



CASES IN GLOBAL HEALTH DELIVERY

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CONCEPT NOTE

HIV Prevention

With nearly 7,000 new HIV infections and 5,000 deaths from HIV/AIDS daily, there is an urgent need to prevent HIV transmission.¹ For every two people treated, five more become infected.² The failure to develop and implement broad-based effective prevention strategies threatens to exacerbate the epidemic significantly and undermine even the most effective treatment approaches. Although significant global expansion of access to proven prevention strategies could avert half of the 62 million new HIV infections projected to occur between 2005 and 2015,³ it was estimated in 2008 that key prevention services reached less than 10% of individuals at risk worldwide.⁴ About 80% of HIV infections occur through sexual contact with an infected partner; about 10% are transmitted perinatally or during breastfeeding; and the remaining 10% are transmitted through exposure to infected blood.⁵ Blood-borne HIV transmission most commonly occurs when injecting drug users (IDU) share contaminated injecting equipment.

Over the past 30 years, scientists have made significant progress in understanding the virus, but numerous attempts to create a working vaccine have fallen short.⁶ Without a vaccine, global public health workers must rely on other biological and behavioral interventions to interrupt HIV transmission and curb the pandemic. Recent data on new tools for HIV prevention have reinvigorated the field, with hopes the epidemic can be controlled.⁷ This paper reviews the global epidemiological landscape, the history and challenges of HIV prevention, the known interventions, and several important concepts underlying successful prevention efforts.

The Epidemiological Landscape of HIV/AIDS

The World Health Organization (WHO) and the Joint United Nations Program on HIV/AIDS (UNAIDS) created four categories of HIV epidemics: 1) low-level, 2) concentrated, 3) generalized, and 4) hyperendemic.⁸ In low-level scenarios, HIV prevalence levels are below 1%, and HIV has not spread to significant levels within any subpopulation. In large countries, such as the United States, China or Brazil, there might be rural geographic sections that have low-level epidemics; the urban areas might have concentrated scenarios, where HIV prevalence is 5% or higher in one or more sub-populations, but the virus is not circulating in the general population. Epidemics in Latin America, the Middle East, Europe, and Asia—i.e., most of the world—are and most likely will remain concentrated (see **Exhibit 1** for table on

Sarah Arnquist, Julie Rosenberg, Joseph Rhatigan, Rebecca Weintraub, and Rebeca Plank prepared this note with assistance from Mehreen Iqbal for the purpose of classroom discussion rather than to illustrate effective or ineffective health care delivery practice.

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various epidemics and strategies). Epidemics are concentrated if transmission occurs largely in a defined vulnerable group—such as sex workers, men who have sex with men, and IDUs and their sexual partners. Prevention activities in concentrated epidemics should target the most heavily impacted groups.⁹

In generalized epidemics, HIV prevalence is between 1% and 15% in pregnant women attending antenatal clinics, indicating that HIV prevalence is present among the general population at sufficient levels to enable heterosexual networking to drive the epidemic. Generalized epidemics are found in most of southern Africa and parts of eastern Africa. Most hyperendemic scenarios are also found in these regions. Epidemics are generalized if transmission is sustained by heterosexual behavior in the general population and would persist despite effective programs for what have been traditionally the most vulnerable groups.⁹ Heterosexual intercourse is the primary driver of generalized epidemics. In these settings, infection rates among men and women are about equal.⁴

In hyperendemic scenarios, which includes parts of southern and eastern Africa, such as South Africa, Swaziland, Botswana, and Kenya, HIV prevalence exceeds 15% in the adult population, and infection is driven through heterosexual, multiple concurrent partner relations with low or inconsistent condom use, among other factors that have not been completely elucidated.

Parts of the Caribbean and South Pacific have mixed epidemics. Most infections are concentrated in high-risk subpopulations, but certain geographic areas have infection rates above 1% in the general population. Haiti and Indonesia are two countries with mixed epidemics.¹⁰

The History and Challenge of HIV Prevention

Following the identification of HIV and AIDS in 1983, the global response was “delayed, grossly insufficient, fragmented, and inconsistent (see **Exhibit 2** for HIV/AIDS timeline).”⁴ Scientists figured out how HIV was transmitted soon after its discovery, but bringing the infection under control would have required an unprecedented, aggressive policy response addressing sensitive social issues, such as sexual behavior, drug use, gender inequalities, community structures, and social norms. Because HIV has been associated with marginalized populations, sexual transmission, and death, the disease became synonymous with widespread stigma, discrimination, and denial. Many religious organizations, for example, compassionately cared for patients dying of AIDS, but they refused to promote condoms or provide sexual education to youth due to fears of encouraging or condoning promiscuity, and the disease spread unabated.⁴

