Proceedings of the National Roundtable on Evaluation of Multilevel/Combination HIV Prevention Interventions

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Summary & Recommendations

The National Roundtable on Evaluation of Multilevel/Combination HIV Prevention Interventions had the goals of examining the present state of the art of multilevel and combination HIV prevention interventions, both domestically and internationally; to define the significant challenges and scientific gaps in current evaluation methods and identify the most promising methodological approaches to address these gaps; and to guide the future agenda for HIV prevention research.

To address these methodological gaps, we must combine the methodological and statistical rigor associated with clinical trials, the conceptual framework of implementation science, the on-the-ground strategies of programmatic monitoring and evaluation, and the strengths of pre- and post-intervention mathematical modeling.

In looking at the HIV epidemic in the US, the group discussed current initiatives guided by the National HIV/AIDS Strategy and the increased optimism over treatment as prevention. We noted that considerable progress has been made in developing core metrics to evaluate outcomes along the “treatment-as-prevention cascade” that could be captured through public health surveillance—number of new HIV cases detected and proportion linked to care, retained in care, on active treatment, and virally suppressed. Our understanding of the optimum package of interventions with regard to both effectiveness and efficiency remains incomplete. Progress was reported, however, in the collection of process data at the local level to better assess how to improve programs. Devising epidemic impact measures to quantify reductions in HIV incidence attributable to combination interventions remains challenging, mostly due to barriers to testing impact through methods like community cluster randomization in the US.

Looking globally, the group discussed a number of planned clinical trials of combination interventions also spurred by optimism over treatment as prevention. Common elements of combination approaches included expansion of voluntary counseling and testing, adult male circumcision, prevention of mother-to-child transmission, and management of sexually transmitted infections, along with expanding ART treatment. Outcome measures were generally framed in terms of the treatment-as-prevention cascade, though these data are not available from current surveillance systems, pointing to the need to create improved systems of data collection. The most common approach to measuring epidemic impact was clustered community randomization, with incident infections measured through cohorts or newer cross-sectional, multi-assay algorithms.

Recommendations from the roundtable include the following:

- A new coalition of interventionists, implementation scientists, public health program and surveillance specialists, mathematical modelers, and behavioral scientists is needed to adequately address the evaluation of multilevel/combination HIV interventions at the community-level.
- The use of the conceptual frameworks of the HIV prevention continuum and engagement-in-HIV-care cascade should be used in structuring evaluation of combination HIV interventions.
- Common public health surveillance systems to evaluate combination HIV prevention interventions at the community level are recommended, and this capacity should be further developed internationally.
- Mathematical modeling before, during, and after multilevel/combination HIV interventions should be incorporated in the design, implementation, and interpretation of intervention results.
- Because an emphasis on efficiency as well as effectiveness from implementation science is helpful, costing and cost-effectiveness evaluations of combination HIV prevention interventions are recommended and are important to policy makers.
- Use of innovative trial and observational study designs outside of the traditional randomized, controlled trial paradigm should be used to account for the complex multilevel and combination nature of new HIV prevention interventions, and emerging design and analysis methods (e.g., stepped-wedge designs, adaptive trial designs, causal inference modeling of “natural experiments”) should be considered to address the challenges of community-level effectiveness evaluation.
- Because social factors and human behaviors are integral factors all along the HIV care and treatment cascade, it is crucial to include social and behavioral science in the design, implementation, and evaluation of combination interventions (e.g., community engagement and mobilization interventions).
- Mixed methods, including qualitative data collection (e.g., key informant interviews with implementers, in-depth interviews with target population members), are recommended to increase our understanding of how and why interventions are successful or not.
- Increased funding opportunities for methods development, whether as stand-alone projects or as supplements to large trials, is recommended as is funding for career development in methods research (e.g., methods-focused K awards).

Introduction and Background

In May 2012, the Center for AIDS Prevention Studies (CAPS) hosted a National Roundtable on Evaluation of Multilevel/Combination HIV Prevention Interventions. The agenda for the meeting and a list of expert participants are included in the Appendix.

The goals of this meeting were to examine the present state of the art of multilevel and combination HIV prevention interventions, both domestically and internationally; to define the significant challenges and scientific gaps in our current evaluation methods; to identify the most promising innovative approaches to addressing these gaps; and to guide the future research agenda for evaluation methods.

This monograph summarizes presentations and discussions during the meeting, identifying areas of agreement and divergence of opinion, and provides a set of recommendations to guide future research.

The roundtable was structured around topical panels over two days, each followed by a facilitated discussion among panelists with questions and comments from expert participants.

- **National Approaches**—looked at current studies and core components of multilevel/combination approaches to HIV prevention; identified process, outcome, and impact measures being used and shared challenges to population-based impact evaluation in the US.
- **IOM Recommendations**—in the context of recent IOM recommendations on monitoring HIV care in the US, explored the recommendations as a potential impact evaluation framework for multilevel/combination HIV prevention in the US.
- **International Approaches**—described core components of several international multilevel/combination approaches to HIV prevention and their process, outcome, and impact measures; and defined some of the challenges to population-based impact evaluation in developing countries.
- **Developing a Framework for International Impact Evaluation: Indicators and Data Systems**—discussions were initiated to explore the potential for a parallel framework to the IOM approach for impact evaluation in developing countries.
- **Economics, Sustainability, and Policy**—the role of cost in impact evaluation and implementation decision-making was presented, as well as issues of sustainability and ethics in multilevel/combination prevention studies in developing countries.

- **Future Directions for Impact Evaluation**—promising statistical approaches for impact evaluation of multilevel/combination HIV prevention interventions were identified.

The Promise of Combination and Multilevel Prevention

In the early era of the HIV/AIDS epidemic, advances in prevention were painfully slow.[1] There were no proven biomedical interventions, and many behavioral prevention programs focused on isolated approaches to changing individual behaviors; the social, economic, and political environments in which populations negotiate behaviors were not central to interventions or to policy. Two major shifts took place over the past several years. The first is the availability of new biomedical approaches: landmark trials have demonstrated the efficacy of providing antiretroviral therapy (ART) to prevent transmission to uninfected partners[2, 3] and ART to high-risk, HIV-negative individuals to prevent acquisition of the virus.[4, 5] The provision of "treatment as prevention" and medical male circumcision now offer effective biomedical approaches to prevention.

The second shift was that of the prevention paradigm, with growing consensus recognizing that HIV prevention programs that operate in isolation and fail to modify the social and structural context or address the multiple factors that influence an individual's behavior will fail to bring about sustained prevention.[6-12] Addressing the larger social and structural context in communities while simultaneously offering powerful integrated biomedical and behavioral strategies to individuals and their partners and families can produce what was coined "highly active" prevention.[12] Renewed hope around combination prevention is great.

Methodological Challenges for Evaluation of Combination Prevention

Programs based on synergies of multiple components, particularly those interventions that aim to change structures and environments using multilevel prevention, are difficult to design, implement, and evaluate.[14-16] The historical "gold standard" of community randomized controlled trials (cRCTs) combining community-based interventions with biomedical and behavioral approaches is logistically challenging, time-consuming to set up and implement, and generally quite expensive. As a result, there have been few experimental trials of multilevel and combination prevention interventions. Moreover, communities with elevated HIV prevalence and incidence often cannot wait for a randomized trial to be conducted in their communities; this has resulted in community-inspired combination prevention strategies with little empirical backing. Despite the uncontrolled settings of many such efforts, much can be learned from them through observational or partially controlled study designs, especially important in an era of limited economic resources to fund large cluster randomized trials. While observational research is often considered a less rigorous alternative to the randomized trial, observational and partially controlled designs have potential to evaluate HIV prevention programs and measure the magnitude of their effects and synergies in their natural environments. Thus, we see a need to explore novel study designs to move our community-level evaluation methods forward.

