

The U.S. President's Emergency Plan for AIDS Relief



**GUIDANCE FOR THE
PREVENTION OF SEXUALLY
TRANSMITTED HIV
INFECTIONS**

August 2011

1. Table of Contents

1. Table of Contents.....	2
1. INTRODUCTION.....	6
1.1 Purpose.....	6
1.2 The global HIV prevention context.....	6
1.3 PEPFAR’s strategy: combination prevention.....	7
2. KNOW YOUR EPIDEMIC, CONTEXT, RESPONSE, AND COSTS.....	7
2.1 The Four “Knows”.....	7
2.2 Using computer modeling to estimate population-level effects of HIV prevention activities ...	11
3. HIV PREVENTION AS PART OF THE COUNTRY CONTINUUM OF RESPONSE.....	12
3.1 Supporting the country continuum of response.....	12
3.2 Overarching principles of PEPFAR prevention programming.....	14
4. EVIDENCE AND IMPLEMENTATION GUIDANCE ON SPECIFIC INTERVENTIONS.....	15
4.1 Levels of evidence for elements of combination prevention.....	15
4.2 Biomedical interventions for prevention of sexual transmission.....	16
4.2.1 Male and female condoms.....	16
4.2.2 Voluntary medical male circumcision (VMMC).....	19
4.2.3 HIV testing and counseling (HTC).....	21
4.2.4 Diagnosis and treatment of sexually transmitted infections (STIs).....	24
4.2.5 Antiretroviral drug (ARV)-based prevention.....	26
4.3 Behavioral interventions for prevention of sexual transmission.....	30
4.3.1 Standalone behavioral interventions to minimize sexual risk or increase protection.....	30
4.3.2 Supportive behavioral interventions to optimize biomedical prevention.....	35
4.4 Structural supports for sexual prevention.....	36
4.4.1 Legal and policy reform.....	36

4.5	Prevention packages for specific populations	39
4.5.1	Comprehensive package for most-at-risk populations (MARPs)	39
4.5.2	Positive Health, Dignity and Prevention (PHDP): Prevention for people living with HIV	40
4.5.3	Prevention interventions for young people.....	42
5.	ASSEMBLING A PORTFOLIO OF INTERVENTIONS.....	45
5.1	Categories of activities.....	46
5.2	Prioritizing and assembling the portfolio: defining the continuum of response by population and geography	49
Table 1: Examples of how to apply prevention priorities across different epidemic-types. Appendix: HIV prevention and the Global Health Initiative (GHI): connecting to the broader country continuum of response.....		51
Appendix: HIV prevention and the Global Health Initiative (GHI): connecting to the broader country continuum of response		52

List of Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Clinic
ART	Antiretroviral Therapy
ARV	Antiretroviral Drug
CDC	Centers for Disease Control and Prevention
COP	Country Operational Plan
CRT	Cluster Randomized Trial
FDA	Food and Drug Administration
GBV	Gender-Based Violence
GHI	Global Health Initiative
GUD	Genital Ulcer Disease
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HSV-2	Herpes Simplex Virus-Type 2
HTC	HIV Testing and Counseling
MARPs	Most At Risk Populations
MAT	Medication-Assisted Treatment
MNCH	Maternal, Neonatal, and Child Health
MOVE	Models for Optimizing Volume and Efficiency
MSM	Men who have Sex with Men
NGO	Non-Governmental Organization
OGAC	Office of the U.S. Global AIDS Coordinator
OI	Opportunistic Infection
OVC	Orphans and Vulnerable Children
PEP	Post-Exposure Prophylaxis
PEPFAR	President's Emergency Plan for AIDS Relief
PHDP	Positive Health, Dignity, and Prevention
PLWH	People Living With HIV
PMI	President's Malaria Initiative
PMTCT	Prevention of Mother-to-Child Transmission
PrEP	Pre-Exposure Prophylaxis
PWID	People Who Inject Drugs
PwP	Prevention with People Living with HIV/AIDS
PWUD	People Who Use Drugs
RH	Reproductive Health
SBCC	Sexual Behavior Change Communication
SMS	Short Message Service
STI	Sexually Transmitted Infection

SW	Sex Workers
TB	Tuberculosis
TG	Transgender
UD	Urethral Discharge
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNFPA	United Nations Population Fund
USG	United States Government
VCT	Voluntary Counseling and Testing
VMMC	Voluntary Medical Male Circumcision
WHO	World Health Organization

1. INTRODUCTION

1.1 Purpose

The purpose of this guidance is to assist PEPFAR country teams in developing Country Operational Plans (COPs) that align activities to prevent sexual transmission of HIV with country-specific epidemiology and country-owned responses, and that support the continuum of response at the country level. This guidance seeks to aid teams in identifying and implementing the optimal combination of prevention activities needed to maximize reduction of new infections as part of the continuum of country HIV response, while reflecting the following key principles:

- Identifying and addressing gaps in scope and reach of prevention activities among priority populations
- Ensuring that interventions address populations and communities in such a way that the level of investment matches the level of risk
- Using resources so that they have maximum impact on HIV incidence
- Prioritizing the most effective biomedical, behavioral, and structural interventions in the country context
- Enhancing coordination across prevention, care, and treatment activities.

1.2 The global HIV prevention context

Thirty years into the global HIV epidemic, HIV prevalence and incidence remain alarmingly high. An estimated 1.8 million people were newly infected with HIV worldwide in 2010. In addition to the human toll of these infections, each of these people will ultimately need a lifetime of antiretroviral treatment (ART) in order to stay alive. HIV prevention is the single most important challenge in the fight against HIV/AIDS.

At the same time, the world has witnessed remarkable declines in HIV incidence over the past decade—coinciding with the dramatic increase in global HIV/AIDS resources through PEPFAR and other donors. Globally, new infections dropped from approximately 16,000 a day in 2001 to about 7,000 a day in 2009. The largest reductions occurred in the region with the most people living with HIV — sub-Saharan Africa. Twenty-two African countries experienced declines in new infections of 25% or more among young people. Many of the largest reductions were in countries in southern Africa with the most severe HIV burdens — e.g. an 81% reduction in Namibia, 57% in Zimbabwe, 49% in Botswana, and between 30 and 40% in South Africa, Swaziland, Zambia, Mozambique, and Malawi¹.

The contributors to these declines in incidence remain poorly understood, but likely include the increasing coverage of both HIV treatment and prevention activities. In addition, improved HIV surveillance and the natural evolution of the HIV epidemic may have contributed to these declines.

Even with these successes, multiple factors have made HIV prevention a continuing challenge:

- First, the arsenal of effective interventions has been limited

¹ Ghys PD, Gouws E, Lyerla R, et al. (2010). Trends in HIV prevalence and sexual behavior among young people aged 15-24 years in countries most affected by HIV. *Sexually Transmitted Infections*, 86, ii72-ii83.

- Second, it has been difficult to implement effective prevention interventions at sufficient scale and intensity relative to the need
- Third, interventions have sometimes been scattered across geographic areas, so synergies from having multiple interventions in one location are not realized
- Fourth, interventions have not been sufficiently targeted to key affected populations, especially in concentrated and mixed epidemics
- Finally, prevention services are frequently not linked with other prevention, care, and treatment services, nor across clinical and community-based settings.

1.3 PEPFAR's strategy: combination prevention

The 2009 PEPFAR Five-Year Strategy focuses on improving health outcomes, increasing program sustainability and integration, and strengthening health systems. All prevention activities are to be pursued within an overarching principle of the strategy: support for country-owned programs that provide a continuum of linked prevention, care, and treatment services. PEPFAR sexual prevention efforts, like efforts in other program areas, must be undertaken in close partnership with partner governments and civil society and must build their commitment and capacity to lead effective country responses.

The Strategy endorses combination prevention for all PEPFAR country programs². Combination prevention approaches HIV prevention using a suite of mutually reinforcing interventions to address the risks of transmission and acquisition as thoroughly and strategically as possible. It is predicated on the idea that no single intervention is efficacious enough to bring an HIV epidemic under control on its own, but that the optimal set of interventions implemented with quality and to scale can significantly reduce HIV incidence³.

Combination prevention recognizes three broad categories of interventions: **biomedical, behavioral, and structural**. As noted below, many interventions span multiple categories — for example, behavioral interventions are always needed to support biomedical interventions. Evidence in support of this approach was presented at PEPFAR's Expert Consultation on HIV Prevention in November 2010.

2. KNOW YOUR EPIDEMIC, CONTEXT, RESPONSE, AND COSTS

2.1 The Four "Knows"

In every national and subnational situation, there are prevention investments that are more effective at reducing HIV infection than others. For example, voluntary medical male circumcision (VMMC) may be a top priority in country X, while a targeted program for migrant workers is more suitable in country Y, and a targeted program for men who have sex with men (MSM) is more appropriate in country Z. Knowing the realities of a country is the first, essential

² U.S. President's Emergency Plan for AIDS Relief Five-Year Strategy (2009).

<http://www.pepfar.gov/strategy/index.htm>

³ Hankins CA, de Zaluondo BO. (2010). Combination prevention: a deeper understanding of effective HIV prevention. *AIDS*, 24, S70.

step in identifying, selecting, and funding the most appropriate and effective HIV prevention measures for that country.

Critical to building an effective portfolio of HIV prevention interventions is having and using accurate and comprehensive information about both the epidemic and the current response, commonly referred to as “Know Your Epidemic, Know Your Response”^{4,5}. In this guidance, we add two new “Knows” to this list: Know Your Context and Know Your Costs. The collection and analysis of data for the Four Knows should be ongoing and reflected in the COP.

Developing and maintaining these categories of data should be a primary objective of all PEPFAR prevention programs. At the Expert Consultation, the critical role of the four “Knows” was highlighted during an exercise in balancing a mock HIV prevention portfolio. Faced with the limited data PEPFAR country teams typically have to make decisions, experts often found themselves at a loss in making defensible decisions about difficult trade-offs. A major recommendation of the consultation was to increase our investment in obtaining data and strategic information.

1. **Know Your Epidemic:** This category includes epidemiological data on incidence and prevalence of HIV, the likely next 1,000 infections, the geographical hotspots of the epidemic, the drivers of transmission, the populations at highest risk of acquiring HIV, and the HIV prevalence and incidence (where available) within sub-populations⁶. These data come from population-based surveys, modes of transmission studies, modeling, size-estimation studies for most-at-risk populations (MARPs), and both qualitative and other quantitative research.

Ideally, much of this data collection and analysis should be done at the national level, led by partner governments. PEPFAR funds can and should be spent in support of these activities; most of these funds should come from strategic information budgets. Prevention budgets may be used to cover some of the costs for Know Your Epidemic studies, in particular for qualitative research and geographical mapping of high-risk populations.

HIV epidemics can be categorized broadly into three main types: concentrated epidemics, mixed epidemics, and generalized epidemics. Recently, epidemiologists have moved away from threshold-based categories for these epidemics and toward definitions that are based upon in-country transmission dynamics. Concentrated, mixed and generalized HIV epidemics can be defined in the following ways⁷:

⁴Merson MH, O'Malley J, et al. (2008). The history and challenge of HIV prevention. *The Lancet*, 372(9637), 475-488.

⁵Wilson D, Halperin DT. (2008). Know your epidemic, know your response?: a useful approach, if we get it right. *The Lancet*, 372(9637), 423-426.

⁶UNAIDS. (2008). Know Your Epidemic, Know Your Response. *UNAIDS HIV Prevention Toolkit*. Accessible at: http://hivpreventiontoolkit.unaids.org/Knowledge_Epidemic.aspx.

⁷Wilson D, Fraser N. (2011). Mixed HIV epidemic dynamics: epidemiology and program implications. *HIV Prevention in Mixed Epidemics Technical Consultation*. Accra, Ghana.

- Concentrated epidemics: transmission mainly occurs within most-at-risk populations, including sex workers (SW), MSM, and people who inject drugs (PWID)
- Mixed epidemics: transmission occurs in both most-at-risk populations (including SW, MSM, and PWID) and the general population
- Generalized epidemics: transmission occurs largely in the general population. It is important to note that even in generalized epidemics, pockets of most-at-risk populations exist and transmission needs to be arrested in both groups.

In concentrated epidemics, the bulk of HIV transmission can be interrupted by effective interventions targeting SW, MSM and PWID, while in generalized epidemics, transmission will persist in the general population even with effective, high-coverage interventions for MARPs. The situation in mixed epidemics is more complex; transmission will continue even if it is interrupted in either MARPs or the general population. Only by targeting interventions to both MARPs and general populations can transmission be effectively reduced.

Of particular importance for PEPFAR country teams is improving our understanding of MARPs in concentrated, mixed, and generalized epidemics. In addition to SW, MSM, and PWID, other MARPs to consider are people in HIV-discordant relationships, migrants, mobile populations, prisoners, women and girls engaged in transactional sex, and military populations, among others. MARPs are often highly stigmatized and partner countries may be reluctant to invest in surveillance and programming for them. Without data, these risk groups and key drivers of epidemics go unaddressed. PEPFAR teams should make breaking down these barriers a priority for both policy and programs in order to most effectively address the epidemic. In many PEPFAR programs, efforts to safely and accurately estimate the size and HIV prevalence of stigmatized populations is ongoing, and these techniques should be rapidly deployed in all PEPFAR countries where knowledge of these key affected populations is limited.

PEPFAR country teams should evaluate the type of epidemic that exists in their countries, including epidemic variations within their countries, and accordingly target prevention resources by population and geography. See Section 5 below for more information on compiling a country portfolio.

2. **Know Your Context:** This category includes information that contextualizes epidemiological data and assists program designers to most effectively target specific populations and structural drivers⁸. Lack of contextual information can lead to prevention programs that miss the mark by failing to take into account key factors shaping behavior⁹.

⁸ Merson, et al. 2008.

⁹ Laher F, Cescon A, Lazarus E, et al. (2011). Conversations with mothers: exploring reasons for prevention of mother-to-child transmission (PMTCT) failures in the era of programmatic scale-up in Soweto, South Africa. *AIDS and Behavior*, epub ahead of print.

They can include information on laws or policies that shape the environment by penalizing or supporting PLWH, such as laws that make transmission of HIV illegal or that make denial of health care to PLWH illegal. They might also include factors that more subtly shape the enabling environment for preventing HIV transmission, such as poorly-enforced laws regarding gender-based violence (GBV), restrictions on women's inheritance of property, or conflicting laws/policies which impede access and delivery of HIV services to those who need them. While most PEPFAR staff will be aware of some of these factors, understanding their ramifications may require more focused research.

Know Your Context data also include information on the socio-cultural contexts that shape behaviors and attitudes towards health, disease, sex, and other factors in HIV transmission. Examples include traditional use of male circumcision and concepts of marriage and fidelity which vary widely across cultures and can lead to confusion around safer-sex practices in stable relationships¹⁰. Also important are cultural attitudes and constraints that shape concepts of health and health-seeking behavior, including high-risk traditional practices such as wife inheritance and sexual cleansing of widows¹¹. Understanding these can play a critical role in shaping culturally relevant prevention programs. Typically, more qualitative research is appropriate for this category of information, especially from anthropological and sociological perspectives¹². PEPFAR country teams should make investments in capacity-building in this area as needed to inform their programs.

Data on patterns of population movement are another kind of critical contextual information. Mobile and migrant populations who spend long periods of time away from home and have reduced access to health services are especially at risk of acquiring and transmitting HIV¹³. PEPFAR programs need data on exactly who is moving where and when in order to provide effective programs that meet the right population at the right time in the right place. Sources for data on mobile and migrant populations include national demographic and labor databases, the International Labor Organization, and the UN Department of Economic and Social Affairs¹⁴. Formative and qualitative studies may also be necessary to understand health-related factors in these populations. Ideally, partner governments will lead efforts to track and understand mobile and migrant populations, and PEPFAR country teams can invest in capacity-building as necessary to support this work.

3. **Know Your Response:** As HIV prevention portfolios grow in complexity and scale, it has become increasingly challenging and important to track their scope and coverage.

¹⁰ Laher, et al. 2011.

¹¹ Mills EJ, Ford N, Mugenyi P. (2009). Expanding HIV care in Africa: making men matter. *The Lancet*, 374(9698), 275-276.

¹² Leclerc-Madlala S. (2009). Cultural scripts for multiple and concurrent partnerships in southern Africa: why HIV prevention needs anthropology. *Sexual Health*, 6, 103-110.

¹³ Coffee M, Lurie MN, Garnett GP. (2007). Modeling the impact of migration on the HIV epidemic in South Africa. *AIDS*, 21(3), 343-350.

¹⁴ United Nations. (2009). Trends in international migrant stock: the 2008 revision. Department of Economic and Social Affairs, Population Division. New York: United Nations.

The Know Your Response category includes mapping of all prevention activities — both those funded by PEPFAR, as well as those funded by partner governments and other donors. This mapping needs to include the geographical and population coverage of each intervention — for example, what percentage of all pregnant women is receiving PMTCT in each district. Know Your Response mapping should also provide information on the “dose” of prevention interventions (for those that require multiple doses), as well as track fidelity of scaled-up efforts to the original model. For example, if a demand creation program was planned to include four contacts with each individual in a village, Know Your Response mapping would show what percentage of participants are receiving that dose and assess whether the content and structure of these interactions match that of the original model for the campaign. Know Your Response mapping should also take into account the accessibility of interventions, asking whether services, commodities and programs are available to target populations in locations and at times of day appropriate to those populations who need and should be using them. Sites or programs with a history of under-utilization should be identified, and either de-funded or altered to address the causes of poor uptake.

