

Vaccines and SARS-CoV2

Your questions answered?

Koleka Mlisana, Elizabeth Mayne and
Melinda Suchard

1. What is a vaccine

- Any preparation which acts to induce or confer artificial immunity to a disease or substance.
- Vaccines stimulate the body to produce a response to pathogens
- Vaccines have been called the greatest public health intervention of all time



2. What do we want a vaccine to do?

- Control – reduction of disease morbidity or mortality in a defined geographical region
- Elimination – reduction of incidence of disease or a specific infection to 0 in a specific geographic area
- Eradication – reduction of worldwide incidence to 0 so that deliberate intervention is no longer requires

3. How do we assess if a vaccine has worked?

- Immunogenicity – does the vaccine elicit (cause) an immune response i.e. does the body make a response to the vaccine
- Efficacy – under ideal conditions with ideal laboratory monitoring, does the vaccine work (often part of a clinical trial)
- Effectiveness – in the real world, does the vaccine work

4. What are the different types of vaccines ?

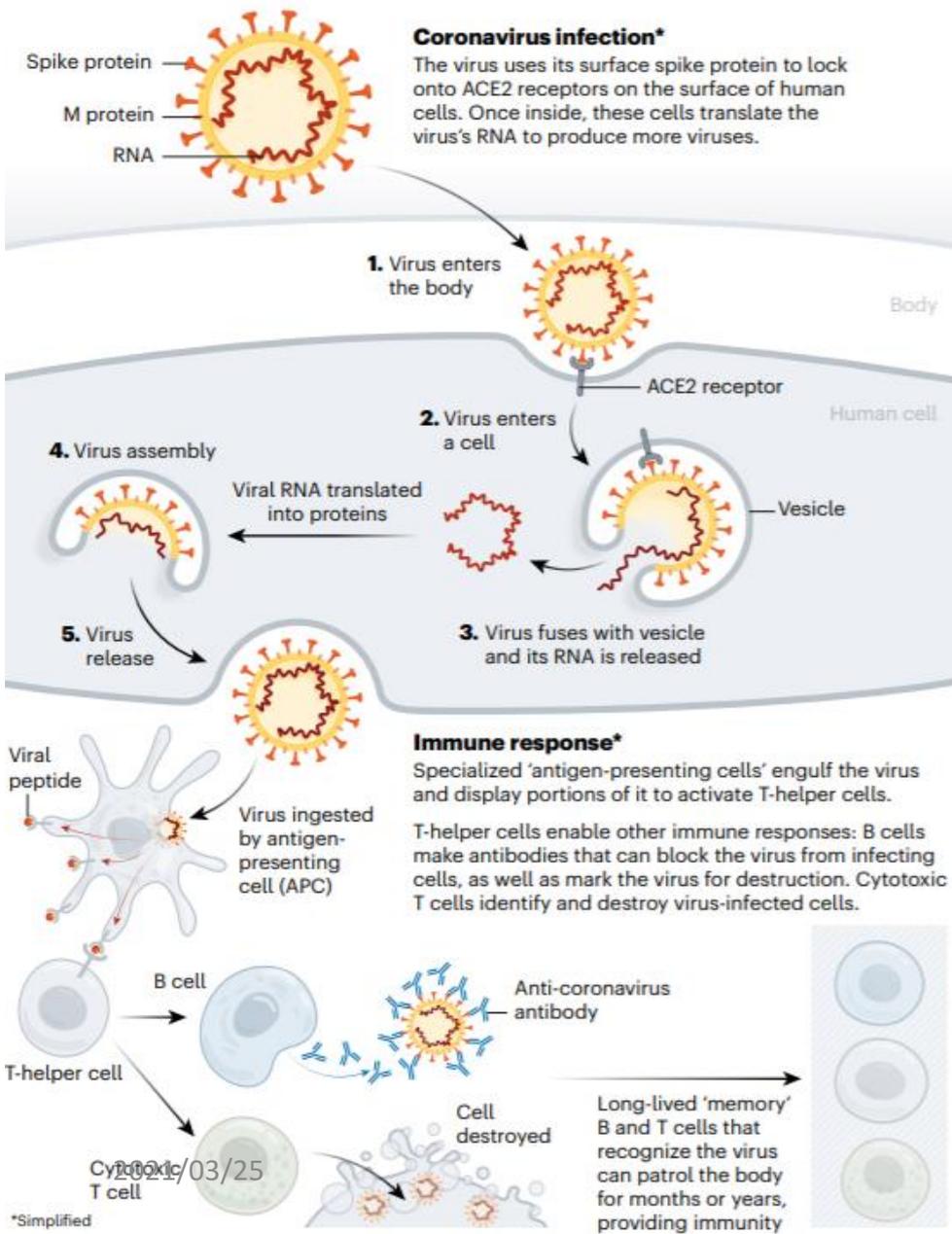
- Subunit vaccines
 - These consist of components of a microbe. These subcomponents are often virulence factors e.g. acellular pertussis (against whooping cough)
- Live attenuated vaccines
 - These are organisms which have been weakened (attenuated) to reduce the chance that they will cause disease e.g. polio, BCG (against polio and TB)
- Killed organism vaccines
 - The organism is killed and this is injected
- DNA and RNA vaccines:
 - DNA and RNA nucleic acids are introduced which allow the cells of the body to make proteins associated with the organism

