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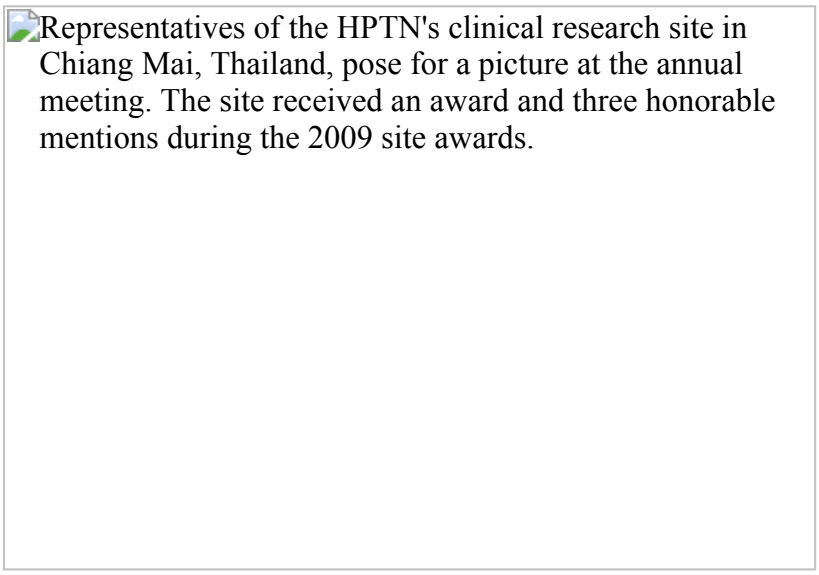
What's New in the HPTN?



Representatives of the HPTN's clinical research site in Chiang Mai, Thailand, pose for a picture at the HPTN's annual meeting in June. The site received an award and three honorable mentions during the 2009 site awards.

Annual Meeting Emphasizes Combination Prevention

In June, nearly 500 HPTN members and other partners from around the world convened in Washington, DC, for the fifth annual meeting of the HPTN. The meeting focused on the HPTN's recent successes, its current domestic and international research agendas, and the direction of its future HIV prevention research. Additional highlights included a joint plenary session and a joint poster session with the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Group.

According to Dr. Anthony Fauci of the National Institute of Allergy and Infectious Diseases (NIAID), who spoke to the meeting participants via satellite, evidence-based HIV prevention strategies are reaching only about one-fifth of the people who need them globally.

The experts at the meeting agreed that using multiple HIV prevention strategies at the same time, focusing on the most vulnerable subpopulations, will be the most effective way to curb the HIV pandemic.

2009 Site Awards

Six Sites Honored for Outstanding Performance
During the HPTN annual meeting in June, six clinical research sites were recognized for their exceptional performance over the past year. The awards, which were determined by the HPTN's performance evaluation committee, were presented in six categories. Congratulations to all the recipients!

Best Accrual
University of North Carolina (UNC) AIDS Clinical Research Site
Chapel Hill, NC, USA

Best Retention
National AIDS Research Institute (NARI) Clinical Research Sites
Pune, India

Best Data Management
Y.R. Gaitonde Centre for AIDS Research and Education (YRG Care)
Chennai, India

Best Laboratory Performance
Research Institute for Health Sciences (RIHES) Laboratory
Chiang Mai, Thailand

Best Community Engagement
San Francisco Department of Public Health
San Francisco, CA, USA

Overcoming Extraordinary Circumstances
Xinjiang Uighur Autonomous Region Center for Disease Control and Prevention
Xinjiang, China

Just as combination antiretroviral treatment has become the gold standard for treating HIV infection throughout the world, "combination prevention" is likely the future of global prevention efforts. **HPTN 065**, HPTN 068, and HPTN 070 are among the trials that are embracing this approach (see '**Making Progress**' for updates on these trials).

Access the **agenda and a sample of plenary presentations** from the annual meeting.

What's New in Prevention?

