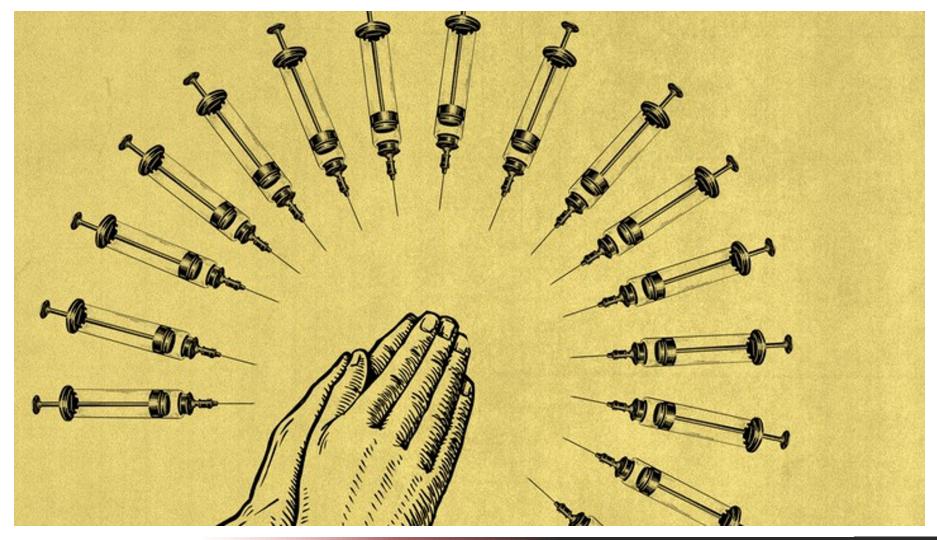
### SARS-CoV-2 Vaccines: Current Status



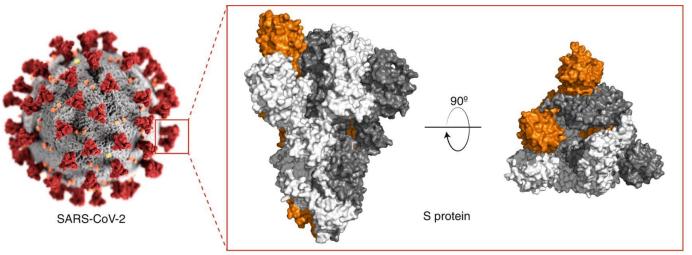


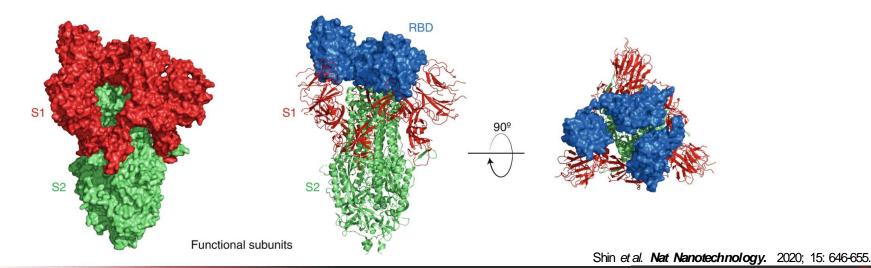
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### **COVID-19:** *Prevention - Vaccines*









