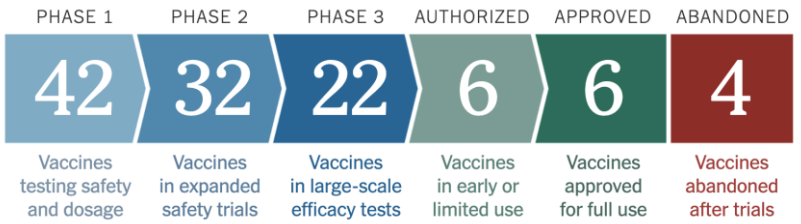
COVID-19 Vaccine Candidates: Characteristics, Efficacy and Safety Profile

Omar Okasha

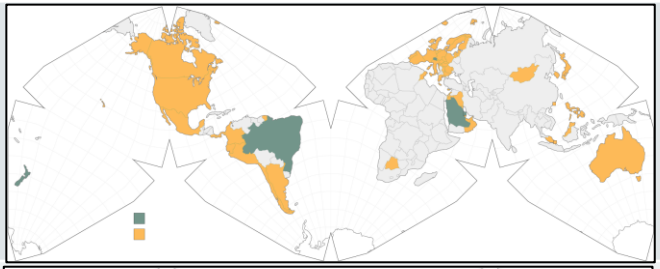
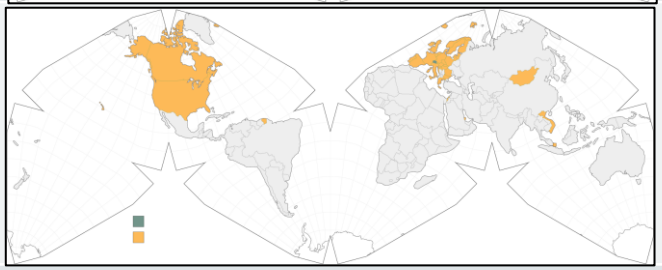
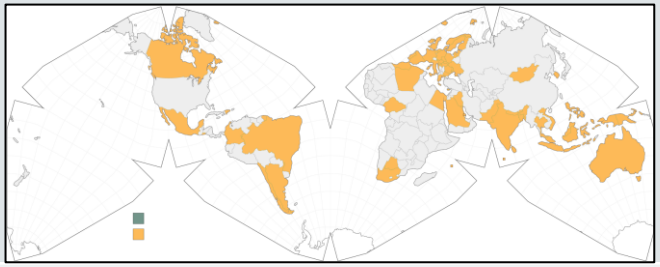
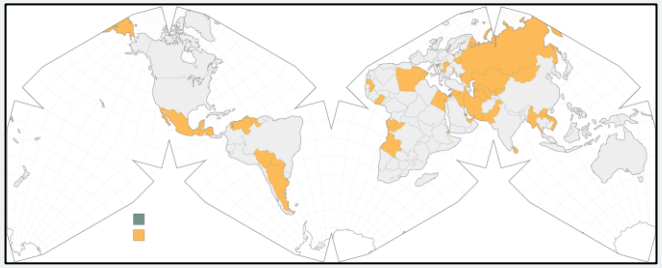
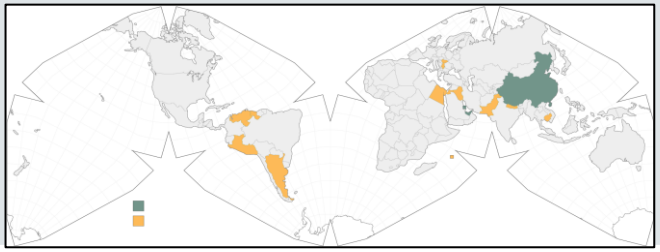
15-March-2021

Introduction



- Landscape Summary of COVID-19 vaccines **currently licensed for use,** including their efficacy and safety:
  - *Data mainly from pivotal trials, authorised labelling and Risk Management Plans*
- **Candidate** COVID-19 vaccine landscape is not within the scope of the presentation but regularly updated by the London School of Hygiene and Tropical Medicine* and WHO**.

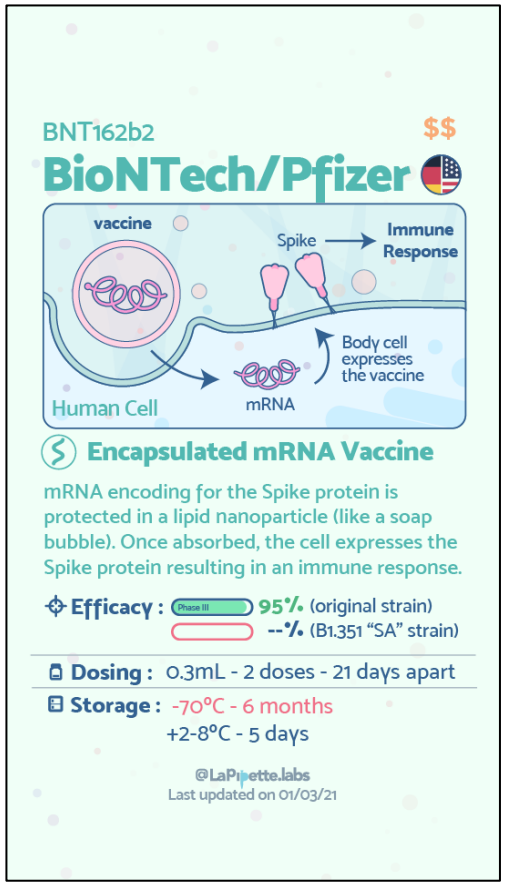
*https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/
**https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