Common Definitions

As a common starting point, we summarized existing definitions in the literature for multilevel and combination prevention, terms that are used interchangeably at times, but which have different origins.

- **Multilevel Interventions.** The multilevel prevention framework has roots in the "ecological model," borrowed from Bronfenbrenner's work in human ecology.[17] This model understands the individual as embedded in societal, community, familial, and peer contexts and posits that behavior is shaped by economic, political, and social structures; sociocultural contexts; and social relationships in which people negotiate behaviors (e.g., condom use, partnerships, health care utilization). As a result, multilevel interventions aim to address the multiple levels that influence an individual; these include interpersonal processes, community factors, institutional factors, and other structural or sociocultural factors and processes together.[10]

- **Combination Prevention.** Combination prevention implies delivery of a package of complementary, evidence-based strategies offered together, because no single intervention strategy is sufficient to stem the spread of HIV. Offering intervention components in combination increases the likelihood of meeting the needs of a diverse population (with varied approaches) and improves the potential to increase potency of the approaches due to components' synergy (e.g., enhanced counseling may increase the effectiveness of pre-exposure prophylaxis).

  Discussions of combination prevention specify that the combined intervention approaches should include complementary behavioral, biomedical, and structural strategies and ideally should target each recognized level of influence (e.g., couples, families, social and sexual networks, communities, society).[12, 18] UNAIDS also contends that combination interventions should be "rights-based [and] community-owned" and should "mobilize community, private sector, government and global resources in a collective undertaking; require and benefit from enhanced partnership and coordination; and the incorporate mechanisms for learning, capacity building and flexibility to permit continual improvement and adaptation to the changing environment."[19]

  In practice, individual-level combination prevention programs typically include behavioral and biomedical strategies but are less likely to include community- or structural-level components or components aimed to change community contexts, social norms, or structures. This is usually attributed to the relative difficulty in demonstrating efficacy of social and structural interventions as compared to behavioral or biomedical interventions. Without RCT-backed evidence for social-structural approaches (e.g., changing gender norms and adjusting social policies), these components are often excluded.

- **Comprehensive Prevention.** A third term, “comprehensive prevention,” has been used by CDC and PEPFAR programs and denotes scaled (state or national) biomedical, behavioral, and structural strategies that focus on strengthening health systems for sustained and integrated programming targeting the specific needs of priority populations. Like combination prevention, these programs are predicated on the idea that no single intervention is efficacious enough to bring an HIV epidemic under control. Comprehensive prevention programs often include a broad range of programmatic actions and integrated efforts (e.g., scaled and integrated programs for male medical circumcision, voluntary HIV counseling and testing, prevention with positives, community engagement, capacity building in the health sector).[20]

Conceptual Frameworks

For many years HIV prevention was conceptualized as comprising behavior-change interventions focused on high-risk, HIV-negative individuals. Treatment programs were directed at HIV-diagnosed individuals. Prevention and treatment goals were supported by separate funding streams, which often led to difficult discussions over budget priorities. To a large extent, the evolving idea of *treatment as prevention* has lessened these conflicts.

In facing the challenges of evaluating multilevel and combination HIV prevention interventions, a continual evolution of suggested frameworks has developed to conceptualize and assess prevention activities. Figure 1 presents how prevention intervention scientists have conceptualized the HIV prevention continuum.[21]

Figure 1. HIV Prevention Continuum

<table>
<tr><td rowspan="5">Potential Interventions</td><td colspan="8">Positive Policy Environment</td></tr>
<tr><td colspan="8">Prevention Social Marketing and Condom Availability</td></tr>
<tr><td colspan="5">Test</td><td colspan="3">and Treat</td></tr>
<tr><td colspan="4">Community-Based Outreach & Mobilization</td><td colspan="4">Clinic-Based Prevention with Positives</td></tr>
<tr><td>Public Education/ Routine Testing</td><td>Targeted Community-Level</td><td>Acute Detection & Awareness</td><td>Linkage to Care</td><td>Tx Engagement</td><td colspan="3">Tx Monitoring, Adherence, Retention in Care & Stigma Reduction</td></tr>
<tr><td>Prevention Opportunities</td><td>General Population</td><td>At-Risk HIV(-)</td><td>Acute/Newly Infected</td><td>Unknown Status HIV(+)</td><td>Tx Eligible, Not Rx'd</td><td>HIV(+) Not Tx Eligible</td><td>Rx'd Non-AIDS</td><td>Rx'd AIDS</td></tr>
</table>

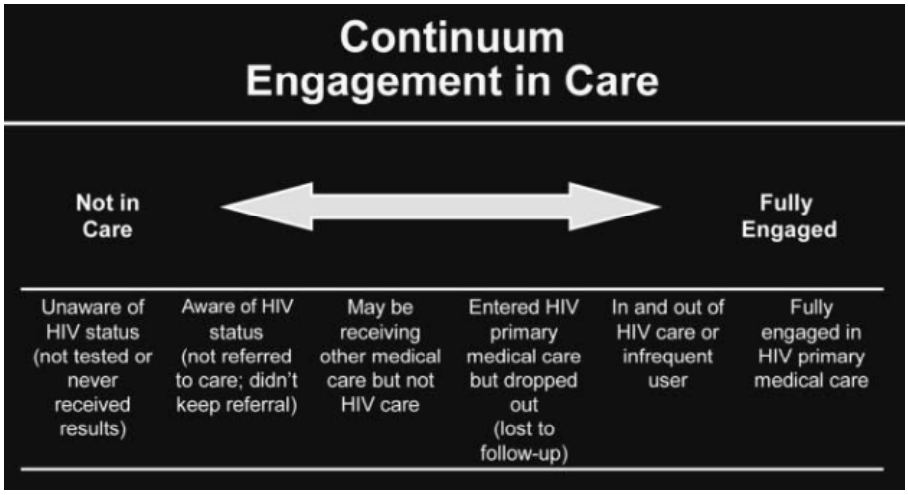
From a behavioral science prevention perspective, it has been important to focus at least some effort on the general population, both because of the significance of HIV as a public health challenge and to reduce the impact of stigma directed at HIV-infected persons. It has also been important to direct intervention at groups with increased risk of HIV infection, in particular men who have sex with men (MSM) and injection drug users (IDUs). Three strategies have proven important: First, the promotion of barrier protection, i.e., male and female condoms—FDA-approved devices—where the behavioral goal is to consistently use the products; second, the availability and use of safer injection materials such as sterile needle exchange for IDUs; and third, increasing awareness of HIV status through HIV antibody testing—again, an FDA-approved

diagnostic—as studies have demonstrated significant reductions in HIV transmission risk behaviors among those who test positive.

More recently our appreciation of the importance of acute HIV infection has led to the development of both screening programs for acute HIV infection—nucleic acid amplification testing (NAAT)—as well as counseling and public information campaigns around acute and early-phase HIV infection and infectiousness to others. Prevention scientists have also focused increased attention on strategies to improve HIV detection by increasing testing availability, frequency, and acceptability in specific groups and geographic locations. In addition, behavioral scientists have taken the lead in improving health outcomes in HIV-infected persons through ART adherence counseling, screening and treatment for HIV comorbidities such as poor mental health and substance abuse, and addressing structural and sociocultural drivers of health behaviors.