Microbicide Gel Garners International Attention

Researchers from the **Centre for the AIDS Programme of Research in South Africa (CAPRISA)** and its partners recently achieved an important scientific breakthrough in the fight against HIV and genital herpes. Through the CAPRISA 004 trial, they showed that a 1% tenofovir gel, formulated as a vaginal microbicide, was 39% effective at reducing a woman's risk of becoming infected with HIV and 51% effective at preventing genital herpes infections. The results were presented in July at the **XVIII International AIDS Conference** in Vienna, Austria.

"The results of the trial signal a major advance for both the microbicide field and the PrEP [pre-exposure prophylaxis] field," says Dr. Quarraisha Abdool Karim, the associate director of CAPRISA, co-principal investigator of the trial, and co-principal investigator of the HPTN. "Much more needs to be done before the product can be licensed and available to women at risk of acquiring HIV, but the results are an important first step for preventing sexual transmission of HIV, especially for women. They also reinforce the HPTN's priorities in PrEP and its potential role in combination prevention."

The women in CAPRISA 004 were advised to use the tenofovir gel up to 12 hours before sex and soon after having sex, for a maximum of two doses in 24 hours. In the approach known as PrEP, researchers are beginning to study whether oral tenofovir, taken once a day, can also reduce the risk of acquiring HIV.

In August, experts from the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) gathered in Johannesburg to further discuss the implications of CAPRISA 004. They recommended that two more clinical trials be conducted soon to confirm the results and that a separate trial (comparing two strategies for delivering tenofovir in the community) be conducted to inform the eventual roll-out of the gel.

Should the safety and effectiveness of the gel be confirmed, widespread use (at the current level of protection) could prevent more than half a million infections in South Africa alone over the next decade.

Access the **results of the trial**, published in the journal *Science*.

United States Launches National HIV/AIDS Strategy

In July, the White House launched the first comprehensive U.S. strategy to confront its domestic HIV epidemic in a coordinated fashion. Despite advances in HIV prevention and care, an estimated 56,000 people in the United States are still becoming infected with HIV every year.

The new National HIV/AIDS Strategy has three aggressive goals for reducing new HIV infections: 1) increasing access to HIV care, 2)

Making Progress

Successful Pilot for HPTN 068

HPTN 068 will help determine whether cash incentives for attending school can help prevent HIV among young women in South Africa. A recent pilot study showed that this intervention is acceptable to the families and communities in the study area. The study protocol has been finalized, and enrollment is expected to begin in early 2011, pending institutional review board (IRB) approval.

HPTN 065 Moving Forward

HPTN 065 (also known as TLC-Plus) is a three-year study evaluating the feasibility of a community-focused test, link to care, plus treat approach to HIV prevention in the United States. The U.S. Centers for Disease Control and Prevention (CDC) and the Departments of Health in Washington, DC, and New York City are collaborating with the HPTN to implement five interrelated components: 1) expanded HIV testing, 2) linkage to HIV care, 3) viral suppression, 4) prevention strategies for HIV-positive individuals, and 5) patient and provider surveys. So far the provider survey, which is designed in part to assess knowledge and attitudes regarding the use of antiretroviral therapy for HIV treatment and prevention, is being sent to providers at HIV care sites in the study areas. The Strategic Working Group of the National Institute of Allergy and Infectious Diseases (NIAID) recently reviewed and applauded the study's progress. **More background information and answers to frequently asked questions** about the study are available.

Concept Approved for HPTN 070

The HPTN's executive committee approved the international test and linkage to care and treatment (iTLCT) concept for protocol development in September, and a study team is beginning to develop the protocol and select study sites. Also known as HPTN 070, the study will test the feasibility of multi-component home-based HIV testing and linkage to care and treatment as a way to prevent HIV infection in international settings. The feasibility study, which will be conducted among four communities in Africa, will help inform a larger future trial. Key elements

improving outcomes for people living with HIV, and 3) reducing HIV-related disparities and health inequities over the next five years.

