Towards Defining an

# HIV Implementation Science Agenda

for Key Populations in Low- and Middle-Income Countries

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## INTRODUCTION

Never in the history of the AIDS response has optimism been more warranted. In 2015, the world for the first time reached a global treatment target: providing antiretroviral therapy to more than 15 million people.[1] Globally, new HIV infections fell by 35% between 2000 and 2014, due to the combined effects of changes in sexual behavior and, more recently, the prevention benefits of scaled-up antiretroviral therapy.* Since peaking in 2004, AIDS-related deaths globally declined by 42% through 2014,[1] and studies indicate that antiretroviral therapy virtually restores a normal lifespan for people living with HIV.[2] There is now growing confidence that the tools exist to end AIDS as a serious pandemic within the next generation.[3]

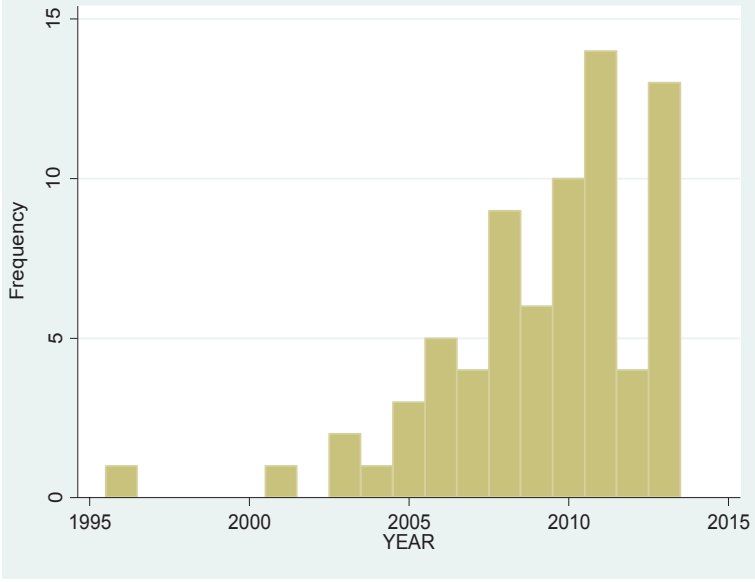
Yet there is often a considerable gap between the potential of existing prevention and treatment tools for HIV and their actual impact for people affected by the virus. For example, while antiretroviral therapy has the potential to basically eliminate the risk of HIV transmission and add decades of life for people living with HIV,[4] gaps in the implementation of HIV testing and treatment programs diminish the public health impact of HIV treatment. Due to such implementation gaps, only 32% of people living with HIV in sub-Saharan Africa achieved viral suppression in 2014.[1] Similar implementation gaps undermine the effectiveness of other proven prevention strategies, such as voluntary medical male circumcision, condom distribution, and pre-exposure prophylaxis (PrEP).

Implementation gaps are typically most pronounced for key populations, such as gay men and other men who have sex with men (MSM), people who inject drugs (PWID), sex workers (SWs), and transgender (TG) people. Members of key populations often struggle to access life-saving prevention and treatment services due to the deterrent effects of stigma and discrimination faced in society and healthcare settings, punitive laws that criminalize their behaviors, and the lack of user-friendly and competent healthcare options.[5]

Implementation science seeks to expand understanding of the causes of HIV-related implementation gaps and to identify effective strategies for closing these gaps, with the ultimate aim of maximizing the health impact of available HIV prevention and treatment tools. Although implementation science has often been neglected in the realm of HIV in comparison with clinical efficacy trials, this has begun to change, as gaps in translating research regarding efficacious HIV technologies and strategies into practice have prompted HIV research funders to increase support for implementation science studies.[6] However, relatively few implementation science studies have focused on overcoming the implementation barriers experienced by key populations, and implementation science has largely failed to improve outcomes for key populations, as evidenced by the estimate that key populations and their sex partners accounted for 40–50% of new HIV infections worldwide in 2014.[7]

In May 2015, amfAR, The Foundation for AIDS Research, hosted an expert consultation on defining an HIV implementation agenda for key populations in low- and middle-income countries.** The meeting provided an opportunity for experts to brainstorm how implementation science research might improve HIV outcomes for key populations in resource-limited settings, with the ultimate goal of persuading key decision makers to increase investments in HIV implementation science research focused on key populations. In addition, the meeting aimed to strengthen the foundation for using implementation science to improve HIV prevention and treatment outcomes for key populations.

### Figure 1: Publication Dates of Identified Implementation Science Definitions




Source: Odeny, T., et al. Definitions of implementation science in HIV/AIDS. *Lancet HIV*. 2015.

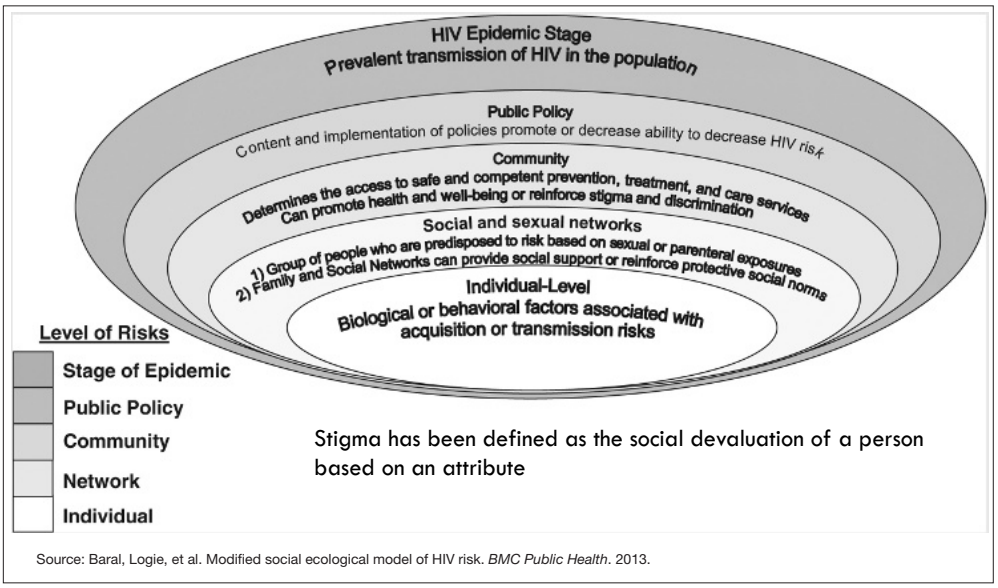
* Antiretroviral therapy reduces the chances that an HIV-positive person will transmit the virus by 96%.[1]

