Navigating the COVID-19 Vaccine Landscape: A review of vaccine modalities studied in COVID-19

A presentation for HealthTrust Members

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Disclosures

- The presenter and her preceptor have no financial relationships with any commercial interests pertinent to this presentation.
- This program may contain the mention of drugs or brands presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes and should not be perceived as an endorsement of any particular supplier, brand, or drug.

Pharmacist & Nurse Objectives

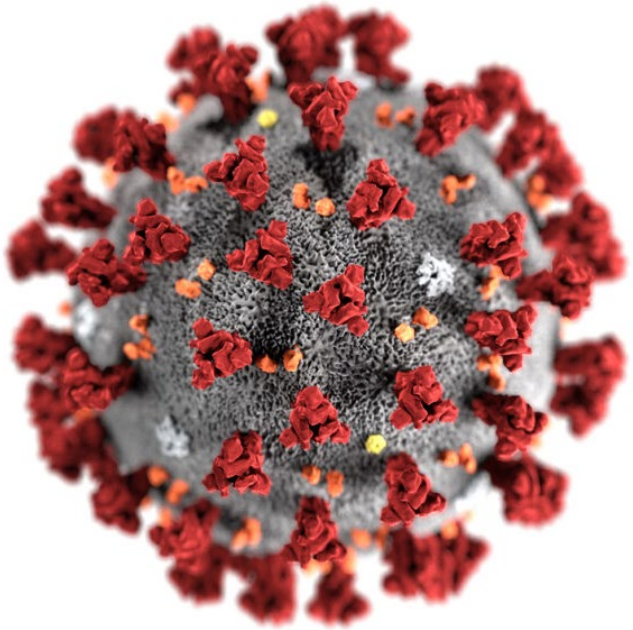
List	List the vaccine platforms approved and under review for COVID-19 including the advantages and drawbacks to each method.
Discuss	Discuss the utility of adjuvants in vaccines, especially in the prevention of COVID-19.
Describe	Describe the clinical trials of COVID-19 vaccines to determine utility and current knowledge gaps.

Pharmacy Technician Objectives

Identify	Identify the differences between the types of vaccine platforms.
Outline	Outline manufacturer recommendations for the storage and handling of COVID-19 vaccines.
Discuss	Discuss strategies for educating patients about the benefits and risks of the COVID-19 vaccines.

COVID-19 & The Immune Response

COVID-19 Pandemic

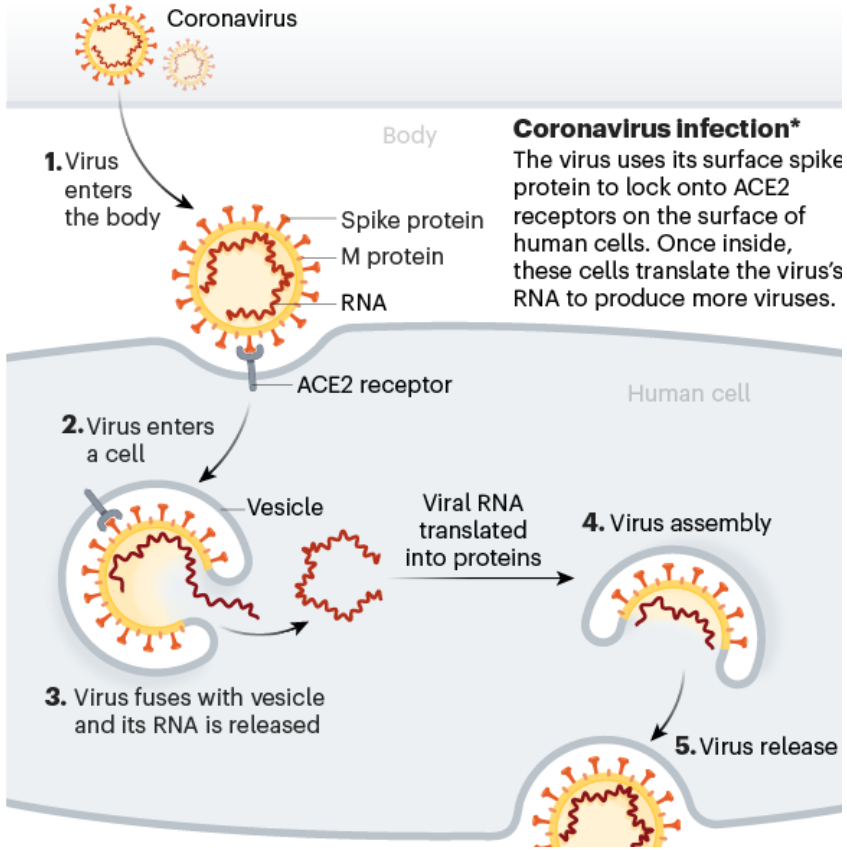


- SARS-CoV-2 is a novel, zoonotic coronavirus that emerged in late 2019
  - >28 million cases, >1.8 million hospitalizations, >500,000 deaths in the U.S. to date
  - Highest 7-day average reported on January 11, 2021: >200,00 new cases, >16,000 hospitalizations, >3,000 deaths
- SARS-CoV-2 is an enveloped, positive sense, single stranded RNA virus
- Similar to coronaviruses responsible for Severe Acute Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS-CoV)

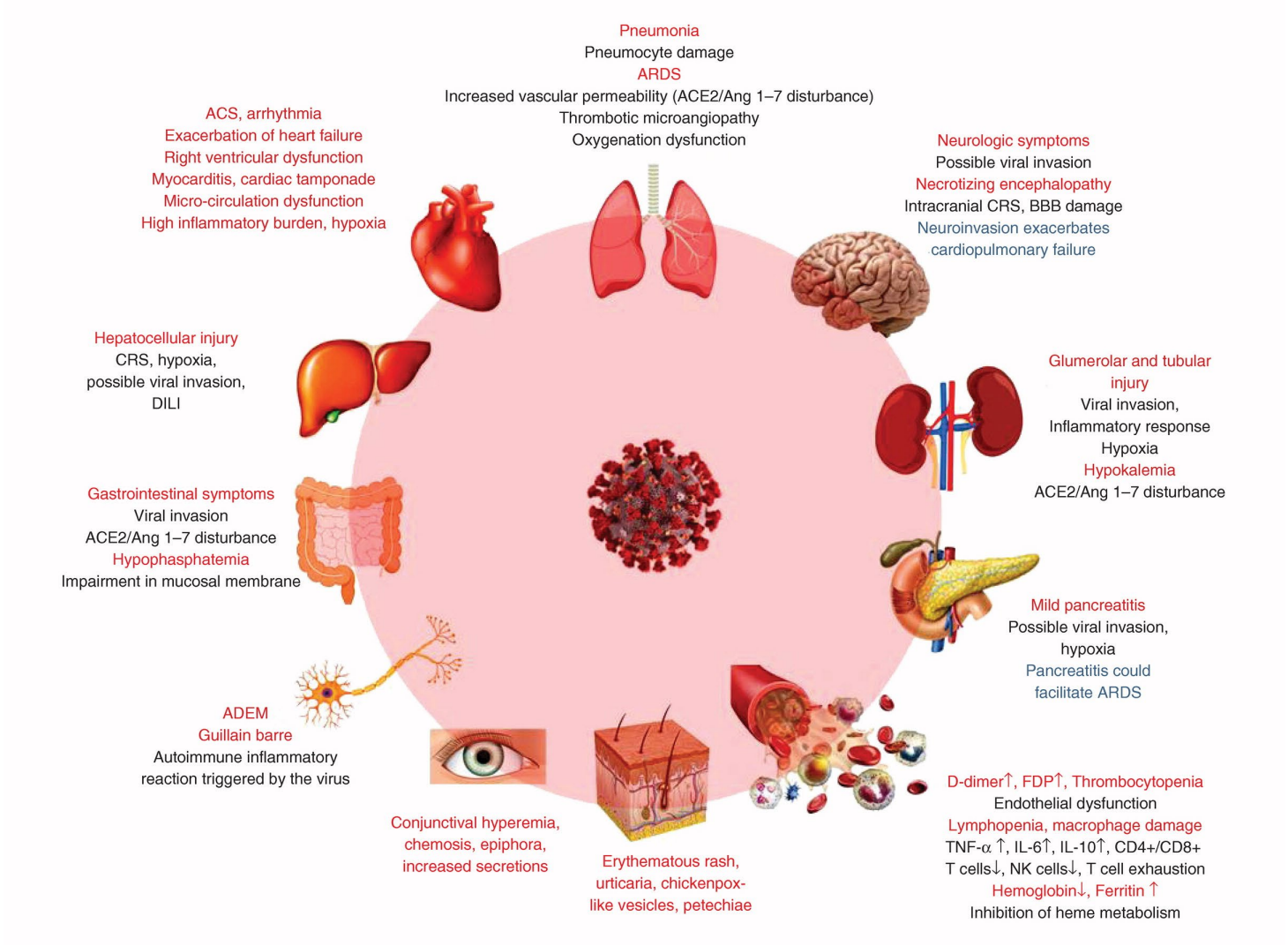
Sources: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html
Zhu N. *N Engl J Med*. 2020;382(8):727-33.

SARS-CoV-2 Pathogenesis

- Vaccine research with SARS-CoV and MERS-CoV helped determine the antigenic target
  - These coronaviruses caused recent zoonotic infections and epidemics (2002-2004 SARS outbreak & 2012 MERS-CoV epidemic)
  - Development of vaccines became low priority because coronaviruses circulating at the time caused relatively mild diseases or the viruses causing these outbreaks were eradicated
- SARS-CoV-2 spike glycoprotein binds to the receptor human angiotensin converting enzyme 2 (hACE2) to initiate infection



Source: Krammer F. *Nature*. 2020;586(7830):516-27.