DNA vaccines

- If you need to improve response to an intracellular pathogen, you need to ensure that peptides are presented effectively
- This presentation needs to occur through MHC1 or stimulate a Th1 response
- The idea with a DNA vaccine is to ensure that viral associated peptides are transcribed as part of cellular replication

VACCINE BASICS: HOW WE DEVELOP IMMUNITY

The body's adaptive immune system can learn to recognize new, invading pathogens, such as the coronavirus SARS-CoV-2.



Vaccine Basics

- All vaccines aim to expose the body to an antigen that won't cause disease but will provoke an immune response that can block or kill the virus if a person becomes infected.
- Vaccines teach the body how to defend itself when microorganisms invade it.

VIRAL-VECTOR VACCINES

Around 25 groups say they are working on viral-vector vaccines. A virus such as measles or adenovirus is genetically engineered so that it can produce coronavirus proteins in the body. These viruses are weakened so they cannot cause disease. There are two types: those that can still replicate within cells and those that cannot because key genes have been disabled.

Replicating viral vector (such as weakened measles)

The newly approved Ebola vaccine is an example of a viral-vector vaccine that replicates within cells. Such vaccines tend to be safe and provoke a strong immune response. Existing immunity to the vector could blunt the vaccine's effectiveness, however.

Non-replicating viral vector (such as adenovirus)

No licensed vaccines use this method, but they have a long history in gene therapy. Booster shots can be needed to induce long-lasting immunity. US-based drug giant Johnson & Johnson is working on this approach.