17 - TAL

# SARS-CoV-2 Vaccines: Rapid Development

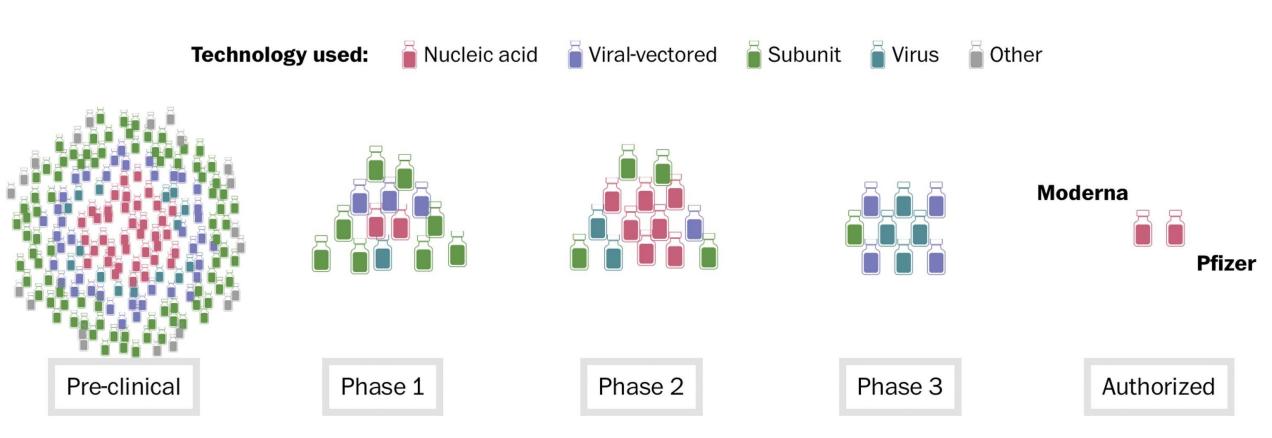
Date	Milestone
Dec 1	Covid-19 illness documented (unpublicized Nov 17 <sup>th</sup> )
Jan 10	SARS-CoV-2 virus sequenced
Jan 15	NIH designs mRNA vaccine in collaboration with Moderna
Mar 16	Moderna Phase 112 trial begins
May 2	Pfizer/BioNTech Phase 112 trial begins
July 14	Moderna Phase 112 trial published in NEJM
July 27, 28	Moderna and Pfizer/BioNTech Phase 3 trial begins
Aug 12	Pfizer/BioNTech Phase 112 published in Nature
October 22,27	Enrollment in both Phase 3 trials complete; >74,000 participants
Nov 9	Pfizer/BioNTech announces interim analysis efficacy > 90%
Nov 16	Moderna announces interim analysis efficacy 94.5%
Nov 18	Pfizer/BioNTech announces 95% efficacy as final result
Nov 20	1 <sup>st</sup> EUA submitted by Pfizer/BioNTech
Nov 27	Distribution of vaccine by UAL charter flights throughout US
Dec 10	FDA External review of Pfizer/BioNTech EUA
Dec 11	Phase 1a Vaccination begins for health care professionals*

\*Provisional on positive external review





## **COVID-19:** Prevention - Vaccines

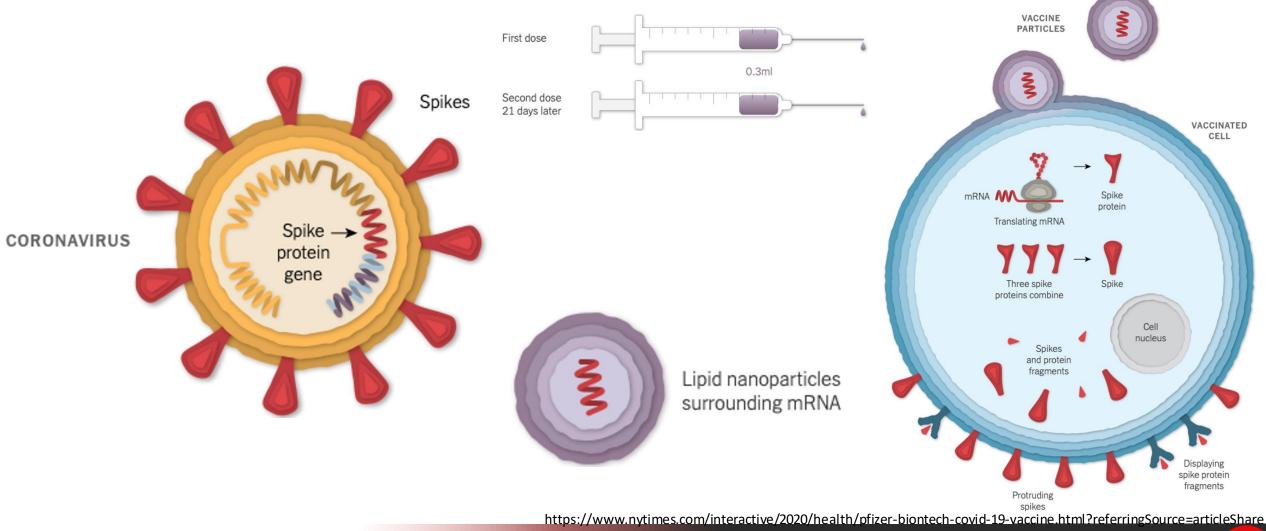


"These are the Top Coronavirus Vaccines to Watch." Washington Post 18 December 2020.