HIV prevention is complex, and numerous obstacles have impeded effective, widespread HIV prevention programs. These obstacles include: shortfalls in funding, inadequate data,¹¹ disagreement over core prevention activities,¹² an overemphasis on individual-level interventions,¹³ insufficient focus on operations research, a failure to effectively target, select, and deliver services, and continued discomfort with topics such as sexuality and drug use.¹¹ Even where the tools and knowledge to prevent HIV have been disseminated, structural risk—the way in which aspects of the environment increase vulnerability to disease or promote risky behavior—can impede their uptake and efficacy. Structural risk is created by the interplay between social, political, and economic forces.¹³ Economic inequity and gender dynamics hamper an individual’s ability or agency to make healthy choices and explain why the incidence in women is on the rise. One example is the case of married women who may, because of gender dynamics and cultural constructs, be unable to negotiate safer sex with their spouses. Commercial sex workers may take part in unsafe sex, as another example, despite having access to condoms due to financial insecurity as well as an unregulated industry. HIV prevention programs must address structural risk, which can be challenging, to

ensure both that both the legal and political environments at the local and national levels are conducive to program success.

Until recently, policymakers also often considered prevention and treatment as distinct activities and failed to achieve the right balance and synergies between funding and implementing both.⁴

Despite this, there have been some “islands of success in a sea of failure” over the past 30 years.¹¹ From the beginning of the HIV/AIDS pandemic, civil society—the broad swath of society that functions outside of government and includes community-based organization, religious groups, and nonprofit organizations—has played many critical roles in HIV prevention efforts worldwide. Civil society advocates for funding, new public policies, and delivers prevention services to hard-to-reach risk groups.¹⁴

In the 1980s activists began viewing the global response to HIV/AIDS as a human rights issue, partly in response to widespread discrimination and human rights violations.¹⁵ This included mandatory HIV testing for those wanting to marry;¹⁶ restrictions on international travel; barriers to employment and housing, access to education, medical care, and/or health insurance; and names-based reporting, partner notification, and confidentiality.¹⁵ Advocates recognized these issues were contributing to individuals’ vulnerability to HIV either by denying access to services or discouraging them from accessing available services.¹⁵

In the 1990s, several United Nations agencies, international nongovernmental organizations (NGOs), and donor governments explicitly adopted human-rights-based approaches to their work. The Joint United Nations Program on HIV/AIDS (UNAIDS) formed in 1996 and integrated a human-rights-based approach into its global strategy for addressing HIV, including HIV prevention.

New funding initiatives in the 2000s changed the HIV/AIDS landscape further and brought more attention to the issue. Three new funding sources became available: the Bill and Melinda Gates Foundation (1999), the Global Fund to Fight AIDS, Tuberculosis and Malaria (2002), and the US government’s President’s Emergency Plan for AIDS Relief (PEPFAR) (2003). Through PEPFAR, the US government pledged USD 15 billion over five years to fund HIV/AIDS prevention, treatment, and care in the 15 most affected countries. The US government assistance for the global HIV epidemic has increased from USD 595 million in 2001 to a proposed USD 5.6 billion in the 2012 budget request.¹⁷ While PEPFAR funding emphasized scaling up treatment efforts and focused less on prevention, the program’s endorsement of only certain types of prevention approaches—namely the ABC (abstinence, be faithful, use condoms) approach—stoked global controversy.¹⁸ Proponents of the ABC approach, often from conservative groups, frequently cited Uganda’s early reduction in HIV prevalence as evidence to support this approach.¹⁹

Critics of the ABC approach said it oversimplified the complexity of prevention, over-emphasized sexual transmission, and placed the onus of prevention on individual choices rather than highlighting the structural factors that contributed to an individual’s risk of infection. They attributed Uganda’s reduction in HIV prevalence in part to high death rates of infected individuals. Furthermore, PEPFAR’s promotion of the ABC approach fueled raging debates about promoting abstinence over condom use. Many considered these debates distractions from the true need to develop strategies that addressed all routes of transmission and create supportive environments that allowed and encouraged individuals to avoid high-risk behaviors.²⁰ Since the introduction of ABC, there has been an outpouring of work exploring other products and services to avert infection.

Preventing Sexual Transmission of HIV

About 80% of HIV infections are transmitted through sexual intercourse. The risk of transmission is related, in large part, to the amount of circulating HIV in the blood stream (viral load) in HIV-infected

individuals and may vary according to viral subtype.²¹ Monogamy, delaying sexual debut, and using condoms consistently are all behavioral-based methods to prevent sexual transmission of HIV. Biomedical approaches, such as male circumcision, treating sexually transmitted infections, and treating HIV itself, can also reduce the likelihood of sexual HIV transmission.⁷