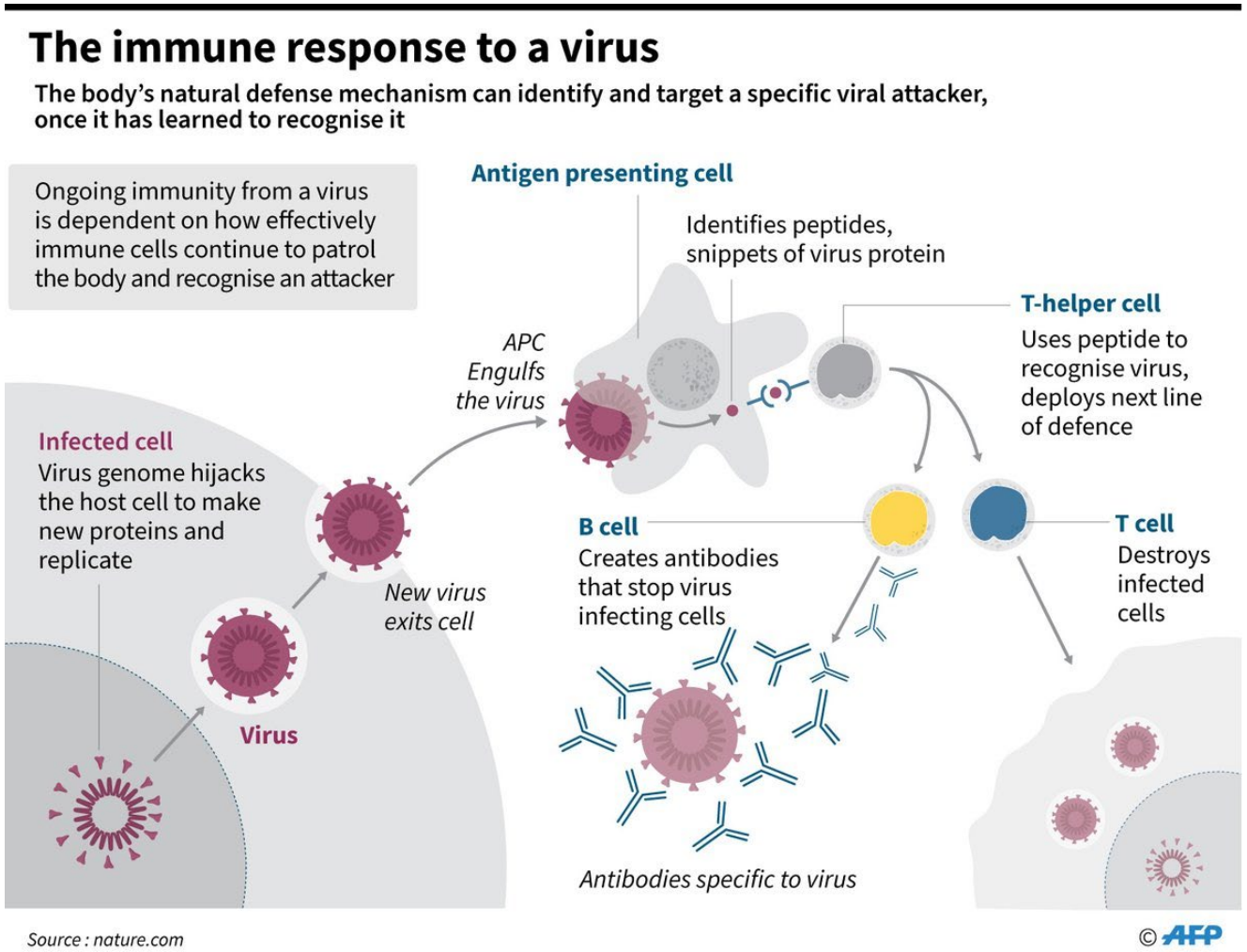
COVID-19 Complications

Syndromes

- Cytokine release syndrome
- Acute respiratory distress syndrome
- Septic shock
- Disseminated intravascular coagulation
- Post-COVID-19 syndrome
- Post-intensive care syndrome

Sources: Kordzadeh-Kermani E. *Future Microbiol*. 2020;15(13):1287-305.
COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed [February 1, 2021].

Acquired Immunity Overview

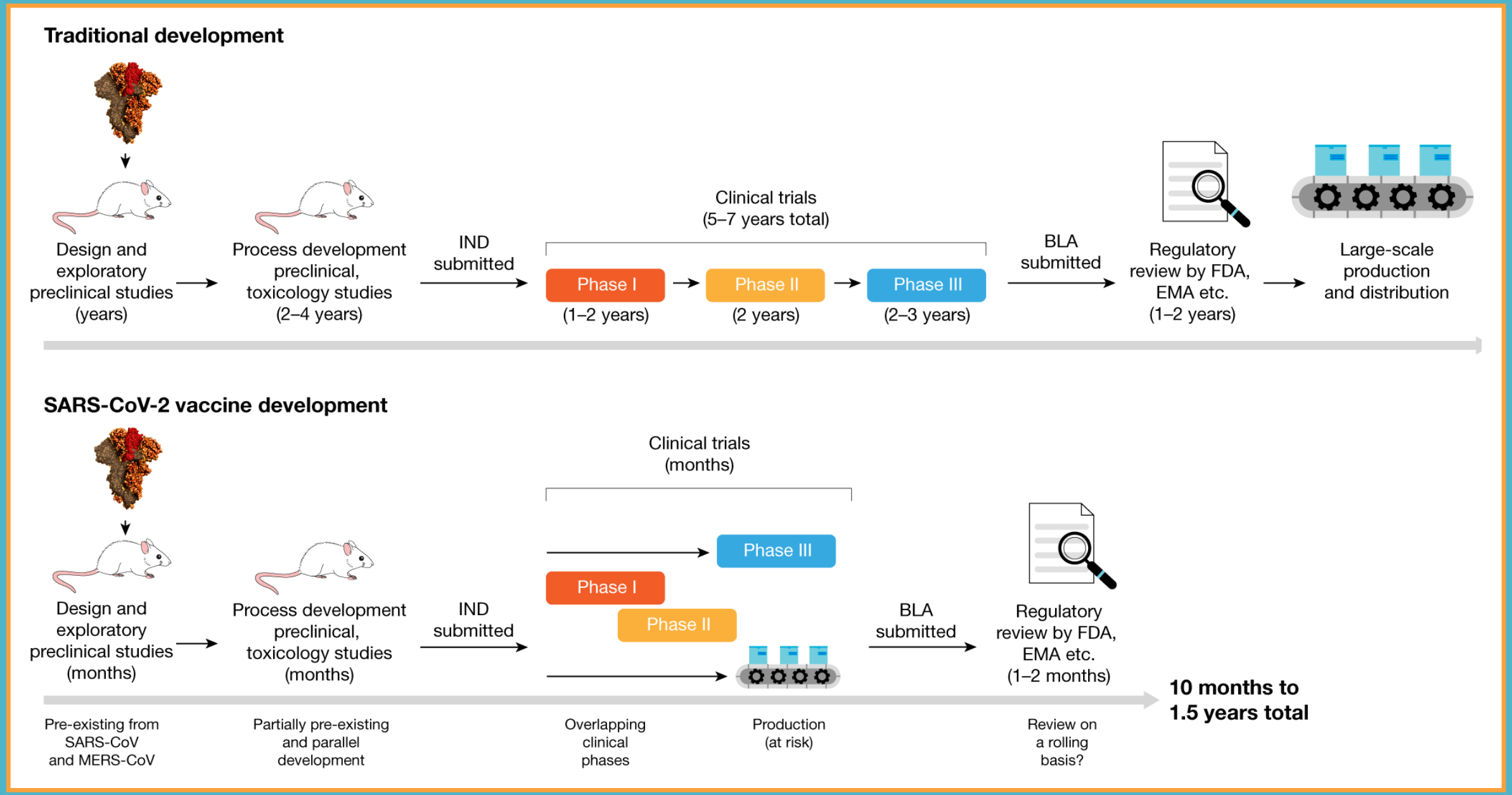


Source: Callaway E. *Nature*. 2020;580(7805):576-7.

Steps to Achieving an Immune Response

- Immune response varies against each virus
- Patient factors such as sex, age, pregnancy, comorbidities, and route of infection can also influence response
- Humoral vs. cell-mediated responses
  - Question of which type of response is most effective against the virus remains unanswered
  - Several data suggest that the major protective effect is to be attributed to antibodies against the spike protein and in particular against its receptor-binding domain (RBD)

Source: Hodgson SH. *Lancet Infect Dis*. 2021;21(2):e26-e35.



Source: Krammer F. *Nature*. 2020;586(7830):516-27.

Vaccine Modalities

COVID-19 Vaccine Platforms

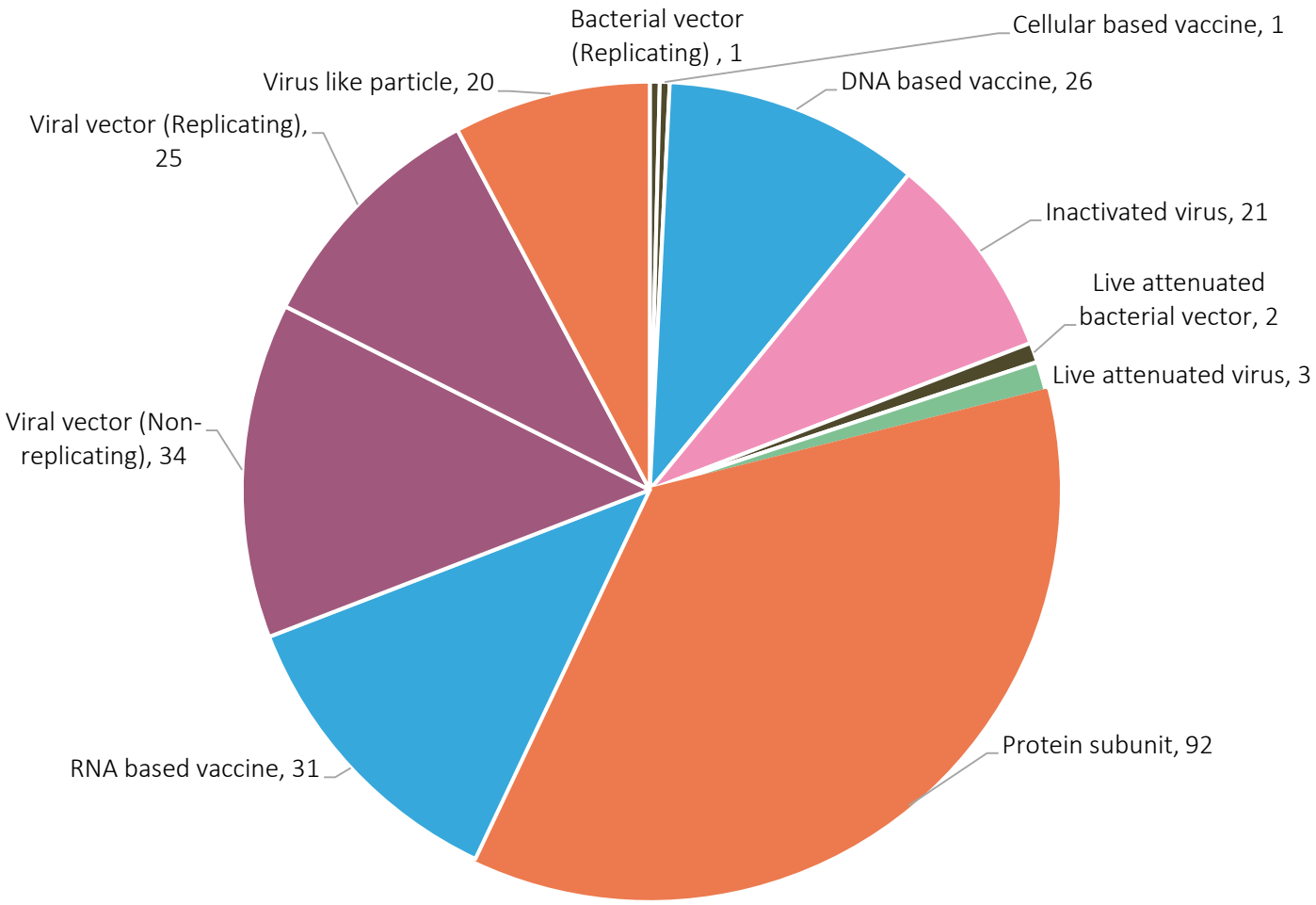
Traditional

- Live attenuated virus
- Inactivated virus

Non-traditional

- Protein subunit
- Viral vector
- Nucleic acid

COVID-19 Vaccine Landscape

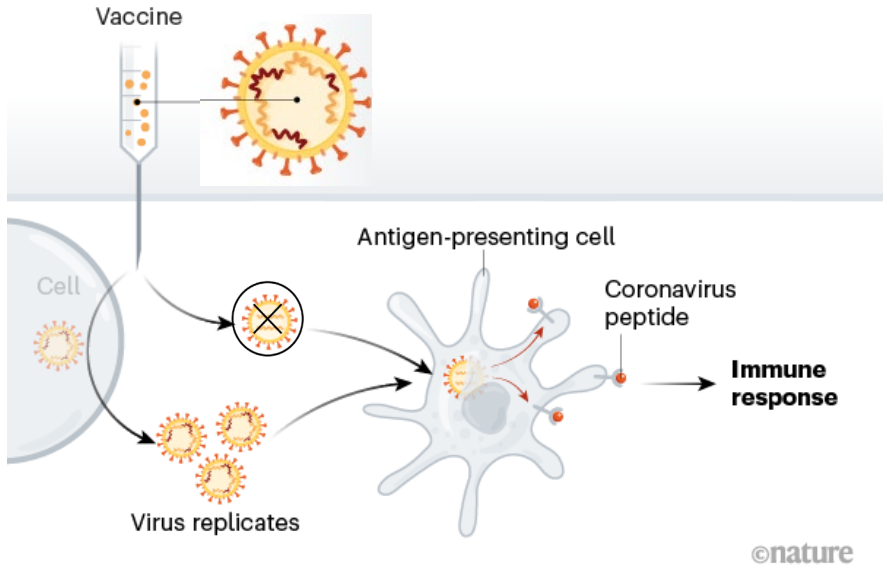


Modality	Phase 2/3	Phase 3	Phase 4
Live attenuated virus	0	0	0
Inactivated virus	0	5	1
Protein subunit	3	2	0
Viral vector	0	3	1
Nucleic acid	2	2	2
Total	5	12	4

