
NEW APPROACHES TO HIV PREVENTION

ACCELERATING RESEARCH AND
ENSURING FUTURE ACCESS

EXECUTIVE SUMMARY

GLOBAL HIV PREVENTION WORKING GROUP

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ABOUT THE GLOBAL HIV PREVENTION WORKING GROUP

The Global HIV Prevention Working Group is a panel of 50 leading public health experts, clinicians, biomedical and behavioral researchers, and people affected by HIV/AIDS, convened by the Bill & Melinda Gates Foundation and the Henry J. Kaiser Family Foundation. The Working Group seeks to inform global policy-making, program planning, and donor decisions on HIV prevention, and to advocate for a comprehensive response to HIV/AIDS that integrates prevention, treatment, and care. Working Group publications are available at www.gatesfoundation.org and www.kff.org.

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NEW APPROACHES TO HIV PREVENTION

ACCELERATING RESEARCH AND ENSURING FUTURE ACCESS

ABOUT THIS REPORT

A growing number of promising new HIV prevention approaches are in the late stages of clinical research, and have the potential to dramatically reduce the burden of HIV/AIDS around the world. Research on some of these approaches, such as male circumcision and diaphragms, could show results within the next two years.

But there are serious obstacles that could significantly delay, or even derail, critical prevention trials—including inadequate resources and capacity to launch and complete trials, and emerging ethical concerns. Moreover, the world is unprepared to capitalize on the potential success of prevention research currently underway. Very little has been done to mobilize resources and develop the public health guidance, provider training, and public education needed to ensure rapid implementation of new prevention methods.

This executive summary of a new report by the Global HIV Prevention Working Group, *New Approaches to HIV Prevention: Accelerating Research and Ensuring Future Access*, summarizes the state of HIV prevention research, and makes recommendations to speed research on promising new HIV prevention methods, and ensure rapid access to new tools and strategies as soon as they are proven effective.

The full report is available at www.gatesfoundation.org, www.kff.org, and www.care.org.

Twenty-five years into the global HIV/AIDS epidemic, HIV infection rates are alarmingly high, and more than 4 million people become infected every year. Despite the proven effectiveness of existing prevention approaches, fewer than one in five people at high risk for HIV have access, and current prevention approaches are not practical for everyone, especially women. New approaches to HIV prevention are urgently needed.

This Global HIV Prevention Working Group report addresses three critical areas:

1. HIV Prevention Research: State of the Science

A wide range of promising new HIV prevention approaches are being tested in clinical trials, including male circumcision, cervical barriers, pre-exposure prophylaxis with antiretroviral drugs, herpes suppression, microbicides, and HIV vaccines. The results of some of these studies could be available within the next two years.

2. Accelerating HIV Prevention Research

Prevention research faces serious challenges that could delay the completion of critical trials, or prevent planned trials from moving forward—including a lack of adequate research infrastructure in developing countries, limited resources, emerging ethical concerns, and inadequate community engagement.

3. Preparing for Access

Despite the fact that some new HIV prevention methods could be shown to be effective in the near future, virtually no planning or resources have been dedicated to

ensuring future access to new prevention approaches. Key implementation issues that must be addressed immediately include ensuring adequate resources, developing public health guidelines, providing health care worker training, and ensuring that risk behavior does not inadvertently increase with the introduction of new prevention methods.

Unless the world acts now to accelerate HIV prevention research and prepare for implementation of effective new approaches, we risk letting new prevention methods sit idle while 4 million people become infected every year. Averting that fate is the goal of this report, and should be a top priority in the fight against HIV/AIDS.

No “Magic Bullet” for HIV

There is no “magic bullet” for HIV prevention. None of the new prevention methods currently being tested is likely to be 100 percent effective, and all will need to be used in combination with existing approaches if they are to reduce the global burden of HIV/AIDS.

As research proceeds on new HIV prevention approaches, it is critical to expand access to existing prevention methods, including behavior change programs, condoms, HIV testing, and treatment for other sexually transmitted diseases. Greater access to existing HIV prevention tools could avert half of the new infections projected to occur over the next decade. For a detailed discussion, see the Working Group’s 2003 report, *Access to HIV Prevention: Closing the Gap*.

