COVID-19 Vaccination Education

December 14, 2020





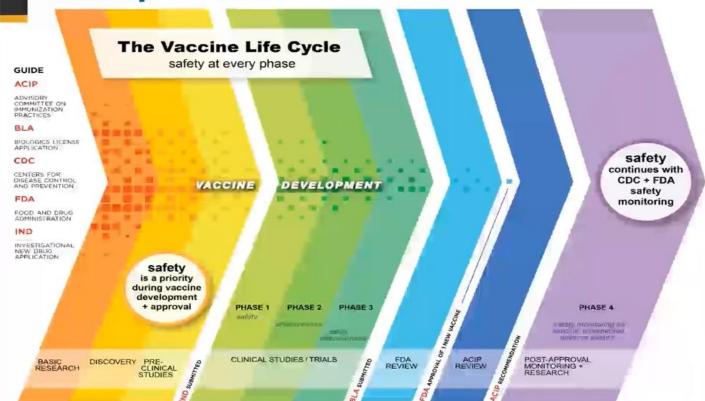
Is the Vaccine Safe?





The Vaccine Life Cycle

Safety Focused

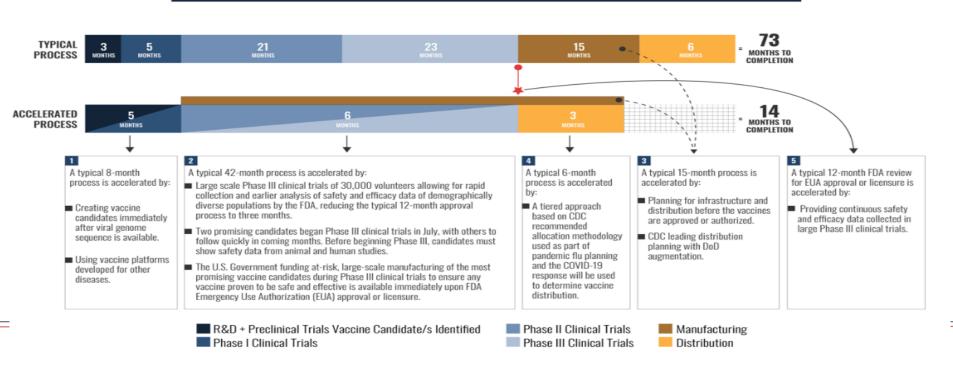


- Safety is a priority during all phases of vaccine development, approval, and use
- Post-licensure (postauthorization) safety monitoring is an established part of the vaccine life cycle
- Monitoring COVID-19 vaccine safety will be a coordinated effort by multiple federal agencies

Operation Warp Speed



MISSION: Deliver 300 million doses of safe and effective vaccine by 1 January 2021.



How do vaccines compare?

	Pfizer &BioNtech COVID-19 Vaccine	Moderna	Flu shot	MMR Vaccine
Туре	RNA-virus genetic code (mRNA)	RNA-virus genetic code (mRNA)	Inactivated virus	Live attenuated
Doses	2 injections 21 days apart	2 injections 28 days apart	Annual injection	Two injections at least 28 days apart
How effective	95%	95%	40-60 %	97% against Measles and rubella, 88% against mumps
Storage	-75 C (Ultra Cold)	-20 C (Cold)	2-8 C (refrigerator)	2-8C (refrigerator)





How do mRNA vaccines work?

mRNA vaccines give the immune system genetic instructions to recognise the virus 'Spike' mRNA lipid Antibodies protein nanoparticle Cell cells Scientists focus on the The synthetic mRNA is Once inside the cell, its genetic sequence for the packaged in a lipid cellular machinery follows the nanoparticle that delivers virus's 'spike' protein. This is mRNA instructions to produce used to synthesise an mRNA the instructions to a cell the viral protein. This is sequence - instructions that displayed on the surface of cells can use to make the the cell and stimulates an 'spike' protein immune system response Source: Pfizer





Vaccine mRNA

- After the vaccine is injected, mRNA encapsulated in a lipid nanoparticle delivers instructions into the muscle cells. It guides the spike protein production within these cells, which reaches peak levels for 24 to 48 hours after vaccination and can last for a few more days.
- Once the mRNA creates enough of the spike protein to be expressed on the cell surface to activate the immune response, translation and protein production stops. The vaccine mRNA degrades after a few days which happens similar to the way our naturally produced mRNA degradation.
- Vaccine mRNA is <u>NOT</u> replicated within the cells. Once it creates enough protein, it STOPS producing the spike protein so there is no overproduction of protein to remain within cells to cause damage.
- Vaccine mRNA will <u>not</u> cause permanent changes to your DNA as it not incorporated into your genetic code; therefore, this mRNA will not be reproduced to create more spike protein once it degrades.
- Since it is not incorporated into your DNA, it cannot be transmitted to your offspring