Data for Know Your Response mapping will come from diverse sources. Data on target population size will come from appropriate methodologies conducted to obtain a size estimation, as well as more general demographic data for the localities in question. Data on coverage, dose, and quality should emerge from routine monitoring and evaluation of programs. The challenge in achieving a truly national map of prevention activities lies in coordinating across multiple funders and implementing partners. While partner governments should take the leading role in this coordination, PEPFAR can and should play a facilitating role where this capacity is limited. UNAIDS is also a key resource for assistance with coordination and typically takes on this leadership role within a country. While the costs of data collection will fall mostly in the strategic information budgets for individual activities, costs of capacity-building may be covered within the prevention budget and should be considered a health systems strengthening activity.

4. **Know Your Costs:** Accurate costing of HIV prevention activities is essential to the success of our programs. Knowing exactly what our dollars are buying in terms of prevention outputs is challenging but critical to ensuring PEPFAR is as efficient as possible with US taxpayer funds. PEPFAR agencies are supporting costing exercises to help country teams understand the unit costs of interventions, but much work remains to be done to better understand the cost of prevention activities in different contexts.

As our capacity to measure infections averted improves, PEPFAR country teams should also begin to work with experts to determine the cost per infection averted of our prevention programs. This information is important to ensuring that our investments are as targeted and effective as possible.

2.2 Using computer modeling to estimate population-level effects of HIV prevention activities

Recent advances in computer modeling of HIV epidemics have generated excitement and controversy. These models offer the possibility of estimating the impact of specific prevention

interventions on the future trajectory of the epidemic, potentially allowing donors and governments to determine the optimal mix of interventions for a given population.

Computer models are already playing an important role in shaping decisions around specific interventions. For example, the use of computer models demonstrating the potential impact of male circumcision on epidemics in southern Africa has been a key tool in garnering support for rapid scale-up of that intervention.

However, the output of any given model is only as good as the data used to generate it. Where data on population size, impacts and unit costs of interventions, and current prevalence are poor, the accuracy of the projections produced by the models will also be poor.

Quality “Four Knows” data can make strong models, which serve as powerful tools for PEPFAR country teams to use to maximize and provide advocacy for the impact of their prevention investments, as well as to win support from key stakeholders. All country teams should carefully consider the use of computer models where they have good data to support them. For more information on modeling and assistance in locating expertise, please contact OGAC.

3. HIV PREVENTION AS PART OF THE COUNTRY CONTINUUM OF RESPONSE

3.1 Supporting the country continuum of response

A highly effective public health response must be comprehensive. Isolated, disconnected contacts with PLWH or individuals at risk of infection do not change the course of a country’s epidemic. The continuum of response means a national system organized to follow populations and their needs in both the health and broader development sectors, rather than being organized around particular donors, agencies, or budget codes. In the case of HIV, this means a national AIDS program that identifies populations at risk and defines specifically what services should be available to each of these populations. For each target population in each geographic setting, the continuum addresses their changing needs over time for HIV prevention, and then, if infected, for care and treatment and preventing further transmission. HIV services, including prevention, are part of the larger continuum of response that addresses the entirety of the population’s health needs.

All countries have adopted national strategies; each national program has the responsibility to turn that into an actual plan for an effective continuum of care. PEPFAR supports country ownership of prevention activities and a continuum of response that can be sustained over the long term.

PEPFAR country teams should consider the place of HIV prevention in the continuum of HIV services in each country, and within the larger continuum of all health and social services. Teams should approach prevention activities with the goal of strengthening and refocusing existing efforts to significantly reduce the number of new HIV infections and increase access to and use of HIV care and treatment. The goal is to contribute to a country prevention program that provides for coordinated implementation of HIV prevention, care, and treatment services using the best mix of interventions, intervention targets, and intervention scale to optimize the impact on new infections.

Country programs will help reach the goal of reducing new HIV infections by intensifying HIV prevention efforts in communities where HIV is most heavily concentrated. Key approaches include expanding targeted efforts to prevent HIV infection using a combination of effective, evidence-based biomedical, behavioral, and structural interventions. PEPFAR supports countries in increasing access to care and improving health outcomes for PLWH by linking them to services that can help them meet their health care needs and avoid onward transmission of the virus.

PEPFAR programs should support the continuum of response in each country by:

- Emphasizing interventions that are prioritized in the national plan, and that are well-coordinated, cost-effective, focused on high-risk populations/areas, and/or not adequately funded through other resources
- Aligning the distribution of PEPFAR prevention, care, and treatment resources to maximally reduce HIV incidence, including:
 - appropriate targeting of current services and combinations of services
 - support for interventions that are evidence-based and effective in reducing HIV at the individual and population level
 - resource allocation proportional to the risk of HIV acquisition or transmission for each population
- Addressing gaps in coverage to maximally reduce HIV incidence in designated areas, including coordination of services at different points along the continuum of HIV prevention, treatment and care.

PEPFAR's authorizing legislation supports this country-focused approach, calling for "balanced funding for prevention activities for sexual transmission of HIV/AIDS" and reliance on "objective epidemiologic evidence as to the source of infections in consultation with the government of each host country involved in HIV/AIDS prevention activities"¹⁵. In any country, three overall approaches are crucial to reducing new HIV infections:

1. Increasing knowledge of HIV status among people living with HIV and their partners
2. Reducing risk of HIV transmission from people living with HIV
3. Reducing HIV acquisition among persons at risk for infection

In working with country partners to implement their national plans and the background guiding plans as established through the "Four Knows," PEPFAR teams should prioritize funding of programs that are:

- Scientifically proven to reduce HIV infection and/or increase access to care
- Able to demonstrate sustained and long-standing outcomes that contribute to HIV prevention goals
- Scalable to produce outcomes at the community level

¹⁵ The Tom Lantos and Henry J. Hyde United States Global Leadership Against HIV/AIDS, Tuberculosis and Malaria Reauthorization Act of 2008. (2008). Public Law 110-293, Sec. 403(a)(1). Accessible at: <http://www.gpo.gov/fdsys/pkg/PLAW-110publ293/pdf/PLAW-110publ293.pdf>.

- Cost-effective
- Sustainable

Realizing the benefits of these strategies depends on implementing strategies that are known to reduce risk of HIV transmission and acquisition. As teams work to expand coverage, they should recognize that some prevention investments can be implemented relatively quickly and have a rapid impact on the epidemic. Others, including those that address cultural, structural, and institutional determinants of vulnerability, may require more time to achieve change. These longer-term investments are important. Without them, the HIV epidemic cannot be successfully contained and reversed, as factors that drive vulnerability will remain in place.

3.2 Overarching principles of PEPFAR prevention programming

1. Set epidemiologically sound priorities

Use available HIV incidence, prevalence, behavioral, and epidemiological data to determine the appropriate balance of prevention activities among different gender, sexual behavior, and age groups. Tailor the response to the geographic distribution of the epidemic in the country. Be responsive to changes in HIV transmission over time, localized spatial clustering of HIV infections, and the local context. It is especially important to address PLWH and couples in sero-discordant relationships to reduce the risk of HIV transmission.

2. Program to the social and cultural context

- In collaboration with governments, partners, and communities, consider social determinants of health in the development, implementation, and monitoring and evaluation of programs, and select culturally appropriate interventions that are tailored for the communities for which they are intended. All sectors of the population should be actively involved in the response, including national and regional governments, employers, religious groups, NGOs, members of key affected populations, and PLWH and their communities. Many of the world's most successful HIV prevention efforts have been led by the affected communities
- Use data, including social determinants data, to identify communities that are disproportionately affected by HIV
- Identify the social and structural factors that may increase HIV risk or vulnerability, such as population mobility, and cross-generational and transactional sex
- Identify opportunities to empower women and engage men to address harmful gender norms that increase risk.

3. Support a coordinated response

- Work with government, partners, and communities to coordinate and harmonize prevention efforts, foster clear and consistent messaging that is mutually reinforcing across different partners, share lessons learned, ensure referrals and linkages as needed, and avoid duplication of efforts
- Foster strong linkages from HIV testing and counseling (HTC) programs to the appropriate follow-up services, including HIV prevention, care, and treatment. Establish clear processes and mechanisms to ensure the appropriate integration of

prevention programming into care and treatment initiatives (across both clinic and community-based settings) and broader health and development work.

4. Establish quality assurance, monitoring, and evaluation mechanisms

- Establish mechanisms to assure the quality of implementation and the use of available data to inform program improvement. These mechanisms can include, but need not be limited to:
 - Establishment of standard operating procedures
 - Comprehensive program monitoring, which includes:
 - Development of meaningful program-level indicators to reflect the optimal mix and quality of prevention approaches (e.g. dose, intensity, multi-level strategies)
 - Development and ongoing revision of monitoring plans which feed back into program implementation
 - Training and supportive supervision for USG staff and partners in collecting and analyzing data to improve implementation, including periodic refresher trainings and quality assessments with plans to transfer these skill sets to country ownership.
 - Use of formative assessments to improve the design, implementation, revision, messaging, focus, and relevance of prevention programming
 - Ongoing evaluation of the impact of prevention programs where:
 - Interventions of known efficacy are closely monitored and implementation science is used to effect more rapid and effective scale-up
 - Interventions of unknown efficacy that address known critical drivers are piloted and their impact on behavioral and biological outcomes and/or HIV incidence measured, with full scale-up dependent upon impact (see PEPFAR Impact Evaluation Guidance)
 - Interventions that play an enabling role are evaluated based upon their ability to drive provision and uptake of services

4. EVIDENCE AND IMPLEMENTATION GUIDANCE ON SPECIFIC INTERVENTIONS

4.1 Levels of evidence for elements of combination prevention

In reviewing the evidence base for specific interventions, it is important to note that the highest level of evidence is data showing that particular prevention interventions have demonstrated *specific impact on HIV incidence*. Although studies that show behavioral outcomes or other biological outcomes of particular interventions provide important indications that the interventions might avert HIV infections, programs that have been shown to have a direct impact on HIV incidence are of particular importance.

This is the case for several reasons. First, as the primary objective is HIV prevention, direct evidence that an intervention unequivocally prevents HIV transmission is the most powerful evidence. By contrast, an intervention that succeeds in reducing high-risk behaviors may or may not be potent enough to reduce them sufficiently to reduce HIV incidence. Similarly, a study

that shows effect on prevention of other STIs, which are easier to transmit than HIV, may also not be sufficient to prevent HIV incidence. Finally, many studies have demonstrated that reporting of sexual behavior is problematic and potentially unreliable, especially among young people. This is particularly problematic during implementation of an intervention, and even more so for stand-alone behavioral interventions when over-reporting of “desired” behaviors is likely due to social desirability bias.

Thus in reviewing the evidence base for particular interventions, the greatest ‘weight’ should be given to those supported by evidence of *specific impact on HIV incidence*.

4.2 Biomedical interventions for prevention of sexual transmission

These interventions are those that act directly on the biological systems through which the virus infects a new host.

It should be noted that other forms of biomedical prevention that do not address sexual transmission and thus are beyond the scope of this guidance (but for which details are available in other PEPFAR guidance) include:

- Prevention-of-mother-to-child-transmission (PMTCT) to prevent vertical transmission of HIV from infected mothers to their infants during either labor and delivery or breastfeeding¹⁶
- Comprehensive programs to prevent transmission among PWID¹⁷.

4.2.1 Male and female condoms

Evidence

Male Latex Condoms¹⁸: When used consistently and correctly, male latex condoms are highly effective in preventing the sexual transmission and acquisition of HIV and other STIs at the individual level^{19,20}. Among MARPs, increasing condom availability, accessibility, acceptability, and use has had a demonstrable population-level effect in several epidemics^{21,22}. In heterosexual serodiscordant relationships in which condoms were consistently used, HIV-negative partners were 80% less likely to become infected compared with persons in similar relationships in which condoms were not used²³. Correct and consistent condom use significantly reduces the risk of HIV transmission from both men to women and also from

¹⁶ Integrating PMTCT, Maternal, Neonatal, and Child Health and Pediatric HIV Services. Accessible at: <http://www.pepfar.gov/guidance/pmtct/158785.htm>

¹⁷ Technical Guidance: Prevention for People Who Inject Drugs. Accessible at: <http://www.pepfar.gov/guidance/combinationprevention/combprevidu/index.htm>

¹⁸ Additional information on male condoms is accessible at: www.cdc.gov/condomeffectiveness/latex.htm.

¹⁹ Foss AM, Hossain M, et al. (2007). A systematic review of published evidence on intervention impact on condom use in sub-Saharan Africa and Asia. *Sexually Transmitted Infections* 83(7), 510-516.

²⁰ Weller SC, Davis K. (2002). Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database of Systematic Reviews*. CD003255.

²¹ Saphonn V, Heng S, et al. (2004). Current HIV/AIDS/STI epidemic: intervention programs in Cambodia, 1993-2003. *AIDS Education and Prevention*, 16(Suppl A), 64-77.

²² Mehendale SM, Gupte N, et al. (2007). Declining HIV incidence among patients attending sexually transmitted infection clinics in Pune, India. *Journal of Acquired Immune Deficiency Syndromes*, 45(5), 564-569.

²³ Weller S, Davis, K. (2003). Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Review*. In: The Cochrane Library, Issue 4,. Chichester, UK: John Wiley & Sons, Ltd.

women to men²⁴. Studies show condoms can reduce the risk for other STIs including chlamydia, gonorrhea, and trichomoniasis²⁵. Use of condoms also appears to reduce the risk for HPV-associated diseases (e.g. genital warts and cervical cancer) and mitigate the adverse consequences of infection with HPV²⁶.

To ensure safety and efficacy, condoms must be manufactured to the highest international standards. They must be procured according to the quality assurance procedures established by WHO, UNFPA, and UNAIDS, and they should be stored away from direct heat sources. In the United States, condoms are regulated as medical devices and are subject to random sampling and testing by the U.S. Food and Drug Administration (FDA). Each latex condom manufactured in the United States is tested electronically for holes before packaging. Rates of male condom breakage during sexual intercourse and withdrawal are approximately two broken condoms per 100 condoms used in the United States²⁷. The failure of male condoms to protect against HIV, STI transmission or unintended pregnancy usually results from inconsistent or incorrect use rather than condom breakage²⁸.

Female Condoms: Laboratory studies indicate that the female condom is an effective mechanical barrier to semen and viruses, including HIV²⁹. In 2006, WHO concluded that female condoms, when used consistently and correctly, have comparable effectiveness to male condoms. In 2009, the FDA approved the second generation of the female condom (FC2) for prevention of HIV, other STIs, and unintended pregnancy. The female condom is the only female-initiated method currently available that can be worn by women for protection against both unintended pregnancy and STIs, though men can also initiate use.

A growing body of evidence shows that effective female condom promotion to both women and men can increase the proportion of protected sex acts^{30, 31, 32}. Studies conducted in a variety of contexts show that the female condom is widely acceptable and a realistic alternative to the male condom³³. One study found that providing a choice of condoms successfully increased acceptability³⁴.

²⁴ Holmes KK, Levine R, Weaver M. (2004). Effectiveness of condoms in preventing sexually transmitted infections, *Bulletin of the World Health Organization*, 82, 454–461.

²⁵ Ibid.

²⁶ Ibid.

²⁷ Weller SC. (1993). A meta-analysis of condom effectiveness in reducing sexually transmitted HIV. *Social Science Medicine*, 1635-44.

²⁸ CDC. (2008). Male latex condoms and sexually transmitted diseases. Fact sheet for public health personnel.

²⁹ Drew WL, Blair M, et al. (1990). Evaluation of the virus permeability of a new condom for women. *Sexually Transmitted Diseases*, 17(2), 110-112.

³⁰ Shane B, Herdman C, et al. (2006). The female condom: significant potential for STI and pregnancy prevention. *Outlook*, 22(2).

³¹ Vijayakumar G, Mabude Z, Smith J, et al. (2006). A review of female-condom effectiveness: patterns of use and impact on protected sex acts and STI incidence. *International Journal of STD and AIDS*, 17(10), 652-9.

³² Hatzell T, Feldblum PJ, et al. (2003). The female condom: is “just as good” good enough? *Sexually Transmitted Diseases*, 30 (5), 440-442.

³³ French PP, Latka M, Gollub EL, et al. (2003). Use-effectiveness of the female versus male condom in preventing sexually transmitted disease in women. *Sexually Transmitted Diseases*, 30(5), 433–9.

³⁴ Steiner, MJ, Hylton-Kong T, Figueroa P, et al. (2006). Does a choice of condoms impact sexually transmitted infection incidence? A randomized, controlled trial. *Sexually Transmitted Diseases*, 33(1), 31–35.

There have been reports of use of the female condom for STI/HIV protection during receptive anal intercourse³⁵. Although a female condom might provide some protection in this context, its efficacy remains unknown.

Program Implementation

Condoms are an integral and essential part of comprehensive prevention, treatment, and care programs, and condom promotion to increase use must be accelerated. Prevention, treatment and care programs should seek to ensure that high-quality condoms are accessible to those who need them, when they need them, and that people have the knowledge and skills to use them correctly. Condoms must be made readily available as widely as possible, either free or at low cost, and promoted in ways that help overcome social and personal obstacles to their use. Effective condom promotion targets not only the general population, but also people at higher risk of HIV exposure, especially women, SW and their clients, PWID, and MSM. The search for new preventive technologies such as HIV vaccines and microbicides continues to make progress, but condoms will remain a key component of PEPFAR combination prevention strategies.

Need to Increase Availability: The current supply of condoms in low- and middle-income countries falls well short of the number required. PEPFAR teams should engage with multiple groups in countries (including both the reproductive health and HIV sectors as well as the government) to address eliminating stock-outs and improving supply chain management, distribution, and programming.