** Meeting agenda and participant list are attached as appendices.

## IMPLEMENTATION SCIENCE: A WORKING DEFINITION

As interest in HIV implementation science has grown (reflected in the recent increase in publications in scientific journals that address implementation science in the context of HIV, Fig. 1), various definitions of the term have been used. At the request of the World Health Organization, Thomas Odeny and colleagues reviewed the definitions used in published literature on HIV implementation science, with the goal of finding a working definition for the term. After analyzing 73 definitions in the medical and public health literature, this team of experts proposed the following working definition of implementation science:

**Figure 2: Levels of HIV Acquisition and Transmission Risks**




Source: Baral, Logie, et al. Modified social ecological model of HIV risk. *BMC Public Health*. 2013.

> *Implementation science is a multidisciplinary specialty that seeks generalizable knowledge about the behavior of stakeholders, organizations, communities, and individuals in order to understand the scale of, reasons for, and strategies to close the gap between evidence and routine practice for health in real-world contexts.*[8]

The multidisciplinary imperative for HIV implementation science stems from the widely varying factors that give rise to HIV risk and vulnerability (Fig. 2). These include a combination of biological and behavioral factors that increase or reduce HIV risk, as well as individual-level and broader social or structural factors that increase vulnerability and diminish the effectiveness of prevention and treatment efforts.

For key populations and other marginalized groups in low- and middle-income country settings, implementation science research must take account of the lived realities of these populations. As a result, ethnographers, human rights experts, and social scientists are potentially useful partners in implementation science research. Similarly, because decision makers require an understanding of the balance between costs and individual and population-level benefits of any intervention, economists have an important role to play in implementation science.

There is an inherent tension between the implementation science goal of generating results that can be generalized across different settings and the need to ground implementation science research in the realities of specific settings. For example, as the lived realities of urban MSM in more tolerant settings (e.g., São Paulo) may differ markedly from those living in settings where punitive anti-LGBT laws are in place (e.g., Lagos), implementation science research may reach varying conclusions regarding the scope of the problem or the most effective interventions against it, depending on the location. Ideally, implementation science will produce findings that can be adapted to diverse local contexts. Furthermore, research to characterize the various contexts in which implementation science work is taking place is vital to support the interpretation of the results across settings.

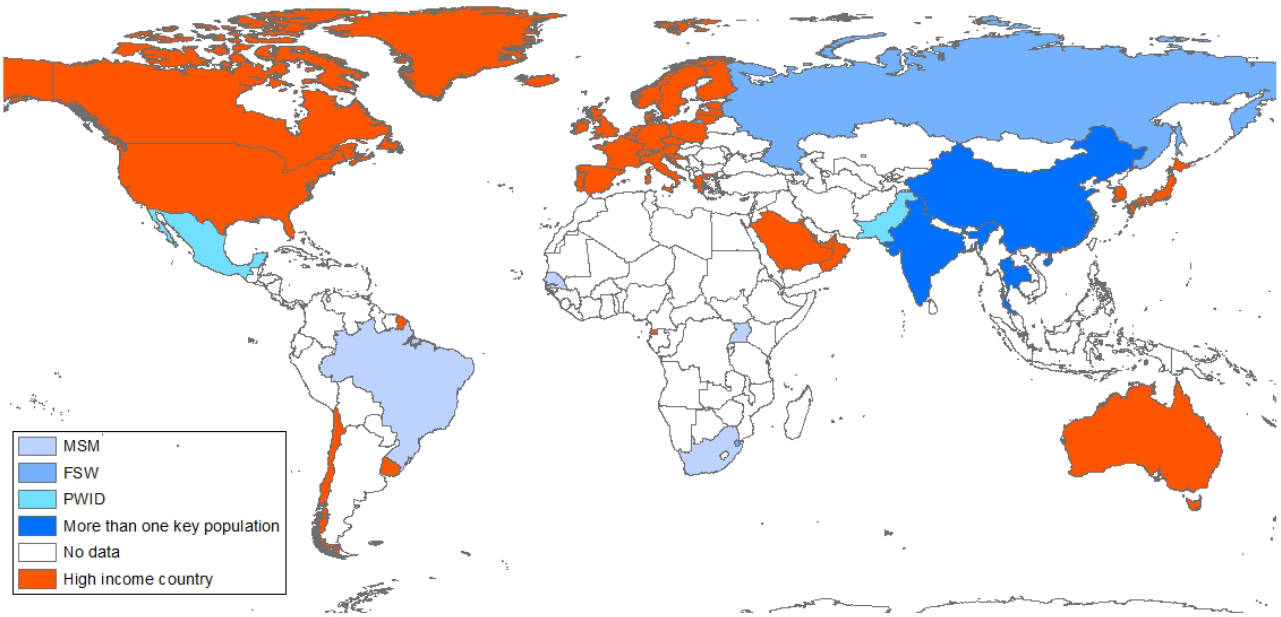
## IMPORTANCE OF HIV IMPLEMENTATION SCIENCE FOR KEY POPULATIONS

For key populations, implementation science has at least three potential roles: (1) clarify the scope and characteristics of the health problem; (2) evaluate ongoing interventions; and (3) identify the reasons why programmatic targets were missed, as well as potential solutions.

