



FEM-PrEP

Trial Update

Pre-Exposure Prophylaxis for HIV

Putting HIV in its Place in Pretoria

FEM-PrEP scientists use an innovative strategy to recruit participants

A few years ago, the massive metropolis that includes Pretoria, South Africa, was renamed *Tshwane*—a word that means, “we are the same,” according to city officials. The name change, and even the meaning of the word *Tshwane*, are controversial subjects in South Africa. What remains uncontroversial is that the HIV epidemic has not affected the two million residents of Tshwane in the same way.

For various reasons, the virus has affected some communities more than others. The FEM-PrEP researchers need to identify these communities because an HIV-prevention trial can only be effective in places where there is a high incidence of HIV. In other words, the women who volunteer for the trial must be at “higher risk” of acquiring the virus.

Finding and recruiting these women is often a significant challenge for HIV-prevention trials. However, FEM-PrEP’s socio-behavioral and community (SBC) team is taking a novel approach to recruiting participants for the clinical trial. “The approach combines a method called *Priorities for Local AIDS Control Efforts* (PLACE) with computer-based mapping strategies to identify promising recruitment areas to focus recruitment efforts,” says Amy Corneli, the SBC principal investigator.

The PLACE method was originally developed to improve the reach of AIDS-prevention programs. The SBC researchers are using modified PLACE questionnaires to interview members of the community, asking them about the places where people go to meet potential sex partners. The researchers visit these places—*shebeens* (informal taverns), guesthouses, and even bushes by the side of the road—where they talk to the people who go there to socialize.

Business owners are asked about the clientele and about the busiest times at the establishment. The interviewers also collect information from the patrons about their alcohol consumption, sexual practices, and risky behaviors.

Local research staff based at the Setshaba Research Centre conduct these interviews. Among them is Dimakatso Molete, who has extensive knowledge of the social networks in the area. Molete, who is known as *Aus Maki*, has conducted hundreds of interviews with establishment owners and patrons. It’s a task that has its challenges.

“Establishment owners are difficult to get in touch with,” says Aus Maki. “This takes much of our time as we may visit the place several times before we can find them. At first, their staff are suspicious of people they do not know,” she says.

(continued on page 4)



Stella Kirkendall/FHI

Interviewers, Dimakatso Molete and Ross Malamatsho, use a global positioning system device to map the coordinates of a recruitment area.



USAID
FROM THE AMERICAN PEOPLE



Issue No. 2 July 2009



Lut Van Damme/FHI

Lut Van Damme, clinical principal investigator of FEM-PrEP.

FEM-PrEP Trial Background

What is the FEM-PrEP Clinical Trial?

The FEM-PrEP (pre-exposure prophylaxis) clinical trial—led by Family Health International—is designed to test the safety and effectiveness of a daily oral dose of a pill called Truvada for HIV prevention.

Truvada combines two antiretroviral drugs—emtricitabine and tenofovir disoproxil fumarate—into a single pill that is taken once a day. Truvada prevents HIV from reproducing itself inside the cells of people already infected with the virus, and it has been proven safe and effective as a *treatment* for HIV-positive people. But it's not clear whether Truvada could also help to *prevent* an infection in an HIV-negative person who is exposed to the virus. Another key objective of the trial is to determine whether Truvada is safely tolerated by HIV-negative women.

Nearly 3,900 HIV-negative women (between the ages of 18 and 35)—who have a higher risk of becoming infected with the virus—will be enrolled in the clinical trial. The trial will take place at six different sites in five countries: Bondo (Kenya), Arusha/Moshi (Tanzania), Blantyre (Malawi), Lilongwe (Malawi), Pretoria (South Africa), and Mazabuka (Zambia).

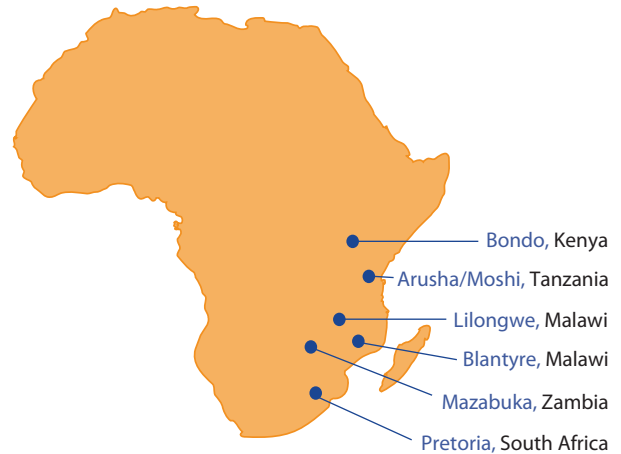
Behavioral Research and Community Engagement

The FEM-PrEP team consists of socio-behavioral and community (SBC) experts who engage local community members and collect behavioral data prior to and during the clinical trial to facilitate its success. The data we gather will help us to recruit and retain participants and to counsel them on contraception, HIV-risk reduction, and adherence to the study pill.

