COVID-19 Vaccines – Updates on Delta, Children, Immunity, and Boosters

August 19, 2021

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Disclosures

- Pfizer
- AstraZeneca
- Sanofi-Pasteur
- Seqirus
- Nestle

- I do not intend to discuss unapproved/investigative use of commercial products/devices in my presentation.

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Objectives

- Update on current COVID-19 status
- Review current vaccine recommendations
- Examine adverse effects
- Discuss guidance in younger children and special populations
- Learn the latest data on vaccine immunity and anticipation of booster doses

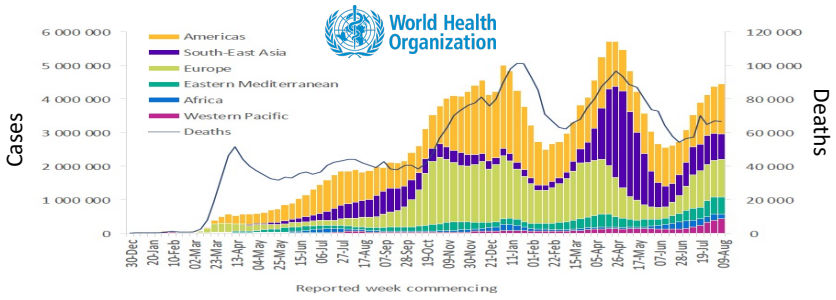
3

COVID-19 Statistics (as of Aug 18, 2021)

Global

Confirmed Cases: 209,076,320

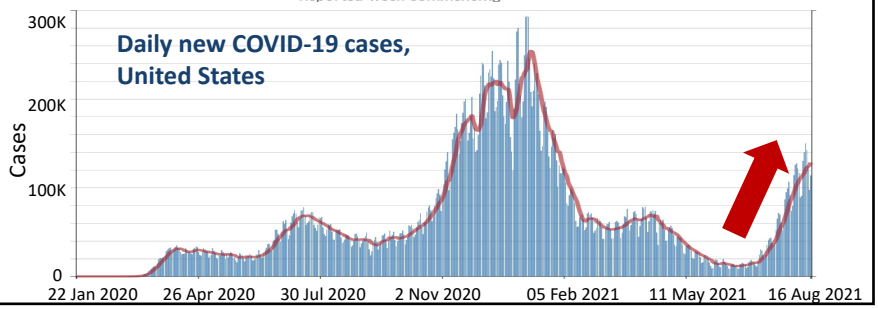
Confirmed Deaths: 4,389,211



U.S.

Confirmed Cases: 37,138,759

Confirmed Deaths: 624,344



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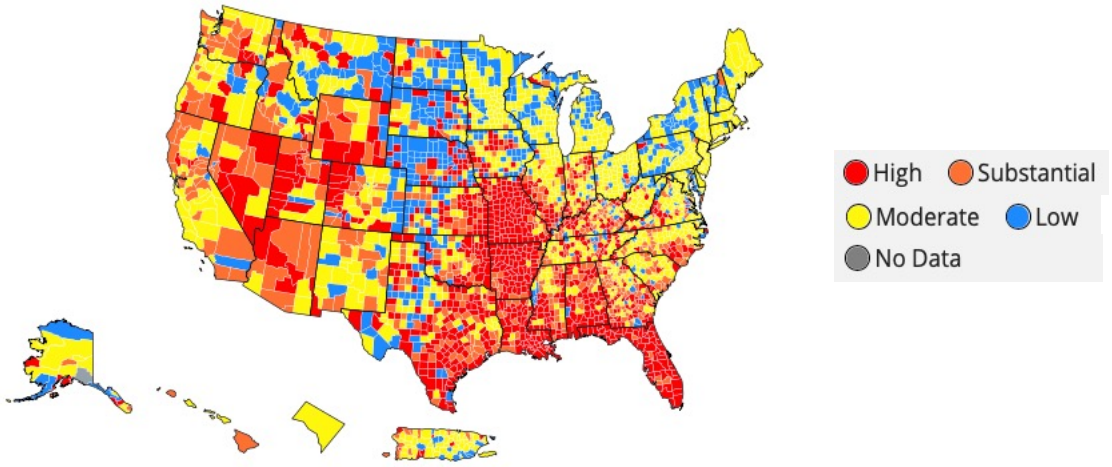
United States – Community Transmission, July 18, 2019



CDC.gov

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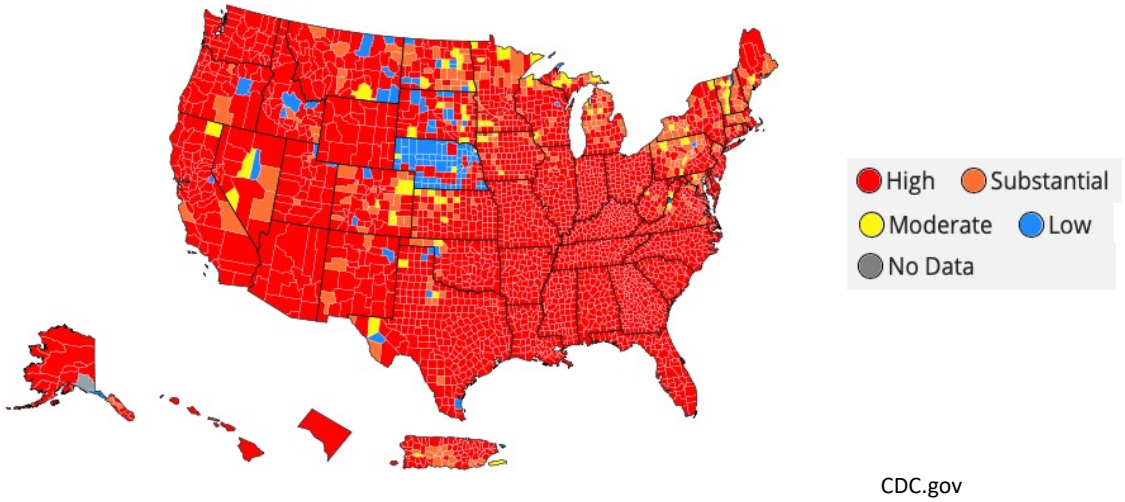
United States – Community Transmission, Aug 16, 2019



CDC.gov

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COVID-19 Variants

- Ability to spread more quickly in people
- Ability to cause either milder or more severe disease in people
- Ability to evade detection by specific viral diagnostic tests
- Decreased susceptibility to therapeutic agents such as monoclonal antibodies
- Ability to evade natural or vaccine-induced immunity

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Variants of Concern, U.S.

WHO label	Alpha	Beta	Gamma	Delta
Scientific Name	B.1.1.7	B.1.351	P.1	B.1.617.2
First identified	United Kingdom	South Africa	Brazil	India
First detected	September 2020	December 2020	January 2021	December 2020
Detected in U.S.	December 2020	January 2021	January 2021	March 2021
Transmissibility	↑29%	↑25%	↑38%	↑55-97%
Severity	↑ hospitalization risk, possible ↑ severity/mortality	possible ↑ mortality	possible ↑ hospitalization	↑ hospitalization risk
Risk of Reinfection	Same	↓neutralization	↓neutralization	↓neutralization
Diagnostic	Limited	None	None	None
Treatment with monoclonal Ab (Bam-Etes)	--	↓	↓↓	(↓)

WHO COVID-19 Weekly Epidemiological Update, 10 Aug 2021

Campbell et al. Euro Surveill 2021 Jun 26

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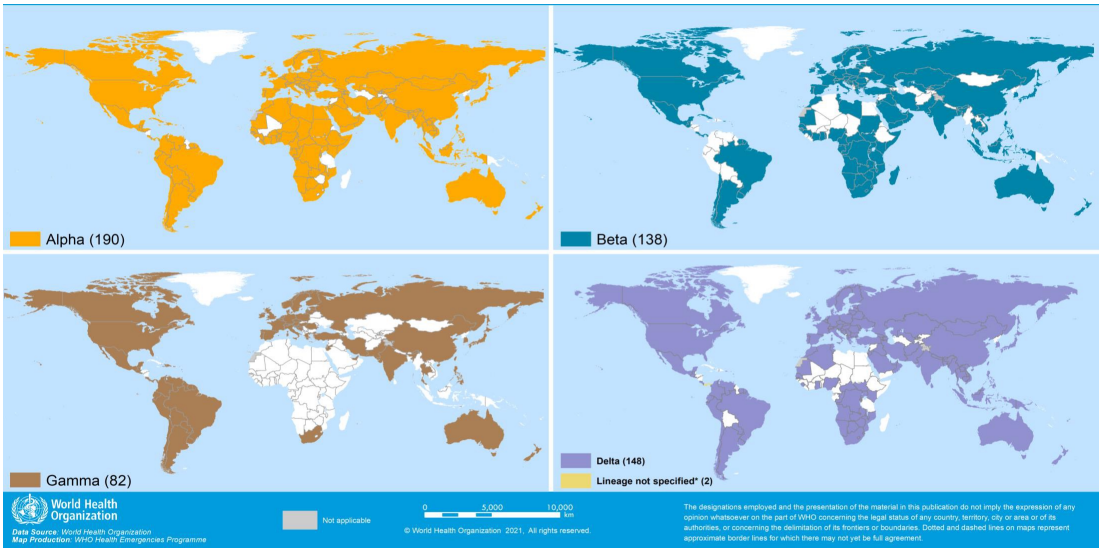
Spread of Variants of Concern (as of 8/17/21)