Need to improve knowledge, acceptability, and demand for male and female condom: Condoms are an important prevention tool for the general population as well as marginalized groups, including people living with HIV. Multiple channels can be deployed to ensure that all people receive accurate, culture- and age-appropriate information about how male and female condoms prevent HIV infection. HIV prevention education and condom promotion should address the challenges of complex gender and cultural factors, ensuring that gender issues are not a barrier to information about and access to condoms. In many social contexts, females do not have the power to negotiate the use of condoms, and males are resistant to the use of condoms. This lack of power needs to be recognized in designing condom promotion programs. Female condoms can provide women with more control in protecting themselves.

Increased access to ART creates the need and the opportunity for accelerated condom promotion: The success of ART in reducing illness and prolonging life has shown that it can alter the perception of risk associated with HIV. With good adherence, ART can significantly reduce infectiousness, but some risk of transmission persists, especially if viral load suppression has not been fully achieved. Promotion of correct and consistent condom use within treatment and care programs and within reproductive health and family planning services is essential to reduce further risk of transmission.

³⁵ Gross M, Buchbinder SP, Holte S, et al (HIVNET Vaccine Preparedness Study Protocol Team). (1999). Use of reality “female condoms” for anal sex by US men who have sex with men. *American Journal of Public Health*, 89, 1739-41.

4.2.2 Voluntary medical male circumcision (VMMC)

Evidence

Voluntary medical male circumcision is the surgical removal of the foreskin from the penis by trained medical personnel under aseptic conditions. Three randomized control trials indicated that VMMC reduces men's risk of HIV acquisition by 50-60%^{36,37,38}. Extended follow-up of participants at up to five years post-trial indicated that the protective effect increased to 68%³⁹.

WHO and UNAIDS have concluded that VMMC should be actively promoted as part of comprehensive HIV prevention efforts in settings where circumcision rates are low and HIV prevalence is high⁴⁰. Current evidence strongly supports VMMC's effectiveness in preventing infection of men in penile-vaginal intercourse, but not in penile-anal intercourse⁴¹. While statistics have been inconclusive thus far on the efficacy of circumcising MSM to prevent infection, the procedure may be worthwhile for individual MSM, especially those who also engage in sex with women. In the United States, heterosexual males with a genital ulcer, who were more likely to report not being circumcised, were found to have a 3.5-fold higher risk of HIV infection compared to men without a genital ulcer⁴².

The effect of circumcision on male-to-female HIV transmission has not been extensively researched. One trial involving 922 HIV-positive men in Uganda found circumcision did not reduce HIV transmission to uninfected female partners⁴³. Another study found that male circumcision was not significantly associated with decreasing women's HIV risk⁴⁴. However, a prospective study enrolling HIV sero-discordant couples found a promising, although not statistically significant, 40% reduction in sero-conversions of women whose male partners were circumcised⁴⁵.

Regardless of a direct benefit to women, there is no doubt of an indirect benefit that accrues over time. Modeling has confirmed that properly implemented VMMC programs that lower HIV prevalence among the male population would thereby also reduce women's risk of exposure to

³⁶ Auvert B, Taljaard D, Lagarde E, et al. (2005). Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 trial. *PloS Medicine*, 2(11).

³⁷ Bailey RC, Moses S, Parker CB, et al. (2007). Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *The Lancet*, 369(9562), 643-656.

³⁸ Gray RH, Kigozi G, Serwadda D, et al. (2007). Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *The Lancet*, 369(9562), 657-666.

³⁹ Kong X, et al. (2011). Long term effects of male circumcision on HIV incidence and risk behaviors during post trial surveillance in Rakai, Uganda. CROI.

⁴⁰ WHO and UNAIDS. (2007, 28th March). WHO and UNAIDS announce recommendations from expert meeting on male circumcision for HIV prevention. Accessible at: <http://www.who.int/hiv/mediacentre/news68/en/index.html>.

⁴¹ Sanchez J, et al. (2010). Male circumcision and risk of HIV acquisition among men who have sex with men. *AIDS*, 24.

⁴² Tobian AAR, Serwadda D, Quinn TC, et al. (2009). Male circumcision for the prevention of HSV-2 and HPV infections and syphilis. *The New England Journal of Medicine*, 360, 1298-309.

⁴³ Wawer MJ, Makumbi F, Kigozi G, et al. (2009). Circumcision in HIV-infected men and its effect on HIV transmission to female partners in Rakai, Uganda: a randomised controlled trial. *The Lancet*, 374(9685) 229-37.

⁴⁴ Turner AN, et al. (2007). Men's circumcision status and women's risk of HIV acquisition in Zimbabwe and Uganda. *AIDS*, 21, 1779-1789.

⁴⁵ Baeten JM, Donnell D, Kapiga SH, et al. (2010). Male circumcision and risk of male-to-female HIV-1 transmission: a multinational prospective study in African HIV-1 serodiscordant couples. *AIDS*, 24(5), 737-744.

men infected with the virus⁴⁶. Circumcision may also help protect women from contracting HPV and thus help prevent cervical cancer: a study conducted in Uganda found that circumcision reduced HPV incidence among the female long-term partners of study participants by 77%⁴⁷.

WHO recommends that men abstain from sex for 6 weeks following circumcision, until proper healing occurs⁴⁸. Concerns have been raised about the possible increased risks of transmitting HIV immediately following the circumcision procedure. A study conducted among African men found that most avoided sex until healing had occurred. Of those who did engage in sexual activity, it was not associated with an increased risk of acquiring HIV⁴⁹. However, another study conducted in Uganda revealed that post-circumcision sexual activity among HIV-positive men prior to complete healing may have led to an increased risk of HIV transmission to their wives, although this risk was not demonstrated once the study was completed⁵⁰.

A recent study suggests that VMMC, with the life-long protection it provides, is a cost-effective strategy to prevent HIV in high-prevalence areas⁵¹. Additionally, 13 studies conducted across nine sub-Saharan countries demonstrated that attitudes toward the procedure were consistently positive among both men and women.

Program Implementation

Countries with a low prevalence of male circumcision and high HIV prevalence should initiate and accelerate steps to increase the availability of VMMC services. As with other prevention methods, considerations of access and cost, as well as cultural, ethical, and religious factors can hinder the widespread implementation of VMMC. Engagement of key stakeholders, and educational and behavior change campaigns are needed to increase awareness about the benefits of VMMC and diminish cultural barriers to the procedure.

Implementation of the comprehensive HIV package: Where VMMC services are provided, they must be part of a comprehensive HIV prevention package along with provision of HTC, treatment for STIs, promotion of safer sex (including counseling of men and their sexual partners to prevent them developing a false sense of security), and provision of condoms (including instructions about how to use them correctly). Country teams are advised to consider providing VMMC to men free of charge or at the lowest possible cost to the client, as with other essential services. PEPFAR will support programs, in keeping with national strategies, that: implement the comprehensive package; adopt culturally-appropriate strategies; utilize well-trained practitioners working in sanitary conditions; maintain informed consent and confidentiality; and avoid any form of coercion.

⁴⁶ Weiss H, Hankins C, Dickson K. (2009). Male circumcision and risk of HIV infection in women: a systematic review and meta-analysis. *The Lancet Infectious Diseases*, 9(11).

⁴⁷ Wawer MJ, Tobian AAR, Kigozi G, et al. (2011). Effect of circumcision of HIV-negative men on transmission of human papillomavirus to HIV-negative women: a randomised trial in Rakai, Uganda. *The Lancet*, 377(9761), 209-218.

⁴⁸ WHO. (2008). Operational guidance for scaling up male circumcision services for HIV prevention.

⁴⁹ Mehta SD, Gray RH, Auvert B. (2009). Does sex in the early period after circumcision increase HIV-seroconversion risk? Pooled analysis of adult male circumcision clinical trials. *AIDS*, 23, 1557-64.

⁵⁰ Tobian AAR, et al. 2009.

⁵¹ UNAIDS/WHO/SACEMA. (2009). Male circumcision for HIV prevention in high HIV prevalence settings: what can mathematical modeling contribute to informed decision making? Accessible at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2731851/>.

Targeted implementation: UNAIDS and WHO advise that the greatest public health benefit results from prioritizing circumcision for young males (such as those aged 12-30 years), as well as men thought to be at higher risk for HIV (such as those in discordant couples or being treated for STIs)⁵². Circumcision of newborn babies should be promoted as a longer-term strategy. VMMC for men living with HIV is not recommended but should not be denied if requested.

Short-term, accelerated implementation: Programs to provide VMMC for HIV prevention differ from other programs such as care and treatment services in that personnel and facility capacity are not required for the long term. Once intensive service provision accomplishes “catch-up” circumcision for adolescent and adult males, sustainable services need to reach only successive cohorts of young adolescents and/or newborns. These “catch up” programs require awareness and behavior change communication campaigns wherein political and social leaders promote VMMC. Rapidly deployable and high-volume service delivery approaches that are self-contained, time-limited, independently staffed, fairly mobile, and use implementation models for optimizing volume and efficiency (MOVE) have been developed and are being successfully implemented in several countries (e.g. Kenya, Tanzania, Swaziland, South Africa).

4.2.3 HIV testing and counseling (HTC)

Evidence

The evidence for the direct impact of HIV testing and counseling on HIV incidence is mixed. However, HTC, knowledge of HIV sero-status, and successful linkages to other services are critical for access to effective prevention interventions for those who test negative, and to treatment and other HIV-specific services for PLWH. In particular, the HTC process allows for identification of PLWH, which in turn supports programs like treatment that can protect their HIV negative partners from infection⁵³. Data from nationally representative surveys and studies continue to point to low proportions of people who have ever been tested for HIV, and a lack of knowledge about partners’ HIV status^{54,55,56,57}. Recent Demographic and Health Surveys from 13 sub-Saharan African and five non-African countries show a median of 12% of women and 7% of men having been tested in the 12 months preceding the survey, and a median of 34% of women and 17% of men reporting having ever been tested⁵⁸. Specific approaches to HTC differ

⁵² WHO and UNAIDS. (2008). Operational guidance for scaling up male circumcision services for HIV prevention. August 2008. Accessible at: http://www.malecircumcision.org/programs/documents/MC_OpGuideFINAL_web.pdf.

⁵³ Cohen MS, Chen YQ, et al. (2011). Prevention of HIV-1 infection with early antiretroviral therapy. *New England Journal of Medicine*, 365, 561-562.

⁵⁴ WHO Report 2010.

⁵⁵ Kaiser R, Bunnell R, Hightower A, et al (KAIS Study Group). (2011). Factors associated with HIV infection in married or cohabitating couples in Kenya: results from a nationally representative study. *PLoS One*, 6(3), e17842.

⁵⁶ Loubiere S, Peretti-Watel P, Boyer S, et al. (2009). HIV disclosure and unsafe sex among HIV-infected women in Cameroon: results from the ANRS-EVAL study. *Social Science and Medicine*, 69(6), 885-91. E-published 2009 Jun 25.

⁵⁷ WHO Report 2010.

⁵⁸ Ibid.

in ability to reach specific populations (e.g. HIV-positive, first-time testers, pregnant women, TB patients, and MARPs)⁵⁹.

For PLWH, HTC is a critical entry point to accessing HIV prevention, care, and treatment, as well as other health services including TB screening and family planning. Couples-based or individual HTC with partner testing can also assist in identifying sero-discordant couples, among whom significant HIV transmission occurs in some epidemics. While the definition of a “partner” in couples-based HTC requires further clarification, this form of HTC can aid in promoting disclosure and preventive behaviors^{60,61}. Continued scale-up of quality HTC may contribute to the reduction of HIV risk behaviors among these specific populations. Some published evidence suggests that HTC is correlated with a positive impact on behavior change, among PLWH^{62,63,64}, and sero-discordant couples^{65,66}, but other studies have not shown this^{67,68,69}. Among individuals who test HIV-negative, some studies have reported reductions in risk behaviors^{70,71}, while others have reported no reductions in risk behaviors^{72,73}.

Program Implementation

HTC is an essential component of country HIV programming as a prerequisite for access to ART, pre-ART care and support, and for most biomedical interventions such as PMTCT and VMMC^{74,75}. Couples HTC in particular is a critical element of emerging interventions promoting

⁵⁹ See for example: Sweat M, Morin S, Celentano D, et al. (2011). Community-based interventions to increase HIV testing and case detection in people aged 16-32 years in Tanzania, Zimbabwe, and Thailand (NIMH Project Accept, HPTN 043): a randomized study. *The Lancet Infectious Diseases*, 11(7), 525-32.

⁶⁰ Burton J, Darbes L, et al. (2010). Couples-focused behavioral interventions for prevention of HIV: Systematic review of the state of evidence. *AIDS and Behavior* 14(1), 1-10.

⁶¹ Dunkle KM, Stephenson R, Karita E, et al. (2008). New heterosexually transmitted HIV infections in married or cohabiting couples in urban Zambia and Rwanda: an analysis of survey and clinical data. *Lancet*, 371, 2183-91.

⁶² Denison JA, McCauley AP, Dunnett-Dagg WA, et al. (2008). The HIV testing experiences of adolescents in Ndola, Zambia: do families and friends matter? *AIDS Care*, 20(1), 101-5.

⁶³ Sherr L, Lopman B, Kakowa M, et al. (2007). Voluntary counselling and testing: uptake, impact on sexual behaviour, and HIV incidence in a rural Zimbabwean cohort. *AIDS*, 21(7), 851-860.

⁶⁴ Voluntary HIV-1 Counseling & Testing Efficacy Study Group. (2000). Efficacy of voluntary HIV-1 counselling and testing in individuals and couples in Kenya, Tanzania, and Trinidad: a randomised trial. *Lancet*, 356(9224), 103-12.

⁶⁵ Dunkle KM, et al. 2008.

⁶⁶ Bunnell R, Cherutich P. (2008). Universal HIV testing and counselling in Africa: Comment. *Lancet*, 371, 2148-50.

⁶⁷ Huchko M, Montandon M, Nguti R, et al. (2011). The association of HIV counseling and testing with HIV risk behaviors in a random population-based survey in Kisumu, Kenya. *AIDS and Behavior*, 15(4), 718-724.

⁶⁸ Eisele T, Mathews C, Chopra M, et al. (2008). High levels of risk behavior among people living with HIV initiating and waiting to start antiretroviral therapy in Cape Town South Africa. *AIDS and Behavior*, 12(4), 570-577.

⁶⁹ Denison JA, O'Reilly KR, Schmid GP, et al. (2008). HIV voluntary counseling and testing and behavioral risk reduction in developing countries: a meta-analysis, 1990-2005. *AIDS and Behavior*, 12(3), 363-373.

⁷⁰ Coates TJ, Sweat M, Gregorich S, et al. (2000). Efficacy of voluntary HIV-1 counselling and testing in individuals and couples in Kenya, Tanzania, and Trinidad: a randomised trial. *The Lancet*, 356(9224), 103.

⁷¹ Turner AN, Miller WC, Padian NS, et al. (2009). Unprotected sex following HIV testing among women in Uganda and Zimbabwe: short- and long-term comparisons with pre-test behaviour. *International Journal of Epidemiology*, 38(4), 997-1007.

⁷² Corbett EL, Makamure B, Cheung Y, et al. (2007). HIV incidence during a cluster-randomized trial of two strategies providing voluntary counselling and testing at the workplace, Zimbabwe. *AIDS*, 21(4), 483-489.

⁷³ Sherr L, et al. 2007.

⁷⁴ WHO. (2011). Guide for monitoring and evaluating national HIV testing and counselling (HTC) programmes: field-test version. Accessible at: <http://www.who.int/hiv/pub/vct/9789241501347/en/index.html>.

⁷⁵ WHO. (2010). Delivering HIV test results and messages for re-testing and counselling in adults. Accessible at: http://www.who.int/hiv/pub/vct/hiv_re_testing/en/index.html. Last accessed: May 20, 2011.

the use of ART as prevention in sero-discordant couples. HTC is a critical component of the comprehensive package of services for MARPs. HTC will also be central in any future implementation of prevention interventions such as PrEP and ART for prevention in sero-discordant couples. Assuming efficient linkages from HTC to proven prevention interventions programs, 80% population coverage will likely be required for HTC among high-burden populations to realize population-level impacts. Importantly, the strength of linkages between HTC points of diagnosis and other HIV services — both clinic-based and community-based — will fundamentally impact the effectiveness of any HTC programming.

The overarching goals of HTC programs are to:

- Ensure that individuals, couples/partners, and families learn their HIV status—with particular emphasis on identifying HIV-positive individuals and sero-discordant couples — including appropriate pre-test information and post-test risk-reduction counseling and linkage to services based on sero-status
- Implement strategies for ensuring that individuals, couples, and families are linked with appropriate follow-up HIV treatment, care and support, and prevention services based on their sero-status (see Figure 1).

There are a range of settings and approaches available to deliver HTC to specific populations. These include provider-initiated HTC, and outreach or community-based HTC, as well as traditional stand-alone VCT sites. Each of these approaches has the potential to reach different population segments depending upon how and where implemented. Priority settings for provider-initiated HTC include TB, STI and antenatal care settings. In generalized epidemics, WHO recommends that HTC be routinely offered in all clinical settings, including antenatal, sexually transmitted infection, and tuberculosis clinics; medical and surgical inpatient wards; and out-patient departments. In addition to standalone voluntary HTC sites, considerable uptake of HTC delivered via mobile and home-based testing has been demonstrated in several countries.

To ensure efficient and effective use of funds, HTC programming should ensure that:

- The mix of HTC approaches is strategically applied to communities and populations most likely to be affected by HIV
- An emphasis is placed on strengthening linkages and referrals to appropriate follow-up services and ensuring initial enrollment in these services
- HTC services are implemented according to international and national minimum standards and guidelines.