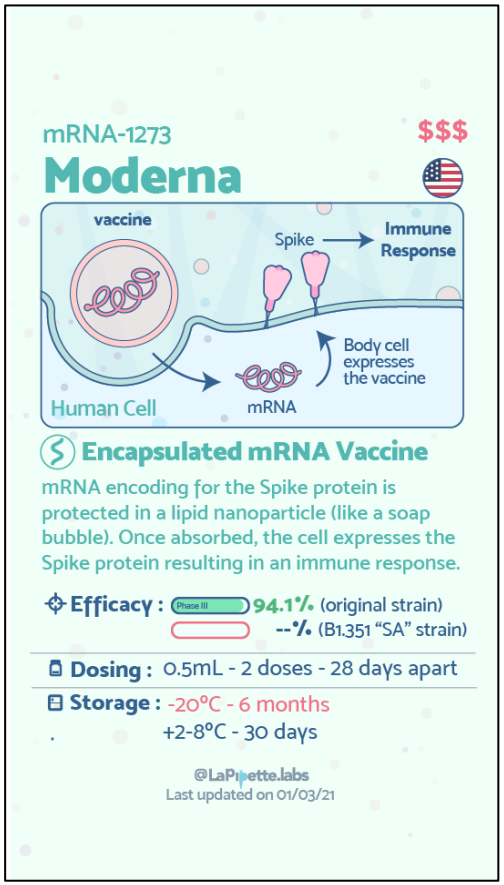
Vaccine Name	Vaccine Type	Developers	Approval (green)/early, limited, or emergency use (orange)
Comirnaty (BNT162b2)	mRNA-based vaccine	Pfizer, BioNTech; Fosun Pharma	
Moderna COVID-19 Vaccine (mRNA-1273)	mRNA-based vaccine	Moderna, BARDA, NIAID	
COVID-19 Vaccine AstraZeneca (AZD1222/ChAdOx 1 nCOV-19); also known as Covishield	Non-replicating viral vector	Astrazeneca, University of Oxford	
Sputnik V	Non-replicating viral vector	Gamaleya Research Institute, Acellena Contract Drug Research and Development	
BBIBP-CorV	Inactivated vaccine	Beijing Institute of Biological Products; Sinopharm	

Regulatory Affairs Professional Society [https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker] Updated on 18 February 2021. Accessed on 8-Mar-20201;
Source of maps: https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