Pfizer Vaccine





Clinical Development To Date

Study BNT162-01	Study C4591001
Ongoing Phase 1, dose-	Ongoing Phase 1/2/3
finding, safety and	randomized, placebo-
immunogenicity in individuals	controlled, observer-blind in
18 to 55 years of age	individuals ≥12 years of age





Subtitle

Initial design included ~30,000 adults 18 to 85 years of age

- Later expanded to include participants ≥12 years and those with stable, chronic disease and/or infections with HIV, HBV, HCV
- Participants received 2 doses of vaccine or placebo, 21 days apart

Phase 1 (N=90): observer-blinded, dose-finding, vaccine candidate selection

- N=15 per dose level, randomized 4:1
- 2 age cohorts: 18 to 55; 65 to 85 years of age
- Dose and age escalation between vaccine candidates and dose levels
 - N=72 received BNT162b2 at 10-, 20-, and 30-μg dose levels (N=18 placebo)
 - N=84 received BNT162b1 at 10-, 20-, 30- and 100-μg dose levels (N=21 placebo)





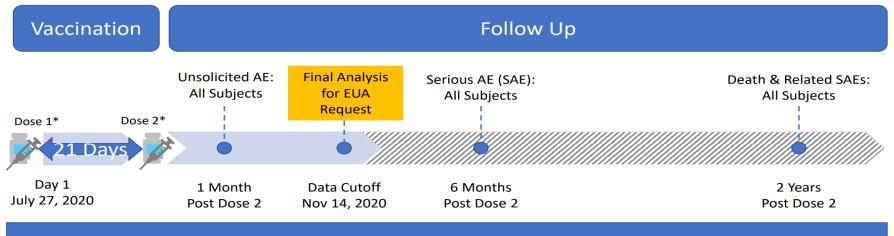
Subtitle

Phase 2/3: randomized 1:1, safety and efficacy

- Phase 2: first 360 participants enrolled, 18 to 85 years of age, for an expanded cohort for safety and immunogenicity
- All COVID-19 cases contribute to efficacy evaluation
- Stratified by age: 12 to 15 yrs; 16 to 55 yrs; >55 yrs (goal of 40% enrollment in oldest group)
- N=43,551 (21,774 vaccine, 21,777 placebo) participants ≥16 yrs of age randomized, as of cutoff November 14, 2020







Active Surveillance begins after 1st dose

Potential COVID -19 symptoms trigger telehealth or in-person visit and nasal swab

^{*}Reactogenicity subset: all phase 1, phase 2/3 (~6500 US, 500/per country: Argentina, Brazil, and S. Africa). Solicited reactions collected for 7 days following each vaccination





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Case definition

COVID-19 disease Severe COVID-19 disease Positive SARS-CoV-2 PCR* within 4 days of Confirmed COVID-19 plus at least one of the symptomatic period plus at least one of following symptoms: the following symptoms: Severe systemic illness: RR ≥30 breaths/minute, Fever HR ≥ 125 beats/minute, Chills SPO₂ ≤93% on RA or Diarrhea PaO2/FiO2 <300mm Hg Vomiting Respiratory failure: Sore throat · high-flow O2, · New or increased cough · noninvasive ventilation. New or increased shortness of breath · mechanical ventilation, or ECMO New loss of taste or smell Shock: · New or increased muscle pain SBP <90 mm Hg, DBP <60 mm Hg or *Confirmed by Central Lab Using: Cepheid Xpert Xpress SARS-CoV-2 need vasopressors Or Local Lab, if no central lab results available:

ICU admission

Death



-Roche cobas SARS-CoV-2 real-time RT-PCR test (EUA200009/A001)
-Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001)