Partner and family HTC programs are especially important for the identification of HIV sero-discordant couples, for whom the HIV prevention benefits of HTC may be the greatest. Additionally, disruptions in HTC commodities represent a missed opportunity for diagnosis. As supply chain challenges with HTC test kits may be a critical barrier to ensuring service availability, PEPFAR teams should work with partner governments and the donor community to jointly address these problems.

Creating strong linkages from HTC to care and treatment for those found HIV-positive has been a challenge. This challenge requires ongoing attention and the development of strategies for

enhanced linkages to HIV prevention, care and treatment. The new data on impact of effective treatment on prevention reinforces the importance of HTC to identify seropositives and prevent new transmission. Successful HIV prevention also includes attention to specific HIV-negative sub-populations. PEPFAR-supported HTC programs should develop clear protocols for HIV-negative individuals that include risk-reduction counseling, provision of condoms, and referral as appropriate to other prevention interventions such as VMMC, youth activities, and community mobilization programs. It is also important to harmonize messages for HIV-negative people provided through HTC with broader HIV prevention messages communicated through behavior change programs (e.g. on partner reduction).

4.2.4 Diagnosis and treatment of sexually transmitted infections (STIs)

Evidence

Studies have shown that STIs, including those that are asymptomatic, increase susceptibility to HIV infection two- to five-fold for several reasons, including direct damage to the mucosa through ulceration that facilitates infection, and through inflammatory processes that increase the proliferation of immune cells that are also targets for HIV^{76,77}. STIs also lead to higher HIV loads in the genital secretions of HIV-positive individuals, thereby increasing the chance of infecting their sexual partners⁷⁸. STIs are biological markers for risky sexual behaviors, increase susceptibility to HIV acquisition through genital ulcers, and increase onward transmission of HIV associated with HIV viral spikes^{79,80,81}. Despite these data, numerous clinical trials have not been able to demonstrate a decline in HIV incidence as a result of STI treatment^{82,83,84}. Some researchers have speculated that the success of STI treatment as an HIV prevention strategy depends on the epidemic stage, the prevalence of viral versus treatable bacterial STIs, and the treatment of choice. Targeting HIV prevention and testing to populations with STIs remains key, especially as many may be co-infected with HIV and STIs, or be acutely HIV infected and therefore at greater risk of transmitting HIV. There is a substantial potential for co-benefits and synergies in treating STIs in those who are co-infected with HIV including: delaying HIV progression; ensuring optimal HIV care, including for opportunistic infections; and providing an entry point for other HIV prevention and care services.

⁷⁶ Fleming DT, Wasserheit JN. (1999). From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sexually Transmitted Infections*, 75,3-17.

⁷⁷ Wasserheit JN. (1992). Epidemiologic synergy: interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. *Sexually Transmitted Diseases*, 9, 61-77

⁷⁸ Galvin R, Cohen MS. (2004). The role of sexually transmitted diseases in HIV transmission. *Nature Reviews Microbiology*, 2(1), 33-42 .

⁷⁹ Holmes KK, et al. (2008). *Sexually Transmitted Diseases, 4th Edition*. New York, McGraw Hill, (eds), 1958-76.

⁸⁰ Sobngwi-Tambekou J, Taljaard D, Lissouba P, et al. (2009). Effect of HSV-2 serostatus on acquisition of HIV by young men: results of a longitudinal study in Orange Farm, South Africa. *Journal of Infectious Disease*, 199,958–64.

⁸¹ Barnabas RV, Wasserheit JN. (2009). Riddle of the Sphinx revisited: the role of STDs in HIV prevention. *Sexually Transmitted Diseases*, 36(6),365-7.

⁸² Celum C, Wald A, Lingappa JR, et al. (2010). Acyclovir and transmission of HIV-1 from persons infected with HIV-1 and HSV-2. *New England Journal of Medicine*, 362(5), 427-439.

⁸³ Kamali A, Quigley M, Nakiyingi J, et al. (2003). Syndromic management of sexually-transmitted infections and behaviour change interventions on transmission of HIV-1 in rural Uganda: a community randomised trial. *Lancet*, 361(9358), 645.

⁸⁴ Kaul R, Kimani J, Naglekerke NJ, et al. (2004). Monthly antibiotic chemoprophylaxis and incidence of sexually transmitted infections and HIV-1 infection in Kenyan sex workers: a randomized controlled trial. *Journal of the American Medical Association*, 291(21), 2555-2562.

Program Implementation

Patients at STI clinics are likely to have engaged in high-risk behaviors which place them at risk for incident HIV infection. The high viral loads associated with acute infection, coupled with the high-risk behavior of patients in STI treatment clinics, make this population a high priority for HIV prevention messages and services including HTC and risk reduction counseling. Providing HTC as part of the routine services offered to patients in STI treatment clinics can also identify patients co-infected with HIV, so that these patients can be linked with HIV prevention, care, and treatment programs.

PEPFAR support for STI control for HIV prevention is dependent on the type of HIV epidemic (concentrated or generalized).

In Concentrated Epidemics:

The population focus should be:

- MARPs
- People who present for care with symptomatic STIs (especially genital ulcer disease (GUD) and urethral discharge (UD))
- HIV-positive persons with ongoing high-risk behavior (symptomatic and asymptomatic STIs)
- Others at risk defined locally (e.g. sexually active adolescents and sexually active mobile or displaced populations).

The programmatic focus should be:

- Syndromic management of GUD and UD
- Presumptive treatment or screening of STIs for high-risk women and men
- Syndromic management of anal discharge and etiologic or risk-based diagnosis of anal STIs for high-risk women and high-risk men who have sex with men with persistent vaginal or anal discharge.

Generalized Epidemics

The population focus should be:

- High-risk sub-populations
- People who present for care with symptomatic STIs
- HIV-positive persons (asymptomatic and symptomatic STIs)
- HIV testing and counseling services for persons with STIs
- Sexually active adolescents.

The programmatic focus should be:

- Syndromic management of GUD
- Etiologic diagnosis of HIV-positive and most-at-risk populations
- Syndromic management of UD and vaginal discharge and etiologic or risk based diagnosis of cervical infection
- Interventions with sex partners for curable GUD.

An additional factor to consider is whether there is good potential for STI control (high proportion of curable, bacterial STIs) or poor potential for STI control (high proportion of viral STIs and low proportion of curable STIs)^{85, 86, 87}.

Within the parameters above, PEPFAR funds may be used for the diagnosis and treatment of STIs in persons attending STI clinics, HIV treatment and care services, MARPs services, ANC clinics, VMMC services, and youth health services. PEPFAR funds may support syndromic treatment of urethral discharge and genital ulcers in any clinical setting. PEPFAR funds may support HTC in STI clinics, syphilis testing in ANC clinics, and STI biomarkers in surveillance activities. However, PEPFAR funds may not be used to support syndromic treatment of vaginal discharge in primary health care or family planning clinics, especially in low/concentrated epidemics.

4.2.5 Antiretroviral drug (ARV)-based prevention

There are four opportunities for HIV prevention: before exposure, at the moment of exposure, immediately after exposure, and as prevention focused on infected persons. Until recently, most prevention resources have been directed toward strategies aimed at preventing exposure. There is growing evidence that ART of infected individuals has an added prevention benefit. Treatment of HIV and prevention of HIV must be considered as elements of a single continuum and deployed together.

Post-exposure Prophylaxis (PEP) for HIV

Evidence

PEP refers to the set of services that are provided to manage specific aspects of exposure to HIV and to help prevent HIV infection in a person exposed to the risk of infection. These services might include first aid, counseling including assessing the risk of HIV exposure, HTC, and, depending on the outcome of exposure assessment, a limited course of ARVs, with appropriate support and follow-up. Exposures can be occupational (e.g. among health workers, emergency response staff, waste disposal workers, law enforcement) or non-occupational (e.g. sexual assault).

Strong evidence suggests that a short course of ARVs started within 72 hours after exposure effectively reduces HIV transmission rates following needle stick exposure to HIV-infected blood. This comes largely from a single-case control study involving health care workers from France, the United Kingdom, and the United States that revealed a strong inverse association between the likelihood of HIV infection following a needle stick injury and the post-exposure use of zidovudine⁸⁸. For ethical reasons, a randomized, placebo-controlled clinical trial cannot be performed to definitely determine the efficacy of PEP. However, data available from animal

⁸⁵ Holmes KK, et al. (2008).

⁸⁶ Sobngwi-Tambekou J, et al. (2009).

⁸⁷ Barnabas RV, Wasserheit JN. (2009).

⁸⁸ Cardo DM, Culver DH, Ciesielski CA, et al. (1997). Case-control study of HIV seroconversion in health-care workers after percutaneous exposure to HIV-infected blood *New England Journal of Medicine*, 1997, 337, 1485–1490.

transmission models⁸⁹, perinatal clinical trials⁹⁰, studies of health-care workers receiving prophylaxis after occupational exposures⁹¹, and observational studies⁹² indicate that PEP may reduce the risk of HIV infection after non-occupational exposures as well.

Program Implementation

While the impact of PEP on population-level transmission is minimal, the resources required to ensure its availability are modest and should be made available as a critical foundational intervention. WHO and CDC guidance exists for PEP administration after both occupational and non-occupational exposure⁹³. To support and preserve the healthcare workforce, PEP and related services for occupational exposure should be available in all health facilities. Small clinics with limited need for PEP may provide PEP starter packs that can provide prophylaxis for a short time until the exposed individual can access higher-level care. Facilities need clear PEP policies related to occupational exposure including testing, counseling, risk assessment, ARV provision, and linkages to appropriate follow-up care and services.

Including PEP for HIV and STIs as part of a package of service for women and men who experience sexual violence is important to ensure quality services within GBV programs. Such services should also include access to psychosocial and legal services, with proper referral systems for survivors of GBV. Broader support to the prevention of GBV is also closely tied to PEPFAR objectives.

Treatment as Prevention

Evidence

An important determinant of risk of HIV transmission from an HIV-positive person to an HIV-negative person is the concentration of HIV in plasma. ART for the HIV-positive partner is associated with both reduced viral load^{94,95} and reduced risk of HIV transmission to sex partners within discordant partnerships, potentially by over 90%^{96,97,98,99}. These observational data were

⁸⁹ Otten RA, Smith DK, et al. (2000). Efficacy of postexposure prophylaxis after intravaginal exposure of pig-tailed macaques to a human-derived retrovirus (human immunodeficiency virus type 2). *Journal of Virology*, 74, 9771–5.

⁹⁰ Shaffer N, Chuachoowong R, Mock PA, et al. (1999). Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomized controlled trial. *Lancet*, 353, 773–80.

⁹¹ Cardo DM, Culver DH, Ciesielski CA, et al. (1997). A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *New England Journal of Medicine*, 337, 1485–90.

⁹² Harrison LH, Do Lago RF, et al. (2001). Post-sexual-exposure chemoprophylaxis (PEP) for HIV: a prospective cohort study of behavioral impact [Abstract 225]. Presented at the 8th Conference on Retroviruses and Opportunistic Infections, Chicago, Illinois, February 4–8.

⁹³ WHO. (2007). Post-exposure prophylaxis to prevent HIV infection: joint WHO/ILO guidelines on post-exposure prophylaxis (PEP) to prevent HIV infection. *MMWR, Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States*, 54(RR02), 1-20.

⁹⁴ Coetzee D, Hildebrand K, Boule A, et al. (2004). Outcomes after two years of providing antiretroviral treatment in Khyelitsha, South Africa. *AIDS*, 18(6), 887-95.

⁹⁵ Crum NF, Riffenburgh RH, Wegner S, et al. (2006). Comparisons of causes of death and mortality rates among HIV-infected persons: analysis of the pre-, early, and late HAART (highly active antiretroviral therapy) eras. *Journal of Acquired Immune Deficiency Syndrome*, 41, 194-200.

⁹⁶ Quinn TC, Wawer MJ, Sewankambo N, et al (Rakai Project Study Group). (2000). Viral load and heterosexual transmission of human immunodeficiency virus type 1. *New England Journal of Medicine*, 342, 921-929.

⁹⁷ Attia S, Egger M, Muller M, et al. (2009). Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS*, 23(11), 1397-1404.

recently confirmed by HPTN 052, a randomized trial among 1,763 HIV serodiscordant couples in which the HIV-positive partner had a CD4 count between 350 and 550 cells/ μ L. The trial evaluated the effect of immediate versus delayed ART (initiated at CD4 of 250 cells/ μ L) in the HIV-positive individual. Immediate initiation of ART by HIV-positive individuals substantially protected their HIV-negative sexual partners from acquiring HIV infection, with a 96% reduction in risk of HIV transmission. HPTN 052 is the first randomized clinical trial to definitively demonstrate that treating an HIV-positive individual with ART can reduce the risk of sexual transmission of HIV to an HIV-negative partner.

Program Implementation

Early identification of HIV-discordant couples, through routine HIV testing programs and linkage of the HIV-positive individual to prevention, care, and treatment services, represents an opportunity to prevent transmission of new infections to the negative spouse or partner(s). In keeping with country guidelines and acknowledging those populations already identified as high priority for treatment, to maximize the prevention, care, and treatment benefits of ART among sero-discordant couples, programs should consider offering treatment to all HIV-positive partners who are in known discordant relationships and have CD4 counts of 350/mm³ or lower¹⁰⁰. HPTN 052 results are likely to strengthen the recommendation to consider ART at CD4 >350 cells/ μ L, especially for sero-discordant couples who cannot use condoms or are attempting to conceive, where resources make ART feasible. **Additional guidance will be developed in consultation with the PEPFAR Scientific Advisory Board to guide programming after WHO normative guidance is available.**

Pre-exposure Prophylaxis (PrEP) for HIV

Evidence

Ongoing research has been devoted to understanding the penetration of ARVs into the male and female genital tract and the protective effects of pre-exposure oral or topical (i.e. microbicide) agents on HIV acquisition¹⁰¹. In 2010 the first results were reported. In the CAPRISA 004 study in South Africa, 889 high-risk women used 1% tenofovir gel vaginally up to 12 hours before intercourse and within 12 hours after intercourse¹⁰². This study reported a 39% reduction in HIV acquisition overall, and maximal reduction of 54% in women who were the most adherent. HIV acquisition was inversely correlated with detection of tenofovir in the vaginal secretions, an indication of the strong association between product adherence and efficacy. An ongoing trial aims to reproduce or even improve on these results by examining daily use of gel as well as oral PrEP and compares these to placebo regimens¹⁰³. Tenofovir gel

⁹⁸ Donnell D, Baeten JM, Kiare J, et al (Partners in Prevention HSV/HIV Transmission Study Team). (2010). Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet*, 375(9731), 2092-8.

⁹⁹ Del Romero J, Castilla J, Hernando V, et al. (2010). Combined antiretroviral treatment and heterosexual transmission of HIV-1: cross sectional and prospective cohort study. *British Medical Journal*, 340, c2205.

¹⁰⁰ WHO. (2009). Rapid advice antiretroviral therapy for HIV infection in adults and adolescents. Accessible at: http://www.who.int/hiv/pub/arv/rapid_advice_art.pdf. Last accessed: March 18, 2011.

¹⁰¹ Cohen MS, Gay C, Kashuba AD, et al. (2007). Narrative review: antiretroviral therapy to prevent the sexual transmission of HIV-1. *Annals of Internal Medicine*, 146(8), 591-601.

¹⁰² Karim QA, Karim SS, Frohlich JA, et al. (2010). Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*, 329(5996), 1168-74.

¹⁰³ Microbicide Trials Network. (2011) MTN-003. Accessible at: <http://www.mtnstopshiv.org/node/70>.

also inhibits HSV-2 replication, and reduced acquisition of HSV-2 was noted in the CAPRISA trial.

In the iPrEx study completed in 2010¹⁰⁴, HIV-negative MSM were provided daily emtricitabine and tenofovir disoproxil fumarate (TDF+FTC) for up to 2.8 years. The study found a 44% reduction in HIV acquisition, and as with the CAPRISA trial, efficacy was strongly associated with ARV drug concentrations. Some study subjects suffered mild renal dysfunction or decrease in bone mineral density, and two subjects who had unrecognized acute (seronegative) HIV infection on PrEP developed an HIV-resistant variant.

The iPrEx study showed that PrEP reduced HIV transmission among MSM, but it was not known if the strategy could prevent HIV infection among heterosexuals. The FEM-PrEP trial of TDF+FTC offered to high-risk women was discontinued because an equal number of infections occurred in both the placebo group and the group provided with drugs¹⁰⁵. The precise explanation for the difference between the iPrEx and FEM-PrEP studies is not yet known. One strong possibility is that the concentration of tenofovir in the female genital tract was not sufficient to prevent HIV acquisition¹⁰⁶. Encouraging results from two additional trials were presented July 2011. The Partners PrEP Study enrolled 4,758 discordant couples in Uganda and Kenya¹⁰⁷. Researchers evaluated daily use of two ARVs: tenofovir and TDF+FTC. The couples were randomly assigned to three groups which determined whether the HIV uninfected partner would use tenofovir, Truvada or placebo during the study. Those who received TDF had an average of 62% fewer HIV infections and those who received TDF+FTC had 73% fewer HIV infections than those who received placebo. TDF and TDF+FTC were statistically similar in their levels of protection against HIV and reduced HIV risk in both women and men. Importantly, PrEP was found to be safe: the rate of serious medical events was similar for those assigned to TDF, TDF+FTC, and placebo. The second study, conducted by CDC in partnership with the Botswana Ministry of Health, found that a once-daily tablet containing TDF+FTC reduced the risk of acquiring HIV infection by roughly 63% overall in the study population of uninfected heterosexual men and women¹⁰⁸. Eight trials with oral antiretroviral agents for pre-exposure prophylaxis are currently ongoing.

