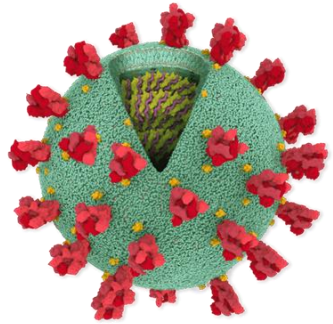


COVID-19 vaccines: An overview

MANJURUL/GETTY IMAGES

Dr. Simba Takuva

Outline

- Aim of a vaccine
- How does a vaccine or COVID-19 vaccine work ?
- Types of COVID-19 vaccines
- How is vaccine research conducted
- Speed of COVID-19 vaccine development
- How safe are COVID-19 vaccines
- COVID-19 rollout strategy RSA
- Closing thoughts

Conflicts to declare

- Safety physician and Medical monitor in ongoing COVID-19 and HIV vaccine trials. Some trials are sponsored by industry.

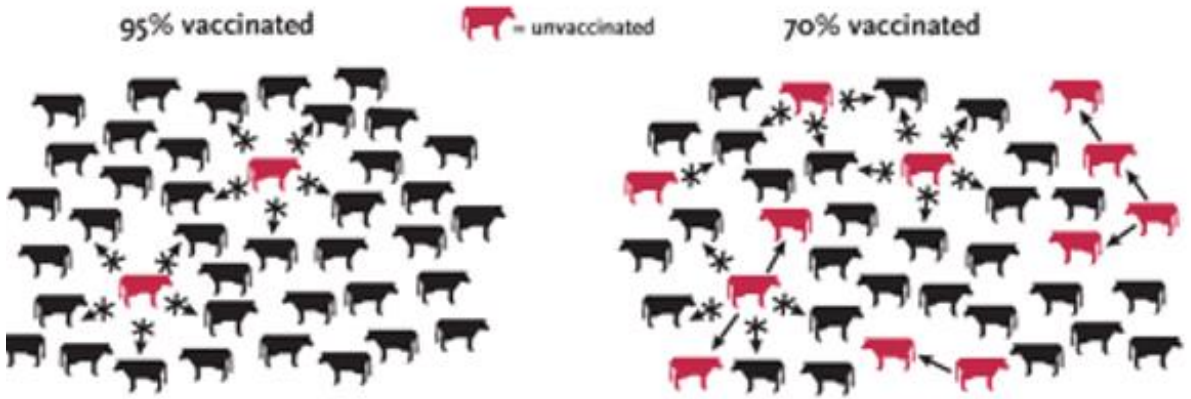
What could a SARS-CoV-2 vaccine do ?

Benefit the individual

- Reduce the severity of illness
- Prevent infection

Benefit the community

- Reduce transmission
- Healthier communities
- Less stress on health systems



SARS-CoV-2 and its Spike Protein (the vaccine target)

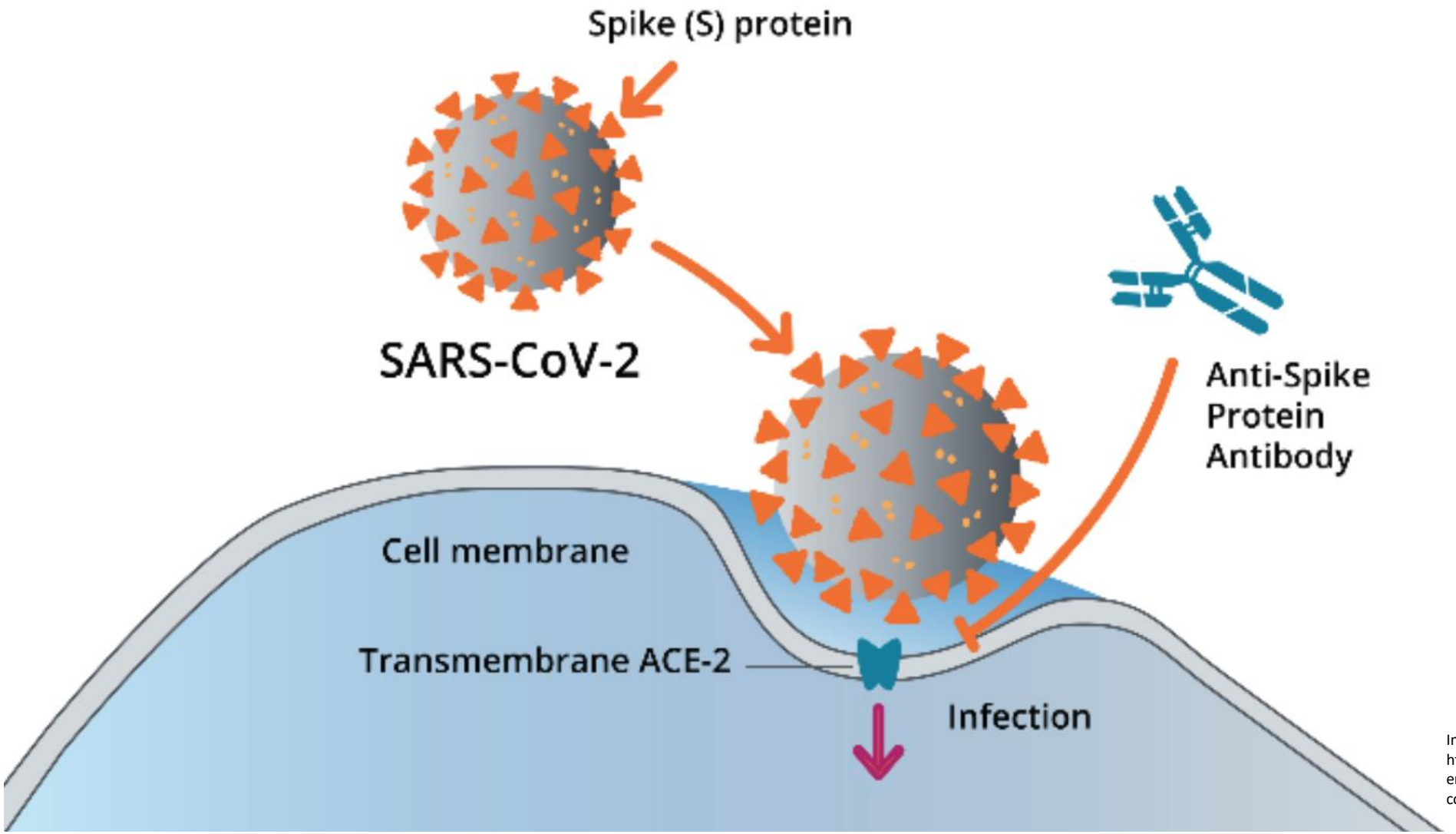
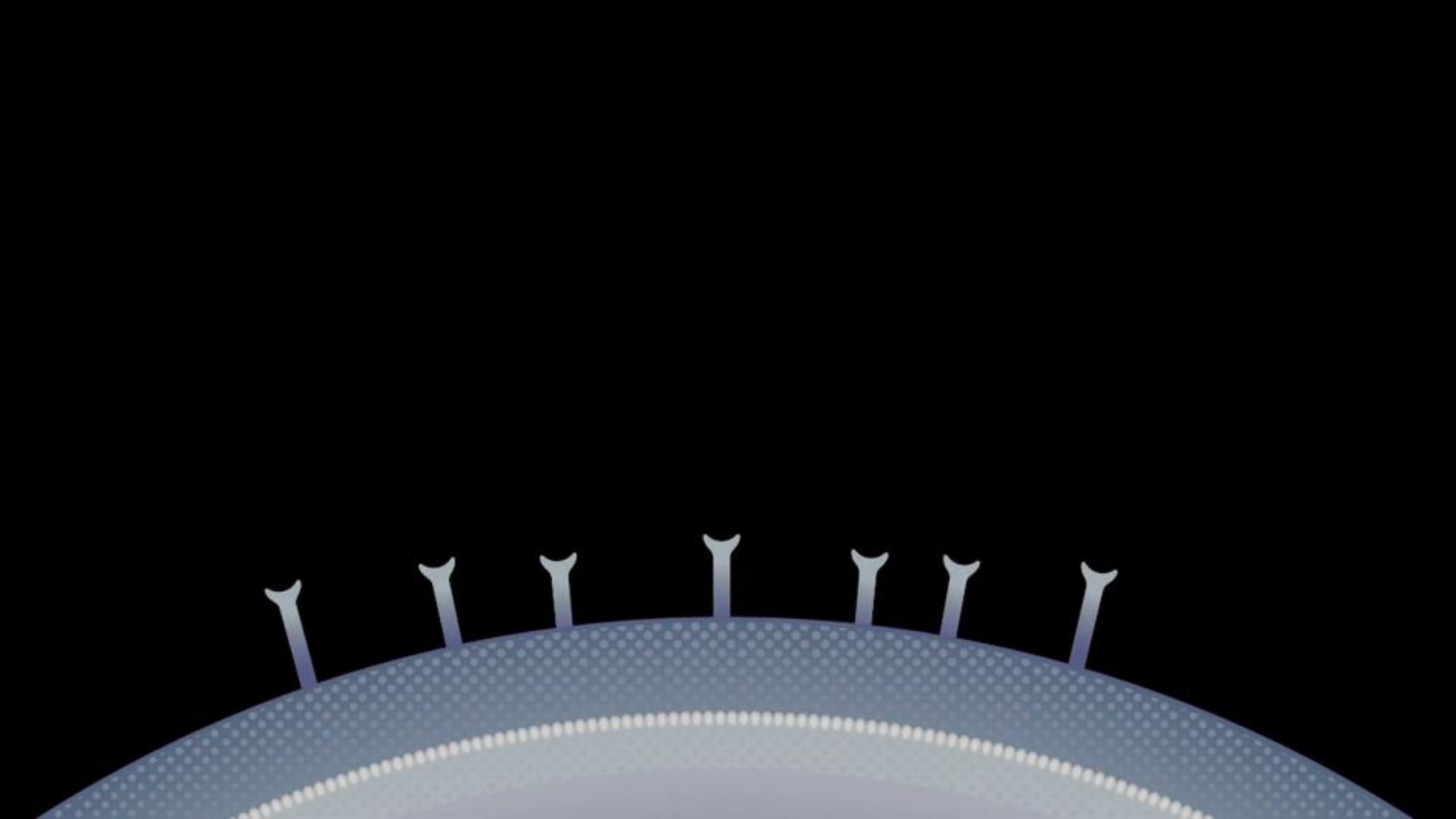