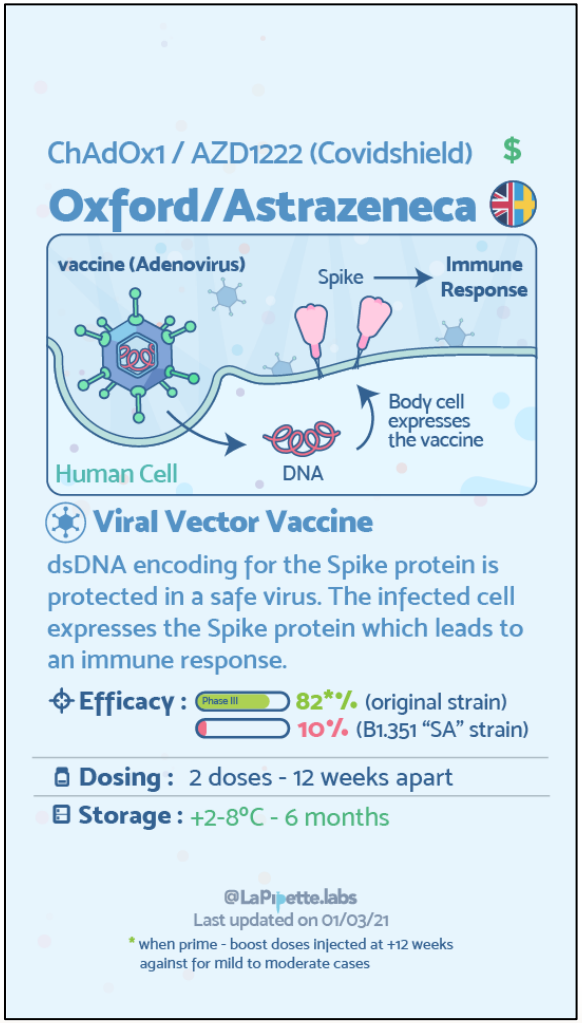
5 examples of COVID-19 vaccines

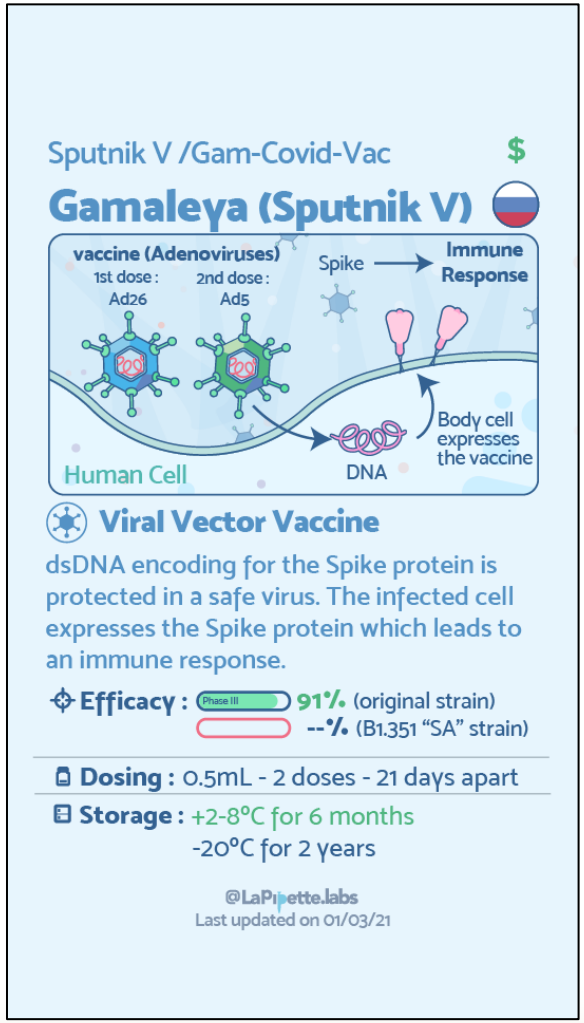
2 examples of **encapsulated mRNA vaccines**



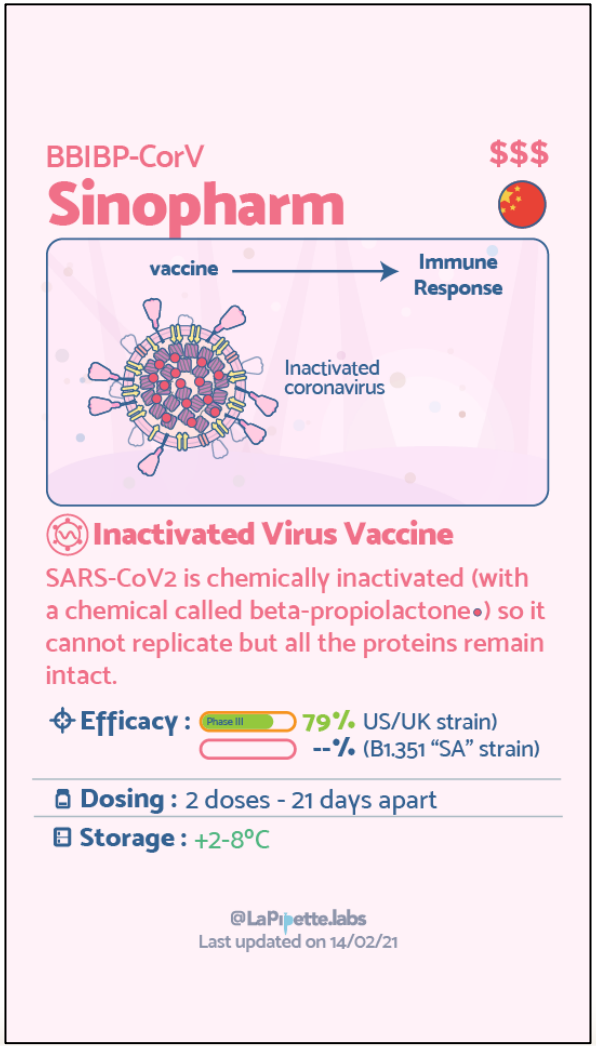


2 examples of **viral vector vaccines**





1 example of an **inactivated virus vaccine**



mRNA Vaccines – Comirnaty (BNT162b2)

https://www.aerzteblatt.de/nachrichten/118189/SARS-CoV-2-Impfstoff-von-Biontech-Pfizer-verhindert-in-Phase-3-Studie-mehr-als-90-der-bestaetigten-Infektionen

- Lipid nanoparticle-formulated mRNA encoding full-length spike (S) protein
- 51,358 subjects in registered trials

The NEW ENGLAND JOURNAL of MEDICINE

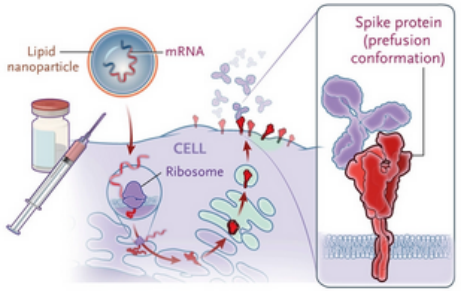
RESEARCH SUMMARY

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

F.P. Polack, et al. DOI: 10.1056/NEJMoa2034577

CLINICAL PROBLEM

Safe and effective vaccines to prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Covid-19 are urgently needed. No vaccines that protect against betacoronaviruses are currently available, and mRNA-based vaccines have not been widely tested.