Source: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

*As of March 2, 2021

Live attenuated virus

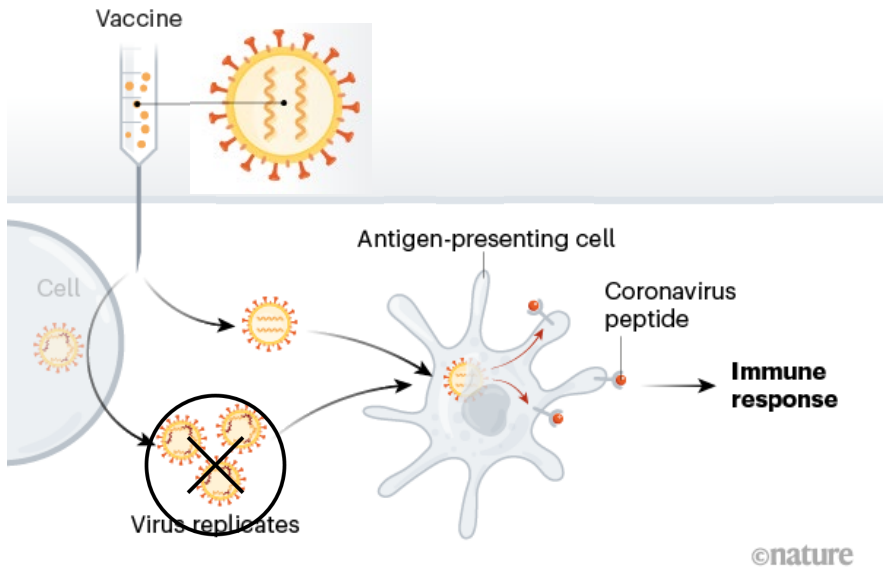


- Most traditional
- Mechanism: viruses are grown in unfavorable conditions or generated as genetically weakened versions
- Examples: Measles, Mumps, Rubella

Advantages	Disadvantages
• Immune response has broad target range • Can be given intranasally • Familiar, proven technology	• Time-consuming to grow • Specific facilities for production, storage, and handling • Safety concerns (may regain virulence)

Sources: Krammer F. *Nature*. 2020;586(7830):516-27.
Forni G. *Cell Death Differ*. 2021;28(2):626-39.
Callaway E. *Nature*. 2020;580(7805):576-7.
Chung YH. *ACS Nano.* 2020;14(10):12522-37.
Li Y. *J Biomed Sci*. 2020;27:104.

Inactivated virus



- Mechanism: actual virus is inactivated or chemically rendered non-infectious
- Examples: Hepatitis A, Rabies, most Influenza vaccines

Advantages

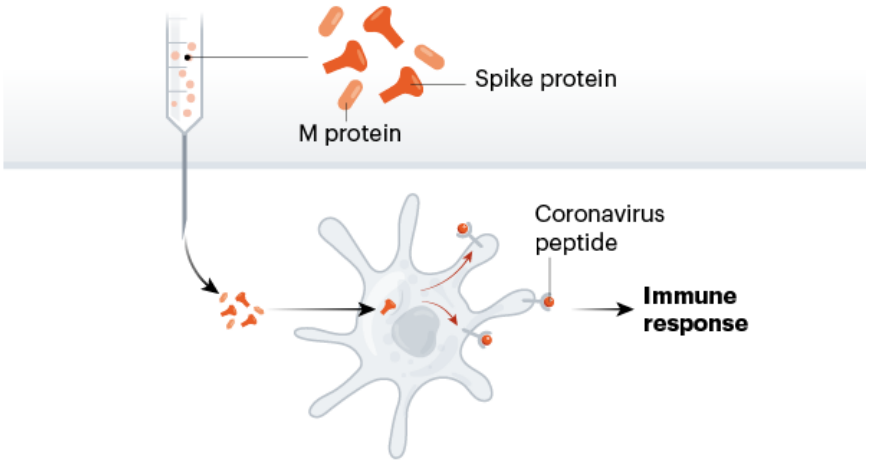
- Immune response has broad target range
- Familiar, proven technology

Disadvantages

- Induced response is generally weaker than live-attenuated
- Time-consuming to grow
- Specific facilities for production, storage, and handling

Sources: Krammer F. *Nature*. 2020;586(7830):516-27.
Forni G. *Cell Death Differ*. 2021;28(2):626-39.
Callaway E. *Nature*. 2020;580(7805):576-7.
Chung YH. *ACS Nano.* 2020;14(10):12522-37.
Li Y. *J Biomed Sci*. 2020;27:104.

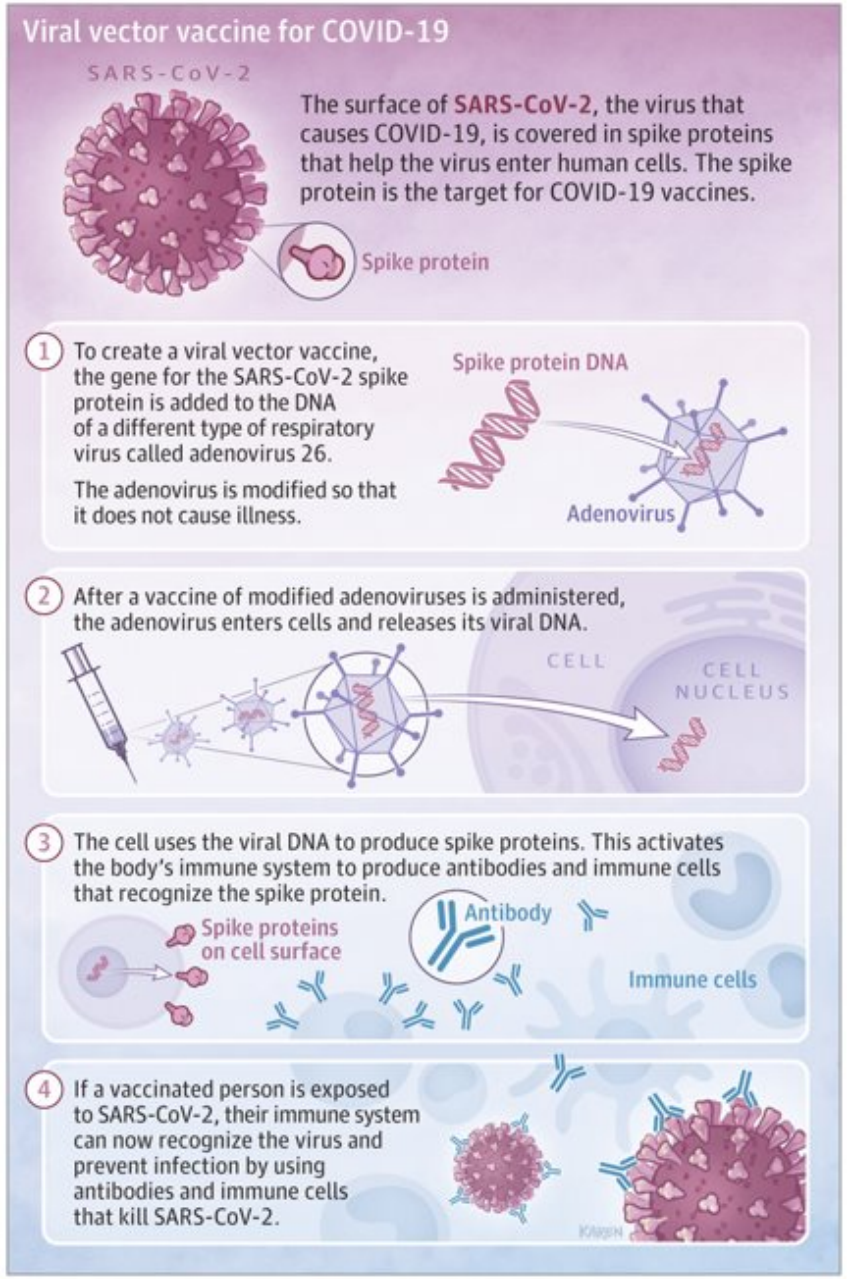
Protein subunit



- Mechanism: viral subunits expressed via various cell lines to stimulate immune response
- Spike protein, RBD, virus-like particle (VLP)
- Examples: recombinant influenza vaccine, acellular pertussis, pneumococcal vaccines

Advantages	Disadvantages
• Produced without handling live virus • Experience producing	• Spike protein hard to express • RBD-based easier to express, but prone to impact of antigenic drift

Sources: Krammer F. *Nature*. 2020;586(7830):516-27.
Forni G. *Cell Death Differ*. 2021;28(2):626-39.
Callaway E. *Nature*. 2020;580(7805):576-7.
Chung YH. *ACS Nano.* 2020;14(10):12522-37.
Li Y. *J Biomed Sci*. 2020;27:104.