Program Implementation

These interventions are awaiting further trials, FDA approval and normative guidance before they can be implemented in PEPFAR programs. Additional data from ongoing trials in heterosexual populations and normative guidance about PrEP for heterosexual populations are

¹⁰⁴ Grant RM, Lama JR, Anderson PL, et al. (2010). Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *New England Journal of Medicine*, 363(27), 2587-99.

¹⁰⁵ Family Health International. (2011). FHI Statement on the FEM-PrEP HIV Prevention Study. Research Triangle Park, North Carolina.

¹⁰⁶ Patterson K, Prince H, Kraft E, et al. (2010). Exposure of extracellular and intracellular tenofovir and emtricitabine in mucosal tissues after a single of fixed-dose TDF/FTC: implications for pre-exposure HIV prophylaxis (PrEP). XVIII International AIDS Conference. Vienna, Austria.

¹⁰⁷ Baeten J, Celum C, on behalf of The Partners PrEP Study Team. (2011). Antiretroviral Pre-Exposure Prophylaxis for HIV-1 Prevention among Heterosexual African Men and Women: The Partners PrEP Study. 6th International Conference on HIV Pathogenesis, Treatment and Prevention. July 17-20 2011, Rome, Italy. Abstract Late Breaker.

¹⁰⁸ Thigpen MC, Kebaabetswe PM, Smith DK, et al. (2011). Daily oral antiretroviral use for the prevention of HIV infection in heterosexually active young adults in Botswana: results from the TDF2 study. 6th International Conference on HIV Pathogenesis, Treatment and Prevention. July 17-20 2011, Rome, Italy. Abstract WELBC01.

likely in 2013. **Additional guidance will be developed in consultation with the PEPFAR Scientific Advisory Board to guide programming after WHO normative guidance is available.**

4.3 Behavioral interventions for prevention of sexual transmission

Behavioral interventions seek to promote a range of behavioral objectives related to reducing HIV transmission. These objectives include, among others, those enumerated in PEPFAR's authorization as "abstinence, delay of sexual debut, monogamy, fidelity, and partner reduction"¹⁰⁹. Behavioral interventions fall into two broad categories:

- Standalone interventions that seek to minimize sexual risk behaviors or increase protective behaviors
- Supportive interventions that seek to optimize biomedical interventions by creating demand for services and improve adherence and aftercare.

4.3.1 Standalone behavioral interventions to minimize sexual risk or increase protection

Evidence

Behavioral interventions include sexual behavior change communications (SBCC) that employ a variety of channels to communicate a range of messages. Studies have been undertaken to assess both channels of communication and the content of the messages.

Channels of communication

Mass media: Much of the research on mass media has focused on changes in intermediary indicators such as knowledge, risk perception, and self-efficacy. Reviews of this research have generally found small but positive effects on each of these indicators¹¹⁰. Studies have also linked mass media to reported positive behavioral outcomes such as delay of sexual debut¹¹¹, decreases in number of sexual partners^{112,113,114}, increases in condom use^{115,116,117}, and utilization of HTC and PMTCT services^{118,119}. In some SBCC programs, impact on these

¹⁰⁹ Public Law 110-193, Section 403 (a)(1)(B).

¹¹⁰ Bertrand JT, O'Reilly K, Anhang R, et al. (2006). Systematic review of the effectiveness of mass communication programs to change HIV/AIDS-related behaviors in developing countries. *Health Education Research*, 21(4), 567-597.

¹¹¹ FHI. (2003). Abstinence, fewer partners, and condom use are complementary messages. Arlington, FHI.

¹¹² Noar, S. (2006). A 10-Year retrospective of research in health mass media campaigns: where do we go from here? *Journal of Health Communication*, 11, 21-42.

¹¹³ Snyder LB, Huedo-Medina TB, et al. (2011). Effectiveness of media interventions to prevent HIV transmission, 1986-2006: a meta-analysis. In Review.

¹¹⁴ Vaughan PW, Rogers EM, et al. (2000). Entertainment-education and HIV/AIDS prevention: a field experiment in Tanzania. *Journal of Health Communication*, 5(1), 81-100.

¹¹⁵ Wakefield MA, Loken B, Hornik RC, et al. (2010). Use of mass media campaigns to change health behaviour." *The Lancet*, 376(9748), 1261-1271.

¹¹⁶ Bertrand JT, et al. 2006.

¹¹⁷ Noar S. (2006).

¹¹⁸ Marum E, Morgan G, Hightower A, et al. (2008). Using mass media campaigns to promote voluntary counseling and HIV-testing services in Kenya. *AIDS*, 22(15), 2019-2024.

¹¹⁹ Sebert Kuhlmann AK, Kraft JM, et al. (2008). Radio role models for the prevention of mother-to-child transmission of HIV and HIV testing among pregnant women in Botswana. *Health Promotion International*, 23(3), 260-268.

behaviors has increased significantly over time, suggesting integration of lessons learned and improved programmatic quality, although the durability of these effects is unknown¹²⁰.

Current research suggests that mass media is most effective when used to: facilitate advocacy efforts¹²¹; promote branded products and programs¹²²; and complement other community-level and interpersonal activities¹²³. Mass media programming has been shown to produce a dose-response effect, in which higher exposure to messaging resulted in increased self-reported positive behavioral change¹²⁴. Mass media campaigns have the ability to reach large segments of the population in a cost-effective manner, and can have a role in creating awareness and demand for core prevention interventions.

Community-level interventions: Community mobilization campaigns have been shown to increase uptake of HTC in discordant couples¹²⁵ and youth¹²⁶. Specific activities such as community-based dramas have been shown to increase HTC utilization and condom use¹²⁷. Locally-based media programs have been shown to impact social norms, including perceptions of HIV-positive individuals¹²⁸. While their geographic reach is often limited, effective community-based activities generally provide good results at a low cost per beneficiary, although the duration of these effects is unknown¹²⁹. Community level activities are most effective when they: focus explicitly on community norms; develop key opinion leaders with the abilities and desire to diffuse messages widely; and facilitate support systems and networks¹³⁰.

Interpersonal communication: Interpersonal communication and counseling is defined as person-to-person or small group interaction and exchange^{131,132}. A recent meta-analysis of research examining interpersonal communication found that exposure was significantly

¹²⁰ Snyder LB, et al. 2011.

¹²¹ Abrams LC, Maibach EW. (2008). The effectiveness of mass communication to change public behavior." *Annual Review of Public Health*, 29(1), 219-234.

¹²² Marum E, et al. 2008.

¹²³ Ibid

¹²⁴ Van Rossem R, Meekers D. (2007). The reach and impact of social marketing and reproductive health communication campaigns in Zambia. *BMC Public Health*, 7(1), 352.

¹²⁵ Chomba E, Allen S, Kanweka W, et al. (2008). Evolution of couples' voluntary counseling and testing for HIV in Lusaka, Zambia. *Journal of Acquired Immune Deficiency Syndromes*, 47(1), 108-115.

¹²⁶ Ngubane T, et al. (2008). Innovative mobilization strategies for attracting at risk youth and young adults to participate in community-based voluntary counselling and testing in rural Kwa-Zulu Natal, South Africa (Project Accept - HPTN 043). XVII International AIDS Conference, August 3-8, 2008. Mexico City, Mexico.

¹²⁷ Harvey B, Stuart J, Swan T. (2000). Evaluation of a drama-in-education programme to increase AIDS awareness in South African high schools: a randomized community intervention trial. *International Journal of STD and AIDS*, 11(2), 105-111.

¹²⁸ Goldstein S, et al. (2005). Communicating HIV and AIDS, what works? A report on the impact evaluation of Soul City's fourth series. *Journal of Health Communication*, 10(5), 465-483.

¹²⁹ Donahue J, Williamson J. (1999). Community mobilization to mitigate HIV/AIDS. Report prepared by the Displaced Children and Orphans Fund and War Victims Fund Project for the United States Agency for International Development.

¹³⁰ Khumalo-Sakutukwa G, Morin S, Fritz K, et al. (2008). Project Accept (HPTN 043): a community-based intervention to reduce HIV incidence in populations at risk for HIV in sub-Saharan Africa and Thailand. *Journal of Acquired Immune Deficiency Syndrome*, 49(4), 422-431.

¹³¹ Aggleton P. (1997). Behavior Change Communication Strategies. *AIDS Education and Prevention*, 9 (2), 111-23.

¹³² AED Center for Global Health and Communication Marketing. Accessible at:
http://www.globalhealthcommunication.org/strategies/interpersonal_communication_-_counseling

associated with increased knowledge and condom use¹³³. In addition to these outcomes, peer education has demonstrated some success in changing community attitudes and norms¹³⁴. Cost-effectiveness studies have shown that interpersonal communication has the ability to reach hard-to-reach population groups in a cost-effective manner¹³⁵. Beyond its direct effects upon behavior, there is increasing consensus that interpersonal communication interventions may have important secondary or indirect effects through the diffusion of program messages through social networks.

Sexual risk reduction interventions include those addressing partner reduction and concurrency, intergenerational and transactional sex, condom use, and delay of sexual debut. It should be noted that many of these behaviors are closely linked, and, as such, interventions often promote changes in more than one behavioral area (intergenerational sex and transactional sex, for example).

Focus of messages:

Multiple partnerships: Sexual activity with more than one partner plays a central role in all sexually-driven HIV epidemics. Ecological and associational evidence from generalized and concentrated epidemics points to a consistent pattern of significant decline in the proportion of men and women reporting multiple partners, followed by population-level declines in HIV infection^{136,137,138}. Behavioral interventions utilizing various communication channels have had a demonstrable impact on reducing numbers of sexual partners in numerous populations including MSM, adult men and women, and young people^{139,140}. While debate exists around the role of concurrent, as opposed to sequential, partnerships in HIV transmission¹⁴¹, efforts to evaluate concurrency reduction interventions are on-going¹⁴².

¹³³ Medley A, Kennedy C, O'Reilly K, et al. (2009). Effectiveness of peer education interventions for HIV prevention in developing countries: a systematic review and meta-analysis. *AIDS Education and Prevention*, 21(3), 181-206.

¹³⁴ Maticka-Tyndale E, Barnett JP. (2010). Peer-led interventions to reduce HIV risk of youth: a review. *Evaluation and Program Planning*, 33(2), 98-112.

¹³⁵ Fung IC, Guinness L, Vickerman P, et al. (2007). Modeling the impact and cost-effectiveness of the HIV intervention programme amongst commercial sex workers in Ahmedabad, Gujarat, India. *BMC Public Health*, 7, 195.

¹³⁶ Green EC, Mah TL, Ruark A, et al. (2009). A framework of sexual partnerships: risks and implications for HIV prevention in Africa. *Studies in Family Planning*, 40(1), 63-70.

¹³⁷ Shelton JD. (2009). Why multiple sex partners? *The Lancet*, 374, 367-369.

¹³⁸ Mishra V, Hong R, Bignami-Van Assche S, et al. (2009). The role of partner reduction and faithfulness in HIV prevention in sub-Saharan Africa: evidence from Cameroon, Rwanda, Uganda, and Zimbabwe. *DHS Working Papers No. 61*. Calverton, Maryland, Demographic and Health Research Division, Macro International Inc.

¹³⁹ Herbst JH, Sherba RT, Crepaz N, et al. (2005). A Meta-Analytic Review of HIV Behavioral Interventions for Reducing Sexual Risk Behavior of Men Who Have Sex With Men. *Journal of Acquired Immune Deficiency Syndrome*, 39(2), 228-241.

¹⁴⁰ Noar S. (2008). Behavioral interventions to reduce HIV-related sexual risk behavior: review and synthesis of meta-analytic evidence. *AIDS and Behavior*, 12(3), 1090-1165.

¹⁴¹ World Bank, USAID. (2010) World Bank debate series: debate 4. Concurrent sexual partnerships. <http://siteresources.worldbank.org/INTHIVAIDS/Resources/375798-1297872065987/Debate4SUMMARYConcurrentSexualPartnerships.pdf> (accessed June 17, 2011).

¹⁴² Tanser F, Barnighausen T, Hund L, et al. (2011). Effect of concurrent sexual partnerships on rate of new HIV infections in a high-prevalence, rural South African population: a cohort study. *Lancet*, 378: 247-55.

Intergenerational and transactional sex: In many settings, intergenerational sex and transactional sex are closely related^{143,144}. Both practices are driven by economic needs or wants, as well as deeply-entrenched norms supporting age differences between partners and male dominance in relationships¹⁴⁵. Women's ability to refuse sex or negotiate condom use, which may already be limited, may be further compromised by age differences between partners or exchange of money or gifts. These factors, in combination with young women's biological vulnerability to HIV infection, contribute to heightened risk for both young women and their male partners¹⁴⁶.

Age of sexual debut: A number of national population-based surveys^{147,148} have found a correlation between early initiation of sex and higher HIV prevalence among young people. Increased mean age of sexual debut is thought to be one contributing factor in declining HIV prevalence in some generalized epidemics in sub-Saharan Africa¹⁴⁹. A multi-country study of youth in sub-Saharan Africa found that programs promoting abstinence, including those utilizing mass media, could produce increases of up to one year in mean age of sexual debut¹⁵⁰.

Alcohol use: Alcohol use plays a critical role in sexual risk behavior that can lead to HIV transmission. Multiple studies have found that persons who use alcohol in sexual situations are more likely to have unprotected sex, casual sex, and multiple partners, than persons who do not use alcohol in sexual situations¹⁵¹. Alcohol consumption is linked with increased risk of STI and HIV infection¹⁵², gender-based violence, and non-adherence to ART. However, there is no evidence that any particular intervention reliably reduces alcohol consumption in low-resource settings. Country teams should wait for conclusive evidence of an effective intervention before making significant investments in programs that aim to reduce consumption.

¹⁴³ Hawkins K, Price N, Mussa F, et al. (2009). Milking the cow: young women's construction of identity and risk in age-disparate transactional sexual relationships in Maputo, Mozambique. *Global Public Health: An International Journal for Research, Policy and Practice*, 4(2), 169-182.

¹⁴⁴ Luke N, Kurz K. (2002). Cross-generational and transactional sexual relations in sub-Saharan Africa: prevalence of behavior and implications for negotiating safer sexual practices. Washington, DC, AIDSMark, Population Services International and International Center for Research on Women.

¹⁴⁵ Dunkle KL, Jewkes RK, Brown HC, et al. (2004). Transactional sex among women in Soweto, South Africa: prevalence, risk factors and association with HIV infection. *Social Science and Medicine*, 59(8), 1581-1592.

¹⁴⁶ Leclerc-Madlala, S. (2008). Age-disparate and intergenerational sex in southern Africa: the dynamics of hypervulnerability. *AIDS*, 22(Suppl 4), S17-S25.

¹⁴⁷ Munjoma MW, Mhlanga FD, et al. (2010). The incidence of HIV among women recruited during late pregnancy and followed up for six years after childbirth in Zimbabwe. *BMC Public Health*, 10, 668.

¹⁴⁸ Busza JR, Balakireva OM, et al. (2010). Street-based adolescents at high risk of HIV in Ukraine. *Journal of Epidemiology and Community Health*, Sept 23.

¹⁴⁹ Bessinger R, Akwara P, Halperin DT, (2003). Sexual behavior, HIV, and fertility trends: a comparative analysis of six countries. Chapel Hill, MEASURE Evaluation Project.

¹⁵⁰ FHI. (2003). Abstinence, fewer partners, and condom use are complementary messages. Arlington, FHI.

¹⁵¹ Kalichman, SC, Leickness CS, Vermaak R, et al. (2007). HIV/AIDS risk reduction counseling for alcohol using sexually transmitted infections clinic patients in Cape Town, South Africa. *Journal of Acquired Immune Deficiency Syndrome*, 44, 594-600.

¹⁵² Li Q, Li X, Stanton B. (2010). Alcohol use among female sex workers and male clients: an integrative review of global literature. *Alcohol and Alcoholism*, 45(2), 188-199.

Program Implementation

Multiple studies^{153,154,155,156} in various contexts over the past two decades indicate that behavioral interventions can best impact behaviors if they:

- Involve target populations and their communities in setting priorities, identifying locally appropriate behavioral objectives, developing messages, and designing activities
- Are based upon formative research
- Are guided by behavioral theory
- Segment audiences into meaningful subgroups
- Feature pretested messages that move beyond delivery of factual information and include salient emotional appeals
- Utilize channels that can effectively reach the target audience
- Communicate harmonized or mutually reinforcing messages through multiple channels
- Use robust evaluation designs that allow for causal correlations about program influence on behaviors of interest¹⁵⁷.

Community-based approaches addressing social norms are essential to reducing intergenerational and transactional sex, multiple partnering, early sexual debut and alcohol-driven infections. Interventions focused on individual behavior change alone will not suffice. Such interventions should include ongoing activities emphasizing dialogue and community problem-solving. Advocacy with local leaders and decision-makers is also essential to addressing social norms that create risk — and to enforcing both healthy norms and formal regulations once they are developed. Because harmful practices are driven in part by inequitable gender dynamics, programs that emphasize transformation of gender norms and male involvement in sexual health may also hold promise. Because concurrency programming is still relatively new, interventions in the area should also emphasize rigorous monitoring and evaluation including sound and appropriate measurement of concurrent partnerships. In recognition of the data on alcohol as a risk factor, alcohol-reduction messages should be included in existing programs, and condom outreach programming should address settings such as bars and other venues where alcohol is sold, and include messaging and referral information appropriate for those at high risk.

Promotion of delayed sexual debut should be integrated with broader sexuality education programs and should begin early, reaching young people with age-appropriate messages that are repeated over time. Programmatic experience in a variety of countries has demonstrated that curriculum-based, adult-led sexuality education programs can impact sexual behavior among young adults, as can promotion and delivery of youth-friendly health services. Multi-

¹⁵³ Rotheram-Borus M, Swendeman D, Flannery D, et al. (2009). Common factors in effective HIV prevention programs. *AIDS and Behavior*, 13(3), 399-408.

