COMBINED CROSS-SECTIONAL AND PROSPECTIVE HIV INCIDENCE STUDY: THE SITE IDENTIFICATION AND DEVELOPMENT INITIATIVE (SIDI)

KEY POINTS

- *Determining the rate of new HIV infections in a population—the incidence rate—can be expensive and complicated. A less expensive and easier method would be a boon to HIV researchers and program planners.*
- *FHI is sponsoring studies at sites in Africa and Asia to evaluate the accuracy of a new laboratory method that may prove superior to the current method of estimating HIV incidence.*
- *Accurate measurements of HIV incidence will reveal whether these sites are suitable for future research on microbicides and other HIV prevention methods. Local staff members who help conduct the incidence studies will gain experience that will prepare them to work on future HIV research projects.*

IMPORTANCE OF MEASURING HIV INCIDENCE

Family Health International (FHI) launched the Site Identification and Development Initiative (SIDI) in July 2006, with funding from the U.S. Agency for International Development (USAID), in an effort to increase the number and improve the readiness of sites for HIV prevention research.

SIDI's primary goal is to assess and fully prepare five or more new sites for clinical trials of microbicides and other products for HIV prevention. SIDI is accomplishing this goal by conducting HIV incidence studies[1] and other HIV research at some of these sites.

The identification of high-risk populations is an essential step in the selection of potential research sites. Incidence figures reveal trends in the HIV epidemic, the rate at which HIV is spreading, and the effectiveness of HIV prevention programs. Researchers depend on these measurements to find populations at unusually high risk for HIV infection.

The measurement of a population's HIV incidence must be accurate for an HIV prevention trial to succeed. If the incidence is lower than predicted, the trial's statistical results may be invalid. Even small differences can have an enormous impact on recruitment, study duration, and estimates of the resources needed for the trial.

LIMITATIONS OF CURRENT HIV INCIDENCE MEASUREMENTS

Accurate measurements of HIV incidence are difficult to obtain and are typically time- and labor-intensive. Traditional HIV surveillance methods have measured prevalence at different points in time to provide a rough estimate of HIV incidence rates, but this approach requires multiple rounds of surveillance over years.

Prospective cohort studies are the gold standard for determining the rate at which people are newly infected, but these studies tend to be large, expensive, and slow. As an alternative, researchers have explored laboratory methods to estimate incidence through cross-sectional testing. If these methods prove accurate, they will offer a more rapid and cost-effective way to predict HIV infection rates.

One of the new methods is called the BED assay ("BED" refers to HIV-1 subtypes B, E, and D). The BED assay is based on the observation that HIV antibody levels increase with the duration of infection. By measuring the amount of HIV-specific antibody, researchers can estimate how long someone has been infected. But the BED assay is affected by variability within a population as well as by host and viral factors that influence the production of antibodies.[2]

To achieve an accurate BED assay, researchers must establish the "false-recent" rate within

1 HIV incidence is the number of new HIV infections in a specific population during a specific period.

2 People with long-term infections or AIDS may experience a drop in antibody titer. Effective HIV treatment may also lead to a decrease in antibody response. As a result, assays mistakenly label 5 percent to 20 percent of long-term infections as recent. This leads researchers to overestimate incidence.

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a population, by testing blood samples from HIV-positive people with long-term infections (greater than 12 months). Researchers can then incorporate the false-recent rate in their BED incidence calculation as a correction factor.

FHI scientists will evaluate the performance of the BED assay at six sites.[3] We will compare the results of the cross-sectionally derived incidence with HIV incidence in a prospective cohort, allowing for a direct comparison of the two methods within the same study population.

DESIGN OF THE SIDI COMBINED INCIDENCE STUDY

The combined HIV incidence study will measure incidence in two ways among populations of women at risk for infection.

- *Cross-sectional phase:* We will test approximately 2,000 sexually active women. Prevalence data gleaned from this phase will help us to determine the accuracy of the BED method for estimating HIV incidence.
- *BED false-recent phase:* We will test a separate group of 400 HIV-positive men and women with established (>1 year) HIV infection and use this information to correct the HIV incidence estimate suggested by the cross-sectional prevalence data.
- *Prospective phase:* We will follow and test approximately 400 sexually active, HIV-negative women for at least six months to measure HIV incidence. We will identify these women from among those we test in the cross-sectional phase and find to be free of HIV.

STUDY OBJECTIVES

Primary objectives

- Estimate HIV incidence in a group of women with multiple risk factors for HIV by using a cross-sectional method
- Determine the percentage of BED false-recent samples by testing the HIV antibodies of people with long-term infections, in order to assure a more accurate cross-sectional incidence estimate
- Compare the prospectively measured HIV incidence with the cross-sectional estimate

Secondary objectives

- Demonstrate each site's capacity to recruit and retain participants at higher risk for HIV
- Measure the incidence of pregnancy during follow-up of the prospective cohort
- Describe the epidemiological characteristics of the screened population, of the participants enrolled in the study, and of those followed in the prospective phase
- Identify the local risk factors for infection

We will also evaluate a novel laboratory device—the SMARTube—that detects acute HIV infections in blood samples. Acute infections are typified by high viral loads, which may be associated with a higher rate of viral transmission during the early stages of an infection. The ability to detect infections soon after they occur—and before ordinary tests can detect them—would have enormous public health benefits.

The SMARTube, a product of SMART Biotech, Ltd., is designed to stimulate the immune system to produce HIV antibodies more quickly than normal, so an infection can be detected sooner. The device is simple to use, requires minimal equipment, and is suitable for resource-poor settings. The combined incidence study will assess the usefulness of the SMARTube in diverse settings.

The results of these studies should be available from several sites by mid-2010.

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3 Combined HIV incidence studies are under way in Ho Chi Minh City, Vietnam, and Rustenburg and Bloemfontein, South Africa. Additional studies will commence later in 2009 in Addis Ababa, Ethiopia, and Beira and Chokwe, Mozambique.