Understanding the importance of decreasing infectiousness in HIV-infected individuals to reducing rates of new HIV infections, both at the individual level and within the community, there is increased attention on the *engagement in care spectrum*, or the *HIV care continuum* (see Figure 2).[22]

Figure 2. HIV Care Continuum



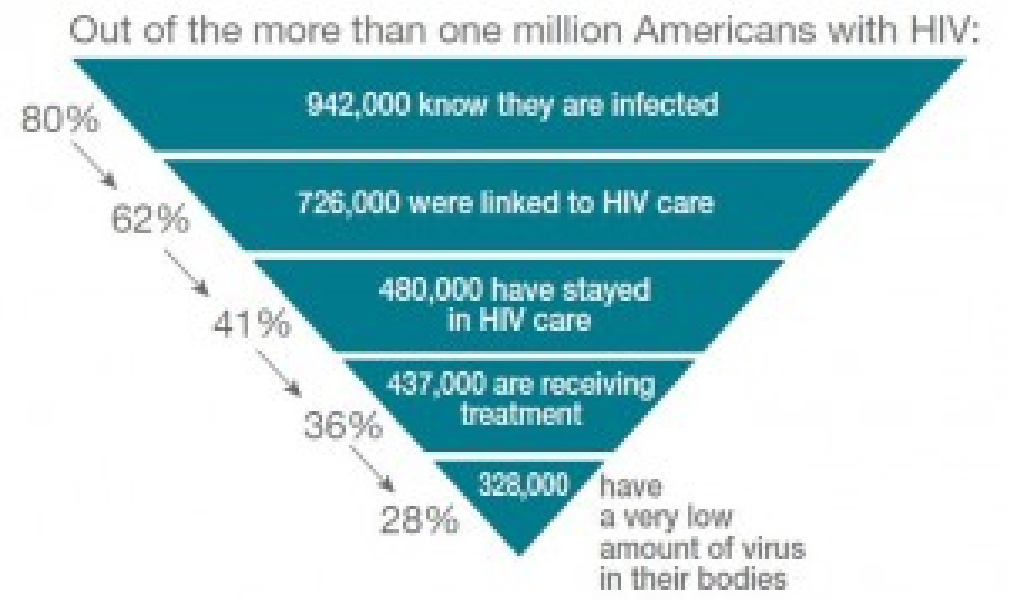
A recently released Institute of Medicine (IOM) report on indicators for care and treatment focused on the continuum of care as a framework for evaluation.[23] The IOM report recommended 14 core indicator measures across the HIV care continuum, with 9 indicators of clinical HIV care and 5 indicators for mental health, substance abuse, and supportive services. The report identified 15 additional indices to assess care quality.

The steps outlined in the HIV care continuum have been used to guide development of intervention and evaluation components. While providing a useful framework, it is important to keep in mind that focus on the care continuum disregards prevention efforts

that take place prior to HIV infection and fails to address the behavioral, societal, and community drivers of the epidemic.

The CDC has published estimates of individuals at various points along an HIV care cascade indicating that approximately 28% of all HIV-infected individuals in the US are virologically suppressed (see Figure 3).[24] Increasing emphasis on implementation issues within the HIV care continuum has focused on assessing significant gaps in the continuum and has generated an increase in care cascade–related research.

Figure 3. HIV Care Cascade



National Approaches

To better understand current research on national approaches to multilevel/combination HIV prevention interventions, the roundtable reviewed three current US studies and their core components. For each study we identified primary HIV outcomes, process and impact measures being used, and challenges to population-based impact evaluation (see Table 1). The three studies reviewed are described below.

HPTN-065 is an NIH-sponsored study to evaluate the feasibility of an enhanced *test, link to care, plus treat* (TLC+) approach to HIV prevention in the United States in the Bronx and Washington, DC, with comparison to surveillance data in Philadelphia, Houston, Chicago, and Miami. Its core components include 1) expanded HIV testing, 2) linkage to care, 3) prevention for positives, 4) incentives for viral suppression, and 5) provider and patient attitude–change interventions.

Enhanced Community HIV Prevention Planning (ECHPP) is a CDC-sponsored project designed to support implementation of the National HIV/AIDS Strategy in the 12 metropolitan areas with the highest AIDS burden. Core components for the intervention include 14 required interventions and 12 optional components ranging from expanded HIV testing to policy interventions, linkage to care, prevention with positives, and targeted condom distribution.

Systems Linkages and Access to Care for Populations at High Risk for HIV Infection (SLAC) is a HRSA-funded Special Project of National Significance study of seven state-level interventions designed to improve access to and retention in high-quality HIV care and services for hard-to-reach populations of HIV-infected persons. Core components are individualized to match each state's target populations and cover the domains of HIV testing, linkage to care, retention in care, and enhancement of HIV virologic suppression.

Several common themes and challenges were identified across the national approaches:

Challenges to use of standard randomized, controlled trial (RCT) designs for evaluation of multilevel/combination HIV prevention. Several significant challenges to the use of classic RCT designs to evaluate multilevel/combination HIV prevention trials in the US were noted. Chief among these is the lack of feasibility of implementing randomization at the individual or community-cluster level. Many of the strategies employed in combination HIV prevention are delivered at the community level and preclude individual-level randomization. For cluster-randomized trial designs, the acceptability of community-level randomization is low or the number of communities required far exceeds the available resources or even the total number of available

Table 1: Examples of Combination/Multilevel Interventions in the United States

Study	HPTN-065: TLC+	CDC: ECHPP	HRSA: SLACETAC
Sites	Bronx, Washington DC	12 MSAs highest in HIV burden	7 states
Interventions	Social media campaign and expanded hospital-based testing, financial incentives for linkage and retention (suppressed viral load)	14 required (testing, regulatory, PEP, PMTCT, P4P, partner svcs, behavioral risk reduction, condom distribution), 10 recommended; priority populations (minority, IDU, high-risk hetero, MSM, PLWHA, high risk with neg/unk HIV status)	Improvements in collaboration for linkage and retention, improved data systems, DIS, navigation, corrections, enhanced testing, social network
Design	Observational social mobilization, clinic-randomized linkage and suppression incentives at testing and care sites, individually randomized P4P, cross-sectional surveys for patients and providers, surveillance data	Each MSA determines its mix of interventions	State-specific, cross-region will focus on pre/post comparisons by state
Study N	2 intervention cities, 16 hospitals, 38 testing sites, 39 care sites, 660 (x2 communities) individuals	12 MSAs	7 states, some analysis within state at individual and clinic/community levels
Process measures	HIV tests, ER or admission to hospital, coupons and financial incentives redeemed, visits with suppressed viral load, qualifying visits among qualified patients	Services and programs provided, populations reached, local objectives met, barriers/ facilitators to implementation, distribution of funding across ECHPP activities/priority populations	Practice and patient characteristics and barriers/facilitators to linkage and retention, intervention activities planned and conducted
Outcomes	# newly tested, % linked to care in 3 mos, # previously diagnosed retested out of care, % retested linked to care in 3 mos, #PLWH in care (2 visits in yr), % with last VL<400	Reduction in HIV risk behaviors for priority populations, increase in service access and prevention activities, better health outcomes among HIV+	Testing, linkage, suppression, and retention measures still being developed
Impact/ outcome data sources	HIV surveillance systems	HIV surveillance systems, other federal agency data (HRSA, SAMHSA, CMS, HOPWA), some cities collecting additional data	Surveillance systems, additional data depending on state
Duration	36 mos	3 yrs	4 yrs (first 2 focused on "learning collaborative," second 2 on evaluation)
Study website	www.hptn.org/research_studies/hptn065.asp	www.cdc.gov/hiv/strategy/echpp/index.htm	spnsetac.ucsf.edu/

communities. The identification of an appropriate comparison group also presents a challenge to standard RCT design.