PROTEIN-BASED VACCINES

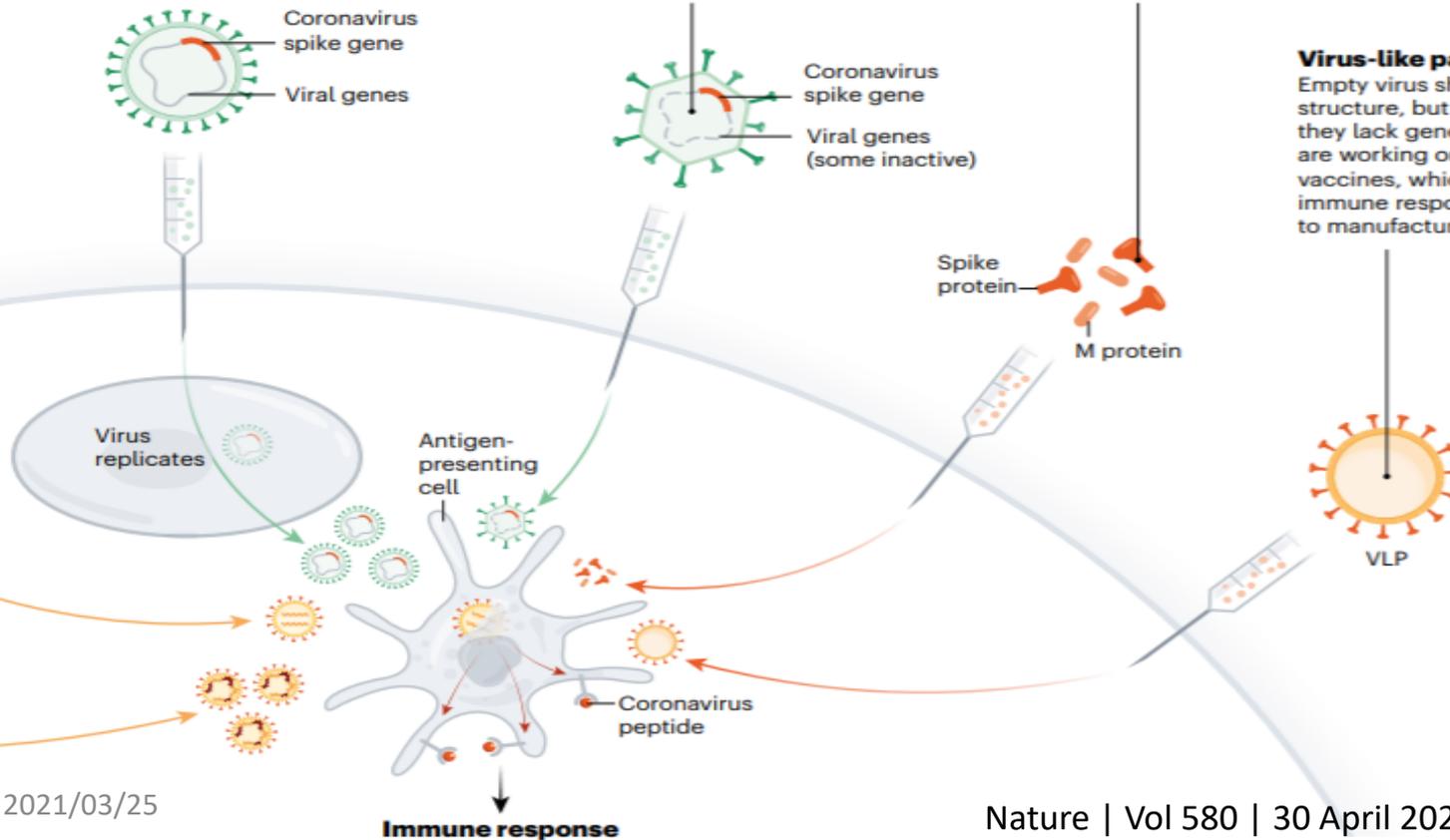
Many researchers want to inject coronavirus proteins directly into the body. Fragments of proteins or protein shells that mimic the coronavirus's outer coat can also be used.

Protein subunits

Twenty-eight teams are working on vaccines with viral protein subunits — most of them are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven't been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.

