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ISSUE BRIEF

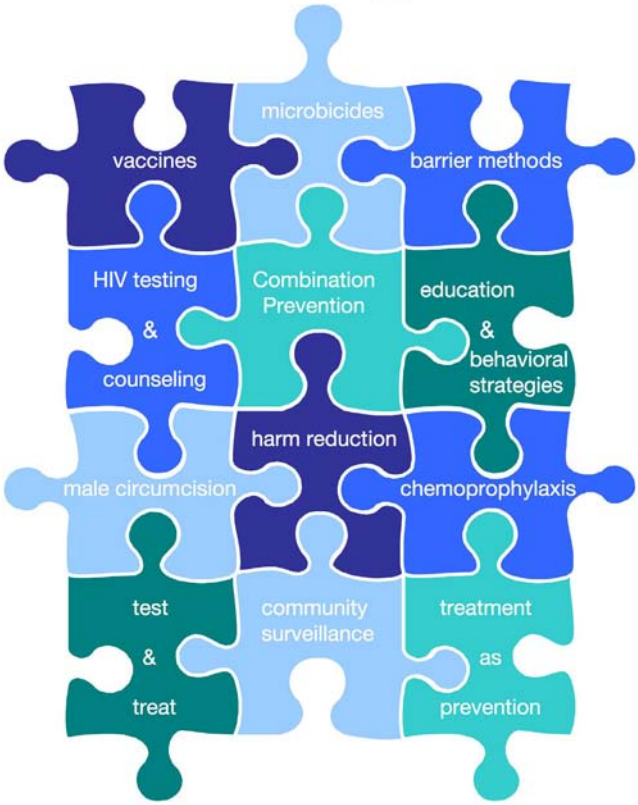
Accelerating an HIV Prevention Revolution: A Roadmap

In 2009, 33.3 million people were living with HIV/AIDS and 2.6 million people were newly infected worldwide.[1] Today, in the United States alone, an estimated 1.1 million adults and adolescents are living with HIV/AIDS.[2] Despite significant progress in knowledge about HIV/AIDS and its treatment over the past 25 years, much remains to be done to slow the rapid spread of this disease: as of 2010, for every two people starting antiretroviral treatment, five more were newly infected worldwide.[3]

Experts agree that stemming the tide of the AIDS epidemic will require a significant emphasis on prevention.[4] A recent report from the Institute of Medicine underscores that prevention must be the central tenet of the long-term response to HIV/AIDS, especially given the significant challenges that treatment scale-up faces in the current global economic downturn.[5] However, recent scientific advances related to the effectiveness of pre-exposure prophylaxis (PrEP), microbicides, and AIDS vaccine development, as well as the establishment of a high-level United Nations Commission on HIV Prevention and the release of the National HIV/AIDS Strategy in the U.S., have reinvigorated the hope for a prevention revolution in the years ahead.

Expansion of preventive interventions could potentially avert more than half of the HIV infections projected to occur by 2015 and could save $24 billion in AIDS treatment costs globally.

HIV prevention consists of a range of educational programs, services, and technologies to reduce HIV transmission. To be successful, interventions must be tailored to the needs of diverse groups at the national and community levels.[6] Federal, state, and local health systems must be strengthened in order to carry out the broad and systematic efforts needed to stop the spread of HIV.



Adapted from: AIDS Vaccine Advocacy Coalition. Piecing together the HIV Prevention Puzzle. 2009.

Prevention is not only the most effective defense against the virus, but also the most cost-effective. Researchers estimate that for every HIV infection prevented in the U.S., approximately $355,000 is saved in medical treatment costs.[7]

Despite their promise and effectiveness, HIV prevention programs have received inadequate resources and attention. Prevention programs currently reach less than half of people at high risk for HIV worldwide (see Figure 1).[1] Additionally, only 28.8% of the U.S. President's

Emergency Plan for AIDS Relief (PEPFAR) budget supports prevention programs including counseling and testing.[8] Expansion of preventive interventions could potentially avert more than half of the HIV infections projected to occur by 2015 and could save $24 billion in AIDS treatment costs globally.[9,10] However, according to a recent UNAIDS report, these efforts could be in jeopardy due to the current global economic crisis, which is projected to have a greater impact on reducing support for prevention initiatives than for treatment programs worldwide.[11]

In the U.S., only 3% of the FY 2011 HIV/AIDS budget was allocated to domestic prevention programs (see Figure 2).[12] Furthermore, the continuing spread of the epidemic has outpaced prevention funding. While the number of people living with HIV/AIDS in the U.S. rose between 2002 and 2007, in the same period HIV prevention spending at the Centers for Disease Control and Prevention (CDC) *decreased* by 19%, when adjusted for inflation.[13]

Prevention also has economic benefits. The CDC has estimated that 40,000 new infections in a single year would ultimately cost approximately $8.4 billion in lifetime HIV-related medical expenses.[14] This means that only 3,430, or 8.6%, of the 56,000 new HIV cases reported annually must be prevented to achieve cost savings.[14] In addition to the financial benefits, preventive measures are the best strategy for reducing the human toll of HIV/AIDS.[14] The bottom line is that prevention saves lives and is cost-effective.

While HIV/AIDS prevention efforts have proven effective in slowing the rate of the epidemic, no single prevention technology or strategy can be 100% effective. Therefore, a *combination prevention approach* that integrates evidence-based behavioral, biomedical, and structural interventions is the most promising strategy for preventing HIV/AIDS in the U.S. and abroad.

This issue brief reviews the scientific evidence regarding the effectiveness of behavioral strategies and prevention technologies that have the potential to avert millions of new HIV infections worldwide. It emphasizes the importance of combining behavioral approaches and prevention technologies and provides research and policy recommendations that serve as a roadmap for future domestic and international HIV prevention efforts.

Education and Behavior Change Strategies

Education and behavior change strategies that target the needs of diverse populations are critical to HIV prevention efforts. Clinical trials have shown that behavioral interventions are essential to reversing the HIV epidemic.[14] For example, reducing high-risk sexual and drug-use behaviors decreases the HIV transmission rate.[15] Furthermore, prevention technologies such as PrEP, microbicides, and condoms are only effective when used consistently and as prescribed. Behavioral research is critical to better understanding how to motivate people to adopt and consistently use a broad range of prevention approaches and technologies.

Figure 1: HIV prevention programs for selected populations
Median coverage of HIV prevention programs for selected population groups, 2008 and 2010.

Source: UNAIDS Report on the Global AIDS Epidemic, 2010.