***Utilization of HIV infection surveillance data for impact evaluation*.** This was a common theme among the three national approaches examined. Local, state, and national HIV surveillance systems and electronic medical records were designed primarily for epidemic monitoring and not for evaluation of HIV interventions. One significant limitation of existing surveillance systems is that they track newly reported HIV cases, not necessarily incident HIV infections. On the other hand, surveillance systems can easily measure impact in terms of the proportion of individuals in the care system who are virologically suppressed.

Process measures. One innovation present in the evaluation of these three interventions is the use of an evaluation framework from implementation science focused on process measurements as is typical among programmatic monitoring and evaluation activities. Thus, each of these three studies measures the number of HIV tests performed and various *units of service* delivered for respective components of the combination interventions. These process measures are increasingly critical as we move away from the RCT design into the setting of community-level interventions with significant heterogeneity of intervention dose delivered to individuals and communities. This is key to analyzing and understanding health disparities and the ability of interventions to reduce disparities' effects.

Outcome measures. These three studies were all developed concurrently with the National HIV/AIDS Strategy (NHAS), and two of them (the HRSA and CDC studies) respond to the NHAS directly. The other study, HTPN-065, arose out of the test-and-treat and TLC+ concepts. Not surprisingly, the outcome measures of these three trials reflect gaps in the HIV care cascade. Common outcome elements include new HIV infections detected, proportion linked into HIV-specific care within 90 days, retention in care, proportion on treatment, and proportion with virologic suppression.

Challenges identified. Participants at the meeting identified challenges such as the struggle to harmonize a set of common indicators across surveillance systems and regional, state, and national prevention and treatment programs. Alignment of reporting systems and measures across "silos" and health divisions or departments is essential to improved monitoring and evaluation. This harmonization of metrics includes the need for high-quality indicators of both process and intervention exposure and outcome measures. The lack of common data collection systems and electronic medical records at clinics and within laboratory reporting systems also impedes the ability to find common, comparable metrics. Often unique identifiers are different across systems, making data merges problematic. Some of the barriers to interoperability stem from differences in laws and HIPAA regulations around reportability between jurisdictions.

Common challenges in the development and implementation of interventions largely reflected the lack of harmonization or consensus building across jurisdictions responsible for local programming in terms of program components and delivery. There

is a tension between providing broad principles for programming behavioral, community, and social-structural efforts and the need for local adaptation and flexibility. Adaptation, however necessary, disrupts uniformity, thereby complicating evaluation of the impact of a specific protocol or intervention. Efficacy as established in highly controlled conditions must give way to effectiveness evaluation in real-world community level interventions.

International Approaches

The roundtable group reviewed five international trials and their approaches. Four of the five studies presented were randomized designs, the exception being the Avahan Project in India. A summary of the design, components, and measures used in the international studies presented appears in Table 2. The studies are described below.

NIMH Project Accept (HPTN-043) is a recently completed Phase-III cluster-randomized community trial. The project took place in four countries (Zimbabwe, South Africa, Tanzania, and Thailand). It utilized social science and qualitative ethnography to develop 24 matched pairs of communities of approximately 10,000 persons that were then randomized to receive either standard of care or the combination HIV intervention. Core elements of the intervention consisted of 14 manualized components including community mobilization, increased access to HIV testing (mobile VCT), and post-test support for all testers. One of the methodological innovations used was a one-time, cross-sectional multiassay algorithm to measure HIV incidence.

The Avahan Project started in 2003 and received funding from the Bill and Melinda Gates Foundation. Avahan provided funding and support to targeted HIV prevention programs in the six Indian states having the highest HIV prevalence along the nation's major trucking routes. Avahan-supported programs were targeted toward groups most vulnerable to HIV infection, including sex workers, their clients and partners, high-risk MSM, and IDUs. Key program components included condom and clean needle distribution, peer outreach, STI testing and treatment, risk reduction counseling, community mobilization, stigma reduction, and access to HIV care and treatment.

The PopART Study (HPTN 071) is a three-arm, cluster-randomized, controlled trial to take place in Zambia and South Africa. This 21-cluster study of communities of approximately 30,000–60,000 persons will compare two intervention arms (ART for all HIV-infected persons and ART for those with CD4<350) to standard of care. HIV incidence will be assessed utilizing a cohort design from subjects randomly selected from within cluster communities. At the time of the roundtable, this study was still in the design phase. Core elements of the intervention in addition to ART will include male circumcision for HIV-negatives, counseling and condom provision, enhanced PMTCT, and syndromic STI treatment at clinics.

Table 2A: Examples of Combination/Multilevel Interventions in International Settings – Overview

Study	***HPTN 043: Project Accept***	***Avahan***	***HPTN 071: The PopART Study*** *(protocol not finalized)*	***OGAC: Iringa, Tanzania*** *(protocol not finalized)*	***OGAC: Botswana*** *(protocol not finalized)*
Site(s)	Zimbabwe, Tanzania, South Africa, Thailand	India – 4 southern states, 2 northern states	Zambia and South Africa	Iringa, Tanzania	Botswana
Interventions	Community mobilization to change norms about knowing status; VCT with mobile vans/community settings with same-day results, post-test support for HIV	Large-scale core group intervention to reduce high-risk behavior and increase condom use during commercial sex acts by addressing proximal (through peer-led outreach and education) and distal determinants of HIV risk (through community mobilization, crisis management, national and state-level advocacy)	Arm A/B: Community VCT Arm A: immediate ART offer to all HIV-positive Arm B: ART offer at CD4<350 Arm C: SOC HIV testing and ART Arms A/B/C: Male circumcision for HIV-negative; counseling and condom provision; enhanced PMTCT; syndromic STI treatment at clinic	Enhanced/scaled-up services—HTC, including mobile outreach and enhanced linkage to treatment; MMC, including outreach to older men; increased ART access with treatment at CD4≤350 and point-of-care CD4; scaled-up SBCC; scaled-up MARP outreach and expanded interventions; cash transfer for women aged 15–24	ART for HIV positive individuals with CD4 < 350 cells/ml or AIDS + ART for high viral load (>10,000) + combination prevention that include enhanced HIV testing and counseling, prevention of mother-to-child transmission, enhanced linkage to care in relation to ART initiation and follow-up, and male circumcision
Design	Phase III randomized, controlled trial	Combined approach/enhanced observational study: extensive data collections combined with tailored mathematical models	3-arm, 2-country, cluster-randomized	2-arm, community cluster-randomized, controlled trial (24 clusters: 12 intervention, 12 control)	Two arm with 15 villages receiving SOC and 15 villages receiving intervention.
Study N	24 community pairs (48 communities) randomized to a community-level intervention or comparison condition	Target population of 200,000 FSWs; 82,000 MSM; 5 million clients; 18,000 IDUs	21 clusters (health centre catchment area): 12 in Zambia, 9 in SA, 30–60K in each, with 50% adults; 2,500 adults in each cluster followed after 1 and 2 yrs	12,000 HIV-negative individuals (500/cluster)	30 villages (15 matched pairs)
Duration	36 mos	7 yrs	2 yrs of follow-up	2 yrs of follow-up	4-year period
Study website	www.cbvct.med.ucla.edu/	www.gatesfoundation.org/avahan/Pages/overview.aspx	www.hptn.org/web%20documents/AnnualMeeting2012/Plenary1/03Fidler071Jun25.pdf	www.jhsph.edu/research/centers-and-institutes/research-to-prevention/research-activities/structural.html	www.hsph.harvard.edu/bhp/research/index.html