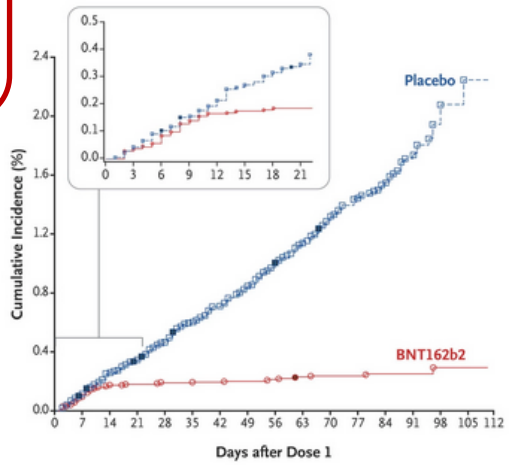


CLINICAL TRIAL

A randomized, double-blind study of an mRNA vaccine encoding the SARS-CoV-2 spike protein.

43,548 participants ≥16 years old were assigned to receive the vaccine or placebo by intramuscular injection on day 0 and day 21. Participants were followed for safety and for the development of symptomatic Covid-19 for a median of 2 months.

Pivotal trial



RESULTS

Safety:
Vaccine recipients had local reactions (pain, erythema, swelling) and systemic reactions (e.g., fever, headache, myalgias) at higher rates than placebo recipients, with more reactions following the second dose. Most were mild to moderate and resolved rapidly.

Efficacy:
The vaccine showed protection 7 days after the second dose; 95% efficacy was observed.

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

LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

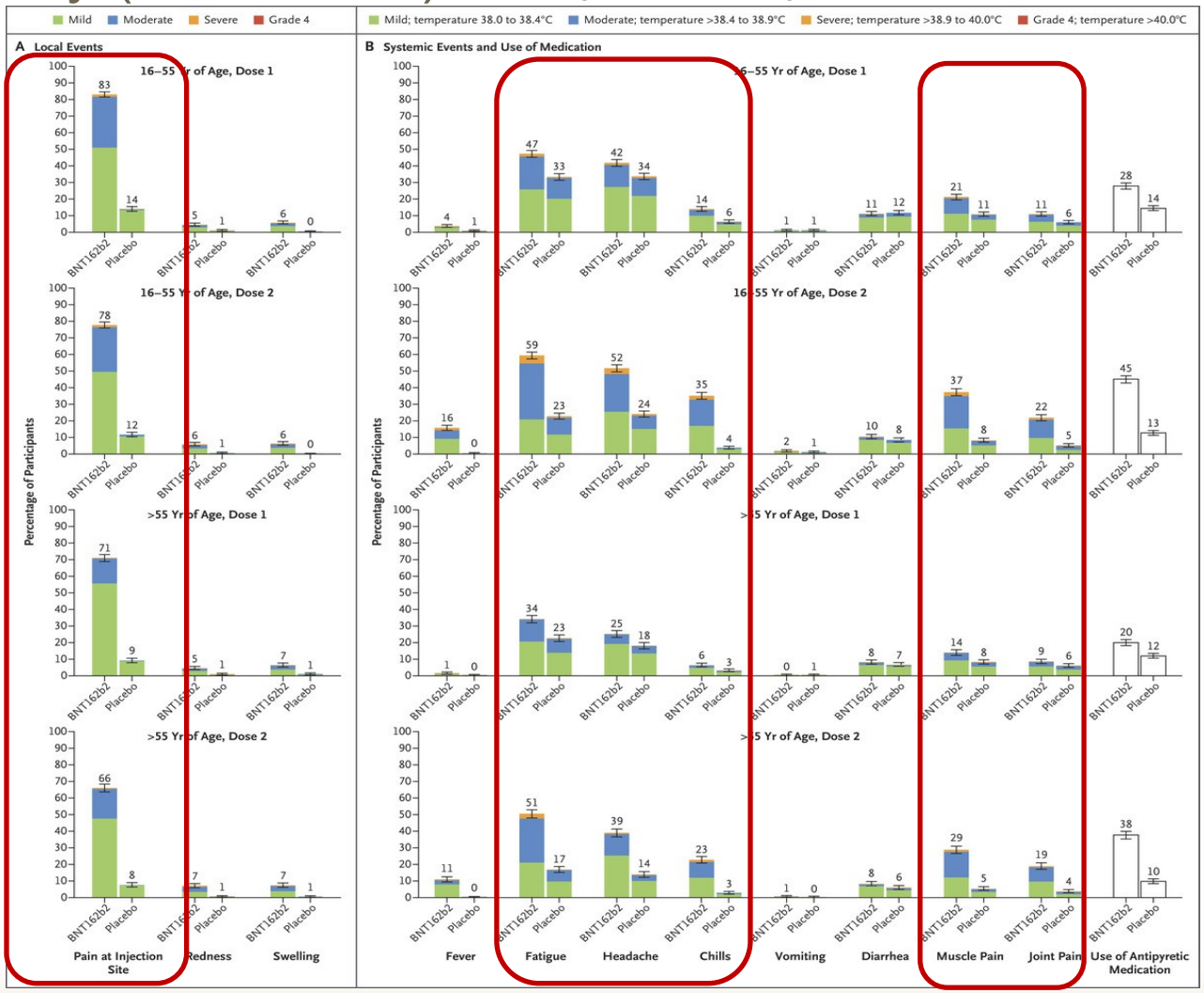
- Safety and efficacy beyond 2 months and in groups not included in this trial (e.g., children, pregnant women, and immunocompromised persons).
- Whether the vaccine protects against asymptomatic infection and transmission to unvaccinated persons.
- How to deal with those who miss the second vaccine dose.

