Vaccine development and implementation

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Objectives: After today you should be able to understand:

- How a vaccine works
- How vaccines are developed.
- How vaccines are tested.
- How they are approved.

Useful sources of information on vaccines

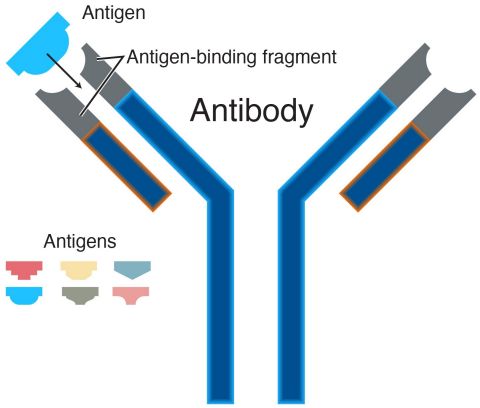
- www.nicd.gov.za (National Institute of Communicable Diseases, South Africa)
- www.who.int (World Health Organisation [WHO] + Africa office)
- www.cdc.gov (Centers for Disease Control, USA)

How vaccines work (1) WHO

- Vaccination is a simple, safe, and effective way of protecting people against harmful diseases, before they come into contact with them. It uses your body's natural defenses to build resistance to specific infections and makes your immune system stronger.

How vaccines work (2) WHO

- Vaccines train your immune system to create antibodies, just as it does when it's exposed to a disease. However, because vaccines contain only killed or weakened forms of germs like viruses or bacteria, they do not cause the disease or put you at risk of its complications.



How vaccines work (3) WHO

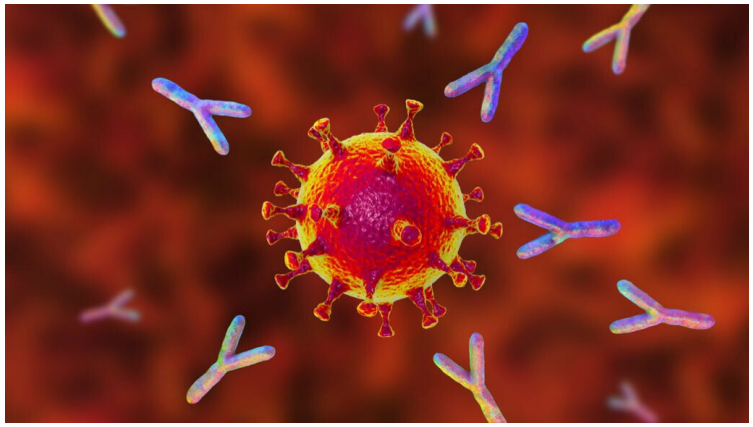
- Most vaccines are given by an injection, but some are given orally (by mouth) or sprayed into the nose.

How vaccines work (4) WHO

- When you get a vaccine, your immune system responds. It:
- Recognizes the invading germ, such as the virus or bacteria.
- Produces antibodies. Antibodies are proteins produced naturally by the immune system to fight disease.
- Remembers the disease and how to fight it..

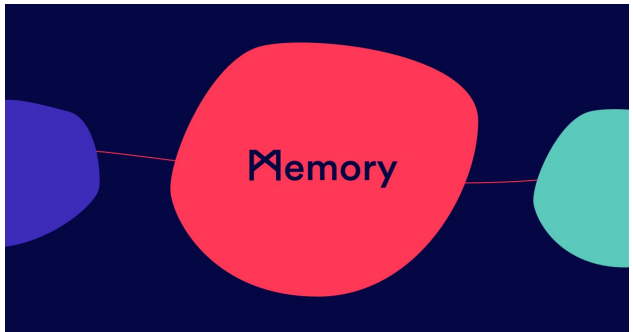
How vaccines work (5) WHO

- If you are then exposed to the germ in the future, your immune system can quickly destroy it before you become unwell.
- The vaccine is therefore a safe and clever way to produce an immune response in the body, without causing illness.