Image credits:
https://www.berkeleylights.com/blog/everything-you-need-know-about-coronavirus/

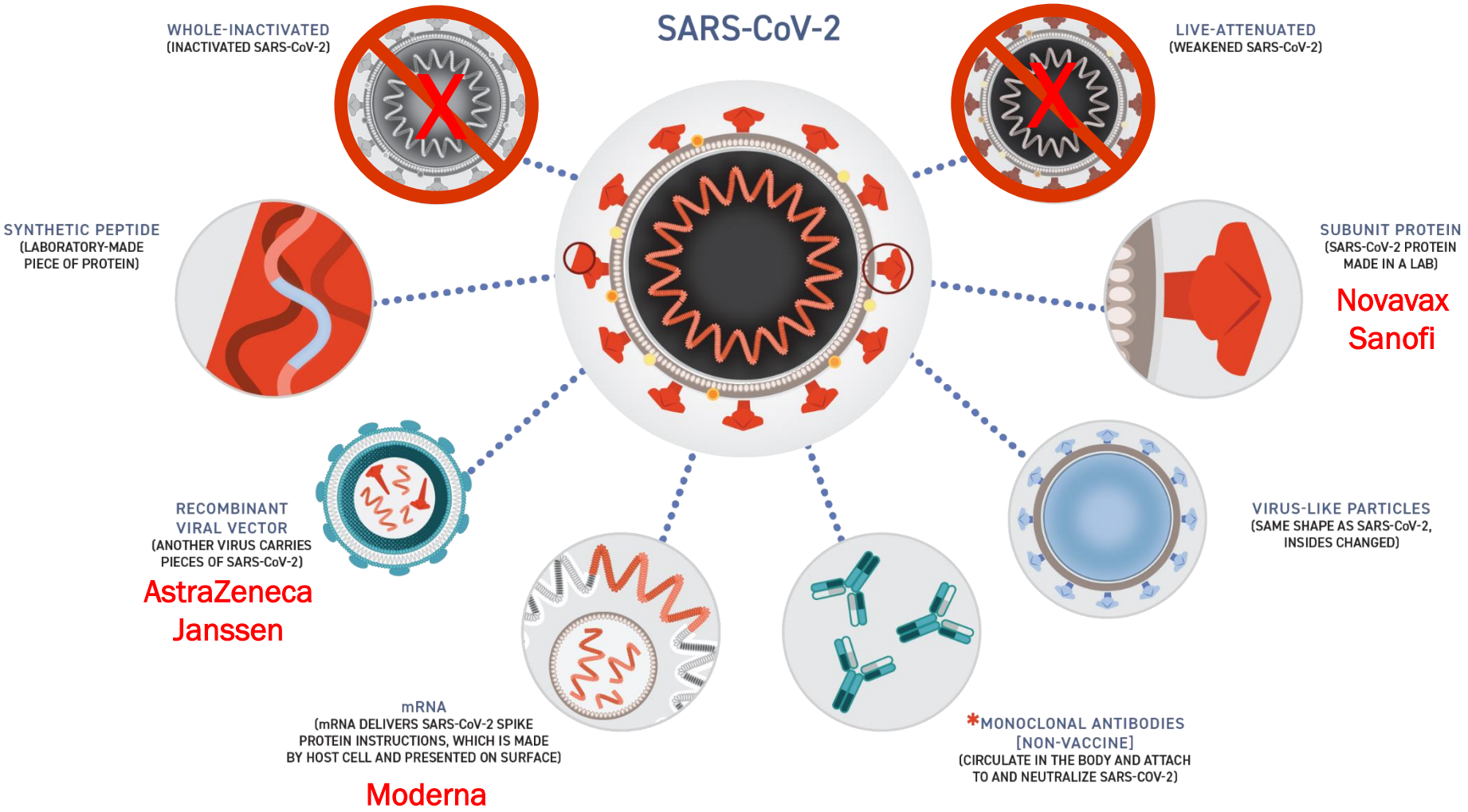
How does a COVID-19 vaccine work ?

- The first time you are infected by a virus you will develop antibodies against that virus
- The next time you come in contact with that same virus, you will already have antibodies prepared to fight against that particular virus
- This is what vaccines try to mimic!
- A vaccine presents an antigen to stimulate an immune response that can block or destroy the virus



Vaccine Designs

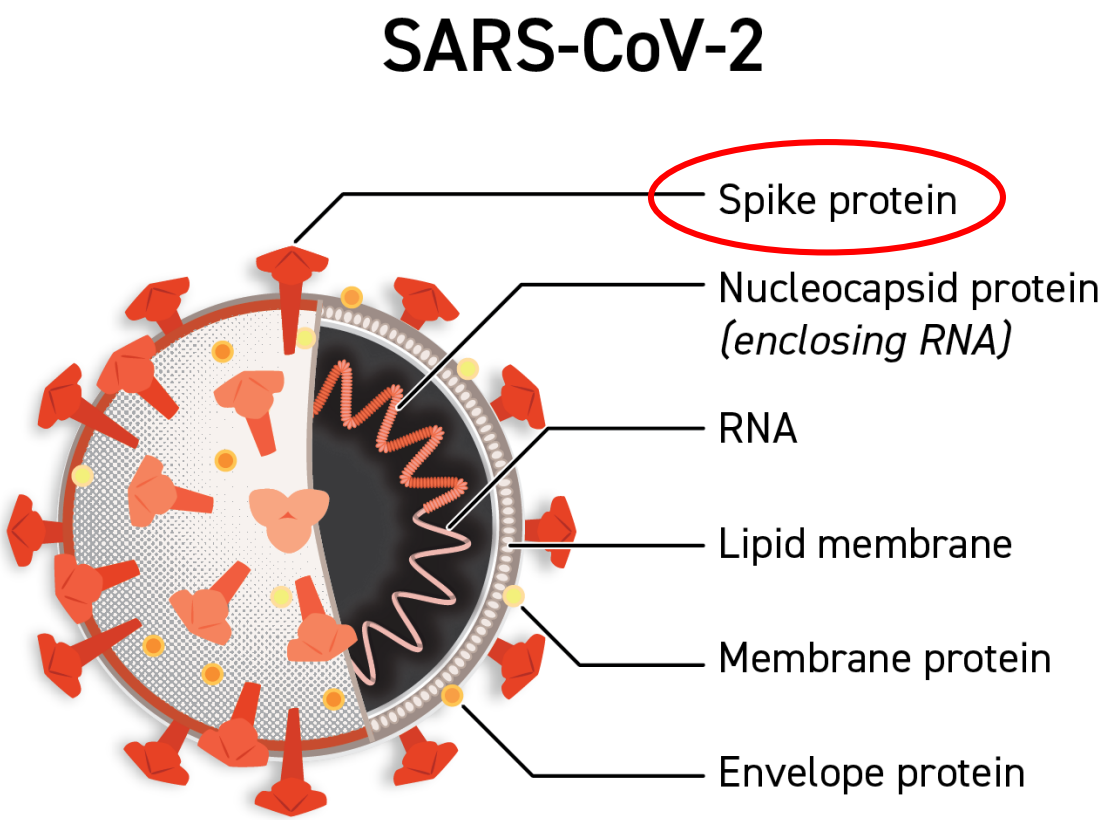
SARS-CoV-2 VACCINE AND RELATED* DESIGNS



COVID-19
Prevention Network

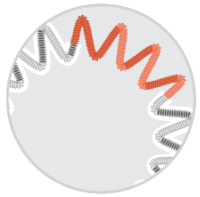
Vaccine Antigen

- To understand how these vaccines are made, we first need to understand what parts of the virus are used.
- The vaccines in Operation Warp Speed focus on the spike protein of the SARS-CoV-2 virus, which is used as the **antigen**.
- An antigen is the ingredient in a vaccine that triggers your body's immune system to build a defense and create antibodies against a virus.
- Remember that the antigen is only a copy of a piece of the virus, usually made in a laboratory, and cannot cause illness.



COVID-19
Prevention Network

Pieces of the vaccine “sandwich”



Genetic Code

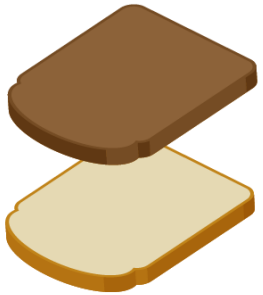
↓

(recipe)

Vector

↓

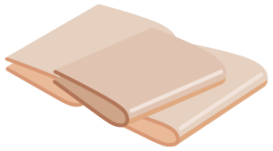
(bread)



Antigen

↓

(meat)