CONCLUSIONS

Two doses of an mRNA-based vaccine were safe over a median of two months and provided 95% protection against symptomatic Covid-19 in persons 16 years of age or older.

Links: Full article | Quick Take | Editorial

Comirnaty (BNT162b2): Safety Summary*



FP Polack et al. N Engl J Med 2020;383:2603-2615.

Comirnaty (BNT162b2)

Safety Summary*

Other relevant adverse reactions:

- **Bell's palsy**
- **Lymphadenopathy**
- **Anaphylaxis**

Potential Risks:

- **Vaccine-associated enhanced disease** (VAED)
  - Is atypical/modified presentation of clinical infection affecting individuals exposed to a wild-type pathogen after having received a prior vaccination for the same pathogen
  - A theoretical risk either before the full vaccine regimen is administered or in vaccinees with waning immunity over time.
  - Not observed or identified in clinical studies, yet

*European Public Assessment Report and EU Risk Management Plan [https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty] Accessed on 24/02/2021

mRNA Vaccines – Moderna COVID-19 Vaccine

https://www.pharmazeutische-zeitung.de/zweiter-covid-19-impfstoff-erhaelt-zulassungsempfehlung-122856/

- Lipid nanoparticle-formulated mRNA encoding full-length spike (S) protein
- 34,320 subjects in registered trials

The NEW ENGLAND JOURNAL of MEDICINE

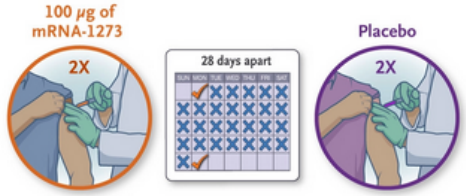
RESEARCH SUMMARY

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

L.R. Baden, et al. DOI: 10.1056/NEJMoa2035389

CLINICAL PROBLEM

The Covid-19 pandemic continues and expands. Additional data regarding vaccines to prevent symptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are needed. The mRNA-1273 vaccine is a lipid-encapsulated mRNA vaccine encoding the prefusion stabilized spike protein of SARS-CoV-2.

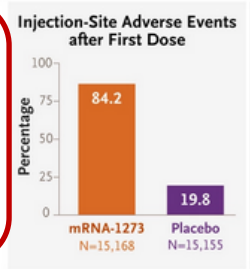


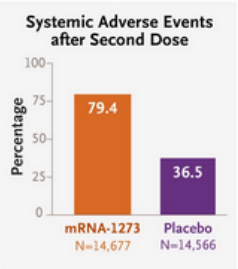
CLINICAL TRIAL

A randomized, double-blind trial to evaluate the efficacy and safety of mRNA-1273.

30,420 participants ≥18 years old were assigned to receive either the vaccine or placebo in two intramuscular injections 28 days apart. Participants were followed for safety and the development of laboratory-confirmed, symptomatic Covid-19 over a median of 2 months after the second dose.

Pivotal trial

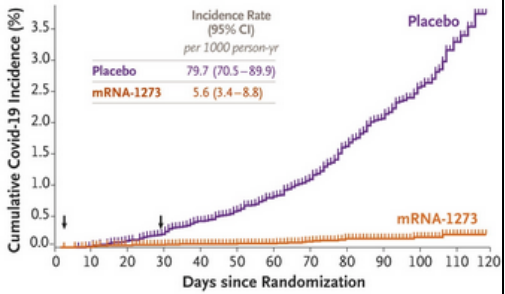




RESULTS

Safety:
Vaccine recipients had higher rates of local reactions (e.g., pain, erythema, swelling) and systemic reactions (e.g., headache, fatigue, myalgia) than placebo recipients. Most reactions were mild to moderate and resolved over 1–3 days.