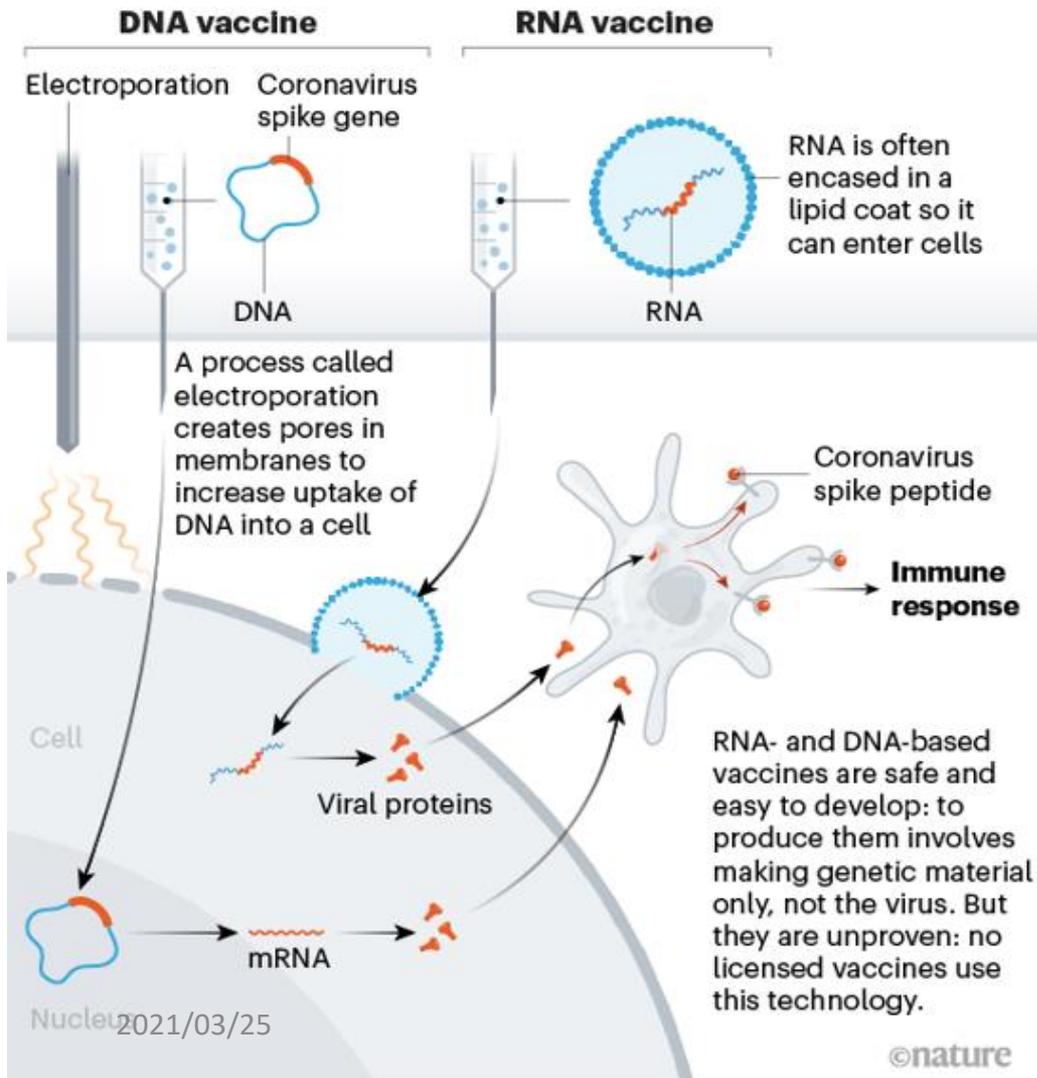
Virus-like particles

Empty virus shells mimic the coronavirus structure, but aren't infectious because they lack genetic material. Five teams are working on 'virus-like particle' (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.