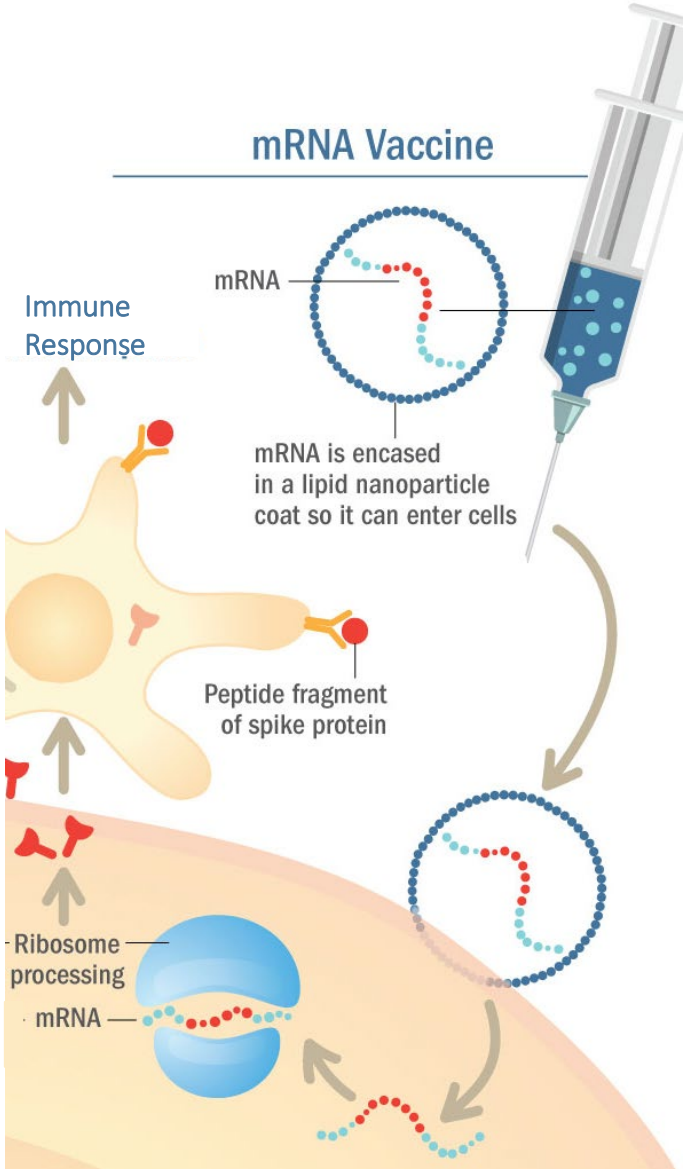


Viral vector

- Mechanism: virus is genetically engineered to include DNA that will produce antigen once injected
- Replicating vs. non-replicating
- Example: Ebola vaccine

Advantages	Disadvantages
• Produced without handling live virus • Familiar, proven technology • Good immune response	• Preexisting immunity against virus vector may affect efficacy • Subsequent exposure to vector may not produce intended response

Sources: Krammer F. *Nature*. 2020;586(7830):516-27.
Forni G. *Cell Death Differ*. 2021;28(2):626-39.
Callaway E. *Nature*. 2020;580(7805):576-7.
Li Y. *J Biomed Sci*. 2020;27:104.
Chung YH. *ACS Nano.* 2020;14(10):12522-37.
Livingston EH. *JAMA*. Published online March 1, 2021.



Nucleic acid

- Mechanism: uses DNA or RNA to create antigens for immune system to target
- Encode for spike protein, RBD, VLP
- Examples (mRNA): Rabies, Zika, Cytomegalovirus, and Influenza

Advantages	Disadvantages
• Produced without handling live virus • Easy and quick to design • Large-scale production	• DNA vaccines often show low immunogenicity and must be administered via delivery devices (e.g. electroporators) to increase efficiency • Relatively new technology • Stability issues

Sources: Krammer F. *Nature*. 2020;586(7830):516-27.
Forni G. *Cell Death Differ*. 2021;28(2):626-39.
Callaway E. *Nature*. 2020;580(7805):576-7.
Chung YH. *ACS Nano.* 2020;14(10):12522-37.
Li Y. *J Biomed Sci*. 2020;27:104.

Summary of Vaccine Modalities

	Live attenuated virus	Inactivated virus	Protein subunit	Viral vector	Nucleic acid
Mechanism	Weakened version of virus that replicates to extent without causing disease	Inactivated version of actual virus grown and chemically rendered un-infectious	Viral subunits expressed via various cell lines to stimulate immune response	Based on another virus with spike protein which has been disabled from replication	Uses DNA or RNA to create antigens for immune system to target
Advantages	• Immune response has broad target range • Can be given intranasally • Familiar, proven technology	• Immune response has broad target range • Familiar, proven technology	• Produced without handling live virus • Experience producing	• Produced without handling live virus • Familiar, proven technology • Good immune response	• Produced without handling live virus • Easy and quick to design • Large scale production
Disadvantages	• Time-consuming to grow • Specific facilities for production • Safety concerns	• Time-consuming to grow • Specific facilities for production	• Spike protein hard to express • RBD-based prone to impact of antigenic drift	• Partial neutralization by existing immunity • Subsequent exposure to vector may not produce intended response	• Relatively new technology • Stability issues
Candidates	• Codagenix • Indian Immunologicals Ltd.	• Sinovac • Sinopharm	• Novavax • AdaptVac	• AstraZeneca • CanSino Biologics • Janssen	• Moderna • Pfizer-BioNTech

Sources: Krammer F. *Nature*. 2020;586(7830):516-27.
Forni G. *Cell Death Differ*. 2021;28(2):626-39.
Callaway E. *Nature*. 2020;580(7805):576-7.
Chung YH. *ACS Nano.* 2020;14(10):12522-37.
Li Y. *J Biomed Sci*. 2020;27:104.

Adjuvants

- Live attenuated vaccines are considered the most effective and safe because they usually result in asymptomatic infections that result in long-lasting immunity
  - For certain pathogens, attenuated vaccines have not been successfully developed
- Nonliving vaccine antigens often are poorly immunogenic and require an adjuvant
- Adjuvants **stimulate the innate immune system** through pattern recognition receptors, which recognize pathogen-associated molecular patterns
  - Boost humoral immunity and some play a role in stimulating cell-mediated immunity as well
- Adjuvants include aluminum, emulsions, toll-like receptor agonists

Sources: Medzhitov R. *Cell*. 1997;91:295-8.
Liang Z. *Front Immunol*. 2020;11:589833.
Coffman RL. *Immunity*. 2010;33(4):492-503.

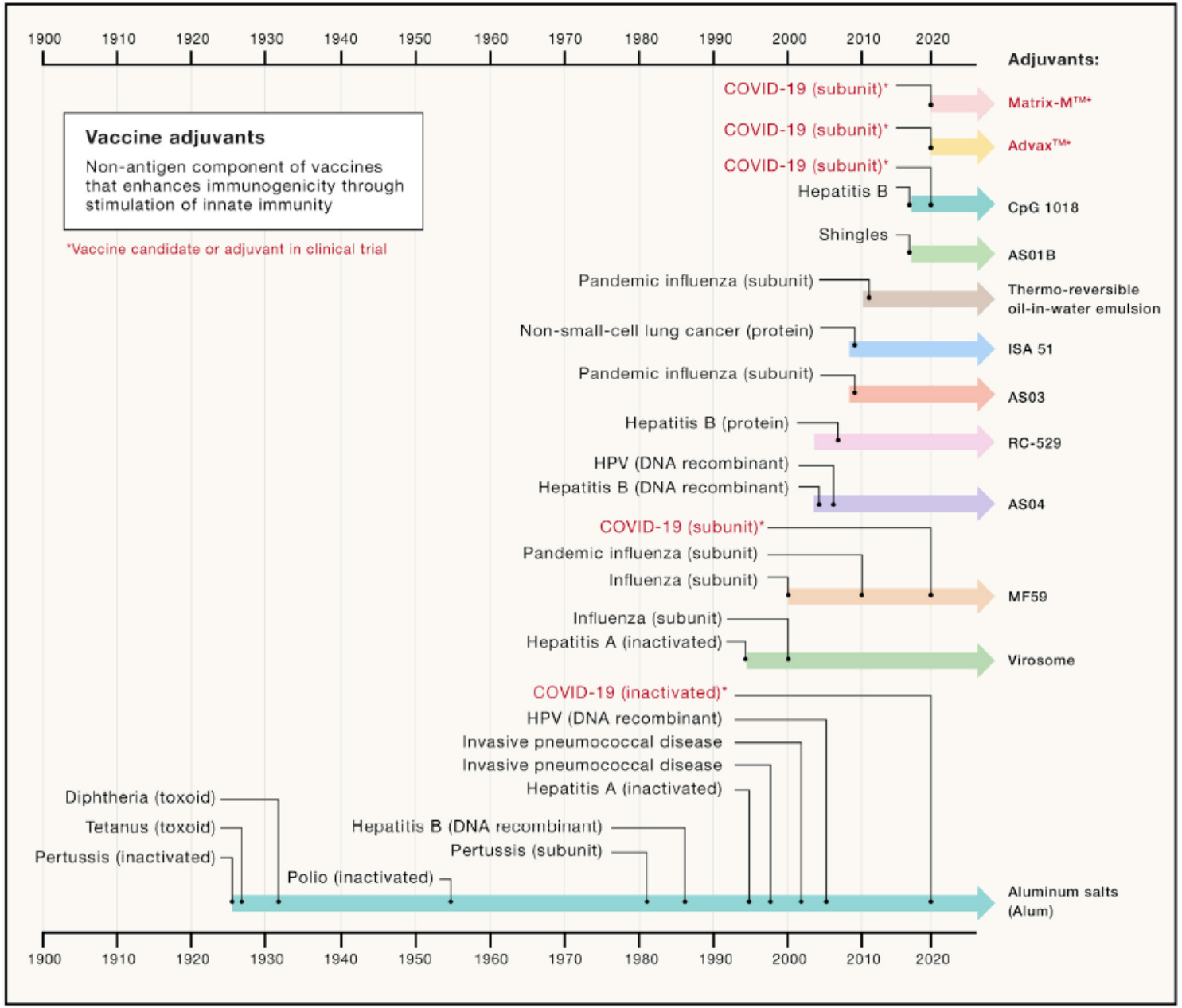


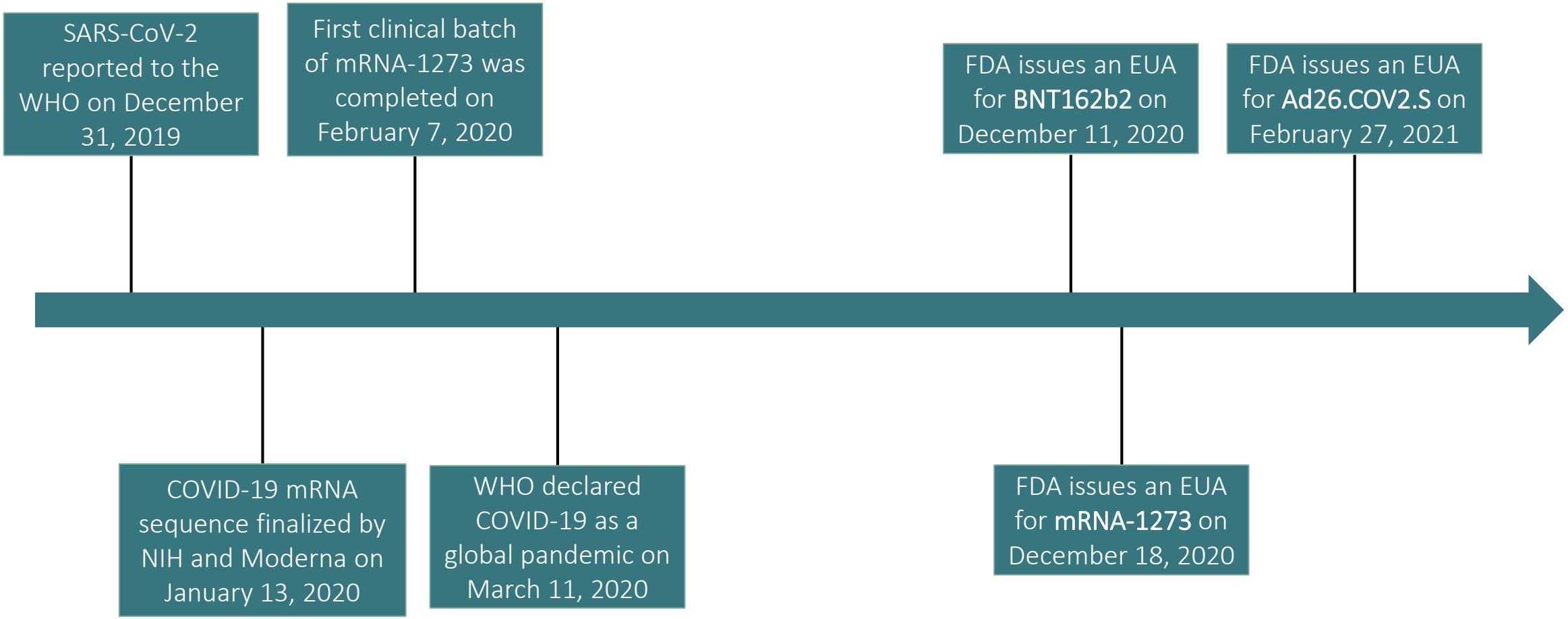
Figure 1. Timeline of Adjuvant Used in Human Vaccines

Adjuvants are non-antigen components of vaccines that stimulate the innate immune system. Adjuvants are indicated by thick arrows from the time of introduction. Vaccines that use the adjuvants are indicated as dots on the arrow at the earliest time of use. Image was made by BioRender.