### *Clarifying the Scope and Characteristics of the Problem*

Although key populations account for up to one-half of new HIV infections worldwide, yawning gaps in basic epidemiologic and service coverage data persist, which hobbles efforts to reduce the HIV burden among these groups. Information regarding HIV burden and the sources of risk and vulnerability these populations face is frequently lacking. While there has been an increase in

## Figure 3: Lower-Middle-Income Countries with Community-Level Measurements for HIV Risk Among Key Populations, 2000–2014




Source: Baral, Stefan. Importance of implementation research for key populations. Presentation, amfAR Implementation Science Consultation, Washington D.C., May 19, 2015.

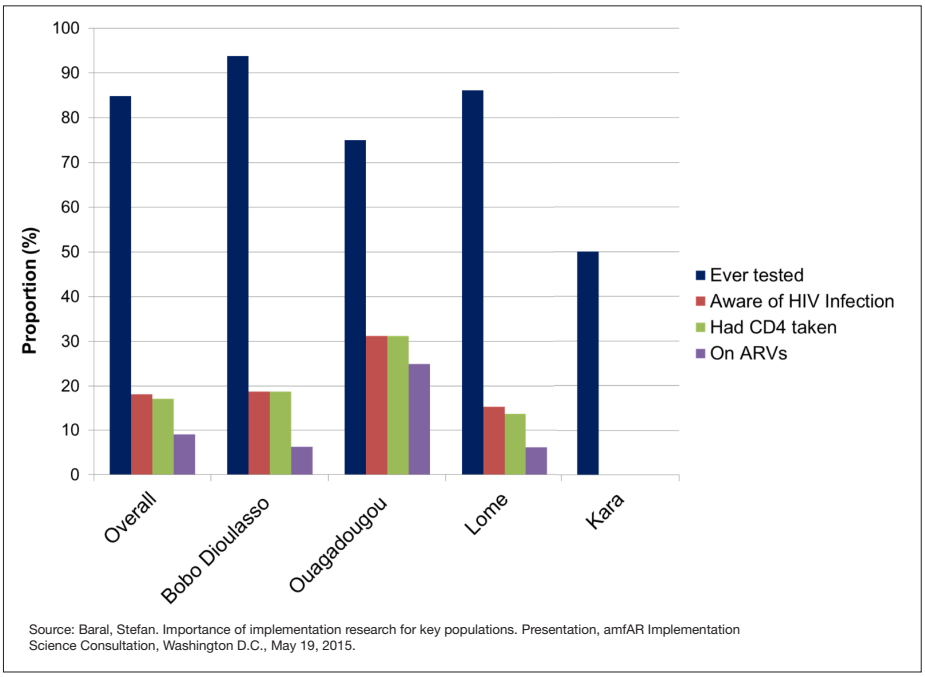
the quantity of HIV prevalence studies, there is limited data on HIV incidence and limited quality assessments of these studies. In most low- and middle-income countries, no quantifiable information whatsoever is available regarding HIV risk among key populations (Fig. 3). Moreover, in only a handful of countries has HIV risk been measured in more than one key population.

Where studies have been undertaken among key populations, they have primarily focused on HIV prevalence and individual risk behaviors, such as whether a condom was used during the last sexual encounter or clean injecting equipment during the most recent episode of drug use. While there has been increasing rhetoric about the importance of structural determinants of HIV risk, including stigma, comparatively few studies have focused on social or structural determinants of HIV risk and vulnerability for key populations.

In addition to the ultimate goal of identifying effective ways to improve HIV-related health outcomes, implementation science also plays a more basic role in helping clarify the extent, nature, and causes of service bottlenecks, thereby helping close data gaps that impede a more effective response. For example, well-designed implementation science research can help identify the root causes for the persistent and well-documented gaps in access to harm reduction services (e.g., lack of political will, organizational shortcomings, resistance by healthcare workers, deterrents to PWID's utilization of services, etc.). Importantly, the multi-disciplinary approach of implementation science extends beyond the singular focus on individual behaviors to take account of environmental factors that increase risk for HIV acquisition or transmission.

By clarifying the scope and nature of the problems that cause poor health outcomes, implementation science aids in identifying optimally effective strategies to improve programmatic results. In the case of programmatic gaps for harm reduction programs, for example, implementation science can help determine whether the most effective intervention to increase harm reduction uptake in a particular setting would be a change in government policy, strategies to motivate and sensitize healthcare workers to improve provision, social network approaches to increase awareness and support for harm reduction among PWID themselves, or some combination of the above.

## Figure 4: Engagement in the HIV Care Continuum Among MSM in Togo and Burkina Faso




Source: Baral, Stefan. Importance of implementation research for key populations. Presentation, amfAR Implementation Science Consultation, Washington D.C., May 19, 2015.