Nucleic acid based vaccine

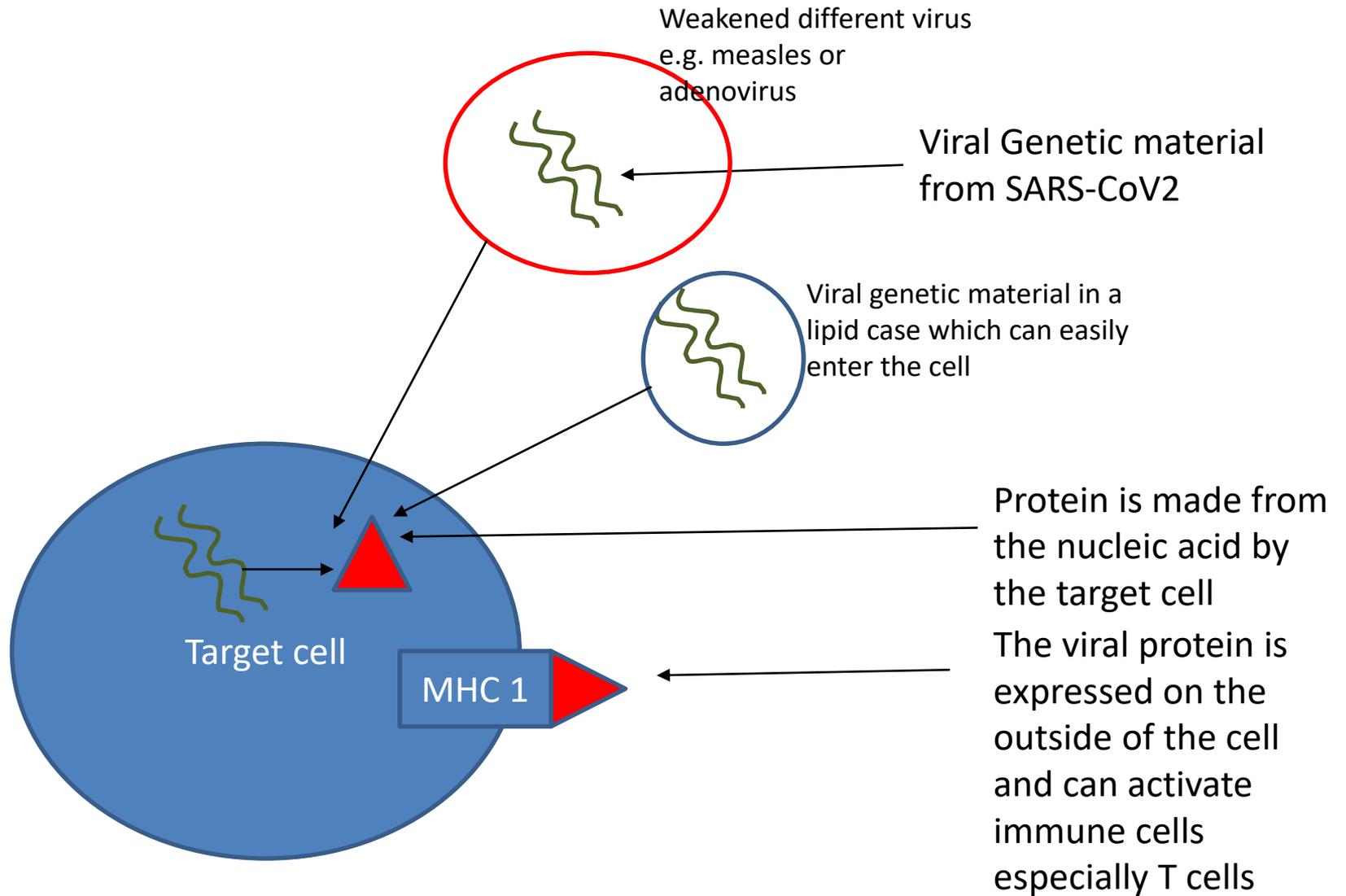
NUCLEIC-ACID VACCINES



- mRNA are not molecules or biological units
- mRNA medicines **are sets of instructions.**
- These are instructions for the cells on how to make 'spike proteins' which in turn induce an immune response to prevent or fight disease.
- Once the proteins are made, the cell destroys the mRNA using its enzymes

mRNA vaccines

- COVID-19 mRNA vaccines have also been rigorously tested for safety before authorization for use.
- mRNA technology is new, but not unknown. They have been studied for more than a decade in cancer research and development of other vaccines.
- mRNA vaccines do not contain a live virus and do not carry a risk of causing disease in the vaccinated person
- mRNA from the vaccine never enters the nucleus of the cell and does not affect or interact with a person's DNA



Immune presentation

- In order to stimulate the immune response to an organism, T-cells need to be switched on
- The best way for this to happen is for protein to be introduced to the T-cells in the context of a molecule called the MHC
- DNA and RNA vaccines both mimic infection to do this

SARS-CoV2 vaccines

What is out there, what is approved,
should I get it and when?