Condoms

Conclusive evidence shows that consistent and correct condom use significantly reduces the risk of HIV transmission during sex.²² The male latex condom is the single most efficient, available technology to reduce the sexual transmission of HIV and other sexually transmitted infections, including chlamydia, genital herpes, gonorrhea, and syphilis. The female condom was created in 1992. Global distribution is far lower for female condoms than for male condoms, reflecting higher cost as well as limited demand based on lack of awareness of its availability. Successful condom programming must focus on both supply and demand issues. UNAIDS estimates that about 13 billion condoms are needed each year for prevention of HIV and other sexually transmitted infections; the current supply falls far short of that need. Although knowledge about condoms and their availability, while critically important, do not guarantee their use, HIV prevention programs must develop behavior change campaigns focused on increasing demand for and use of condoms. Effective condom promotion should be aimed at both the general population and targeted at people with the highest risk of infection, especially young people, sex workers and their clients, injecting drug users, and men who have sex with men.²² Negotiating condom use can be difficult and should be addressed when possible. Studies have shown that condom uptake is higher in non-traditional outlets, such as in bathrooms, hotel rooms, and from dispensers than in traditional outlets such as in clinics and pharmacies, and efforts should be made to ensure such outlets remain stocked²²

Counseling and Testing

Testing is a crucial component of HIV prevention, particularly in light of new evidence suggesting early initiation of antiretroviral drug treatment can prevent transmission (reference Cohen NEJM 2011).²³ It is estimated that in the United States approximately 20% of HIV-infected persons are unaware of the infection.²⁴ HIV testing identifies infected individuals so they can reduce the risk of transmitting the virus. Research suggests this “prevention with positives” can be an effective targeted behavioral intervention. Those infected with HIV can take measures to prevent transmission to others, such as abstinence, consistent condom use, not sharing injection equipment, and initiating treatment. Testing also identifies negative individuals who need reinforcement about safe behaviors.⁷

Overall coverage of counseling and testing remains low. A median of 17% of women and 14% of men in sub-Saharan Africa were tested and knew their results between 2005 and 2009.⁷ Factors affecting demand for HIV testing include access to care, perception of risk, fear, stigma, and the threat of violence. To increase demand for testing, new approaches using rapid tests door-to-door and offering economic incentives are being tried. Additionally, many programs are shifting from client-initiated testing (also called voluntary testing and counseling or VCT) to routine testing, also called provider-initiated testing. Evidence suggests this could normalize and reduce stigma around HIV testing.⁷

Behavior Change Campaigns

Many known behaviors directly and indirectly lead to HIV transmission, including unprotected intercourse, sex with concurrent partners, and intravenous drug use. Prevention therefore requires individuals to avoid these behaviors or employ risk reduction strategies.¹² Increasing consistent and correct

use of condoms, reducing or eliminating concurrent partnerships, and delaying onset of sexual debut are examples of common behaviors targeted. Key approaches include mass media and communications campaigns, as well as community mobilization.

Mass Media

Mass media interventions aim to prevent HIV by increasing knowledge, improving risk perception, changing sexual behaviors, and questioning potentially harmful social norms. Campaigns may use radio, television, and other outlets and ideally operate as part of multi-pronged efforts, in which mutually reinforcing messages are offered through interpersonal, community, and national channels. Mass media campaigns aim to influence social norms and spur dialogue at the population level. “Edutainment” is a combination of education and entertainment through radio or television series and can be used to model and demonstrate behavioral patterns that affect people’s risk of HIV, such as partner communication. Messages need to change frequently and be reinforced continually to sustain behavior change. Additionally, researchers have noted a “dose-response effect” to mass media messages in that higher exposure to mass media corresponds to increased positive behavioral change.²⁵

Community Mobilization

Mobilizing communities around HIV prevention is critical to generating demand for services and promoting behavior change among high-risk and marginalized groups.²⁶ Community mobilization hinges on empowerment of these vulnerable populations. Outreach activities to engage people in HIV prevention services should be tailored to specific groups. Often, this is best done by hiring peer educators or outreach workers from the communities of focus. Mobilizing people who already are receiving services can prompt them to advocate for enhanced quality or services. Community mobilization includes empowering individuals to advocate for services and transparency to hold providers and public officials accountable to their commitments.

Diagnosing and Treating Sexually Transmitted Infections

Individuals already infected with human papillomavirus and other sexually transmitted infections (STI) are two to five times more likely than uninfected individuals to acquire HIV infection via sexual contact.²⁷ Studies have shown that treating STI in HIV-infected individuals decreases both the amount of HIV in genital secretions and how frequently HIV is found in those secretions, thus reducing the likelihood of transmission. However, a meta-analysis of several studies found that the overall findings were inconclusive.²¹ According to the US Centers for Disease Control and Prevention, STI prevention, testing, and treatment can play a vital role in comprehensive HIV prevention programs and examining STI trends may offer insights into where the HIV epidemic is growing.²⁷ Many programs use surveillance of STI as a useful proxy measure for risky behavior and potentially important facilitators of transmission.¹¹