https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

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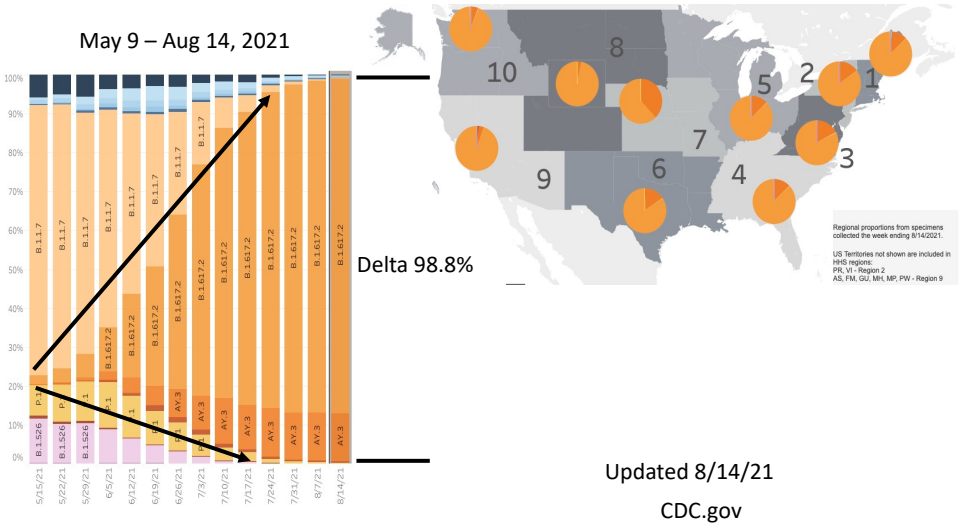
Delta Variant B.1.617.2

- Has spread to all 50 states
- Now accounts for 83% of current US cases



Updated 8/14/21

CDC.gov

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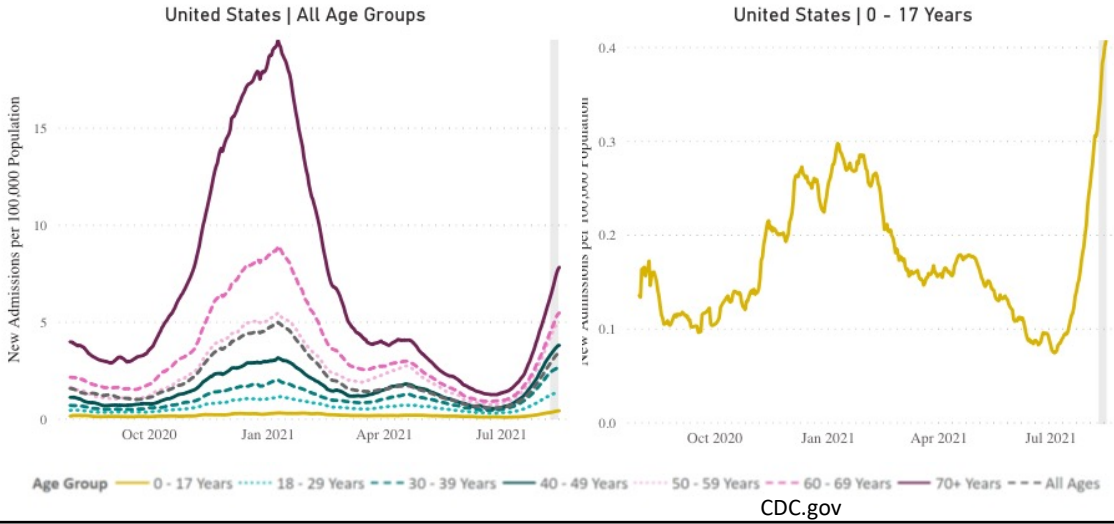
New admissions of patients with COVID-19 per 100,000 by age group
(through Aug 15, 2021)



CDC.gov

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U.S. Vaccination Rates

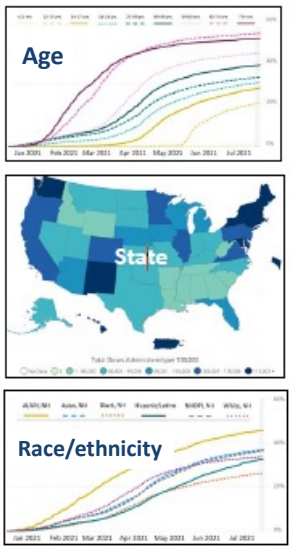
- >357 million doses administered
- 198.9 million people ≥1 dose
- 168.9 million fully vaccinated

United States vaccinations

	At least one dose	Fully vaccinated
All ages*	59.9%	50.9%
12 and up	70.1%	59.5%

*Includes those not yet eligible for the vaccine.

Coverage varies by



CDC.gov

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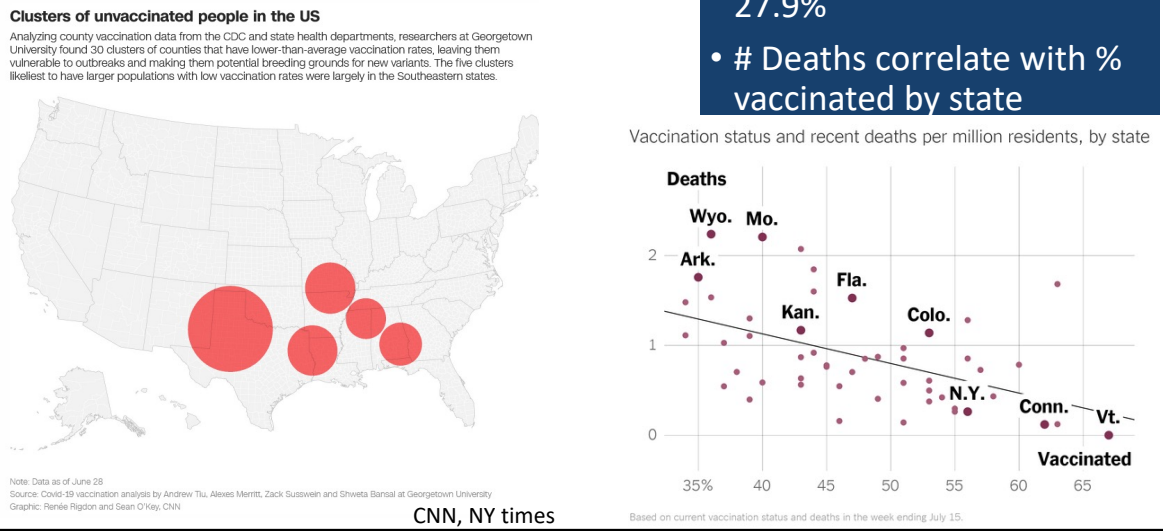
Clusters of Unvaccinated Persons, U.S.

- 15 million people live in these 5 clusters
- Vaccination frequency = 27.9%
- # Deaths correlate with % vaccinated by state



CNN, NY times

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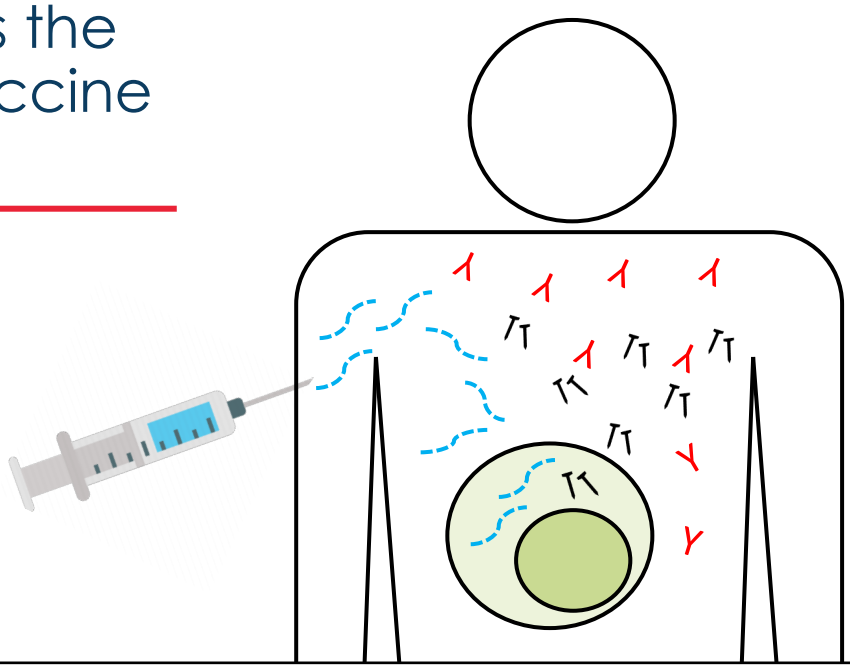
How does the mRNA vaccine work?