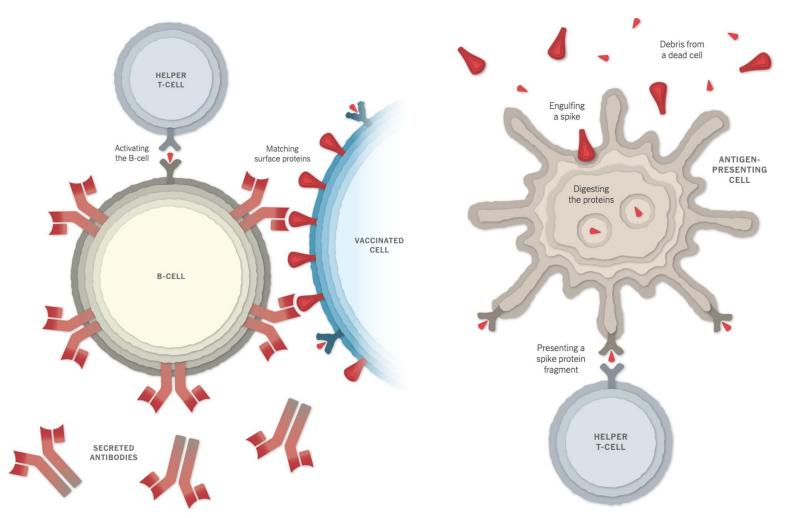
## SARS-CoV-2 Vaccines: mRNA Vaccines







## SARS-CoV-2 Vaccines: mRNA Vaccines

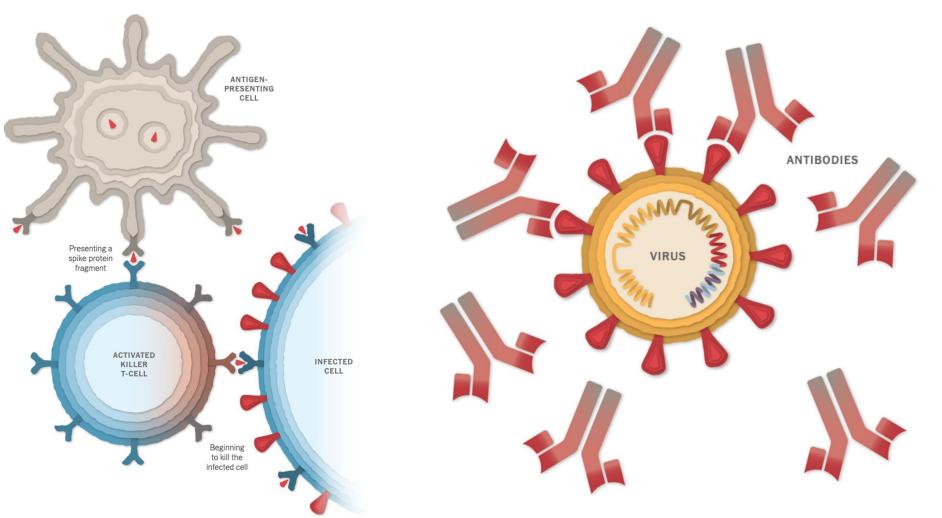


https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html?referringSource=articleShare





# SARS-CoV-2 Vaccines: What They Do

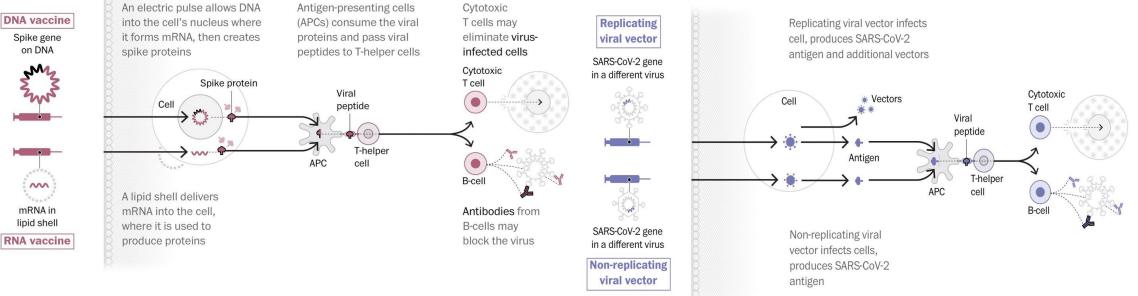


https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html?referringSource=articleShare





### **COVID-19:** *RNA/DNA and Viral Vaccines*



#### Nucleic acid vaccines, developed by...

Moderna: National Institutes of Health	PC	P1	P2	P3	٨
	FU	PI	FZ	P3	A
Pfizer; BioNTech; Fosun Pharma	PC	P1	P2	P3	A
AnGes; Osaka University; Takara Bio	PC	P1	P2	P3	A
Arcturus Therapeutics; Duke-NUS	PC	P1	P2	P3	A
CureVac	PC	P1	P2	P3	А
Genexine	PC	P1	P2	P3	A
Imperial College London; VacEquity Global Health	PC	P1	P2	P3	А
Inovio Pharmaceuticals	PC	P1	P2	P3	A

#### Viral-vectored vaccines, developed by...

AstraZeneca; University of Oxford	PC	P1	P2	P3	A
CanSino Biologics; Beijing Institute of Biotechnology*	PC	P1	P2	P3	A
Gamaleya Research Institute*	PC	P1	P2	P3	A
Johnson & Johnson, Beth Israel Deaconess Medical Center	PC	P1	P2	P3	A
Institut Pasteur; Themis; University of Pittsburgh CVR; Merck Sharp & Dohme	PC	P1	P2	P3	A

