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Scientists See Breakthrough in the Global AIDS Battle

By MARK SCHOOFS



A new study reveals a major breakthrough in AIDS prevention. Kelsey Hubbard talks with WSJ's Mark Schoofs about the success of antiretroviral drugs in reducing the transmission of the HIV virus in heterosexual couples.

In a landmark finding that scientists say could help stem the global AIDS pandemic, researchers announced Thursday that treating HIV patients with AIDS drugs makes them strikingly less infectious.

The results were so overwhelming that an independent panel monitoring the research recommended they be released four years before the large, multicountry study had been scheduled to end.

Epidemic Update



"I was bowled over," said Salim Abdool Karim, an AIDS researcher and professor at the University of KwaZulu-Natal in South Africa who wasn't involved in the study but was briefed on its results. "If we can implement this," he said, "we have a real chance to turn the tide on the HIV epidemic."

The randomized trial of 1,763 couples—in which one partner had HIV and the other didn't—confirms a growing body of less rigorous research and is likely to inject new urgency into treatment campaigns, especially in Africa, home to two thirds of the more than 33

See data on AIDS deaths, new infections and the number of people world-wide living with the disease.

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million people estimated to have HIV world-wide. There, a global effort now under way to treat millions of patients with antiretroviral drugs could have the added benefit of slowing the spread of HIV. AIDS workers have dubbed this "treatment as prevention."

The \$73 million study, conducted in nine countries, was funded by the National Institutes of Health and led by Myron Cohen, director of the Institute for Global Health and Infectious Diseases at the University of North Carolina at Chapel Hill.

The hopeful results come at a potential turning point in the epidemic, almost 30 years to the day after the disease was identified among five homosexual men in Los Angeles. A vaccine remains the holy grail of AIDS prevention research. But a combination of new and emerging HIV prevention methods have convinced many leading AIDS experts that they can dramatically constrict the torrent of new infections. In 2009, 2.6 million people were newly infected with HIV, according to United Nations estimates.



Dominic Nahr for The Wall Street

Ugandan women infected with HIV hold their babies at a clinic in 2009. Females account for about 60% of HIV cases in sub-Saharan Africa, the U.N. says.

"Although it is still important to develop an HIV vaccine," said Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, "we have significant tools already at our disposal that can make a major impact on the trajectory of this epidemic."

Along with treating HIV patients to render them less infectious, the main prevention tools for Africa are male circumcision, which reduces the odds a man will acquire HIV, and a virus-blocking "microbicide" gel that women apply vaginally.

Each has received considerable attention, though usually as a stand-alone intervention. But it is the deployment of all of them—added to behavioral methods such as condom promotion and limiting one's sexual partners—that could finally curb the epidemic. Dr. Fauci calls it "combination prevention" and said it

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has been "dominating my thinking lately."

Thursday's results are likely to end, or at least diminish, a bitter feud within the AIDS world over how much funding should go to treatment versus prevention. In recent years, many experts argued that more emphasis should be put on prevention, but the new study now provides evidence that treatment can function as prevention.

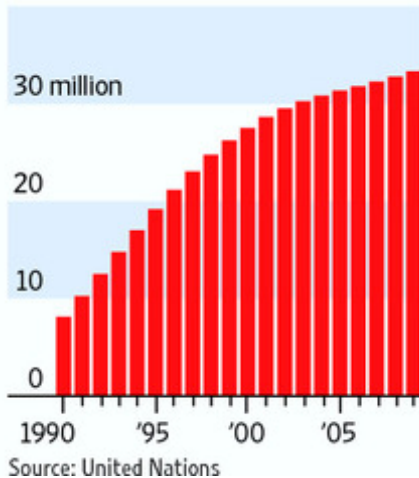
Funding will be a major obstacle. The global community has been struggling to come up with enough funds to treat those with advanced AIDS symptoms—let alone those at earlier stages of the disease. From 2008 to 2009, overall spending against the epidemic in low- and middle-income countries stayed virtually flat, at a little under \$16 billion annually, according to estimates prepared by the Joint United Nations Programme on HIV/AIDS and the Kaiser Family Foundation.

At the end of 2009 more than five million people were on treatment—but another 10 million needed the drugs, according to UNAIDS, and the funding shortfall was estimated at more than \$7.5 billion. Antiretroviral drugs don't cure AIDS, but merely keep it in check. So the pills must be taken every day for life.

Still, treatment has one financial advantage: "It's basically free

Growing Epidemic

People living with HIV



in terms of a prevention impact, because we're talking about treating people who need treatment anyway," said David Barr, a veteran AIDS advocate.

Another obstacle: the difficulty of implementing programs, especially in impoverished settings with tattered health-care systems, poor education and other challenges.

