million persons died from AIDS, 4.1 million were newly infected with HIV, and 38.6 million were living with HIV. HIV continues to disproportionately affect certain geographic regions (eg, sub-Saharan Africa, the Caribbean) and subpopulations (eg, women in sub-Saharan Africa, men who have sex with men [MSM], injection drug users [IDUs], sex workers). Although effective prevention and treatment of HIV infection with highly active antiretroviral therapy (HAART) are now available, even in countries with limited resources, there remains an urgent need to develop comprehensive programs and expand access to reach all persons who require treatment and prevention services.

At the core of the HIV epidemic is “behavior.” Although HIV is the etiologic agent associated with AIDS, it is people’s behavior, or rather the lack of appropriate HIV-preventive behavior, that propels the epidemic. However, HIV-associated risk behavior is not random, uncontrollable, or inevitable. Indeed, HIV-associated risk behavior is modifiable. Whether the behavior in question is condom use, reducing the number of sexual partners, cleaning IDU equipment, or adherence to HAART, it is behavior that is the root cause of the epidemic and it is that behavior that must be modified to stem the epidemic.

Currently, correct and consistent condom use is one of most efficacious methods for the prevention of sexually transmitted HIV. New biomedical interventions for HIV prevention, such as prophylactic microbicides, pre-exposure prophylaxis (PrEP), suppression of genital herpes (herpes simplex virus-2 [HSV-2]), and cervical barriers, are in various stages of development and evaluation. Underlying all these prevention approaches is behavior, with behavioral and biomedical approaches requiring the adoption and maintenance of HIV prevention strategies over protracted periods of time. As new biomedical prevention technologies are developed, however, social/behavioral science needs to be integrated with biomedical science to understand acceptance, adoption, and adherence to these technologies better and to address such concerns as condom migration, behavioral disinhibition, partial...
efficacy of the technologies, and access to these technologies should they be efficacious in reducing HIV infection. Indeed, even the advent of an effective prophylactic microbicide for men or women would not be optimally efficacious without adherence. Thus, social/behavioral scientists and biomedical scientists need to collaborate to enhance HIV-preventive behaviors, whether that behavior is condom use, adherence to HAART, adherence to microbicide use, or acceptance of an HIV vaccine.

As the HIV epidemic continues to evolve, so too must we as social and behavioral scientists evolve our thinking, our research, our interventions, and our methodologies to confront this epidemic. In this issue, we report a series of publications that emerged from the First Social and Behavioral Sciences Research Network (SBSRN) Conference held in Philadelphia in October 2006. The SBSRN conference was designed to create an infrastructure for social/behavioral scientists and biomedical scientists to interact in a collegial environment with the endpoint being the exchange of topical and relevant information and the formation of research ideas and interdisciplinary research teams. By marshaling new data, we hope to address new research questions, create new opportunities for interdisciplinary collaboration, and utilize more efficiently limited existing resources.

The articles presented in this issue reflect the collaborative exchange of ideas in task groups. They address emergent issues that are critical for confronting the HIV epidemic. They do not, however, represent an exhaustive portfolio of topic areas for HIV prevention. That would be beyond the scope of this supplement. Moreover, rather than attempt to recapitulate these articles, our goal is to highlight key recommendations for future HIV prevention research.

RECOMMENDATIONS
1. Enhance support for developing and evaluating mentoring models, whereby social/behavioral and biomedical scientists collaborate in providing interdisciplinary training and support to nurture the next generation of HIV prevention scientists.
2. Enhance support for developing much needed tools in the area of HIV prevention, including user-friendly automated computer software packages to enhance the standardization and collection of cost data and mathematic modeling to examine the effects of a diverse array of determinants on HIV transmission dynamics.
3. Enhance support for developing models that guide the adaptation of evidence-based HIV interventions and promote the development of phase 4 HIV prevention effectiveness trials to facilitate quantization of an intervention’s "true" public health benefit.
4. Enhance support for understanding HIV risk among understudied populations, such as African-American men, and for examining barriers to providing integrated services for populations, such as doubly and triply diagnosed patients with HIV/substance abuse/mental illness.
5. Enhance support for collaborative research designed to examine and reduce health disparities that fuel the HIV epidemic.
6. Enhance support to foster collaboration between social/behavioral and biomedical scientists in the development, implementation, and evaluation of biomedical HIV prevention approaches.

CONCLUSIONS
The challenge of preventing HIV is formidable. Our experience over the past 2 decades has shown that the HIV epidemic continues to evolve, is relentless, and is devastating from an individual and societal perspective. The SBSRN conference and the articles spawned from that conference represent an attempt to capitalize on the interdisciplinary collaboration of prevention scientists to accelerate innovation in the field of HIV prevention. Although the research agenda charted through our recommendations are not exhaustive, they do reflect critical gaps in the field. Addressing these gaps through the development of targeted research programs requires mobilizing support for the allocation of resources to countenance these critical issues adequately. Without adequate resources to conceptualize, stimulate, and support the HIV prevention agenda further, we miss an opportunity to advance the science of HIV prevention significantly and, more importantly, to have an impact on the HIV epidemic.

REFERENCE