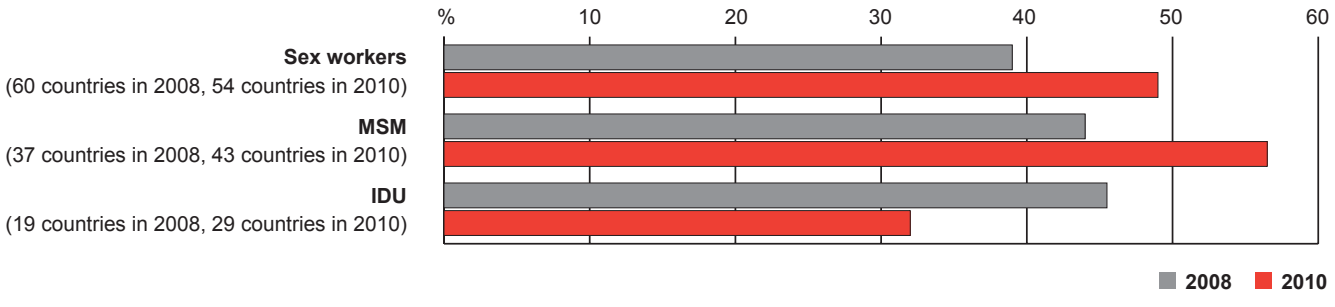
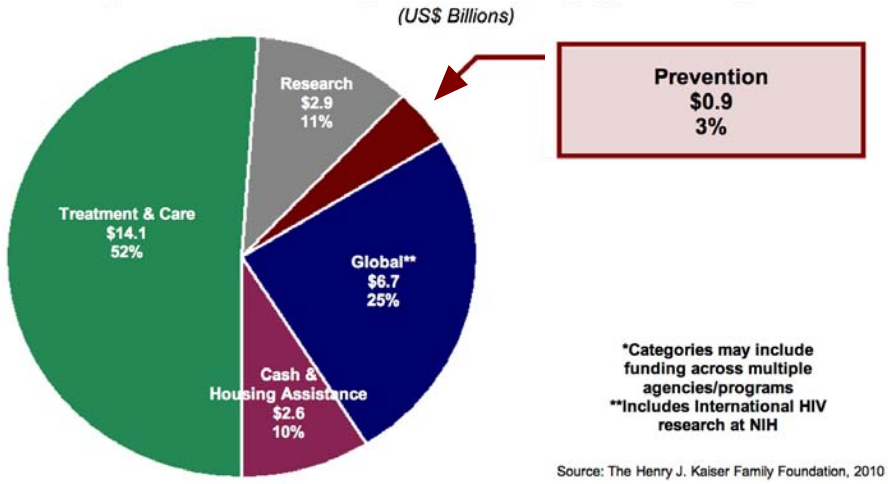


Figure 2: U.S. Federal Funding for HIV/AIDS by Category, FY 2011 Budget



Educational strategies such as comprehensive, evidence-based, age-appropriate sex education, rather than abstinence-only programs, are needed in schools and communities. A recent CDC study found that 84.2% of public secondary schools in the U.S. included HIV prevention in their curriculum, but only 21.1% addressed all eleven CDC-recommended HIV prevention topics, which include 1) abstinence as an effective method to avoid pregnancy, HIV, and STDs; 2) correct condom usage; 3) condom efficacy; 4) the risks associated with having multiple sexual partners; 5) social and cultural influences on sexual behavior; 6) prevention of HIV infection; 7) HIV transmission methods; 8) the effects of HIV on the human body; 9) the influence of alcohol and other drugs on HIV-related risk behaviors; 10) where to find information and services related to HIV and testing; and 11) compassion for persons living with HIV or AIDS.[16]

Educational efforts and interventions are needed to reduce the number of individuals' concurrent sexual partners, which is greatest in areas of the world with the highest HIV prevalence rates.[17] In countries such as Zimbabwe, Botswana, and Swaziland, it is common practice to have multiple long-term sexual partners, which is a high-risk practice with regard to the spread of HIV. Long-term partners are more inclined to engage in sexual activity without the use of protection, increasing the risk of HIV transmission. This behavior also creates a sexual network that can extend across large regions of countries when one person infected with the virus transmits it to his or her partners.[18] Education should encourage both HIV testing prior to initiating relationships and safe sex practices even in monogamous relationships.[19] Research supports the efficacy of these strategies in reducing rates of HIV infection. However, in the U.S. and worldwide, there are significant social, religious, cultural, financial, and political barriers that continue to impede the widespread implementation of evidenced-based HIV/AIDS education programs.

Innovative new strategies should be employed in tandem with conventional prevention approaches to create an additional line of defense. Two recent studies supported by the World Bank in Malawi and Tanzania suggest that "conditional cash transfer" programs, in which financial incentives are used to encourage positive behaviors, could be used to reduce the incidence of HIV and other sexually transmitted infections. In the Malawi study, for example, small monthly cash payments to poor schoolgirls, aged 13 to 22, and their families as an incentive to continue their education resulted in these young women delaying the onset of sexual activity and having sex less often and with fewer partners.[20] The study also demonstrated a 60% lower prevalence of HIV and herpes infections compared to the girls who did not receive any payments in the 18 months following implementation of the program.[21] These small financial incentives made it less likely that young women living in poverty participated in sexual activity with men in exchange for gifts or money.

Another important social factor fueling the AIDS epidemic is the widespread stigma that still surrounds HIV/AIDS despite decades of progress in the fight against this disease. This stigma is promoted by myths, lack of knowledge regarding disease transmission, homophobia, and value-judgments associated with its acquisition.[22] Educational and behavioral strategies, when coupled with effective use of the media, can reduce the stigma and discrimination associated with HIV/AIDS. These interventions may encourage individuals at risk for HIV infection to seek testing and treatment,[23] while those already infected and receiving medication will be more likely to adhere to their treatment.[24]

Further research is needed to determine the most effective delivery models for behavioral and educational interventions and whether a combination of strategies would be more beneficial. Priority must be given to evaluating preventive interventions for vulnerable populations, as well as investigating the scale-up of these programs in a broad range of community settings in the U.S. and globally. A better understanding is needed of the factors that motivate individuals to initiate behavior changes and use prevention technologies. Additionally, the social "drivers" that make people more vulnerable to HIV infection, such as poverty, homelessness, social stigma, discrimination, and unequal power dynamics in relationships, must be effectively addressed.

HIV Behavioral Counseling and Testing

The availability and effectiveness of new prevention technologies and treatment options for HIV/AIDS have increased the importance and benefits of routine HIV testing and counseling.[25] HIV behavioral counseling and testing (BCT) involves access to an array of medical, preventive, psychosocial, and referral services.[26] Almost 11% of HIV infections in the U.S. are transmitted by undiagnosed HIV-positive individuals,[27] and up to 25% of HIV-positive people do not know their serostatus. Education and early detection help to facilitate early treatment and changes in high-risk behaviors.[28] Data suggest that HIV-infected individuals who are aware of their serostatus are more likely to adopt risk-reduction behaviors than those who do not have this knowledge.[29]

BCT is important both for individuals with HIV and those at risk of contracting HIV. Counseling should occur before and after HIV testing with the purpose of encouraging behavioral changes, and should include a risk reduction plan for alcohol and drug use as well as risky sexual behaviors to avoid infection and/or transmission of the virus. Though it often follows HIV-positive diagnoses, counseling should also be offered to those with an HIV-negative diagnosis. Counseling assesses an individual's HIV risk while identifying and implementing strategies for risk reduction.