I. HIV PREVENTION RESEARCH: STATE OF THE SCIENCE

A wide range of promising HIV prevention approaches are in late-stage clinical trials:

► **Male circumcision:** Researchers have long observed that countries with higher rates of male circumcision have lower rates of HIV infection. In 2005, the first randomized efficacy trial of male circumcision for HIV prevention, conducted in South Africa, showed that circumcised men were 60 percent less likely than uncircumcised men to become infected with HIV from female partners.

Three additional efficacy trials of male circumcision are underway in Kenya and Uganda, to assess the applicability of the South African findings in other settings and populations, and to determine if male circumcision also reduces the risk of HIV transmission from men to their female partners. Results are expected in 2007.

► **Cervical barriers:** Researchers hypothesize that cervical barriers such as diaphragms, which are currently used for contraception, may help protect women from HIV and other sexually transmitted diseases. An efficacy trial of the diaphragm for HIV prevention is nearing completion in South Africa and Zimbabwe, and results are expected in 2007.

► **Pre-exposure prophylaxis with antiretrovirals:** Research in animals suggests that antiretroviral drugs used for HIV treatment may also be effective at preventing infection in HIV-uninfected adults, an approach called pre-exposure prophylaxis, or **PREP**. Efficacy trials of this approach are underway in Botswana, Peru, and Thailand. Results could be available as early as 2007 or 2008.

► **Herpes suppression:** Herpes, which infects up to 70 percent of people in some parts of sub-Saharan Africa, can triple the risk of HIV acquisition, as well as increase the risk of transmission to others. The inexpensive, off-patent drug acyclovir is approved for herpes suppression, and two trials are being conducted in Africa, Latin America, and the U.S. to test the efficacy of suppressing herpes to lower HIV risk. Results are expected in 2007 and 2008.

► **Microbicides:** Microbicides are topical substances, such as gels or creams, that could be applied to the vagina or rectum to reduce HIV transmission. Five first-generation vaginal microbicide candidates are currently in late-stage clinical trials; results from some of these trials could be available by 2008. In addition, a number of second-generation microbicide candidates—which specifically target HIV or molecules of the cells it infects—are in earlier stages of research, and could complete clinical trials within 10 years.

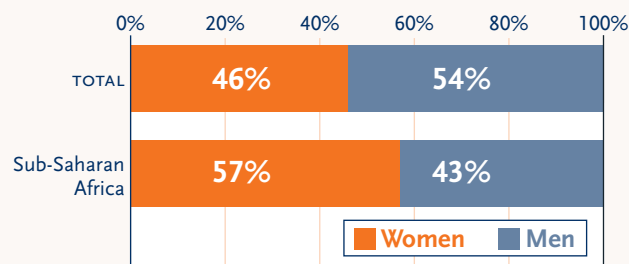
► **HIV vaccines:** The best long-term hope for HIV prevention is a vaccine, although developing an effective vaccine has proven to be a highly complex scientific challenge. Most experts predict that it could be 10 years or more before an HIV vaccine candidate is shown to be effective. An effective vaccine will likely need to stimulate two types of immune response, although most of the vaccine candidates developed to date are designed to target only one arm of the immune system. Currently, 30 HIV vaccine candidates are in clinical trials, including two in advanced efficacy or proof-of-concept trials.

WOMEN, HIV, AND NEW PREVENTION METHODS

Many of the new HIV prevention methods in development could be particularly beneficial for women, who account for roughly one-half of people living with HIV globally. For many women, current prevention methods are inadequate—women often do not have the social or economic power to refuse sex or negotiate condom use.

New tools such as cervical barriers, pre-exposure prophylaxis, and microbicides may provide women with HIV prevention methods that they could initiate—potentially without the knowledge or consent of their partners.