Source: Iwasaki A. *Cell*. 2020;183(2):290-5.

COVID-19 Vaccine Interim Clinical Trial Results

Emergency Use Authorization (EUA) Timeline for COVID-19 Vaccines



Defining Key Terms in Vaccine Trials

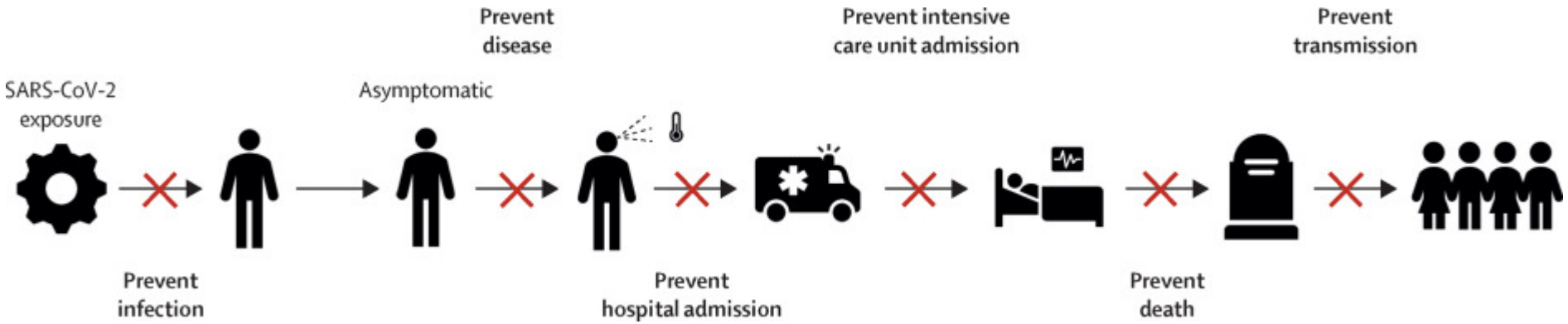
- **Reactogenicity**: physical manifestation of the inflammatory response to vaccination, and can include injection-site reactions and systemic symptoms
- **Vaccine efficacy**: measures prevention of illness in a direct population (i.e. controlled clinical trial)
  - Often presented as proportional reduction in disease between participants who were vaccinated and control participants to calculate the reduction that is attributable to the vaccine
  - **Vaccine efficacy does not always predict effectiveness**
- **Immunogenicity**: measures capacity of a vaccine to elicit a measurable immune response

Source: Hervé C. *npj Vaccines*. 2019;4(1):1-11.

Considerations in Study Design

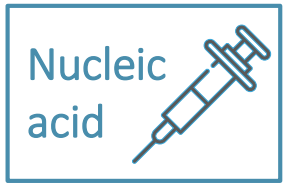
- Patient population
  - High risk groups: age, occupation, race/ethnicity, comorbidities

- Possible endpoints:



Source: Hodgson SH. *Lancet Infect Dis*. 2021;21(2):e26-e35.

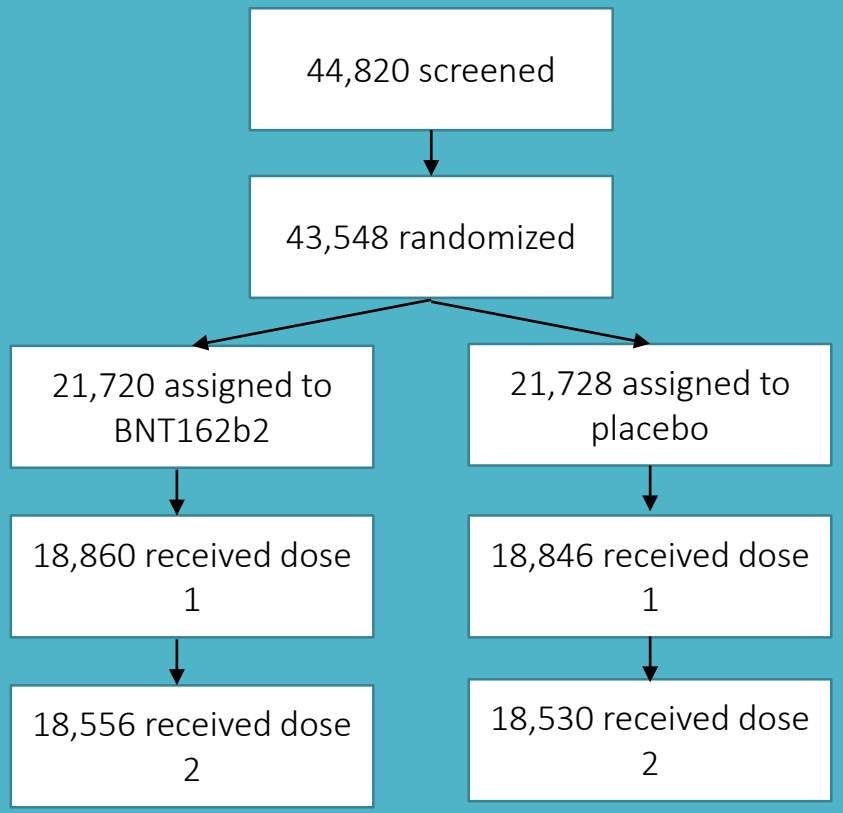
Pfizer-BioNTech - BNT162b2



Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine		
Study Design	Phase III, multinational, placebo-controlled, observer-blinded, efficacy trial	
Patient Population	Adults ≥16 years of age who were healthy or had stable chronic medical conditions, excluding pregnant or breastfeeding, medical history of COVID-19, immunocompromised or treatment with immunosuppressive therapy	
Intervention	1:1 ratio to receive two doses of 30 mcg of BNT162b2 or placebo 21 days apart	
Endpoints	Safety: • Local/systemic reactogenicity • All adverse drug events during specified time frames	Efficacy: • Efficacy of vaccine against symptomatic, lab-confirmed COVID-19 7 days after second dose • Efficacy in participants with and participants without evidence of prior infection Secondary Endpoint: • Prevention of severe COVID-19 disease

Source: Polack FP. *N Engl J Med*. 2020;383(27):2603-15.

Patient Population



Source: Polack FP. *N Engl J Med*. 2020;383(27):2603-15.

Table 1. Demographic Characteristics of the Participants in the Main Safety 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)

* Percentages may not total 100 because of rounding.
† Race or ethnic group was reported by the participants.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

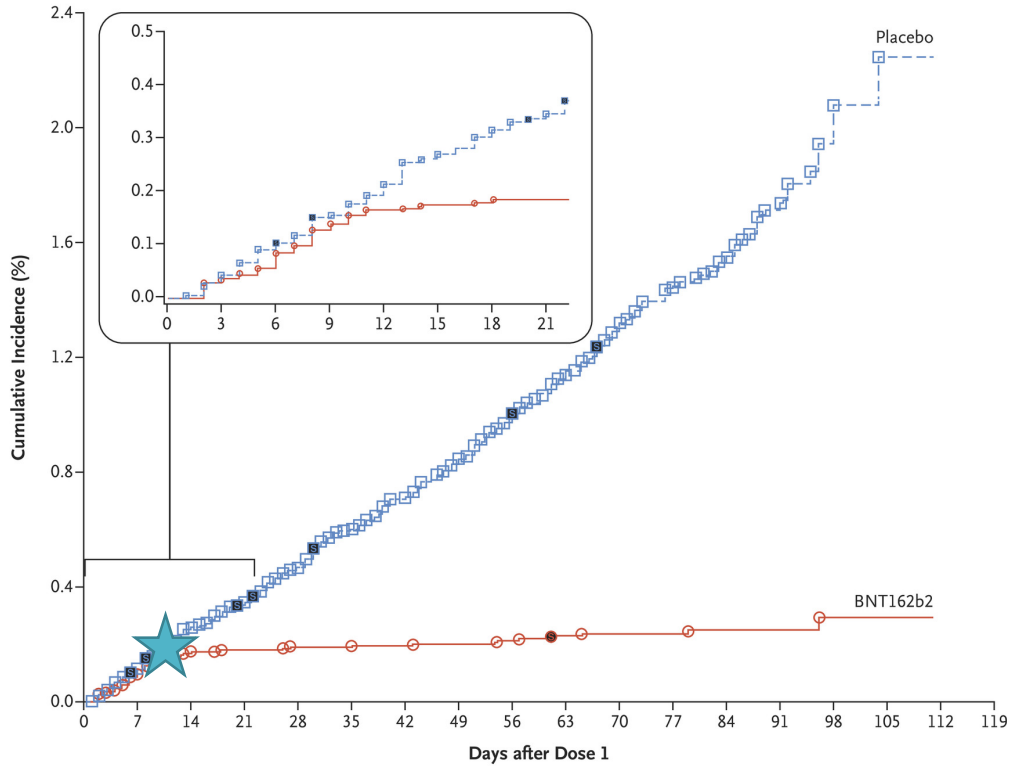
Reactogenicity & Adverse Events

- Older patients had lower rates of local reaction and were less likely to have systemic events
- Most common local event reported was **pain** at injection site, which was common between both age groups
- Commonly reported systemic events include **fatigue** and **headache**
- Fever more common after second dose
- Most reactions resolved within 1-2 days
- More BNT162b2 recipients than placebo recipients reported any adverse event or a related adverse
  - Transient reactogenicity events were reported as adverse events more commonly by vaccine recipients

Source: Polack FP. *N Engl J Med*. 2020;383(27):2603-15.

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

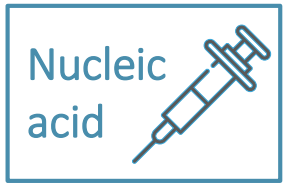


Efficacy

- BNT162b2 was **95% effective** (95% CI, 90.3-97.6) in preventing COVID-19 disease
- Of the 10 cases of **severe COVID-19** that were observed after the first dose, only 1 occurred in the vaccine group vs. 9 in placebo indicating **88.9% efficacy** (95% CI, 20.1-99.7)
  - No deaths were related to COVID-19 infection
- **Observed efficacy between first and second dose was 52.4%** (95% CI, 29.5-68.4)

Source: Polack FP. *N Engl J Med*. 2020;383(27):2603-15.