Male Circumcision

Three large randomized control trials in South Africa, Kenya, and Uganda in the mid 2000s confirmed that medical male circumcision (MC) reduces men’s risk of acquiring HIV heterosexually.²¹ The protective effect of MC against HIV infection results from removing the foreskin and its high density of cells targeted by HIV, and also indirectly by reducing the risk of ulcerative STI. A meta-analysis of 28 observational studies revealed that overall, circumcised men were 48% less likely than uncircumcised men to be HIV-positive. Adjusting for confounding factors such as age and sexual behaviors increased it to 58%.²⁸ Although circumcision of HIV-infected men might not reduce HIV transmission to women,²⁹ women would benefit

from the population effects of scaled-up MC because less HIV would be circulating, essentially a “herd immunity” effect as is seen with vaccines. The WHO identified 14 priority countries with generalized HIV epidemics and low prevalence of MC, such as Kenya, Swaziland, and South Africa. Starting around 2008, significant HIV prevention funding and efforts began focusing on scaling up circumcision.³⁰ One important advantage of MC as a prevention strategy is that it is a one-time intervention, like a vaccine. Challenges to scaling up voluntary medical MC include a shortage of trained providers, distrust, and cultural and religious practices. Nonetheless, scaling-up of MC as an HIV prevention strategy is calculated to be highly cost-effective.³¹

Preventing HIV Transmission Due to Blood Exposure

Blood Safety

Adoption of safety measures, such as blood donor selection and screening guidelines, makes the risk of HIV transmission through blood transfusions today virtually non-existent in developed countries. In many resource-constrained settings, however, where guidelines for blood safety have not been implemented universally, HIV infection remains a risk associated with receiving blood transfusions. In 2007 more than 85 million blood donations occurred in 162 countries, of which 41 countries lacked the resources to screen for transfusion-transmissible infections.³² The WHO recommends a nationally coordinated blood transfusion service, using voluntary unpaid donors, testing all donated blood, and ensuring quality systems checks throughout the blood transfusion process to help maintain a constant blood supply safe from contamination with HIV, hepatitis B and C, and syphilis.

Reducing Occupational Risk

Contaminated needles and syringes used in medical practice can also result in HIV infection. PEPFAR funded the “Making Medical Injections Safer” campaign in 11 countries to work with host governments to promote the safe use and disposal of injections through training and education. Newer technologies, such as single dose, pre-filled auto-disable injection devices (used for vaccinations) and auto-disable syringes, which work only one time, can make injections safer in developing countries.

Taking antiretroviral drugs soon after an accidental prick or other exposure to HIV reduces the risk of transmission. This short-course, month-long treatment is called post-exposure prophylaxis. The WHO recommends that post-exposure prophylaxis be provided within the health care sector as part of a comprehensive universal occupational precautions package.³³

Harm Reduction Strategies Among Injecting Drug Users

About 30% of HIV infections outside of sub-Saharan Africa result from injecting drug use, and about one in five IDUs worldwide are infected with HIV.³⁴ HIV prevention efforts targeting IDUs fall under a broad category of activities aiming to reduce the negative aspects of drug use referred to as “harm reduction strategies.” Harm reduction programs do not try to eliminate drug use itself; rather they aim to decrease needle use or sharing and stabilize IDUs, medically, economically, and socially.³⁵ Numerous studies have demonstrated that harm reduction programs for IDUs reduce HIV risk without increasing drug use.³⁶ The most common harm reduction activities are opiate substitution therapy and needle and syringe exchange programs. Additionally, harm reduction programs distribute and promote condoms and link IDUs to

counseling and testing, substance abuse treatment, and antiretroviral treatment if required (see **Exhibit 3** for the WHO's recommended 12 components for comprehensive harm reduction).³⁷

Needle and syringe exchange programs distribute clean needles and syringes to increase the availability of clean injecting equipment circulating among IDUs. They also collect dirty needles to prevent their re-use. Numerous types of needle-exchange programs have been developed, including free needles at fixed and mobile sites; vending machines selling injecting equipment; pharmacy sales of injecting equipment; and distribution of equipment by IDUs or their peers. Strong evidence shows that these programs increase safe injections. The direct link between needle and syringe programs and reduced HIV incidence is less clear, but the impact likely depends on the proportion of IDUs receiving sufficient sterile syringes to cover all injections.³⁵

Oral opiate substitution therapy is a type of harm reduction that seeks to substitute the use of heroin—the most common drug injected worldwide—with other (oral) opioids, most commonly methadone or buprenorphine to reduce drug dependency and, therefore, decrease injection frequency and chances for contracting the virus. Such practices, like methadone maintenance therapy, help stabilize drug users through improvements in health and social functioning. This stabilization is associated with declines in risky behaviors, such as sharing dirty needles, selling sex for drugs, and having unprotected sex with multiple partners.³⁵

Current coverage of harm reduction is low. It is estimated that annually worldwide sterile needles and syringes provided by needle and syringe programs are used in just 5% of total drug injections; 8% clients receive opiate substitution therapy; and 4% of HIV positive IDUs receive antiretroviral treatment.³⁷ Harm reduction policies face legal and political objections for concerns it is promoting criminal activity. The United States, for example, banned federal funding for needle exchange programs until 2009. The adoption of laws supporting needle-exchange programs and opioid substitution therapy are essential to increasing their uptake. Thus, HIV prevention efforts also focus on sensitizing police officers and changing legal and regulatory environments.³⁴