People Living with HIV/AIDS, by Gender, 2005



Source: UNAIDS

CURRENT EFFICACY TRIALS OF NEW HIV PREVENTION METHODS

Prevention Method	Trial Sites and Participants	Primary Sponsors and Funders
Male Circumcision	Kenya—2,500 men	University of Illinois, U.S. National Institutes of Health (NIH)
	Uganda—5,000 men	Johns Hopkins University, NIH
	Uganda—1,361 men and 7,000 women	Columbia University, Gates Foundation
Cervical Barriers Female diaphragms	South Africa and Zimbabwe—5,045 women	University of California at San Francisco, Gates Foundation
Pre-Exposure Prophylaxis with Antiretrovirals		
Tenofovir	Thailand—1,600 injection drug users	U.S. Centers for Disease Control and Prevention (CDC)
Tenofovir plus emtricitabine	Botswana—1,200 men and women	CDC
	Peru—1,400 men who have sex with men	NIH
Herpes Suppression	Peru, South Africa, Zambia, Zimbabwe, and U.S.—3,277 men and women	University of Washington, NIH
	Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, and Zambia—3,000 male-female couples in which one partner is also HIV-infected	University of Washington, Gates Foundation
Microbicides		
C31G (Savvy)	Nigeria—2,142 women	Family Health International (FHI), U.S. Agency for International Development (USAID)
Carbopol 974p (BufferGel)	Malawi, South Africa, Tanzania, Zambia, Zimbabwe, and U.S.—3,220 women	NIH
Cellulose sulfate	Nigeria—2,160 women	FHI, USAID
	Benin, Burkina Faso, India, South Africa, and Uganda—2,574 women	CONRAD, Gates Foundation, USAID
Naphthalene sulfonate (PRO2000)	Same as Carbopol trial (see above)	NIH
	South Africa, Tanzania, Uganda, Zambia, and Zimbabwe—10,000 women	U.K. Medical Research Council, U.K. Department for International Development
PC-515 (Carraguard)	South Africa—6,299 women	Population Council, Gates Foundation, USAID
HIV Vaccines		
<i>gag, pol, nef</i> in adenovirus type 5 (MrkAd5)	Australia, Brazil, Canada, Dominican Republic, Haiti, Jamaica, Peru, and U.S.—3,000 men and women	Merck & Co., NIH
<i>env, gag, pol</i> in canarypox + gp120 (ALVAC + AIDSVAX)	Thailand—16,000 men and women	Thailand Ministry of Public Health, NIH, U.S. Military HIV Research Program

2. ACCELERATING HIV PREVENTION RESEARCH

As new HIV prevention approaches move forward into advanced stages of development, the world faces serious financial, logistical, and ethical challenges in completing ongoing prevention trials, and in mounting the additional large-scale trials that will be needed to fully test new prevention tools and strategies. Key challenges—and recommendations from the Global HIV Prevention Working Group—include:

- ▶ **Clinical trials capacity:** Current efficacy trials of new HIV prevention approaches will require a total of approximately 80,000 study participants. Even more participants will be needed to mount additional efficacy studies and to conduct confirmatory trials. Yet current global clinical trials capacity—including an adequate number of participants, properly equipped study sites, and trained research staff—falls far short of the need. **Recommendations:** Trial sponsors, national governments, and international donors should make significant new investments in global capacity for HIV prevention trials. Agencies should work together to inventory existing capacity, determine specific needs in key regions, and identify sites for scaling up capacity. Given limited capacity, trial sponsors should better coordinate decision-making about which prevention interventions to prioritize for large-scale trials, and share trial sites as necessary.
- ▶ **Ethical issues:** While current HIV prevention trials are being conducted according to internationally and locally accepted ethical standards, existing guidelines do not sufficiently address some key issues that have emerged in recent years. These include defining the standard set of existing prevention methods that

should be provided to all trial participants; defining and ensuring fully informed consent; and determining how to facilitate HIV treatment access for participants who become HIV-infected during the course of a trial, or who are found to be HIV-infected at the initial screening for a trial.