Demography

	BNT162b2	Placebo	Total
Characteristic	(N=20033) N (%)	(N=20244) N (%)	(N=40277) N (%)
Sex	14 (70)	14 (70)	14 (70)
Female	9794 (48.9)	10107 (49.9)	19901 (49.4)
Male	10239 (51.1)	10137 (50.1)	20376 (50.6)
Age at vaccination	, ,	,	
Mean years (SD)	50.3 (15.73)	50.1 (15.78)	50.2 (15.76)
Median (years)	51.0	51.0	51.0
Min, max (years)	(12, 89)	(12, 91)	(12, 91)
Age group	•	•	
16 to <18 years	77 (0.4)	76 (0.4)	153 (0.4)
16 to 54 years	11589 (57.8)	11743 (58.0)	23332 (57.9)
>55 years	8396 (41.9)	8454 (41.8)	16850 (41.8)
≥65 years	4294 (21.4)	4319 (21.3)	8613 (21.38)
≥75 years	860 (4.3)	852 (4.2)	1712 (4.3)
Race			
American IndianAlaska Native	131 (0.7)	122 (0.6)	253 (0.6)
Asian	880 (4.4)	883 (4.4)	1763 (4.4)
Black/African American	1957 (9.8)	1972 (9.7)	3929 (9.8)
Native Hawaiian/Pacific Islander	54 (0.3)	29 (0.1)	83 (0.2)
White	16387 (81.8)	16619 (82.1)	33006 (81.9)
Multiracial	523 (2.6)	493 (2.4)	1016 (2.5)
Not reported	101 (0.5)	126 (0.6)	227 (0.6)
Ethnicity			
Hispanic or Latino	5272 (26.3)	5281 (26.1)	10553 (26.2)
Not Hispanic or Latino	14652 (73.1)	14847 (73.3)	29499 (73.2)
Not reported	109 (0.5)	116 (0.6)	225 (0.6)
Comorbidities			
Yes	9278 (46.3)	9314 (46.0)	18592 (46.2)
No	10755 (53.7)	10930 (54.0)	21685 (53.8)
Obesity	6934 (34.6)	7093 (35.0)	14027 (34.8)





Solicited local reaction

Up to 7 days from injection

Age group	18 to 55 y	years*	>55 y	years .
	BNT162b2	Placebo	BNT162b2	Placebo
Local Reaction - Dose 1	N=2291	N=2298	N=1802	N=1792
	%	%	%	%
Pain ^a				
Mild	51.1	13.4	55.9	8.9
Moderate	31.0	0.5	15.0	0.3
Severe	1.0	0.1	0.2	0.0
Redness ^b				
Mild	3.1	0.7	3.1	0.7
Moderate	1.2	0.3	1.5	0.3
Severe	0.3	0.2	0.2	0.1
Swelling ^b				
Mild	3.8	0.1	3.9	0.6
Moderate	1.7	0.2	2.5	0.6
Severe	0.2	0.1	0.1	0.0

%: n/N. n = number of participants with the specified reaction. N = number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

Data analysis cutoff date: November 14, 2020.





^a Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.

^b Mild: 2.0 to ≤5.0 cm; moderate: 5.0 to ≤10.0 cm; severe: >10.0 cm.

^{*}Includes <10 participants 16 and 17 years of age.

Age group	18 to 55 y	/ears*	>55 y	years
	BNT162b2	Placebo	BNT162b2	Placebo
Local Reaction - Dose 2	N=2098	N=2103	N=1660	N=1646
	%	%	%	%
Pain ^a				
Mild	49.5	10.7	47.7	7.6
Moderate	27.1	1.0	18.0	0.1
Severe	1.2	0.0	0.5	0.0
Redness ^b				
Mild	3.5	0.4	3.6	0.5
Moderate	1.9	0.3	3.2	0.2
Severe	0.5	0.0	0.5	0.1
Swelling ^b				
Mild	3.8	0.1	4.1	0.3
Moderate	2.1	0.1	3.2	0.3
Severe	0.3	0.0	0.2	0.1

^{%:} n/N. n = number of participants with the specified reaction. N = number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

Data analysis cutoff date: November 14, 2020.





^a Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.

^b Mild: 2.0 to ≤5.0 cm; moderate: 5.0 to ≤10.0 cm; severe: >10.0 cm.

^{*}Includes <10 participants 16 and 17 years old.