The study announced Thursday involved couples, 97% of whom were heterosexual. The HIV-infected partners started off with a moderately healthy immune system.

About half of the couples were randomly assigned so that the infected partner went on antiretroviral drugs right away. In the other couples, the infected partner waited to start treatment until later in the course of the disease, a common practice in many countries. All participants were counseled on how to protect against HIV transmission and were given free

condoms and other prevention services.

In the group that waited to start treatment, 27 infections occurred in which the virus was genetically linked to the infected partner. All of those infections occurred when the patient wasn't yet taking antiretroviral drugs.

In the group that started treatment right away, only one genetically linked infection occurred.

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Comparing the two rates of infection, patients taking antiretroviral drugs were 96.3% less likely to pass on the virus.

Because almost all couples in the study were heterosexual, the new findings don't apply to homosexual couples, researchers cautioned.

"Most authorities would still recommend use of other preventive methods such as condoms," even if the HIV-positive sexual partner is on antiretroviral treatment, Kevin De Cock, director of the Center for Global Health at the U.S. Centers for Disease Control and Prevention, wrote in an email. The study is new, and he said CDC hasn't issued guidance on the prevention benefit of

antiretroviral therapy.

The researchers learned the results on April 28 and cautioned they are still analyzing the data. Study subjects who aren't yet on treatment are being offered antiretroviral drugs.

Beyond reducing transmission, starting treatment right away appeared better for the health of patients. For example, compared to those who delayed therapy, those who went on drugs immediately were less likely to contract a type of tuberculosis that occurs outside the lungs.

Patients on antiretroviral medication are less infectious because the drugs sharply suppress the amount of HIV in the body, meaning people on treatment have less virus to transmit.

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places have measured what they call "community viral load," or the amount of virus in all known HIV-positive people in those cities. As more individuals go onto antiretroviral therapy, the total amount of virus in the community falls, reducing the overall danger. "If someone slips up and makes a bad decision because they're in love or drunk or whatever, each individual act is less risky," explains Moupali Das, director of research in the HIV prevention section of the San Francisco Department of Public Health. Indeed, the Vancouver and San Francisco research suggests that as the amount of HIV in a community drops, so too does the rate of new infections.

Treatment as prevention has long been debated. But only in the past couple of years has the evidence convinced a critical mass of AIDS scientists that it can play a major role in curtailing the epidemic.

That evidence helped persuade China, the world's most populous country, to change its AIDS strategy earlier this year, according to Zunyou Wu, director of AIDS control efforts at the Chinese Center for Disease Control and Prevention.

He said that China is intensifying its efforts to locate people with the virus so that they can be put on treatment for their own sake and to render them less infectious. Local health officials will no longer be evaluated on how many people they merely test for HIV, but rather on how many HIV-positive people they actually identify, said Dr. Wu. All those with HIV who meet China's treatment guidelines will be offered free antiretroviral drugs, he said, adding that China expects enrolling more people into treatment will slow the spread of the epidemic.

There are potential pitfalls to applying treatment as prevention in the real world. To prevent transmission, infected people must rigorously adhere to their pill-taking regimen, which can cause side effects.



Another problem is people who are newly infected. They are considered extremely infectious, because they typically have massive amounts of the virus.

But it's hard to identify people who just got infected—and if these highly infectious people can't be found, they can't be treated. Dr. Cohen, lead investigator of Thursday's study, believes this is a potentially gaping loophole.

In short, treating infected people likely isn't a panacea that can squelch the epidemic on its own.

But in recent years, there have been other breakthroughs. From 2005-2007, three large, randomized, controlled clinical trials in different parts of Africa all showed that circumcision reduces the chance a man will acquire HIV by about 60%.

Unlike treatment, which requires patients to adhere to a daily regimen, circumcision is a one-time intervention—a surgical vaccine, some call it.

A U.S. government study looked at 14 African countries and estimated that widespread circumcision could avert more than a fifth of adult infections that would have occurred by 2025.

Still, "circumcision is not going to do it alone," said Dr. Fauci. "Fifty percent of the world is women." And females account for about 60% of HIV cases in sub-Saharan Africa, according to U.N. figures.

Last year, a placebo-controlled study showed that a vaginal gel containing the AIDS drug tenofovir reduced the chance a woman would contract HIV by 39%. Among women who used it consistently, the gel more than halved the chance they would get infected.

"What's been missing is that we are just not able to protect young women," said Dr. Abdool Karim, one of the lead investigators of the gel trial. Indeed, women often can't make their male partners wear a condom.

A second, confirmatory trial is needed to approve a gel for general use. But work has already begun on more convenient products, such as vaginal rings that would dispense the virus-blocking drug for a month or more.

—Betsy McKay contributed to this article.

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