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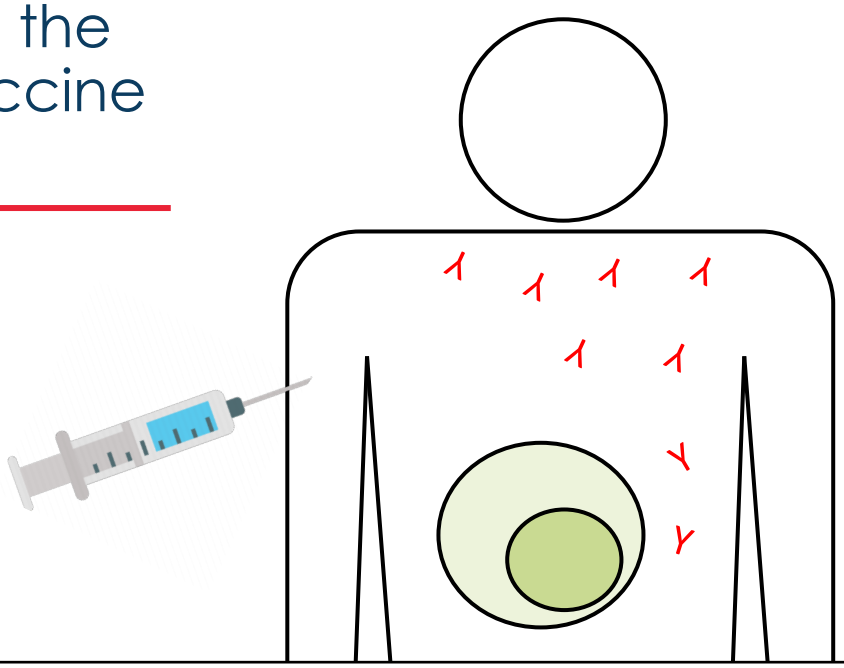

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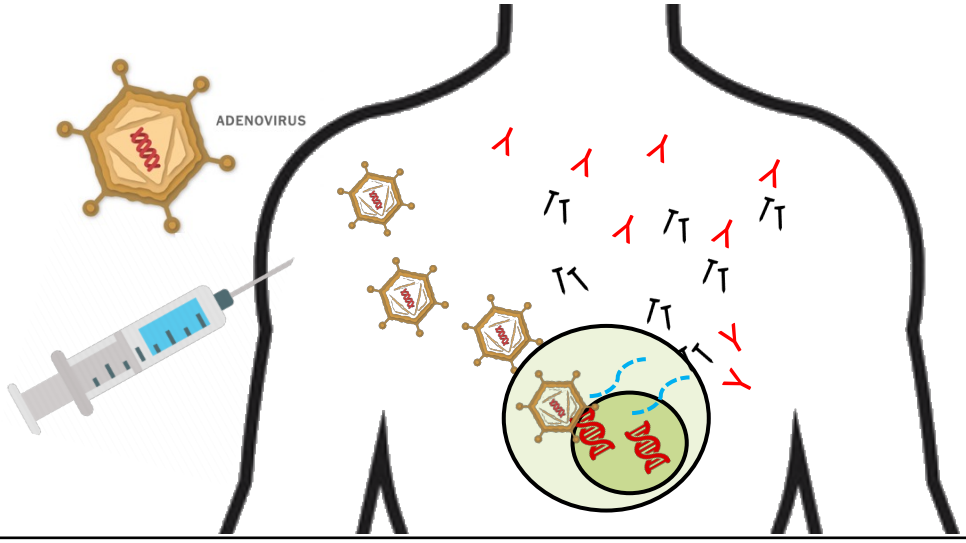
How does the adenovirus - DNA vaccine work?



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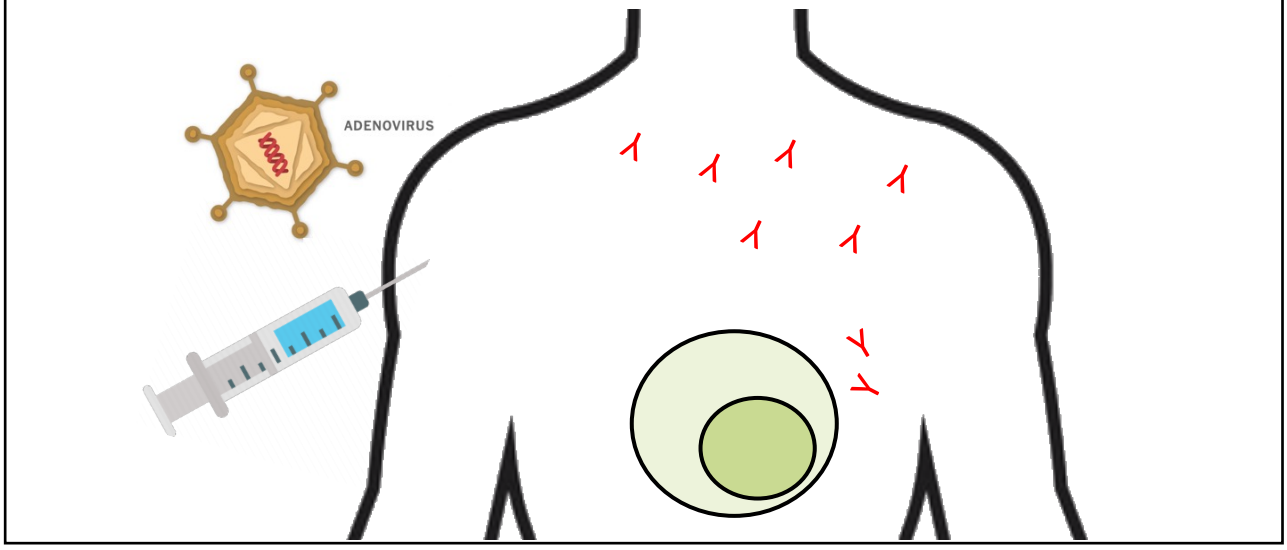
How does the adenovirus - DNA vaccine work?



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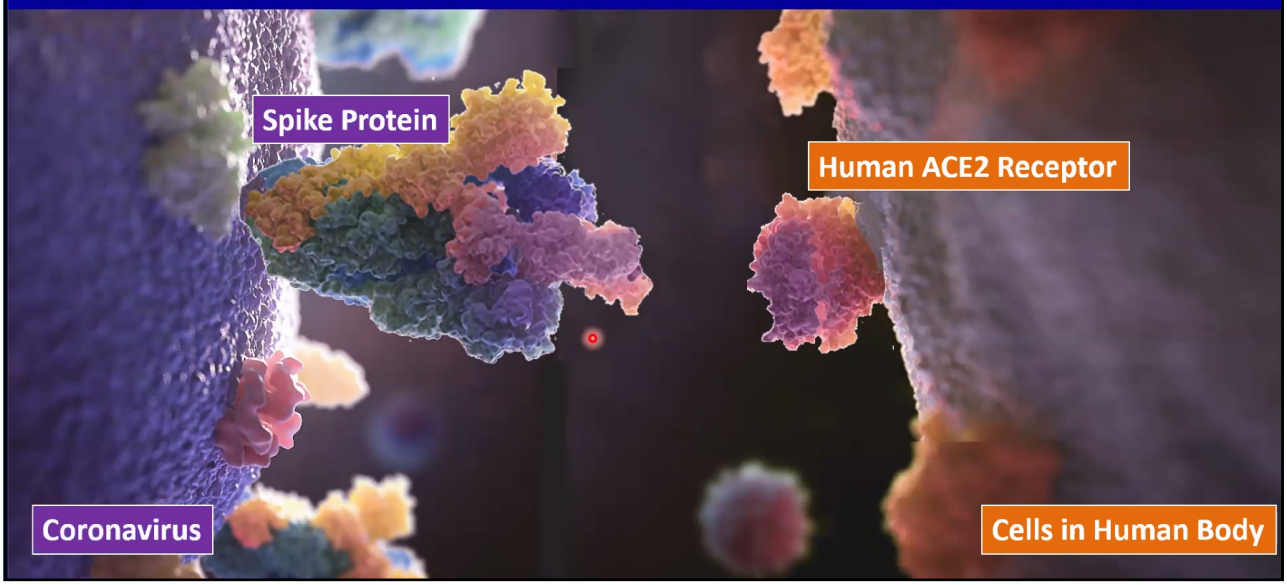
Vaccine Target: Coronavirus Spike Protein

- Coronavirus spike protein is on the viral surface and mediates attachment to cells to start the infection process
- Ideal vaccines target coronavirus spikes in order to block viral infection