Vaccine Update: Excellent News

Johnson and Johnson vaccine

1. Contains the instructions for the Spike protein packaged in an adenovirus
2. Can be administered as a single dose
3. Stable at 20 degrees for up to 2 months

How effective is the J and J vaccine

How Safe and Effective Is the Johnson & Johnson Vaccine?

Initially, the Johnson & Johnson vaccine was shown to produce antibodies against SARS-CoV-2 in 90% of people who received it after the first dose. The amount of antibodies was greater for those who received 2 doses of the vaccine. Data released by Johnson & Johnson suggest that 1 dose of vaccine was 66% effective in preventing moderate to severe COVID-19 and 100% effective in preventing COVID-19-related hospitalization and death. These data are being reviewed by the US Food and Drug Administration to consider whether to grant an Emergency Use Authorization (EUA) to allow use of this vaccine.

In the studies of this vaccine, no one developed a severe allergic reaction, and side effects of the vaccine were similar to those of other vaccines, including fever experienced by 9% of volunteers. The vaccine did not appear to cause any excess serious complications.

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No serious safety concerns



- Moderna's COVID-19 vaccine shows 94.5% efficacy in **30 000 volunteers**
- Used 2 doses of mRNA-1273 vaccine
- Recorded 90 cases on the placebo vs 5 on the vaccine arm from diverse communities
- May be stored at standard fridge temp (2-4°C) for 30 days and -20°C for up to 6mths
- Company expected to have 20mil doses by end of 2020 (for the US only)
- Costs about \$35 a dose

- Pfizer and BioNTech's vaccine with 95% efficacy in the final analysis of **45 000 volunteers**
- Had 162 cases on placebo vs 8 on the vaccine arm
- Also uses 2 doses of mRNA vaccine
- **Vaccine must be shipped and stored at -70 degrees Celsius**
- The companies expect to have about 50mil doses globally by the yearend
- Pfizer expects to produce up to 1.3 billion doses in 2021
- Costs about \$20 a dose



- The vaccine showed an average efficacy of 70% in > 23 000 volunteers
- Uses a crippled chimpanzee adenovirus as a “vector” to deliver the gene
- 2 doses 1 mnth apart (efficacy improved to 90% in those receiving a reduced initial dose)
- Stored in a standard refrigerator fridge
- Costs \$3 - \$4 a dose
- 3 billion doses could be ready in 2021

