

**Project Accept (HPTN 043):
A Phase III Randomized Controlled Trial of
Community Mobilization, Mobile Testing, Same-Day Results, and Post-Test Support
for HIV in Sub-Saharan Africa and Thailand**

Overview and Significance

There is no more compelling crisis in the world today than the HIV epidemic in sub-Saharan Africa. Since the epidemic began, more than 60 million people have been infected with HIV. With an estimated 2.8 million new HIV infections in sub-Saharan Africa in the past year alone, 24.7 million Africans are now living with the virus. In addition to death and disease burden, the epidemic has had an enormous impact on economies and life expectancies, and left a legacy of millions of orphans. There is concern that this magnitude of epidemic burden could devastate parts of Asia as well.

Evidence-based strategies that mobilize communities are required to achieve significant and lasting reductions in the incidence of HIV in countries hit hard by the HIV/AIDS epidemic. This study is the first randomized controlled Phase III trial to determine the efficacy of a behavioral/social science intervention with an HIV incidence endpoint in the developing world.

In this HIV prevention trial sponsored by the National Institute of Mental Health (NIMH), 34 communities in Africa (in South Africa, Tanzania, and Zimbabwe) and 14 communities in Thailand will be randomized to receive either a community-based voluntary counseling and testing (CBVCT) intervention in addition to standard clinic-based VCT (SVCT) services, or SVCT services alone. The CBVCT intervention has three major strategies:

1. To make VCT more available in community settings
2. To engage the community through outreach
3. To provide post-test support

These strategies are designed to change community norms and reduce risk for HIV infection among all community members, irrespective of whether they participated directly in the intervention. Thus, a community-level sampling approach is used, as opposed to a cohort design.

Provided that we can document efficacy with regard to HIV incidence and incremental cost-effectiveness, we expect that resources for widespread implementation of CBVCT will become available from the U.S. Agency for International Development (USAID) or the Global Fund to Fight AIDS, Tuberculosis and Malaria. We have worked closely with representatives of national AIDS programs in the host countries to ensure that the intervention is sustainable even in countries with limited resources.

Study Objectives and Design

The primary objective of this study is to test the hypothesis that communities receiving 3 years of CBVCT, relative to communities receiving 3 years of SVCT, will have significantly lower prevalence of recent HIV-1 infection. This will be evaluated by comparing the post-intervention incidence of HIV infection in CBVCT and SVCT communities. The method used to estimate HIV incidence rates will be determined based on the performance of currently available test methods. It is likely that these estimates will take into account results of two serologic HIV incidence assays (the BED-CEIA assay (Calypte) and an avidity assay), as well as non-serologic measures (eg, CD4 cell count and HIV viral load). Samples from HIV seronegative individuals may also be analyzed for evidence of early/acute HIV infection.

The secondary objective of this study is to test the hypotheses that CBVCT communities, relative to SVCT communities, will at the end of the intervention period report significantly less HIV risk behavior, higher rates of HIV testing, more favorable social norms regarding HIV testing, more frequent discussions about HIV, more frequent disclosure of HIV status, less HIV-related stigma, and fewer HIV-related negative life events.

Cost-effectiveness analyses will be conducted to determine whether CBVCT is cost-effective compared to SVCT. This will be evaluated in terms of cost per HIV infection averted and disability-adjusted life years (DALYs) saved. Qualitative analyses will also be performed through community ethnography and in-depth interviews.

The assessment of efficacy is based on changes in communities using repeat cross sectional data collected using household probability samples. A baseline behavioral assessment will be conducted in all communities using a household probability sampling technique. Pairs of communities will be matched using one or more variables; each community in a pair will then be randomized to receive either CBVCT or SVCT (CBVCT communities will be provided with both CBVCT and SVCT services, while SVCT communities will only be provided with SVCT services). A qualitative cohort in each community will be recruited in order to collect data on how stigma changes over time in the communities, and will allow for an assessment of attitudes toward HIV-infected persons.

A post-intervention assessment will be conducted using the same household probability sampling technique as for the baseline behavioral assessment. Recruited individuals from each community will provide biological samples for HIV testing, with a subsample of individuals from each community receiving a second cross-sectional behavioral assessment.

The intervention component of the study will last 3 years. The entire study project, from planning work through data analysis, is scheduled to last 8 years.

