

Another HIV vaccine has failed – so what happens next?

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Scanning electron micrograph of HIV particles infecting a human H9 T cell - National Institutes of Health/Stocktrek Images

“We hope to have a vaccine ready for testing in about two years. Yet another terrible disease is about to yield to patience, persistence and outright genius.”

So said Margaret Heckler, US Secretary of Health, on the HIV epidemic in 1984.

Yet four decades and some 40 million deaths later, the world still doesn't have a vaccine to protect against HIV.

Last week, Johnson and Johnson became the latest pharmaceutical firm to withdraw a possible contender.

The US company announced that its vaccine, the world's only candidate to have still been in late-stage trials, was ineffective.

The study, known as Mosaico, tested the shot in 3,900 men and transgender people across North America, South America and Europe. But while analysts found it was safe, the trial was halted because the vaccine did not prevent more HIV infections than a placebo.

It is yet another blow for an important area of research that has become used to disappointment.

To date, eight HIV candidate vaccines have reached late-stage clinical trials. [All have failed at the final hurdle](#), with just one showing signs of modest efficacy in a trial in Thailand between 2003 and 2006.

Johnson and Johnson was attempting to build upon the modest success of the Thai study, but in the end it just didn't work.

So why is developing a vaccine for HIV proving so difficult? After all, scientists had a jab for Covid developed and in trials within months of the virus emerging.

'With HIV, nobody has recovered'

Experts are still confident that one day they will produce a successful HIV vaccine, but they point to several formidable challenges that have yet to be overcome.

Perhaps most notably, there's no "roadmap in nature" for scientists to copy or enhance.

"When we get measles, we recover from measles and there's an immune response that our body mounts, [and we can design a vaccine] that copies that response," said Professor Salim Abdool Karim, director of Centre for the Aids Programme of Research in South Africa.

"With HIV, nobody has recovered. There's no immune response that is naturally occurring. Nature doesn't have anything for us to copy."

He added that when Sars-Cov-2 emerged, earlier research into the first Sars outbreak had already identified what component of a coronavirus should be targeted – the so-called 'spike protein'. But this is not the case with HIV.

"Even though we have the technology to make a vaccine, we don't know what [part of the virus] it needs to make," Prof Karim said.

The HIV virus also lurks in chromosome CD4 cells, where it's not easily visible to the immune system," said Tomáš Hanke, a professor of vaccine immunology at Oxford University, who has been working on HIV vaccines for 30 years.

He added that the genetic composition of the pathogen also changes rapidly – far more quickly than Sars-Cov-2, the Covid virus. This means that by the time you have created a vaccine for fighting it, the virus may have already moved on.

And finally, said Prof Karim, there is no reliable animal model that can work as a basis for HIV virus research.

"We have got these real problems which make an HIV vaccine so, so difficult," he said.

But optimism remains.

"[The latest setback] is disappointing, but the positive thing is that we have learned," said Prof Hanke. "[The Johnson and Johnson vaccine] was designed several years ago, when perhaps we knew less. But the trial confirmed that some ways of using T cells and antibodies are just not working, and we have a good idea how to improve."

In 2010, scientists made a possible breakthrough when they found people who produce antibodies that work across a broad range of targets – called 'Broadly neutralising Antibodies' or bNAbs.

Normally HIV antibodies are strain specific, so are beaten by quick viral evolution. But bNAbs seem to work against many strains all at once.

"The idea is that maybe if you can create a vaccine that generates a broadly neutralising antibody, maybe that will work," said Prof Karim, who's part of a project to develop one such antibody, called CAP256.

Meanwhile, Prof Hanke's team at Oxford University – who are using the same technology that formed the backbone of the AstraZeneca Covid jab – are targeting T cells.

He suspects that any effective vaccine will actually be a multi-dose shot – with different doses using different approaches to trigger a broad, robust immune response.

He says he is optimistic about “positive signals” from several vaccine candidates currently in laboratory-based phase one and two trials.

“The scientific process is slow for a difficult infection,” he said. “But if the vaccines that we have in our hands today do something useful, we will know in five years.”

Prof Hanke added that some of the experiences of the Covid pandemic, including the advance of technology such as mRNA, could also help in the development of HIV vaccines – with adequate funding and focus.

“From every trial, from every failure, we learn – we design the next one based on our experience and results... Eight efficacy trials have failed in the HIV field over 40 years, but there were 35 efficacy trials for Sars-Cov-2 in the first year of the pandemic. Do you see the difference?”

“We need a new incentive to stick with HIV vaccine development.”

Thankfully, there have been significant breakthroughs over the years in combating HIV through other means beyond vaccination, helping turn the virus from a death sentence, as it was in the 80s and early 90s, into a manageable disease.

Pre-exposure prophylaxis, or PrEP, can be taken by people at risk of the virus in advance of any potential exposure, while antiretrovirals reduce the amount of HIV in the bloodstream to undetectable levels among those infected.

Condoms remain an important form of protection and in more recent years, an antiretroviral-infused vaginal ring has proven effective at lowering women’s risk of HIV infection.

“The disappointment of the vaccine trial further underlines the importance of rolling out available HIV treatment and prevention innovations,” said Winnie Byanyima, executive director of UNAIDS.

“The search for a vaccine must continue, but it’s important to remember that despite this setback the world can still end Aids by 2030 by delivering all the proven prevention and treatment options to all the people who need them.”

Nonetheless, Prof Hanke believes a vaccine will still be “a key component of any package which truly ends the HIV pandemic”. But unlike Margaret Heckler, he won’t be making any predictions on when this day comes.