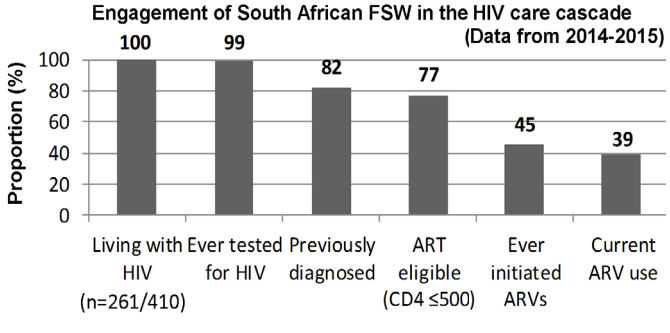
### *Evaluation of Ongoing Interventions*

In addition to the shortage of quality data on HIV burden and determinants of HIV risk and vulnerability among key populations, there is often little, if any, evidence regarding HIV-related outcomes for members of key populations living with HIV who access HIV services. For example, while considerable efforts have been made to document or estimate outcomes along the HIV treatment cascade, few such efforts have specifically focused on key populations. This gap is vividly illustrated in the 2014 UNAIDS *Gap Report*, which sought to survey the full array of HIV-related evidence regarding key populations, but was not able to provide any quantifiable evidence regarding linkage to care, retention in care, or rates of viral suppression among these groups.[5] In part, these gaps may be easily explained, as few clinical sites track patients based on their membership in a key population, and many members of such groups may actively work to conceal their membership as a result of stigma and discrimination. Where studies have been undertaken to evaluate interventions among key populations, including members living with HIV, they have typically focused on process indicators (e.g., number of people enrolled or retained) rather than on the actual health impact of the intervention.

Through carefully focused studies, implementation science can help close this evidence gap by documenting outcomes experienced by key populations. Although implementation science researchers confront the familiar challenge of estimating the size of key populations, well-designed studies can help shed light on service coverage among them. Implementation science can increase knowledge regarding the acceptability of services among key populations, the quality of services they receive, and their impact on participants' health.

For example, one study among MSM in Togo and Burkina Faso has documented the percentage of the population that has ever been tested for HIV, as well as outcomes across the HIV treatment cascade for MSM diagnosed with HIV infection (Fig. 4). The study, undertaken on behalf of PEPFAR by a team from Johns Hopkins Bloomberg School of Public Health, found that while HIV-diagnosed MSM in Ouagadougou largely accessed HIV treatment services and obtained antiretroviral therapy, outcomes were far less favorable in other study sites (Bobo Dioubasso and Lome). This study helped identify settings where intensified efforts are needed to engage and retain HIV-positive MSM in care and to ensure timely initiation of antiretroviral therapy. By collecting data regarding the legal and social environment, experience of HIV stigma and discrimination, drug use, and other indicators, the study clarified the social and structural factors that contribute to sub-optimal outcomes for MSM in these settings, highlighting the need for interventions addressing multiple levels of risk.[9]

## Figure 5: HIV Among Female Sex Workers in South Africa




Source: Schwartz, Lambert, Phaswana-Mafuya, Baral, 2015.

A separate study among female SWs in South Africa similarly detected sub-optimal outcomes across the treatment cascade for this vulnerable population (Fig.5). Also undertaken by Johns Hopkins researchers, this study found that only 39% of South African female SWs living with HIV were receiving antiretroviral therapy at the time of the study. Whereas 82% of all SWs living with HIV have been diagnosed—a degree of success that approaches the global target of 90% knowledge of HIV status among people living with HIV—nearly half of SWs who were eligible for antiretroviral therapy were not obtaining the treatment in 2014–2015—far below the global target of 90% access. This study strongly suggests that interventions that are focused on scaling up linkage into HIV treatment programs for SWs living with HIV are crucial to improve clinical outcomes and minimize risks of onward sexual and vertical transmission.

### *Analyzing Missed Targets and Identifying Possible Solutions*

Implementation science not only helps identify where a programmatic failure or shortcoming has occurred, but it also sheds light on the reasons why programs have failed to meet their targets.

For example, implementation science has clearly demonstrated that punitive laws and policies, combined with the stigmatizing social environments that give rise to them, substantially deter key populations from accessing HIV prevention and treatment services. In The Gambia, where under the law, persons convicted of "aggravated homosexuality" can be sentenced to life imprisonment, a study found that only 15% of MSM had disclosed their sexual orientation to a healthcare worker and only 4% to a family member.[10]

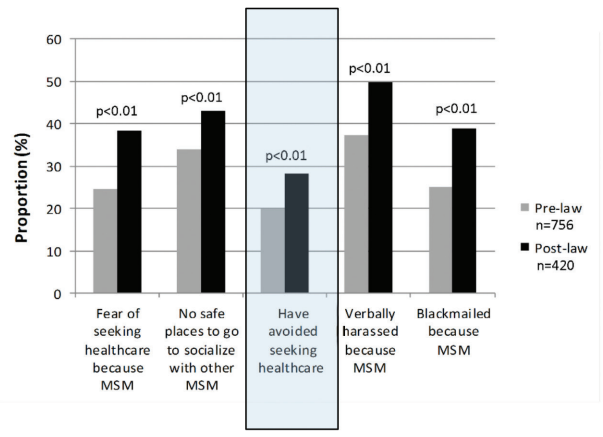
Likewise, implementation science research has correlated passage of repressive anti-gay legislation in Nigeria with reductions in utilization of healthcare services among MSM (Fig. 6). Following enactment of the law, fears among MSM about seeking healthcare services spiked, as did instances of harassment and blackmail experienced by MSM.

In addition to documenting the impact of structural factors on service utilization, studies have also found that such factors can increase sexual risk behaviors. Research by Da, Baral, et. al., in Lesotho, for example (Fig. 7), linked depression and alcohol use with increased risk behaviors among MSM. Based on study findings in Lesotho, investigators sketched causal pathways whereby stigma increases HIV risks, potentially pointing the way towards novel interventions to reduce sexual risk among MSM, including interventions focused on the antecedents of sexual risk practices.