Matrix-M / AS03

Adjuvant

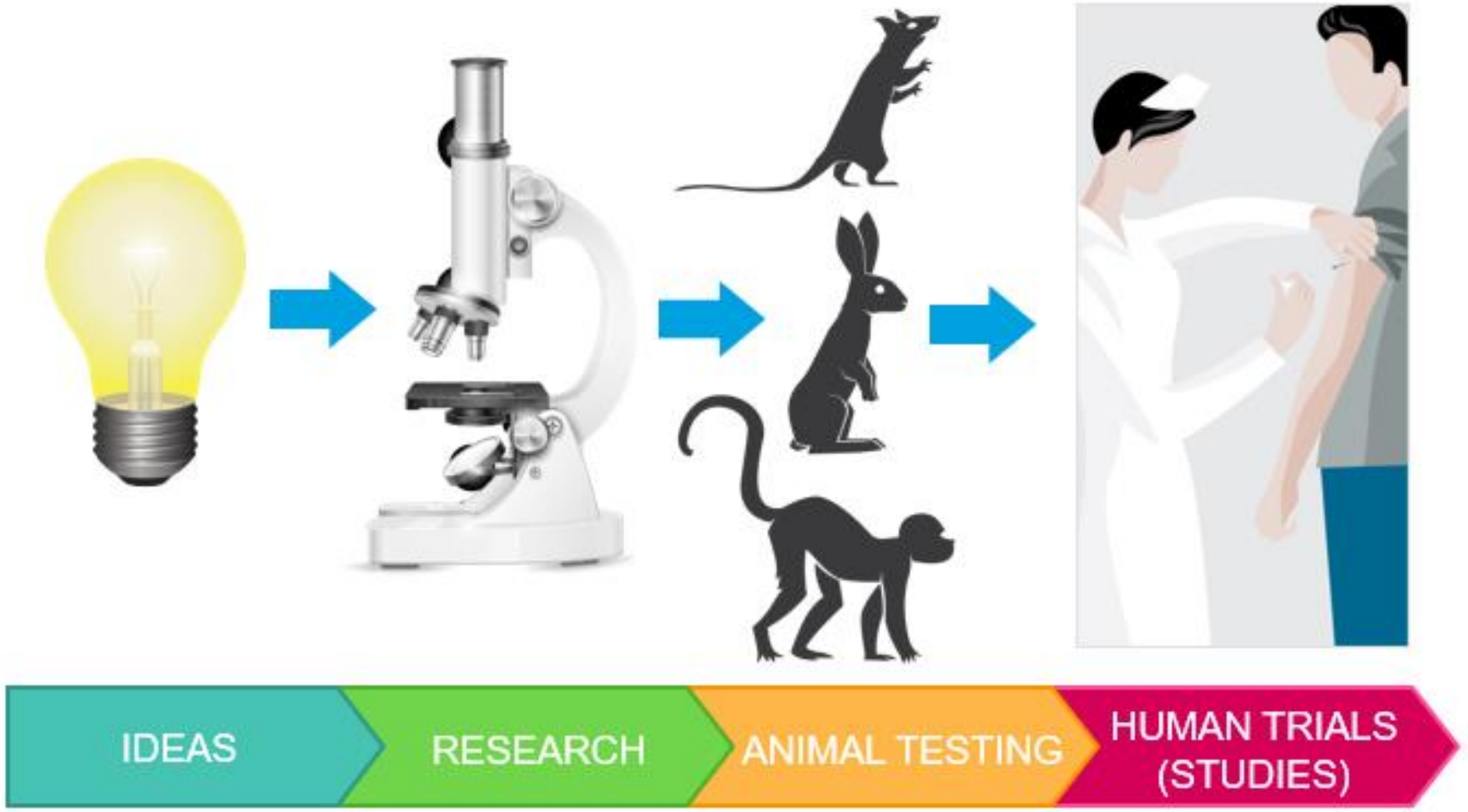
↓

(condiment)

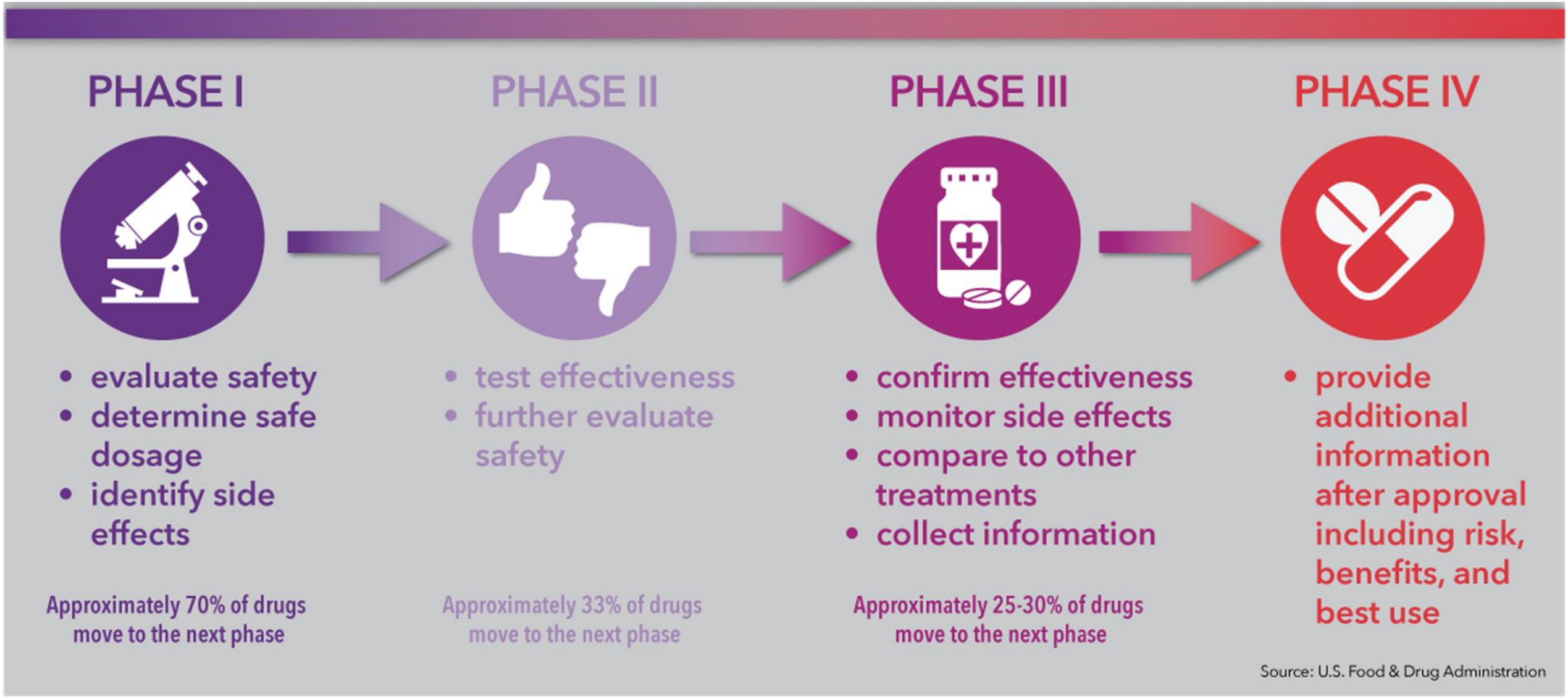
=

COVID-19
Prevention Network

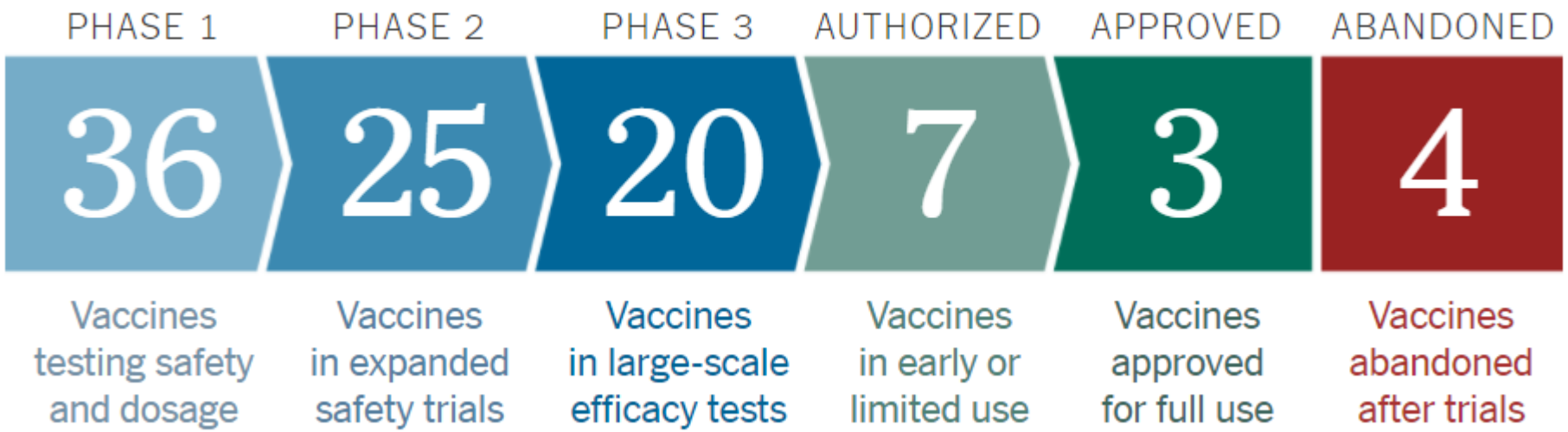
How do we conduct vaccine research?



How do we conduct vaccine research?