Age group	18 to 55	18 to 55 years*		ears
	BNT162b2	Placebo	BNT162b2	Placebo
Adverse Event- Dose 1	N=2291 %	N=2298 %	N=1802 %	N=1792 %
Fever				
≥38.0°C	15.8	0.5	1.4	0.4
>38.0°C to 38.4°C	9.2	0.2	1.3	0.1
>38.4°C to 38.9°C	5.2	0.1	0.1	0.2
>38.9°C to 40.0°C	1.2	0.1	0.1	0.1
Fatigue ^a				
Mild	21.1	11.8	20.7	14.1
Moderate	33.7	10.3	13.3	8.4
Severe	4.6	0.7	0.1	0.2
Headache ^a				
Mild	25.6	15.3	19.3	13.5
Moderate	22.9	8.1	5.8	4.5
Severe	3.2	0.7	0.1	0.2
Chillsa				
Mild	17.1	3.1	4.8	2.2
Moderate	15.9	0.7	1.4	0.9
Severe	2.1	0.0	0.0	0.1
New or worsened muscle				
pain ^a				
Mild	15.5	5.3	9.3	5.6
Moderate	19.5	2.8	4.6	2.6
Severe	2.2	0.1	0.1	0.2

%:n/N. n = number of participants with the specified reaction.

N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.

a Mild: does not interfere with activity; moderate:

some interference with activity; severe: prevents daily activity.
*Includes <10 participants 16 and 17 years of age.

*Includes <10 participants 16 and 17 years of age. Data analysis cutoff date: November 14, 2020.





Solicited reaction Dose 1

	18 to 55	years*	>55	years
	BNT162b2	Placebo	BNT162b2	Placebo
Adverse Event	N=2291	N=2298	N=1802	N=1792
	%	%	%	%
New or worsened joint pain ^a				
Mild	6.4	4.1	5.6	3.8
Moderate	4.3	1.9	2.9	2.2
Severe	0.2	0.0	0.1	0.1
Diarrheac				
Mild	9.0	9.4	6.5	5.6
Moderate	2.0	2.3	1.4	0.9
Severe	0.1	0.0	0.2	0.1
Vomiting ^b				
Mild	1.0	1.0	0.4	0.5
Moderate	0.2	0.2	0.1	0.0
Severe	0.0	0.0	0.0	0.0

%:n/N. n = number of participants with the specified reaction.

N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.

- ^a Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
- ^b Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.
- ^c Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.
- *Includes <10 participants 16 and 17 years of age. Data analysis cutoff date: November 14, 2020.





Age group	18 to 55	years*	>55	years
	BNT162b2	Placebo	BNT162b2	Placebo
Adverse Event- Dose 2	N=2291	N=2298	N=1802	N=1792
	%	%	n (%)	n (%)
New or worsened joint pain ^a				
Mild	9.8	2.6	9.7	2.1
Moderate	11.2	2.4	8.7	1.5
Severe	1.0	0.2	0.4	0.1
Diarrhea ^c				
Mild	8.5	6.8	6.9	4.4
Moderate	1.7	1.5	1.3	1.3
Severe	0.2	0.0	0.1	0.2
Vomiting ^b				
Mild	1.3	8.0	0.5	0.3
Moderate	0.4	0.4	0.1	0.0
Severe	0.2	0.0	0.1	0.0

%:n/N. n = number of participants with the specified reaction.

N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.

^a Mild: does not interfere with activity: moderate:

Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
 Mild: 1 to 2 times in 24 hours; moderate: >2 times

in 24 hours; severe: requires intravenous hydration.

c Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.

*Includes <10 participants 16 and 17 years of age. Data analysis cutoff date: November 14, 2020.





Study C4591001 Unsolicited AEs (non-serious)

Higher frequency in vaccine group vs. placebo

- Primarily AEs consistent with solicited reactions/AEs reported by reactogenicity subset participants (vaccine 18.7%, placebo 3.9%)
- Lymphadenopathy
 - Vaccine n=64, placebo n=6
 - Plausible relation to vaccination
- Bell's palsy
 - Vaccine n=4, placebo n=0
 - Observed frequency consistent with background rate in general population
 - No clear basis upon which to conclude a causal relationship at this time





Study C4591001 Serious Adverse Events

Deaths: 6 total (2 vaccine, 4 placebo)

Vaccine group deaths (both >55 years of age):

- Cardiac arrest 62 days after Dose 2; died 3 days later
- Atherosclerotic disease; died 3 days after Dose 1, with baseline obesity

Non-fatal SAEs

Appendicitis (8 vaccine, 4 placebo)

 Vaccine group: 2 participants aged >55 years, of which 1 was perforated

Possibly-related SAEs (FDA conclusion)

Shoulder injury: vaccine administration or vaccine itself





Study C4591001 - Other Safety Evaluations

Clinical laboratory (Phase 1)

- Transient decreased lymphocytes at 1-3 days after Dose 1
- Generally normalized by next study visit (6-8 days after Dose 1)
- Did not occur after Dose 2

Subgroup analyses

- Assessed by race, ethnicity, medical comorbidities, prior SARS-CoV-2 infection
- No safety concerns





Is the Vaccine Effective?