BCT providers should tailor programs to their clients' needs, provide an explanation of HIV and STD infection, the testing process, confidentiality, and the meaning of a positive or negative test result, as well as refer patients to medical care or substance abuse treatment if needed. Community-level interventions with local input on the design and implementation of programs are necessary. Studies have shown that BCT has beneficially changed the behavior of HIV-positive individuals, but has been less

successful in reducing the risky behavior of HIV-negative individuals.[15] While sustained reductions in high-risk behavior have proven difficult over the long term, behavior change interventions have been associated with a decrease in HIV incidence.[30] The effectiveness of most HIV prevention technologies depends on patient behavior and adherence; thus, research is needed to learn how to better tailor BCT to the needs of specific populations in order to alter high-risk behaviors.

New approaches and technologies for HIV testing are also needed. For example, health professionals use the number of CD4 cells present in the blood to evaluate when an HIV-infected individual should begin treatment with ARVs.[31] Conducting this test requires sophisticated lab equipment that many communities lack. A portable, inexpensive device to confirm an HIV diagnosis is currently in development. Such a device would allow health care providers to conduct these tests in underserved areas and could be used to yield accurate test results within minutes, aiding all those who now must wait a critical number of days, if not weeks, before learning whether they should be receiving ARV treatment. Rapid testing of pregnant women and provision of ARV therapy would also further reduce mother-to-child transmission of HIV worldwide.

Prevention Technologies

Barrier Methods

Male Condoms

Male condoms are currently the most effective available means of preventing HIV transmission. Research has demonstrated that most latex and polyurethane condoms cannot be penetrated by particles the size of HIV; in contrast, lambskin condoms have pores large enough for HIV to pass through. Studies have shown that latex condoms, when used consistently and correctly, can reduce the risk of sexually transmitted infections (STIs), including HIV, by 90–96%.[32,33,34] For HIV-positive individuals, condom use during sexual intercourse is still an important preventive measure, both to avoid onward transmission and prevent further infection with other strains of HIV, which could increase the severity of their condition.[33]

Condoms are relatively inexpensive, are sold without a prescription, and have no side effects. Due to their effectiveness and the number of educational campaigns aimed at promoting their use, condoms as a means of preventing HIV have risen in popularity in many parts of the world. Male condom sales have increased dramatically across the globe as a result of successful social marketing campaigns.[33] Free condom distribution programs have also increased their availability and use. Condoms have played an important role in decreasing prevalence of HIV/AIDS in high-risk populations, such as sex workers and their clients.[35]

However, male condoms are not well accepted by some populations. In the U.S., condom use has been difficult to sustain among men who have sex with men (MSM), with a less than 75% usage rate, depending on whether a partner has HIV.[36] Obstacles that impede the use of condoms include social and cultural stigma, religious beliefs, unequal power dynamics between sexual partners, lack of awareness of condoms' effectiveness, personal reluctance, quality, and availability.[33] Strategies to combat these barriers include persuading people to reframe their attitudes and behaviors regarding condoms; ensuring widespread condom distribution and use; promoting condom use as responsible, acceptable, and health promoting; and providing easier access to condoms through price reductions or free distribution.[33]

Female Condoms

HIV continues to spread at an alarming rate among women, who account for 50% of HIV cases worldwide.[37,38] In the developing world, lack of economic, social, or cultural empowerment for women can impede access to currently available HIV prevention strategies. The female condom is one method that can be initiated by women and can lead to an increased sense of empowerment;[29] it can also serve as an alternative barrier method for intercourse among MSM, though further studies are needed to evaluate efficacy.[39] It provides protection against most STIs including HIV, and is sold without a prescription. The female condom is made of a material that is stronger than latex, is odorless, causes no allergic reactions, and can be safely used with both oil-based and water-based lubricants. Inserted prior to intercourse, it usually neither hinders male erection nor requires immediate withdrawal after ejaculation.[40] A new formulation of the female condom has made it easier to use and less expensive.

Although the female condom is widely accepted[41] and represents a significant advance in female-initiated protection, significant impediments exist to its widespread utilization, including conspicuous appearance, insertion

difficulties, the possibility of reduced sensation, reluctance of male partners, imbalances in relationships in many countries, and cost.[42,43] Campaigns addressing enhanced access to and education about female condoms, as well as recent reductions in cost, will help to increase its use.

Cervical Barriers

Diaphragms and cervical caps are soft latex or silicone cups that fit at the anterior end of the female genital tract to cover the cervix. These barriers can be inserted before intercourse and remain in the body for several hours.

Cervical interventions aim to fortify the cervix, which, due to its thinness, is the preferential infection site for many STIs, including HIV.[44] Compared to the vaginal mucosa composed of stratified squamous epithelium, which is more than thirty cell layers thick, the endocervical mucosa of the cervix is covered by only a single layer of columnar epithelial cells.[45]

Although cervical barriers have been approved for contraceptive use around the world, their distribution has been limited and usage rates have been low compared to those of other contraceptive methods.[46] Clinical trials have demonstrated that cervical barriers alone do not prevent HIV infection, but these devices have significant potential for improving topical delivery of microbicides and may prove in the future to play an important role in increasing the overall efficacy of microbicides.[47]

Male Circumcision

Research provides compelling evidence that male circumcision prevents the transmission of HIV/AIDS in heterosexual populations,[48] reducing HIV infection by 50-60%.[49] The WHO and UNAIDS have concluded that male circumcision should be actively promoted as part of comprehensive global HIV prevention efforts.[50]

Several studies have demonstrated a correlation between male circumcision and decreased rates of HIV infection among heterosexual males,[51] with results from recent randomized controlled trials in Africa confirming this relationship.[52] Studies conducted in Kenya and Uganda demonstrated a 53% and 48% reduction, respectively, in heterosexually acquired HIV infection in circumcised men.[53,54] While statistics have been inconclusive thus far on the efficacy of circumcising MSM to prevent infection,[55] the procedure may be worthwhile for MSM, especially those who concurrently engage in sex with women.[56] Furthermore, in the U.S., 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 ulcer.[57] Circumcision may also help protect women from contracting HPV (and thus help prevent cervical cancer): a study conducted in Uganda in 2005-6 found that circumcision reduced HPV incidence among the female long-term partners of study participants by 77%.[58]

Recent studies suggest that male circumcision is a cost-effective, enduring, and proven strategy to prevent HIV in high-prevalence areas.