Table 2B: Examples of Combination/Multilevel Interventions in International Settings – Measures

Study	*HPTN 043: Project Accept*	*Avahan*	*HPTN 071: The PopART Study* (*protocol not finalized*)	*OGAC: Iringa, Tanzania* (*protocol not finalized*)	*OGAC: Botswana* (*protocol not finalized*)
Primary process measures	Utilization data and feedback from community	Monitored quality of Avahan-supported clinics; quality of STI care using simulated patient surveys and refresher training activities; annual condom coverage surveys; 40 core indicators incl. # of STI clinics, DIC, or paid staff, # of peer educators/FSW, # of FSWs registered, # of condoms distributed/FSW	Community HIV provider performance (Arm A/B only); proportion men circumcised; proportion known HIV-infected, linked to care, on ART; magnitude clinic treatment in HIV-infected population; case-cohort studies: refuse HIV testing, not linked to care, refuse ART	Biometrics (fingerprinting at clinics), service delivery snapshots, qualitative research with cohort members (community members and sex workers)	Coverage of: HIV testing and counseling, male circumcision, prevention of mother to child transmission, and ARV linkage to care and adherence
Outcomes	Reduction in HIV incidence; easy community access to VCT; community outreach and mobilization; post-test support as individuals	Trends in commercial sex acts toward consistent condom use; STI/HIV prevalence trends among high-risk groups; HIV incidence/HIV infections averted among HRGs and LRGs over time	Primary: HIV infection in cohort. Secondary: HIV-free survival of children/provision of PMTCT; HIV-related stigma; community viral load; ART drug resistance; prevalence and case notification rates of TB. Impact: population HIV seroincidence in each community; mortality/ morbidity in infants; prevalence of TB	Primary: cumulative HIV incidence at 24 months. Secondary: cost-effectiveness of combination package per HIV infection averted; implementation and utilization of combination HIV prevention. Impact: decrease in HIV incidence at population level; change the course of an HIV epidemic	Primary: viral load, CD4 count, prevalence of TB, drug resistance, adverse events. Impact: HIV incidence in both arms from cohorts (20% of population) followed longitudinally over 4-year period; cross-sectional incidence estimation at end of study
Outcome data sources	Blood specimens, behavioral risk questionnaires, HIV testing rates, HIV testing norms, frequency of HIV discussions in communities, community-level HIV-related stigma	Biobehavioral surveys addressing proximal determinants of HIV risk (STI, condom use) and distal determinants of HIV risk (stigma, violence, barriers to services)	Intervention and control arm study cohort data; incidence measured in a population cohort randomly selected from communities	Survey data of all eligible per household to assess risk/ utilization data with more assessment on subsample; HIV testing; CD4 and viral load at each visit for those who test HIV-positive; additional data collection from cohorts of PLWHA and sex workers, cross sectional survey MSM	Population cohorts in control and intervention communities, cross-sectional incidence estimation at end of study

The Iringa Combination Prevention Study in Tanzania. The Iringa Combination Prevention Study, funded by USAID in 2011, is a large-scale public health evaluation to assess the impact of an integrated set of biomedical, behavioral, and structural prevention interventions on HIV incidence in the Iringa region of Tanzania. At the time of the roundtable, the evaluation protocol and interventions were still in development. The evaluation will consist of a two-armed, cluster-randomized trial of 12,000 HIV-negative individuals in 24 communities. Core components of the program will include HIV counseling and testing, HIV care and treatment, PMTCT, voluntary male circumcision, home-based care, and strategic behavior change communication.

The Botswana Combination Prevention Project. This project, funded by the CDC in 2011, will evaluate the effect of expanding population coverage of an integrated set of HIV prevention interventions on HIV incidence in Botswana. At the time of the roundtable, the protocol and interventions for this project were still in development. The evaluation will include a two-armed, cluster-randomized trial of 20,000 individuals in 30 matched communities. Core intervention components will include enhanced HIV counseling and testing, enhanced voluntary male circumcision, refined PMTCT, improved linkage to care and treatment, and expanded ART to all individuals with viral load greater than 10,000 copies/mL, regardless of CD4 cell count.

Discussion of combination prevention intervention in international settings. An important point of discussion was the tension between prioritizing service delivery and program rollout versus prioritizing RCT designs to answer research questions. The expense and time required for community randomized trials present barriers to their usefulness in making program decisions responsive to changing conditions and new prevention options. Further themes of the discussion of international prevention efforts are summarized below.

Key components of combination/multilevel interventions in international settings. Among the international approaches in the preparatory phase, a general theme of HIV treatment as prevention was present, with elements of the combination approach focused on increased detection of HIV infection and linkage to care, PMTCT, and male circumcision for HIV uninfected males. Another focus is on health services strengthening and workforce development to facilitate the expansion of treatment as a prevention strategy. Engaging social and community support for the combination HIV prevention interventions was a key strategy to be employed in all three cluster-randomized trials. There was also discussion of a planned trial in Eastern Europe where the epidemic among IDUs required intervention to provide clean needles. There appeared to be less general agreement on specific behavioral interventions in the trials being planned, although a clear recognition emerged that adherence and other behavior change were central to the reduction in HIV incidence.

Commonly identified implementation challenges and needs. Discussion of the major challenges faced in implementation and impact evaluation of these multilevel/ combination interventions identified the lack of human resources for health and the need for workforce development as major barriers to success. On a practical level, the limited availability of in-country community partners and insufficient government research infrastructure were seen as major challenges. Another challenge found to impact evaluation was the push to roll out programs as fast as possible, which can limit the planning and resources available for research data collection and evaluation.

Commonly identified challenges for data collection. Developing countries often lack data systems for such things as vital statistics, health records, or public health surveillance records. There is also considerable heterogeneity in the data collected; thus, research studies generally have to establish these data systems. Long-term, planned system strengthening must include investments in these data collection mechanisms. To monitor progress toward HIV treatment and prevention goals, innovation is needed to move beyond paper-based data collection and systems that do not allow tracking of individuals.

Methodological Options

Researchers designing and implementing multilevel/combination HIV prevention intervention studies face many challenges in study design, data collection and harmonization, and measurement. Prior to the analysis of intervention data, particular care is needed in design of the study; selection, development, and pilot testing of measurements; and assuring data quality. Once these steps have been addressed, investigators may select an optimal analysis method or set of methods to address key research questions. Of course, some evaluation is done post hoc; in such cases, careful selection of analytical methods and modeling approaches can help mitigate some of the biases inherent in “natural experiments.”