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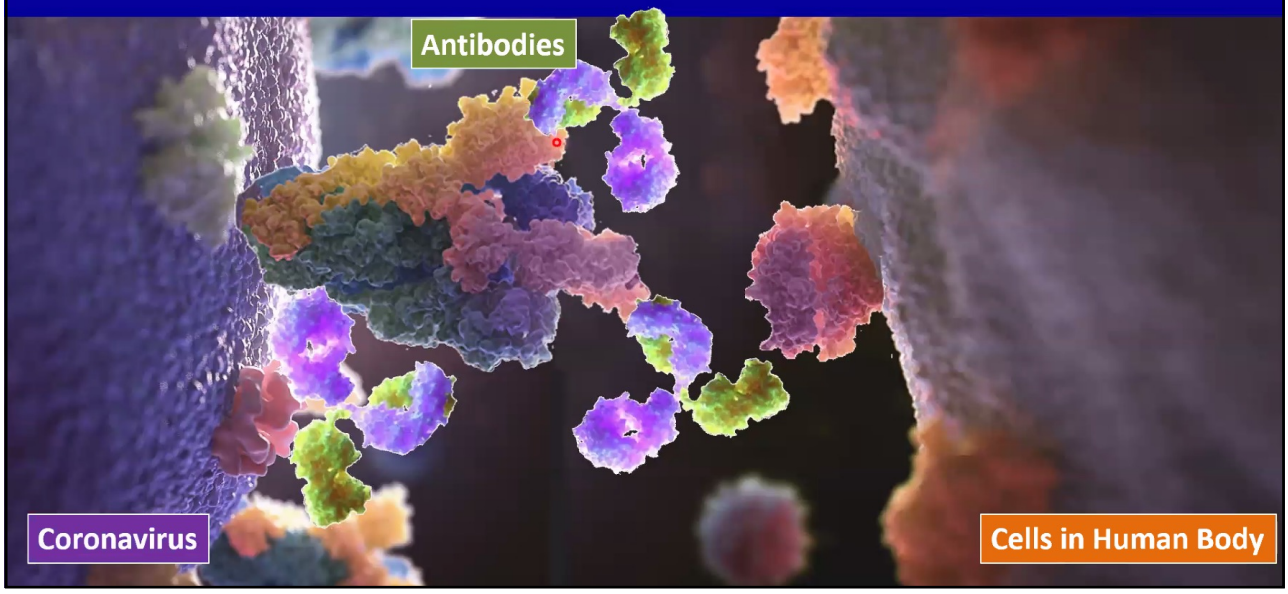
Vaccine Target: Coronavirus Spike Protein

- Vaccine-induced antibodies will block the interaction and function of CoV spike protein



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Comparing COVID Vaccines

	Pfizer-BioNTech	Moderna	Johnson & Johnson	AstraZeneca/ Oxford
Countries of Use	US, Europe + others	US, Europe + others	US + others	Europe + others (US – not approved)
Vaccine type	mRNA	mRNA	Viral vector	Viral vector
Number of doses	2 doses	2 doses	1 doses	2 doses
Eligible age (years)	≥12	≥18	≥18	≥18
Severe disease prevention in clinical trials	94.6%	94.1%	85%	76%
Hospitalization and death prevention	100%	100%	100%	100%

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Real-world effectiveness data

- Prospective cohort of health care personnel and essential workers
- Dec 2020 - Apr 2021

Table 2. Effectiveness of mRNA Vaccines in Preventing SARS-CoV-2 Infection with Full and Partial Vaccination.*

Characteristic and Vaccination Status	Contributing Participants†	Person-Days		SARS-CoV-2 Infections	Vaccine Effectiveness‡	
					Unadjusted	Adjusted
	no.	*total no.*	*median (IQR)*	*no.*	*percent (95% CI)*	
Overall						
Unvaccinated	3964	127,971	19 (8–41)	156	—	—
Partially vaccinated	3001	81,168	22 (21–28)	11	86 (74–93)	81 (64–90)
Fully vaccinated	2510	161,613	69 (53–81)	5	92 (80–97)	91 (76–97)

Thompson MG et al. NEJM 2021 Jul 22

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Real-world effectiveness data

Table 3. Viral RNA Load, Duration of Viral RNA Detection, Frequency of Febrile Symptoms, and Duration of Illness in Vaccinated and Unvaccinated Participants with SARS-CoV-2 Infection.*

Variable	Unvaccinated	Partially or Fully Vaccinated	Difference (95% CI)
Viral RNA load			
No. assessed	155	16	—
Mean — $\log_{10}$ copies/ml†	3.8±1.7	2.3±1.7	40.2 (16.3–57.3)‡
Duration of viral RNA detection			
No. assessed	155	16	—
Mean — days	8.9±10.2	2.7±3.0	6.2 (4.0–8.4)
Detection of viral RNA for >1 week — no./total no. (%)	113/156 (72.4)	4/16 (25.0)	0.34 (0.15–0.81)§
Febrile symptoms — no./total no. (%)¶	94/149 (63.1)	4/16 (25.0)	0.42 (0.18–0.98)‖
Total days of symptoms			
No. assessed	148	16	—
Mean — days	16.7±15.7	10.3±10.3	6.4 (0.4–12.3)
Days spent sick in bed			
No. assessed	147	15	—
Mean — days	3.8±5.9	1.5±2.1	2.3 (0.8–3.7)

Thompson MG et al. NEJM 2021 Jul 22

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Vaccine effectiveness on variants of concern, U.S.

WHO label	Alpha	Beta	Gamma	Delta
Scientific Name	B.1.1.7	B.1.351	P.1	B.1.617.2
First identified	United Kingdom	South Africa	Brazil	India
Vaccine effectiveness				
Severe disease	↔ Moderna, Pfizer ↓ AstraZeneca	↔ Janssen	No evidence	↔ AstraZeneca, Pfizer
Symptomatic disease	↔ Moderna, Pfizer ↔ to ↓ AstraZeneca	↔ Janssen ↓↓↓ AstraZeneca	↔ to ↓ Sinovac-CoronaVac	↔ to ↓ Pfizer ↓Bharat-Covaxin ↓↓ AstraZeneca
Infection	↔ Moderna, Pfizer ↔ to ↓ AstraZeneca	↔ Moderna ↓ Pfizer	No evidence	↓AstraZeneca, Pfizer

WHO COVID-19 Weekly Epidemiological Update, 10 Aug 2021

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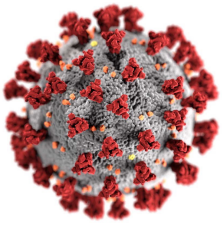
Vaccine effectiveness against Delta

	VE (95% CI)	
	Delta	**Alpha**
1 dose - Pfizer or AstraZeneca	30.7 (25.2-35.7)	48.7 (45.5-51.7)
2 doses -Pfizer	88.0 (85.3-90.1)	93.7 (91.6-95.3)
2 doses – AstraZeneca	67.0 (61.3-71.8)	74.5 (68.4-79.4)



Bernal et al. NEJM 2021 Jul 21

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COVID-19 Vaccines in children

- >4.4 million child COVID-19 cases (14.4% of all cases) in the U.S.
- ~ 400 deaths
- 4,404 MIS-C cases, 37 deaths
- May be important drivers of community spread once restrictions are lifted
- Goal to return to school and "normal life" while protected

AAP.org, CDC.gov

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Los Angeles Household Exposure and Respiratory Transmission Study – Index Cases

H.E.A.R.T.S

Unpublished material

haka et al. Under revision

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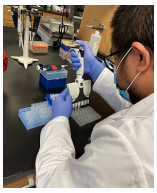
Los Angeles Household Exposure and Respiratory Transmission Study



Unpublished material

ka et al. Under revision

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Pfizer/BioNTech

- Phase 3 trial of adolescents 12-15 years old, Oct 2020 - Mar 2021
- 30 µg dose well tolerated
- Side effects similar to 16-25 year old group
- SARS-CoV-2 neutralizing antibody titer comparable to 16-25 year old group

	Vaccine	Placebo
Number of Participants	1,131	1,129
COVID-19 cases	0	18

Efficacy 100% (95% CI: 78.1-100)

Frenck et al. NEJM 2021 July 15

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Moderna

- Phase 2-3 trial of adolescents 12-17 years old
- 100 µg dose well tolerated
- Side effects similar to 18-25 year old group
- SARS-CoV-2 neutralizing antibody titer comparable to 18-25 year old group

	Vaccine	Placebo	Efficacy % (95% CI)
Number of Participants	2,489	1,243	
Symptomatic COVID-19 cases	1	7	93.3 (47.9-99.9)
Any COVID-19 infection	27	42	69.8 (16.8-76.4)

Ali et al. NEJM 2021 Aug 11

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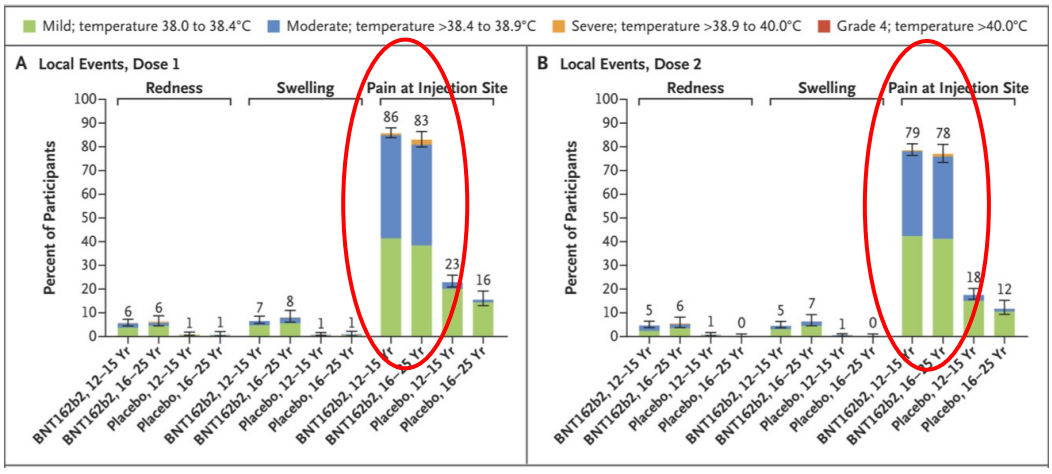
Local Reactions, 12-15 yo