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 HIV.[59] However, another study conducted in Uganda revealed that sexual activity among HIV-positive men after circumcision (prior to complete healing) may have led to an increased risk of HIV transmission to their wives.[60] It is recommended that HIV-positive men abstain from sex for 6 to 8 weeks following circumcision until proper healing occurs.

A recent study suggests that male circumcision is a cost-effective, enduring, and proven strategy to prevent HIV in high-prevalence areas.[17] Additionally, 13 studies conducted across nine sub-Saharan countries demonstrated that attitudes toward the procedure were consistently positive among both men and women.[61]

As with other prevention technologies, considerations of access and cost, as well as cultural, ethical, and religious factors, can hinder the widespread implementation of male circumcision as an intervention. Educational campaigns are needed to increase awareness about the benefits of male circumcision, conducting the procedure in infants, adequately training local health care workers in its administration, and diminishing cultural barriers to the procedure. Research on strategies to promote the continued use of other prevention approaches, including condoms, among circumcised men are also needed.

Treatment of Sexually Transmitted Infections

The U.S. has one of the highest rates of STIs among all developed countries.[62] Studies have shown that STIs, including those that are asymptomatic, increase susceptibility to HIV infection two- to five-fold.[63,64,65] Herpes, for example, causes genital ulcers that function as entry points for HIV, while inflammation caused by other STIs increases the number of cells that HIV targets in genital secretions.[66] STIs also lead to higher HIV loads in the genital secretions of HIV-positive individuals, thereby increasing the chance of infecting their sexual partners.[44]

When STIs are treated, these risk factors can be eliminated. However, there are certain limitations. Studies have shown that the success of STI treatment as an HIV prevention strategy depends on the stage of infection when treatment is administered, with treatment effectiveness decreasing over time as HIV becomes more established.[67] Uncircumcised and HIV-positive men typically require a longer course of treatment and do not respond as well to antibiotic therapy for STIs.[68]

Since STI treatment does not require a sexual partner's consent, it is a particularly valuable tool for women in unequal sexual partnerships. Furthermore, the recent development of a vaccine to prevent HPV infection in women, recently found to be effective for men as well,[69] represents an important STI prevention tool and a step forward in reducing vulnerability to HIV. Increased access to STI diagnosis, therapy, and prevention services can help decrease the spread of HIV and promote sexual health more generally.

Microbicides

Microbicides are virus- and bacteria-killing compounds formulated as gels, creams, films, or suppositories and applied inside the vagina or rectum to protect against STIs, including HIV.[70] These compounds are currently in various stages of development and must be safe, effective, easy to use, and affordable to be considered for widespread use.

Microbicides are a prevention priority because they can be used without the cooperation, consent, or knowledge of a partner. A safe and effective vaginal microbicide would be an important defense for women. Rectal microbicides could also help prevent HIV transmission via receptive anal intercourse for both men who have sex with men and heterosexual women.[71] Studies suggest that the risk of becoming infected from unprotected anal sex is greater than from unprotected vaginal sex, in part because the rectal lining is more fragile than vaginal mucosa, making it easier for the HIV virus to permeate tissue.[72]

Research suggests that an effective microbicidal agent could have a significant impact on curbing the global HIV/AIDS epidemic. A study using epidemiological and economic models reported that if a microbicide with a 60% efficacy rate reached 20% of the at-risk population in 73 low-income countries, approximately 2.5 million HIV infections could be averted over a three-year period.[73,74]

Mathematical modeling studies have shown that a tenofovir-based microbicide gel could possibly prevent up to 1.3 million HIV infections and 800,000 deaths over the next 20 years in South Africa alone.

For the first time in the fight to control the global pandemic, and after two decades of research to develop a safe and effective microbicide, a significant breakthrough was achieved with the July 2010 announcement of the CAPRISA 004 trial results, which evaluated the effectiveness of a 1% tenofovir antiretroviral-based vaginal gel to prevent HIV infection.[75] In this study, the gel was used by 889 HIV-negative women living in two South African communities, one urban and the other rural, who were followed for two and a half years and directed to use the gel before and after sexual activity. The microbicide reduced HIV acquisition by approximately 39% overall, and among women who most regularly used the compound, by 54%.[75] The gel also reduced herpes (HSV-2) transmission by 51%.[76] The effectiveness of this microbicide, however, diminished over time, possibly due to a decline in the diligent use of the product by women in the study. This hypothesis is supported by the finding that participants who achieved higher concentrations of tenofovir in cervicovaginal fluid had lower rates of infection, pointing to the powerful influence of adherence on efficacy.[77] Mathematical modeling studies have shown that a tenofovir-based microbicide gel could possibly prevent up to 1.3 million HIV infections and 800,000 deaths over the next 20 years in South Africa alone.[50]

Improved microbicide products will become a "game changer" for women who wish to self-initiate HIV preven-

tion measures, especially in cases where there are significant barriers to successfully negotiating mutual monogamy or condom use with partners. [20,75] The tenofovir-based gel used in the CAPRISA study will require further evaluation to determine the safety, efficacy, and impact of broader utilization of this and other potential microbicide candidates. A larger clinical trial, VOICE, is currently under way to test daily use.[77] Higher ARV concentrations within the gel, as well as the addition of other ARVs to microbicide formulations, may also boost effectiveness. In 2011, the International Partnership for Microbicides will initiate trials testing vaginal rings containing dapivirine, while USAID will fund a project to develop rings containing tenofovir combined with a contraceptive.[50]

A recent study found that for the first time, a microbicidal gel containing tenofovir protected rectal tissue against HIV. However, significant gastrointestinal side effects were experienced by some of the study participants.[72] Additional research is needed on the development of safe and effective vaginal and rectal microbicide agents. Studies are also needed on the acceptability of and adherence to these products. Investments in the production and evaluation of and innovative marketing strategies for a new generation of microbicides are needed to fill an important HIV prevention gap.