Other activities include working closely with the community to:

- Build partnerships with community representatives and other key stakeholders
- Increase capacity for research practices and research ethics
- Establish trust to minimize rumors and address misinformation

FEM-PrEP Study Sites



Planning for an HIV-Prevention Breakthrough

If Truvada is proven effective, there will be a need to make it available as soon as possible. In anticipation of this need, public health scientists and policy-makers are concentrating on the logistics of providing access to PrEP drugs. This enormous task raises ethical, medical, and economic challenges.

The FEM-PrEP trial is addressing these issues with preparatory “rollout” activities to plan for local access to Truvada. Our research activities include in-depth interviews and focus group discussions with public health stakeholders, civic leaders, and community members.

These activities will help us to develop small-scale pilot interventions for the distribution of an effective PrEP drug. The pilot interventions will serve as models for expanding the rollout to national levels after the pilot period. Governments, communities, funders, and health experts must work together to ensure that this new way of preventing HIV is delivered effectively.



Michael Szpir/FHI

Amy Corneli, behavioral investigator of FEM-PrEP and principal investigator of the SBC preparedness protocol.

FEM-PrEP Trial Highlights

Clinical Trial

- The protocol was approved by the Medunsa Campus Research Ethics Committee for the Pretoria site in August 2008, and by the Kenyatta National Hospital Institutional Review Board for the Bondo site in September 2008.
- We are waiting for ethical approval for the Arusha/Moshi site from the London School of Hygiene and Tropical Medicine and the Tanzanian Food and Drug Administration.
- The site in Bondo had a “refresher” and initiation training in April.
- Staff members at the Pretoria site were trained in research practices and ethics in May and June.
- The Cape Town site was closed in the second quarter of 2009.
- The first trial participant was screened on May 28 at the Bondo site.
- The principal investigators will meet in Nairobi, Kenya, to discuss the clinical protocol in August.
- We added a site in Mazabuka, Zambia. We plan to recruit the first participants at this site in the first half of 2010.

Socio-Behavioral and Community (SBC) Activities

- The Bondo site has completed all SBC data dissemination activities. All SBC data related to recruitment, retention, adherence, informed consent, risk-reduction counseling, community engagement, and contraceptive counseling have been incorporated into clinical trial procedures. Interviews with community stakeholders will continue throughout the course of the clinical trial. Interviews with trial participants will soon begin to inform SBC-related components of the clinical trial and will continue throughout the trial.
- The Bondo site continues to engage the community to build support for the FEM-PrEP clinical trial, address any community concerns, and to correct misinformation. The community advisory board (CAB) participated in a data dissemination meeting and reviewed the interview guides for the PrEP rollout protocol.
- Training for the PrEP rollout protocol was conducted in Bondo in May. Training will be conducted at the Pretoria site in July and at the Arusha site by the end of 2009.
- The Pretoria site has completed all components of the SBC preparedness research and SBC data analysis. The SBC data are now being incorporated into clinical trial procedures. SBC data dissemination activities began in June.
- The Pretoria site continues to be involved in outreach activities, including participation in World TB Day, Vaccine Awareness Day, candlelight memorials, and a variety of local events. The CAB also participated in an SBC data dissemination meeting and reviewed the PrEP rollout interview guides.
- The Arusha site will complete the main components of the SBC preparedness research at the end of July. The site will continue mapping potential recruitment sites until the clinical trial begins. We have begun to analyze the SBC data.
- The Arusha site held a stakeholders meeting in February that included the community advisory group (CAG). A three-day training was held with the Moshi CAG the same week. Community program activities will start as soon as SBC research activities are completed.
- Training for SBC preparedness research is scheduled for the Mazabuka site in August.
- Training for Mazabuka's CAB is planned for the week of August 17.
- SBC closeout procedures and data dissemination activities took place at the Cape Town site in June and July.



Stella Kirkendale/TH

SBC research and community staff (left to right), Vu Mtimkulu, Khatija Ahmed, Stella Kirkendale, and Malebo Ratlhagana.

(continued from page 1)

Interviewing the patrons presents similar obstacles. “Since they do not know you, it can be very difficult to get them to be honest about their sexual behavior,” Aus Maki says. “It is very difficult to get these women during the day, and at night they come very late to these places, when our time on duty is over,” she says.

Even so, Aus Maki’s ties to the community have enabled her to forge strong connections with the people she has interviewed. “Once they get to know me, and trust develops, some of them tell me about their personal problems, about their relationships, or what made them to behave in the way they are now,” she says. That kind of trust also encourages the interviewees to tell Aus Maki about the other places where people meet new sex partners.