Frenck et al. NEJM 2021 July 15

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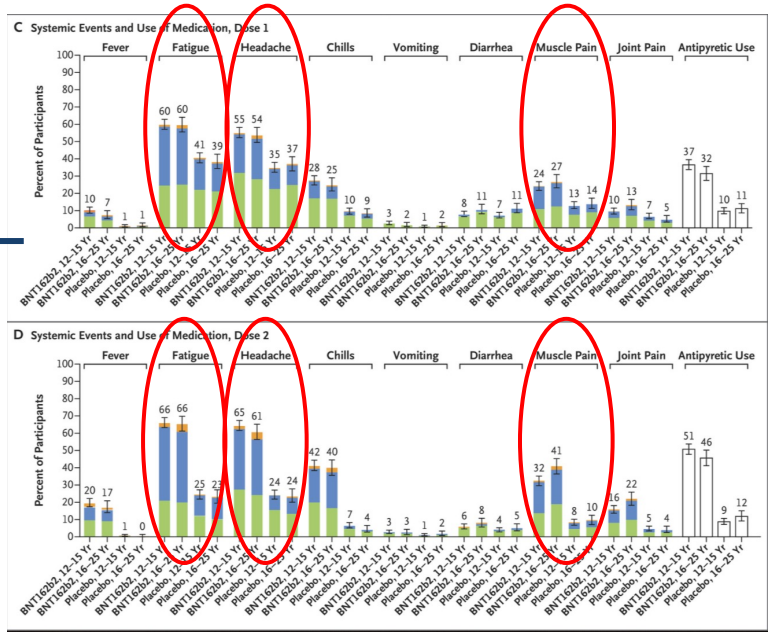
Systemic Reactions, 12-15 yo



Frenck et al. NEJM 2021 July 15

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VAERS Vaccine Adverse Event Reporting System
www.vaers.hhs.gov

CDC + FDA

VAERS is the nation's early warning system for vaccine safety.

12–15 years old* (N= 2,540) of 6.0 million doses administered

Adverse event‡	n (%)
Dizziness	618 (24.3)
Syncope	446 (17.6)
Nausea	308 (12.1)
Headache	281 (11.1)
Vomiting	221 (8.7)
Pallor	218 (8.6)
Loss of consciousness	217 (8.5)
Pyrexia (fever)	215 (8.5)
Hyperhidrosis	211 (8.3)
Fatigue	182 (7.2)

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Potential harms reported after COVID-19 vaccination

mRNA vaccines

Myocarditis:

3.5 cases per million doses among adults

Janssen vaccine

Thrombosis with thrombocytopenia syndrome:

3.0 cases per million doses among adults

Guillain-Barré syndrome:

7.8 cases per million doses among adults

- Risk for each varies by age and sex

ACIP Meeting July 22, 2021

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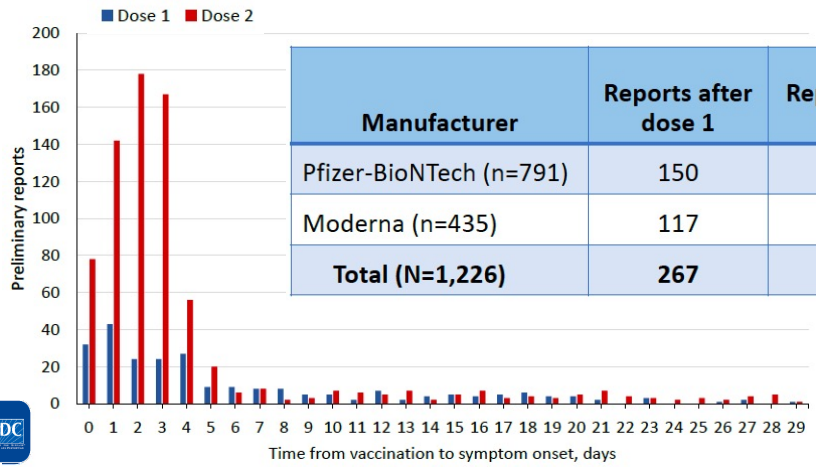
Myocarditis/Pericarditis

- After 300 million mRNA doses administered



Manufacturer	Reports after dose 1	Reports after dose 2	Reports after unknown dose
Pfizer-BioNTech (n=791)	150	563	78
Moderna (n=435)	117	264	54
Total (N=1,226)	**267**	**827**	**132**

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Gargano et al. MMWR 2021 July 9

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Characteristics of myocarditis/pericarditis reports to VAERS

Characteristics	Dose 1 (n=267)	Dose 2 (n=827)
Median age, years (range)	30 (12–94)	24 (12–87)
Median time to symptom onset, days (range)	4 (0–61)†	3 (0–98)†
Sex (%)		
Male	176 (66%)	655 (79%)
Female	88 (33%)	165 (20%)
Not reported/not available	3 (1%)	7 (1%)

Symptoms/ Diagnostic findings:

- Chest pain
- Dyspnea
- St or T wave change
- Elevated cardiac enzymes
- Abnormal echo

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Gargano et al. MMWR 2021 July 9

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Myocarditis/Pericarditis, expected vs. observed within 21 days after dose 2

Age groups	Females			Males		
	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*
12–17 yrs	2,189,726	1–7	20	2,039,871	1–12	132
18–24 yrs	5,237,262	2–18	27	4,337,287	2–25	233
25–29 yrs	4,151,975	1–15	11	3,625,574	2–21	69
30–39 yrs	9,356,296	5–54	14	8,311,301	5–48	71
40–49 yrs	9,927,773	6–57	23	8,577,766	5–49	40
50–64 yrs	18,696,450	11–108	25	16,255,927	9–94	34
65+ yrs	21,708,975	12–125	17	18,041,547	10–104	16
Not reported	—	—	1	—	—	9

ACIP Meeting, June 23, 2021, Gargano et al. MMWR 2021 July 9

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Myocarditis/ pericarditis rates and outcomes

Product (dose)	Female cases	Female rates per million doses (95% CI)	Male cases	Male rates per million doses (95% CI)
Any mRNA (both doses)	6	3.2 (1.2–6.9)	26	16.9 (11.0–24.8)
Any mRNA (dose 1)	2	1.9 (0.2–7.0)	4	4.7 (1.3–12.0)
Any mRNA (dose 2)	4	4.7 (1.3–12.0)	22	32.0 (20.1–48.5)

Care and status	n (%)
Highest level of care received	
Outpatient	1 (3.4)
Emergency department	4 (13.8)
Inpatient hospitalization	22 (75.9)
Intensive care unit (ICU)	2 (5.7)
Median length of hospital stay (days, range)	1 (0–13)
Discharged to home at time of chart review	29 (100)
Follow-up visit noted at time of chart review	27 (93.1)

ACIP Meeting, June 23, 2021; Gargano et al. MMWR 2021 July 9

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COVID-19 infection and myocarditis

- 1597 young athletes with recent SARS-CoV-2 infection had cardiac MRI
  - 37 (2.3%) with abnormal MRI findings
    24 (65%) of 37 had **normal** lab findings and **no symptoms**
  - Another study suggested some MRI findings may be related to remodeling from athletic training
- Retrospective study —children with acute myocarditis treated at a single center from 2018–2020
  - 27 children <18 years of age identified
  - 7/27 (26%) had evidence of prior SAR-CoV-2 infection or exposure; 6 MIS-C
  - Individuals with myocarditis/MIS-C related to SARS-CoV-2 had better clinical course

Daniels CJ, et al. *JAMA Cardiol.* 2021 May 21; Clark DE, et al. Circulation 2021; Vukomanovic et al. PIDJ 2021

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Predicted cases prevented vs. myocarditis cases for every million second dose vaccinations over 120 days

Females 12–17 Years	Males 12–17 Years
8,500 COVID-19 cases prevented	**5,700** COVID-19 cases prevented
183 hospitalizations prevented	**215** hospitalizations prevented
38 ICU admissions prevented	**71** ICU admissions prevented
1 death prevented	**2** deaths prevented
8-10 myocarditis cases	**56-69** myocarditis cases

Hospitalizations, ICU admissions and deaths based on data for week of May 22, 2021.