Chemoprophylaxis, Including PrEP and PMTCT

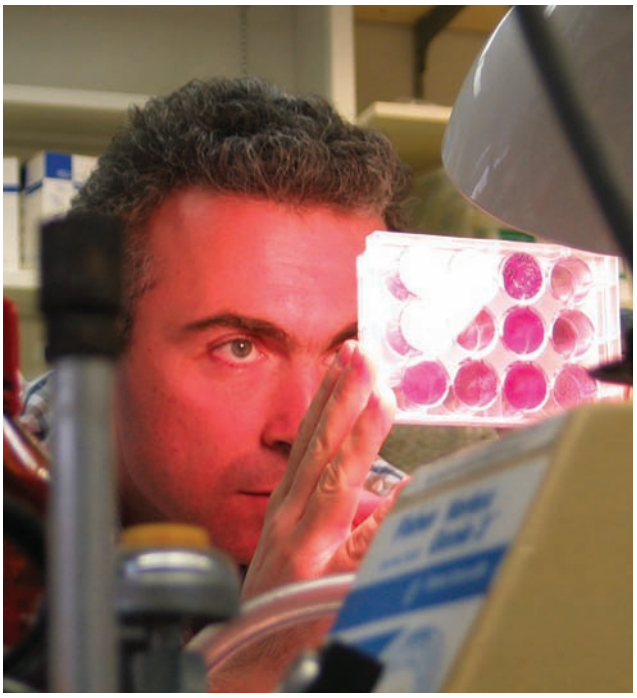
Chemoprophylaxis is the administration of antiretroviral therapies and other medications to prevent HIV infection. ARVs prevent HIV infection by disrupting various stages of viral replication, thereby interfering with the life cycle of HIV. Chemoprophylaxis may be used as an HIV prevention strategy for: 1) post-exposure prophylaxis (PEP) for individuals following a high-risk situation that could potentially result in HIV infection; 2) prevention of mother-to-child transmission (MTCT) during pregnancy, labor, and delivery; and 3) pre-exposure prophylaxis (PrEP) for individuals at high risk of contracting HIV.

PEP is a strategy that uses ARVs to reduce the risk of HIV after high-risk events, such as unprotected sex, rape, needle sticks, or the sharing of needles. When initiated promptly (within 72 hours of exposure) and administered for 28 days, PEP has been shown to reduce the risk of HIV infection by 80%.[78]

ARVs given to HIV-positive pregnant women for purposes of prevention of mother-to-child transmission (PMTCT) have proven extremely effective in preventing transmission of the virus to newborns. When women are treated with ARVs during pregnancy, labor, and delivery, the newborn is treated with ARVs, and delivery is performed via caesarian section, MTCT can be reduced to less than 2%, as has occurred in the United States.[64] Even when mothers begin ARVs during labor and delivery, the rate of MTCT can be reduced to 10% or less.[79] In 2010, UNITAID and UNICEF began implementing a "Mother-Baby Pack" program, which provides pregnant women with an "all-in-one" take-home package of drugs for before, during, and after delivery, as well as ARV medication for the infant to prevent HIV transmission for six weeks after delivery. The packages are designed for easy use and are in unmarked bags to avoid stigma within communities.[80] It is estimated that with sufficient funding, this drug delivery method could help reduce MTCT to 5% or less globally.[80] A recent study has shown that mothers who were continued on ARV treatment until breastfeeding was completed were 43% less likely to transmit HIV to their babies than women who stopped receiving therapy one week after delivery.[81] Intensified efforts to prevent MTCT could lead to an HIV-free generation in the years ahead.

Injection drug use accounts for about 10% of HIV infections worldwide, rising to 80% in some regions of the world such as Eastern Europe and Central Asia.[82] A 2010 study supported by the National Institute on Drug Abuse demonstrated that ARVs can decrease the spread of HIV among those with a history of injection drug use, as well as in the general population. The study found that increased levels of ARV use in the community corresponded with decreased viral load and fewer new HIV diagnoses on a population level.[99]

These important results about the effectiveness of chemoprophylaxsis led scientists to study whether ARV administration on a daily (PrEP) or intermittent basis (iPrEP) to high-risk populations would reduce the likelihood of acquiring HIV. PrEP had been found to reduce the transmission of a virus analogous to HIV in primate studies. In November 2010, the first definitive results of PrEP use in humans were released from the iPrEx study.[83] The study demonstrated an overall 43.8% efficacy rate for tenofovir and emtricitabine-based PrEP among gay men, transgender women who have sex with men, and other men who have sex with men in six



countries. Efficacy climbed to 92% among men in the study who had diligently adhered to the PrEP regimen, as determined by medication levels detected in their blood.[83]

In 2011, four other major clinical trials of PrEP are under way, including the Bangkok Tenofovir Study, Partners PrEP, FEM-PrEP, and VOICE (MTN 003). These studies are testing the safety and efficacy of tenofovir and a combination of tenofovir and emtricitabine in several countries. Results are expected in 2012 or 2013.[84] Preliminary analysis of a phase II clinical safety trial using tenofovir among MSM populations in the U.S. suggests that daily administration of the medication has no significant side effect safety issues to date.[85]

While PrEP, if proven to be safe and effective, has the potential to revolutionize HIV prevention with its use as a "prevention pill," widespread implementation will require further research and the establishment of evidence-based policies. Issues that must be addressed include: 1) evaluation of candidate drugs; 2) use in various populations, including women of childbearing age, adolescents, and MSM; 3) schedule of administration and dosage (continuous vs. intermittent); 4) cost; 5) health insurance reimbursement policies; 6) impact on sexual behavio; and 7) potential risk of developing drug resistance and other side effects of long-term use.[50]

Vaccines

Since the discovery of HIV in 1983, the development of a safe and effective vaccine has been a prevention priority. While significant advances in scientific knowledge about HIV have been made, the development of a suitable vaccine candidate has been particularly difficult due to challenges stemming from the virus' rapid mutation rate as it replicates, the differing strains found around the world, and the virus' ability to remain latent in cells.

A vaccine is a product that produces immunity, thereby protecting the body from disease. Vaccines can be administered orally, through needle injections, or by nasal sprays.[86] A successful HIV vaccine may need to induce both antibodies to broadly neutralize the virus and cytotoxic T lymphocytes to destroy HIV-infected cells. Vaccine candidates that primarily induce the latter are a particular focus of current research efforts. Such vaccines would not be expected to prevent infection; rather, they would control virus levels, reduce early destruction of CD4 helper T cells, delay disease progression, and reduce secondary transmission. Recent T-cell vaccines used in both the STEP and Phambili clinical trials unfortunately proved unsatisfactory in these large-scale efficacy studies.[87] The HIV Vaccine Trials Network (HVTN) 505 study is currently testing a new T-cell-based vaccine.[88]

While more than 80 clinical vaccine trials have been conducted to date without success, in December 2009, more than 25 years after the virus was identified, a study in Thailand revealed the first evidence of a vaccine providing any level of protection against HIV infection.[89] Researchers reported that a combination of two vaccines tested over a six-year period had a modest but statistically significant impact on protecting people from HIV infection. Though the study involved only a small sample size, the vaccine was the first to make any headway against HIV in humans and is providing valuable clues for future vaccine development (it should be noted that some experts have challenged the validity of the study's findings). Scientists are now exploring the mechanism by which this vaccine decreased infection risk, since it did not affect the level of virus in the blood of volunteers.