COVID-19 Vaccines in Clinical Development



Example candidates
(not exhaustive)

Clover Biopharmaceuticals · NOVAVAX · The University Of Queensland · CSL

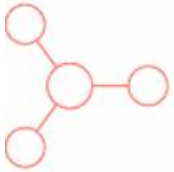
inovio · CUREVAC · moderna · BIONTECH

MERCK · THEMIS · University of Oxford · AstraZeneca

sinovac · SINOPHARM

BioNTech/Pfizer	Authorized
Moderna	Authorized
Oxford/AstraZeneca	Authorized
Sinovac/Instituto Butantan	Phase III
Wuhan Inst./Sinopharm	Phase III
Beijing Inst./Sinopharm	Phase III
Gamaleya Research Inst.	Phase III
CanSino Biologics	Phase III
Janssen Pharma	Phase III
Novavax	Phase III

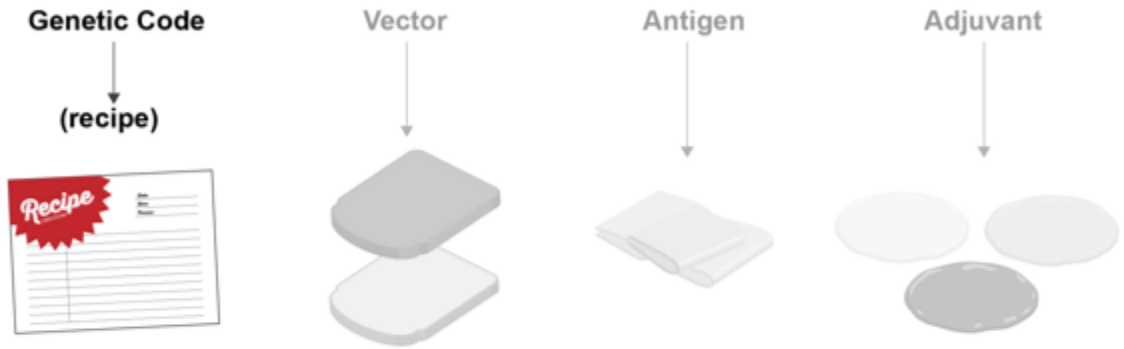
Types of COVID-19 vaccines

Technology		Description	Example candidates *(not exhaustive)*
	**Protein**	**Purified or recombinant proteinaceous antigens** from a pathogen to elicit immune response	Clover Biopharmaceuticals, NOVAVAX, The University Of Queensland, CSL
	**Nucleic Acid**	**Genetically engineered plasmid containing the DNA sequence** containing sequence for disease-specific antigen **Messenger RNA** containing sequence for a disease-specific antigen	inovio, CUREVAC, moderna, BIONTECH
	**Viral vector**	**Chemically weakened viruses to carry DNA**, containing sequence for disease-specific antigen, into human cells	MERCK, THEMIS, University of Oxford, AstraZeneca
	**Inactivated**	**Chemically "killed" virus or subunits of the virus** grown under controlled conditions	sinovac, SINOPHARM

Moderna Vaccine (mRNA vaccine)

- The “Cove Study.” N=30,423 across 99 sites in the US, mRNA-1273.

Moderna’s vaccine “sandwich” recipe



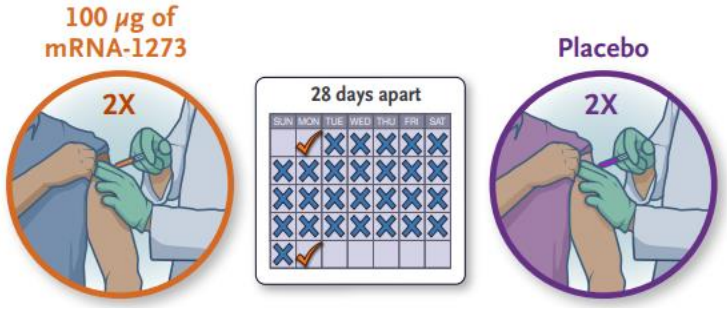
- Moderna’s vaccine delivers the instructions for making the spike protein from SARS-CoV-2
- Once inside a human cell, the vaccine delivers the message: “Make protein from SARS-CoV-2”
- Human cells makes the protein and display it on the surface
- The immune system sees the protein, recognizes it as foreign, and creates an immune response to block infection and prevent disease

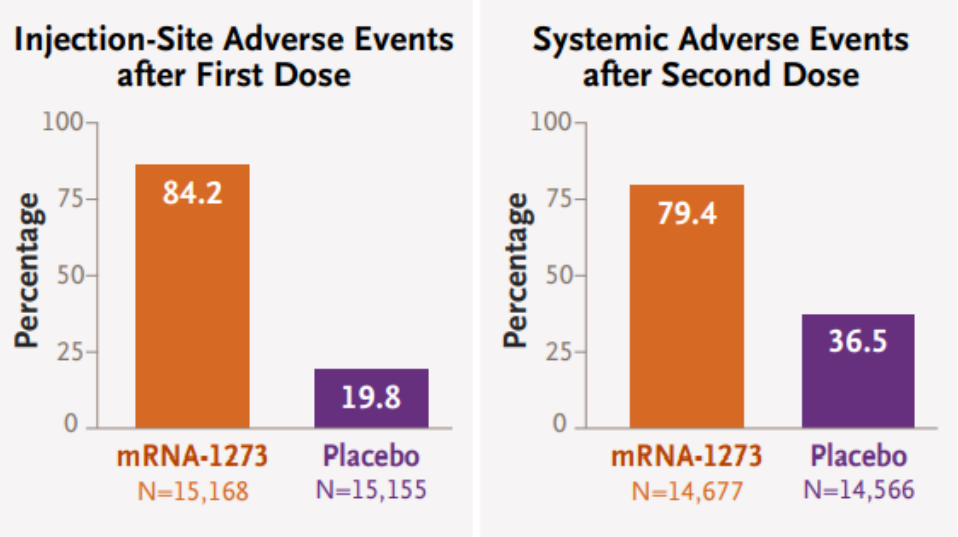
Moderna Vaccine (mRNA vaccine) continued

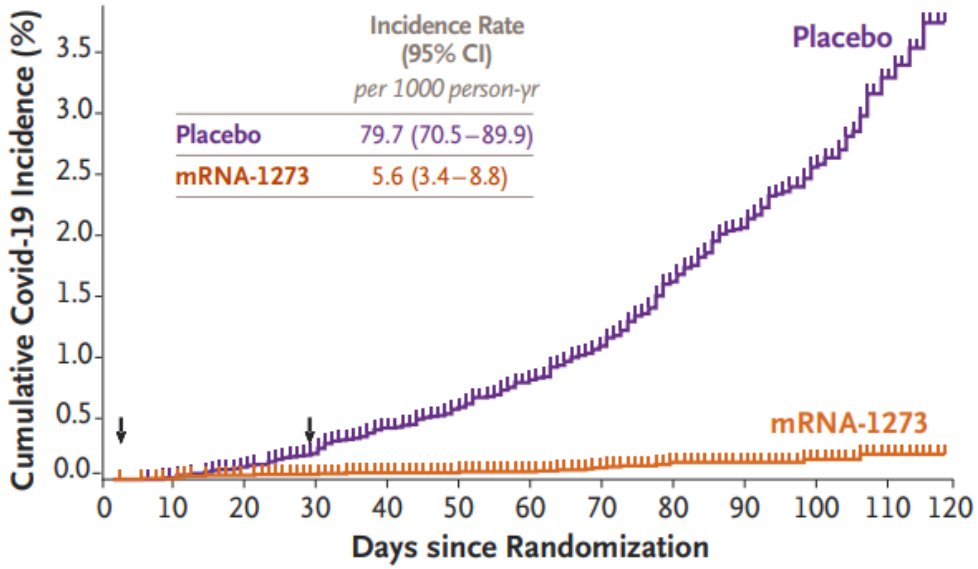
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 FEBRUARY 4, 2021 VOL. 384 NO. 5

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

L.R. Baden, H.M. El Sahly, B. Essink, K. Kotloff, S. Frey, R. Novak, D. Diemert, S.A. Spector, N. Rouphael, C.B. Creech, J. McGettigan, S. Khetan, N. Segall, J. Solis, A. Brosz, C. Fierro, H. Schwartz, K. Neuzil, L. Corey, P. Gilbert, H. Janes, D. Follmann, M. Marovich, J. Mascola, L. Polakowski, J. Ledgerwood, B.S. Graham, H. Bennett, R. Pajon, C. Knightly, B. Leav, W. Deng, H. Zhou, S. Han, M. Ivarsson, J. Miller, and T. Zaks, for the COVE Study Group*







	mRNA-1273 Vaccine N=14,550	Placebo N=14,598
Symptomatic Covid-19	11	185
Severe Covid-19	0	30

Vaccine efficacy of 94.1% (95% CI, 89.3–96.8%; P<0.001)

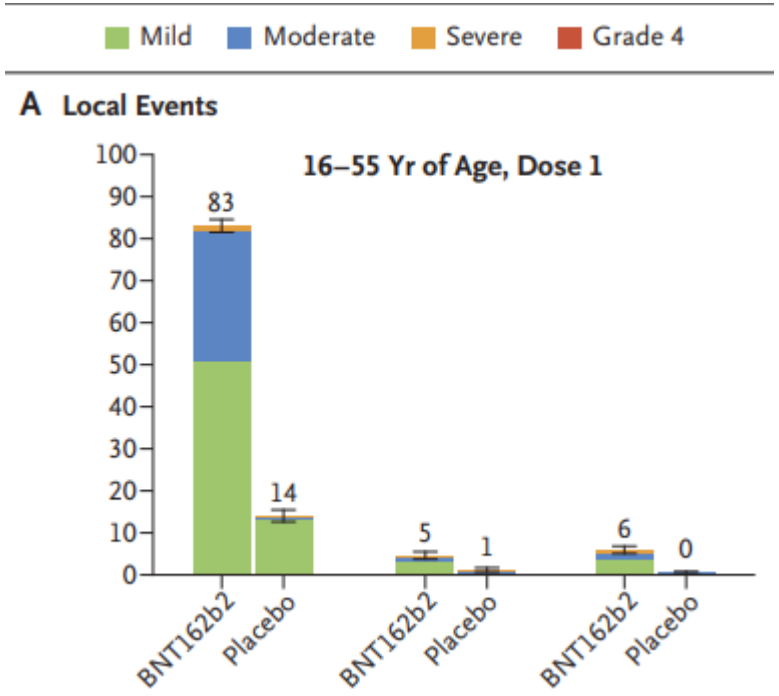
Pfizer/BioNTech Vaccine (mRNA vaccine)