Recommendations: Key stakeholders in HIV prevention research—including trial sponsors, affected communities, and developing country governments—should work with UNAIDS and the World Health Organization (WHO) to convene a broadly inclusive panel of experts to develop updated ethical guidelines for conducting HIV prevention research. This guidance should be continually revised as HIV prevention research evolves.

- ▶ **Community engagement:** Community involvement and support are vital to successful clinical research. Yet some HIV prevention trials have been criticized for not properly reaching out to communities. In some cases, misinformation and lack of communication between researchers and communities have been factors in the cancellation of HIV prevention trials.

Recommendations: Investigators and sponsors of HIV prevention trials should foster strong partnerships with the communities where trials are conducted—through Community Advisory Boards, regular communications to the broader community, and involvement of key local and national officials. Community input should inform key aspects of the clinical research process, including development of trial protocols, recruitment of participants, and ongoing trial oversight. International agencies such as UNAIDS and WHO should compile and publish best practices in community engagement.



3. PREPARING FOR ACCESS

As soon as they are shown to be effective, new HIV prevention methods should be made accessible and affordable for people at risk. But the world is virtually unprepared to ensure rapid access. Key challenges and recommendations include:

► **Resources:** While there have been significant increases in global spending to fight the HIV/AIDS epidemic in recent years, there are still severe resource gaps. UNAIDS estimates that \$11.4 billion will be needed annually for HIV prevention by 2008—two-and-a-half times current spending. Ensuring timely, widespread access to new prevention methods will require significant additional resources. Many countries will need donor assistance to purchase new prevention tools such as pre-exposure prophylaxis, microbicides, and vaccines. New resources will also be needed to support provider training and community education programs, to ensure that new prevention methods are safely and properly implemented.

Recommendations: *The international community—including major donors such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria, and the U.S. government's President's Emergency Plan for AIDS Relief—should commit to providing the resources necessary to ensure the roll-out of new HIV prevention tools as soon as they are shown to be effective. It is critical to begin now to estimate the resources that will be needed to implement new prevention methods. It is also vital that these resources do not take funding away from current HIV prevention, treatment, and care programs.*

► **Public health guidance:** As results become available from clinical trials, national and global decision-makers will need to carefully determine how to integrate new HIV prevention methods into health programs. In the case of new technologies such as microbicides and HIV vaccines, regulatory review and licensure will be required as well. Yet there are significant gaps in global capacity to provide timely public health guidance and regulatory review for new HIV prevention interventions.

Recommendations: *Key stakeholders in HIV prevention—including national governments, donors, and international agencies such as UNAIDS and WHO—should establish systems to anticipate and provide needed guidance on the introduction of new prevention methods. Key issues include developing formal public health guidance on the proper use*

of new prevention approaches, and developing tools to help decision-makers in developing countries assess the relative cost and benefit of new prevention interventions. In addition, regulatory agencies in the U.S. and Europe should provide assistance to their counterparts in developing countries on evaluating new prevention methods.

► **Provider training:** Health care professionals and community health providers will require training in the safe and proper use of new HIV prevention methods. For example, in many developing countries, few health care providers have experience in circumcising adult males, and if the procedure is improperly performed it can result in serious injury or death. The problem of health worker training is compounded by the fact that many developing countries suffer acute shortages of qualified health care personnel in general.

Recommendations: *International agencies such as UNAIDS and WHO should develop regional and country-level provider training programs to help promote the safe and proper use of new HIV prevention methods. Where possible, training in providing new HIV prevention methods should be integrated into ongoing health provider training programs, and traditional healers should be included in these programs.*

► **Preventing “disinhibition”:** It is essential that the introduction of new prevention methods does not lead people to become complacent about HIV risk behavior. Such behavioral disinhibition could cancel out the benefits of new HIV prevention methods, and lead to an inadvertent increase in HIV infections.

Recommendations: *Strong communications and public education campaigns, grounded in scientific evidence of effectiveness, should accompany the introduction of new prevention methods, to reinforce the importance of minimizing risk behavior and using new prevention methods in combination with existing tools and strategies. It is also critical to monitor and evaluate efforts to counter potential disinhibition on an ongoing basis to ensure they are effective.*