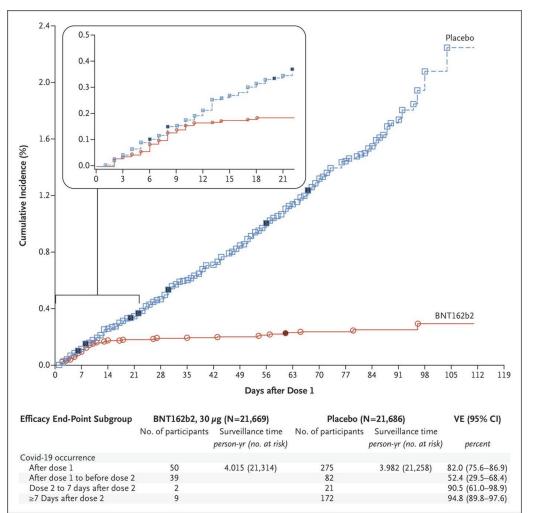
"These are the Top Coronavirus Vaccines to Watch." Washington Post 18 December 2020.





### SARS-CoV-2 Vaccines: mRNA Pfizer Vaccine

Table 1. Demographic Characteristics of the Pa	articipants in the Main S	afety Population.*	
Characteristic	BNT162b2 (N=18,860)	Placebo (N=18,846)	Total (N=37,706)
Sex — no. (%)			
Male	9,639 (51.1)	9,436 (50.1)	19,075 (50.6)
Female	9,221 (48.9)	9,410 (49.9)	18,631 (49.4)
Race or ethnic group — no. (%)†			
White	15,636 (82.9)	15,630 (82.9)	31,266 (82.9)
Black or African American	1,729 (9.2)	1,763 (9.4)	3,492 (9.3)
Asian	801 (4.2)	807 (4.3)	1,608 (4.3)
Native American or Alaska Native	102 (0.5)	99 (0.5)	201 (0.5)
Native Hawaiian or other Pacific Islander	50 (0.3)	26 (0.1)	76 (0.2)
Multiracial	449 (2.4)	406 (2.2)	855 (2.3)
Not reported	93 (0.5)	115 (0.6)	208 (0.6)
Hispanic or Latinx	5,266 (27.9)	5,277 (28.0)	10,543 (28.0)
Country — no. (%)			
Argentina	2,883 (15.3)	2,881 (15.3)	5,764 (15.3)
Brazil	1,145 (6.1)	1,139 (6.0)	2,284 (6.1)
South Africa	372 (2.0)	372 (2.0)	744 (2.0)
United States	14,460 (76.7)	14,454 (76.7)	28,914 (76.7)
Age group — no. (%)			
16–55 yr	10,889 (57.7)	10,896 (57.8)	21,785 (57.8)
>55 yr	7,971 (42.3)	7,950 (42.2)	15,921 (42.2)
Age at vaccination — yr			
Median	52.0	52.0	52.0
Range	16-89	16–91	16–91
Body-mass index‡			
≥30.0: obese	6,556 (34.8)	6,662 (35.3)	13,218 (35.1)