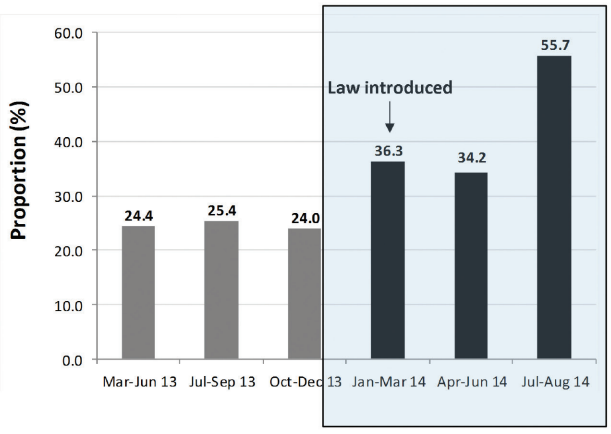
Likewise, studies among female SWs in Swaziland have found that higher rates of social cohesion among SWs are significantly associated with consistent condom use and organizing to promote

## Figure 6: The Impact of Criminalization on HIV Risks Among MSM in Nigeria

Reporting of discrimination and stigma during study visits pre- and post-legislation

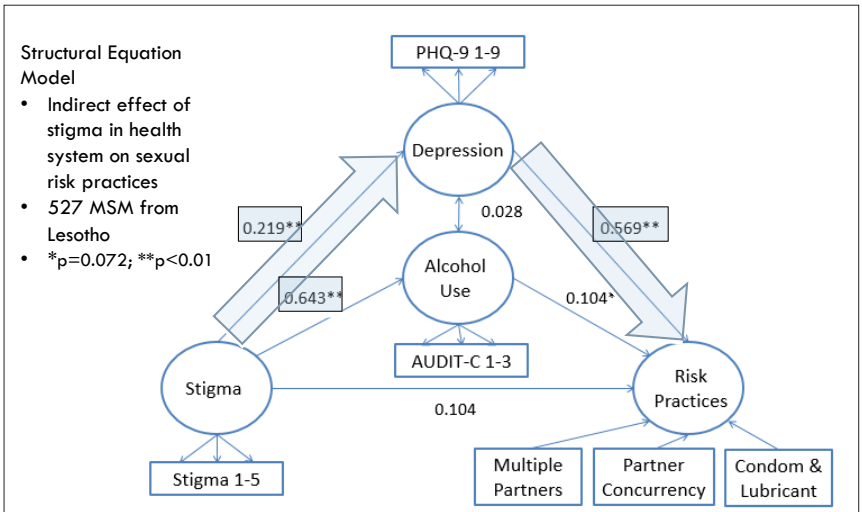



Cumulative lifetime experiences of reported fear of seeking healthcare services across study visits (n=1,175 visits).



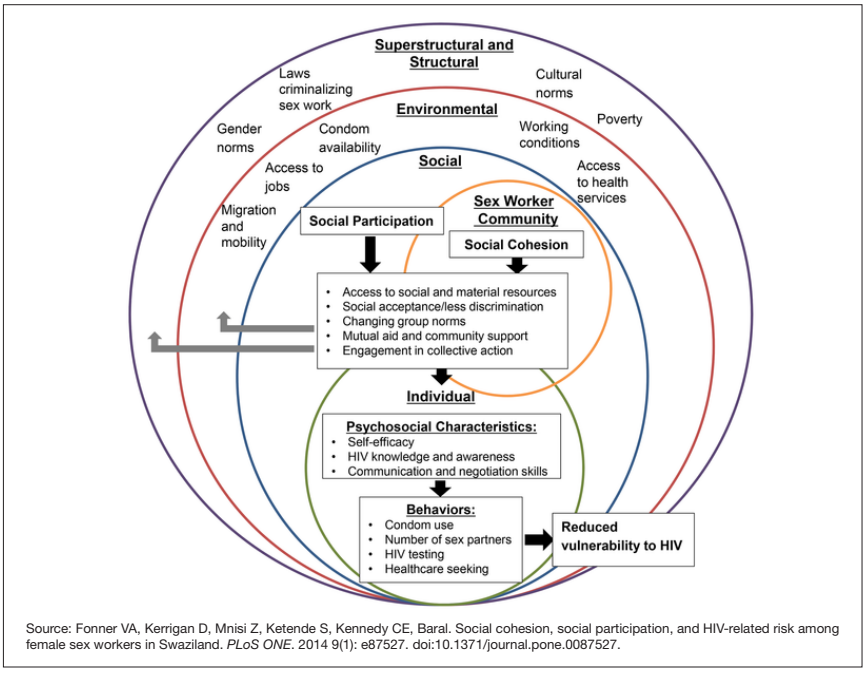

Source: Schwartz, Nowak, Orazulike, Blattner, Charurat, Baral, TRUST Study Group (UMD, MHRP, ICARH, JHU). The immediate HIV-related impact of enacted legislation that further criminalizes same-sex practices in Nigeria. Forthcoming.

## Figure 7: Potential Causal Pathway for Stigma and HIV Risks Among MSM




Source: Da, W and Baral, S. Depressive symptoms and alcohol use as mediators of HIV-related risk practices and stigma affecting men who have sex with men in Lesotho: a structural equation modelling approach, 2015.

## Figure 8: Theoretical Framework of Social Capital and HIV-Related Risk Among Female Sex Workers in Swaziland




Source: Fonner VA, Kerrigan D, Mnisi Z, Ketende S, Kennedy CE, Baral. Social cohesion, social participation, and HIV-related risk among female sex workers in Swaziland. *PLoS ONE*. 2014 9(1): e87527. doi:10.1371/journal.pone.0087527.

their own health and human rights. SWs who reported higher levels of social participation were more than twice as likely as those with lower social participation to have been tested for HIV in the previous year and were also substantially more likely to use a condom with non-paying partners.