Intervention

The CBVCT intervention consists of four components—Community Mobilization, Community-Based (mobile) VCT, Post-Test Support Services, and Quality Assurance. The intervention in each of the countries and sites will be derived from the same theoretical model and contain the same strategies. The implementation of the elements of the intervention will be tailored to each local culture and context. The CBVCT intervention is based on the premise that HIV sexual risk behavior and HIV incidence will decrease in communities with increased knowledge of HIV status and more supportive community norms.

Communities randomized to SVCT (the “standard-of-care”) will only receive the installment of clinic-based VCT services at existing facilities. The training for VCT counselors will be the same in the CBVCT and SVCT communities; however, no active outreach/community mobilization, mobile/enhanced-access VCT services, or special post-test clubs will be provided in the SVCT arm.

Communities randomized to CBCVT will receive, in addition to the SVCT services, deployment of a mobile or easily accessed VCT unit including a nurse or trained phlebotomist, outreach worker/driver, and HIV test counselors. The counselors, outreach workers, and recruited volunteers will provide information on HIV/AIDS and the VCT process to the community to encourage people to consider testing. Post-test clubs will be available to people who have tested, regardless of their test results, in order to provide support and offer health and social service referrals.

Community Participation

All aspects of the design and implementation of the study are determined through strong collaboration among host-country investigators and institutions and their U.S.-partner investigators and institutions.

A partnership with each study community and its leadership shall be established through Community Advisory Boards (CABs). Throughout the duration of the study, regular CAB meeting will be held to ensure ongoing two-way communication between the study team and the study communities. Communication with relevant local, district, and national leadership will also continue as needed throughout the study.

For the 4 African sites, it is expected that a total of approximately 68,000 participants will access CBVCT services through the study, with another 34,000 accessing SVCT services. The baseline and post-intervention behavioral assessments will each enroll a total of 10,200 participants; 33,800 participants will be evaluated for the post-intervention biological assessment.

For the Thailand site, it is expected that a total of approximately 24,500 participants will access CBVCT services through the study, with another 19,600 accessing SVCT services. The baseline and post-intervention behavioral assessments will each enroll 2,800 participants; 7,000 participants will be evaluated for the post-intervention biological assessment.

Collaborating Institutions and Investigators

This trial is a National Institute of Mental Health (NIMH) Cooperative Agreement involving Johns Hopkins University (JHU) Bloomberg School of Public Health, the Medical University of South Carolina (MUSC), and the University of California at San Francisco (UCSF) and Los Angeles (UCLA). The Statistical Center for HIV/AIDS Research & Prevention (SCHARP) at Fred Hutchinson Cancer Research Center (FHCRC) in Seattle, University of North Carolina at Chapel Hill, and Charles University in Prague, Czech Republic, are also participating as the statistical and data management experts for the study. The host country institutions are Chiang Mai University in Chiang Mai, Thailand; Human Sciences Research Council in Durban, South Africa; Perinatal HIV Research Unit and the University of the Witwatersrand in Johannesburg, South Africa; Muhimbili University of Health and Allied Sciences in Dar es Salaam, Tanzania; and the University of Zimbabwe in Harare, Zimbabwe. The HIV Prevention Trials Network (HPTN) is also providing support to the project (HPTN 043); support has also been provided by the Office of AIDS Research of the National Institutes of Health.

Christopher M. Gordon, PhD, is the study's program officer at NIMH's Division of AIDS and Health and Behavior Research. The primary investigators from the United States are David Celentano, ScD, MHS (PI, JHU); Thomas J. Coates, PhD (PI, UCLA); Stephen F. Morin, PhD (PI, UCSF); and Michael Sweat, PhD (PI, MUSC). Primary host-country investigators are Suwat Chariyalertsak, MD, DrPH (PI, Thailand); Alfred Chingono, MSc (PI, Zimbabwe); Glenda Gray, MBBCh, FCPaed(SA) (PI, Soweto, South Africa); Jessie Mbwambo, MD (PI, Tanzania); Linda Richter, PhD (PI, Vulindlela, South Africa); G.P. Kilonzo, MBChB, Mmed, FRCP, MD (co-PI, Tanzania); James McIntyre, MBChB, MRCOG (co-PI, Soweto, South Africa); and Surasing Visrutaratna, PhD (co-PI, Thailand). Deborah Donnell, PhD, and Michal Kulich, PhD, are providing statistical and data management expertise for the study.

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