Efficacy:
The incidence of Covid-19 was lower among vaccine recipients than among placebo recipients as early as 14 days after the first dose. Protection in the vaccine group persisted for the period of follow-up.



	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)

LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- Safety and efficacy over a longer period of time, in a larger population, and in pregnant women and children.
- Whether the vaccine protects against asymptomatic infection and transmission to unvaccinated persons.
- How to care for those who miss the second vaccine dose.

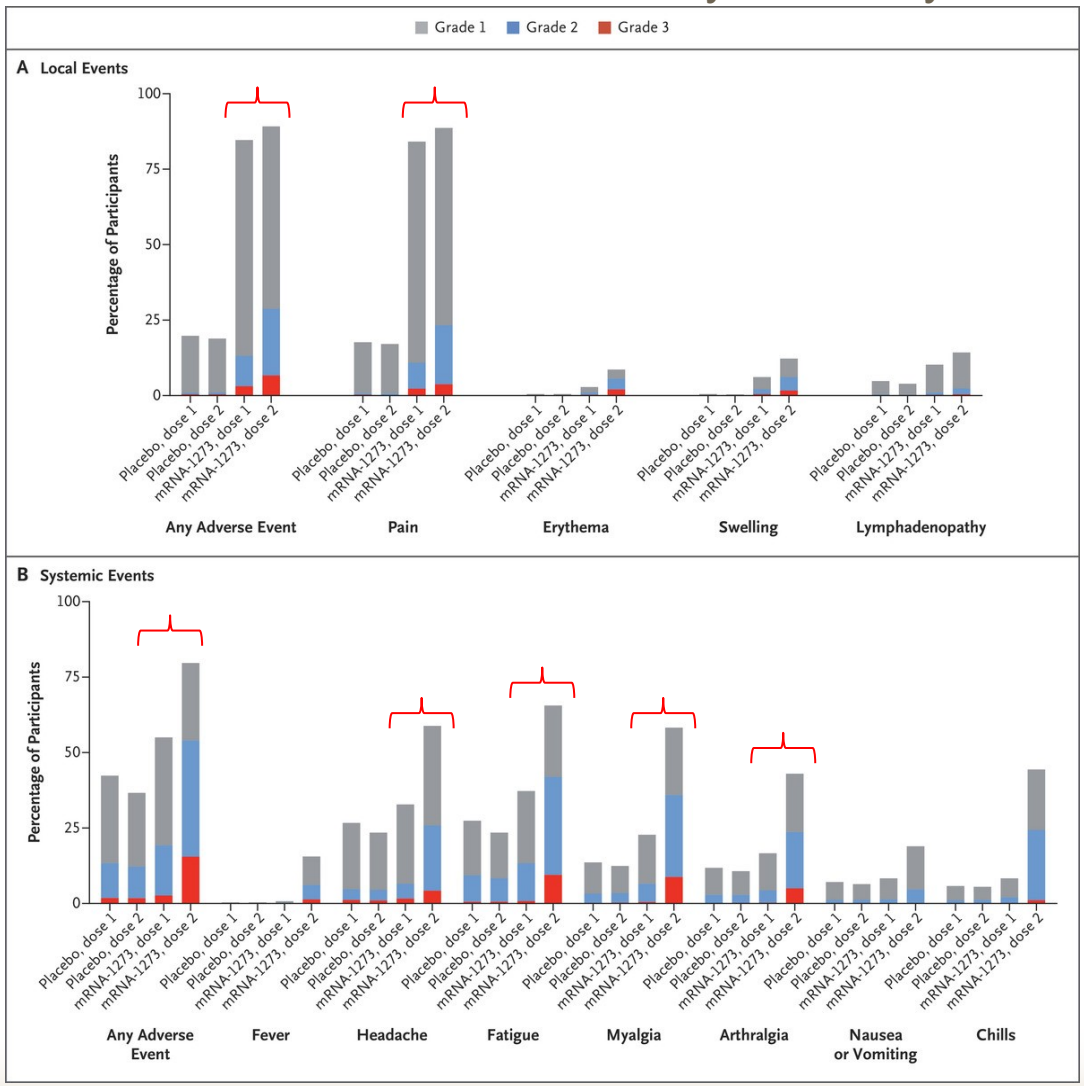
CONCLUSIONS

Two doses of a SARS-CoV-2 mRNA-based vaccine were safe and provided 94% efficacy against symptomatic Covid-19 in persons 18 or older.