¹⁵⁴ Kirby DB, Laris BA, Roller L. (2007). Sex and HIV education programs: their impact on sexual behaviors of young people throughout the world. *Journal of Adolescent Health*, 40(3), 206-217.

¹⁵⁵ Lyles CM, Kay LS, Crepaz N, et al. (2007). Best-evidence interventions: findings from a systematic review of HIV behavioral interventions for US populations at high risk, 2000-2004. *American Journal of Public Health*, 97(1), 133-143.

¹⁵⁶ Schensul S, Saggurti N, Singh R, et al. (2009). Multilevel perspectives on community intervention: an example from an Indo-US HIV prevention project in Mumbai, India. *American Journal of Community Psychology*, 43(3), 277-291.

¹⁵⁷ Noar S. 2006.

channel communication programs targeting young people while involving broader community structures and stakeholders can also impact behaviors, particularly if they explicitly address key issues of concern to young people¹⁵⁸. Many interventions promoting delay of sexual debut target in-school youth. Opportunities for reaching out-of-school youth, who may face heightened risks, should be identified as well.

4.3.2 Supportive behavioral interventions to optimize biomedical prevention

Creating Demand for Services

Evidence

SBCC has been widely used over the past decade to create demand for biomedical prevention approaches, including HTC and VMMC. HTC-focused mass media campaigns in Kenya and South Africa have been shown to increase uptake of testing services, with clear dose-response effects^{159,160}. Evidence from South Africa further indicates that exposure to SBCC programs is associated with discussing HIV and that discussion of HIV is associated with testing — suggesting a possible indirect effect of HTC promotion interventions^{161, 162}. Demand creation for VMMC is newer and considerably less -evaluated, although anecdotal evidence from national and sub-national programs in sub-Saharan Africa strongly suggests that targeted communication addressing key barriers to circumcision is essential to creating or “conditioning” demand¹⁶³.

Program Implementation

Promotion of biomedical prevention strategies, like that of any health product or service, must be carefully balanced to ensure that demand does not outstrip supply. Joint planning between health service partners and SBCC implementers can greatly improve outcomes in this area.

Historically, VMMC programs have tended to focus heavily upon development and scale-up of clinical services, with demand creation activities carried out on a more informal basis. There is increasing acknowledgement that VMMC communication interventions should draw upon lessons learned in SBCC for other health behaviors, including use of proven processes to design, implement, and evaluate communication activities. Demand creation for VMMC should: include development of a comprehensive national or sub-national communication strategy; target a range of well-segmented primary and secondary audiences, including healthcare providers and traditional leaders; communicate complex subject matter in simple and audience-appropriate terms; and ensure proper timing and sequencing of messages¹⁶⁴. Although efforts to date have focused heavily upon interpersonal communication and small-group community mobilization,

¹⁵⁸ Ross D, Dick B, Ferguson J. (2006). Preventing HIV/AIDS in young people: a systematic review of the evidence from developing countries. Geneva, World Health Organization.

¹⁵⁹ Marum E, et al. 2008.

¹⁶⁰ Kincaid L. (2006). AIDS communication programs, HIV prevention, and living with HIV/AIDS in South Africa. Pretoria, JHHESA.

¹⁶¹ Gay J, Hardee K, Croce-Galis M, et al. (2010). What works for women and girls: evidence for HIV/AIDS interventions. New York, Open Society Institute.

¹⁶² Johnson S, et al. (2009). Second National HIV Communication Survey. Pretoria, JHHESA.

¹⁶³ Bertrand, J. (2010). Male Circumcision Communication: Achievements and Challenges. Keynote Presentation: UNAIDS-PEPFAR Regional Meeting on VMMC Communication. September 22, 2010. Durban, South Africa.

¹⁶⁴ Population Services International (PSI). (2009). Regional communication strategy: male circumcision.

mass media promotion may become increasingly important as services are scaled up and latent demand is fulfilled^{165, 166}.

Improving Adherence and Aftercare through Client Education

Evidence

Creating demand for services, while essential, is not sufficient in isolation to ensure positive outcomes. Helping clients identify side effects and adverse events, take medication correctly, and care for themselves following medical procedures can all contribute to optimal use of medical technologies. A randomized control trial in Kenya found that SMS reminders significantly improved ART adherence among patients¹⁶⁷. Similar approaches have been used to support attendance at VMMC follow-up visits. VMMC counseling and client education has not been well evaluated to date and is widely recognized as a priority area for future operations research and process evaluation¹⁶⁸.

Program Implementation

ART adherence communication should emphasize open and effective client-provider communication (including promotion of client assertiveness/engagement and provider tolerance when appropriate), as well as increased treatment literacy among both PLWH and their families and communities. Experience to date suggests that a combination of training, provider job aids and client materials, and mass media can be used to achieve this. New media applications, including SMS reminders and virtual buddy systems, also hold promise.

VMMC client counseling and education provide an important opportunity to increase understanding of the procedure and its benefits (which may support secondary discussion and demand creation through social networks), provide risk reduction counseling as part of HTC, and promote safe aftercare practices. It may also offer an entry point for discussion of gender as it relates to health-seeking behaviors and sexual risk-taking. SBCC in this area should include flexible and efficient counseling procedures (including offsite counseling and group counseling when appropriate), provider job aids, client materials, and activities targeting clients' partners and caregivers.

4.4 Structural supports for sexual prevention

As would be expected, there is significantly less of an evidence base around activities that create and support an enabling environment for HIV prevention than around biomedical and behavioral interventions. These activities tend to fall into five broad categories.

4.4.1 Legal and policy reform

In order to ensure fair access to HIV prevention and treatment services for all people and protect those affected by HIV/AIDS, countries need sound laws and policies regarding HIV. PEPFAR country teams should fund activities to support sound legal and policy reform, as

¹⁶⁵ Bertrand JT, 2010.

¹⁶⁶ PSI, 2009.

¹⁶⁷ Lester R, et al. (2010). Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya: a randomized control trial. *Lancet*, 376, 1838-1845.

¹⁶⁸ UNAIDS/PEPFAR. (2010). Meeting Report: Southern and Eastern Africa Region Male Circumcision Communication Meeting.

appropriate in the context, recognizing that enforcement is as critical as good policy^{169, 170, 171}. These activities may support work directly with partner governments, but should also support civil society, in particular organizations of PLWH. Legal and policy reform that supports HIV prevention, care, and treatment with MARPs is especially critical.

Reducing stigma and discrimination against PLWH and marginalized groups

Stigma and discrimination — against both PLWH and marginalized groups often at high risk for HIV — are significant barriers to increasing demand and access to services, and dedicated efforts are needed to overcome this obstacle^{172, 173}. Like gender inequality, stigma and discrimination are cross-cutting issues that can limit the effectiveness of all programs in a prevention portfolio^{174, 175}. While programs should incorporate stigma-reduction components into all their activities, specific programs to address stigma and discrimination at the community and national level may also be implemented with PEPFAR funds. Such programs help create a safe space for peer-peer interactions that serve as a referral mechanism to the entire continuum of response for HIV and other health services.

Gender inequality and gender-based violence (GBV)

Gender inequality and related GBV contribute through multiple pathways to the transmission of HIV¹⁷⁶. Gender inequality is a cross-cutting issue: all PEPFAR prevention programs must take gender dynamics into account in order to be effective. For example, school-based programs targeting girls will not be fully effective in reducing incidence among girls as a whole if they do not take into account the many girls not in school because of gender discrimination and other factors.

At the same time, PEPFAR country teams may fund programs that directly address harmful gender norms and GBV. In particular, country teams should scale up delivery of PEP as part of a comprehensive protocol for victims of GBV in all PEPFAR-funded clinical facilities, and to address GBV and harmful gender norms in the context of HIV prevention. Screening for GBV should be part of all routine and emergency health care.

Economic empowerment and other multi-sectoral approaches

While the relationship between income and HIV risk is complex and not always linear, there is substantial evidence that economic insecurity is often a critical factor in shaping risky

¹⁶⁹ Ayala G, Beck J, Lauer K, et al. (2010). Social discrimination against men who have sex with men (MSM): implications for HIV policy and programs. The Global Forum on MSM and HIV, Oakland, CA.

¹⁷⁰ Tucker J, Ren X, Sapio F. (2010). Incarcerated sex workers and HIV prevention in China: social suffering and social justice countermeasures. *Social Science and Medicine*, 70,121-129.

¹⁷¹ Wolfe D, Cohen J. (2010). Human rights and HIV prevention, treatment, and care for people who inject drugs: key principles and research needs. *Journal of Acquired Immune Deficiency Syndromes*, 55,S56-S62.

¹⁷² Mahajan AP, Sayles JN, Patel VA, et al. (2008). Stigma in the HIV/AIDS epidemic: a review of the literature and recommendations for the way forward. *AIDS (London, England)*, 22, S67.

¹⁷³ Fay H, Baral S, Trapence G, et al. (2010). Stigma, health care access, and HIV knowledge among men who have sex with Mmen in Malawi, Namibia, and Botswana. *AIDS and Behavior*, (epub ahead of print), 1-10.

¹⁷⁴ Mawar N, Sahay S, et al. (2005). The third phase of HIV pandemic: social consequences of HIV/AIDS stigma & discrimination & future needs. *Indian Journal of Medical Research*, 122, 471.

¹⁷⁵ Skinner D, Mfecane S. (2004). Stigma, discrimination and the implications for people living with HIV/AIDS in South Africa. *Sahara*, 1,157-164.

¹⁷⁶ WHO, Department of Gender, Women and Health. (2009). Integrating gender into HIV/AIDS programmes in the health sector: Tool to improve responsiveness to women's needs.

behaviors¹⁷⁷. PEPFAR funds may be used to support economic empowerment programs for populations at risk. These programs should be well-targeted to ensure that increased access to resources does not put recipients at greater risk for other negative outcomes, and they should be carefully monitored. Consideration should also be given to linking PEPFAR HIV programs to economic empowerment programs already funded by the USG, both within and outside of PEPFAR¹⁷⁸. Modifications or enhancements to these existing programs might offer significant opportunities for HIV prevention. PEPFAR prevention staff are strongly encouraged to work closely with programs for orphans and vulnerable children (OVC), as well as with food and nutrition programs, to identify possible synergies in these efforts, while remembering that impact on HIV incidence is the desired outcome. Operations research may be helpful in determining how existing programs for OVC and other populations might be adapted to enhance their protective effects against HIV transmission. The topic of integrating HIV prevention with other USG programs is also addressed in the Appendix.

Education

UNAIDS estimated in 2008 that in 17 African and four Latin American countries, better-educated girls tended to delay having sex^{179, 180}. Studies have shown that sexual initiation is later among young women enrolled in school than among those not enrolled¹⁸¹. Research in Zambia finds that young women with more education are less likely to be HIV infected than those with less education¹⁸². While PEPFAR has long-standing HIV prevention efforts in schools, country teams should also bear in mind that sustained school attendance on its own is correlated with lower rates of HIV infection^{183, 184, 185, 186}. While PEPFAR prevention funds should not be spent directly on supporting school attendance (e.g. on tuition reimbursement), PEPFAR prevention staff should look for opportunities to strengthen or refine existing education programs in a way that enhances their protective effect on HIV transmission. Such programs might be funded through the USG or through partner governments and other donors. At a minimum, PEPFAR prevention workers should work closely with their OVC colleagues on developing approaches to tuition and school support that maximize the preventive effects of these activities.

¹⁷⁷ Gillespie S, Kadiyala S, Greener R. (2007). Is poverty or wealth driving HIV transmission? *AIDS*, 2, S5.

¹⁷⁸ Kim J, Pronyk P, Barnett T, et al. (2008). Exploring the role of economic empowerment in HIV prevention. *AIDS*, Suppl 4, S57-71.

¹⁷⁹ UNAIDS. (2000). Report on the Global HIV/AIDS Epidemic. Geneva.

¹⁸⁰ McGrath N, Nyirenda M, Hosegood V, et al. (2009). Age at first sex in rural South Africa. *Sexually Transmitted Infections*, 85 Suppl 1, i49-55.

¹⁸¹ Gupta N and Mahy M. (2003). Sexual initiation among adolescent girls and boys: trends and differentials in sub-Saharan Africa. *Archives of Sexual Behavior*, 32(1), 41-53.

¹⁸² Michelo C, Sandoy IF, Fylkesnes K (2006). Marked HIV prevalence declines in higher educated young people: evidence from population-based surveys (1995–2003) in Zambia. *AIDS*, 20, 1031-38.

¹⁸³ Birdthistle I, Floyd S, Nyagadza A, et al. (2009). Is education the link between orphanhood and HIV/HSV-2 risk among female adolescents in urban Zimbabwe? *Social Science and Medicine*, 68, 1810-1818.

¹⁸⁴ Gakidou E, Cowling K, et al. (2010). Increased educational attainment and its effect on child mortality in 175 countries between 1970 and 2009: a systematic analysis. *Lancet*, 376, 959-974.

¹⁸⁵ Hargreaves JR, Bonell CP, Boler T, et al. (2008). Systematic review exploring time trends in the association between educational attainment and risk of HIV infection in sub-Saharan Africa. *AIDS*, 22(3), 403-414.

¹⁸⁶ Pettifor AE, MacPhail C, Rees H, et al. (2008). HIV and sexual behavior among young people: the South African paradox. *Sexually Transmitted Diseases*, 35(10), 843-844.

4.5 Prevention packages for specific populations

4.5.1 Comprehensive package for most-at-risk populations (MARPs)

Evidence

There is substantial evidence for the effectiveness of a core set of interventions for populations at high risk for HIV, including SW, MSM and PWID. Please see PEPFAR's Guidance for MSM and PWID for information and citations^{187,188}. PEPFAR will continue to evaluate the need for additional guidance documents and respond as needed.

Program Implementation

Many countries continue to lack or under-utilize existing bio-behavioral data for MARPs; such data are key to informing programming. A stronger link between epidemiologic, behavioral, and socio-cultural data and prevention activities is needed to ensure that study results and surveillance information become the basis for prioritizing and implementing prevention programs. Both qualitative and quantitative data are important. Qualitative methods should be employed to understand the social and behavioral dynamics of HIV transmission, and as formative work to design interventions. Country teams should strengthen the links between strategic information and prevention to develop data-driven programs that characterize MARPs and other vulnerable populations based on population-based surveillance and quantitative and qualitative research.

Based on the data gained from country strategic information activities, PEPFAR country teams should scale up a minimum, core set of interventions adapted for different sub-groups especially vulnerable to HIV. The package of prevention services includes: risk reduction, including partner reduction; counseling; condom, condom-compatible lubricants and skills building; HIV and STI screening and treatment; HIV care and treatment; and comprehensive services for PWID. A comprehensive approach to HIV prevention with MARPs should also include linkages to psycho-social support services; legal services; Positive Health, Dignity and Prevention programs; economic strengthening projects; prevention, diagnosis, and treatment of tuberculosis; family planning and reproductive health services; and other appropriate services.

MARPs often engage in behaviors that are criminalized and stigmatized, creating barriers to accessing HIV prevention, care, and treatment services. The ability of HIV prevention programs to make a real and lasting impact in preventing the spread of HIV will largely be determined by the broader social environment in which these services are implemented. Where the environment is constrained, the effectiveness and impact of services are limited. However, where the environment enables effective services, impact will be maximized. For HIV prevention, an enabling environment includes the social, economic, and legal determinants that facilitate the behavior change process and encourage MARPs and PLWH to participate in all levels of the response to the epidemic. A good example of an enabling environment is one that supports effective HIV prevention interventions among PWID, coupled with the involvement of PWID in program design, implementation, and evaluation.

¹⁸⁷ Accessible at: <http://www.pepfar.gov/guidance/combinationprevention/combprevmsm/index.htm>

¹⁸⁸ Accessible at: <http://www.pepfar.gov/guidance/combinationprevention/combprevidu/index.htm>

Country teams should take steps to ensure that scale-up of prevention programs for MARPs is accompanied by appropriate protections of their rights, including the review of policies and regulations that criminalize or deter MARPs seeking services and training for service providers to reduce stigma and discrimination. For more information on the comprehensive package of services for MARPs, please see guidance documents for PWID¹⁸⁹ and MSM¹⁹⁰.

4.5.2 Positive Health, Dignity and Prevention (PHDP): Prevention for people living with HIV

HIV prevention for PLWH integrated into routine care is a core component of a comprehensive and integrated HIV prevention, care, and treatment strategy. Guidelines have been issued by WHO (2008)¹⁹¹ and CDC (2003)¹⁹² on prevention interventions for PLWH in both clinic and community settings. They also address the myriad health and prevention needs of HIV-positive individuals outlined in the Positive Health, Dignity, and Prevention (PHDP) framework¹⁹³.

Evidence

Evidence supports PHDP interventions with PLWH as an effective strategy for reducing sexual risk behavior^{194,195,196} (including multiple partnering¹⁹⁷), STI incidence^{198,199}, and unintended pregnancies²⁰⁰ while providing opportunities for counseling and support for safer pregnancy options if children are desired. Evidence indicates that couples counseling can increase the uptake of PMTCT interventions among HIV-positive pregnant women in antenatal clinics²⁰¹. Effective treatment that reduces viral load is a strong correlate of effective prevention.

These interventions can be effectively delivered by health care providers^{202, 203}, counselors/social workers²⁰⁴, and lay or peer counselors^{205, 206, 207} in both clinic and community settings. Models also suggest that prevention interventions with PLWH are cost-effective²⁰⁸.