The researchers also log the coordinates of recruitment areas with a handheld global positioning system (GPS) device. The coordinates are transmitted to Caleb Parker, a geographer, who maps the areas. The maps are combined with data from the PLACE interviews to prioritize recruitment areas, according to Parker.

“We have identified hundreds of potential places in the recruitment areas that need to be prioritized before the trial begins in order to recruit efficiently,” says Parker.

Mapping data will then be combined with screening data on HIV prevalence, which is collected when the women are tested for HIV during the screening process for the clinical trial. “When monitored monthly, this combination will help to determine whether we are reaching areas where women might be at higher risk, and we can modify where we are recruiting as needed,” says Corneli.

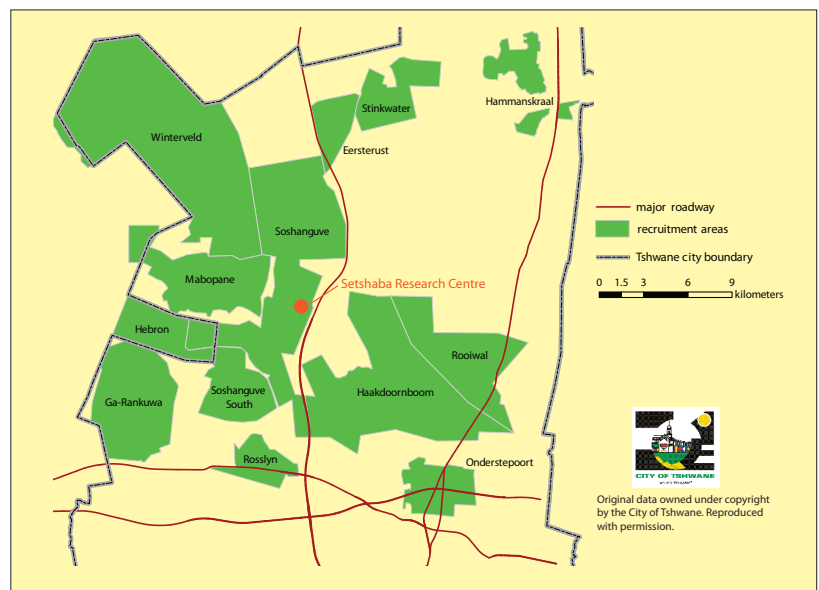
This form of community mapping is new to the region, according to Khatija Ahmed, the principal investigator of the Setshaba Research Centre in Soshanguve. “It was not used in previous trials and will certainly assist us in recruitment for the study,” she says.

Like many other townships in South Africa, Soshanguve endured poverty and a poor health care system during the apartheid era. Soshanguve and the surrounding townships contain more than 1.2 million people, and they will be a vital part of the trial’s catchment area. It’s an area that has been hit hard by HIV—about 25 percent of the women are infected with the virus, according to Ahmed.

Ahmed is optimistic about the trial’s approach to finding participants. “I have met the best of people in these areas and am very positive that we have good potential to recruit and retain within this group of people,” she says.

Malebo Ratlhagana, the community liaison officer at the Pretoria site, agrees. “People around here are welcoming, and we believe they will be willing to participate,” she says.

(continued on page 5)



Recruitment areas in Tshwane are identified by researchers using the PLACE method.

(continued from page 4)

Ratlhagana's work takes her outside the office and into the community, where she enjoys educating others and attending events. "Tshwane has many taverns and she-beens, where people go to relax and enjoy, and those are the places that we are looking for. It's a place where the fun never ends," she says.

By late May, the SBC team had spent eight months mapping potential recruiting sites and building relationships with the people in the community. "I think they are happy that their area is going to try something again in the HIV field," says Ratlhagana, "and that gives them hope and something to be proud of in the fight against the virus."

HIV-Prevention News

Intriguing Results for PRO 2000 Topical Gel

Scientists conducting the HIV Prevention Trials Network (HPTN) 035 study of 3,099 women found that a 0.5-percent dose of the PRO 2000 vaginal gel reduced a woman's risk of HIV infection by 30 percent, but the effect was not statistically significant. The results were presented by Salim Abdool Karim, of the Centre for the AIDS Programme of Research in South Africa (CAPRISA), and his colleagues, at the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal (February 8–11).

The HPTN 035 results are the first indication that a vaginal gel containing a candidate microbicide might reduce a woman's risk of becoming infected with HIV. Because the effectiveness of PRO 2000 was just short of reaching statistical significance, further research is needed to determine the product's potential for HIV prevention.