As with MSM in Lesotho, researchers have used the implementation research findings to diagram the relationship between social capital and HIV-related risks among SWs in Swaziland (Fig. 8), helping identify key points at which to intervene to improve health outcomes for these women.

## LEVERAGING IMPLEMENTATION SCIENCE TO STRENGTHEN AIDS RESPONSES FOR KEY POPULATIONS

Given the severe and growing burden of HIV among key populations, there is an urgent need to move forward on a comprehensive, prioritized implementation science research agenda for key populations. In addition to further expanding understanding of the scope and nature of the HIV challenges these populations face, implementation science efforts need to characterize the optimal implementation methods for priority interventions targeting them that include strategies for overcoming or mitigating structural barriers to service provision and uptake.

To further efforts to leverage implementation science to improve HIV-related outcomes for key populations, participants in the amfAR-sponsored consultation divided into three work groups, with each group charged with exploring an implementation science research agenda for a different priority intervention for key populations. Each group was asked to describe the intervention, identify the target population and delivery model, describe desired outcomes and indicators, and brainstorm strategies for evaluating the intervention. Groups were encouraged to take account of cost-benefit issues.

The three interventions explored by the work groups were:

- Oral PrEP for MSM, transgender women, the negative partners in serodiscordant couples, and women who have sex with men who are living with HIV;
- Peer navigators to support linkage to care for MSM in Eastern and Southern Africa; and

- Adherence clubs to support retention in care for female SWs.

Several important themes emerged from efforts to design an implementation science approach for these three interventions:

### *Lack of Data Increases Implementation Science Challenges*

Even as implementation science works to build the evidence base for action to address the HIV-related needs of key populations, such efforts suffer from important, underlying data gaps. Lack of understanding of the size of key populations in different settings may make it difficult to draw conclusions regarding coverage trends. Moreover, where size estimations have been done there is significant variability in quality. Few interventions focused on linkage to HIV treatment and retention in care have been rigorously evaluated, and there is very little information regarding the acceptability of PrEP among key populations. While linkage-to-care and treatment rates generally are known to be sub-optimal for members of key populations who test HIV positive, little information is available regarding the proportion of MSM who test positive who are linked to care in a timely manner. Although the evidence base regarding anti-stigma interventions has expanded, the information on effective programmatic and policy strategies to minimize stigma and discrimination remains quite limited.

### *Implementation Science Helps Clarify the Essential Components of Specific Interventions*

For each of the three interventions, work groups deconstructed the interventions, identifying key steps in the service cascade, as well as key factors that influence the impact of the intervention. For example, in the case of peer navigation for MSM in Eastern and Southern Africa, key aspects of the intervention would include:

- Agreement on criteria for good navigators
- Recruitment of a corps of peers from the target population
- Training and orientation of peer navigators (including development of a training protocol and curriculum)
- Development of a strong and well-defined relationship between the peer navigation program and a suitable health facility
- Training and orientation of health facility staff to ensure their competence and readiness to address the needs of the target population
- Sustained compensation for peer navigators
- HIV testing (including provisions for commodity purchase and protocols for testing procedures)
- Linkage to health facility (including development of clear protocols to guide linkages)
- Follow-up monitoring to ensure entry to care
- Supervision of peers and clinic staff
- Monitoring and evaluation procedures

Deconstructing each intervention into its components helps identify pivot areas where services can fail or be less successful than they might otherwise be. In the case of adherence clubs for female SWs, for example, ensuring the availability of child care may have an important effect on participation in the intervention. Separating the intervention into key steps also aids in development of a service cascade for purposes of performance monitoring.

### *Key Population Interventions Must Take Account of Stigma, Discrimination, and Hostile Legal and Political Environments*

Each of the work groups noted the negative role of stigma and discrimination in healthcare access, and focused considerable attention on how the various interventions could be framed and implemented in a manner to overcome or mitigate the deterrent effects of these social environments. In many respects, the peer navigation and adherence clubs for key populations specifically aim to mobilize communities to provide services themselves as a way to lessen the negative impact of stigma. For example, the development of peer navigation systems for MSM would leverage community expertise to direct MSM to non-judgmental and quality health services.

The political climate may play an important role in the feasibility or success of an intervention. In the case of PrEP, for instance, even if the intervention is acceptable to the target populations and well-planned to address all relevant programmatic factors, it is unlikely to be implemented at scale if national decision makers are not convinced that PrEP represents a cost-effective use of finite health dollars. Similarly, some interventions for key populations may not be feasible in especially repressive environments, such as countries with laws that impose an obligation on healthcare workers to report MSM, PWID, or SWs to law enforcement authorities.

Taking account of the social, legal, and political environments may influence strategies for intervention delivery. For example, given the reality that members of key populations are often ill-served by mainstream health services, in many social contexts implementation of PrEP will likely need to move beyond the clinic setting and use innovative community-centered approaches.

### *Implementation Science Helps Identify Opportunities to Leverage Community Resources*

Each of the three interventions analyzed by the work groups aim in some measure to mobilize and effectively leverage community resources. Adherence clubs, for example, use the wisdom and experience of people living with HIV to support robust treatment adherence and retention in care and treatment. Likewise, peer navigation looks to trained members of the population to provide individually tailored and competent support to ensure linkage to care for people who test HIV positive.

Most HIV interventions for key populations will need to include a component of demand creation. Here, too, communities are ideally placed to lead the efforts. For example, many, if not most, MSM in resource-limited settings are poorly informed about PrEP. Given the lack of education about PrEP in low- and middle-income countries, community education and outreach will be required to alert people to the availability of PrEP and dispel myths about the intervention.

### *Implementation Science Can Help Clarify Total Intervention Costs*

Each of the work groups agreed that implementation research would need to define the unit cost for each intervention, in part to address the cost-benefit calculus that program planners will use to determine whether to fund a particular programmatic approach. This is another area where the deconstruction of the intervention and delineation of all pertinent activities is useful, aiding in the identification of all direct and indirect costs associated with an intervention, as well as in facilitating comparisons with the standard of care.

