FEATURE

These 4 Covid-19 Vaccines Are Closest to Becoming Reality

There are hundreds of trials currently in the works. Here's everything you need to know about the ones edging ahead in the global race.

This story originally appeared on WIRED UK.
https://www.wired.com/story/these-4-covid-19-vaccines-are-closest-to-becoming-reality/

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AS THE WORLD waits eagerly for a Covid-19 vaccine, several candidates are starting to be put through their paces in clinical trials. More than 100 vaccine candidates are being developed by teams around the world, with more than 20 now in or about to enter clinical evaluation, meaning they are being tested in humans.

"When the world got the virus [RNA] sequence through on January 11, we knew pretty well immediately what kind of vaccine one would need and what bit of virus you would need to put in it, so the world of immunology was in a very good state to get going on that," says Danny Altmann, a professor of immunology at Imperial College London.

On July 20, two vaccine candidates published preliminary results from Phase I and II trials showing they induced an immune response and didn't trigger any major safety concerns, marking a positive step forward. But there's still a way to go. Inducing an immune response doesn't necessarily mean that the vaccine will actually protect people from Covid-19. Only a Phase III trial, which involves giving a large number of people the vaccine and tracking if they get the disease, will show this. "They've done everything we wanted, so that's good news," Altmann says. "Now it's the difficult bit."

The vaccine candidates currently in development make use of a range of different vaccine technology platforms, some of which are tried-and-tested and others that are really cutting-edge. While some first results have started to come out, it's not possible to draw direct comparisons, as different labs can test with different doses and populations, and use different assays to measure the immune response. "The question of which one is better cannot be

answered at this point," says Beate Kampmann, director of the Vaccine Centre at the London School of Hygiene and Tropical Medicine.

With that in mind, here are some of the vaccine candidates that are currently furthest along:

Oxford/AstraZeneca

The world has heard a lot about a vaccine being developed at the University of Oxford in partnership with the pharmaceutical firm AstraZeneca. The UK government has already ordered 100 million doses of the vaccine, and it is currently one of the front-runners in terms of testing.

The Oxford vaccine is a viral vector vaccine: It is based on a chimp adenovirus (a virus that causes an illness like the common cold in chimpanzees), which has been modified to contain a genetic sequence of the coronavirus "spike protein," which is thought to play a large role in infecting cells. This is a way of exposing the body to the spike protein without exposing it to coronavirus, so that it creates an immune response. "The chimp adenovirus is kind of the Trojan horse to bring the Covid protein information into the immune system," Kampmann explains. If the immune system then comes into contact with the actual coronavirus, it's primed to react.

On July 20, researchers published a preliminary report in *The Lancet* on Phase I and II studies of their vaccine, ChAdOx1 nCoV-19, which they report induced an immune response and didn't have any major side effects. It is now moving into Phase III trials in Brazil and South Africa.

Altmann says the immune response shown in the Oxford data is promising and emphasizes the importance of triggering T cells as well as antibodies. T cells are a type of white blood cell that help B cells create antibodies and kill infected cells to help stop an infection from spreading. "For any good response from a vaccine, you need both on board," Altmann says. He says that all the data he has seen from vaccine candidates looks good for both—"although I thought the Oxford data had really truly impressive T cell data."

CanSino

China's CanSino Biologics reported results from its Phase II trial, which was conducted in Wuhan, on the same day as the Oxford group, also in *The Lancet*. It similarly reported that its vaccine was safe and induced a significant immune response.

The CanSino vaccine, which is being developed with the Beijing Institute of Biotechnology, also uses an adenovirus as a viral vector to deliver the coronavirus spike protein, but in this case it is a common cold virus that infects humans. One potential downside to this, Kampmann says, is that, as the virus circulates in human populations, some people may already have antibodies to it, which could affect the immune response. "It could be that people with preexisting antibodies against that adenovirus won't make as much of an immune response to the adenovirus Covid vaccine," she says.

The vaccine has been approved for use by the Chinese military.

Moderna

The US company Moderna is one of several groups working on an RNA vaccine, a new type of vaccine that involves making a synthetic version of the coronavirus spike protein's RNA—the genetic instructions that tell cells how to make the protein. This tricks the body into making the spike protein itself, which induces an immune response.

On July 14, preliminary results from a Phase II trial of the Moderna vaccine were published in The New England Journal of Medicine and stated that the vaccine had induced an immune response and raised no major safety concerns. Moderna began Phase III trials on Monday.

The advantage to the RNA approach is that you don't have to make lots of material, as

the body essentially creates the vaccine itself. This could make it easier to scale and cheaper to produce. “You can get away with very, very small quantities,” Kampmann says. However, it is relatively new in the world of vaccine technology; no RNA vaccine has previously been licensed.

Other groups working on RNA vaccines include Imperial College London and the German company BioNTech; the latter is working with pharma giant Pfizer and has an agreement with the UK government to supply 30 million doses.

Sinovac

Beijing-based Sinovac Biotech’s vaccine candidate, called CoronaVac, is an inactivated vaccine—a comparatively old-fashioned type of vaccine that consists of virus particles that have been killed or inactivated and so no longer cause infection. The immune system still recognizes the virus, provoking an immune response that it can call upon if the recipient later comes into contact with the real thing.

In June, the company said in a press release that preliminary results from its Phase I and II studies in humans showed that the vaccine induced neutralizing antibodies and had no severe side effects. It is now moving on to Phase III studies in Brazil.

One advantage of the inactivated virus approach, says Altmann, is that it is tried and tested; the same technique has been used for decades to make vaccines to protect against diseases such as polio. “I like that logic,” Altmann says. This also means we already have the infrastructure to make this kind of vaccine.

A disadvantage, however, is that making the vaccine requires growing the material in vast quantities, which may make it harder to scale than other vaccine types—an important consideration given the scope and urgency of demand for a Covid-19 vaccine.

China’s SinoPharm is also developing an inactivated vaccine and is conducting a Phase III trial in Abu Dhabi.

A Long Way to Go

There are of course many other vaccines being worked on, and picturing the quest for a Covid vaccine as a “race” may be misleading. “This isn't actually a quick sprint, this is a marathon,” Kampmann says.

Being first doesn’t necessarily mean being best, and there are other issues beyond just making a vaccine that works. We will need to manufacture and distribute the vaccine at great scale, and we won’t know how long a vaccine protects a person from Covid-19 until later down the line. A vaccine that takes longer to develop may prove more effective, longer-lasting, cheaper, or easier to scale. Or different vaccines may prove more effective in different geographies or age groups. “It might well be there’s going to be more than one vaccine,” Kampmann says. “I would be very surprised if there was only one vaccine that came through.”

For now, Altmann says, it’s important to invest in lots of different platforms and candidates rather than put all our eggs in one basket in a rush to back a single “winner.” “It’s an argument for trying to be slow and wise and careful, and not jumping at it as if it was the Eurovision Song Contest of vaccines,” he says.

This story originally appeared on WIRED UK.