"The White House has asked the agencies of the U.S. Public Health Service, such as the NIH [National Institutes of Health] and the CDC [Centers for Disease Control and Prevention], to synergize their research efforts to help reach the goals of the new strategy," says Dr. Sten Vermund, principal investigator of the HPTN. "This underscores the relevance of the HPTN, as our BROTHERS, ISIS, TLC-Plus, and PrEP [pre-exposure prophylaxis] protocol teams have already anticipated these goals. Increasing access, improving outcomes, and reducing disparities are what the HPTN is all about."

Learn more about the strategy at **whitehouse.gov** or **aids.gov**.

In the Community

Cross-Network Collaboration Brings Communities Together
Approximately 60 community educators, community advisory board (CAB) members, study coordinators, project directors, and other key stakeholders in Soweto, South Africa, met for a two-day CAB training workshop in August.

The workshop was a cross-collaboration between the HPTN, the Microbicide Trials Network (MTN), and three clinical trials units in Soweto (the Perinatal Health Research Unit, the Reproductive Health Research Unit, and the Clinical Health Research Unit).

Participants listen intently during the training workshop in South Africa.

Participants listen intently during the training workshop, which was hosted by the Perinatal Health Research Unit.

"One of the unique aspects and key outcomes of this workshop was that the participants requested that the cross-network training be repeated, as it was especially effective at keeping community staff and CAB representatives informed of all the research studies in their communities," says Dr. Janet Frohlich, who co-chairs the HPTN's Community Working Group, leads the community program at the Centre for the AIDS Programme of Research in South Africa (CAPRISA), and directs CAPRISA's Vulindlela site.

The first day of the workshop focused on updates and training related specifically to **HPTN 052**, **MTN 003** (also known as VOICE), and the **South African Studies on HIV in Adolescents (SASHA) project**.

CAB representatives from the **South African AIDS Vaccine Initiative (SAAVI)** and five of the clinical trials networks supported by the Division of AIDS (DAIDS) within the National Institute of Allergy and Infectious Diseases (NIAID) were invited to participate in the second day of the workshop. The second day addressed cross-cutting community issues, results and implications of the CAPRISA 004 trial, ethical

that will be evaluated in HPTN 070 include 1) strategies for implementing home-based HIV testing, 2) strategies for improving linkage to care, 3) the feasibility of using HIV viral load to determine eligibility for antiretroviral therapy, 4) the feasibility of syndromic screening for tuberculosis, and 5) the feasibility of assessing the prevalence of HIV among women attending antenatal clinics.

HPTN 069 Under Development
HPTN 069 will evaluate the safety and tolerability of several antiretroviral drug combinations used as pre-exposure prophylaxis to prevent HIV transmission among men who have sex with men in the United States. In this Phase II study, participants will be randomized to receive maraviroc (MVC), MVC plus emtricitabine (FTC), or the fixed-dose combination of tenofovir (TDF) and FTC (also known as Truvada). MVC works by blocking HIV from entering a person's cells. Tenofovir and FTC are two different types of reverse transcriptase inhibitors, which interfere with HIV replication. The study is expected to start in the first half of 2011.

Coming Soon

HPTN Leadership Retreat
November 11–12, 2010
Atlanta, GA

HPTN Prevention Management Group Meeting
February 2–3, 2011
Arlington, VA

2010 HIV Prevention Leadership Summit
December 12–15, 2010
Washington, DC

2011 National African American MSM Leadership Conference on HIV/AIDS and other Health Disparities
January 20–23, 2011
Brooklyn, NY

Hot Off the Press

Burns DN, Dieffenbach CW, Vermund SH. Rethinking prevention of HIV type 1 infection. *Clin Infect Dis* 2010;51(6):725–731.

responsibilities for community representatives, and collaboration within communities.

More information on how DAIDS-supported networks stay connected is available from the **HIV/AIDS Network Coordination (HANC) project**, which recently launched a new Web site.