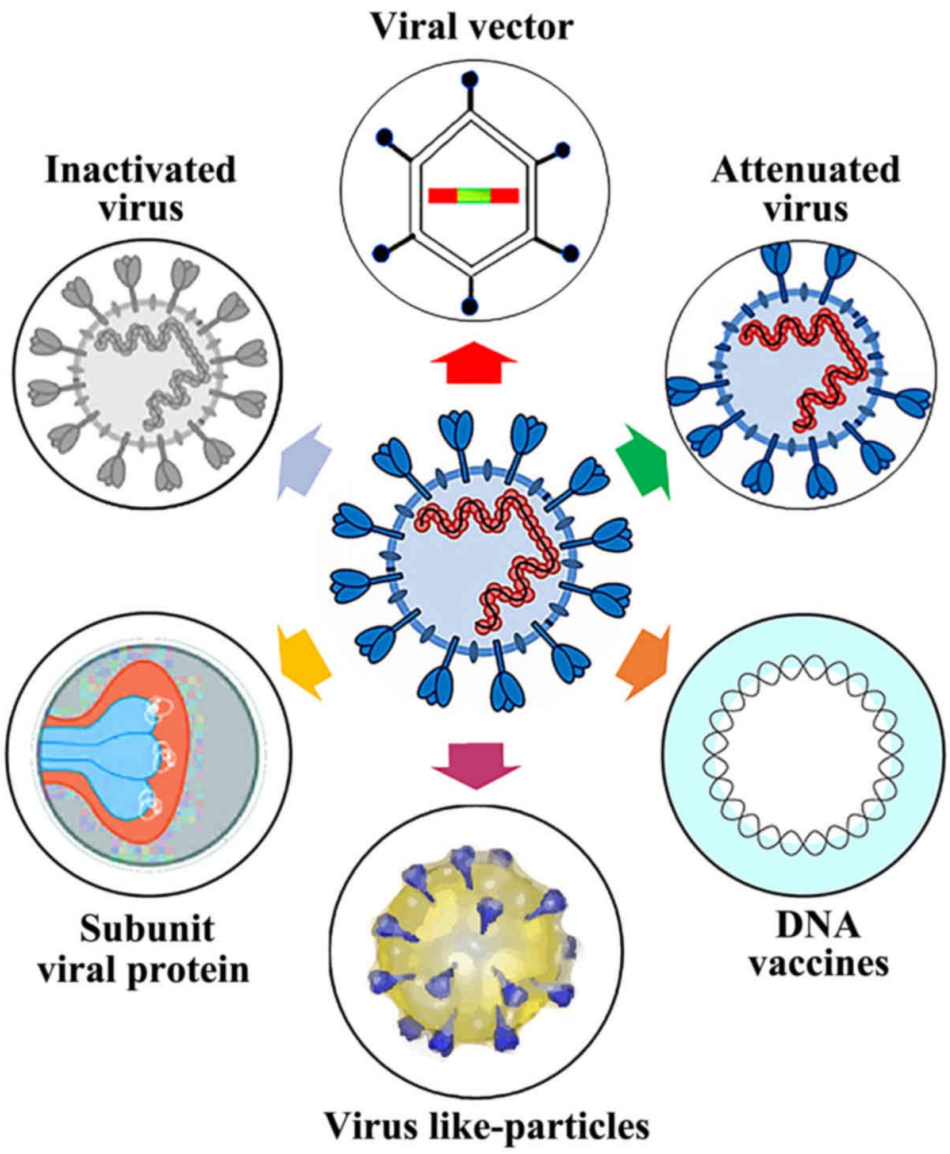


How vaccines work (6) WHO

- Our immune systems are designed to remember. Once exposed to one or more doses of a vaccine, we typically remain protected against a disease for years, decades or even a lifetime. This is what makes vaccines so effective. Rather than treating a disease after it occurs, vaccines prevent us in the first instance from getting sick



Types of vaccines



- Live attenuated (weakened) vaccines (measles)
- Whole cell killed vaccines (whooping cough)
- Viral vectored vaccines (J&J Covid vaccine)
- Protein based vaccines (Novavax)
- DNA based vaccines (Hepatitis B)
- mRNA vaccines (relatively new) (Pfizer)