Harm Reduction in Prisons

The rates of HIV among prisoners in many countries are significantly higher than the general population. Countries in the European Region, in particular, face this burden. Five countries report greater than 10% HIV prevalence among the prison population, including Estonia (9% to 90% at the various prisons), Lithuania (Altyus Prison 15%), Romania (13% overall), Slovakia (0% to 34%) and Ukraine (0% to 26%).³⁸ Harm reduction programs geared specifically toward prisoners have been developed, but their degree of implementation varies widely depending on policy makers' willingness to allow condoms, methadone, and clean needles in prisons. HIV prevention experts agree that policies of mandatory testing and segregation are counterproductive and may result in negative health consequences for the segregated prisoners.³⁹

Prevention of Mother-To-Child Transmission

In 2008, 430,000 children under 15, 90% of whom lived in Africa, were newly infected with HIV. About 90% of all new HIV infections in children occur as a result of mother-to-child transmission.⁴⁰ HIV can be transmitted from mothers to infants in three ways: across the placenta during pregnancy; during labor and delivery; and through breast milk. Effective interventions have reduced the risk of transmission from mother to baby to less than 2% in high-income nations. Risk can also be reduced in resource-limited settings

to less than 2% through antiretroviral (ARV) prophylaxis and treatments in concert with elective caesarean-sections (C-section) and avoidance of breastfeeding.⁴¹

The WHO and UNICEF recommend a four-pronged strategy for prevention of mother-to-child transmission (PMTCT) that includes:

1. Primary HIV prevention in women of childbearing age;
2. Prevention of unintended pregnancies in women with HIV infection;
3. Prevention of HIV transmission from women with HIV to their infants via use of antiretroviral drugs; and
4. Provision of treatment, care, and support to women with HIV and their families.

The most effective means of preventing mother-to-child transmission involves administration of antiretroviral therapy (ART) to all HIV-positive pregnant women (regardless of their clinical stage or CD4 count) late in their pregnancy and during labor, as well as the initiation of long-term ART for HIV-positive women who meet criteria for treatment. In 2010 the WHO updated its PMTCT and infant feeding guidelines, suggesting giving ART to pregnant women earlier in their pregnancy and for a longer duration. For the first time, the WHO also said it was safe for women on ART to breastfeed rather than formula feed, although expert opinion is still divided on this issue. Exclusive breastfeeding may protect the infant's intestinal mucosa, thus providing a better barrier against HIV.⁴² Even though formula feeding reduces the risk of infant HIV, without reliable access to safe drinking water to prepare the formula, it increases the risks of diarrhea, malnutrition, and death.⁴³ The relative risks and benefits of formula versus breastfeeding must be considered by location and level of resources.

In most cases, under administration of ART, the risk of HIV transmission from mother to infant during labor and delivery is low, thus removing the need for a c-section. Recommendation for a c-section delivery depends on the mother's HIV viral load, and both medicinal and surgical interventions depend upon a community's socioeconomic and cultural access to healthcare services and drugs.⁴⁴ For example, many women already face adversity and barriers to seeking health care. Many women drop out of PMTCT programs because they fear discrimination and rejection by their male partners and families. PMTCT programs must consider these issues in their program design.⁴¹

Pre-Exposure Prophylaxis

The success of PMTCT and post-exposure prophylaxis stimulated interest in the concept of pre-exposure prophylaxis. Pre-exposure prophylaxis refers to the use of antiretroviral drugs by HIV-negative people prior to HIV exposure to prevent HIV infection. Using prophylactic medications to prevent other infections, such as malaria, is standard practice, but it remains experimental for HIV prevention.⁴⁵

Microbicides

Microbicides, a subset of pre-exposure prophylaxis, are products formulated for individuals to apply topically (vaginally or rectally) to reduce the risk of contracting HIV and possibly other sexually transmitted infections. After two decades of disappointing research to develop a microbicide for women, a 2010 clinical trial run by the Centre for the AIDS Programme of Research in South Africa proved promising. The study found that a microbicide containing 1% tenofovir (an antiretroviral drug) reduced a woman's risk of HIV infection by 39%.⁴⁶ Women who used it most consistently in more than 80% of sex acts had a 54% reduction in HIV infection. If these findings are confirmed with future studies, microbicides could be added to the

arsenal of HIV prevention strategies and specifically give women an additional mechanism they themselves can control to decrease their risk of infection.¹

Treatment as Prevention

The concept of “treatment as prevention” describes the public health or community benefits from using ART to decrease transmission.⁷ In 2009, data supported the notion that by lowering viremia in treatment-adherent HIV-infected persons, ART can be greatly effective in preventing transmission.⁴⁷ Interest in this approach increased significantly around 2010 after several studies definitely showed that treatment with antiretroviral drugs reduced an infected individual’s viral load and infectiousness such that their likelihood of passing on the virus was very low.^{48,49}