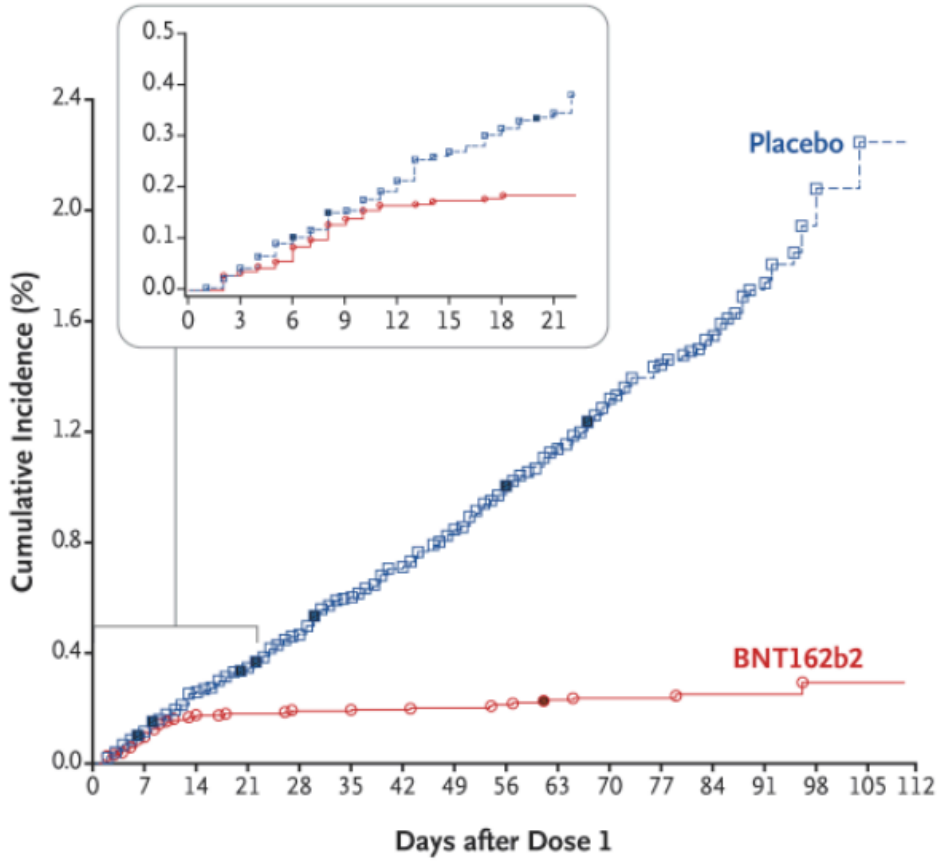
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 31, 2020 VOL. 383 NO. 27

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Fernando P. Polack, M.D., Stephen J. Thomas, M.D., Nicholas Kitchin, M.D., Judith Absalon, M.D., Alejandra Gurtman, M.D., Stephen Lockhart, D.M., John L. Perez, M.D., Gonzalo Pérez Marc, M.D., Edson D. Moreira, M.D., Cristiano Zerbini, M.D., Ruth Bailey, B.Sc., Kena A. Swanson, Ph.D., Satrajit Roychoudhury, Ph.D., Kenneth Koury, Ph.D., Ping Li, Ph.D., Warren V. Kalina, Ph.D., David Cooper, Ph.D., Robert W. Frenck, Jr., M.D., Laura L. Hammitt, M.D., Özlem Türeci, M.D., Haylene Nell, M.D., Axel Schaefer, M.D., Serhat Ünal, M.D., Dina B. Tresnan, D.V.M., Ph.D., Susan Mather, M.D., Philip R. Dormitzer, M.D., Ph.D., Uğur Şahin, M.D., Kathrin U. Jansen, Ph.D., and William C. Gruber, M.D., for the C4591001 Clinical Trial Group*



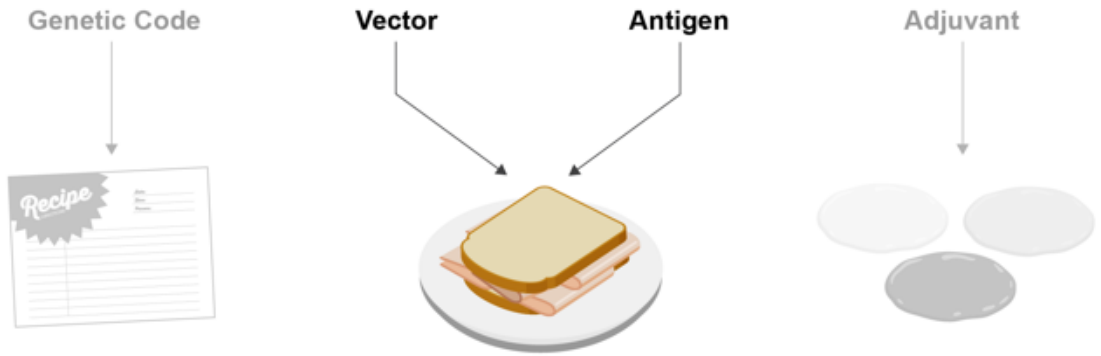


Vaccine efficacy of 95% (95% credible interval, 90.3 –97.6%)

AstraZaneca/Oxford Vaccine (viral vector)

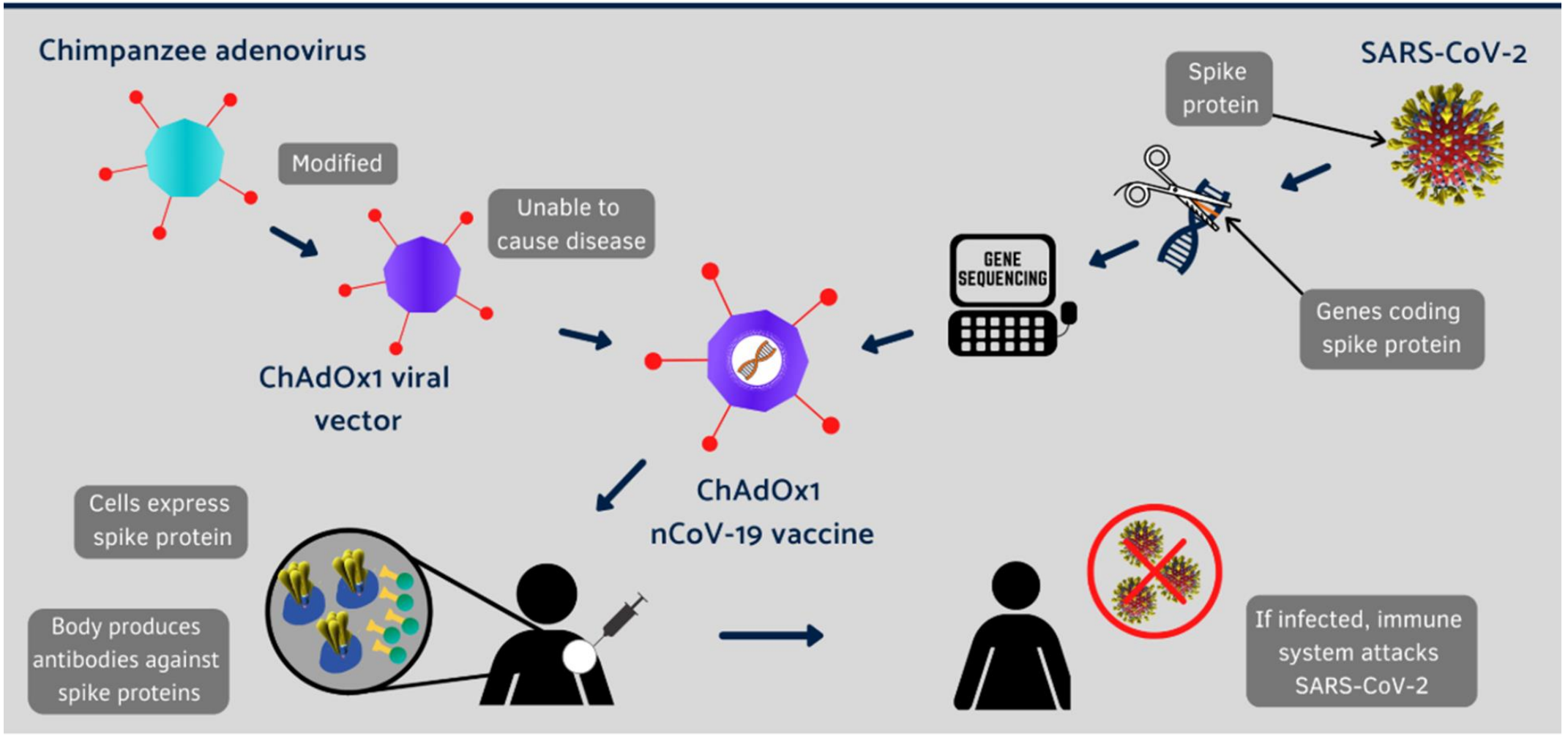
- This study tests the experimental vaccine called AZD1222.
- The study vaccine is commonly known as the “Oxford vaccine” or as “ChAdOx.”

AstraZeneca’s vaccine “sandwich”



- AstraZeneca’s vaccine uses a type of chimpanzee adenovirus as the **vector** (bread). Adenoviruses cause common colds.
- Because the adenovirus is from another species, the human body can easily recognize it as something foreign and the immune system can be put on alert.
- The vaccine **antigen** (sandwich filling) uses copies of the spike protein from SARS-CoV-2.
- This helps the immune system to produce the antibodies and T-cells specific to SARS-CoV-2 in order to protect you if you are ever exposed.