¹⁸⁹ <http://www.pepfar.gov/guidance/comboinvention/comboinvention/index.htm>

¹⁹⁰ <http://www.pepfar.gov/guidance/comboinvention/comboinvention/index.htm>

¹⁹¹ WHO. (2008). Essential prevention and care interventions for adults and adolescents living with HIV in resource-limited settings.

¹⁹² CDC. (2003). Incorporating HIV prevention into the medical care of persons living with HIV. Recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *Morbidity and Mortality Weekly Report*, 52, 1-24.

¹⁹³ GNP+ and UNAIDS. (2009). Positive health, dignity and prevention: a policy framework.

¹⁹⁴ Crepaz N, Lyles CM, Wolitski RJ, et al. (2006). Do prevention interventions reduce HIV risk behaviours among people living with HIV? A meta-analytic review of controlled trials. *AIDS*, 20, 143-57.

¹⁹⁵ Kennedy C, Medley A, et al. (2010). Behavioural interventions for HIV positive prevention in developing countries: a systematic review and meta-analysis. *Bulletin of World Health Organizations*, 88, 615-623.

¹⁹⁶ Johnson BT, Carey MP, et al. (2006). Sexual risk reduction for persons living with HIV research synthesis of randomized controlled trials, 1993 to 2004. *Journal of Acquired Immune Deficiency Syndrome*, 41, 642-50.

¹⁹⁷ Allen S, Meinzen-Derr J, Kautzman M, et al. (2003). Sexual behavior of HIV discordant couples after HIV counseling and testing. *AIDS*, 17(5), 733-40.

¹⁹⁸ Saleh-Onoya D, Reddy P, Ruiters R, et al. (2009). Condom use promotion among isiXhosa speaking women living with HIV in the Western Cape Province, South Africa: a pilot study. *AIDS Care*, 21(7), 817-825.

¹⁹⁹ Wingood GM, DiClemente RJ, Mikhail I, et al. (2004). A randomized controlled trial to reduce HIV transmission risk behaviors and sexually transmitted diseases among women living with HIV: The WILLOW program. *Journal of Acquired Immune Deficiency Syndrome*, 37, S58-S67.

²⁰⁰ King R, Estey J, et al. (1995). A family planning intervention to reduce vertical transmission of HIV in Rwanda. *AIDS*, 9(Suppl 1), S45-51.

²⁰¹ Farquhar C, Kiarie JN, Richardson BA, et al. (2004). Antenatal couple counseling increases uptake of interventions to prevent HIV-1 transmission. *Journal of Acquired Immune Deficiency Syndrome*, 37(5), 1620-6.

²⁰² Crepaz N, et al. 2006.

Program Implementation

Prevention interventions with PLWH should include both behavioral and biomedical interventions aimed at reducing the morbidity and mortality experienced by PLWH and reducing the risk of transmission to HIV-negative partners and infants. Implementation of comprehensive PHDP interventions, including practical integration of prevention into care and treatment settings, is an important HIV prevention approach. This should include provision of a continuum of consistent and reinforcing messages and services across settings. PLWH accessing care at the facility or community level should receive the following minimum set of services and messages:

- Assessment of patients' adherence to ART and treatment for OIs (including TB medications) at every visit
- Assessment for signs and symptoms of STIs and other OIs including TB, screening and treatment or referral for treatment where indicated
- Assessment of partners' status and disclosure — couple/partner counseling, testing and support for safe disclosure if indicated
- Assessment of reproductive health/family planning intentions of patient/client and provision or referral for appropriate services
- Assessment of clients' sexual risk behavior, alcohol, and other substance use — providing or linking PLWH to appropriate support services if indicated
- Providing condoms and lubricants at all care and treatment encounters
- Referring to appropriate and functional community-based programs for relevant non-clinical support and services, and referring back for relevant clinical services from community-based encounters
- In keeping with country guidelines and recognizing the priority populations for treatment established in PEPFAR guidance, to maximize the prevention, care, and treatment benefits of ART among sero-discordant couples, programs should consider offering treatment to all HIV-positive partners who are in known discordant relationships and have CD4 counts of 350/mm³ or lower.

PHDP interventions contribute to the identification of HIV-positive individuals and sero-discordant couples and partnerships. Partners who are newly identified as HIV-positive can then be linked into HIV prevention, care, and treatment services. Identification of discordant couples

²⁰³ Gardner LI, Marks G, O'Daniels, et al. (2008). Implementation and evaluation of a clinic-based behavioral intervention: Positive STEPS for patients with HIV. *AIDS Patient Care and STDs*, 22, 1-9.

²⁰⁴ Myers J, Shade S, Rose C, et al. (2010). Interventions delivered in clinical settings are effective in reducing risk of HIV transmission among people living with HIV: results from the Health Resources and Services Administration (HRSA)'s Special Projects of National Significance Initiative. *AIDS and Behavior*, 14, 483-492.

²⁰⁵ Comman DH, Kiene SM, Christie S, et al. (2008). Clinic-based intervention reduces unprotected sexual behavior among HIV-infected patients in KwZulu-Natal, South Africa: results of a pilot study. *Journal of Acquired Immune Deficiency Syndrome*, 48(5), 553-60.

²⁰⁶ Peltzer K, Tabane C, et al. (2010). Lay counselor-based risk reduction intervention with HIV-positive diagnosed patients at public HIV counseling and testing sites in Mpumalanga, South Africa. *Evaluation and Program Planning* (epub).

²⁰⁷ Torpey K, Kabaso M, Mutale L, et al. (2008). Adherence support workers: a way to address human resource constraints in antiretroviral treatment programs in the public health settings in Zambia. *PlosOne*, 3(5), e2204.

²⁰⁸ Marseille, E, Shade S, et al. (2011). The cost-effectiveness of HIV prevention interventions in HIV-infected patients in clinical settings. *Journal of Acquired Immune Deficiency Syndrome*, 56(3), e87-e94.

and partnerships represents an opportunity to prevent new infections of the negative spouse or partner(s) through provision of prevention services, including routine re-testing and counseling of the HIV-negative partner. As noted, VMMC has been shown to reduce the risk of HIV acquisition by HIV-negative males by at least 60 percent²⁰⁹. Thus, offering circumcision to the HIV-negative male partners of HIV-positive women should be routine when addressing the prevention needs of discordant couples. To help ensure that the couple is able to maintain their HIV discordancy, the HIV-negative partner in discordant partnerships should be offered HTC at least annually or in line with WHO retesting recommendations²¹⁰.

Finally, ongoing adherence counseling and support services maximize the care and prevention benefits of ART by supporting optimal adherence among patients on treatment. PwP interventions may also help retain persons in care by addressing the multiple prevention needs of HIV-positive individuals in a service continuum that spans both clinic and community level.

4.5.3 Prevention interventions for young people

Evidence

Due to social, cultural, economic, and biological reasons, some young people are particularly vulnerable to HIV infection. Global goals to reduce vulnerability and prevent HIV in young people highlight the growing consensus that HIV prevention efforts must include a focus on young people. Resources for HIV prevention in all countries are limited, and therefore it is imperative that resources be used effectively. A compelling case can be made for the need for focused interventions to prevent HIV among young people, but it is less clear how precisely this should be done. Despite the uncertainties, the rate of new HIV infections has fallen by more than 25% among young people in 15 of the most severely affected countries. In South Africa, the rate of new HIV infections among 18-year-olds declined sharply from 1.8% in 2005 to 0.8% in 2008, and among women 15–24 years-old, it dropped from 5.5% in 2003 to 2.2% by 2008²¹¹.

Research shows that early age of sexual debut puts young people at an increased risk of HIV acquisition. Early sexual debut lengthens the potential period of exposure to HIV, typically resulting in a higher number of lifetime sexual partners as well as increasing the risk of unintended pregnancy. Delayed sexual debut or abstinence can thus reduce an individual's risk of being exposed to HIV. Statistically significant changes in behavioral trends included the following²¹²: a reduction in the proportion of 15-19 year olds with early sexual debut was observed among women in 13 of 17 countries (statistically significant in eight) and among men in 11 of 16 countries (statistically significant in seven). A reduction in the proportion of 15-24 year olds with multiple partners in the past 12 months was found in women in 10 of 14 countries (statistically significant in seven) and in men in 13 of 14 countries (statistically significant in 10). Finally, a reduced proportion of young people not using condoms was seen for women in 6 of 11 countries (statistically significant in six) and for men in 11 of 12 countries

²⁰⁹ Siegfried N, Muller M, et al. (2009). Male circumcision for prevention of heterosexual acquisition of HIV in men. *Cochrane Database Systematic Reviews*, 15(2).

²¹⁰ WHO. (2010). Delivering HIV test results and messages for re-testing and counseling in adults. Accessible at: http://www.who.int/hiv/pub/vct/hiv_re_testing/en/index.html.

²¹¹ Rehle TM, Hallet TB, Shisana O, et al. (2010). A decline in new HIV infections in South Africa: estimating HIV incidence from three national HIV surveys in 2002, 2005 and 2008. *PLoS ONE*, 5(6), e11094.

²¹² Ghys PD, et al (2010).

(statistically significant in five). Significant increases in condom use in both sexes occurred in Cameroon and Uganda.

While the protective effect of delayed sexual debut is clear, more data and further analysis are needed to understand the associations between prevention efforts, behavioral change, and changes in the prevalence and incidence of HIV. Five studies used biologically measured outcomes to assess HIV, STIs, and/or pregnancy among youth. Two large cluster randomized trials (CRTs) in Tanzania²¹³ and Zimbabwe²¹⁴ evaluated multi-component interventions with activities in schools, health services, and geographically-defined communities. Neither demonstrated a significant effect on any of the biological outcomes they measured. In South Africa, a third CRT of an intensive series of group health education sessions, using the Stepping Stones approach, was conducted in 15-26 year old volunteers²¹⁵. The study did not detect a significant impact on HIV, but the incidence of HSV2 was one-third lower in those selected for the intervention than in those who were not selected. A fourth CRT, the IMAGE study in South Africa, aimed to reduce gender-based HIV vulnerabilities through microfinance and HIV education, offered and delivered to self-selected adult women of low economic status²¹⁶. This intervention demonstrated a reduction in reported intimate partner violence among participants; however, there was no significant impact on HIV incidence in the sub-group analysis among young people within participant households or in the participating communities at large. However, it should be noted that two-year follow-up almost certainly did not permit enough time for the impact to diffuse from the targeted women to younger women in the same communities. A cross-sectional survey of young people in South Africa found that HIV prevalence was lower in those who reported exposure to the multi-component *LoveLife* program than in those who had not been exposed to it²¹⁷. While encouraging, the observational design of this study makes it open to potential bias and confounding.

Research has identified the most promising types of interventions among young people in schools, health services, and geographically-defined communities in terms of the evidence base supporting their effectiveness — at least to achieve improvements in reported sexual behavior and/or biological outcomes^{218, 219, 220}.

Interventions in schools were largely successful at demonstrating improvements in reported sexual risk behaviors and other mediating factors. Overall, in-school interventions are a logical and promising means to impart necessary information and skills to school-going young people.

²¹³ MEMA kwa Vijana: Rethinking how to prevent HIV in young people: evidence from two large randomized controlled trials in Tanzania and Zimbabwe. Policy Briefing Paper, No. 10, 2008.

²¹⁴ Cowan FM, Pascoe SJ, Langhaug LF, et al. (2008). The Regai Dzive Shin Project: a cluster randomized controlled trial to determine the effectiveness of a multi-component community-based HIV prevention intervention for rural youth in Zimbabwe. *Tropical Medicine and International Health*, 13(10), 1235-44.

²¹⁵ Jewkes R, Nduna M, Levin J, et al. (2008). Impact of Stepping Stones on incidence of HIV and HSV-2 and sexual behavior in rural South Africa: cluster randomized control trial. *British Medical Journal*, 337, a506.

²¹⁶ Kim JC, Dupas P, et al. (2008). Exploring the role of economic empowerment in HIV prevention. *AIDS*, 22(Suppl 4), S57-71.

²¹⁷ Pettifor AE, Rees HV, Kleinschmidt I, et al. (2005). Young people's sexual health in South Africa: HIV prevalence and sexual behaviors from a nationally representative household survey. *AIDS*, 19(14), 1525-34.

²¹⁸ Kirby, et al. 2006.

²¹⁹ Paul-Ebhohimhen VA, Poobalan A, van Teijlingen ER. (2008). A systematic review of school-based sexual health interventions to prevent STI/HIV in sub-Saharan Africa. *BMC Public Health*, 8, 4.

²²⁰ Ross DA. (2008). Approaches to sex education: peer-led or teacher-led? *PLoS Med*, 5(11), e229.

However, evidence from the two recent trials that included an assessment of the impact of schools-based interventions on biological outcomes suggests that such interventions may not be sufficient to reduce the risk of HIV, other STIs, or early pregnancies^{221, 222, 223, 224, 225}.

There is now strong evidence of the potential efficacy of several interventions that can be delivered by health services to youth, such as VMMC, condom use, and HTC. However, these specific interventions cannot have any direct population-level effect on the HIV epidemic among young people unless they are made accessible and acceptable to, and are therefore used by, young people. Evidence of the most appropriate way to deliver health care to young people in order to maximize their access to, and appropriate use of, such services remains incomplete. Many of the recently published evaluations of interventions to improve health services lacked adequate descriptions of the intervention and process evaluation and had weak intervention and/or impact evaluation designs, making it difficult to decipher which aspect or aspects of the intervention were most effective²²⁶.

Interventions in geographically-defined communities are generally the most difficult to evaluate. Intervention types which target the community as a whole, rather than just young people, were more effective at improving reported sexual risk behavior and impacting biological outcomes, which suggests that it may be important to explore interventions to change the social and sexual norms within the wider community. This highlights the difficulty in disentangling the important elements of community-based interventions and the possibility that the exact nature of the interventions used and the context may be particularly important for interventions in this setting²²⁷.

Program Implementation

For every partner country with a generalized epidemic, PEPFAR's Five-Year Strategy sets a target to provide "100% of youth in PEPFAR prevention programs with comprehensive and correct knowledge of ways HIV is transmitted and ways to protect themselves." There are a number of factors which may mediate behavior change in young people, and the social, cultural, and epidemiological contexts in which interventions are implemented may affect their effectiveness considerably. A one-size-fits-all intervention is thus unlikely to be the most effective approach as evidence needs to move to practice based on age, gender, and country context. Careful evaluation of local risk factors and context is necessary to determine the optimal intervention. There is a growing consensus that to achieve HIV prevention in young people it is necessary to provide a range of tools and address a number of barriers. To accomplish this, it is necessary to implement interventions in different settings simultaneously, and thus have the capacity to promote change using different approaches on a number of

²²¹ Kim JC, et al. 2008.

²²² Kirby DB, et al. 2006.

²²³ Paul-Ebhohimhen, et al. 2008.

²²⁴ Ross DA. 2008.

²²⁵ Duflo E, Dupas P, Kremer M, et al. (2006). Education and HIV/AIDS prevention: evidence from a randomized evaluation in Western Kenya. Accessible at: <http://www.povertyactionlab.org>.

²²⁶ Ross D, Dick B, Ferguson J. (2006). Preventing HIV/AIDS in young people: a systematic review of the evidence from developing countries. Accessible in: Report of the UNAIDS Inter-agency Task Team on Young People. *World Health Organization Technical Report Series*, 938.

²²⁷ Friedman SR, O'Reilly KR. (1997). Sociocultural interventions at the community level. *AIDS*, 11(Suppl A), s201-208.

levels. In the school context, PEPFAR country teams should ensure that any programs supported are curriculum-based, adult-led interventions that include key characteristics described above^{228, 229}. In clinical settings, PEPFAR programs ensure that any interventions supported train service providers and take actions to make facilities more youth-friendly, coupled with activities in the community with or without involvement of other sectors to link or refer young people to health services. Additionally, the evidence base for youth prevention will need to continue to be built, making this an area in which it is important to integrate rigorous evaluation into programming. As it grows, successful interventions should be shared with country leadership across appropriate ministries to integrate into curriculum development, policies, and guidelines in order to promote country ownership and sustainability of evidence-based programming.

5. ASSEMBLING A PORTFOLIO OF INTERVENTIONS

The last step in PEPFAR country programming for sexual transmission is assembling a portfolio of the different interventions described above that optimizes PEPFAR's contribution to the country continuum of response. Prioritizing is perhaps the most essential task, and a helpful way of categorizing different interventions to aid in prioritization has been proposed in a recent paper and adapted by PEPFAR²³⁰. Country prevention investments should span these categories:

Overarching Elements
HIV Testing and Counseling
Foundations
Core Interventions
Critical Enablers
Innovations with Evaluation

Collectively, these categories include both activities focused on sexual prevention, and those focused on other modes of transmission. Each category includes all three components of combination prevention — structural, behavioral, and biomedical interventions. A PEPFAR country's entire prevention budget should be distributed across all or some of these interventions, based on the evidence of their ability to decrease HIV incidence in that country context, as well as other conditions such as investments by other donors, evidence of special populations or drivers within the epidemic or other technical considerations. It is understood that a range of factors will influence the investment by PEPFAR in these areas.

The following set of diagrams may be helpful in prioritizing the elements and assembling a country portfolio.

²²⁸ Kim JC, et al. 2008.

²²⁹ Duflo E, et al. 2006.

²³⁰ Schwartländer B, Stover J, et al. (2011). Towards an improved investment approach for an effective response to HIV/AIDS. *Lancet*, 377(9782), 2031-41.

