What If the New Experimental HIV Vaccine Cuts Risk by Only Half?

With a major new HIV vaccine trial under way, cautious optimism is stirring that the vaccine will prove effective enough for a rollout.

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By the early 2020s, the world could at last have an HIV vaccine. But before chilling the champagne to toast the news that a series of simple shots will forever wipe out HIV risk, consider that in all likelihood such a vaccine would be only partially effective. In other words, it would reduce but not eliminate the chance of contracting the virus.

What good is a vaccine that cuts HIV risk by, say, only half? Plenty. Scientists generally consider that level of efficacy the minimum threshold for rolling out an HIV vaccine on a grand scale.

At the end of 2016, the first new major HIV vaccine trial in seven years began enrollment in South Africa. The Phase IIb/III trial is slated to include 5,400 men and women and is expected to yield results in late 2020. Participants will be randomized to receive the experimental vaccine or a placebo consisting of five injections over the course of a year. Called HVTN 702, the South African trial is investigating a retooled version of the so-called RV144 HIV vaccine that in 2009 showed a modest benefit among people in Thailand.

In the Thai trial, the RV144 vaccine reduced HIV risk by 31 percent during a 3.5-year period following vaccination. This is the only HIV vaccine trial ever to produce a successful result—even a modest one. Nevertheless, scientists did not deem RV144 strong enough to move into real-world use.

As it turned out, RV144's prevention was highly front-loaded: The vaccine cut HIV risk by 60 percent during the first year, but this benefit dropped off considerably during subsequent years. So researchers have sought to adjust various components of the RV144 vaccine, including its injection schedule, to improve the vaccine's overall efficacy and extend its benefits over a greater amount of time.

The new version of the vaccine has also been reconfigured to provide protection against HIV subtype C, which is predominant in South Africa. The vaccine tested in Thailand applied to subtypes B and E, which are most prevalent there. It is unknown whether the new vaccine, if effective, will protect against other viral subtypes in addition to subtype C.

Initial results from a smaller pilot study of the retooled vaccine, presented at the 21st International AIDS Conference in Durban, South Africa, in July 2016, were encouraging. The vaccine proved safe and met various criteria to show that it stimulates the immune system.

According to Anthony S. Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID), which is sponsoring the South African trial, the efficacy of 31 percent seen in the Thai trial meant that vaccine "was not ready for prime time." However, he says, "If someone came to me and said, 'We've got a solid 50 percent [efficacy],' I would say, 'Go.'" He adds, though, that 60 percent is a more preferable minimum level of efficacy for an HIV vaccine.

As a parallel, three major randomized controlled trials published in the mid-aughts showed that circumcising men is associated with about a 60 percent reduction in the risk of female-to-male HIV transmission. This finding led a massive push to expand voluntary male medical circumcision (VMMC) in sub-Saharan Africa.

Recent research has found that the VMMC effort is already likely lowering HIV rates in the region. Additionally, scientists have not found that men who receive VMMC wind up engaging in riskier sex as a result. This finding bodes well for the prospects of widely distributing an HIV vaccine with about the same general level of efficacy, as it suggests that the recipients of such a vaccine could be properly counseled to understand that the vaccine is not foolproof but will provide a substantial benefit to the population at large nevertheless.

Another reason that an HIV vaccine doesn't have to have as high an efficacy as, for example, a measles vaccine, is that there are so many different ways to prevent HIV. While a vaccine is the only way to prevent measles, the HIV-prevention tool box includes condoms, sexual behavior modification, treatment as prevention (successfully treating the virus likely all but eliminates the risk of transmission), pre-exposure prophylaxis, or PrEP, (which is likely more than 99 percent effective) and VMMC (60 percent effective). Widespread use of all these methods can pack quite the wallop against the global pandemic. They already are: Global infection rates fell from 3.2 million in 2000 to 2.1 million in 2015 according to the World Health Organization.

"All you need is another little boost of prevention with a vaccine," says Fauci.

A recent paper published in the Proceeding of the National Academy of Sciences backs Fauci's suggestion. Using mathematical modeling, the study's authors predicted future global HIV transmission rates and found that even a 50 percent effective vaccine could be key to sending the epidemic into retreat.

Currently, an estimated 37 million people are living with HIV worldwide. Based on today's levels of HIV diagnosis and treatment, the new study's authors predict that 49 million people will contract the virus between 2015 and 2035. They also project that 25 million of these infections could be averted if the global HIV population hits key Joint United Nations Programme on HIV/AIDS (UNAIDS) targets by 2030: 95 percent are diagnosed, 95 percent of that group are on ARVs, and 95 percent of that group has an undetectable virus.

If on top of that “95-95-95” achievement, a vaccine that is 50 percent effective were rolled out starting in 2020 and gradually scaled up to immunize 70 percent of the population, this would prevent a projected additional 6.3 million new infections, the researchers predict.

Fauci says he isn’t “purely optimistic” that the newly launched South African trial will yield a vaccine as effective as 50 percent. “I would say cautiously optimistic,” he says.

Even if the vaccine were significantly effective for just five years, Fauci notes, it would still mark an important victory, considering that many people are at high risk for HIV during only a limited period in their lives.

“You don’t need to have something that lasts forever,” he says.

Additionally, if subsequent scientific efforts produced a vaccine that appeared more effective than one put into widespread use, a major clinical trial could compare its efficacy to the established vaccine, thus negating the need for a placebo. In an ideal world, such a trial would be powered not just to prove that the new vaccine had comparable effectiveness to the old one (known as a non-inferiority trial) but was in fact more effective (a superiority trial).

So hopefully, a partially effective vaccine would signal the beginning of an exciting trend that may spell an eventual end to the pandemic.