How are vaccines developed? WHO

- As with all medicines, every vaccine must go through extensive and rigorous testing to ensure it is safe before it can be introduced in a country.
- An experimental vaccine is first tested in animals to evaluate its safety and potential to prevent disease. It is then tested in human clinical trials, in three phases

Note: experimental vaccines are usually developed in laboratories often using samples of the organism itself

Phases of clinical trials? (WHO)(1)

- In phase I, the vaccine is given to a small number of volunteers to assess its safety, confirm it generates an immune response, and determine the right dosage.
- In phase II, the vaccine is usually given hundreds of volunteers, who are closely monitored for any side effects, to further assess its ability to generate an immune response.
- .

Phases of clinical trials? (WHO)(2)

- In phase II, data are also collected whenever possible on disease outcomes, but usually not in large enough numbers to have a clear picture of the effect of the vaccine on disease. Participants in this phase have the same characteristics (such as age and sex) as the people for whom the vaccine is intended. In this phase, some volunteers receive the vaccine and others do not, which allows comparisons to be made and conclusions drawn about the vaccine.

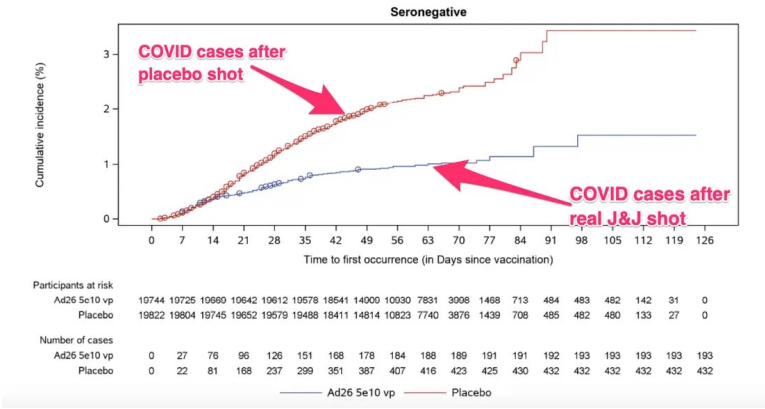
Phases of clinical trials? (WHO)(3)

- In phase III, the vaccine is given to thousands of volunteers – some of whom receive the investigational vaccine, and some of whom do not, just like in phase II trials. Data from both groups is carefully compared to see if the vaccine is safe and effective against the disease it is designed to protect against.

Vaccine efficacy/ effectiveness

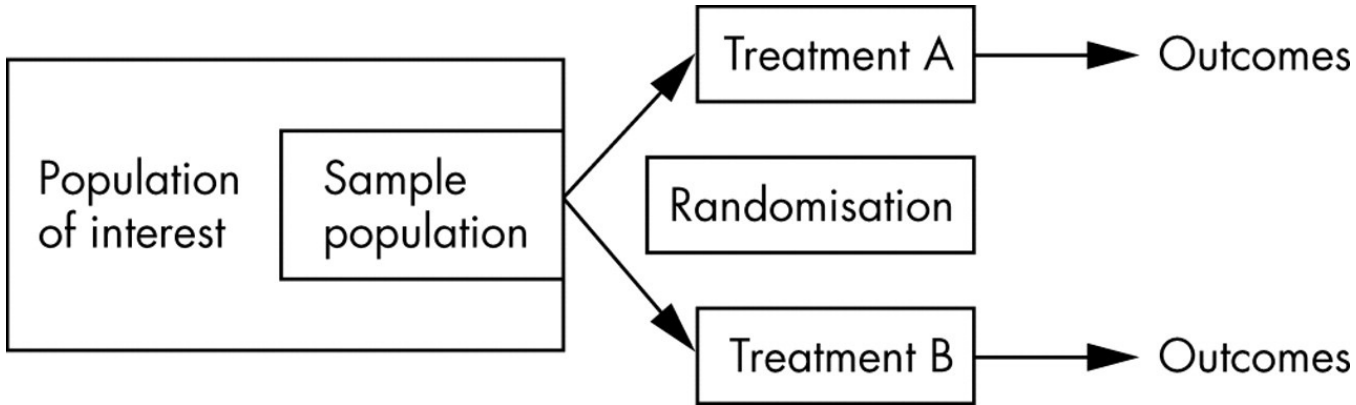
- The degree to which a vaccine reduces the number of cases due to a disease.
- Can it work (under controlled conditions)? = vaccine efficacy.
- Does it work (when implemented under programme conditions)?
- = vaccine effectiveness

