

BREAKTHROUGH OF THE YEAR

HIV Treatment as Prevention

On 1 December, George Washington University in Washington, D.C., hosted “The Beginning of the End of AIDS,” a splashy World AIDS Day event that featured three U.S. presidents, business magnates, and rock stars. The catalyst that brought them together was something Anthony Fauci, the top U.S. government HIV/AIDS scientist, told the crowd even 1 year ago would have seemed “wishful thinking”: a clinical trial dubbed HPTN 052 and its “astounding” result.

HIV/AIDS researchers have long debated whether antiretroviral drugs (ARVs) used to treat HIV-infected people might have a double benefit and cut transmission rates. To some it was obvious: ARVs reduce HIV levels, so individuals should be less infectious. Skeptics contended that this was unproven. Indeed, a consensus statement issued by the Swiss Federal Commission for HIV/AIDS in 2008 that said effective ARV

to which the viral load in blood predicts the risk of HIV transmission,” they cautioned.

Then in May of this year, the 052 clinical trial conducted by the HIV Prevention Trials Network reported that ARVs reduced the risk of heterosexual transmission by 96%. “Now we have absolute, confirmed data,” said Fauci at an AIDS conference this summer in Rome where researchers first presented the HPTN 052 data in detail. Fauci, who heads the U.S. National Institute of Allergy and Infectious Diseases—the main funder of the \$73 million trial—said the challenge now was to apply the results. “We just need to take that data and run with it,” he said. “The idea of the tension between treatment and prevention, we should just forget about it and just put it behind us, because treatment is prevention.” Because of HPTN 052’s profound

implications for the future response to the AIDS epidemic, *Science* has chosen it as its Breakthrough of the Year.

Myron Cohen, an HIV/AIDS researcher at the University of North Carolina, Chapel Hill, who heads the ongoing HPTN 052 trial, said the finding’s impact surprised him. “People were interested in the idea of treatment as prevention, but it created a hurricane-force wind behind the strategy,” Cohen says. “The result was so unambiguous.”

As Cohen and colleagues explained in the 11 August *New England Journal of Medicine*, HPTN 052 enrolled 1763 “discordant” couples in which one person at the study’s start had a known HIV infection. The infected partner

could not be taking ARVs and had to have between 350 and 550 CD4 cells per milliliter, which indicates that the person had some immune damage but had yet to develop AIDS (defined as fewer than 200 CD4s). Five countries in sub-Saharan Africa participated, as did Brazil, India, Thailand, and the United States. The study randomly assigned half the infected people to start ARVs immediately, while the other half delayed treatment until CD4 counts dropped below 250.

The researchers planned to compare the groups until 2015. But on 28 April, an independent monitoring board that periodically reviewed the data stunned Cohen and his collaborators when it recommended that the results of the trial be made public as soon as possible. Of the 28 people who become infected with HIV that genetically matched the viruses in their long-term partners, only one was in the early treatment group—which also experienced 41% fewer serious health problems associated with HIV. Infected people in the delayed arm of the study were offered ARVs immediately.

The HPTN 052 results and other recent successes have raised hopes that combining such interventions can now end AIDS epidemics in entire countries, if not the world. ARVs are not a vaccine:

People must take them for decades, which is difficult to do and costly. But many call HPTN 052 a “game changer” because of its near 100% efficacy. “It has had an impact on our vision for the future,” says Françoise Barré-Sinoussi, a virologist at the Pasteur Institute in Paris who shared the Nobel Prize for helping to discover HIV. Researchers must continue—and even intensify—efforts to develop an effective AIDS vaccine and cure, Barré-Sinoussi stresses, but she notes that countries can apply treatment as prevention today.

Julio Montaner, a prominent advocate of the strategy at the University of British Columbia, Vancouver, in Canada says HPTN 052 has persuaded leaders such as U.S. President Barack Obama—whose administration recently announced a policy goal of creating “an AIDS-free generation”—to take action. “Clinicians and policymakers are always asking for the ultimate evidence,” Montaner says. “HPTN 052 was the unequivocal piece of the puzzle to close any doubts.”

Given resource constraints and logistical hurdles, treatment as prevention isn’t going to sweep the world anytime soon. But HPTN 052 has made imaginations race about the what-ifs like never before, spotlighting the scientifically probable rather than the possible. And now a growing number of HIV/AIDS experts are insisting that the irresponsible and appalling thing to do is nothing. —JON COHEN

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Double duty. This year a study proved that anti-HIV drugs both treat and prevent HIV infections.

treatment could virtually stop heterosexual transmission was denounced as “appalling,” “inconclusive and irresponsible,” “dangerous,” and “misleading.” The Joint United Nations Programme on HIV/AIDS and the World Health Organization also responded with alarm, urging people to continue using condoms and stressing that semen or vaginal secretions might harbor the virus even when blood tests showed no trace of it. “More research is needed to determine the degree

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