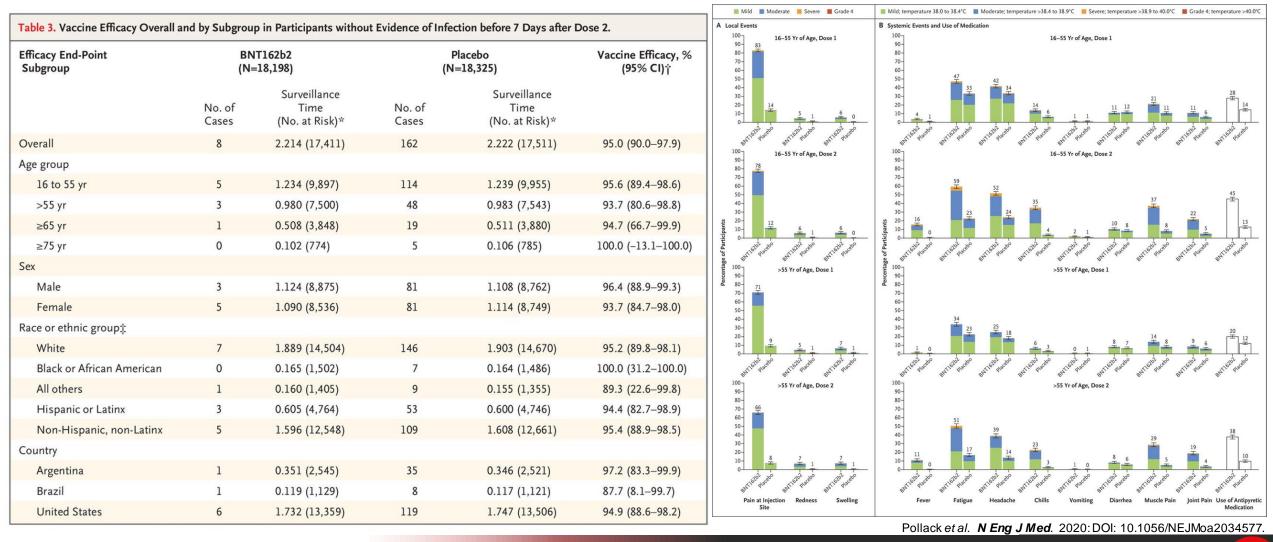


Pollack et al. N Eng J Med. 2020: DOI: 10.1056/NEJMoa2034577.





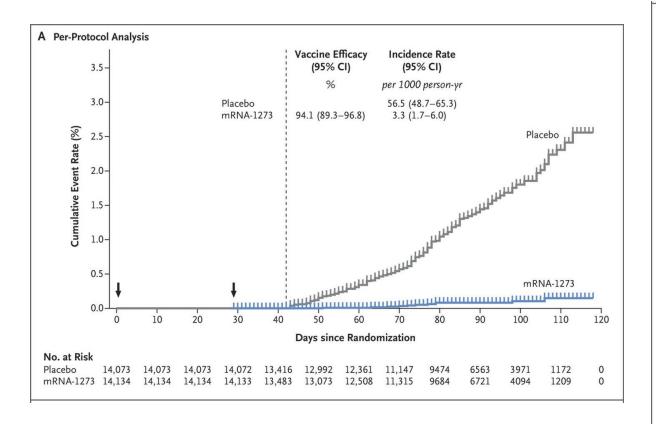
### SARS-CoV-2 Vaccines: mRNA Pfizer Vaccine

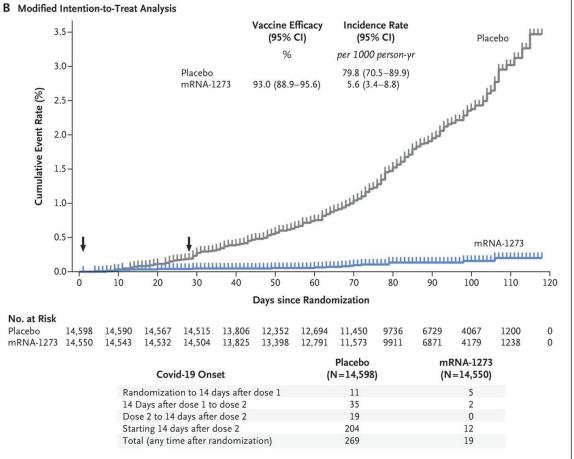




dkb

### SARS-CoV-2 Vaccines: mRNA Moderna Vaccine





Baden et al. N Engl J Med. 2020. DOI: 10.1056/NEJMoa2035389.





# SARS-CoV-2 Vaccines: mRNA Moderna Vaccine

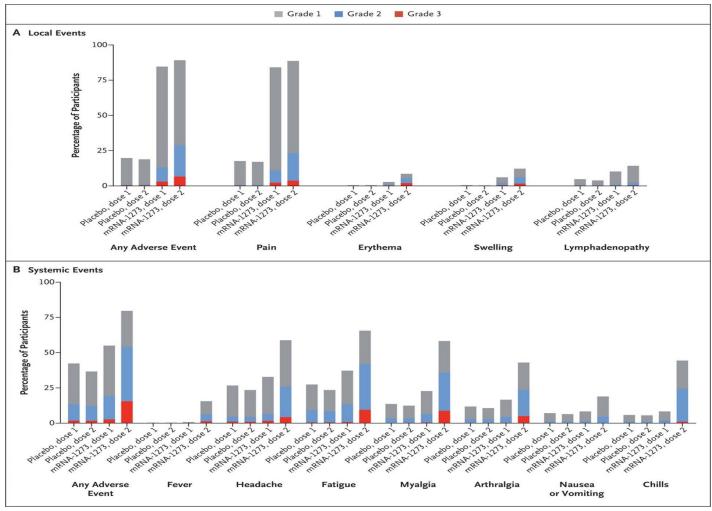
Subgroup	Placebo (N=14,073)	mRNA-1273 (N=14,134)	Vaccine Efficacy (95% CI)
	no. of even	ts/total no.	
All patients	185/14,073	11/14,134	94.1 (89.3–96.8)
Age			
≥18 to <65 yr	156/10,521	7/10,551	
≥65 yr	29/3552	4/3583	<b>86.4 (61.4–95.2)</b>
Age, risk for severe Covid-19			
18 to <65 yr, not at risk	121/8403	5/8396	
18 to <65 yr, at risk	35/2118	2/2155	94.4 (76.9–98.7)
≥65 yr	29/3552	4/3583	86.4 (61.4–95.2)
Sex			
Male	87/7462	4/7366	
Female	98/6611	7/6768	
At risk for severe Covid-19			
Yes	43/3167	4/3206	90.9 (74.7–96.7)
No	142/10,906	7/10,928	<b>−■</b> 95.1 (89.6−97.7)
Race and ethnic group			
White	144/8916	10/9023	
Communities of color	41/5132	1/5088	97.5 (82.2–99.7)
			0 25 50 75 100

Baden et al. N Engl J Med. 2020. DOI: 10.1056/NEJMoa2035389.