5.1 Categories of activities

a. Overarching Elements

i. Treatment coverage



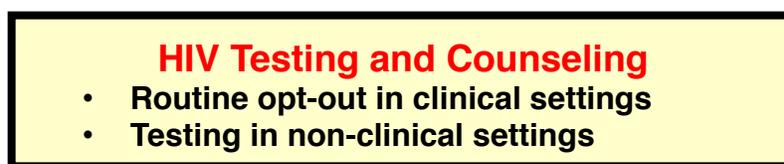
As noted, ART is an important component of HIV prevention, both through its direct impact on the infectivity of people living with HIV, as well as its function as a gateway to other prevention services and to partners. As part of the 'Four Knows,' knowing the levels of treatment coverage within a community is important to understanding risks of transmission at the community level. ART should continue to be funded under the HTXS, PDTX, and HTXD codes under the treatment budget, but PEPFAR country teams should look for opportunities to exploit natural synergies between prevention, treatment, and care activities, for example through wraparounds and co-location of services.

ii. Addressing behavior



Addressing behavior is integral to every dimension of the country prevention effort. The importance of behavior extends beyond standalone behavioral interventions, described in Innovation/Evaluation below. Explicit addressing of relevant behavioral factors should be a part of *all* prevention interventions, including biomedical ones.

b. HIV Testing and Counseling



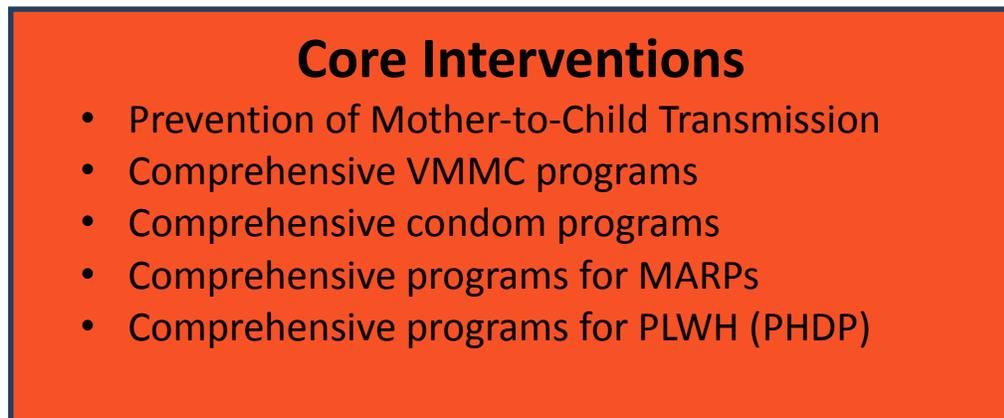
HTC is an essential component of HIV programming as a prerequisite for ART, pre-ART care and support, and biomedical prevention interventions including PMTCT and VMMC. Couples HTC in particular is a critical element of emerging interventions promoting the use of ART as prevention in sero-discordant couples. HTC is a critical gateway to other core prevention interventions such as the minimum package of services for MARPs and PwP and is strongly linked with behavioral HIV prevention interventions and foundational prevention interventions such as blood and injection safety. HTC will also be central in future prevention interventions currently under evaluation such as PrEP.

c. Foundations



Foundations are activities that support systems critical to sustainable, long-term HIV prevention. They include a safe blood supply, universal medical precautions, and school-based and non-school based HIV prevention for youth. In many countries with PEPFAR programs, these activities are already embedded within national budgets and require little or no investment from PEPFAR. In other places technical assistance or minimal program support may be required.

d. Core Interventions



Core interventions include PMTCT; condom procurement, distribution and promotion (including female condoms); comprehensive VMMC programs; evidence-based comprehensive packages for MARPs which include (but are not limited to) CSW, PWID, and MSM; and comprehensive PHDP programs for PLWH. In some epidemic contexts, all of the core interventions will be appropriate; in other contexts, only some should be implemented. As discussed in Section 2 above, country teams should consider "Four Knows" data on epidemiology, country context, inputs by other donors and national strategies in determining which core interventions should be supported at which levels.

In a review of the FY 2011 proposed prevention spending by budget code across regions and epidemic types, investments in core interventions were found to be the majority of PEPFAR programs' prevention budgets. **These interventions should continue to comprise the large majority of prevention funding** and reflect a combination prevention approach in which biomedical, behavioral and structural interventions work synergistically to complement and reinforce one another. The balance across these interventions will vary based upon the nature and extent of the epidemic in each country.

e. Critical Enablers

Critical Enablers
Create gateways to HIV prevention services; support successful scale-up; and create enabling environments to maximize impact, e.g. addressing STIs, GBV, structural constraints, stigma reduction

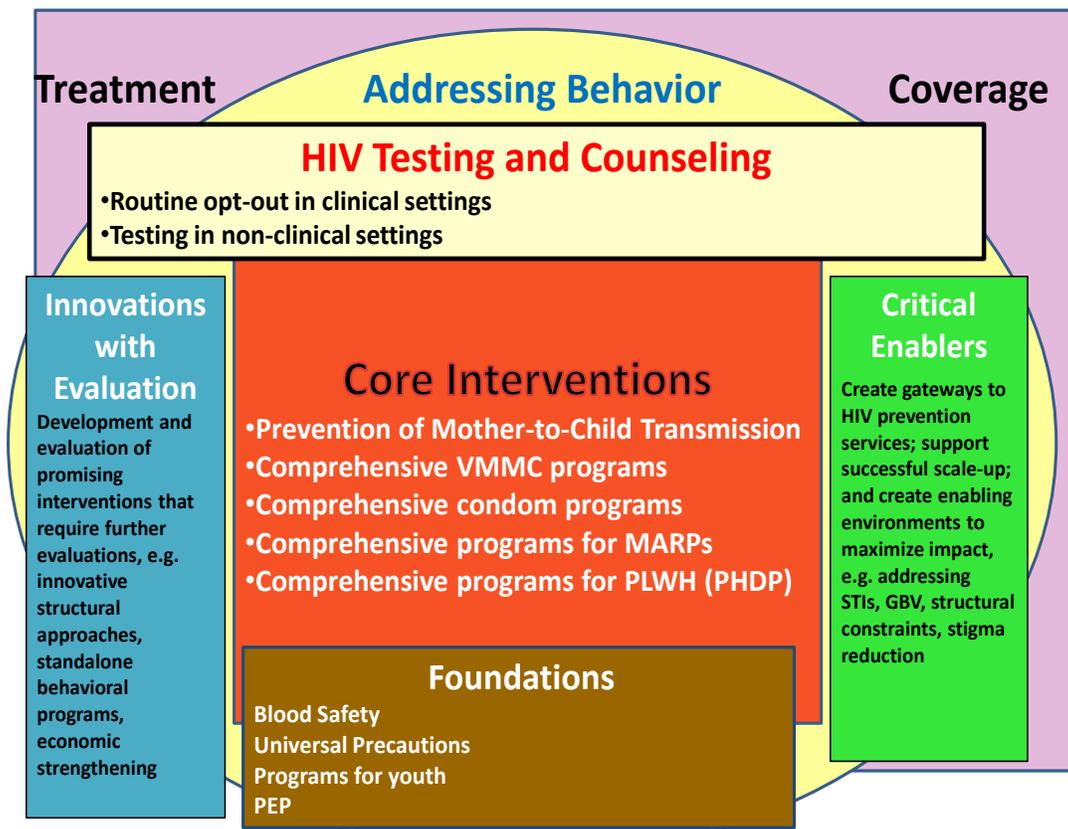
Critical enablers create gateways to HIV prevention services, support the successful scale-up of HIV prevention activities, and create an enabling environment in which such activities' impacts are maximized. They include treatment of other STIs; programs to address GBV and the social norms that support it; mass media focused on creating an enabling environment; structural activities to strengthen and enforce supportive policies at the national, regional and local levels; and stigma-reduction activities.

f. Innovations with Evaluation

Innovations with Evaluation
Development and evaluation of promising interventions that require further evaluations e.g. innovative structural approaches, standalone behavioral programs, economic strengthening

This category includes interventions that are promising but require further evaluation of impact on HIV incidence, or are not yet approved for scale-up. All activities in this category should be designed and implemented with full impact evaluation, and scale-up should be predicated upon clear evidence of reduction of HIV incidence. This category should be used generally to invest in the development and evaluation of innovative approaches to HIV prevention, including the

development of models, multi-sectoral approaches and novel structural interventions²³¹. Examples include standalone behavioral programs to minimize risk or increase protective behaviors, and economic strengthening.



5.2 Prioritizing and assembling the portfolio: defining the continuum of response by population and geography

Step 1: Review and validate the “Four Knows” data

- Begin with data on the epidemic, prioritize high-transmission geographic areas and populations
- Select the appropriate continuum of response for each population
- Plan for adequate coverage/scale for population-level impact
- Ensure that content of interventions directly addresses key drivers and incorporates clear behavioral messages
- Assure adequate quality, dose, and intensity of interventions
- Coordinate implementation of interventions, including harmonizing messages across partners
- Incorporate process, outcome, and impact evaluation

²³¹ Padian NS, McCoy SI, et al. (2011) HIV prevention transformed: the new prevention research agenda. *Lancet*. 378(9787), 269-78.

Step 2: Define packages of interventions

A. Targeting (who): Extent to which effective interventions reach the people at high risk of contracting the virus.

Includes:

- Are we where we need to be, what's the current gap?
- Geography, urban/rural
- Coverage
- Risk group
- Age / gender

B. Selection (what):

- Emphasizing interventions that are prioritized in the national plan and that are well-coordinated, cost-effective, focused on high-risk populations/areas, and not adequately funded through other resources; resource allocation proportional to populations' risk of HIV acquisition or transmission
- Interventions that are evidence-based and effective in reducing HIV at the population level

C. Delivery (how): Determine the ideal mix of interventions for the focus populations. Ensure your mix adequately addresses the following considerations:

- Sufficient coverage to reach population impact
- Sufficient quality to achieve program goals
- Interventions that are effective enough to reach the desired outcomes
- M&E to track progress and maintain quality

D. Cost optimization (how much): How much does the prevention of an additional HIV infection cost, and what is that cost worth to the country? If cost is less than the value, more funds should be provided for the intervention.

Includes:

- Allocation of funds — reduce or increase?
- Single or multiple implementing partners
- Assuring the most impact for the prevention investment by shifting funding from programs with uncertain effectiveness to those with known effectiveness

Step 3: Prioritize

1. Determine relative importance of the target groups (in percentage)
2. Determine distribution of funding by target groups
3. Determine interventions *within* the target groups (by percentage)
4. Determine distribution of funding by intervention

Examples:

Table 1 provides some examples of how PEPFAR country teams might consider the relative importance of each core intervention depending upon the type of HIV epidemic in the country. These examples are not meant to be prescriptive and in all cases, country teams should rely on relevant country epidemiological data to determine intervention and priority areas on which to focus. As noted above, levels of PEPFAR investment should be determined by "Four Knows"

data. For example, where investment in a particular intervention by other donors or the partner government is high, PEPFAR should take particular care to be additive or complementary, rather than duplicative.

Intervention Area	Concentrated Epidemic	Mixed Epidemic	Generalized Epidemic
Core Intervention: PMTCT	Invest minimally; investments often made by national governments.	Medium to high levels of investment; achieve 80% HCT coverage and 85% ART coverage.	High levels of investment; achieve 80% HCT coverage and 85% ART coverage.
Core Intervention: VMMC	Provided to individuals when requested but not a focus of country prevention efforts.	Targeted investments based upon geographic prevalence of MC and regional HIV prevalence.	High levels of investment; achieve near universal coverage.
Core Intervention: Comprehensive Condom Programs	Condom promotion with a focus on most at-risk populations.	High levels of investment; condoms should be available, accessible, and affordable.	High levels of investment; condoms should be available, accessible, and affordable.
Core Intervention: Comprehensive programs for MARPs	Bulk of prevention funding; funding targeted to specific sub-populations based upon data.	High levels of investment; interventions targeted to specific sub-populations based upon data.	Targeted investments to reach high levels of coverage of specific MARP populations.
Core Intervention: PHDP	Targeted investments within care, treatment, and MARPs-focused programs.	High levels of investment; achieve near universal coverage.	High levels of investment; achieve near universal coverage.
Foundational: Blood Safety	Invest minimally; investments often made by national governments.	Invest minimally; investments often made by national governments.	Targeted investments; investments often made by national governments.
Foundational: Universal Precautions	Invest minimally; investments often made by national governments.	Invest minimally; investments often made by national governments.	Targeted investments; investments often made by national governments.
Foundational: Programs for youth	Invest minimally; investments often made by national governments.	Targeted investments; investments often made by national governments.	Targeted investments with a focus on complementing gaps in existing national programs.
HIV Testing and Counseling	HTC as part of a comprehensive package of services for MARPs.	Targeted investments focusing on MARPs, other vulnerable populations and specific geographic regions.	High levels of investment.
Innovations with Evaluation	Impact evaluations of programs targeting MARPs.	Impact evaluations of promising biomedical, behavioral, and structural interventions.	Impact evaluations of promising biomedical, behavioral, and structural interventions.
Critical Enablers	Targeted investments focused on creating an enabling environment for MARPs interventions.	Targeted investments depending upon national context.	Targeted investments depending upon national context.
Treatment Coverage	Linkages to care and treatment as part of a comprehensive package of services for MARPs.	High levels of investment to achieve strong linkages to treatment and care.	High levels of investment to achieve strong linkages to treatment and care.

Table 1: Examples of how to apply prevention priorities across different epidemic-types.

Appendix: HIV prevention and the Global Health Initiative (GHI): connecting to the broader country continuum of response

The first goal of the US Global Health Initiative (GHI) is the prevention of 12 million new HIV infections²³², making prevention activities a key component of the USG's global GHI strategy. The GHI principles should be reflected in all PEPFAR prevention portfolios:

1. Implement a woman, girl, and gender equality centered approach
2. Increase impact through strategic coordination and integration
3. Strengthen and leverage key multilateral organizations, global health partnerships, and private sector engagement
4. Encourage country ownership and invest in country-led plans
5. Build sustainability through health systems strengthening
6. Improve metrics, monitoring, and evaluation
7. Promote research and innovation

Other parts of this guidance address gender, partnerships, country ownership, sustainability, monitoring and evaluation, and research. This section addresses Principle 2, increasing impact through strategic coordination and integration.

PEPFAR prevention programs should seek opportunities for synergy and collaboration with other USG activities. Many aspects of development and public health are intertwined, and as USG colleagues learn more about programs in other areas, they may identify areas where HIV prevention could be added. While each country and region is unique, and therefore these collaborations will be unique, there are some areas that all country teams should consider:

- **Malaria:** In countries where the President's Malaria Initiative (PMI) is active, PEPFAR and PMI colleagues should look for opportunities for joint prevention programming. PEPFAR country teams may fund joint activities that combine malaria prevention with HIV prevention (for example, combining an HTC event with handing out bed nets). More sustained, integrated programs may also be funded with approval from headquarters; contact your CSTL for more guidance.
- **Maternal, Neonatal and Child Health (MNCH):** PEPFAR released guidance on integrating HIV services within MNCH programs in January 2011²³³. This guidance identifies an essential package of integrated PMTCT/pediatric HIV/MNCH services and health systems strengthening activities and recommends possible action steps to operationalize and evaluate integration efforts. While these steps focus on integration across PMTCT and treatment activities, their principles can and should be extended to broader HIV prevention, especially as primary prevention of HIV infection is a core pillar of PMTCT programs.

²³² United States GHI Targets. Accessible at: <http://www.ghi.gov/about/goals/index.htm>

²³³ Integrating PMTCT, Maternal, Neonatal, and Child Health and Pediatric HIV Services. Accessible at: <http://www.pepfar.gov/guidance/pmtct/158785.htm>

Therefore, PEPFAR prevention staff should work closely with MNCH programs to incorporate HIV prevention activities into these programs and to ensure that PEPFAR-funded prevention activities refer and link appropriately to MNCH resources.

- Family Planning: For information on linkages between PEPFAR programs and family planning programs, please see the current version of the annual Country Operating Plan Guidance²³⁴.

The above examples involve natural linkages between HIV prevention and other public health initiatives. Recent studies also indicate rich opportunities for HIV prevention across other development sectors^{235,236}. These studies suggest that activities in diverse sectors such as economic strengthening and agriculture can have measurable impacts on HIV transmission. PEPFAR prevention staff should reach out to other USG programs targeting a range of sectors and look for opportunities to enhance the HIV prevention effect of existing programs. These enhancements might include adding HIV prevention content to existing programs such as a class on HIV prevention and gender empowerment for women in a USG-sponsored agriculture program, but they might also entail simple “tweaks” to existing programs such as ensuring that food security programs are designed to be accessible by those living with HIV.

Many of these areas need further research. For example, a recent study in Malawi demonstrated that giving cash transfers directly to adolescent girls decreased risky sexual behavior and improved HIV-related health outcomes for the girls²³⁷. While this intervention needs to be tested in varied social and cultural environments before being replicated on a large scale, it suggests that changes in how existing cash-transfer programs target recipients could have a significant impact on HIV transmission. For more on integrating HIV prevention with programs in the non-health sectors, see Section 4.4 of this guidance.

²³⁴ PEPFAR Fiscal Year 2012 Country Operational Plan (COP) Guidance (August 2011). Accessible at: <http://www.pepfar.gov/guidance/cop2012/index.htm>

²³⁵ Bundy D, Patrikios A, Mannathoko C, et al. (2010). Accelerating the education sector response to HIV. *Accelerating the Education Sector Response to HIV*, 1, 1-93.

²³⁶ Kim J, et al. (2008).

²³⁷ Baird S, Chirwa E, McIntosh C, Ozler B. (2010). The short-term impacts of a schooling conditional cash transfer program on the sexual behavior of young women. *Health Economics*, 19, 55-68.