AstraZaneca/Oxford Vaccine (viral vector) continued

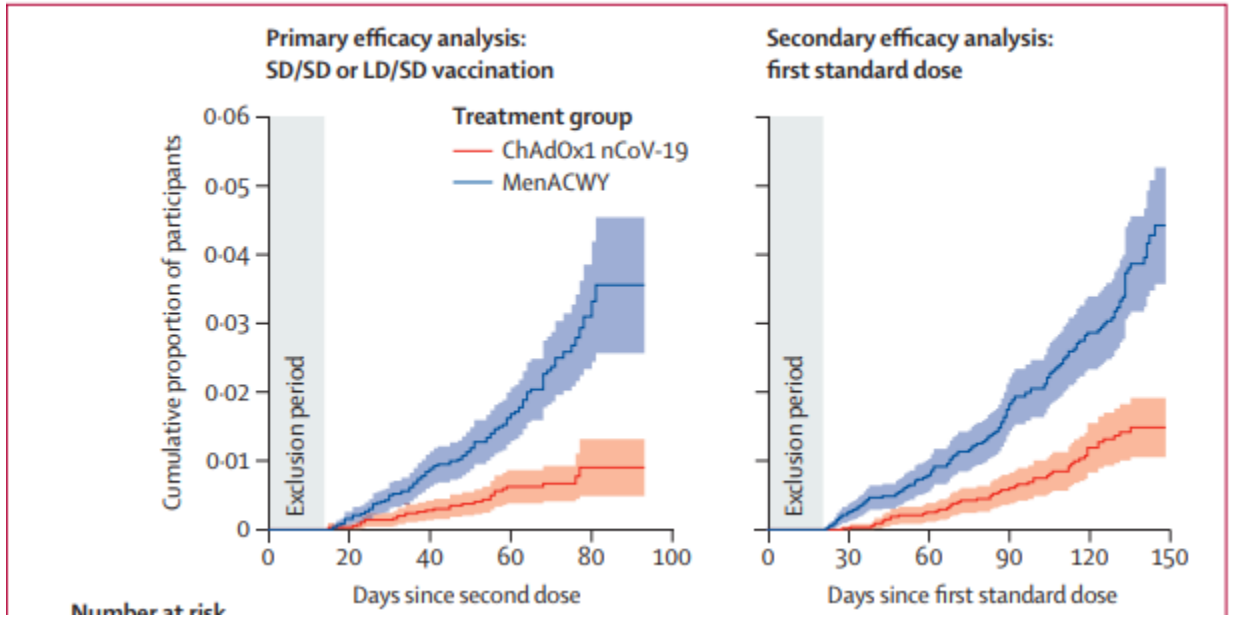


AstraZaneca/Oxford Vaccine (viral vector) continued

THE LANCET

Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK

Merryn Voysey, Sue Ann Costa Clemens*, Shabir A Madhi*, Lily Y Weckx*, Pedro M Folegatti*, Parvinder K Aley, Brian Angus, Vicky L Baillie, Shaun L Barnabas, Qasim E Bhorat, Sagida Bibi, Carmen Briner, Paola Cicconi, Andrea M Collins, Rachel Colin-Jones, Clare L Cutland, Thomas C Darton, Keertan Dheda, Christopher J A Duncan, Katherine R W Emary, Katie J Ewer, Lee Fairlie, Saul N Faust, Shuo Feng, Daniela M Ferreira, Adam Finn, Anna L Goodman, Catherine M Green, Christopher A Green, Paul T Heath, Catherine Hill, Helen Hill, Ian Hirsch, Susanne H C Hodgson, Alane Izu, Susan Jackson, Daniel Jenkin, Carina C D Joe, Simon Kerridge, Anthonet Koen, Gaurav Kwatra, Rajeka Lazarus, Alison M Lawrie, Alice Lelliott, Vincenzo Libri, Patrick J Lillie, Raburn Mallory, Ana V A Mendes, Eveline P Milan, Angela M Minassian, Alastair McGregor, Hazel Morrison, Yama F Mujadidi, Anusha Nana, Peter J O'Reilly, Sherman D Padayachee, Ana Pittella, Emma Plested, Katrina M Pollock, Maheshi N Ramasamy, Sarah Rhead, Alexandre V Schwarzbold, Nisha Singh, Andrew Smith, Rinn Song, Matthew D Snape, Eduardo Sprinz, Rebecca K Sutherland, Richard Tarrant, Emma C Thomson, M Estée Török, Mark Toshner, David P J Turner, Johan Vekemans, Tonya L Villafana, Marion E E Watson, Christopher J Williams, Alexander D Douglas*, Adrian V S Hill*, Teresa Lambe*, Sarah C Gilbert*, Andrew J Pollard* on behalf of the Oxford COVID Vaccine Trial Group†*

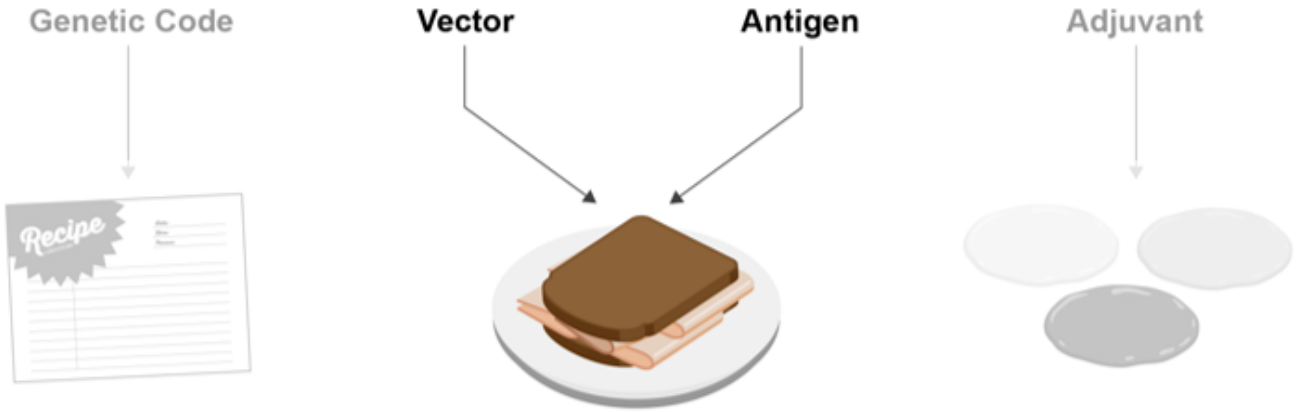


	Total number of cases	ChAdOx1 nCoV-19		Control		Vaccine efficacy (CI*)
		n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	
All LD/SD and SD/SD recipients	131	30/5807 (0·5%)	44·1 (248 299)	101/5829 (1·7%)	149·2 (247 228)	70·4% (54·8 to 80·6)†
COV002 (UK)	86	18/3744 (0·5%)	38·6 (170 369)	68/3804 (1·8%)	145·7 (170 448)	73·5% (55·5 to 84·2)
LD/SD recipients	33	3/1367 (0·2%)	14·9 (73 313)	30/1374 (2·2%)	150·2 (72 949)	90·0% (67·4 to 97·0)‡§
SD/SD recipients	53	15/2377 (0·6%)	56·4 (97 056)	38/2430 (1·6%)	142·4 (97 499)	60·3% (28·0 to 78·2)
COV003 (Brazil; all SD/SD)	45	12/2063 (0·6%)	56·2 (77 930)	33/2025 (1·6%)	157·0 (76 780)	64·2% (30·7 to 81·5)‡
All SD/SD recipients	98	27/4440 (0·6%)	56·4 (174 986)	71/4455 (1·6%)	148·8 (174 279)	62·1% (41·0 to 75·7)

Johnson and Johnson Vaccine (viral vector)

- Ensemble study tests the experimental vaccine called Ad26.COV2.S
- The study vaccine is commonly known as the “Oxford vaccine” or as “ChAdOx.”

Janssen’s vaccine “sandwich”



- Janssen uses a similar method for making its vaccine as AstraZeneca does.
- Their vector (bread) is a human Adenovirus called Adenovirus-26, or Ad26 for short.
- They also use the spike protein copied from SARS-CoV-2 as the meat, or antigen.
- You can think of the Janssen and AZ vaccines as similar sandwiches using different bread, such as turkey on sourdough and turkey on wheat.

COVID-19 Prevention Network

Johnson and Johnson Vaccine (viral vector)

Efficacy of Johnson & Johnson Single-Shot Janssen COVID-19 Vaccine
Phase 3 ENSEMBLE Trial

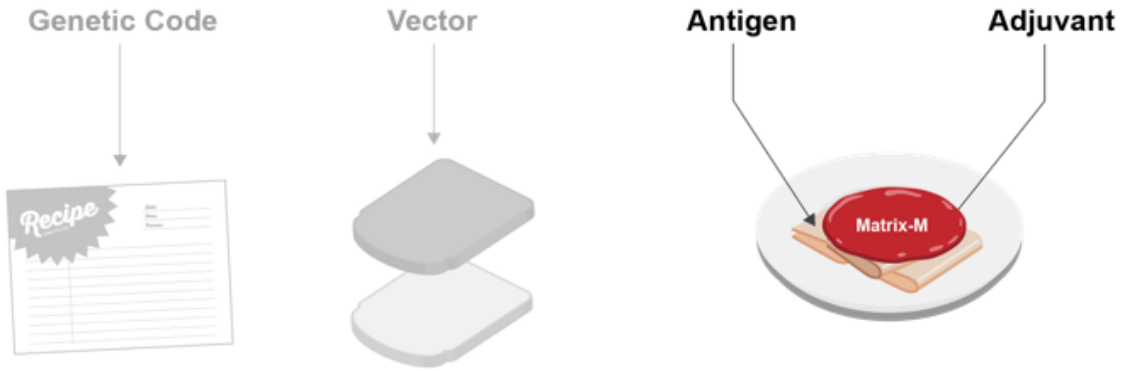
	Moderate & Severe (28 days)	Severe (28 days)	Severe (>49 days)
US	72% ⬇	85% ⬇ (100% ⬇ death)	100% ⬇
Latin America	66% ⬇		
South Africa (95% B.1.351 variant)	57% ⬇		

Novavax Vaccine (spike protein nanoparticle)

NOVAVAX
Creating Tomorrow's Vaccines Today

- This study tests the experimental vaccine called SARS-CoV-2 rS.
- The study vaccine is known as a recombinant spike protein nanoparticle vaccine.

The Novavax vaccine "sandwich"



- Novavax makes copies of the spike protein from SARS-CoV-2 in the laboratory, which is once again the antigen/meat of this "sandwich."
- These proteins are delivered on a microscopic particle. Since this particle isn't really a vector, we can't use any bread for this sandwich, just a plate.
- The tiny particle carrying spike proteins puts the immune system on alert that something foreign has entered the body.
- The adjuvant called Matrix-M™ is added to give the immune system an extra kick, similar to how the ketchup gives the meat a lot of added flavor.