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Predicted cases prevented vs. myocarditis cases for every million second dose vaccinations over 120 days

Females 18-29 Years	Males 18-29 Years
12,800 COVID-19 cases prevented	**9,600** COVID-19 cases prevented
750 hospitalizations prevented	**300** hospitalizations prevented
50 ICU admissions prevented	**60** ICU admissions prevented
5 deaths prevented	**3** deaths prevented
3-4 myocarditis cases	**22-27** myocarditis cases

Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

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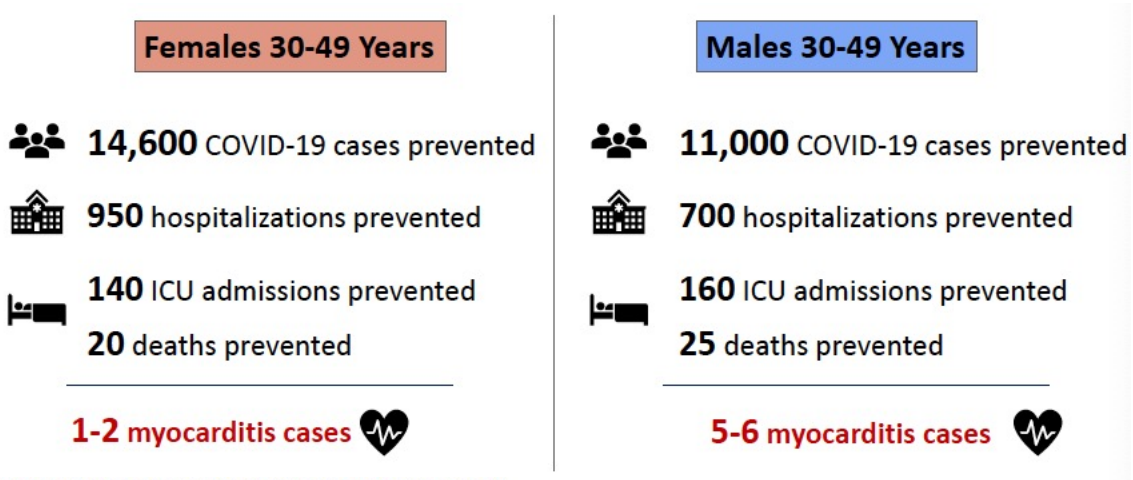
Predicted cases prevented vs. myocarditis cases for every million second dose vaccinations over 120 days



Hospitalizations, ICU admissions and deaths based on data for week of June 19, 2021

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Vaccination consideration in people with a history of myocarditis/pericarditis

Scenario	Recommendation
Myocarditis/Pericarditis prior to COVID-19 vaccination	Proceed with any COVID-19 vaccine
Myocarditis/Pericarditis after 1st dose mRNA vaccine but before 2nd dose	Defer receiving the 2nd dose until more data available Consider: - proceeding with 2nd dose after resolution of symptoms - personal risk of severe acute COVID-19 - level of community transmission - timing of any immunomodulators

CDC Interim Considerations, updated July 16, 2021

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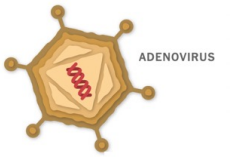
Thromboses

VAERS Vaccine Adverse Event Reporting System
www.vaers.hhs.gov

- Rare clotting events after COVID-19 adenovirus vector vaccines



AstraZeneca

- Approved in 118 countries
- Awaiting EUA in US

Janssen / J&J

- EUA in U.S. Feb 2021
- Requires only 1 dose
- Easier storage

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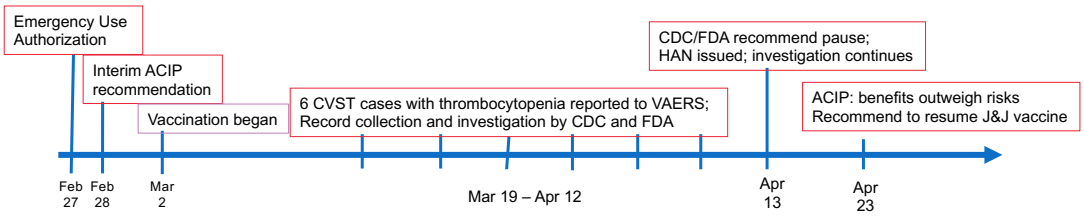
Thrombosis with Thrombocytopenia Syndrome, Janssen / Johnson & Johnson



- 12.6 million J&J vaccine doses given
- 38 cases of CVST with thrombocytopenia
- Age 18-64, 74% women
- Onset 6-13 days

Thrombosis with Thrombocytopenia, as of July 8, 2021

	Females n= 28			Males n=10		
Age group	Cases	Doses admin	Reporting rate†	Cases	Doses admin	Reporting rate†
18-29 years old	4	946,358	4.2 per million	3	1,281,479	2.3 per million
30-49 years old	**17**	**1,934,574**	**8.8 per million**	4	2,440,773	1.6 per million
50-64 years old	7	1,865,372	3.8 per million	3	2,130,473	1.4 per million
65+ years old	0	1,028,190	0.0 per million	0	943,098	0.0 per million

MacNeil et al. MMWR 2021 Apr 30
ACIP Meeting July 22, 2021

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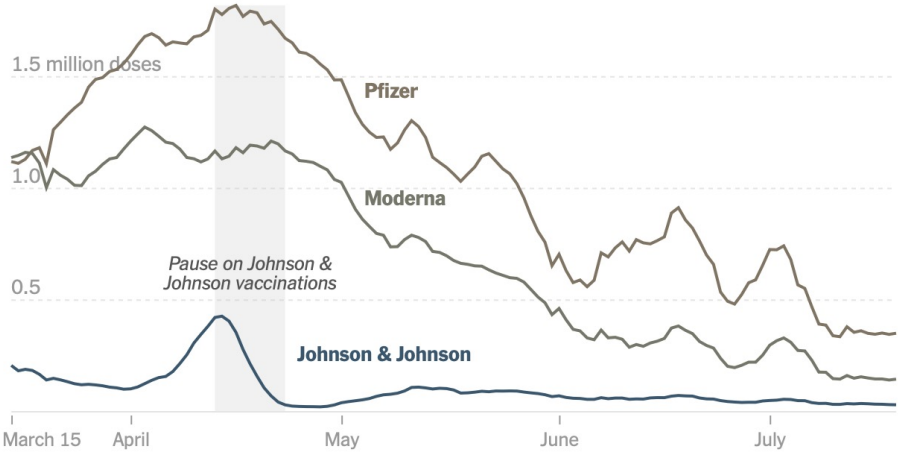
Vaccine doses administered by day



Source: Centers for Disease Control and Prevention

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Guillain-Barré Syndrome after Janssen/Johnson &Johnson vaccine

- Normally ~3000-6000 cases/year in U.S.
  - Highest risk in males >50 years old
- 100 GBS cases after Janssen vaccine
- 12.6 million doses administered

Characteristics		n = 100
Sex [a]		
Male		61 (61%)
Female		38 (38%)
Seriousness [b]		
Serious	(10 intubated)	95 (95%)
Hospitalized		95 (95%)
Died		1 (1%)
Non-serious		5 (5%)

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Guillain-Barré Syndrome after Janssen/Johnson &Johnson vaccine

Characteristics	
Age [a]	
Median	57 years
Mean (standard deviation)	53.6 (12.46) years
Range	24 – 76 years
Number of reports with age 18 – 64 years	83 (83%)
Number of reports in with age ≥ 65 years	16 (16%)
Time to onset [a]	
Median	13 days
Mean (standard deviation)	13.8 (9.80) days
Range	0 – 75 days
Number of cases in 21-day risk window	84 (84%)
Number of cases in 42-day risk window	98 (98%)

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Guillain-Barré Syndrome after Janssen/Johnson &Johnson vaccine

- Crude comparison with mRNA vaccine

COVID-19 Vaccine	VAERS reports with GBS screening*	Doses administered	Crude** VAERS GBS reporting rate per million doses administered
Janssen	100	12,235,978	8.1
Moderna	162	134,076,668	1.21
Pfizer-BioNTech	190	181,347,436	1.05

VAERS reports processed through June 30, 2021

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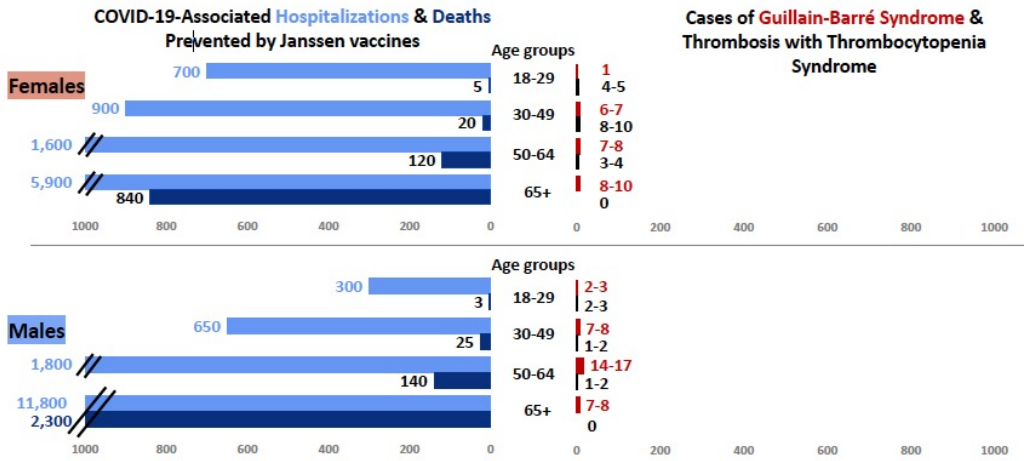
Benefits of COVID-19 vaccination continue to outweigh risks