Another major discovery reported in July 2010 has rekindled hope for an effective vaccine. Scientists at the National Institute of Allergy and Infectious Diseases (NIAID) identified two antibodies that naturally occur in the blood of HIV-positive individuals. These antibodies neutralize more HIV strains with greater overall strength than previously known antibodies to the virus, marking a significant advance in HIV vaccine design research.[90] Additionally, computer modeling work in a separate May 2010 study has shed light on how white blood cells develop in some individuals who, when exposed to HIV, either progress slowly to AIDS or never develop the disease at all.[91] This study has significant implications for developing vaccines that might stimulate a similar response to HIV that individuals with "natural immunity" appear to have. The researchers found that an HIV-protective gene in these individuals results in more potent CD8 killer T cells that bind to HIV more effectively.[91] These promising results highlight the urgent need for intensified efforts, increased investments, and new approaches to vaccine development.

Public Health Strategies for HIV Prevention

Harm Reduction

Injection drug use accounts for 15.6% of HIV infections in the U.S. and an estimated 10% globally.[93] Notably, people who inject drugs are believed to constitute up to one-third of new HIV infections outside of sub-Saharan Africa.[92] In some regions of Eastern Europe and Central Asia, as many as 80% of HIV infections are linked to injection drug use.[93] The term "harm reduction" refers to public health programs that work to minimize the consequences of high-risk behaviors such as drug use and unsafe sex.[94] It uses a hybrid approach combining education, behavior change strategies, counseling, and syringe and needle exchange programs (SEPs/NEPs), which provide injection drug users (IDUs) with sterile syringes in exchange for used syringes at no cost.

SEPs provide a range of services. A survey found that 77% of these programs provided referrals to substance abuse treatment, 72% provided on-site voluntary counseling and HIV testing, and more than two-thirds provided supplies such as bleach to disinfect needles, alcohol pads, and male and female condoms. Many also provided screening for hepatitis and tuberculosis and offered on-site medical care to address wounds caused by frequent injections. Notably, many IDUs who use SEPs often informally provide information about health maintenance and risk reduction to other drug users outside the exchange program.[95] Since the mid 1980s, SEPs in conjunction with other harm reduction strategies have been associated with reductions of up to 80% in

risk behaviors and 30% in HIV incidence among IDUs in the U.S. and have been shown to be cost-effective.[96,97,98] Furthermore, studies have demonstrated that SEPs do not increase drug use[99] and help to keep communities and law enforcement personnel safe from contaminated syringes.[100]

Despite the success of SEPs, more than 8,000 new HIV infections still occur among IDUs in the U.S. every year, representing 16% of new infections and 24% of Americans living with HIV/AIDS.[101] Around the world, up to 20% of IDUs are HIV positive.[102] While the number of IDUs infected with HIV could be significantly reduced with increased usage of SEPs in conjunction with other prevention strategies, only 8% of IDUs worldwide receive HIV prevention services.[103]

Until recently, there was a ban on the use of federal funds for SEPs/NEPs in the U.S. even though states and localities have supported some of these programs in the past. On December 16, 2009, a significant legislative victory was achieved when the ban was removed. By July 7, 2010, the US Department of Health and Human Services released the interim guidance for state health departments interested in implementing SEPs with FY 2010 appropriated dollars as part of a comprehensive HIV prevention program.[104] While not guaranteeing an increase in funding for SEPs, the lifting of the ban ensures that federal money can now be provided to states and localities to support SEPs.[105] Federal funding for SEPs helps to increase the prevalence and acceptability of these programs, which would reduce the rate of new HIV infections among IDUs and their sexual partners and children.

As of January 2011, there are 211 SEPs in 32 states, the District of Columbia, the Commonwealth of Puerto Rico, and the Indian Nations.[106] One study found that 90% of IDUs who lived within a 10-block radius of an SEP participated in the program.[107] SEP attendance was also positively correlated with both safer injection and sexual practices.[107] IDUs who did not acquire syringes exclusively from SEPs or pharmacies were more than twice as likely to report high-risk behavior compared to those who did.[108]

"Test and Treat"

A new prevention concept termed "test and treat" focuses on diagnosing and treating people early in the course of a confirmed HIV infection. This strategy involves two steps: 1) promoting and providing annual, universal, and voluntary testing of all people aged 15 or older; and 2) immediately providing ART to those who test positive for HIV. In 2010, a mathematical model developed by the World Health Organization (WHO) demonstrated that global universal treatment with antiretroviral drugs could reduce HIV incidence and mortality to less than one case per thousand by 2016 while reducing the worldwide HIV prevalence rate to 1% in 50 years.[109] This model suggests that the test-and-treat strategy could move the AIDS epidemic from an endemic phase into an "elimination phase," in which most adults living with HIV are on ART, within five years of the program's implementation.[110] Furthermore, recent studies suggest that expanded ART utilization combined with increased access to HIV screening and counseling could reduce HIV incidence in the United States by 24% over the next 20 years.[111] Extending these efforts to include harm reduction strategies could add considerable additional benefit, with an estimated 65% reduction in the size of the epidemic in the U.S. within approximately 20 years of implementation.[111]

Some experts, however, suggest that this approach is unrealistic considering the low rates of testing worldwide, the high costs involved, and the wide range of epidemic settings. An additional concern is treatment adherence. In theory, an increase in the number of patients on ARVs worldwide, some of whom do not adhere to their regimen, could result in an elevated risk of drug resistance.

Furthermore, a British research team developed a model suggesting that the success of the "test and treat" program would be dependent upon the characteristics of local epidemics. In areas where concurrent sexual partners were frequent, new infections would be reduced by 85%, but not completely eliminated.[112] In this case, HIV could be reduced by 95% in most areas if 80% of the population were to be tested every three to four years; in "hyperendemic" regions, testing would be needed in 80% of the population every two to three years to achieve the WHO estimates for HIV reduction.[112]

Currently, the NIH is collaborating with the Washington, D.C., and New York City Health Departments on studies to determine the efficacy of an aggressive "test and treat" strategy on HIV infection rates in the U.S.[113] If the results from this research support WHO's predictions, the findings could have important implications for national policies, resulting in a bold new strategy to stop the spread of AIDS by routinely testing everyone in the community and promptly starting those who test positive on treatment.[113] The recent

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Treatment as Prevention

The "treatment as prevention" concept is gaining ground as an innovative public health approach, in light of recent findings that suggest a significant reduction in HIV transmission rates when an HIV-positive person takes ARVs, lowering their viral load and thereby decreasing the likelihood of transmitting HIV to others. The effectiveness of ART in reducing HIV transmission is estimated to be as high as 92%.[84] Among serodiscordant couples, a 2009 meta-analysis of cohort studies found that HIV transmission was 92% lower if the affected partner was taking ARVs.[84] A phase III clinical trial (HPTN 052), ongoing as of 2011, is directly examining the effect of ARV administration on HIV transmission rates in serodiscordant couples at sites in Africa, India, Brazil, and Thailand.[84] However, numerous challenges in implementing "treatment as prevention" programs exist. A recent review found that only 60% of individuals who were aware of their HIV status were linked to care.[84] Furthermore, the study found that among those who were offered ART, some did not accept treatment because of denial of their condition, worries about potential medication side effects, or concerns regarding stigma.[84]