Many researchers perceive a large gap in analysis methods options between a formal cRCT and an observational study. Some designs, such as the stepped wedge, have become more common, but a false perception persists that any design other than a formal RCT is not sufficiently rigorous. More recent work, however, has shown that creative designs where protocols can be adapted as a study progresses (e.g., “drop the loser”) or analysis strategies that can compensate for differences in treatment groups are able to generate results as unbiased as those associated with a traditional randomized design and, in some cases, less biased than with an “intent-to-treat” analysis. Results from less traditional designs may also be more generalizable to the population scale than

traditional randomized trials requiring intensive study involvement from individual research participants.

The cost of cluster-randomized designs and the time required to implement and analyze them are major constraints to using such designs for many research questions. In addition, loss to follow-up and missing data, particularly with mobile or otherwise hard-to-reach populations, can create major stumbling blocks to randomized designs. Finally, one could question the benefit of investment in cRCTs when, given careful collection and use of surveillance data, one can generate a rigorous evaluation of prevention programs at a fraction of the cost.

Roundtable participants reviewed a variety of design and analytic strategies that can provide rigorous evaluations of multilevel/combination interventions while taking into account the realities of current surveillance and clinic data collection systems and the growing need to document the impact of national prevention programming. Below we summarize multiple methods that may be used alone or in combination and their principal characteristics to address methodological challenges raised during the roundtable.

Potential methodological approaches

Time-series models for surveillance and other summary data. Time-series models describe an approach for observing trends in both exposure and outcome indicators over time and are therefore particularly useful for aggregate data. For example, surveillance efforts may capture aggregate quantities of interest (e.g., community viral load or proportion of persons testing for HIV) across multiple time points at the community level. Time-series models offer an approach to evaluate aggregate data over time, provided that the measurement of a given indicator or outcome is stable over time and that sufficient repeatedly measured data points are available (typically 30 or more). When looking at surveillance level data in a country, state, or local jurisdiction, time series offers a way to try to separate intervention effects from other identifiable trends or exposures such as the beginning of a national treatment program or the scale-up of linkage efforts.

Time-series models are particularly useful when data are collected at the community level only (as opposed to the individual level), when there are few communities available (including situations where only one community is followed over time for trends), and when national surveillance programs are in place to capture key indicators.

Hierarchical linear models and other model-based analysis approaches for individual-level outcome data. This category encompasses a range of analytic strategies that extend statistical models to account for clustering in communities or groups and that analyze data from newer study designs (e.g., stepped wedge). Some model-based approaches such as hierarchical linear models (HLMs), also known as multilevel models or random-coefficient models, explicitly model community-level variability, whereas other model-based approaches like

generalized estimating equations (GEE) focus on population-level estimation and treat community-level variability as a nuisance parameter. In HLM approaches that explicitly model community-level variability, community-specific changes over time may be estimated, and intervention communities' average change in indicators (such as HIV testing) may be compared with those from control communities. As the "hierarchy" in the name implies, these models can be particularly helpful in multilevel prevention programs where some intervention activities target community-level factors and some target individual-level factors. With sufficient data, these models can help tease apart which components of multilevel intervention programs have impact and at which level.

These HLM and other model-based analysis methods work well when intervention and comparison communities are balanced at baseline (i.e., having similar demographics, health outcomes, and health policies or programs), as is the case in a cluster-randomized trial. These approaches may also yield useful results from non-randomized study designs by adding some minor extensions as necessary. For instance, propensity scoring, treatment weighting, or censoring weights may be used to balance intervention and comparison communities using pre-baseline information to "level the playing fields." Using weighted data, one can utilize HLM or GEE estimation of community differences under the assumption of balanced intervention and comparison communities at baseline. When interventions are being rolled out sequentially as in a stepped-wedge design, another alternative is to use HLM to model pre- and post-intervention trajectories separately and compare them. The difference between pre-intervention and post-intervention trajectories, aggregated across the wedges, represents the effect of the intervention.

Causal inference approaches for the analysis of individual-level data. Causal inference approaches are a framework for approaching study design and analysis rather than a specific method. They encompass a range of techniques with the goal of clearly identifying the parameter of interest—the counterfactual argument—and arriving at a marginal (population-level) estimate of the effect of interest. The counterfactual represents a measure of what would have happened if, counter to fact, the investigators were able to fully control the study and administer the intervention to all or none of communities at two equivalent points in time. Since such an ideal is impossible, causal inference helps us to identify the best way to approximate our ideal experiment. For example, causal inference methods could be used to ask the question, How much would HIV incidence have differed if every community studied in rural Uganda had a VCT program versus not having one? Since we cannot actually expose all rural areas to VCT and go back in time to observe HIV incidence in the absence of VCT, causal inference models provide a way to estimate this difference by using all available data (measured confounders) and removing their effects from the model to obtain unbiased estimates of causal effects.

Causal inference tools can be used for either randomized or non-randomized studies, though they are particularly useful in non-randomized designs where treatment or exposure was not assigned and biases are more likely to induce spurious estimates of effect. Additionally, the causal inference framework includes the ability to formally quantify whether a given candidate mechanism of change is responsible (or partly responsible) for the intervention's impact via weighted mediation analysis. These properties make the causal inference approach very attractive for evaluating intervention effects in multilevel and combination prevention intervention studies, though causal inference techniques are less well developed for hierarchically structured or multilevel data.

Mathematical modeling for individual-level and community-level data. Mathematical models encompass a wide variety of strategies to describe a system with mathematical concepts. These types of models can take many forms, including but not limited to dynamic systems, statistical models, differential equations, or game-theoretic models. Models can be constructed to include individual- or community-level relationships or both. In general, theoretical concepts are used to construct mathematical relationships between elements in a mathematical system. In this theory-based system, all relationships are known, and changes to the system can be made to generate estimates of how those changes would impact outcomes. Data generated from these systems can then be compared to empiric or experimental data collected in the real world.

Mathematical modeling can provide ways to integrate many sources of data in a larger analysis framework and to conduct pre- or post-study analyses to draw boundaries around the expected changes related to various intervention components. Lack of agreement between theoretical mathematical models and empiric or experimental measurements can lead to important advances as better theories and estimations of relationships within the mathematical system are developed. For example, the Avahan Project in India has made extensive use of mathematical modeling to integrate results from many intervention components with separate groups.

Methods start with careful design and measurement. While evaluation design is not always contemplated prior to program implementation, as was the case with the Avahan Project and in many US programs, pretrial or -implementation planning work to optimize study design is the first and most important step to evaluating combination/multilevel programs. Evaluation pitfalls can be avoided by developing a clear theoretical framework, by improving study design to detect changes in clearly defined parameters of interest, and by identifying a parsimonious set of markers to measure the factors important for evaluation ahead of time. This includes a clearly stated causal model, clearly defined components of the model (exposures, mediators, and outcomes), and well-developed and validated measures for each. The roundtable's participants were able to identify important process outcome and impact measures for most major

multilevel interventions. Forward planning can also be facilitated by use of mathematical modeling.

Part and parcel of the need to clearly define each component of programs (exposures) and outcomes is understanding what can be gained by utilizing program monitoring data. We have an opportunity to gain much more extensive information from implementation experience than is currently standard practice, and reported program data often are not utilized in impact assessment or used to weight models or control for biases in the absence of a traditional randomization. With the use of more extensive program monitoring indicators (e.g., community prevention dosage measurement or utilization measures), there is also the potential to examine pathways and mechanisms of action. No estimation can be done in the absence of variability, however, making careful documentation of process in each community all the more important. With careful forward planning, process and implementation markers can be used to capture variability in exposure.