## SARS-CoV-2 Vaccines: mRNA Moderna Vaccine



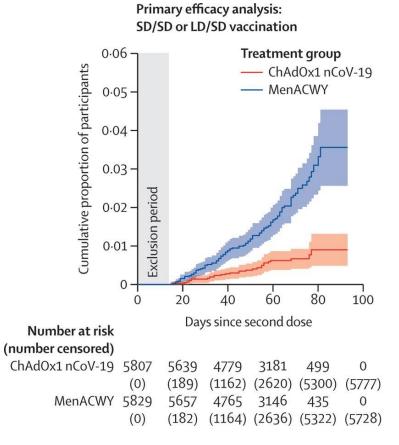
Baden et al. N Engl J Med. 2020. DOI: 10.1056/NEJMoa2035389.





### SARS-CoV-2 Vaccines: Adenovirus Vector – AstraZeneca/Oxford

	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 (170369)	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 (73313)	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 (97056)	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 (76780)	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)
Other non-primary symptomatic COVID-19 disease¶	18	7/5807 (0·1%)	10·3 (248 299)	11/5829 (0·2%)	16·3 (247 228)	36·4% (-63·8 to 75·3)‡
Any symptomatic COVID-19 disease	149	37/5807 (0.6%)	54·4 (248 299)	112/5829 (1·9%)	165.5 (247228)	67·1% (52·3 to 77·3)
Asymptomatic or symptoms unknown (COV002)	69	29/3288 (0.9%)	69.8 (151 673)	40/3350 (1·2%)	96.0 (152 138)	27·3% (-17·2 to 54·9)
LD/SD recipients	24	7/1120 (0.6%)	41.4 (61782)	17/1127 (1·5%)	100.6 (61730)	58·9% (1·0 to 82·9)‡
SD/SD recipients	45	22/2168 (1.0%)	89.4 (89891)	23/2223 (1.0%)	92.9 (90 408)	3·8% (-72·4 to 46·3)
Any NAAT-positive swab	221	68/5807 (1·2%)	100.0 (248 299)	153/5829 (2·6%)	226.0 (247228)	55·7% (41·1 to 66·7)

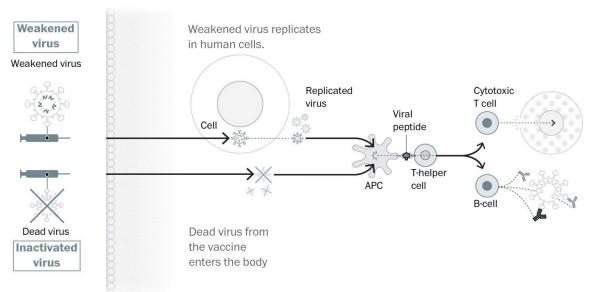


Voysey et al. Lancet. 2020: DOI: 10.1016/S0140-6736 (20)32661-1.



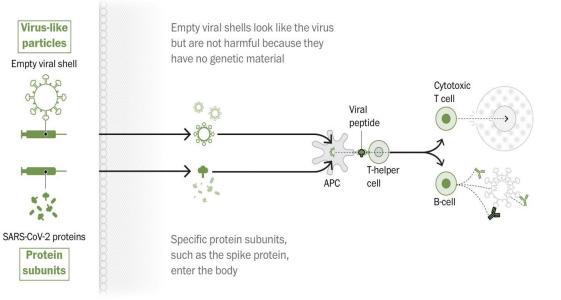


### **COVID-19:** *Protein Vaccines*



#### Weakened and inactivated virus vaccines, developed by...

Beijing Institute of Biological Products; Sinopharm	PC	P1	P2	P3	A
Bharat Biotech	PC	P1	P2	P3	A
Sinopharm	PC	P1	P2	P3	A
Sinovac	PC	P1	P2	P3	А
Chinese Academy of Medical Sciences	PC	P1	P2	P3	A
Research Institute for Biological Safety Problems, Republic of Kazakhstan	PC	P1	P2	P3	А



#### Subunit vaccines, developed by...

Novavax	PC	P1	P2	P3	А
Anhui Zhifei Longcom; Chinese Academy of Sciences	PC	P1	P2	P3	A
Federal Budgetary Research Institution (FBRI) State Research Center of Virology and Biotechnology "VECTOR"	PC	P1	P2	P3	A
Instituto Finlay de Vacunas	PC	P1	P2	P3	A
SpyBiotech; Serum Institute of India	PC	P1	P2	P3	A

"These are the Top Coronavirus Vaccines to Watch." Washington Post 18 December 2020.