### *An Implementation Science Approach Supports Robust Program Evaluation*

For each of the three interventions, participants in the consultation explored optimal ways to evaluate program effectiveness. Each work group identified measurable process and impact indicators. In the case of adherence clubs for female SWs, viral suppression represents the ultimate outcome for measurement, although limited access to viral load testing in many clinical settings poses challenges for researchers and implementing partners alike. A comprehensive evaluation of this retention-in-treatment intervention would also include interim outcomes, such as quality of life (as measured by such indicators as satisfying sex life or return to work), supportive social networks, incidence of other sexually transmitted diseases (STIs), and fertility. Other qualitative measures, such as provider and patient satisfaction with the intervention, may also be monitored.

In some settings, randomized controlled trials (RCT) represent an important evaluation strategy for assessing the effectiveness of different interventions. In the case of adherence clubs for female SWs, all participants in an RCT would receive a group intervention, but only members of the intervention arm would obtain the full package of services. However, traditional RCTs may be difficult in some situations, including in settings where individuals do not wish to be identified as members of key populations in healthcare settings. Innovative methods, such as cluster or community randomization or non-randomized designs, may be required for certain interventions, populations, and particular settings. Moreover, using newer research evaluation approaches, including adaptive randomization based on outcomes, stepped-wedge designs, and pragmatic trials, may help maximize generalizability of the ultimate findings.

## PrEP: A CLOSER LOOK AT THE POTENTIAL ROLE OF IMPLEMENTATION SCIENCE

PrEP provides a useful example of how implementation science can help clarify the need for an intervention and advance efforts to implement and evaluate the intervention in the real world. The PrEP work group identified research questions and outcomes, recognizing that subsequent steps would require identification of implementation measures and specific research methods. As previously noted, the work group examined oral PrEP for MSM, transgender women, HIV-negative partners in serodiscordant couples, and women who have sex with men living with HIV. The work group recognized that PrEP may also be appropriate for other populations, but that the evidence was clearest for these specific populations.

The work group determined that the PrEP intervention consists of five categories of services or related considerations: (1) testing, re-testing, and client monitoring; (2) consumer education and demand creation; (3) care delivery (including associated activities for workforce education, training and sensitization, and management of STIs); (4) dosing (i.e., daily or intermittent); and (5) issues associated with funding and prioritization of the intervention in national AIDS programs. For each category of program components or considerations, the work group identified key questions to be answered by implementation science research, as well as outcomes to be measured.

### *Testing, Re-Testing, and Client Monitoring*

As an intervention for HIV-uninfected individuals, PrEP requires HIV testing prior to enrollment. There is growing interest in the

possible use of self-testing technologies for PrEP screening. To minimize the risk of drug resistance in individuals on PrEP who seroconvert, periodic re-testing is also required. Important testing-related questions for implementation science research include: (1) What are optimal testing algorithms for purposes of determining eligibility to enroll in PrEP? (2) What are the individual decision-making processes relevant to voluntary testing and re-testing for PrEP? (The work group determined that testing-related outcomes to be measured included both frequency and prevalence of HIV testing.) (3) What are the optimal approaches to implementing regular testing (including HIV self-testing), the leveraging of social networks to distribute test kits, and other emerging approaches?

### *Demand Creation*

As PrEP is an entirely new intervention in low- and middle-income countries—and one associated with questions and misperceptions—the work group agreed that investments in demand creation activities would be essential to meaningful PrEP uptake. Important questions for implementation science research regarding demand creation include: (1) What is the best mechanism (or combination or mechanisms) to educate communities about PrEP? (2) What are the best strategies for engaging communities regarding PrEP? (3) What is the optimal messaging to facilitate PrEP uptake (especially among key populations for whom HIV is not the primary concern)? Relevant outcomes for demand creation include the number and coverage of training modules for demand creation, increased uptake of PrEP, and increased evidence of community empowerment.

### *Delivery Model*

Although PrEP has been developed as an intervention to be delivered in healthcare settings, innovative approaches are likely needed for key populations that experience deterrents to utilization of mainstream health services. Important delivery-related implementation science research questions include: (1) What are the optimal community-centered approaches for delivering PrEP—such as the peer educator or peer navigator model, community medicine delivery, or innovative use of the Internet? (2) For MSM, what are the best strategies for linking STI diagnostics and PrEP? (3) What is the best means for preparing and motivating healthcare workers to provide PrEP in a non-judgmental way? (4) Should the intervention be targeted to every member of the target population who is HIV-negative, or should programs use screening to identify members of the target population who are most likely to adhere to the PrEP regimen? Relevant delivery-related outcomes include increased uptake of testing and re-testing, increased uptake of PrEP, and identification of best practices for delivery of PrEP.

### *Costing*

As PrEP is a new intervention—and one whose unit cost may exceed some other prevention methods—decision makers will likely require evidence that PrEP is affordable and that the benefits of PrEP outweigh the costs. For purposes of costing, the work group assumed that generic medicines would be used for administration of PrEP in low- and middle-income countries. Important cost-related implementation science research questions include: (1) What is the cost-benefit ratio for governments to fund PrEP? (2) What is the role of PrEP in the context of the broader array of prevention and treatment programs included in national plans and strategies? (3) In addition to government outlays, what alternative funding sources may be available to support PrEP uptake (e.g., private sector, social entrepreneurship, etc.)? Relevant outcomes include per-person unit cost of the intervention (for both daily and intermittent PrEP), the change in unit costs as HIV incidence changes, and clarity on when to stop the intervention for a particular individual (other than as a result of seroconversion).