Figure 1. Cumulative Incidence Curve of Centrally Confirmed Moderate to Severe/Critical COVID-19 Cases With Onset at Least 1 Day After Vaccination, Full Analysis Set



How is a vaccine efficacy study done?

- Phase III trial.
- Usually double blind, randomised and controlled.
- i.e. conditions are idealised.
- Strict inclusion and exclusion criteria
- Sample size determined based on expected incidence of disease in unvaccinated and estimated incidence in vaccinated.
- Usually for a limited period.



Calculating Vaccine efficacy - example

- Rate of disease in those who got placebo – 100 out of 1000.
- Rate of disease in those who got vaccine – 10 out of 1000.
- What is the vaccine efficacy?

Vaccine efficacy (VE)

$$VE = 1 - \text{Relative Risk} = 1 - \frac{\text{Risk in vaccinated arm}}{\text{Risk in unvaccinated arm}}$$

$$VE = 1 - \text{Risk Ratio}$$

$$VE = 1 - \text{Incidence Rate Ratio}$$

$$VE = 1 - \text{Hazard Ratio}$$

Calculation in our example

- (Incidence in Unvaccinated – Incidence in vaccinated) x 100

  Incidence in Unvaccinated

- $\frac{100/1000 - 10/1000}{100/1000} \times 100 =$
- $\frac{10\% - 1\%}{10\%} \times 100 = \frac{9}{10} \times 100$
- $= 0.9 \times 100 = 90\%$

The Public Health value of vaccines

- Most effective health intervention after provision of safe water
- Have saved millions of lives
- We give them to our children, use them when we are injured
  (e.g. tetanus vaccine) and when we travel (e.g. yellow fever vaccine).
- Small pox has been eradicated and polio exists only in a few countries due to vaccination

EXPANDED PROGRAMME ON IMMUNISATION – EPI (SA) REVISED CHILDHOOD IMMUNISATION SCHEDULE FROM DECEMBER 2015

Age of Child	Vaccines needed	How and where is it given
At Birth	**BCG** Bacilles Calmette Guerin	Right Arm
	OPV (0) Oral Polio Vaccine	Drops by mouth
6 Weeks	**OPV (1)** Oral Polio Vaccine	Drops by mouth
	RV (1) Rotavirus Vaccine	Liquid by mouth
	DTaP-IPV-Hib-HBV (1) Diphtheria, Tetanus, Acellular Pertussis, Inactivated Polio Vaccine, *Haemophilus influenzae* type b and Hepatitis B Combined	Intramuscular / Left thigh
	PCV (1) Pneumococcal Conjugated Vaccine	Intramuscular / Right thigh
10 Weeks	**DTaP-IPV-Hib-HBV (2)** Diphtheria, Tetanus, Acellular Pertussis, Inactivated Polio Vaccine, *Haemophilus influenzae* type b and Hepatitis B Combined	Intramuscular / Left thigh
14 Weeks	**RV (2)** Rotavirus Vaccine*	Liquid by mouth
	DTaP-IPV-Hib-HBV (3) Diphtheria, Tetanus, Acellular Pertussis, Inactivated Polio Vaccine, *Haemophilus influenzae* type b and Hepatitis B Combined	Intramuscular / Left thigh
	PCV (2) Pneumococcal Conjugated Vaccine	Intramuscular / Right thigh
6 Months	**Measles Vaccine (1)****	Subcutaneous / Left thigh
9 Months	**PCV (3)** Pneumococcal Conjugated Vaccine	Intramuscular / Right thigh
12 Months	**Measles Vaccine (2)****	Subcutaneous / Right arm
18 Months	**DTaP-IPV-Hib-HBV (4)** Diphtheria, Tetanus, Acellular Pertussis, Inactivated Polio Vaccine, *Haemophilus influenzae* type b and Hepatitis B Combined	Intramuscular / Left arm
6 Years (Both boys and girls)	**Td Vaccine** Tetanus and reduced strength of Diphtheria Vaccine	Intramuscular / Left arm
12 Years (Both boys and girls)	**Td Vaccine** Tetanus and reduced strength of Diphtheria Vaccine	Intramuscular / Left arm