Current mRNA vaccines

	Pfizer	Moderna
Effectiveness	95%	95%
Doses	2 IM 21 days apart	2 IM 28 days apart
Micrograms	30 mcg	100 mcg
Side effects (Phase 1 and 2 trials)	Fatigue and fever	Fatigue, headaches and muscle pain





Primary efficacy

Vaccine Efficacy — First COVID-19 Occurrence From 7 Days After Dose 2, Subjects Without Prior Evidence of Infection

		BNT162b2 N=18198		Placebo N=18325	
Pre- Specified Age Group	Cases	Surveillance Time in 1000 p- yrs (No. subjects at risk)	Cases	Surveillance Time in 1000 p- yrs (No. subjects at risk)	Vaccine Efficacy % (95% CI)
All participants	8	2.214 (17411)	162	2.222 (17511)	95.0 (90.3, 97.6)
16 to 55 years	5	1.234 (9897)	114	1.239 (9955)	95.6 (89.4, 98.6)
>55 years	3	0.980 (7500)	48	0.983 (7543)	93.7 (80.6, 98.8)





	BNT162b2	Placebo	
	N=19965	N=20172	
	Cases	Cases	Vaccine
Efficacy Endpoint	Surveillance	Surveillance	Efficacy %
Subgroup	Time	Time	(95% CI)
Overall	9	169	94.6 (89.6,
	2.332 (18559)	2.345 (18708)	97.6)
Ethnicity			
Hispanic or Latino	3	55	94.5 (83.2,
	0.637 (5074)	0.638 (5090)	98.9)
Not Hispanic or Latino	6	114	94.7 (88.1,
	1.681 (13380)	1.693 (13509)	98.1)
Race			
American Indian or Alaska	0	1	100.0 (-3511.0,
native	0.011 (104)	0.010 (104)	100.0)
Asian	1	4	74.4 (-158.7,
	0.095 (796)	0.097 (808)	99.5)
Black or African American	0	7	100.0 (30.4,
	0.187 (1758)	0.188 (1758)	100.0)
Native Hawaiian or other	0	1	100.0 (-2112.1,
Pacific Islander	0.006 (50)	0.003 (29)	100.0)
White	7	153	95.4 (90.3,
	1.975 (15294)	1.990 (15473)	98.2)
Multiracial	1	1	10.4 (-6934.9,
	0.047 (467)	0.042 (424)	98.9)
Not reported	0	2	100.0 (-581.6,
	0.010 (90)	0.013 (112)	100.0)
Baseline SARS-CoV-2 Status			
Positive ^h	1	1	-7.1 (-8309.9,
	0.056 (526)	0.060 (567)	98.6)
	0.036 (326)	0.000 (001)	
Negative ⁱ	8	164	95.1 (90.1,
Negative			95.1 (90.1, 97.9)
Negative ⁱ Unknown	8	164	95.1 (90.1,

Primary Efficacy Endpoint: COVID-19 Cases at least 7 days after Dose 2, Subjects <u>with and without</u> prior infection – Evaluable Efficacy Population





Second dose primary efficacy endpoint

di Caranta		Placebo	
	BNT162b2	N=20172	
	N=19965	Cases	Vaccine
Efficacy Endpoint	Cases	Surveillance	Efficacy %
Subgroup	Surveillance Time	Time	(95% CI)
Overall	9	169	94.6 (89.6, 97.6)
	2.332 (18559)	2.345 (18708)	
Age group (years)			
16 to 17	0	1	100.0 (-3969.9,
	0.003 (58)	0.003 (61)	100.0)
18 to 64	8	149	94.6 (89.1, 97.7)
	1.799 (14443)	1.811 (14566)	
65 to 74	1	14	92.9 (53.2, 99.8)
	0.424 (3239)	0.423 (3255)	
≥75	0	5	100.0 (-12.1,
	0.106 (805)	0.109 (812)	100.0)
Obese ⁹			
Yes	3	68	95.5 (86.2, 99.1)
	0.810 (6445)	0.832 (6582)	
No	6	101	94.1 (86.7, 97.9)
	1.522 (12108)	1.513 (12120)	
Sex			
Female	5	84	93.9 (85.2, 98.1)
	1.149 (9102)	1.176 (9366)	
Male	4	85	95.3 (87.6, 98.8)
	1.183 (9457)	1.170 (9342)	