Some people have called for universal voluntary HIV testing followed by immediate treatment regardless of the infected person’s CD4 cell count. Such a Universal Test and Treat (UTT) strategy aims to reduce infectiousness at a population level, thereby reducing HIV incidence. Implementation of UTT or another version of “treatment as prevention” raises numerous questions and concerns.²¹ Many scientists are concerned about adherence to medication regimens and the possibility of increased resistance with more noncompliance. Introducing treatment earlier for prevention purposes would exacerbate existing distribution challenges and begs the question how it will be funded. Of the estimated 15 million HIV-positive people qualifying for treatment under the WHO’s guidelines in 2010, only about 5.2 million were receiving it.⁵⁰

Implementing HIV Prevention Programs

Effective HIV prevention, selection of which interventions to offer and how, requires strong, informed, and committed leaders that are held accountable and a deep understanding of the nature of the epidemic in individual countries and specific communities where prevention strategies are being implemented.⁸

When planning HIV prevention activities, UNAIDS suggests decision makers begin by answering three critical questions:⁸

1. Where, among whom, and why are HIV infections happening now?
2. How fast are infections moving?
3. What are the drivers of the epidemic?

Answering these questions—what UNAIDS terms coming to “know your epidemic and know your response”—requires consideration of structural factors, the social, political, cultural, and economic context that affect the spread of the virus. It means considering the behaviors and social conditions influencing communities’ ability to implement prevention messages; it means understanding the relationship between the epidemiology of HIV infection and the key drivers of the epidemic—the behavioral, biological, and structural factors contributing to the spread of infection. Structural drivers, as previously mentioned, may include poverty, gender inequality, and human rights violations that can be difficult to measure and hard to change.⁸

Risk and vulnerability are two fundamental concepts underlying HIV prevention that must be understood to identify exactly where, among whom, and why HIV infections are happening. Risk is the

¹ See www.mtnstopshiv.org/ for updates.

probability that a person may acquire HIV infection.⁸ Certain behaviors create, enhance, and perpetuate risk, such as having unprotected sex or injecting drugs with contaminated needles. Vulnerability to HIV is the individuals' and communities' lack of power or agency to minimize or modify their risk of exposure to HIV infection and, once infected, to receive adequate care and support.¹⁵ Vulnerability results from a range of factors at the individual, community, and societal levels. Personal factors include a lack of knowledge and skills to protect oneself and others. Community factors include geographic distance to services or availability of prevention commodities, such as condoms and clean needles. Finally, societal factors include social and cultural norms, religious beliefs, cultural constructs and laws that affect gender equality, stigmatize or disempower certain populations.⁸

Women and girls in many parts of the world, for example, have a greater risk of contracting HIV as a result of their lack of control over and access to economic and educational resources. Addressing gender inequality, particularly gender-based violence, deserves special consideration when considering structural drivers of HIV and why infections are happening.^{8,51} Prevention efforts should consider women's dependency on and vulnerability to male partners and not assume they have significant control of decisions related to their sexual practices. Women may be unable to refuse sex, question their partners' fidelity, or request use of a condom, and past or current sexual, physical, or psychological abuse can exacerbate the problems.⁵² Understanding issues that disproportionately impact women has led to several economic interventions that have shown to reduce women's poverty, their dependency on male partners, and their vulnerability to HIV including conditional cash transfers and access to microcredit.⁵²

Another group highly vulnerable to HIV in many places is sex workers. Sex workers are a diverse group of individuals. They can be men or women, work in brothels, their homes, or the streets. They can be high-end escorts or young girls migrating to work in cities. Successful HIV prevention programs will understand these differences and tailor their activities based on a subpopulation's particular needs. Despite differences, sex workers are often disenfranchised, economically desperate, and victims of violence and discrimination. Prevention programs for sex workers must confront stigma and discrimination, reduce violence, and promote enabling environments in which they are encouraged to protect their health.⁵³ Targeted interventions that promote education, condoms, sexual health, solidarity, empowerment, and rights for sex workers have contained HIV in Asia's three main sexually fueled epidemics in Thailand, Cambodia, and South India, showing the importance of understanding the epidemic and those at risk.⁹

Men who have sex with men (MSM) are yet another important group to recognize in program planning because they have a significantly high risk for HIV infection due to biological, behavioral, and structural factors, such as unprotected anal intercourse, multiple sex partners, and the social marginalization and discrimination they often endure. It is also important to realize that some men who have sex with men may or may not identify themselves as gay or bisexual, and may in fact identify as "straight," or transgendered, which underscores the importance of stressing this as a risk behavior, rather than as a risk group. MSM are hidden in many countries, where homosexual behavior can be highly stigmatized or even criminalized, and finding them to deliver HIV prevention services can be difficult. In addition to targeting behavior change strategies described above, legal protections for sexual minorities and efforts to reduce the stigma and discrimination contribute to generating demand for and access to HIV treatment and prevention services.⁵⁴

Recognizing the vulnerabilities of certain groups has led to many unique structural approaches to HIV prevention.^{55,13} The Thai "100% condom campaign" is a commonly cited example of a structural intervention that had dramatic, measurable impact on reducing HIV incidence. A law implemented nationally in 1991 required universal condom use in venues for commercial sex. Politicians and police enforced the law, and subsequently condoms became widely available in all brothels. This policy was no longer regulated by the sex worker but by the other stakeholders, including brothel owners and police.²⁰