Methods gaps that need to be addressed. An important gap in methodological research identified was the need for better attention to measurement. Measures are the building blocks of our evaluative models and merit careful attention. An expanded set of indicators or scales with which to measure causal pathways and a more extensive set of tools to assess quality (validity, reliability) of our measures are needed. Some of the least well-understood pathways in HIV prevention models are those occurring at the community level (e.g., changing norms, reducing stigma), though the prevention community agrees that community-level intervention response is paramount to the framework. Our lack of quality knowledge of the impact of these community-level prevention efforts is due in part to a lack of good social measures—scales to assess stigma, social norms, and social processes that are the target of change; or methods to gather and analyze this data (e.g., aggregated individual survey response vs. a structural indicator of normative behaviors and opinions or community resources). Without more attention to social measurement, it will be difficult to assess the contribution of contextual or community factors at work in shaping vulnerability and to what extent these factors are modified by prevention programming. In addition, the roundtable identified the need to improve assessment of behavioral data, particularly self-reported risk, and measures of clinic performance.

Loss to follow-up and more generally missing data were also cited as barriers to producing rigorous impact evaluations. Particularly in areas where much of the population migrates frequently, loss to follow-up can pose a serious threat to the validity of any evaluation. This is an issue, for example, in the use of current public health surveillance systems. Roundtable participants identified the need to develop improved strategies to capture some information on missing data. Creative approaches to using surveillance systems or other data sources to estimate outcomes for those lost to follow-up may be helpful. Approaches such

as intensive tracking for a subset of persons lost to follow-up can help improve the validity of overall inferences.

Another important gap identified is in understanding how to quantify dose/ exposure to combinations or multiple levels of intervention in order to capture variability and make inferences about which components of complex interventions might be driving the effects we observe. In general, we need better ways to capture dose/exposure and easier ways to utilize such data in our models. As an example, in NIMH Project Accept, utilization data on each of the 14 active components of the intervention were collected and fed back to the staff implementing the intervention biweekly. This feedback of utilization data helped improve the quality of the intervention and allowed a better understanding of the relationship between intervention dose and outcomes.

Promising areas for further development. Roundtable participants identified several crucial areas for extending current methods and developing new methods to inform multilevel/combination HIV prevention interventions. Among these, moving beyond stepped-wedge to other semicontrolled designs and considering adaptive trial designs such as “drop the loser” or other such strategies to make modifications during the course of intervention rollouts would be useful.

Participants also identified the importance of uniting multiple methods described here in a synergistic way. For instance, it is possible to use pretrial mathematical modeling to help select the most parsimonious set of data elements needed for evaluation. In a similar vein, efficiencies can be gained by using a small subsample of a difficult-to-obtain measure to greatly improve and contextualize results from larger data sets with many cases but fewer measures (e.g., surveillance data). Similar approaches have been used recently to address and correct for possible bias due to loss to follow-up.

***The benefits of mixed methods*.** Qualitative methods can be used to assess the feasibility and acceptability of particular interventions or for the evaluation of intervention effects in a randomized, controlled trial. For example, some studies have used qualitative research with intervention staff to explain how the intervention they evaluated through an RCT did or did not work. In addition, qualitative methods can be used to evaluate the experience of participants in clinical trials or community members in a jurisdiction where combination interventions are being implemented. NIMH Project Accept used a longitudinal qualitative cohort where repeat in-depth interviewing was used to assess how changes in social norms regarding HIV testing and changes in stigma related to the intervention.

Economic and costing approaches. In both domestic and international settings, issues of costing and cost-effectiveness are gaining attention. Costing

has become a key part of impact evaluation and implementation decision-making and is key to raising and addressing issues of sustainability and research ethics.

Participants indicated that human rights and health benefits should be the most important drivers of healthcare decisions. However, cost analyses have utility in examining the efficiency of funding. An important concept in implementation science, cost analyses to assess the efficiency of combined or coordinated efforts across programs (e.g., TB, malaria, and reproductive health) are of particular interest currently. Roundtable participants cautioned that capturing the true cost and benefits of a program is a difficult process. Collateral benefits such as the benefit to a household of having a member's health improve are difficult to capture in cost models. Mathematical models were noted to be a useful approach to pretrial planning, costing and estimating what the "next-best" package might be, with the caveat that modeling is not a perfect solution.

In conclusion, participants noted that the research community should strive to become both better consumers and better distributors of novel methods. Innovative approaches will not move the field forward if they are not understood or communicated to others.

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Appendix 1: Agenda
Appendix 2: Participants

National Roundtable on Evaluation of Multi-Level/ Combination HIV Prevention Interventions

UCSF Center for AIDS Prevention Studies (CAPS)

UCSF-Gladstone Institute of Virology and Immunology Center for AIDS Research (CFAR)

May 24-25, 2012, Athens Room, Hotel Monaco

501 Geary Street (at Taylor), San Francisco

Day 1

Continental Breakfast 8:30-9:00

Steve Morin, PhD, Professor of Medicine, UCSF, Director of the Center for AIDS Prevention Studies (CAPS) & **Christopher Gordon, PhD,** Branch Chief, Division of AIDS Research, National Institute of Mental Health 9:00-9:15
Welcome and Introductions

Edwin Charlebois, MPH, **PhD**, Associate Professor of Medicine, UCSF; Co-Director of the Methods Core, Center for AIDS Prevention Studies; Co-Director of Prevention, AIDS Policy Research Center 9:15-9:20
Goals and Process for the National Roundtable

Sten Vermund, MD, PhD, Professor of Medicine, Vanderbilt, Director Institute for Global Health 9:20-9:30
The evolution and importance of combination HIV prevention approaches

Panel 1 – National Approaches 9:30-10:20

Chair: Mallory Johnson, PhD, Associate Professor of Medicine, UCSF, CAPS
The goal of Panel 1 is to better understand core components of multi-level/combination approaches to HIV prevention, to identify process, outcome and impact measures, and to better understand the challenges to population-based impact evaluation in the U.S.

Deborah Donnell, PhD, Principal Staff Scientist, Vaccine and Infectious Disease Institute Statistical Center for HIV/AIDS Research and Prevention, Seattle 9:30-9:45
HPTN 065 - TLC-Plus: A Study to Evaluate the Feasibility of an Enhanced Test, Link to Care, Plus Treat Approach for HIV Prevention in the United States

Holly Fisher, PhD, Behavioral Scientist, CDC, Atlanta 9:45-10:00
CDC: Enhanced Comprehensive HIV Prevention Planning and Implementation for Metropolitan Statistical Areas Most Affected by HIV/AIDS

Janet Myers, PhD, MPH, Associate Professor of Medicine, UCSF CAPS 10:00-10:15
HRSA: Systems Linkages and Access to HIV Care for Populations at High Risk for HIV Infection Initiative – Evaluation and Technical Assistance Center

Facilitated discussion: 10:15-10:45
Robert Remien, PhD, Professor of Clinical Psychology, New York State Psychiatric Institute and Columbia University, Director of the HIV Center Global Community Core
Wayne Steward, PhD, MPH, Assistant Professor of Medicine, UCSF, CAPS

Break 10:45-11:00

Panel 2 – IOM Recommendations

Chair: Starley Shade, PhD, Assistant Professor, UCSF CAPS
The goal of Panel 2 is to better understand the context of the IOM report on Monitoring HIV Care in the United States: Indicators and Data Systems, and to explore the recommendations as a potential impact evaluation framework for multi-level/combination HIV prevention in the U.S.