### **COVID-19:** *Protein Vaccines*

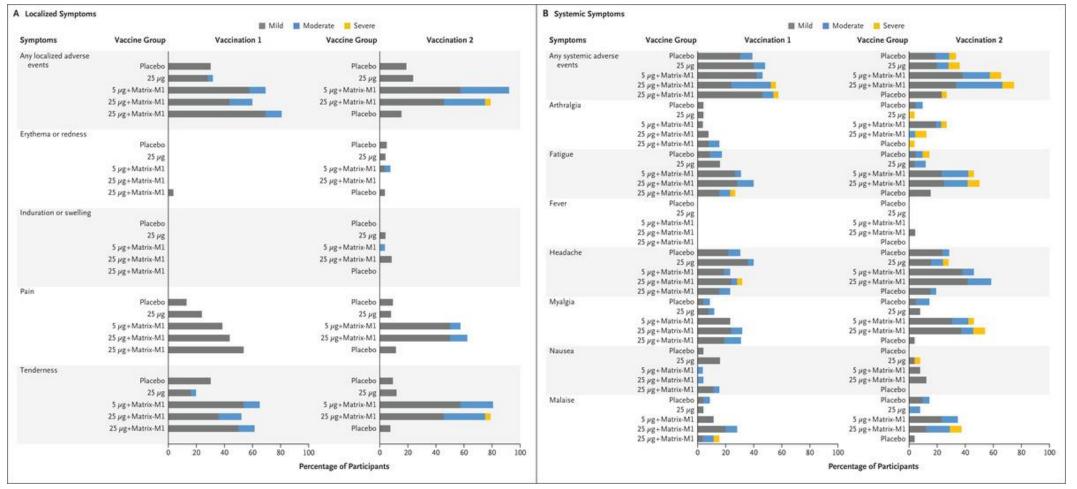
- Novovax: SARS-CoV-2 spike glycoprotein with Matrix-M1, a saponin-based adjuvant
  - 。 Baculovirus Spodoptera frugiperda (Sf9) insect cell-expression system
    - C>99% Wild-Type Virus Neutralization 3906 3305 983 104-104. . 7457 .... . • :  $10^{3}-$ 128 103. 41 837 Human Convalescent -254 Serum  $10^{2}-$ 102-Ī Asymptomatic 20 Outpatient symptomatic 10<sup>1</sup>-10<sup>1</sup>-Hospitalized 21 Day 21 35 21 35 21 35 21 35 0 35 0 0 0 0 Human Convalescent Placebo 25 µg 5µg 25 µg 25 µg Serum (dose 1 and 2) rSARS-CoV-2+Matrix-MI rSARS-CoV-2 rSARS-CoV-2+ (dose 1 and 2) (dose 1 and 2) Matrix-MI (dose 1) and Placebo (dose 2) No. of Patients 23/21 25/25 29/29 28/27 26/26 (dose 1/dose 2)
    - B Wild-Type SARS-CoV-2 Microneutralization

Keech et al. N Engl J Med. 2020: DOI: 10.1056/NEJMoa2026920.



# COVID-19: RNA Vaccines

#### • Novovax:

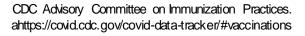


Keech et al. N Engl J Med. 2020: DOI: 10.1056/NEJMoa2026920.





- Two COVID-19 vaccines were authorized by FDA for use in December 2020
- Initial doses of any COVID-19 vaccine will be limited. We expect a constrained supply environment for some months and need to make the best use of available vaccine.
- Initially, the number of doses available by end of December was anticipated to be about 40 million, enough to vaccinate 20 million people, with the expectation that 5 to 10 million doses would be dispensed each week
  - As of January 6, 2021, 17 million doses were distributed and 5.3 million people received their first dose







		Phase1c Adults with high -risk medical cond Adults 65+	litions
		Sector, Food & Agriculture, Utilities, orrections Officers, Transportation)	
Phase 1a Health care personnel LTCF residents			

Time

CDC Advisory Committee on Immunization Practices.