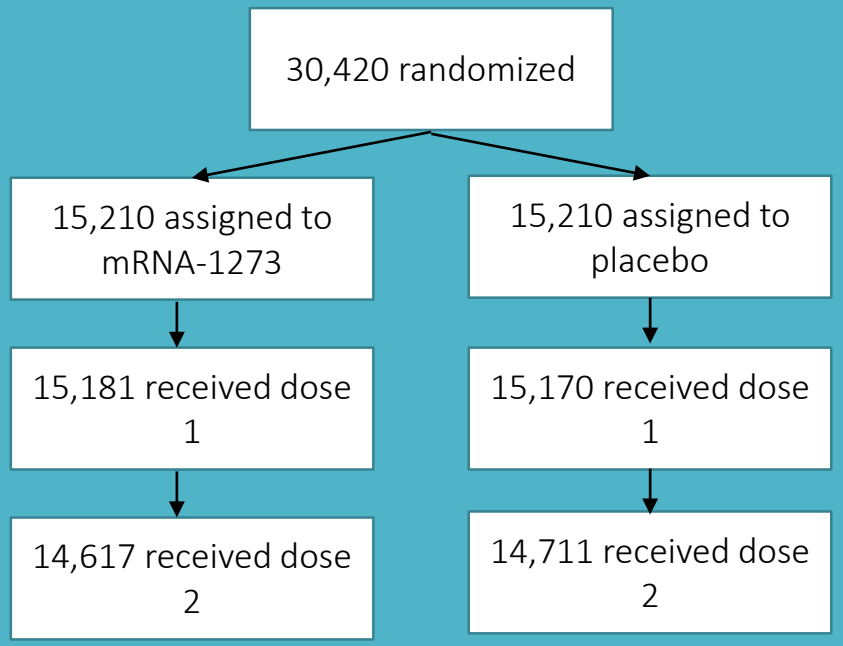
Moderna - mRNA-1273



Safety and Efficacy of the mRNA-1273 SARS-CoV-2 Vaccine		
Study Design	Phase III, randomized, stratified, observer-blinded, placebo-controlled trial	
Patient Population	Adults ≥18 years of age and at high risk of SARS-CoV-2, excluding pregnant or breastfeeding, medical history of COVID-19, immunosuppressed, asplenia, recurrent severe infections	
Intervention	1:1 ratio to receive two doses of mRNA-1273 (100 mcg) or placebo 28 days apart	
Endpoints	Safety: • Local/systemic reactogenicity • All adverse drug events during specified time frames	Efficacy: • Efficacy of vaccine against symptomatic, lab-confirmed COVID-19 14 days after second dose • Efficacy in participants with and participants without evidence of prior infection Secondary Endpoint: • Prevention of severe COVID-19 disease • Prevention of COVID-19 after a single dose

Source: Baden LR. *N Engl J Med*. 2020;384(5):403-16.

Patient Population



Source: Baden LR. *N Engl J Med*. 2020;384(5):403-16.

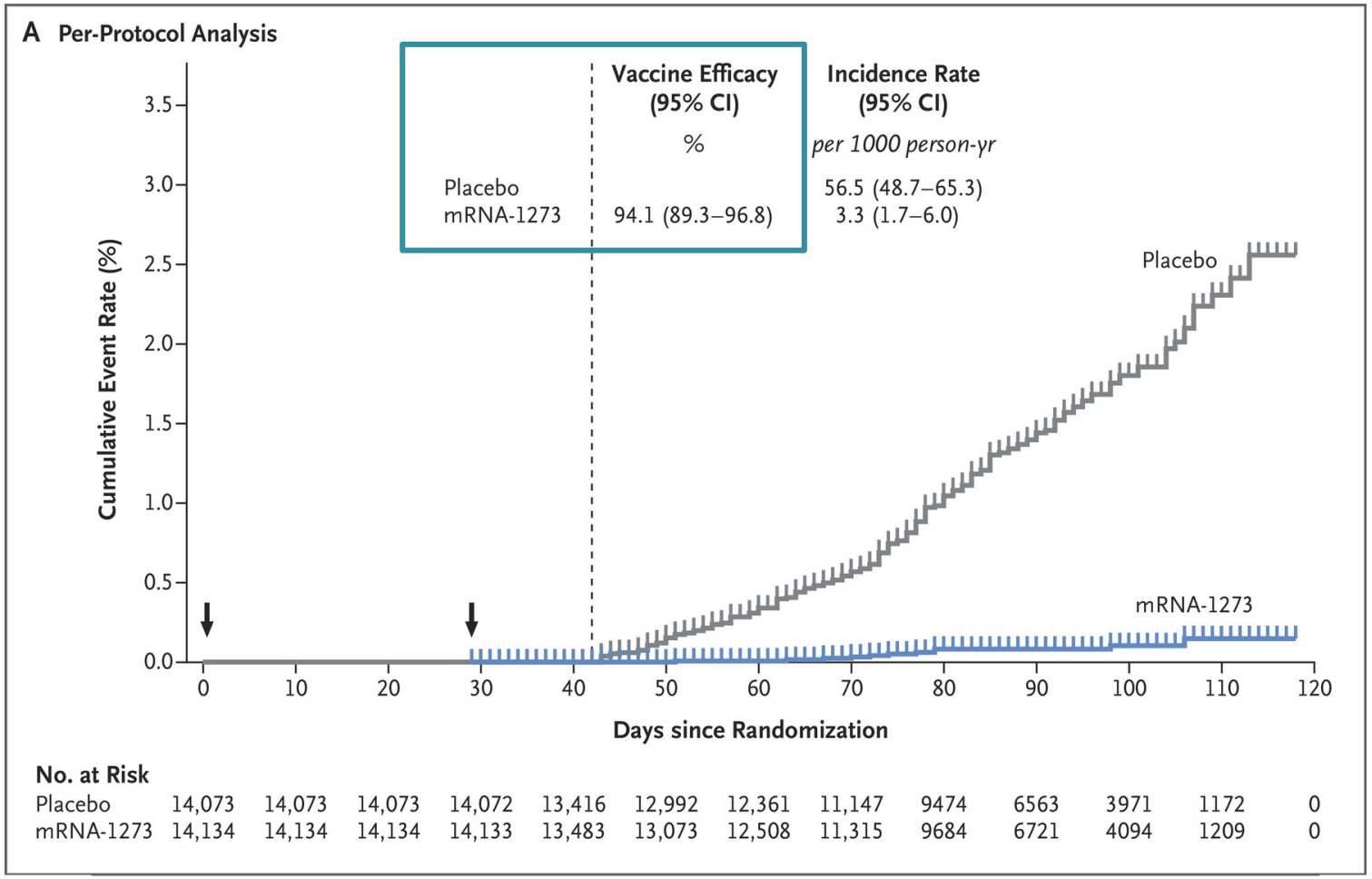
Table 1. Demographic and Clinical Characteristics at Baseline.*

Characteristics	Placebo (N=15,170)	mRNA-1273 (N=15,181)	Total (N=30,351)
Sex — no. of participants (%)			
Male	8,062 (53.1)	7,923 (52.2)	15,985 (52.7)
Female	7,108 (46.9)	7,258 (47.8)	14,366 (47.3)
Mean age (range) — yr	51.3 (18–95)	51.4 (18–95)	51.4 (18–95)
Age category and risk for severe Covid-19 — no. of participants (%)†			
18 to <65 yr, not at risk	8,886 (58.6)	8,888 (58.5)	17,774 (58.6)
18 to <65 yr, at risk	2,535 (16.7)	2,530 (16.7)	5,065 (16.7)
≥65 yr	3,749 (24.7)	3,763 (24.8)	7,512 (24.8)
Hispanic or Latino ethnicity — no. of participants (%)‡			
Hispanic or Latino	3,114 (20.5)	3,121 (20.6)	6,235 (20.5)
Not Hispanic or Latino	11,917 (78.6)	11,918 (78.5)	23,835 (78.5)
Not reported and unknown	139 (0.9)	142 (0.9)	281 (0.9)
Race or ethnic group — no. of participants (%)‡			
White	11,995 (79.1)	12,029 (79.2)	24,024 (79.2)
Black or African American	1,527 (10.1)	1,563 (10.3)	3,090 (10.2)
Asian	731 (4.8)	651 (4.3)	1,382 (4.6)
American Indian or Alaska Native	121 (0.8)	112 (0.7)	233 (0.8)
Native Hawaiian or Other Pacific Islander	32 (0.2)	35 (0.2)	67 (0.2)
Multiracial	321 (2.1)	315 (2.1)	636 (2.1)
Other	316 (2.1)	321 (2.1)	637 (2.1)
Not reported and unknown	127 (0.8)	155 (1.0)	282 (0.9)
Baseline SARS-CoV-2 status — no. of participants (%)§			
Negative	14,598 (96.2)	14,550 (95.8)	29,148 (96.0)
Positive	337 (2.2)	343 (2.3)	680 (2.2)
Missing data	235 (1.5)	288 (1.9)	523 (1.7)
Baseline RT-PCR test — no. of participants (%)			
Negative	14,923 (98.4)	14,917 (98.3)	29,840 (98.3)
Positive	95 (0.6)	87 (0.6)	182 (0.6)
Missing data	152 (1.0)	177 (1.2)	329 (1.1)
Baseline bAb anti–SARS-CoV-2 assay — no. of participants (%)			
Negative	14,726 (97.1)	14,690 (96.8)	29,416 (96.9)
Positive	303 (2.0)	305 (2.0)	608 (2.0)
Missing data	141 (0.9)	186 (1.2)	327 (1.1)
Risk factor for severe Covid-19 — no. of participants (%)			
Chronic lung disease	744 (4.9)	710 (4.7)	1,454 (4.8)
Significant cardiac disease	744 (4.9)	752 (5.0)	1,496 (4.9)
Severe obesity	1,021 (6.7)	1,025 (6.8)	2,046 (6.7)
Diabetes	1,440 (9.5)	1,435 (9.5)	2,875 (9.5)
Liver disease	96 (0.6)	100 (0.7)	196 (0.6)
Human immunodeficiency virus infection	87 (0.6)	92 (0.6)	179 (0.6)
Body-mass index¶			
No. of participants	15,007	14,985	29,992
Mean ±SD	29.3±6.7	29.3±6.9	29.3±6.8

Reactogenicity & Adverse Events

- Local and systemic effects more prevalent with mRNA-1273 group
- Older patients had lower rates of local reaction and were less likely to have systemic events
- Severity of adverse reaction increased after second dose
- Most reactions resolved within 1-3 days
- More mRNA-1273 recipients than placebo recipients reported any adverse event or a related adverse
- **Fatigue** and **headache** were the most common adverse events

Source: Baden LR. *N Engl J Med*. 2020;384(5):403-16.



Efficacy

- 196 cases of COVID-19 were diagnosed
  - 11 cases in mRNA-1273 group
  - 185 cases in placebo group
- 94.1% efficacy (95% CI, 89.3-96.8) for the prevention of symptomatic SARS-CoV-2 infection as compared with placebo
- 30 participants in the trial had severe COVID-19
  - All 30 were in the placebo group (indicating vaccine efficacy of 100% [95% CI, could not be estimated to 1.0])
  - 1 COVID-19 related death in placebo group

Source: Baden LR. *N Engl J Med*. 2020;384(5):403-16.