Understanding the Epidemic

Knowing your epidemic and responding appropriately relies on obtaining quality surveillance data frequently. Surveillance in generalized epidemics usually relies on prevalence rates at antenatal clinics, reported AIDS cases, and population-based surveys. If such surveys include a standardized behavioral component and are conducted at regular intervals (every three to five years), they can be helpful in tracking progress.¹¹ Surveillance in concentrated epidemics relies on integrated behavioral-biomedical surveys of high-risk groups. These surveys are the best method available to understand the drivers of the epidemic and assess trends over time. High-risk groups are often difficult to find and so these surveys are prone to selection bias and small samples. Additionally, estimating the total size (denominator) of the hard-to-reach populations is difficult but necessary to plan and gauge coverage.¹¹ The scarcity of good information and limited capacity to analyze and apply that information leaves many HIV/AIDS program managers “in a fog of uncertainty.”

The surveillance data countries most often have relates to HIV prevalence and is based on reported cases and population surveys. Prevalence reflects infections that happened in the past, and projecting the next 1,000 new HIV infections remains challenging. Data on HIV incidence--new infections—is scarce because no technology exists to distinguish incident infections from prevalent cases. Modeling incidence from prevalence studies is time consuming and costly.¹¹ With the available data, decision makers determine which populations to target, which interventions and in what combination to employ them, and who (i.e., NGOs or government) is best suited to deliver them.⁸

Evaluating Prevention Programs

The evidence base for HIV prevention programs is mixed. One review found that 33 of 39 trials evaluating HIV prevention interventions showed no effect. Only trials of behavioral interventions, which remain the mainstay of HIV control programs, were included. The authors noted that the inconclusiveness may reflect lack of efficacy but also likely reflects inherent difficulties in the trial design, conduct, and measurement.²¹ Providing evidence for the effectiveness of a behavioral prevention program is a more complex task than proving the effectiveness of a drug, vaccine, or even a stand-alone prevention intervention, such as MC.¹¹ Measuring causal relationships between prevention programs and HIV infections averted is especially challenging for large-scale programs operating across diverse environments with multiple players.^{56,57,58}

Combination Prevention: The Way Forward

Decades of well-meaning activities have yet to meaningfully turn the tide in HIV prevention, and leaders are asking for new approaches. Most prevention experts agree that a combination of the interventions described above tailored to specific populations and guided by the wisdom and ownership of local communities offers the best hope for curbing the epidemic going forward.^{4,7,59} “Combination HIV prevention” is a multilevel approach that employs the simultaneous use of biomedical, behavioral, and structural prevention activities.²¹ Combination prevention not only addresses multiple layers of HIV vulnerability, but these layers can be mutually reinforcing. For example, linking biomedical prevention methods with behavioral approaches helps avoid risk compensation and increases adherence.⁶⁰ Successful programs will use a combination of interventions tailored to specific populations.

Population-based prevention efforts also require consideration of scale because sufficient levels of coverage, uptake, intensity, and duration of the right mix of prevention activities are necessary to improve

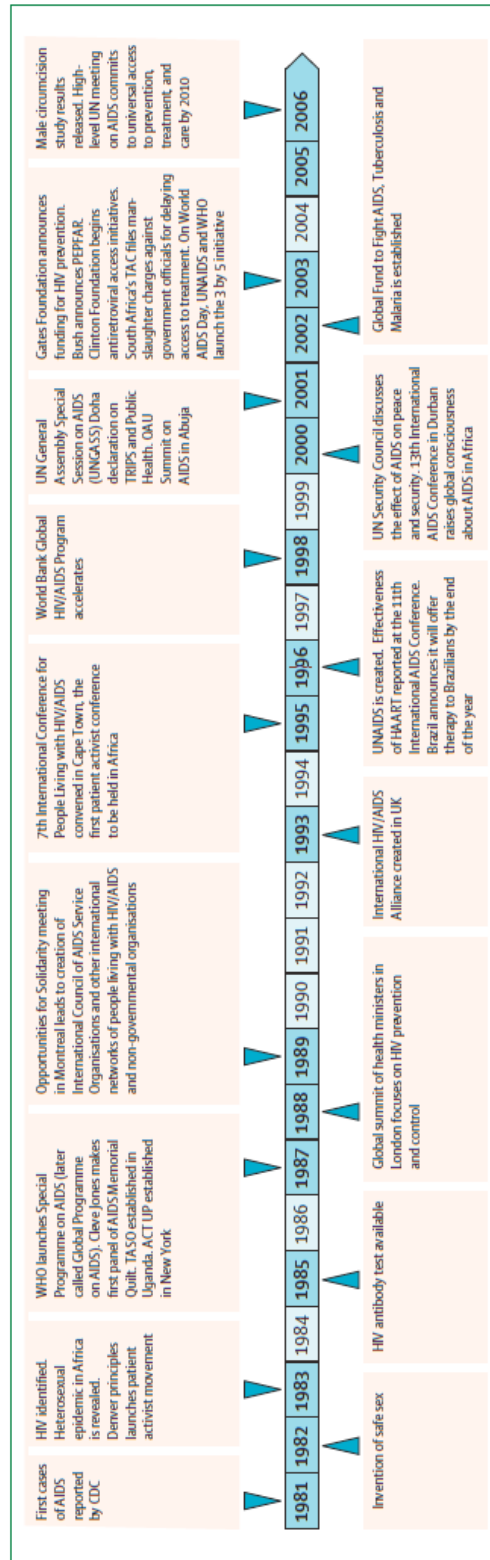
optimal population health outcomes, i.e., generate value.⁹ Thus, in addition to individual-level interventions, programs must consider actions at the community and even national level to promote conditions that enable individuals to protect themselves from infection. Supporting activities, such as generating demand, guaranteeing access to services, and measuring outcomes are vital to effective prevention (see **Exhibit 4** for table of what works in HIV prevention at individual, community, and national levels).⁶¹