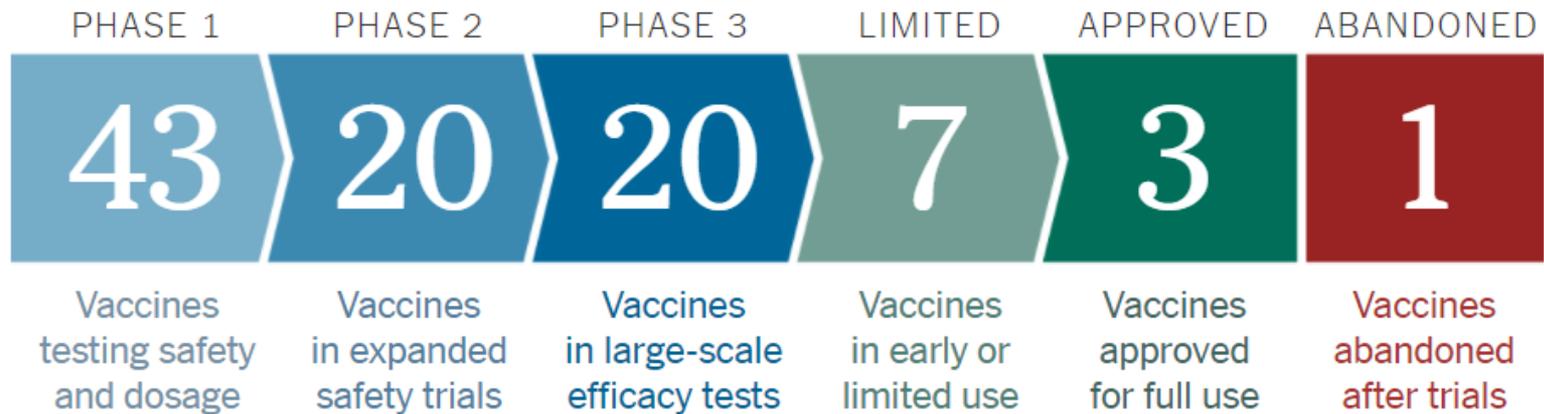


- 2 days ago, Russians reported a 91.4% efficacy from a second interim analysis of > 18,000 people
- 31 cases in placebo vs 8 in vaccine arm
- Also uses Adenovirus (Ad26) as a vector followed by an Ad5-spike 21 days later.
- Stored in a standard refrigerator
- Can cost <\$10 a dose
- Plans underway to produce 1 billion doses in 2021

SARS-CoV-2 Vaccine Tracker

Coronavirus Vaccine Tracker

By Carl Zimmer, Jonathan Corum and Sui-Lee Wee Updated Jan. 6, 2021



Vaccine Approval:

Regulators review the complete trial results and plans for a vaccine's manufacturing, and decide whether to give it full approval.

Moderna



TECHNOLOGY: mRNA
RNA instructs our cells to produce the SARS-CoV-2 spike protein to trigger an immune response.
EFFICACY: 94.1%
CLINICAL TRIALS: Completed Phase 3. Authorized for use in USA, Canada, U.K., Israel, Switzerland, and EU.
DOSE: 2 doses, 28 days apart.
STORAGE: 30 days with refrigeration, 6 months at -20°C.

Pfizer-BioNTech



TECHNOLOGY: mRNA
RNA template for the spike protein.
EFFICACY: 95%
CLINICAL TRIALS: Completed Ph3. Authorized/approved in USA, Canada, U.K., Switzerland, Bahrain, Saudia Arabia, EU, Argentina, Chile, Costa Rica, Ecuador, Jordan, Kuwait, Mexico, Panama, and Singapore.
DOSE: 2 doses, 21 days apart.
STORAGE: Freezer storage at -70°C, 5 days with refrigeration.

Oxford-AstraZeneca



TECHNOLOGY: Viral Vector
A harmless virus is engineered to contain the gene for the SARS-CoV-2 spike protein
EFFICACY: 62% at the approved dosing scheme.
CLINICAL TRIALS: Completed Phase 3, authorized for use in U.K., Argentina, India (called CoviShield), and Mexico.
DOSE: 2 doses, 4 weeks apart.
STORAGE: refrigerated at 2-8° C.

Sinopharm



TECHNOLOGY: Inactivated Virus
SARS-CoV-2 virus is rendered inert through a chemical process that preserves the structure of the virus.
EFFICACY: Reportedly 79.34% (86% in UAE trial); unpublished data.
CLINICAL TRIALS: Phase 3 trials are ongoing; authorized/approved in China, United Arab Emirates (UAE), Bahrain, Egypt, and Jordan.
DOSE: 2 doses, 3 weeks apart.
STORAGE: refrigerated at 2-8° C.

Johnson & Johnson



TECHNOLOGY: Viral Vector
A harmless virus is engineered to contain the gene for the SARS-CoV-2 spike protein
EFFICACY: not yet known
CLINICAL TRIALS: Completed Phase 2a, expected phase 3 trial data to be released soon.
DOSE: 1- and 2-dose schemes are being tested.
STORAGE: 2 years frozen at -20° C, 3 months refrigerated at 2-8° C.

Gamaleya



TECHNOLOGY: Viral Vector
A harmless virus is engineered to contain the gene for the SARS-CoV-2 spike protein
EFFICACY: Reportedly 91.4% (unpublished data).
CLINICAL TRIALS: Phase 3 trials are ongoing; authorized for use in Russia, Belarus, Argentina, Algeria, Bolivia, Palestine, and Serbia.
DOSE: 2 doses, 3 weeks apart.
STORAGE: Freezer storage (-20°C)

Some of your Frequently asked questions

This is an RNA vaccine. Does this mean it will change my genetic makeup?