Janssen – Ad26.COV2.S

A Study of Ad26.COV2.S for the Prevention of SARS-CoV-2-Mediated COVID-19 in Adult Participants (ENSEMBLE)		
Study Design	Phase III, multinational, randomized, double-blind, placebo-controlled trial	
Patient Population	Adults ≥18 years of age and at high risk of SARS-CoV-2, excluding pregnant and breastfeeding women, severe or uncontrolled disease	
Intervention	1:1 ratio to receive one dose of Ad26.COV2.S (5×10^{10} viral particles) or placebo	
Endpoints	Safety: • Local/systemic reactogenicity • All adverse drug events	Efficacy: • Efficacy of vaccine against symptomatic, lab-confirmed COVID-19 14 and 28 days after dose

Source: Janssen/FDA Briefing Document. Data updated Feb 26, 2021.

Patient Population

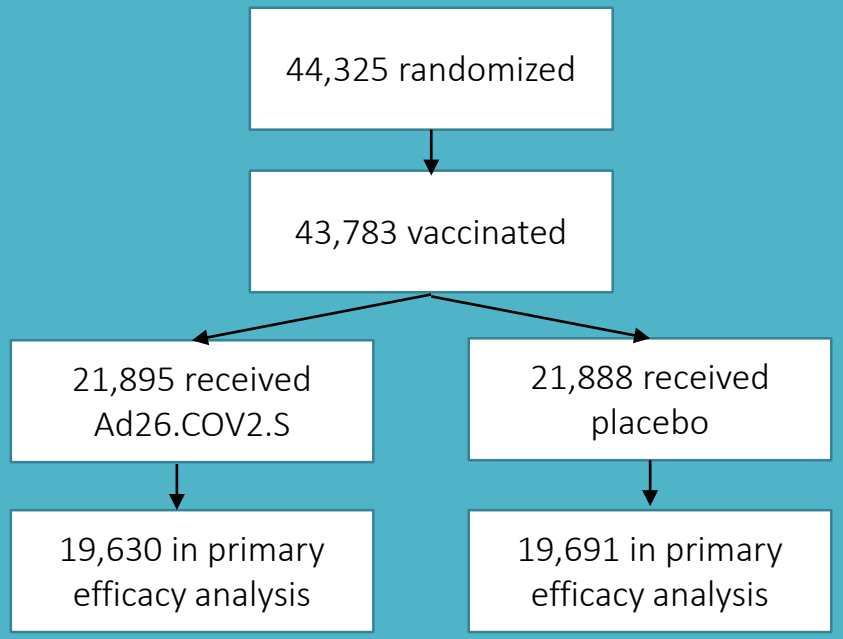


Table 10: Global Baseline Demographics and Comorbidities (Study COV3001)

	Ad26.COV2.S N=21,895		Placebo N=21,888	
Full Analysis Set (FAS)	n	%	n	%
Sex, Female	9820	44.9%	9902	45.2%
Age, years				
Mean (SD)	50.7 (15.1)		50.7 (15.0)	
Age Group				
18-59	14564	66.5%	14547	66.5%
≥60	7331	33.5%	7341	33.5%
≥65	4259	19.5%	4302	19.7%
≥75	809	3.7%	732	3.3%
Country				
Brazil	3644	16.6%	3634	16.6%
South Africa	3286	15.0%	3290	15.0%
Chile	563	2.6%	570	2.6%
United States	9655	44.1%	9647	44.1%
Argentina	1498	6.8%	1498	6.8%
Colombia	2125	9.7%	2123	9.7%
Peru	886	4.0%	885	4.0%
Mexico	238	1.1%	241	1.1%
Race				
American Indian or Alaska Native	2083	9.5%	2060	9.4%
Asian	743	3.4%	687	3.1%
Black or African American	4251	19.4%	4264	19.5%
Native Hawaiian or other Pacific Islander	58	0.3%	48	0.2%
White	12858	58.7%	12838	58.7%
Multiple	1204	5.5%	1245	5.7%
Unknown, not reported	697	3.2%	744	3.4%
Ethnicity				
Hispanic or Latino	9874	45.1%	9963	45.5%
≥1 Comorbidity*	8936	40.8%	8922	40.8%
Obesity	6277	28.7%	6215	28.4%
Hypertension	2225	10.2%	2296	10.5%
Type 2 Diabetes	1600	7.3%	1549	7.3%
Serious heart conditions	497	2.3%	511	2.3%
HIV (positive)	601	2.7%	617	2.8%

*Cut off at ≥2.0% in either group

Source: Janssen/FDA Briefing Document. Data updated Feb 26, 2021.

Reactogenicity & Adverse Events

- Lower reactogenicity was observed for older adults (≥60 years of age)
- Most adverse events were of mild or moderate severity and resolved within 1 to 2 days
- Analyses reported 3 deaths in the vaccine group (0 related to COVID-19) vs. 16 deaths in the placebo group (5 related to COVID-19)

Source: Janssen/FDA Briefing Document. Data updated Feb 26, 2021.

Efficacy

Table 12: Vaccine Efficacy Against Molecularly Confirmed Moderate to Severe/Critical COVID-19 With Onset at Least 14 Days and at Least 28 Days After Vaccination, Per Protocol Population (Study COV3001)

	Vaccine Efficacy Against Molecularly Confirmed Moderate to Severe/Critical COVID-19			
	With Onset at Least 14 Days After Vaccination		With Onset at Least 28 Days After Vaccination	
Per Protocol (PP)	Ad26.COV2.S N=19,630	Placebo N=19,691	Ad26.COV2.S N=19,630	Placebo N=19,691
Number of cases, n	116	348	66	193
Person Years	3116.57	3096.12	3102.00	3070.65
Vaccine efficacy (VE) (Adjusted 95% CI)	66.9% (59.03, 73.40)		66.1% (55.01, 74.80)	

Table 22. Vaccine Efficacy of First Occurrence of Moderate to Severe/Critical and Severe/Critical COVID-19 Including Non-centrally Confirmed Cases With Onset at Least 14 or at Least 28 Days After Vaccination, by Country of Participation, Per-Protocol Set, Study 3001

	Onset at Least 14 Days			Onset at Least 28 Days		
Country Subgroup	Ad26.COV2.S Cases (N) Person-yrs	Placebo Cases (N) Person-yrs	VE%[a] 95% CI	Ad26.COV2.S Cases (N) Person-yrs	Placebo Cases (N) Person-yrs	VE%[a] (95% CI)
United States						
Moderate to severe/critical	51 (9119) 1414.0	196 (9086) 1391.3	74.4% (65.0, 81.6)	32 (8958) 1403.4	112 (8835) 1375.6	72.0% (58.2, 81.7)

- Ad26.COV2.S was **~67% effective** (95% CI, 59.03-73.40) in preventing COVID-19 disease globally
  - The vaccine was **85.4% effective** (95% CI, 54.15-96.9) in preventing **severe or critical COVID-19** at day 28
- It also demonstrated **complete protection against COVID-19 related hospitalization and death at day 28** post-vaccination
- Preliminary analysis of **asymptomatic/undetected COVID-19** infection resulted in **efficacy of 87.8%** (95% CI, 48.27-98.64)

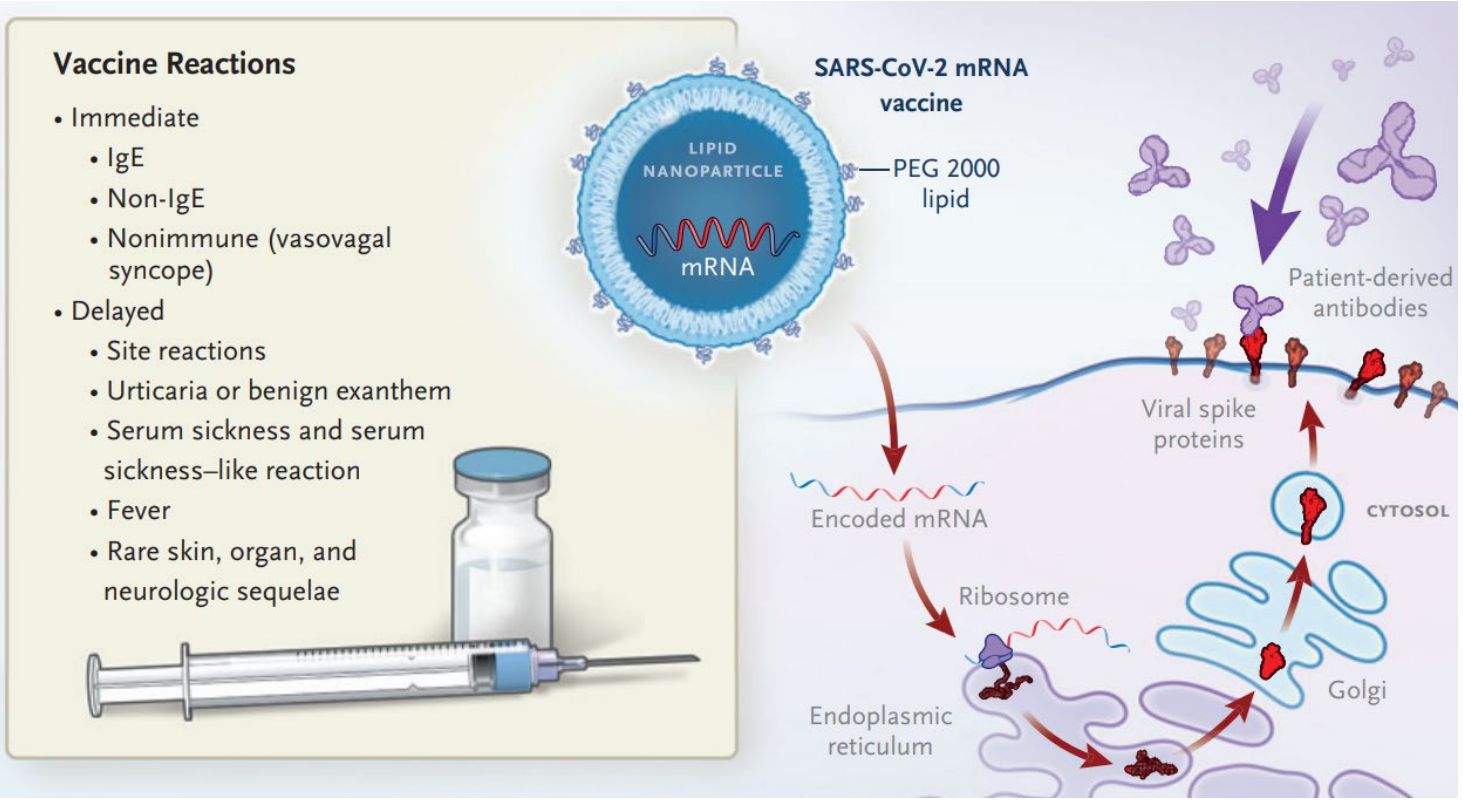
Source: Janssen/FDA Briefing Document. Data updated Feb 26, 2021.

COVID-19 Vaccines Available in the U.S.