Exhibit 1 *Type of Epidemic by Area, Data Collection Strategy, and Intervention*

	Concentrated Epidemics	Generalized Epidemics	Mixed Epidemics
Geographic Areas	North, Central and South America, Europe, Middle East, Asia Australia	Most of southern Africa and parts of East Africa	Parts of the Caribbean, west Africa, horn of Africa, Pacific region
Priorities for Surveillance, Monitoring and Evaluation	Emphasis on biological and behavioral surveillance of vulnerable groups (sex workers, men who have sex with men, injecting drug users)	Antenatal and episodic population-based surveillance	Both vulnerable group and general population surveillance
Interventions	Goal is to saturate coverage of vulnerable groups with tailored prevention activities	Goal is to change community norms and values around sexual behavior at the population level and promote widespread male circumcision	Tailor interventions to primary drivers of infection and maintain balance between targeted and general population activities

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

Exhibit 2 *Critical Events in the Global Response to HIV/AIDS*



Source: Merson MH, O'Malley J, Serwadda D, Apisuk C. The history and challenge of HIV prevention. *Lancet*. 2008;372(9637):475-488.

Exhibit 3 *WHO-Recommended Components for Comprehensive Harm Reduction Programs*

1. Outreach
2. Information, education and communication
3. Risk reduction counseling
4. HIV testing and counseling
5. Disinfection programs (for used needles and syringes)
6. Needle and syringe programs
7. Disposing of used injecting equipment
8. Availability of drug treatment services
9. Drug substitution treatment
10. HIV/AIDS treatment and care
11. Primary health care
12. Peer education.

Source: WHO Policy and Programming Guide for HIV/AIDS Prevention and Care Among Injecting Drug Users, 2005

Exhibit 4 *What Works in HIV Prevention*

	Reducing Structural Risk	Reducing Risky Behavior	Reducing Biological Vulnerability
Individual	Blood screening	Increase consistent and correct condom use Reduce or eliminate multiple concurrent partnerships Delay onset of first intercourse Decrease number of partners Increase condom use Address intergenerational or age-disparate sex Decrease sharing of contaminated injection equipment Behavior change programs to achieve above goals Universal precautions by workers in health care settings Risk reduction in PLWHA	Male circumcision PMTCT ARV regimens for mother and child Breastfeeding alternatives Caesarean delivery
Community	Confronting stigma, discrimination, and denial associated with the disease Addressing gender inequalities Addressing homophobia Building community solidarity among sex workers Creating an enabling community environment to empower sex workers to make their own decisions, including those that protect them from HIV infection	Changing social norms to encourage delayed sexual debut and limit enablers (e.g., alcohol and gender norms) Community-level interventions to reduce risky behaviors.	

National	<p>Rights for sex workers in concentrated epidemics</p> <p>Reducing sexual violence</p> <p>Addressing wealth inequality</p> <p>Addressing poverty</p> <p>High mobility as a driver of the epidemic</p> <p>Political and social leadership that openly acknowledges HIV also facilitates HIV prevention.</p> <p>Policy changes that allow needle exchange and methadone treatment (for IDUs)</p> <p>Stable housing to reduce the risks associated with injecting drug use</p> <p>100% condom use policy for sex workers</p> <p>Creating an open, enabling environment for confronting the epidemic</p> <p>Universal education beyond primary school</p> <p>Revising laws to recognize and enforce women's property rights</p>	<p>Access to prevention information, messages, skills, and technologies</p> <p>Mass media campaigns</p>	
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Appendix *Abbreviations*

ARV	Antiretroviral (drug)
ART	Antireviral therapy
HIV	Human immunodeficiency virus
IDU	Injecting drug user
MC	Male circumcision
PEPFAR	President's Emergency Plan for AIDS Relief
PMTCT	Prevention of mother to child transmission
UNAIDS	United Nations Joint Program on AIDS
WHO	World Health Organization

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