National Meetings Serve as Community Platform

The HPTN continues to find innovative ways to increase community awareness about its research agenda. Most recently, representatives of the network have been delivering presentations at professional meetings to share opportunities for community involvement with a broader audience.

"We are using social media and conference presentations to engage people and organizations who are already concerned about health disparity issues but who may not yet be knowledgeable about HIV prevention research," says HPTN's Senior Community Engagement Officer Georgette King.

Ms. King and HPTN's Jonathan Lucas, in partnership with representatives from all six clinical trials networks supported by the Division of AIDS (DAIDS) of the National Institutes of Health (NIH), co-facilitated a workshop in September at the **United States Conference on AIDS (USCA)** in Orlando, FL. The workshop provided information on increasing community involvement at all levels of the research process. It also provided a brief history of clinical trials and prompted discussion about opportunities to increase cultural competency and diversity in HIV research.

Also, in August, two nurses from HPTN research sites (Rondalya DeShields and Melissa Douglas) delivered a presentation at the 38th annual conference of the **National Black Nurses Association (NBNA)** in San Diego, CA. This presentation focused on how Black health professionals in particular can contribute to the HPTN's domestic research agenda.

See more extensive coverage of the **cross-network workshop at USCA**.

A Closer Look

HPTN 058: Taking 'Control' of Quality in Guangxi, China

In an HIV prevention trial, each case report form can be filled with a massive amount of data, ranging from simple demographic information to complex clinical, laboratory, and behavioral findings. When you consider that some trials include hundreds or thousands of participants and that these forms must be completed for every participant during every study visit, the thought of keeping track of all that data can be overwhelming.

"Assessing the quality of so much data is a continuous and dynamic process, and it requires a very carefully constructed quality-

Chen YQ, Young A, Brown ER, Chasela CS, Fiscus SA, Hoffman IF, Valentine M, Emel L, Taha TE, Goldenberg RL, Read JS. Population attributable fractions for late postnatal mother-to-child transmission of HIV-1 in Sub-Saharan Africa. *J Acquir Immune Defic Syndr* 2010;54(3):311–316.

Kim HN, Wang J, Hughes J, Coombs R, Sanchez J, Reid S, Delany-Moretlwe S, Cowan F, Fuchs J, Eshleman SH, Khaki L, McMahon MA, Siliciano RF, Wald A, Celum C. Effect of acyclovir on HIV-1 set point among herpes simplex virus type 2-seropositive persons during early HIV-1 infection. *J Infect Dis* 2010;202(5):734–738.

Sugarman J, Grace WC. Ethics and the standards of prevention in HIV prevention trials. *AIDS* 2010;24(14):2298-2299; author reply 2299–2300.

Towler WI, James MM, Ray SC, Wang L, Donnell D, Mwatha A, Guay L, Nakabiito C, Musoke P, Jackson JB, Eshleman SH. Analysis of HIV diversity using a high-resolution melting assay. *AIDS Res Hum Retroviruses* 2010;26(8):913–918.

Watson-Jones D, Wald A, Celum C, Lingappa J, Weiss HA, Changalucha J, Baisley K, Tanton C, Hayes RJ, Marshak JO, Gladden RG, Koelle DM. Use of acyclovir for suppression of human immunodeficiency virus infection is not associated with genotypic evidence of herpes simplex virus type 2 resistance to acyclovir: analysis of specimens from three phase III trials. *J Clin Microbiol* 2010;48(10):3496–3503.