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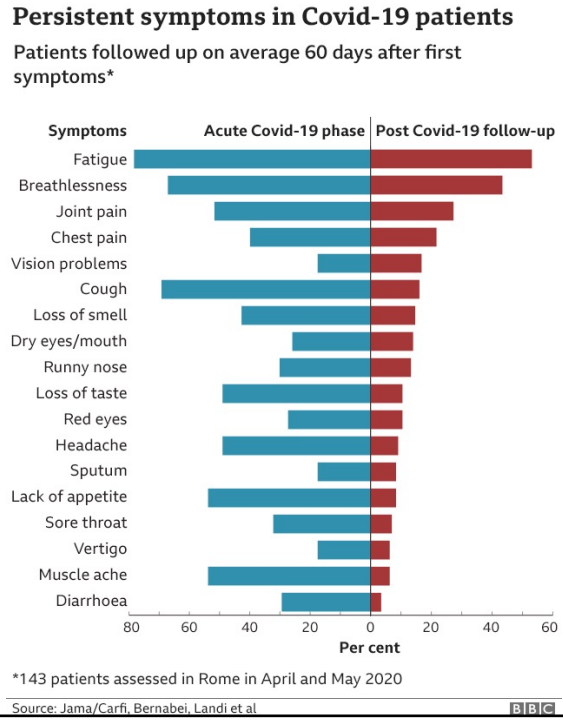
Additional vaccination benefits to prevent post-COVID conditions

- Prevent MIS-C
- Prevent prolonged symptoms
- Protection against variants



54

Vaccine co-administration

- COVID-19 vaccines may be administered at the same time or within 14 days of other vaccines.
- Adolescent routine vaccines are ↓↓
  - Tdap - ↓ 18.9%
  - HPV - ↓ 19.3%
  - Meningococcal conjugate - ↓15.1%

Pediatrics 2021; doi: 10.1542/peds.2021-052336

55

Vaccinations in younger children and special populations

56

Vaccine trials in younger children

- **Pfizer** phase 2/3 trials ongoing
- 5-11 years old
- 10 µg
- Planned enrollment: 4,500 in U.S., Finland, Poland, Spain
- Anticipate initial results in September 2021

- 2-5 years old expected Oct-Nov 2021
- 6 months – 2 years expected Dec 2021

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Vaccine trials in younger children

- **Moderna** – EUA under review for 12-17 year old
- Phase 2/3 in 6 months to 11 yo began Mar 16, 2021 (KidCOVE study)
  - Planned enrollment: 6,750 in U.S. and Canada
  - Three dose levels (25 µg, 50 µg and 100 µg) being tested
  - Safety, tolerability, reactogenicity and effectiveness

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Recent CDC Update to Pregnancy Language

- No evidence that any of the COVID-19 vaccines affect current or future fertility
  - COVID-19 vaccines do not cause infection in the pregnant person or the fetus
  - No safety signals in animal studies
  - Reassuring safety data on mRNA COVID-19 vaccines during pregnancy
  - mRNA COVID-19 vaccines during pregnancy are effective
- **COVID-19 vaccination is recommended for all people aged 12 years and older, including people who are pregnant, lactating, trying to get pregnant now, or might become pregnant in the future**

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

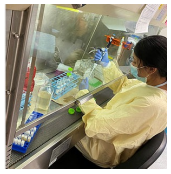
59

Breastfeeding may offer protection against COVID-19

- C… …sists at le…

Brea… …ID-19 in Breast milk

Unpublished material



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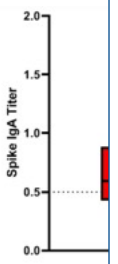
…ez S, et al, in preparation

60

Donor breast milk after COVID-19 infection or vaccination

- Br… …ion
  co…

COVID… …efore …ion,



Van … …reparation

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Vaccination guidance after MIS-C

- Unclear if people with a history of MIS-C are at risk of recurrence following reinfection or in response to vaccination
- Consider vaccination after 90 days from diagnosis/treatment of MIS-C
- Other factors to consider:
  - Clinical recovery from MIS-C and return to normal cardiac function
  - Risk of severe acute COVID-19 due to age or underlying condition
  - Level of community transmission
  - Timing of any immunomodulatory therapies

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html, updated July 16, 2021

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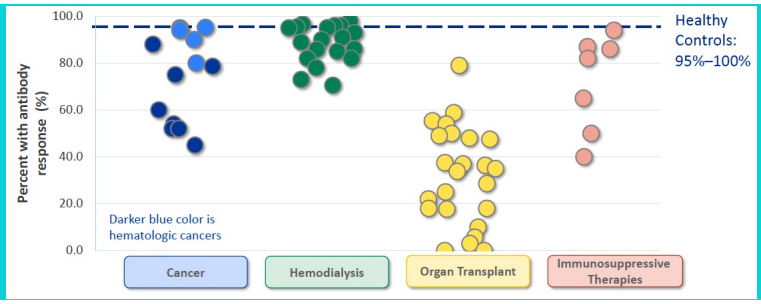
Immunocompromised individuals – clinical considerations

- 2.7% of U.S. adults (7 million adults)
- ↑ risk severe infection, prolonged infection and shedding
- Vaccination breakthrough infection
  - 44% of hospitalized cases are immunocomp in U.S. (40% in Israel)

Percent of subjects with antibody response after two mRNA vaccine doses by immunocompromising condition (n=63 studies)



Truong EbioMedicine 2021; Tenforde medRxiv 2021; Brosh-Nissimov Clin Microbiol Infect 2021; Qin Transplantation 2021; ACIP Meeting Aug 13, 2021

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Emerging data - 3rd vaccine dose

Study	Patient Population	2nd Dose Sample Size	2nd Dose Seronegative N (%)	2nd Dose Seropositive N (%)	3rd Dose Seronegative after 2nd dose Sample Size	3rd Dose Seronegative after 2nd dose Seronegative N (%)	3rd Dose Seronegative after 2nd dose Seropositive N (%)
Kamar et al.	Recipients of solidorgan transplant	99	59 (60)	40 (40)	59	33 (56)	**26 (44)**
Werbel et al.	Recipients of solidorgan transplant	30	24 (80)	6 (20)	24	16 (67)	**8 (33)**
Longlune et al.	Patients on hemodialysis	82	13 (16)	69 (84)	12	7 (58)	**5 (42)**
Epsiet al.	Patients on hemodialysis	106	66 (62)	40 (38)	12	6 (50)	**6 (50)**
Ducloux et al.	Patients on hemodialysis	45	5 (11)	40 (89)	5	3 (60)	**2 (40)**

- Among those who had no detectable antibody response to initial series, 33-50% developed antibody to additional dose

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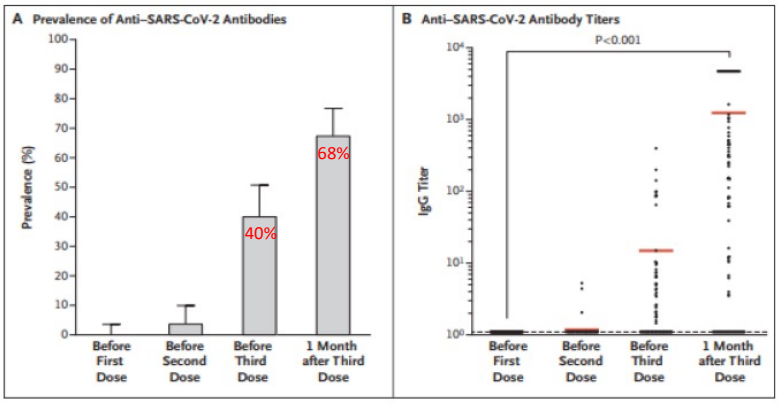
3 doses of an mRNA COVID-19 vaccine in solid-organ transplant recipients (n=99)



- No serious adverse events were reported
- No acute rejection episodes

Kamar et al, NEJM 2021

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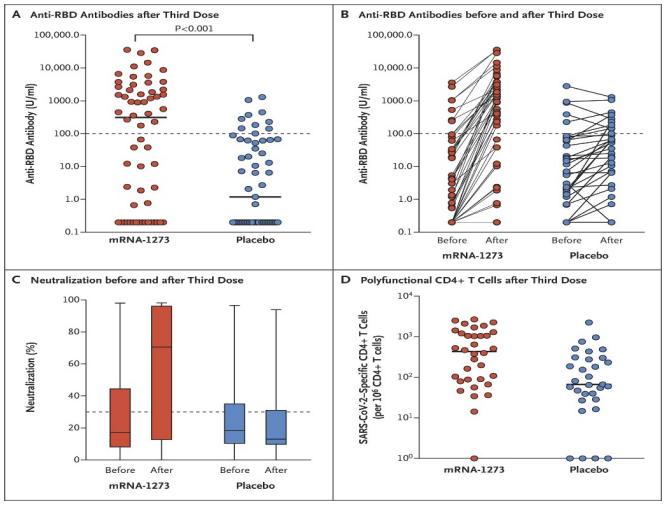
Randomized trial: 3rd dose Moderna in 120 transplant recipients



RBD antibody (≥100 U/ml) at 1 month post-dose 3

- 33 of 60 patients (55%) vaccine group

vs.