Links: Full article | NEJM Quick Take | Editorial

L R. Baden, H M. El Sahly, B. Essink et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med 2021; 384:403-416

Moderna COVID-19 Vaccine: Safety Summary*



*LR Baden et al. N Engl J Med 2021;384:403-416

Moderna COVID-19 Vaccine

Safety Summary*

Other Relevant Adverse Reactions:

- **Bell's palsy**
- **Lymphadenopathy**.
- **Anaphylaxis** (reported from post-authorisation use)

Potential Risks:

- **VAED** (see before)

*European Public Assessment Report and EU Risk Management Plan [https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-moderna] Accessed on 24/02/2021

Viral Vector Vaccines – Oxford/AstraZeneca Vaccine

- Simian adenovirus vector containing codon-optimised spike (S) protein (ChAdOx1 nCOV-19)
- 58,166 subjects in registered trials

Pivotal Trial*:
11 636 participants ≥ 18 years, randomly assigned (1:1) to vaccine or control (meningococcal group ACWY vaccine or saline).

Vaccine group:
- two doses containing 5×10^{10} viral particles (standard dose; SD/SD cohort)
- **a subset in the UK trial received a half dose as their first dose (low dose) and a standard dose as their second dose (LD/SD cohort)**
- followed for symptomatic COVID-19 in seronegative participants more than 14 days after a second dose of vaccine.

Efficacy Results:
In participants who received two standard doses, **vaccine efficacy was 62.1%** and in participants who received a low dose followed by a standard dose, efficacy was **90.0%**. Overall vaccine efficacy across both groups was **70.4%**

*Voysey M, Clemens SAC, Madhi SA et al Oxford COVID Vaccine Trial Group. 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. Lancet. 2021 Jan 9;397(10269):99-111.

Viral Vector Vaccines – Oxford/Astrazeneca Vaccine

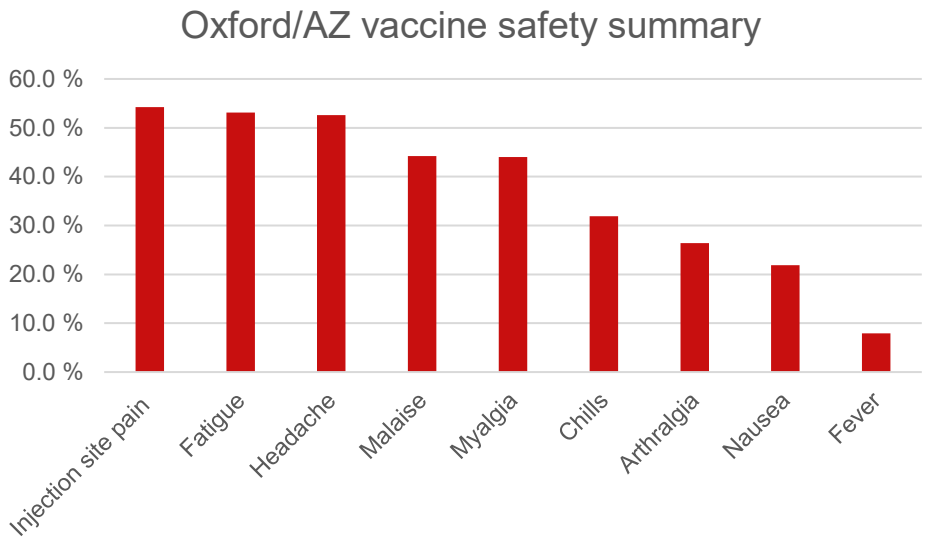
Safety Summary*

Other Relevant Adverse Events:

- **Lymphadenopathy**
- **Anaphylaxis** (reported from post authorisation use)

Potential Risks:

- Bell's palsy
- 1 case of **transverse myelitis**
- **VAED** including VAERD (see before)



*European Public Assessment Report and EU Risk Management Plan [https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-astrazeneca] Accessed on 24/02/2021

Viral Vector Vaccines – Sputnik V

- Recombinant adenovirus expressing full-length spike (S) protein. Two vector components, rAd26-S and rAd5-S. The use of two varying serotypes, given 21 days apart, is intended to overcome any pre-existing adenovirus immunity in the population.
- 44,754 subjects in registered trials

Pivotal Trial*:

21 977 participants ≥ 18 years, randomly assigned to the vaccine group (n=16 501) or the placebo group (n=5476).

- The vaccine (first dose rAd26, second dose rAd5) or placebo administered IM with a 21-day interval between doses.
- 19 866 received two doses of vaccine or placebo and were included in the primary outcome analysis.

Efficacy Results:

From 21 days after the first dose of vaccine (the day of dose 2), 16 (0.1%) of 14 964 participants in the vaccine group and 62 (1.3%) of 4902 in the placebo group were confirmed to have COVID-19; **vaccine efficacy was 91.6%** (95% CI 85.6–95.2).

