

With No Magic Bullet, Researchers Examine One-Two Punch against HIV Acute Infection

Program: Study of a behavioral and biomedical treatment intervention during acute HIV infection

Researchers: William Miller, M.D., Ph.D, and Audrey Pettifor, Ph.D., of the University of North Carolina's Institute for Global Health & Infectious Diseases

Mission: Testing efficacy of a new acute infection diagnostic and studying implications of immediate short-term ARV treatment during the early stages of HIV infection

Funding: \$3.5 million grant from the National Institutes of Health

Policy Challenge: Finding the best combination approaches to HIV prevention in the absence of a "magic bullet," such as an AIDS vaccine

If there's one thing scientists can safely conclude about HIV/AIDS after nearly three decades of research, it's that there is no single "magic bullet" on the horizon to prevent this deadly disease. Until a safe, effective vaccine hits the pipeline, a whole cache of medical weapons will be needed to curb HIV transmission.

That is the driving philosophy behind an innovative new study designed by two scientists at the University of North Carolina's Institute for Global Health & Infectious

Diseases. Funded by the National Institutes of Health and led by co-principal investigators William Miller, MD, Ph.D, and Audrey Pettifor, Ph.D., the study will examine the impact of treating HIV at the earliest stage of infection with a one-two punch of behavioral counseling and biomedical intervention.

Coming as a thorny debate unfolds over whether to initiate HIV therapy earlier, this project will tackle some of the most difficult and provocative questions in AIDS research: Is immediate ARV treatment an effective and worthwhile approach to reduce HIV transmission? Can this early treatment provide a strong public health benefit?

To make sure they do not cause harm to the study participants, they will also examine how aggressive, early treatment might alter the course of infection over the long term and whether early treatment has any implications on drug resistance.

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The underlying hypothesis of the \$3.5 million study is that people with acute HIV infection—which starts with initial transmission of the virus and lasts for up to 12 weeks—are significant drivers of the epidemic, especially in sub-Saharan Africa. During that initial 12 week period, the virus replicates quickly and the probability of transmission is very high, but a standard HIV test cannot detect any HIV antibodies, explains Dr. Miller, a professor of medicine and epidemiology at UNC.

"If someone is tested when they are acutely infected, in most of the world, those people would be told they are HIV negative and told to be retested in 3 to 6 months," Dr. Miller says. "Many, many people never come back And that window is important because during this acute phase, they have very high viral loads and are at risk of transmitting to others."

Estimates vary widely on what percentage of new infections are attributable to transmission during the acute stage, but one study conducted in Rakai, Uganda found that about half of new infections incurred through vaginal sex occurred during acute infection. Data also indicate that during the acute infection phase, individuals are approximately 10 times more likely to transmit the virus as those with chronic infection.

The most common diagnostic tool in the developed world for identifying acute infection is the polymerase chain reaction (PCR) test, but its cost and complexity make unfeasible in resource-poor settings. That is the first problem the UNC study is designed to address.

Miller and Pettifor plan to screen 1,000 patients at two clinics in Malawi with a new rapid test that can detect HIV at the acute stage but that has not been fully validated yet. If they confirm that the new diagnostic, developed by Inverness, is effective, they will move forward with it during the second phase of the study: identifying 90 patients with acute HIV and dividing them into three research groups.

The first will receive standard counseling for HIV-positive patients, with some additional information about acute HIV infection being a period of high risk for transmission. The second group will get a more comprehensive behavioral intervention, with three counseling sessions in the first week aimed at empowering patients to make wise decisions about sexual activity and specific instructions to avoid sex or use a condom during the acute period, plus follow-up sessions at a later stage of the acute infection window. The third group will get that same behavioral counseling, plus immediate ARV therapy.

“This treatment is really geared towards trying to reduce the viral load quickly, so if they do have intercourse, they are less likely to transmit,” says Miller. “And a big chunk of what we’ll be measuring is how quickly the viral load comes down when you treat and where the viral load ends up.”

Miller notes that an HIV-positive patient’s viral load will eventually come down even without treatment, as part of the virus’s natural course of replication and the body’s subsequent immune response. This study will help HIV/AIDS physician-scientists understand how immediate treatment alters that process. The researchers will stop the ARV therapy once the acute infection period is over, when a patient’s viral load would be normalizing on its own.



William Miller, MD, Ph.D., and Audrey Pettifor, Ph.D.
Photo Courtesy of UNC

Dr. Miller and Pettifor will then follow patients to see if their viral load rebounds and if it does, whether it goes higher than the two control groups—in other words, whether it goes higher than it would have without treatment. They will also examine drug resistance, addressing questions about whether a short-term treatment intervention during acute infection could limit ARV options down the line.

Dr. Miller estimates that they will have to screen several thousand patients to find their 90 acute HIV infected participants; this is a four-year pilot project, and a major portion of the grant will be used to take the study data and do mathematical modeling to project potential impacts to a larger population. If the results are promising, Miller and Pettifor will try to proceed with a large scale, longer-term study.

The larger questions the study aims to answer have already put Dr. Miller and his colleagues in the middle of hot-button policy debate about the potential for immediate ARV therapy—and the cost of such a move. Mead Over, an economist with the Center for Global Development, a Washington think tank, described the study inaccurately in a blog post that raised questions about whether it’s feasible to put millions more HIV-positive patients in poor countries on ARV therapy.

Miller noted that his study is limited to probing the potential impact of 12 weeks of immediate treatment—not long-term ARV therapy—and a very narrow set of questions stemming from acute infection. But he still hopes it will inject some sound science into an important policy debate.

For one thing, even if only the first part of the study is successful—proving the efficacy of the Inverness diagnostic—Dr. Miller says that will be a “great advance” because it’s relatively inexpensive, could become widely available in the developing world, and will get people an accurate and immediate answer about their HIV status. Right now, thousands of HIV-positive patients are lost, sometimes forever, at a critical moment because of inadequate or expensive diagnostic tools.

Moreover, if they discover that the behavioral intervention works well, “then you could not have to worry about treating acute infection,” Dr. Miller says. “But the likelihood is that behavioral intervention will get you part way there, and the treatment will get you the rest of the way.”

Regardless of the results of this study, Dr. Miller says the policy and program implications for combating global AIDS are clear: funding agencies and implementers need to try novel, multi-pronged strategies to combat this confounding virus.

“The idea is there is not likely to be one single intervention that’s the magic bullet” to stop HIV/AIDS, says Dr. Miller. “We just have to be open to trying new and innovative prevention efforts that combine different strategies that are interdisciplinary and integrative.”