Mapping Community Viral Load

To facilitate evaluation of the effectiveness of new approaches such as "treatment as prevention" and "test and treat," new methods are needed to determine whether these prevention strategies work and to highlight areas for improvement. While it has been proven that on an individual level, ART mediated virologic suppression reduces perinatal transmission and may reduce sexual transmission as well,[114] it remains uncertain whether increased HIV testing and widespread use of ARVs can actually decrease HIV incidence on a population level. In the 1990's, the introduction and expanded use of ARVs in some regions of the world was accompanied by a reduction in new HIV infections. For example, in Taiwan, the increased utilization of ARVs was matched by a 50% reduction in newly reported HIV cases.[115] However, in other areas, such as San Francisco, the success of ART may have led to complacency about the need for vigilant prevention interventions resulting in a rise in risky sexual behavior and an alarming increase in HIV incidence among MSM. Consequently, the San Francisco Public Health Department intensified its efforts to combat HIV infection by simplifying HIV testing procedures, increasing partner

notification, and providing linkages to care. A recent study found that these actions resulted in a decline in new HIV cases in the city from 2004 to 2008.[116]

Researchers in San Francisco have used surveillance and mapping techniques to chart community viral load (CVL) and assess HIV rates across the city. Total CVL is a measure of the potential infectiousness of a particular geographic population (neighborhood community), while mean CVL is an indicator of treatment effectiveness and transmission risk.[116] Mapping and comparing these numbers across specific populations can illuminate "hotspots" with particularly high HIV incidence, facilitating the targeting of interventions to populations at greatest risk. Such a mapping strategy also helps identify barriers to accessing care that may be based on gender, ethnicity, insurance coverage, and other factors. In this way, mapping CVL provides a window through which we can see the geographic and demographic face of the epidemic in communities, and provides important knowledge that can help eliminate structural barriers, improve services, and address other factors that may keep interventions from reaching individuals most at risk.[116]

Reductions in the mean and total CVL in San Francisco following comprehensive public health measures to increase HIV testing and ART use were consistent with apparent declines in HIV incidence and strongly associated with reductions in newly diagnosed HIV infections. This positive health outcome occurred despite a rise in rectal gonorrhea in the city suggesting that risky sexual behaviors had not diminished; rather, public health interventions to increase HIV testing and treatment had been the major factor in decreasing HIV infection rates in the city.[116] In this way, CVL can serve as a useful biomarker for the overall success of ART use in communities and for HIV prevention efforts. More research on such mapping and surveillance strategies is needed.

For maximum impact, HIV programs must include structural interventions aimed at changing the environment so that all populations can access HIV prevention and treatment services.

Structural Interventions

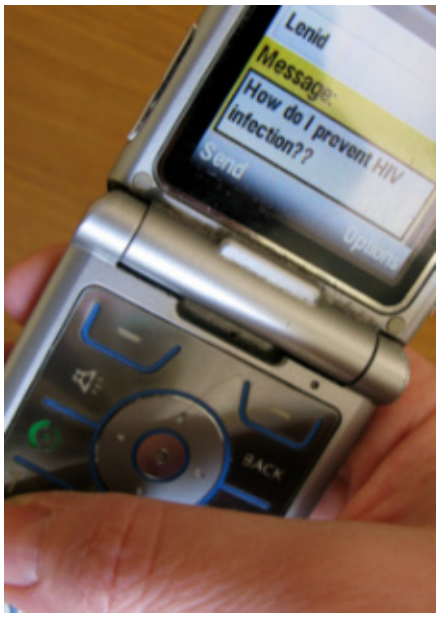
Most-at-risk-populations (MARPs), including men who have sex with men, sex workers, and injecting drug users, bear a disproportionately heavy burden of the HIV epidemic. Many governments codify prevailing hostility toward MARPs into law, effectively institutionalizing stigma and negative attitudes towards these vulnerable groups, isolating them, and impeding the delivery of HIV prevention and care services to the individuals who most need them.[117]

In Eastern Europe and Central Asia, where the HIV epidemic is primarily driven by drug use, nearly 60% of countries report having laws that limit drug users' access to HIV services.[117] Although sex work is a primary driver of the AIDS epidemic in Asia, more than 80% of countries in this region of the world have adopted legal frameworks that hinder sex workers' access to services.[117] Furthermore, although infections among MSM in Asia and the Caribbean are on the rise, approximately 60% of countries in these regions have discriminatory laws in place regarding MSM.[117] In fact, some 76 countries around the world—most of them developing nations—criminalize same-sex sexual behavior.[118] In many countries, criminal penalties for homosexual behavior are extremely severe, including five nations that permit the death penalty to be imposed.[119]

These structural barriers, attitudes, and social conditions undermine the overall response to HIV/AIDS. For maximum impact, HIV programs must include structural interventions aimed at changing the environment so that all populations can access HIV prevention and treatment services.[120] Laws should be revised to prohibit discrimination on the basis of membership in a marginalized group. Specifically, countries should repeal all laws that criminalize same-sex sexual behavior and impede HIV prevention interventions. Laws restricting access to essential health services should be removed, and policies affirming the human rights of vulnerable populations are urgently needed.

HIV Prevention 2.0

New media technologies and social marketing campaigns are being harnessed to empower people to make informed health decisions, to promote adherence to treatment, and to spread the word about HIV prevention strategies. With more than 5 billion mobile phones in use globally[121] and 2 billion Internet users worldwide,[122] new media with its wide



availability and instantaneous reach, can play a powerful role in mobilizing a prevention revolution. Increasingly, the mobile phone is the primary route for accessing the Internet. Recent studies conducted in South Africa and Mexico demonstrated that the use of new media increased patient participation in health services and adherence to medication.[123] These positive behavior changes can be attributed in part to increased connectivity between providers and their patients, as well as patient texting 'support groups' in some cases.

A 2010 review conducted in nine countries that evaluated 12 randomized clinical trials using text messaging in disease prevention efforts yielded promising results. The research found that text messaging was a cost-effective tool for achieving positive behavioral or clinical outcomes related to disease prevention and management.[124] The widespread integration of new media into prevention programs could benefit consumers, patients, researchers, and healthcare providers alike, and the progress seen thus far shows there is great promise in this emerging field. Additionally, the use of video and voice messages would expand the reach of HIV prevention efforts in areas of the world with low literacy rates. More research is needed to assess current and potential applications for reaching diverse population groups and to evaluate the impact of new media approaches on HIV education, prevention, and treatment outcomes. Mobile technology should also be further explored as a platform for conducting research in the U.S. and in the developing world.