- 10 of 57 patients (18%) placebo group

Hall et al.. NEJM 2021

66

International policies on additional doses for immunocompromised people

- France (Announced April 11, 2021)
  - 3rd dose 4 weeks after the 2nd dose for patients who are "severely immunocompromised"
- United Kingdom (Announced July 1, 2021)
  - Proposal for an additional dose for immunocompromised people ≥16 years, to be implemented in Sept 2021
- Israel (Announced July 11, 2021)
  - People living with organ or stem cell transplants, blood cancer, autoimmune disease and treatment with specific immunosuppressive medications
- Germany (Announced Aug 2, 2021)
  - Immunocompromised persons

dgs_urgent_n43_vaccination_modalites_d_administration_des_rappels.pdf (solidarites-sante.gouv.fr); C1327-covid-19-vaccination-autumn-winter-phadvicease-3-planning.pdf; https://govextra.gov.il/media/30095/meeting-summary-15122020.pdf

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U.S guidance

- Aug 12, 2021: FDA authorized additional mRNA vaccine dose for certain immunocompromised individuals
- Attempts should be made to match the additional dose type to the mRNA primary series
- ≥28 days after completion of the primary mRNA COVID-19 vaccine series
- Testing for antibodies following vaccination is not recommended
- Whenever possible, 3 mRNA COVID-19 vaccination doses should be given ≥2 weeks before initiation of immunosuppressive therapies
- EUA amendment does not apply to Janssen vaccine

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Moderately and severely immunocompromised

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of CAR-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge, Wiskott-Aldrich syndromes)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids (i.e., ≥20mg prednisone or equivalent per day), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, TNF blockers, and other biologic agents that are immunosuppressive or immunomodulatory

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

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Booster doses

- Definition: Vaccine doses after primary (1 or 2-dose) series that are needed to increase immunity after waning of initial immune response
- Decisions around strains for vaccine production likely to be made separately
- EUA will require data on **safety**, **immunogenicity** and **public health need**

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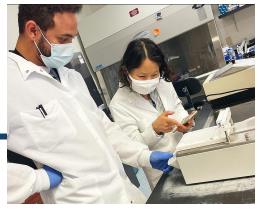
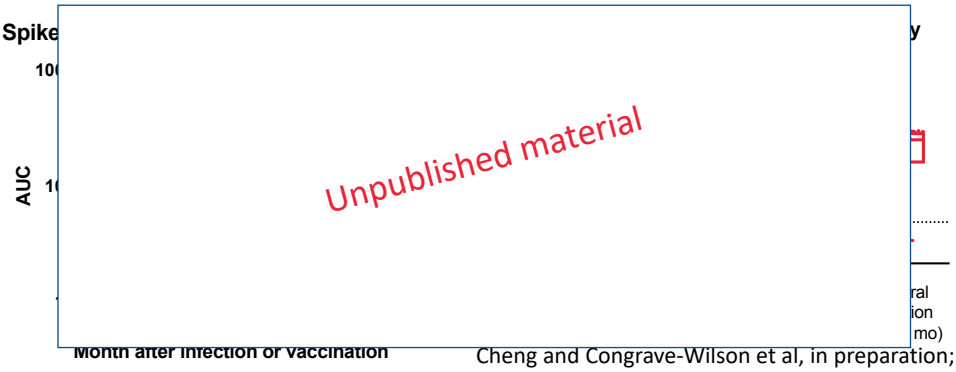
Duration of immunity



- Antibody persistence
  - At least 9 months after natural infection
  - At least 6 months after vaccination



Cheng and Congrave-Wilson et al, in preparation; Dan et al. Science 2021; Choe et al. Emerg Infect Dis 2021; Doria-Rose et al. NEJM 2021

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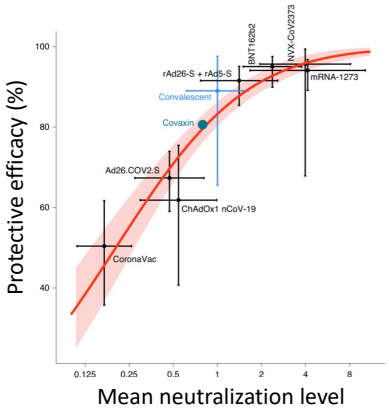
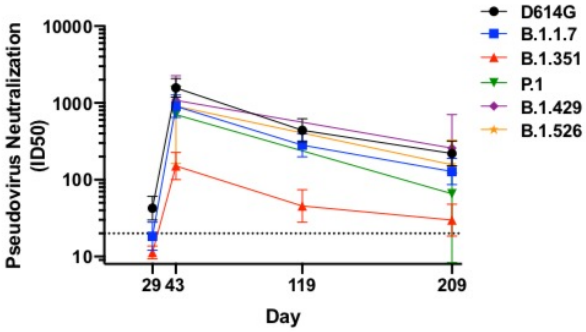
Neutralizing antibody

- Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection



- Neutralizing antibody is lower at 6 months after vaccination, especially against B.1.351



Khoury et al. Nat Med 2021; Pegu et al, bioRxiv 2021

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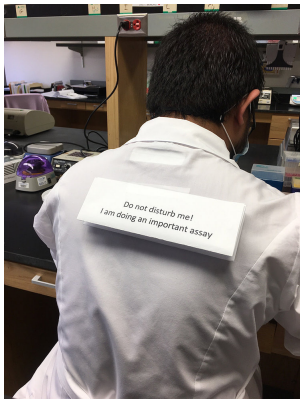
SARS-CoV-2 specific T cells



Unpublished material

73

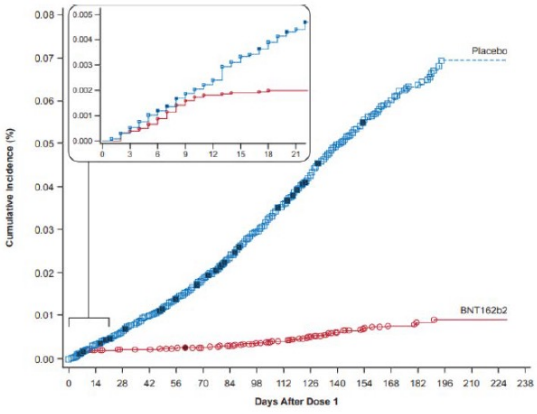
Pfizer vaccine efficacy at 6 months

VE against infection: 91% (89, 93)

Period after dose 2	% VE (95% CI)
≥7 days to <2 mos	96 (94, 98)
≥2 mos to <4 mos	90 (87, 93)
≥4 mos to <6 mos	84 (75, 90)

VE against severe illness: 97% (80,100)

Moderna press release:
93% VE against infection at 6 months (unpublished)



Thomas et al. medRxiv preprint https://doi.org/10.1101/2021.07.28.21261159
Moderna. https://investors.modernatx.com/news-releases/news-release-details/moderna-reports-second-quarter-fiscal-year-2021-financial

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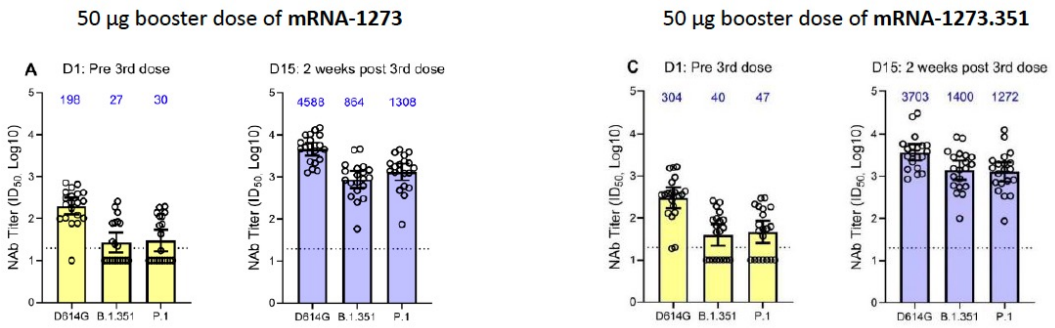
Variant-specific booster - preliminary data



- Booster increased titers against wild-type, B.1.351 and P.1 variants

Wu et al, medRxiv 2021

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Booster doses

- White house: Booster shots will be offered beginning Sept. 20, 2021
  - mRNA vaccines
  - ≥ 8 months after primary series
  - Pending FDA approval
- J&J vaccine second dose recommendations anticipated soon

Press Release, Aug 18, 2021

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Summary

- Vaccination continues to be critical during this period of rapidly increasing cases and spread of variants of concern
- The reported adverse events (TTS, GBS, and myocarditis) are potentially serious and should be transparently communicated with the public
- Benefits of vaccination outweigh risks for most possible adverse events
- Additional pediatric data for (5-11 yo) expected September
- 3rd mRNA dose for immunocompromised now recommended
- Boosters are inevitable, awaiting more data for FDA approval

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Children's Hospital LOS ANGELES | USC University of Southern California | pialab Pediatric Immunization Advancement

Thank you

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