The Microbicide Development Programme (MDP) is also investigating the effectiveness of the 0.5 percent PRO 2000 gel in the MDP 301 study of 9,389 women. The results of that study—expected at the end of 2009—may provide the data needed to confirm the product's effectiveness.



CAPRISA

PRO 2000 gel applicator.

Gels Protect against Simian HIV in Macaques

Topical gels containing antiretroviral (ARV) drugs—tenofovir alone or with emtricitabine—can prevent vaginal transmission of simian HIV (SHIV) in pigtail macaques, according to a study by Charles Dobard, of the U.S. Centers for Disease Control and Prevention, and his colleagues. Their results were presented at the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal (February 8–11).

The macaques were exposed to repeated low doses of SHIV, given vaginally twice a week to simulate a common route of HIV transmission in humans. None of the 12 macaques that received either of the ARV-containing gels became infected with the virus, despite 20 challenges with SHIV. In contrast, 10 of the 11 macaques in the control arms became infected after vaginal exposure to SHIV.

The authors of the study note that the complete protection achieved by the tenofovir gel identifies an effective strategy for human trials and that combinations of topical drugs may not be required for highly effective prophylaxis.



Douglas M. Bowden/Wisconsin National Primate Research Center, Jacobsen Library

Pigtail macaque.

Current HIV PrEP Trials

STUDY/FUNDER	LOCATION	STRATEGY	POPULATION	STATUS	COMPLETION
U.S. Extended Tenofovir Safety Study/CDC	United States	Oral tenofovir	400 men who have sex with men	Fully enrolled	2009
Bangkok Tenofovir Study/CDC	Thailand	Oral tenofovir	2,400 injection-drug users	95% enrolled (May 2009)	2010
iPrEX Study/NIH, BMGF	Brazil, Ecuador, Peru, South Africa, Thailand, United States	Oral Truvada	3,000 men who have sex with men	47% enrolled (January 2009)	2010
CAPRISA 004/USAID, LIFElab	South Africa	Vaginal tenofovir gel	900 sexually active women	Fully enrolled	2010
TDF-2/CDC	Botswana (2 sites)	Oral Truvada	1,800 heterosexual men and women	43% enrolled (May 2009)	2011
Partners PrEP Study/BMGF	Kenya, Uganda	Oral tenofovir, oral Truvada	3,900 serodiscordant heterosexual couples	33% enrolled	2012
FHI FEM-PrEP Study/USAID, BMGF	Kenya, Malawi, South Africa, Tanzania, Zambia	Oral Truvada	3,900 higher-risk women	Started Q2, 2009	2012
MTN VOICE Study/NIH	Malawi, Southern Africa, Uganda, Zambia, Zimbabwe	Oral tenofovir, oral Truvada, vaginal tenofovir gel	4,200 sexually active women	Planning/expected start Q2, 2009	2012

Abbreviations: BMGF—Bill & Melinda Gates Foundation; CAPRISA—Centre for the AIDS Programme of Research in South Africa; CDC—U. S. Centers for Disease Control and Prevention; FHI—Family Health International; iPrEX—Iniciativa Profilaxis Pre-Exposición; MTN—Microbicide Trials Network; NIH—U. S. National Institutes of Health; TDF—tenofovir disoproxil fumarate; USAID—U. S. Agency for International Development; VOICE—vaginal and oral interventions to control the epidemic.

Note: This table does not include vaccine trials.

To learn more about HIV-prevention research

Alliance for Microbicide Development: www.microbicide.org

Prepwatch: www.prepwatch.org/trials.htm

Global Campaign for Microbicides:

www.global-campaign.org/download.htm

AIDS Vaccine Advocacy Coalition (AVAC): www.avac.org

HIV Prevention Trials Network (HPTN): www.hptn.org

Microbicide Trials Network (MTN):

www.mtnstopshiv.org/node/studies

For more information about the FEM-PrEP trial

Beth Robinson, Deputy Director

Research Dissemination

Family Health International

P.O. Box 13950

Research Triangle Park, NC 27709 USA

E-mail: FEM-PrEP@fhi.org



FEM-PrEP

Family Health International (FHI), a nonprofit public health organization, leads the FEM-PrEP trial in collaboration with local scientists at each site. FHI provides scientific oversight, supports the trial's management, monitors the clinical trial activities and the socio-behavioral and community research, and assists with community activities. FHI works closely with the study sites in the day-to-day conduct of the clinical trial.

Gilead Sciences, which makes Truvada, is providing the drug free for this clinical trial. If Truvada is found to be safe and effective for HIV prevention, Gilead Sciences will make a good-faith effort to provide Truvada for this use. The company has also provided technology transfer of Truvada to companies that produce generic drugs.

The U. S. Agency for International Development and the Bill & Melinda Gates Foundation are funding the FEM-PrEP trial.