COVID-19
Prevention Network

Novavax Vaccine Phase 2b and Phase 3

NOVAVAX
Creating Tomorrow's Vaccines Today

- Phase 3 trial results from the UK and phase 2b results from South Africa were recently announced
- Its efficacy in the UK was 89% at least seven days after individuals had received two doses of vaccine (n=15,000)
- In South Africa (n=4,400), the vaccine efficacy was 60% in people living without HIV. A small group of individuals living with HIV – about 150 – was included in the efficacy analysis. However, the study didn't have the statistical power to evaluate for vaccine efficacy specifically in this population.
- The South African efficacy readout is against the B.1.351 variant – 92% of all of the cases in the main analysis developed COVID-19 following infection by this variant.

Sputnik Vaccine (viral vector – prime-boost)

Sputnik V

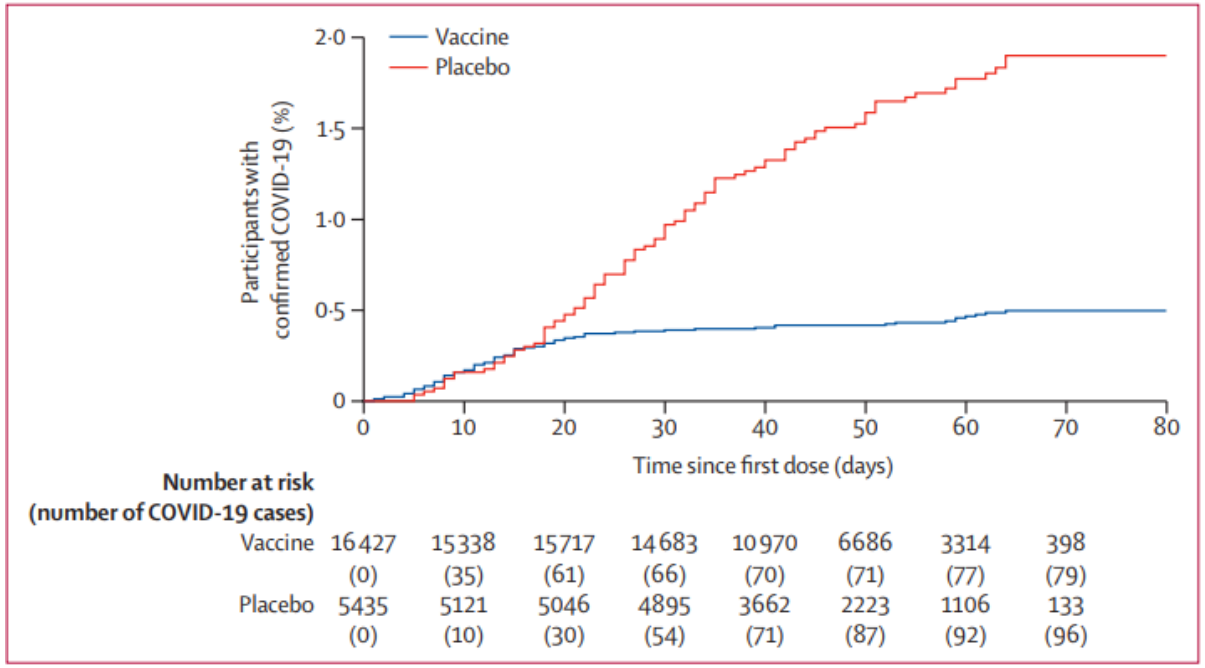


Figure 2: Kaplan-Meier cumulative incidence curves for the first symptomatic, PCR-positive COVID-19 after dose 1, in participants who received at least one dose of vaccine or placebo

	Total cases	Vaccine group	Placebo group	Vaccine efficacy (95% CI)	p value
First COVID-19 occurrence from 21 days after dose 1 (day of dose 2)*					
Overall	78	16/14 964 (0·1%)	62/4902 (1·3%)	91·6% (85·6–95·2)	<0·0001
First COVID-19 occurrence after dose 1†					
Any time after dose 1	175	79/16 427 (0·5%)	96/5435 (1·8%)	73·1% (63·7–80·1)	<0·0001
From 14 days after dose 1	109	30/14 999 (0·2%)	79/4950 (1·6%)	87·6% (81·1–91·8)	<0·0001
First COVID-19 occurrence after dose 2 (28 days after dose 1)*					
All	60	13/14 094 (0·1%)	47/4601 (1·0%)	91·1% (83·8–95·1)	<0·0001

THE LANCET

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

Summary: Variables in Vaccine Development

- **Vaccine platform:** how is the vaccine designed? Does it use:
  - Messenger RNA like in Moderna's design?
  - A viral vector like the adenovirus in AstraZeneca's or Janssen's designs?
  - A microscopic particle delivery like in Novavax's design?
  - Proteins like in Sanofi's design?
- **Adjuvant:** will anything be added to the vaccine for that extra kick?
- **Dose:** how much is given per injection?
- **Route:** where and how is the injection given?
- **Storage and transportation**: cold chain requirements ?
- **Timing:** how many injections and how much time between them?

Summary: Variables in Vaccine Development

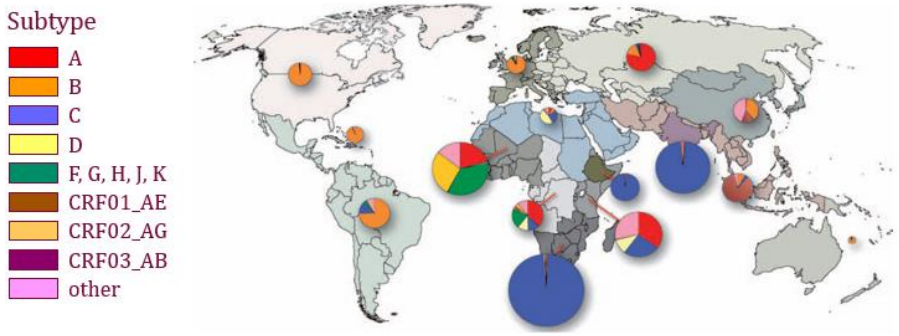
Product	Design	Adjuvant	Cold chain	How do I get the shot?	How often?
Moderna mRNA-1273	mRNA	-	- 20 degreesC	Shot in the deltoid muscle of your upper arm	Twice: Day 0 and Day 29
AstraZeneca AZD1222	Chimp adenovirus vector	-	2 to 8 degreesC		Twice: Day 0 and Day 29
Janssen Ad26.COV2.S	Human adenovirus-26 vector	-	2 to 8 degreesC		**1 dose** – Day 0
Novavax SARS-CoV-2 rS	Protein Subunit Nanoparticle	Matrix-M™	2 to 8 degreesC		Twice: Day 0 and Day 21
Pfizer	mRNA	-	- 70 degreesC		Twice: Day 0 and Day 21

For two dose regimens, looks okay and maybe better to give at least 3 months apart

COVID-19 Prevention Network

Were corners cut ? BIG NO !!

- Bringing Covid-19 vaccines to market in one year instead of 10 has been a monumental task. But was it really developed in 1 year ??
- We did not start from ZERO ! Built on SARS, MERS and HIV vaccine work
- Parallel clinical development. Relay race !
- Genetic engineering advancements i.e. gene sequencing
- Funding for multiple vaccines
- Expedition by regulatory authorities
- How about HIV ???
  - Genetic diversity
  - Animal or human models for recovery



How safe are vaccines ? (V-Safe / CDC tracking data)

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

	Pfizer-BioNTech	Moderna	All COVID-19 vaccines
People receiving 1 or more doses in the United States*	12,153,536	9,689,497	21,843,033
Registrants completing at least 1 v-safe health check-in†	997,042	1,083,174	2,080,216
Pregnancies reported to v-safe	8,633	6,498	15,131

Local and systemic reactions, day 0-7*,†	All vaccines %	Pfizer- BioNTech dose 1 %	Pfizer-BioNtech dose 2 %	Moderna dose 1 %
Pain	70.7	67.7	74.8	70.1
Fatigue	33.4	28.6	50.0	29.7
Headache	29.4	25.6	41.9	26.0
Myalgia	22.8	17.2	41.6	19.6
Chills	11.5	7.0	26.7	9.3
Fever	11.4	7.4	25.2	9.1
Swelling	11.0	6.8	26.7	13.4
Joint pain	10.4	7.1	21.2	8.6
Nausea	8.9	7.0	13.9	7.7

How safe are vaccines ? (V-Safe / CDC tracking data)