COVID-19 cases @ least 7 days after 2d dose,
Subjects with or without prior infection





Subgroup analysis- efficacy by comorbidity

Efficacy Endpoint Subgroup	BNT162b2 N=18198 Cases Surveillance Time	Placebo N°=18325 Cases Surveillance Time	Vaccine Efficacy % (95% Cl)				
				Overall	8	162	95.0
					2.214 (17411)	2.222 (17511)	(90.0, 97.9
				Comorbidity			
No comorbidity	4	76	94.7				
	1.189 (9381)	1.197 (9482)	(85.9, 98.6				
Any comorbidity	4	86	95.3				
	1.025 (8030)	1.025 (8029)	(87.7, 98.8				
Any malignancy	· 1	4	75.				
	0.092 (704)	0.090 (681)	(-145.8, 99.5				
Cardiovascular	Ó	5	100.0				
	0.067 (534)	0.062 (492)	(-0.8, 100.0				
Chronic pulmonary disease	· 1	14	93.0				
	0.175 (1374)	0.171 (1358)	(54.1, 99.8				
Diabetes	· 1	19	94.7				
	0.176 (1372)	0.176 (1374)	(66.8, 99.9				
Obese (BMI≥30.0 kg/m²)	3	67	95.4				
	0.763 (6000)	0.782 (6103)	(86.0, 99.1				
Hypertension	2	44	95.4				
	0.567 (4413)	0.567 (4437)	(82.6, 99.5				
Diabetes (including gestational	1	20	95.0				
diabetes)	0.177 (1381)	0.178 (1384)	(68.7, 99.9				





Vaccination of special populations

- Vaccine may be administered to persons with underlying medical conditions who have no contraindications to vaccination
- Phase 2/3 clinical trials demonstrate similar safety and efficacy profiles in persons with underlying medical conditions, including those that place them at increased risk for severe COVID-19, compared to persons without comorbidities





Immunocompromised

- Persons with HIV infection, other immunocompromising conditions, or who take immunosuppressive medications or therapies might be at increased risk for severe COVID-19
- Data not currently available to establish safety and efficacy of vaccine in these groups
- These individuals may still receive COVID-19 vaccine unless otherwise contraindicated
- Individuals should be counseled about:
 - Unknown vaccine safety and efficacy profiles in immunocompromised persons
 - Potential for reduced immune responses
 - Need to continue to follow all current guidance to protect themselves against COVID-19 I





Pregnancy

COVID-19 vaccines and pregnancy

- There are no data on the safety of COVID-19 vaccines in pregnant women
 - Animal developmental and reproductive toxicity (DART) studies are ongoing
 - Studies in humans are ongoing and more planned
- mRNA vaccines and pregnancy
 - Not live vaccines
 - They are degraded quickly by normal cellular processes and don't enter the nucleus of the cell

COVID-19 and pregnancy

- Increased risk of severe illness (ICU admission, mechanical ventilation and death)
- Might be an increased risk of adverse pregnancy outcomes, such as preterm birth

If a woman is part of a group (e.g., healthcare personnel) who is recommended to receive a COVID-19 vaccine and is pregnant, she may choose to be vaccinated. A discussion with her healthcare provider can help her make an informed decision.





Lactation

Subtitle

- There are no data on the safety of COVID-19 vaccines in lactating women or the effects of mRNA vaccines on the breastfed infant or milk production/excretion
- mRNA vaccines are not considered live virus vaccines and are not thought to be a risk to the breastfeeding infant
- If a lactating woman is part of a group (e.g., healthcare personnel) who is recommended to receive a COVID-19 vaccine, she may choose to be vaccinated





Public health recommendations for vaccinated persons

Subtitle

- Protection from vaccine is not immediate; vaccine is a 2-dose series and will take 1 to 2 weeks following the second dose to be considered fully vaccinated
- No vaccine is 100% effective
- Given the currently limited information on
 - o how well the vaccine works in the general population
 - o how much it may reduce disease, severity, or transmission
 - how long protection lasts
- Vaccinated persons should continue to follow all current guidance to protect themselves and others, including:
 - Wearing a mask
 - Staying at least 6 feet away from others
 - Avoiding crowds
 - Washing hands often
 - Following CDC travel guidance
 - Following quarantine guidance after an exposure to someone with COVID-19
 - o Following any applicable workplace or school guidance





CDC recommendations for vaccine distribution