* Rotavirus Vaccine should NOT be administered after 24 weeks.
** Do not administer with any other vaccine

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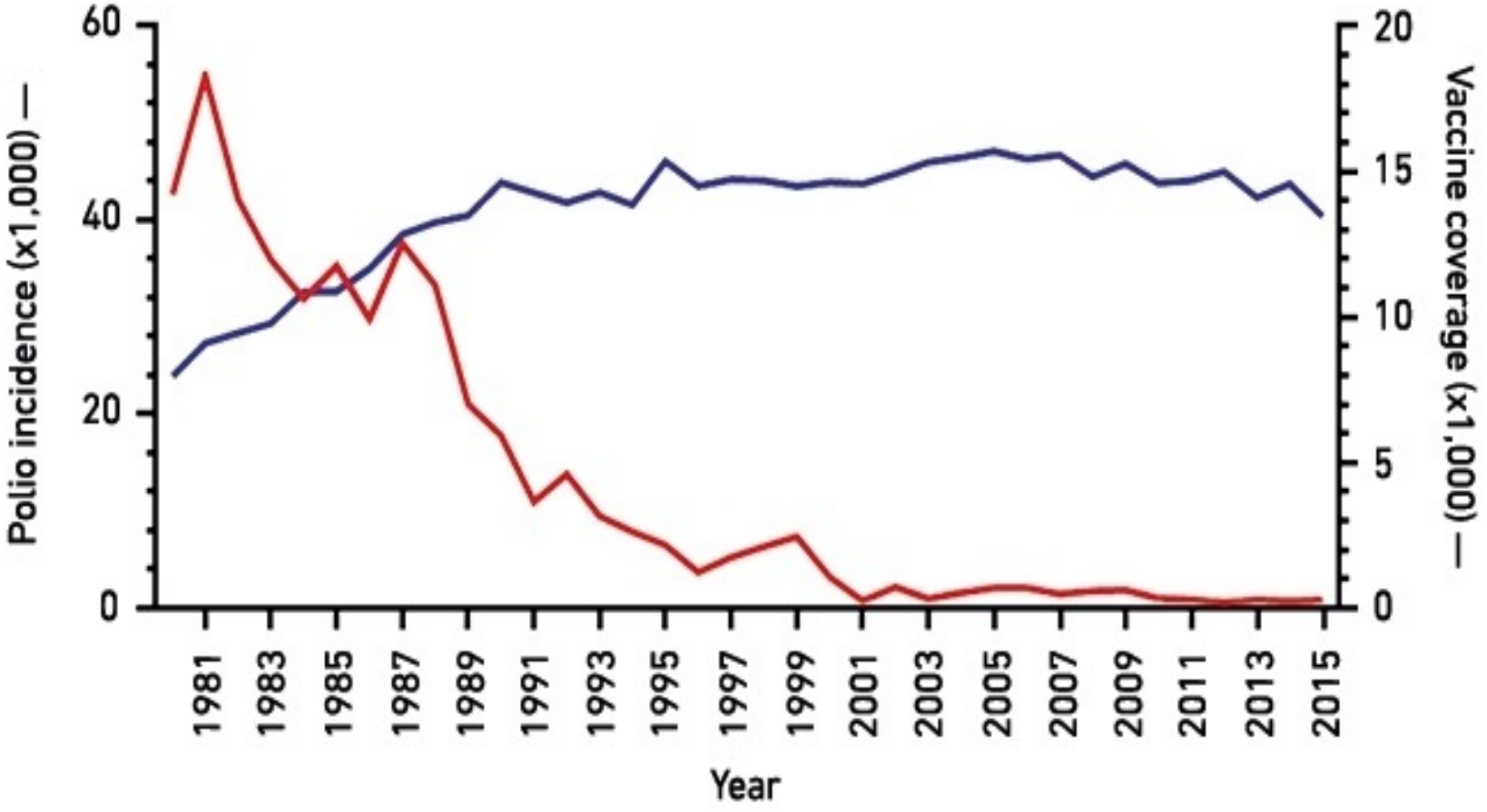
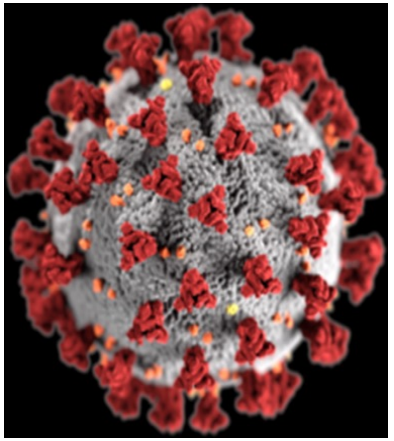
Impact of polio vaccine on polio incidence globally (WHO)