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

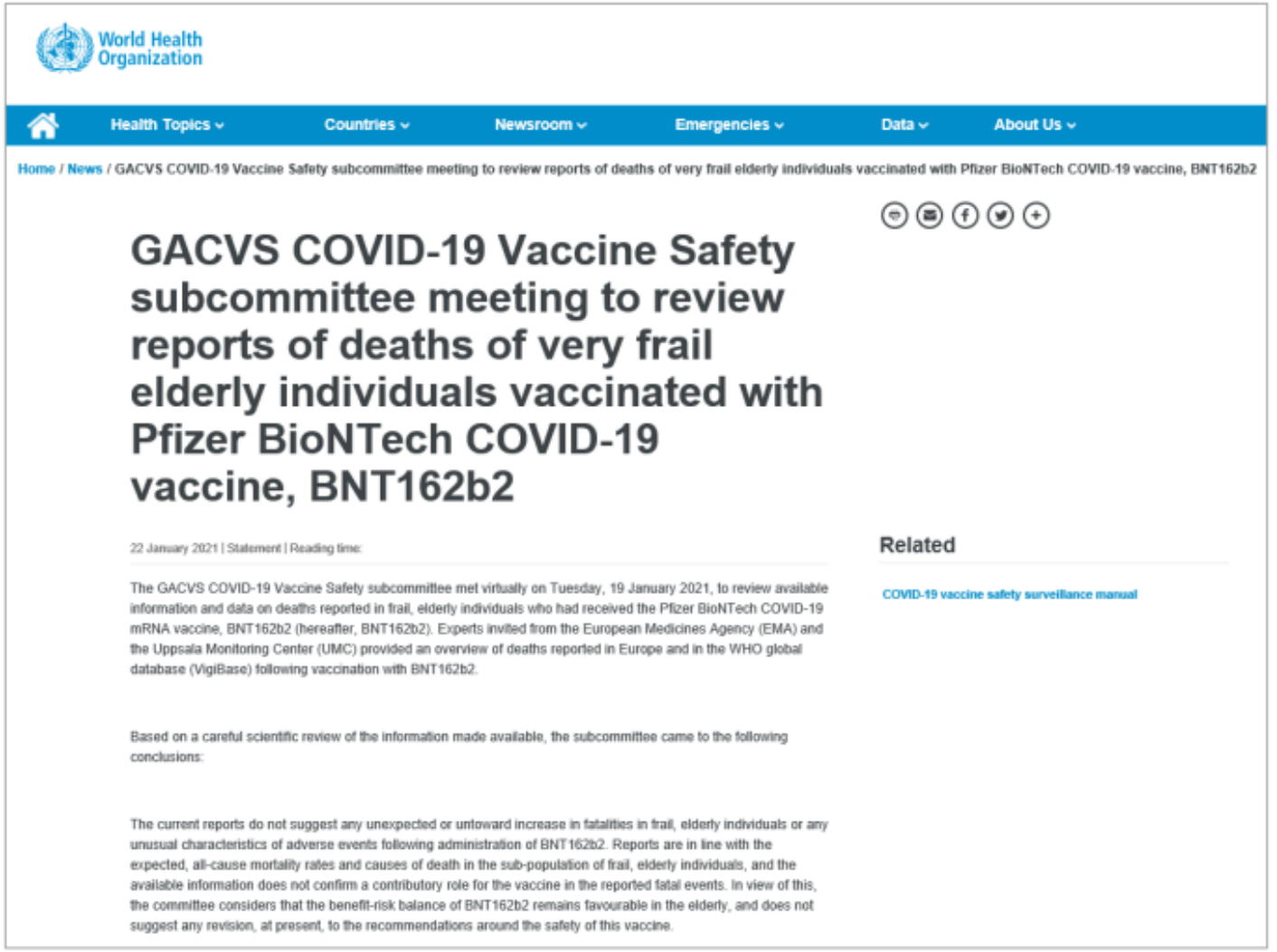
Reported vaccine doses administered	Anaphylaxis cases	Reporting rate (analytic period Dec 14-Jan 18)
Pfizer-BioNTech: **9,943,247**	50	5.0 per million doses admin.
Moderna: **7,581,429**	21	2.8 per million doses admin.

How safe are vaccines ? (V-Safe / CDC tracking data)

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System



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Home / News / GACVS COVID-19 Vaccine Safety subcommittee meeting to review reports of deaths of very frail elderly individuals vaccinated with Pfizer BioNTech COVID-19 vaccine, BNT162b2

GACVS COVID-19 Vaccine Safety subcommittee meeting to review reports of deaths of very frail elderly individuals vaccinated with Pfizer BioNTech COVID-19 vaccine, BNT162b2

22 January 2021 | Statement | Reading time:

The GACVS COVID-19 Vaccine Safety subcommittee met virtually on Tuesday, 19 January 2021, to review available information and data on deaths reported in frail, elderly individuals who had received the Pfizer BioNTech COVID-19 mRNA vaccine, BNT162b2 (hereafter, BNT162b2). Experts invited from the European Medicines Agency (EMA) and the Uppsala Monitoring Center (UMC) provided an overview of deaths reported in Europe and in the WHO global database (VigiBase) following vaccination with BNT162b2.

Based on a careful scientific review of the information made available, the subcommittee came to the following conclusions:

The current reports do not suggest any unexpected or untoward increase in fatalities in frail, elderly individuals or any unusual characteristics of adverse events following administration of BNT162b2. Reports are in line with the expected, all-cause mortality rates and causes of death in the sub-population of frail, elderly individuals, and the available information does not confirm a contributory role for the vaccine in the reported fatal events. In view of this, the committee considers that the benefit-risk balance of BNT162b2 remains favourable in the elderly, and does not suggest any revision, at present, to the recommendations around the safety of this vaccine.

Related

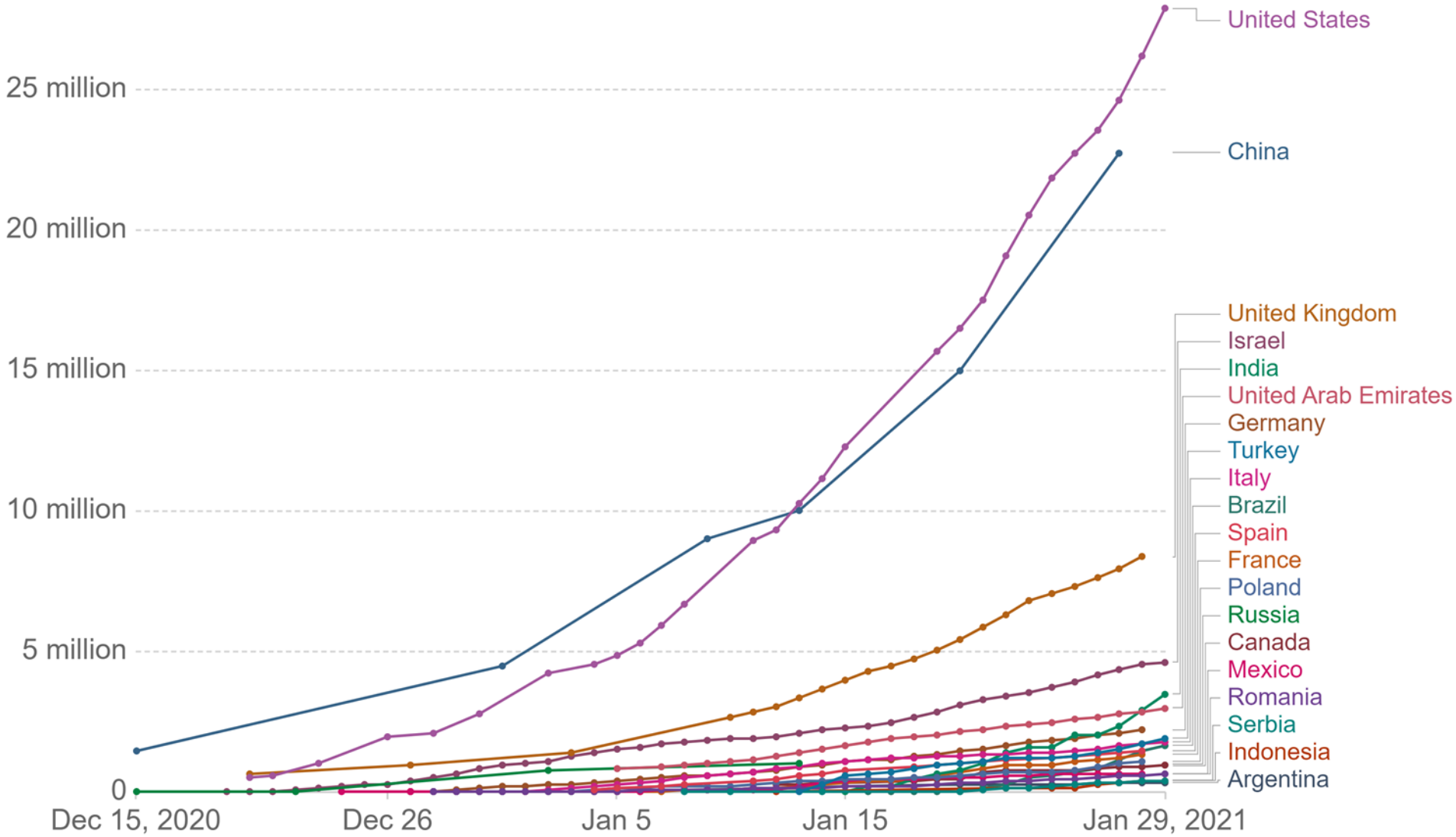
COVID-19 vaccine safety surveillance manual

https://www.who.int/news/item/22 -01-2021-gacvs-review-deaths-pfizer-biontech-covid-19-vaccine-bnt162b2

COVID-19 vaccine doses administered

Total number of vaccination doses administered. This is counted as a single dose, and may not equal the total number of people vaccinated, depending on the specific dose regime (e.g. people receive multiple doses).

Our World in Data



Source: Official data collated by Our World in Data – Last updated 30 January, 09:10 (London time)

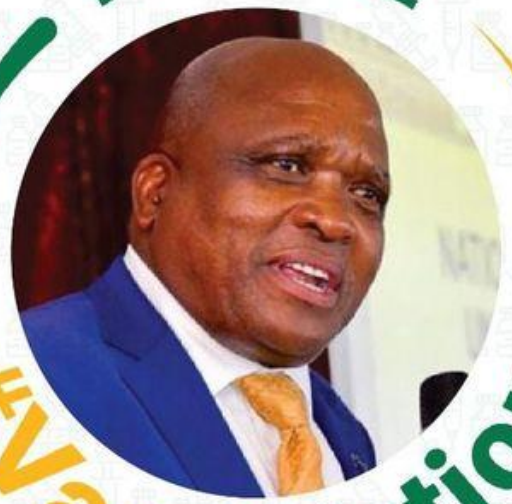
Closing thoughts

- Greater than 100 million COVID-19 vaccine doses have been administered globally
- Overall, the safety profiles of COVID-19 vaccines are reassuring and consistent with that observed from the pre-authorization clinical trials
- Always confirm what you read online with your doctor
- Get vaccinated !! This is not a way to live
- Stay safe from COVID-19: Observe distancing, Sanitize, Wear a mask and get vaccinated

Some Unknowns

- Safety and efficacy of the vaccines in “special” populations.
- Duration of protection provided by these vaccines.
- Degree to which these vaccines protect against infection and transmission.

I CHOOSE



#VacciNation

My choice to vaccinate is an ethical one. I will be vaccinating to protect not just myself, but the lives of others too.

Dr Joe Phaahla - Deputy Minister of Health

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

COVID-19
Prevention Network

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