### *Dosing*

The evidence base on optimal PrEP dosing continues to evolve, with two European studies recently finding that various dosing strategies for PrEP sharply reduced the risks of HIV acquisition among MSM.[11, 12] Important dosing-related implementation science research questions include: (1) For whom is intermittent PrEP appropriate and what is the best way to target those individuals? (2) What are the differences, if any, in adherence levels for daily and intermittent PrEP, and do any such differences have an effect on outcomes and cost-effectiveness of the intervention? (3) When is the optimal time to stop PrEP (other than as a result of seroconversion)? Relevant outcomes include savings to health systems from daily and intermittent PrEP, savings to health systems from timely cessation of PrEP, and improved adherence to the intervention.

### *Cross-Cutting Indicators and Research Questions*

At the macro-level, researchers should track several cross-cutting outcomes of PrEP implementation, including (1) the number of countries that have approved PrEP, (2) the number of countries where PrEP has been implemented, (3) the number of people taking PrEP, (4) the profile of people taking PrEP (e.g., distribution

among key populations, age, gender, etc.), and (5) reductions in HIV incidence as a result of PrEP. From the standpoint of political economy, implementation science research should also help identify the best ways to build robust, sustained political and financial support for PrEP roll-out, both among decision makers and within the AIDS field itself.

## MOVING FORWARD: PRIORITIZING HIV IMPLEMENTATION SCIENCE FOR KEY POPULATIONS

Although the increased attention of late to HIV implementation science is encouraging, specific investments remain far short of what is needed and far below the amount invested in efficacy research. This is especially true for key populations, whose HIV burden and role in the HIV pandemic continue to increase as the pandemic slows among other reproductive-age adults. Rolling back epidemics among these key populations demands much clearer, stronger evidence on effective strategies for delivering essential services and overcoming persistent barriers.

Participants in the amfAR-sponsored consultation called for substantial increases in investments in HIV implementation science research focused on the needs of key populations. All funders of HIV-related research—including biomedical research agencies, development assistance agencies, United Nations organizations, and philanthropic research funders—should urgently review their research portfolios and commit to increasing funding for implementation science research to improve HIV-related outcomes for key populations. A transparent effort should be undertaken to review existing research funding methods to determine the extent to which they meet implementation science needs and to assess their suitability (i.e., staff expertise) to play a growing role in HIV implementation science. Funders and leading researchers should collaborate to standardize implementation science methods and measures to the greatest extent feasible.

The involvement of key populations in the planning, implementation, and monitoring of implementation science is essential, at the funder and organizational levels, as well as in the communities and countries where the research will be conducted. Not only is involvement of key populations the right thing to do—consistent with the notion of “nothing about us without us”—but it also has practical benefits for implementation science projects. This includes insuring that research addresses the actual needs of key populations, takes account of the lived realities of the communities being studied, and contributes to the feasibility and sustainability of the developed interventions.

Given the growing prominence of clinical interventions and outcomes in the HIV response, implementation science research needs to be undertaken where people obtain HIV services—including enabling services such as social and legal support—that help make clinical care effective. Steps are needed to embed the implementation science infrastructure within decentralized health and community service delivery systems. Implementation science research will need to look beyond institutions that are already equipped to host or conduct research and engage the decentralized service providers and implementing partners that will play an essential role in reaching global AIDS goals.

## APPENDIX 1

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## APPENDIX 2

# Defining an HIV Implementation Science Research Agenda for Key Populations in Low- and Middle-Income Countries

May 19, 2015 · 8:30 a.m. – 4:00 p.m.
The Carriage House, 1781 Church Street NW, Washington, D.C.

8:30 – 8:45 – Arrival and Breakfast
8:45 – 9:00 – Introduction/ Welcome: Greg Millett
9:00 – 9:40 – Presentations: How do we define implementation science through the lens of reaching key populations? (12–15 minutes each)
- Dr. Elvin Geng: Defining Implementation Science
- Dr. Stefan Baral: Contextualizing Key Populations Implementation Science Research

9:40 – 10:40 – Discussion: Moving from research to real world application
- What are the priority areas in which implementation science approaches can best improve services for key populations (and e.g., increasing demand and new models for HIV testing, scaling up ART initiation and improved retention in treatment, PrEP availability)?
- How can issues regarding stigma and discrimination be incorporated into implementation science approaches?

10:40 – 11:00 – Group decision making: Breakout group topics
11:00 – 1:00 – Small break out groups
- What are the key components of the intervention in the priority area?
- What are the primary research questions to better understand how to improve the implementation of these interventions?
- What are the potential methods to study optimal approaches to implementation of the intervention?
- What are the external factors that influence the implementation approach (e.g., stigma, criminalization)? How do these impact research design?
- What are key internal factors that influence the implementation approach (e.g., community-based vs. facility-based care settings)? How do these impact research design?
- Who are the key constituents involved in implementation of the intervention and what is their role in the research?
- What are the key outcomes sought from research (e.g., issues to measure, evidence needs to drive policy change, etc.)?

12:00 – 1:00 – Working lunch
1:00 – 2:15 – Report back (10 minutes each group) and discussion with larger group
- Commonalities across group report back
- Notable/important points missing from the discussion

2:15 – 2:30 – Break
2:30 – 3:45 – Discussion: Meeting takeaway and policy, funding, research implications
- Understanding and reducing barriers to investing in successful implementation science initiatives
- Ideas of what would be most useful to encourage sustainable investments in further characterizing optimal strategies of program implementation for HIV prevention, treatment, and care for key populations?
- Peer-review paper (target journal, main points to cover, etc.), white paper, or commentary?

3:45 – 4:00 – Next steps/Thank you: Greg Millett
4:00 – Adjourn

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