* D. Lugonov et al. 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. Lancet 2021; 397: 671–81

Viral Vector Vaccines – Sputnik V

Summary Safety Results (Data from pivotal trial publication):

- Most common AEs:
  - flu-like illness (15.2%)
  - local injection site reaction (5.4%)
- Two episodes of AEs of grade 3 or worse, considered not associated with vaccination: an exacerbation of urolithiasis and acute sinusitis.
- In participants older than 60 years: three SAEs reported in the vaccine group: renal colic and deep vein thrombosis (both associated with pre-existing comorbidities) and extremity abscess.

*D. Lugonov et al. 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. Lancet 2021; 397: 671–81

Inactivated Vaccine – Sinopharm vaccine

- Fragmentary release of data.
- Results from Phase I/II trials*:
  - Vaccine well-tolerated and elicited an immunogenic response.

Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial

Yanjun Zhang, Gang Zeng*, Hongxing Pan*, Changgui Li*, Yaling Hu, Kai Chu, Weixiao Han, Zhen Chen, Rong Tang, Weidong Yin, Xin Chen, Yuansheng Hu, Xiaoyong Liu, Congbing Jiang, Jingxin Li, Minnan Yang, Yan Song, Xiangxi Wang, Qiang Gao†, Fengcai Zhu†*

- Interim analysis of Phase III trials:
  - Indication of **86% efficacy against COVID-19 infection** according to the United Arab Emirates ministry of health**:

MOHAP in collaboration with Department of Health Abu Dhabi (DOH) have reviewed Sinopharm CNBG's interim analysis of the phase III trials, which shows Beijing Institute of Biological Product's inactivated vaccine to have 86% efficacy against COVID-19 infection. The analysis also shows the vaccine to have 99% seroconversion rate of neutralizing antibody and 100% effectiveness in preventing moderate and severe cases of the disease. Furthermore, the analysis shows no serious safety concerns.

*Y. Zhang; G. Zeng et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis 2021; 21: 181–92

**UAE ministry of health and prevention [https://www.mohap.gov.ae/en/MediaCenter/News/Pages/2699.aspx] accessed on 25 Feb 2021

Take home messages

Take home messages

- COVID-19 vaccines are being developed using 3 main vaccine platforms:
  - inactivated viral vaccines
  - viral vector-based vaccines
  - mRNA vaccines
- COVID-19 vaccine candidates are novel vaccines
- Number of individuals exposed to vaccines during clinical trials is limited
- Close safety and effectiveness monitoring post authorization should be carefully conducted to continue to assess the safety profile and efficacy of each vaccine

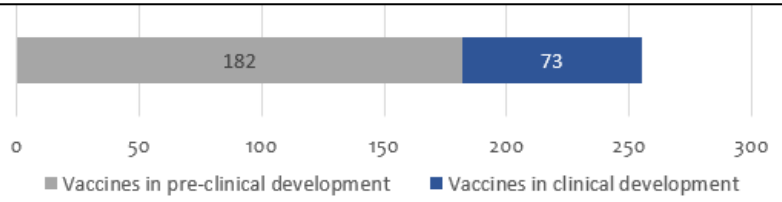

Q&A
SESSION

Back-Up

Summary information of Covid Vaccines in clinical development

1. - Number of vaccines in clinical development 73

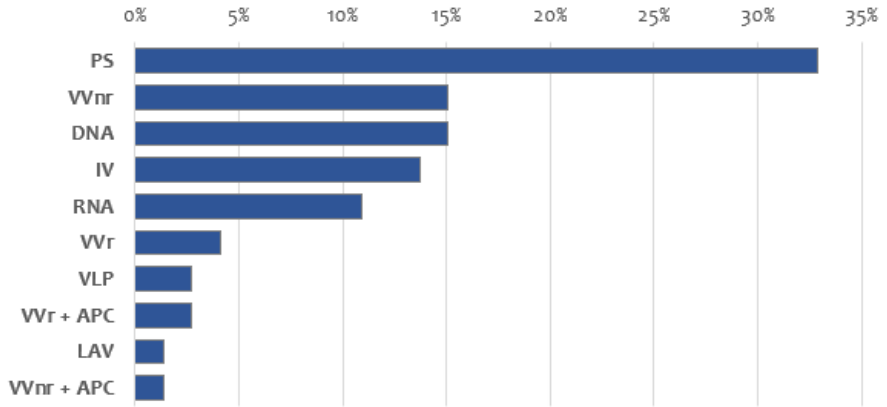
2. - Number of vaccines in pre-clinical development 182



3. - Candidates in clinical phase

Filter: All — Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	24	33%
VVnr	Viral Vector (non-replicating)	11	15%
DNA	DNA	11	15%
IV	Inactivated Virus	10	14%
RNA	RNA	8	11%
VVr	Viral Vector (replicating)	3	4%
VLP	Virus Like Particle	2	3%
VVr + APC	VVr + Antigen Presenting Cell	2	3%
LAV	Live Attenuated Virus	1	1%
VVnr + APC	VVnr + Antigen Presenting Cell	1	1%
		73	



WHO Draft landscape and tracker of COVID-19 candidate vaccines https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines Accessed on 24/02/2021