Accelerating an HIV Prevention Revolution: Policy Recommendations

With more than two million new HIV infections occurring globally each year and 56,000 in the U.S. alone, prevention is essential to stemming the tide of the AIDS epidemic. However, no single prevention strategy by itself is sufficient; rather, a *combination* of interventions is needed including expanded access to lifesaving AIDS treatments. Now is the time for vision, innovation, commitment, and strategic direction to scale up proven interventions and to develop innovative new approaches to HIV prevention.

The following recommendations provide a roadmap for putting prevention into practice in the fight against HIV/AIDS:

Invest in Basic, Clinical, and Public Health Research

- Increase investments by government, foundations, and other donors in research on prevention technologies and behavioral approaches including PrEP, microbicides, vaccines, behavioral/educational interventions, and strategies that utilize a combination of approaches.
- Address the needs and circumstances of diverse populations (e.g., youth, MSM, IDUs, women, and communities of color) to maximize their participation in clinical trials of prevention technologies and behavior change strategies.
- Ensure that clinical trials of prevention technologies appropriately analyze data for any biological and psychosocial differences with respect to age, sex, and race/ethnicity.
- Ensure community engagement in and broad stakeholder support for the development and implementation of clinical trials.
- Support studies that evaluate the "test and treat" and "treatment as prevention" models for HIV prevention in the United States and globally; implement widely if found to be safe and effective.
- Establish systems for data-sharing and collaboration across institutions and countries.
- Conduct public health research, including implementation science, to promote innovation and strengthen current and future HIV prevention efforts.

- Develop new, highly accurate, rapid, and portable HIV testing methods.
- Evaluate multidisciplinary, combined prevention approaches for their effectiveness.

Implement Prevention Strategies

- Fully implement prevention recommendations in the National HIV/AIDS Strategy. Coordinate initiatives across Federal government agencies in partnership with the private sector, and develop new cross-cutting approaches.
- Implement prevention initiatives contained in the recent health care reform legislation, the *Patient Protection and Affordable Care Act*, including those that will ensure increased access to HIV testing, treatment, and prevention services.
- Support the implementation of evidence-based prevention technologies that include barrier methods (male and female condoms), male circumcision, harm reduction programs including SEPs, and STI treatment.
- Expand HIV/AIDS education and counseling programs to increase testing frequency and reduce high-risk behaviors.
- Make the lowering of HIV incidence in communities a prevention priority.
- Train health care personnel to implement HIV/AIDS prevention and testing strategies.
- Target preventive strategies to meet the needs of vulnerable populations including communities of color, MSM, women, IDUs, the economically disadvantaged, and incarcerated populations.
- Develop a toolbox of innovative and effective approaches to prevention to reduce new infections and change the course of the epidemic.

Eliminate Barriers to Accessing Prevention Services

- Ensure that prevention services are delivered at the scale necessary to reach all those who need them.
- Reduce legal barriers and policy restrictions to utilizing effective prevention services and new technologies.
- Make elimination of disparities in access to HIV prevention based on ethnicity, race, gender, sexual identity, and socioeconomic status a priority in policy and program development.
- Reduce stigma experienced by vulnerable populations in health care settings.
- Optimize state policies for implementation and utilization of syringe exchange programs.
- Work to ensure that Congress does not backtrack by reinstating the ban on use of Federal funds to support SEPs.
- Ensure that local and national prevention portfolios are closely informed by the HIV epidemic's profile so that programming reaches those populations that are most affected.
- Use innovative monitoring and evaluation strategies such as mapping of community viral load to better understand where structural barriers are greatest and what opportunities exist to ensure that HIV testing and care reach the most vulnerable populations.

Raise Awareness About the Power of Prevention

- Conduct national and global education campaigns on HIV/AIDS prevention to raise awareness, change attitudes and behaviors surrounding HIV, and decrease stigma.
- Increase policymaker and public awareness about the impact of ARV therapy on lowering HIV viral load in communities, which may reduce the likelihood of transmitting the virus.
- Use new media including text messaging and social marketing techniques to enhance prevention efforts.

Target Funding and Advance Evidence-Based Policies

- Provide national leadership to make prevention a priority in domestic and global programs.
- Increase Federal and private sector funding for prevention research and services in national and global HIV/AIDS programs through the NIH, CDC, PEPFAR, the Global Health Initiative, and contributions to the Global Fund to Fight AIDS, Tuberculosis and Malaria.

Direct resources to programs that can have the greatest impact at the international, federal, state and local levels.

- Establish a National Task Force on HIV Prevention to engage leaders from the government, NGOs, health care, business, and civil society to accelerate an HIV prevention revolution in the United States. Link its work to the newly established UNAIDS Commission on Global HIV Prevention.
- Support demonstration projects in the U.S. and globally to follow up on the promising efficacy results of PrEP. Such projects should investigate questions important to effective use of PrEP including adherence, behavior change, cost-effectiveness, and approaches to delivering PrEP as part of a package of preventive interventions.
- Support structural level interventions to foster HIV prevention efforts by ensuring that policies are evidenced-based and designed to engage organizations, systems, government, the media, and social networks.
- Reform or repeal laws that criminalize same-sex sexual behavior, and protect human rights, which is essential to ensuring access to testing, care, and treatment.
- Direct Federal funding towards domestic and international programs that scale up the implementation of prevention technologies and interventions targeting high-risk groups.
- Engage a broad spectrum of stakeholders worldwide in the development and implementation of prevention clinical trials and service delivery programs.
- Create a collaborative system of advocacy for prevention, research, treatment, and health systems strengthening to ensure that the response to AIDS remains an urgent priority.

Summary

Since the first case of HIV was reported in 1981, scientists have made significant strides in the prevention and treatment of HIV/AIDS. Yet much more remains to be done. Advances in the treatment of HIV/AIDS have made a lifesaving difference, but prevention of the disease is the ultimate goal. This issue brief has reviewed the scientific evidence about currently available prevention technologies and behavioral interventions and has examined the potential of several new approaches that are under development. It underscores the fact that we are on a path to making AIDS history.

Benjamin Franklin once said, “An ounce of prevention is worth a pound of cure.” While Mr. Franklin was referring to fighting fires, his words remind us of the urgency with which we must fight the HIV/AIDS epidemic using a combination of evidenced-based prevention technologies, behavioral approaches, and public health strategies while expanding provision of comprehensive AIDS treatment programs in communities worldwide. These strategies must target the needs of diverse populations with attention to gender, age, and community and cultural issues. Recent research advances demonstrating the effectiveness of new HIV prevention technologies suggest that we are in the midst of a prevention revolution to accelerate progress in eradicating the HIV/AIDS epidemic. If the spread of HIV/AIDS in America and globally is to be halted, critical actions are needed including increasing investments in HIV prevention programs and research, a multidisciplinary, innovative approach, broad stakeholder and community involvement, removing barriers to care, committing adequate resources, and scaling up effective, evidence-based programs. The bottom line: prevention saves lives, averts suffering, is cost-effective, and, in the future, may lead to a world without AIDS.

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