No. Some viruses, retroviruses like HIV, are inserted into the host genetic material and can cause mutations. The genetic material of SARS-CoV2 is not inserted and the vaccines will also not result in genetic manipulation.

What about the side-effects of the vaccines?

These vaccines are designed to activate the immune system. This can produce temporary side effects. This includes injection site pain, low grade fever, rash, muscle aches. In the large scale studies, these were reported by the participants generally as mild and lasted for a few days only. There have been reports of severe allergic responses to some but not all vaccines. These are extremely uncommon (approximately 0.001% of participants) and have not be conclusively linked to the vaccine. Importantly, side-effects are more likely to occur after the second dose of the vaccine.

I have heard stories about individuals getting clots following the vaccine

Clotting is increased in individuals who are inflamed and for this reason any immunological challenge may increase the risk of clotting (including the vaccine) however, the risk of clotting does not appear very high and the risk of abnormal clots with severe COVID-19 are very high indeed. It is therefore better to take the vaccine risk than the risk of severe disease

I am pregnant. Should I have the vaccine?

Limited data are available on the effect of pregnancy. Most vaccines have, however, been effective in pregnant women. Because of the risk of severe SARS-CoV2 infection in pregnant women, the WHO has recently reversed its decision not to recommend vaccination of pregnant women and many countries are now actively vaccinating women in the 2nd and 3rd trimester (www.who.int)

What about my medications – won't they interfere?

A number of individuals are on drugs which may suppress the immune response. This includes corticosteroids. Although there is no current indication that this affects the efficacy of the vaccine this remains something to monitor. Currently, pain medication (like non-steroidal anti-inflammatory drugs) are being used in vaccinated individuals who present with side-effects like injection site pain.

What should I tell the person who is vaccinating me?

1. If you are pregnant or breastfeeding
2. If you have a condition that effects the immune system e.g. if you have HIV or cancer
3. If you have had an allergic response in the past to vaccination
4. If you are susceptible to bleeding
5. If you have any symptoms of active SARS-CoV2 infection or a fever
6. If you have received another vaccine for SARS-CoV2

How long will the vaccine protection last?

We are currently not sure since the majority of the vaccines only have about 6 months of data. It may be necessary to have this vaccine more than once?

Some people have suggested that you can “mix and match” vaccines. Is this true?

Some preliminary data suggests that this may be the case although the vaccine suppliers suggest that there are limited efficacy data on this approach. It has been utilised in some countries however including the United Kingdom.

Is the vaccine effective for children and for individuals >65 years

The vaccine is currently not recommended for children under the age of 16 years. Children are also less likely to have severe disease. There has been some data that elderly patients may not respond as well to the vaccine but in South Africa, we intend to vaccinate elderly patients who are at risk of severe disease and death.

What is “herd immunity”

If a number of individuals in a population have received a vaccine, they become immune and will not transmit the infection. This is generally considered to be about $2/3$ s of the population. This means that these individuals will protect other individuals in the population who cannot receive the vaccine for any reason.

How do I know if the vaccine has worked?

Importantly, a number of individuals have been to have an antibody test after the vaccination. A reminder that serology (antibody tests) often measure antibodies against the nucleocapsid antigen and not against the spike antigen. This means that these tests will not pick up antibodies in people who have not had so-called “natural infection”.

I have had COVID. This means that I am immune and don't need the vaccine?

A number of individuals who have had the disease have become reinfected. In some cases, infection does not result in significant immunity. In addition, there are variants of the disease circulating in South Africa so it is important to be vaccinated even if you had the infection previously. Similarly, there are cases of breakthrough infection even in vaccinated people especially with the variants. For that reason, vaccination does not mean that you are 100% protected. **Importantly, vaccination significantly reduces the risk of severe disease and death.**

I don't want the vaccine. Do I have to have it?

No! Importantly no person can be forced to be vaccinated as per the President's declaration. Individuals cannot be discriminated against in South Africa for not having the SARS-CoV2 vaccine.