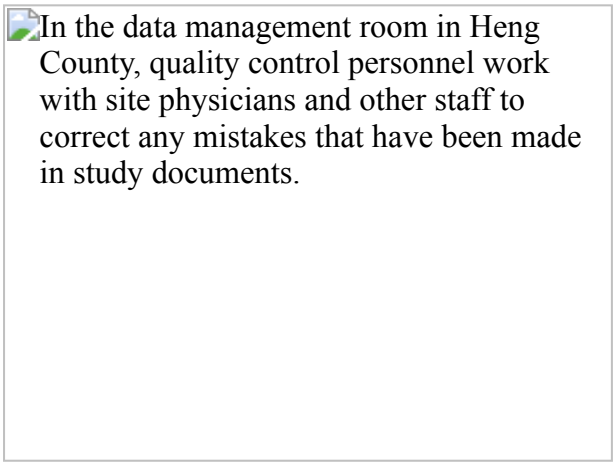
Want to Read More?

HIV Prevention Trials Network
http://www.hptn.org/index.htm

HPTN Annual Meeting
http://www.hptn.org/network_information/MeetingRegFiles/AnnualMeeting2010Presentations.htm

HIV/AIDS Network Coordination
http://www.hanc.info/Pages/default.aspx

HPTN 058
http://www.hptn.org/research_studies/hptn061.asp



In the data management room in Heng County, quality control personnel work with site physicians and other staff to correct any mistakes that have been made in study documents.

management plan," explains Liu Shaifeng, the quality assurance (QA) and quality control (QC) coordinator for the HPTN 058 sites in Guangxi, China.

After each participant visits a study clinic, a QC coordinator typically reviews the participant's case report form and any other research-related documents from the study visit. Data managers then identify and track different types of errors in these site-specific data, and these data are eventually submitted to an off-site data center for further review.

"The purpose of such a plan is to ensure the accuracy of these data and to protect participants by identifying errors early and monitoring outliers that may be cause for concern," says Dr. Huang Jianhua, the site coordinator for HPTN 058's clinical research site in Heng County.

HPTN 058 is a Phase III trial of two strategies for preventing HIV and death among opiate-dependent injectors in Thailand and China. Heng County was the first of two research sites in Guangxi to open to enrollment. So far, about 290 of an expected 405 participants have been enrolled there.

To help improve quality control in Heng County, the entire study team—not just the QC staff—have gotten involved. Before a QC coordinator sees any data, and even before a participant has left the study clinic, each staff member is responsible for checking over the data he or she has collected. This way, errors can be caught immediately and fixed within minutes.

"Because it is now the responsibility of every staff member to ensure the quality of our data, we have been able to create a real culture of quality monitoring" says Carin Busch, the former on-site research coordinator for Johns Hopkins University (JHU), as part of the JHU-Guangxi, China Clinical Trials Unit. Using this strategy, the study team has also been able to catch more errors.

"With the beginning of a project at a new site, it is expected that there will be many errors on case report forms and that the errors will decrease with time and experience," says Ms. Busch. "What our site has done differently is to dramatically decrease errors in monitoring reports as well."

The Statistical Center for HIV/AIDS Research and Prevention (SCHARP) in Seattle, Washington, is the off-site data center that reviews case report forms for all HPTN trials, but SCHARP cannot review all types of data. For instance, the responsibility for reviewing clinical data that are written in doctors' notes falls to the site.

A contract research organization called Pharmaceutical Product Development (PPD) helps monitor the accuracy of these types of data. Monitoring reports from 2009 showed a dramatic decrease in errors during the year. The number of reported procedural errors in source

HPTN 065
http://www.hptn.org/research_studies/hptn065.asp

Blog.AIDS.gov
http://blog.aids.gov/

Future of HIV/AIDS Clinical Trial Networks
http://blog.aids.gov/2010/08/future-directions-for-niaids-hiv-vaccine-clinical-research-consider-and-comment.html

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documents, for example, dropped from 122 in the first quarter of 2009 to just 11 in the fourth quarter.

According to Ms. Busch, the lessons learned in Heng County are being carried over to the clinical research site in Nanning, which began enrolling participants in May 2010 and is the newer of HPTN 058's sites in Guangxi.

"Overhauling a site's existing quality management plan may be time-consuming, but we found its impact to be pervasive," says Ms. Busch. "After all, a trial is only as good as the quality of its data."