### Proposed Phase 1 & 2 allocation, December 2020

Phase	Groups recommended for vaccination	Number of persons in each group (millions)	Number of unique* persons in each group (millions)	Total* (millions)
1a	Health care personnel Long-term care facility residents	21 3	21 3	24
1b	Frontline essential workers Persons aged 75 years and older	30 21	30 19	49
1c	Persons aged 65-74 years Persons aged 16-64 years with high-risk conditions Essential workers not recommended in Phase 1b	32 110 57	28 81 20	129
2	All people aged 16 years and older not in Phase 1, who are recommended for vaccination			

CDC Advisory Committee on Immunization Practices





### Frontline Essential Workers (~30M)

- First Responders (Firefighters, Police)
- Education (teachers, support staff, daycare)
- Food & Agriculture
- Manufacturing
- Corrections workers
- U.S. Postal service workers
- Public transit workers
- Grocery store workers

### Conditions associated with severe COVID-19

- · CDC has identified a list of conditions that make an individual at increased risk of severe disease.
- The list is not exhaustive and only includes conditions with sufficient evidence to draw conclusions.
- High-risk medical conditions may include other individuals based on consultation with a healthcare
  provider about personal risk factors.

•	Obesity
•	Severe Obesity
•	Type 2 diabetes
•	COPD
•	Heart Condition
•	Chronic kidney disease
•	Cancer
•	Immunocompromised state from solid Organ transplant
•	Sickle cell disease
•	Pregnancy
•	Smoker (current of history)

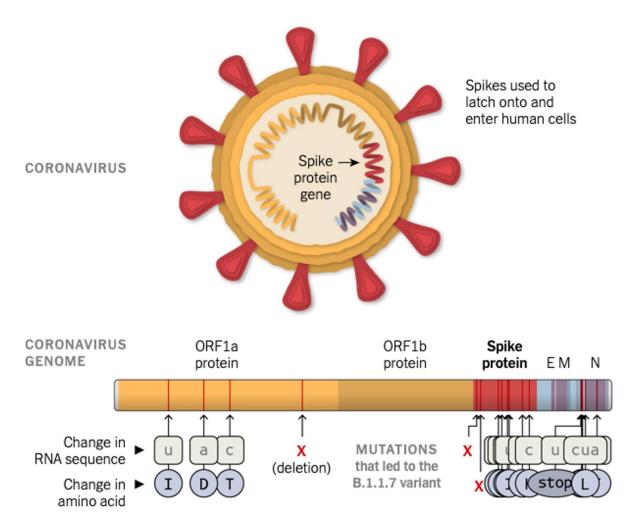
1. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical conditions.html?CDC\_AA\_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov/%2Fneed-extra-precautions%2Fgroups-at-higher-risk.html

CDC Advisory Committee on Immunization Practices





### Variant SARS-CoV-2 and Vaccine Efficacy



gene	nucleotide	amino acid
ORF1ab	C3267T	T1001I
	C5388A	A1708D
	T6954C	I2230T
	11288-11296 deletion	SGF 3675-3677 deletion
spike	21765-21770 deletion	HV 69-70 deletion
	21991-21993 deletion	Y144 deletion
	A23063T	N501Y
	C23271A	A570D
	C23604A	P681H
	C23709T	T716I
	T24506G	S982A
	G24914C	D1118H
Orf8	C27972T	Q27stop
	G28048T	R52I
	A28111G	Y73C
Ν	28280 GAT->CTA	D3L
	C28977T	S235F

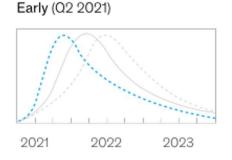
https://virological.org/t/preliminary-genomic-characterisation-of-an-emergent-sars-cov-2-lineage-in-the-uk-defined-by-a-novel-set-of-spike-mutations/563



### SARS-CoV-2 Vaccines: Time to Herd Immunity

Probability of functional end<sup>1</sup> to COVID-19 pandemic in US by guarter (illustrative)

The probability of reaching COVID-19 herd immunity in the United States is highest in the third or fourth quarter of 2021 but could shift.



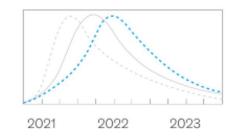
- COVID-19 vaccine with high efficacy arrives sooner than expected
- Timeline of manufacturing, distribution, and administration of COVID-19 vaccine is shorter than expected
- Cross-immunity from other coronaviruses proves significant
- There is broad-based willingness to be vaccinated

Most likely (Q3/Q4 2021)

# 2021 2022 2023

- ≥1 COVID-19 vaccine is authorized by end of 2020 or early 2021
- COVID-19 vaccine is distributed to a sufficient portion of population in ~6 months
- There is broad-based willingness to be vaccinated

Late (2022 or later)



- Early COVID-19-vaccine candidates have low efficacy or low coverage (eg, side effects, slow adoption)
- Timeline of manufacturing, distribution, and administration of COVID-19 vaccine is longer than expected
- Immunity duration is very short

https://www.mckinsey.com/industries/healthcare-systems-and-services/our-insights/when-will-the-covid-19-pandemic-end#







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To ask your own question, email: QA@dkbmed.com