	BNT162b2	mRNA-1273	Ad26.COV2.S
Efficacy	95% efficacy at preventing symptomatic, lab-confirmed COVID-19 7 days after second dose 88.9% efficacy in preventing severe COVID-19 infection	94.1% efficacy at preventing symptomatic, lab-confirmed COVID-19 infection 14 days after second dose 100% efficacy in preventing severe COVID-19 infection	67% efficacy at preventing moderate to severe/critical COVID-19 occurring at least 14 days after vaccination 85.4% efficacy in preventing severe COVID-19 infection
	No comparative trials conducted on efficacy of available vaccines yet		
Safety	• Serious adverse events low and consistent between groups	• Serious adverse events low and consistent between groups	• Serious adverse events low and consistent between groups
Gaps	• Long-term data • Prevention of asymptomatic infection • Not tested in children, immunocompromised people or pregnant women	• Long-term data • Prevention of asymptomatic infection • Not tested in children, immunocompromised people or pregnant women	• Long-term data • Not tested in children, immunocompromised people or pregnant women

Considerations

Allergic Reaction Considerations



- mRNA vaccines contain lipid nanoparticles (i.e. **polyethylene glycol**)
  - BNT162b2A – **4.7 cases per million** doses administered
  - mRNA-1273 – **2.5 cases per million** vaccine doses administered
- Ad26.COV2.S contains **polysorbate-80**
  - Severe allergic reactions, including **one** case of anaphylaxis has been reported in South Africa

Sources: Castells MC. *N Engl J Med*. 2021;384(7):643-9.
Turner PJ. *World Allergy Organ J*. 2021;14(2):100517.
Shimabukoro TT. *JAMA*. Published online February 12,2021.
Janssen/FDA Briefing Document. Data updated Feb 26, 2021.

SARS-CoV-2 Variants

- Variants may differ in virulence and transmissibility
- B.1.1.7 was identified in September 2020 in the United Kingdom
- B.1.351 emerged in October 2020 in South Africa
- P.1 emerged in January 2021 in Brazil

Variant	Reported Cases in the U.S.
B.1.1.7.	2,672
B.1.351	68
P.1	13

*As of March 5, 2021

How do current vaccines fair?

- BNT162b2 promotes immune response against B.1.1.7 and B.1.351
- Pfizer-BioNTech and Moderna are studying additional booster doses to address emergence of variants
- Preliminary data confirm that ~96% of the COVID-19 cases that occurred in the Ad26.COV2.S study in South Africa were due to the SARS-CoV-2 variant 20H/501Y.V2 (belonging to the B.1.351 lineage), implying efficacy against this strain

Sources: CDC. SARS-CoV-2 Variants. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html. Accessed [February 13, 2021].
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Janssen/FDA Briefing Document. Data updated Feb 26, 2021.

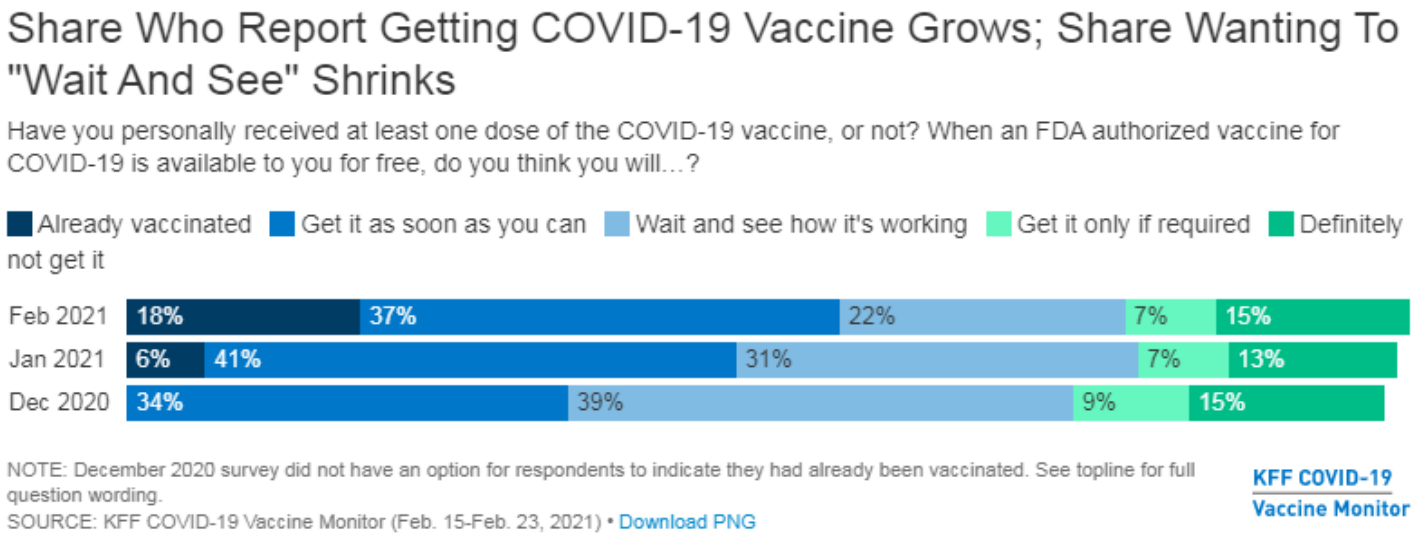
Storage & Handling

	BNT-162b2	mRNA-1273	Ad26.COV2.S
Manufacturer	Pfizer-BioNTech	Moderna	Janssen
Supplied/ Refrigeration Stability	Shipped in thermal container with dry ice Store at ultra-low temperature freezer between -80°C to -60°C OR store at (-25°C to -15°C for up 2 weeks. Thaw then store at 2°C to 8°C for up to 5 days OR thaw at 8°C to 25°C for 30 minutes for immediate use Undiluted vials may be stored at 8°C to 25°C for up to 2 hours	Shipped frozen (-25°C to -15°C) May be stored between (-25°C to -15°C) but must be thawed before use. Store at 2°C to 8°C for up to 30 days OR 8°C to 25°C for up to 12 hours	Initially stored frozen by manufacturer then shipped at 2°C to 8°C Store at 2°C to 8°C OR at 9°C to 25°C for up to 12 hours
Preparation	Dilute the vial contents using 1.8 mL of 0.9% Sodium Chloride Injection, USP	No dilution needed	No dilution needed
Stability	After dilution, vaccine is stable at 2°C to 25°C for 6 hours	After vial puncture, vaccine is stable at 2°C to 25°C for 6 hours	After vial puncture, vaccine is stable at 2°C to 8°C for 6 hours OR at 9°C to 25°C for 2 hours

Sources: Emergency Use Authorization of the Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 [Healthcare Provider Fact Sheet]. U.S. FDA. Revised 2/2021
Emergency Use Authorization of the Moderna COVID-19 Vaccine to Prevent Coronavirus Disease 2019 [Healthcare Provider Fact Sheet]. U.S. FDA. Revised 12/2020
Emergency Use Authorization of the Janssen COVID-19 Vaccine to Prevent Coronavirus Disease 2019 [Healthcare Provider Fact Sheet]. U.S. FDA. Revised 2/2021

Vaccine Hesitancy

- Studies show that to stop the spread of COVID-19 and its mutations, a majority of the population must achieve immunity
- Factors that contribute to hesitancy with COVID-19 vaccines: the novelty of the virus, mixed messages about the severity of the disease, concerns about the rapid vaccine development timeline, and perceived politicization of the process



Sources: Coutasse A. *J Ambul Care Manage.* 2021;44(1):71-5.
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Wood S. *N Engl J Med*. 2021;384(7):e23.
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Strategies to Diminish Hesitancy

Define the goals of vaccine communication (What)

- Assurance of vaccine safety and efficacy
- Explain the vaccine development, FDA approval, monitoring, and distribution process
- Address concerns without judgment or overly directive language
- Educate on misconceptions and dispel misinformation

Identify the needs and perspectives of the intended audience (Who)

- Population-specific concerns, motivations, and information needs must be considered (e.g. old vs. young, racial disparities)

Create and disseminate messages tailored to the intended audience (How)

- Provide verified information from trusted sources
- Establish COVID-19 vaccination as an accepted social norm
- Avoid language of requirement and mandate
- Incorporate the values and beliefs of the target audience

Source: NIH. COVID-19 Vaccination Communication: Applying Behavioral and Social Science to Assess Vaccine Hesitancy and Foster Vaccine Confidence. Available at https://obssr.od.nih.gov/wp-content/uploads/2020/12/COVIDReport_Final.pdf. Accessed [February 28, 2021].

Conclusion

- The urgent need for achieving herd immunity has allowed for the rapid development of vaccines with different modalities
  - There is no single, perfect solution as each vaccine strategy has its advantages and drawbacks
- Interim results of BNT162b2A, mRNA-1273, & Ad26.COV2.S show >50% efficacy and vaccines will continue to be monitored for long-term efficacy and safety
- Healthcare professionals must educate and dispel misconceptions to reduce vaccine hesitancy

Assessment Questions

Question #1

mRNA-based vaccines have been studied in which other disease states?

a) Influenza
b) Rabies
c) Cytomegalovirus
d) A, B, & C
e) mRNA-based vaccines are considered a new approach and have only been studied in coronavirus disease states

Question #1 Response

mRNA-based vaccines have been studied in which other disease states?

a) Influenza
b) Rabies
c) Cytomegalovirus
d) A, B, & C
e) mRNA-based vaccines are considered a new approach and have only been studied in coronavirus disease states

Question #2

True or False: The purpose of the vaccine adjuvant is to boost immune response to the vaccine

Question #2 Response

True or False: The purpose of the vaccine adjuvant is to boost immune response to the vaccine

Question #3

Which vaccine is most effective at preventing COVID-19 infection?

a) Pfizer-BioNTech (BNT162b2)
b) Moderna (mRNA-1273)
c) Janssen (Ad26.COV2.S)
d) Unable to determine since there are currently no head-to-head clinical trials comparing outcomes with different vaccines

Question #3 Response

Which vaccine is most effective at preventing COVID-19 infection?

a) Pfizer-BioNTech (BNT162b2)
b) Moderna (mRNA-1273)
c) Janssen (Ad26.COV2.S)
d) **Unable to determine since there are currently no head-to-head clinical trials comparing outcomes with different vaccines**

Question #4

Which of the following is **not** a characteristic of a viral vector vaccine?

a) Virus is genetically engineered to include DNA that will produce antigen once injected
b) Immune response has broad target range
c) Produced without handling live virus
d) Familiar, proven technology

Question #4 Response

Which of the following is **not** a characteristic of a viral vector vaccine?

a) Virus is genetically engineered to include DNA that will produce antigen once injected

b) **Immune response has broad target range**

c) Produced without handling live virus

d) Familiar, proven technology

Question #5

Which of the following vaccines must be diluted prior to administration?

a) BNT-162b2
b) mRNA-1273
c) Ad26.COV2.S
d) None of the above

Question #5 Response

Which of the following vaccines must be diluted prior to administration?

a) **BNT-162b2**
b) mRNA-1273
c) Ad26.COV2.S
d) None of the above

Question #6

Which of the following strategies should you avoid when speaking to a patient who expresses hesitancy in receiving a COVID-19 vaccine?

a) Explaining the vaccine development process and distribution process
b) Using language of requirement and mandate
c) Incorporating the values and beliefs of the target audience
d) Addressing concerns without judgement

Question #6 Response

Which of the following strategies should you avoid when speaking to a patient who expresses hesitancy in receiving a COVID-19 vaccine?

a) Explaining the vaccine development process and distribution process

b) Using language of requirement and mandate

c) Incorporating the values and beliefs of the target audience

d) Addressing concerns without judgement

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Thank you

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