



HVTN 706/HPX3002 (Mosaico): When “No” Still Moves Science Forward

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Today, we have more ways than ever to prevent HIV, and these tools have helped reduce new HIV infections around the world. But many HIV prevention options need to be used regularly to keep working. Vaccines are different! They have the potential to provide longer-lasting protection and, once available, can help protect entire communities, not just people who are considered to be at higher risk.

The goal of HIV prevention is to build multiple layers of protection, much like modern cars have seatbelts, airbags, and collision-warning systems. Different tools work for different people in different ways, and the more options we have, the better.

So why don't we have an HIV vaccine yet?

It's not because scientists aren't trying. Developing vaccines, or anything in science, is a process of trial and error. In science, understanding what doesn't work is often just as important as discovering what does. Every study helps researchers get one step closer to the answer. Negative results are also results!

This was the case with the **Mosaico study (HVTN 706/HPX3002)**, a large international clinical trial that tested whether a new HIV vaccine could prevent HIV infection in people at higher risk of HIV exposure.

The vaccine used a "mosaic" design, an approach created to address one of the biggest challenges in HIV vaccine development: HIV changes rapidly. Unlike viruses that remain relatively stable, HIV mutates frequently, creating many different strains around the world.

Vaccines work by training the immune system to produce proteins called antibodies, which recognize and block viruses before they can cause infection. However, if a virus changes too much, those antibodies may no longer recognize it. The mosaic vaccine was designed to overcome this challenge by combining pieces of many different HIV strains into a single vaccine, with the goal of generating antibodies capable of recognizing a broad range of HIV variants (known as broad neutralizing antibodies or bnABs).

The study enrolled nearly 3,900 adults from the United States, Latin America, and Europe. Participants were randomly assigned to receive either the experimental vaccine or a placebo (an injection without the vaccine). Neither the participants nor most of the researchers knew who received the vaccine until the study ended. Everyone in the study also received standard HIV prevention services, including HIV testing, counseling, condoms, and access to PrEP.





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Researchers then followed participants over time and compared how many people in each group acquired HIV through natural exposure. The results showed that the vaccine did not prevent HIV infection. The number of HIV infections was similar in the vaccine and placebo groups, meaning the vaccine did not provide HIV protection.

While the Mosaico trial showed that the vaccine was safe, it did not show that the vaccine could prevent HIV. But the trial still taught researchers something important. The results are helping scientists understand what future HIV vaccines may need to do differently.

The results were disappointing, but this was not a failure. Science doesn't always move in a straight line. Sometimes, learning what doesn't work is an important step toward finding what does.

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