Paul Volberding, MD, Professor and Vice-Chair, UCSF Department of Medicine; and Director, Center for AIDS Research & AIDS Research Institute *Monitoring HIV Care in the United States: Indicators and Data Systems*	11:00-11:10
Moupali Das, MD, MPH, Assistant Clinical Professor, Divisions of HIV/AIDS and Infectious Diseases, SFGH; Center for AIDS Prevention Studies, UCSF; Director of Research HIV Prevention Section SFDPH *Strategies for process, outcome, and impact evaluation – role of surveillance systems*	11:10-11:30
Gregorio Millett, MPH, Senior Policy Advisor, White House Office of National AIDS Policy *Harmonization of measures across agencies*	11:30-11:40
Facilitated discussion: **Arleen Leibowitz PhD,** Professor of Public Policy, UCLA **Jeff Kelly, PhD**, Professor and Director Center for AIDS Intervention Research, Medical College of Wisconsin, Milwaukee	11:40-12:00
Lunch	12:00-1:00

Panel 3 – International Approaches

Chair: Maria Ekstrand, PhD, Associate Professor of Medicine, UCSF CAPS
The goal is to better understand core components of multi-level/combination approaches to HIV prevention, to identify process, outcome and impact measures, and to better understand the challenges to population-based impact evaluation in developing countries.

Steve Morin, PhD, Professor of Medicine, UCSF, Director of the Center for AIDS Prevention Studies (CAPS) *HPTN 043: Project Accept – A Phase III Randomized Controlled Trial of Community Mobilization, Mobile Testing, Same-Day Results, and Post-Test Support for HIV in Sub-Saharan Africa and Thailand*	1:00-1:15
Marie-Claude Boily, PhD, Senior Lecturer in Infectious Disease Ecology, School of Public Health Imperial College, London *Gates/Avahan: Assessing Impact of of a large scale intervention targeted to Vulnerable populations across 4 states in southern India.*	1:15-1:30
Deborah Donnell, PhD, Principal Staff Scientist, Vaccine and Infectious Disease Institute Statistical Center for HIV/AIDS Research and Prevention, Seattle *HPTN 071: The PopART Study*	1:30-1:45
Deanna Kerrigan, PhD, MPH, Associate Professor, Bloomberg School of Public Health, Johns Hopkins University, Baltimore *USAID/OGAC and Gates Foundation: Design of the Combination HIV Prevention Trial in Iringa, Tanzania and Formative Research Findings on the Services Package*	1:45-2:00
	2:00-2:15

Rui Wang, PhD, Assistant Professor of Medicine, Brigham and Women's Hospital; Assistant professor of Biostatistics, Harvard School of Public Health, Boston
CDC/OGAC: A study of the impact and cost-effectiveness of a unique combination of HIV prevention strategies in Botswana

Facilitated discussion: 2:15-2:45

Audrey Pettifor, PhD, MPH, Assistant Professor of Epidemiology, University of North Carolina

Tim Lane, PhD, MPH, Assistant Professor of Medicine, UCSF CAPS

Break 2:45-3:00

Panel 4 –Developing a Framework for International Impact Evaluation – Indicators and Data Systems

Moderator: Nancy Padian, PhD, MPH, Professor of Epidemiology UC Berkeley

The goal of the moderated panel discussion is to explore the potential for a parallel framework to the IOM approach for impact evaluation in developing countries. 3:00-4:00

Paulin Basinga, MD, PhD, School of Public Health, National University of Rwanda & the Bill and Melinda Gates Foundation, Seattle

Don Des Jarlais, PhD, Director of Research, Baron Edmund de Rothschild Chemical Dependency Institute at Beth Israel Medical Center, New York

Jim Hughes, PhD, Professor of Biostatistics, Vaccine and Infectious Disease Institute Statistical Center for HIV/AIDS Research and Prevention, Seattle

Martina Morris, PhD, Professor of Sociology and Statistics, University of Washington

Roger Myrick, PhD, MA, Director of Monitoring and Evaluation, Prevention and Public Health Group, UCSF

Panel 5 – Economics, Sustainability, & Policy 4:00 -5:00

Moderator: Marguerita Lightfoot, PhD, Professor of Medicine, UCSF; Co-Director, CAPS

The goal of the moderated discussion is to explore the role of cost in impact evaluation and implementation decision-making, as well as to discuss issues of sustainability and ethical issues in multi-level/combination prevention studies in developing countries

Jim G. Kahn, MD, MPH, Professor Institute of Health Policy Studies, UCSF

Steve Pinkerton, PhD, Professor Medical College of Wisconsin; Director, CAIR Cost-Effectiveness Studies Core; Director, CAIR Postdoctoral Research Fellowship Program

Michael Sweat, PhD, Professor at the Family Services Research Center in the Department of Psychiatry and Behavioral Sciences at the Medical University of South Carolina (MUSC)

Reception: No-host bar, Le Petit Café, Hotel Monaco 5:00-6:30

Day 2

Continental Breakfast 8:30-9:00

Synthesis Discussion of Day 1 topics: 9:00-9:15
Edwin Charlebois, MPH, PhD & Sten Vermund, MD, PhD

Panel 6 – Future Directions for Impact Evaluation, Part I

Chair: Susan Kegeles, PhD, Professor of Medicine, UCSF Co-Director CAPS
The goal is to discuss promising statistical approaches for impact evaluation of multi-level/combination HIV prevention intervention, specifically to identify strengths, gaps and data needs for different existing methods as we move from evaluation of projects to broader implementation and state/national programs and from intervention data to surveillance or other routinely collected population level data.

Ray Catalano, PhD, MRP, Professor of Public Health, UC Berkeley 9:15-9:30
Time Series applications for evaluating health outcomes

Steven Gregorich, PhD, Professor, UCSF School of Medicine *Hierarchical Linear Models and other model-based approaches for analysis of multilevel data* 9:30-9:45

Paul Farnham, PhD, Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta 9:45-10:00
CDC approaches to modeling

Break 10:00-10:15

Panel 7 – Future Directions for Impact Evaluation, Part II

Chair: Mi-Suk Kang Dufour, PhD, Assistant Professor, UCSF CAPS

Peter Vickerman, BSC, Dphil, Senior Lecturer of Mathematical Epidemiology, London School of Hygiene and Tropical Medicine. London 10:15-10:30
Gates Foundation: Modeling the Evaluation of Avahan – the HIV prevention initiative in India

Maya Petersen, MD, PhD, Assistant Professor of Biostatistics and Epidemiology, UC Berkeley 10:30-10:45
Causal inference - applying rigorous methods to observational data and natural experiments.

Facilitated Discussion:
Tor Neilands, PhD, Associate Professor, UCSF; Director Methods Core CAPS 10:45-
Sheri Lippman, PhD, Assistant Professor, UCSF CAPS 11:15

Setting the Research Agenda: Discussion 11:15-
Edwin Charlebois, MPH, PhD & Sten Vermund MD, PhD 12:30

National Roundtable on Evaluation of Multi-Level/ Combination HIV Prevention Interventions
UCSF Center for AIDS Prevention Studies (CAPS)
UCSF-Gladstone Institute of Virology and Immunology Center for AIDS Research (CFAR)
May 24-25, 2012, Athens Room, Hotel Monaco
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