Aims of COVID-19 vaccine in South Africa



- Prevent severe illness and death
- Reduce transmission
- Protect our health system
- As at 6 March 2021, 299 million shots of COVID-19 vaccine had been given.
- (www.bloomberg.com) https://www.bloomberg.com/graphics/covid-vaccine-tracker-global -distribution/
- (70% of vaccines used by China, USA, UK and EU, 130 countries still to administer a single dose)

Vaccines shown to have efficacy against COVID-19

Vaccine	Efficacy	Efficacy against severe disease	Efficacy in high risk groups	Dose regimen	Storage	Comments
Biontech/ Pfizer/ Cominarty	95%	90%	Yes, older age groups	2 doses	-70 degrees	NEJM published
Moderna	94%	100%	Yes, older age groups	2 doses	- 20 degrees	NEJM published
Oxford/ Astrazeneca/ Covishield	62.1-90% (Brazil and UK) 22% (SA)	100% (Brazil and UK)	Older age groups >55, HIV not known	2 standard doses or Low/standard dose	2-8 degrees	Lancet published
Sinopharm (Beijing Strain)	86%	100%		2 doses	2-8 degrees	News reports
Sinovac (coronavac)	50.4 - 91.2%	100%		2 doses		News reports
Sputnik V	91.40%	100%		2 doses	Normal fridge temperatures	Lancet published
Novavax *	49-89%	(yes but small numbers)	? HIV persons	2 doses	2-8 degrees	News reports/ 66% in HIV negative persons
Johnson and Johnson *	66% (57 - 72%)	85%		1 dose	- 20 degrees 2-8 degrees (28 days)	News reports, national presentations, FDA submission

Approval processes

- Medicine regulatory bodies approve clinical trials of new products and ethics committees/ institutional review boards approve research on new products.
- In addition, medicine regulatory bodies approve the public use of medicines – 2 options – normal approval for general use and emergency approval when urgent.

NB, these approvals must be independent of researchers and pharmaceutical companies

Examples of regulatory authorities

- South African Health Products Regulatory Authority (SAHPRA)
- Federal Drug Administration (FDA) (USA)
- Medicines Health Regulatory Authority (MHRA) (UK)
- European Medicines Agency (EMA) (EU)

Conclusion

- Vaccines have played an important part in the control of infectious diseases and continues to do so.
- There is a rigorous scientific and ethical process underlying the design, researching and implementation of new vaccines.
- 8 vaccines have shown efficacy against COVID-19 and have been approved for use in multiple countries.
- Vaccine distribution inequity remains an important stumbling block to global control of COVID-19.

Thank you