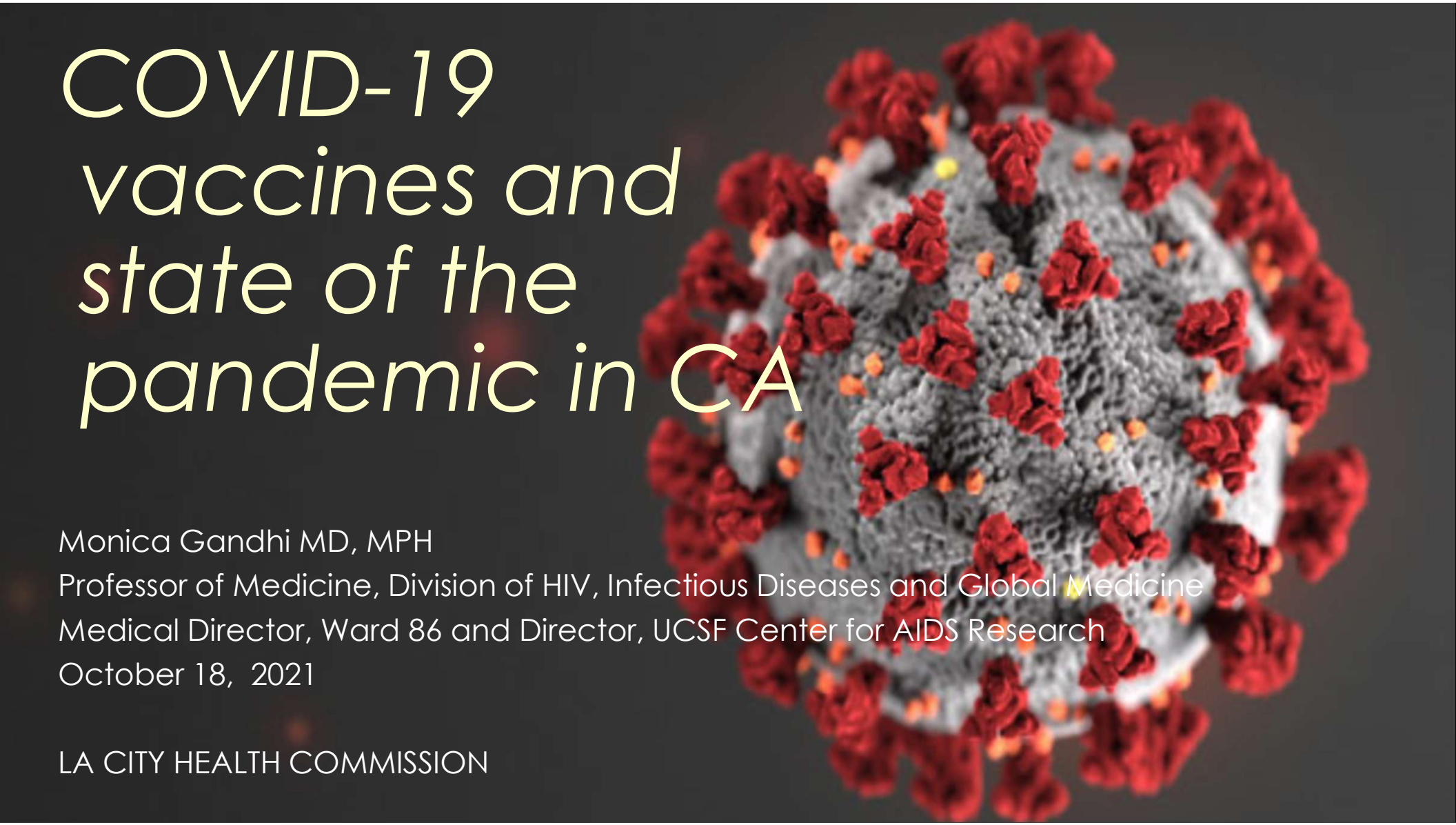
COVID-19 vaccines and state of the pandemic in CA



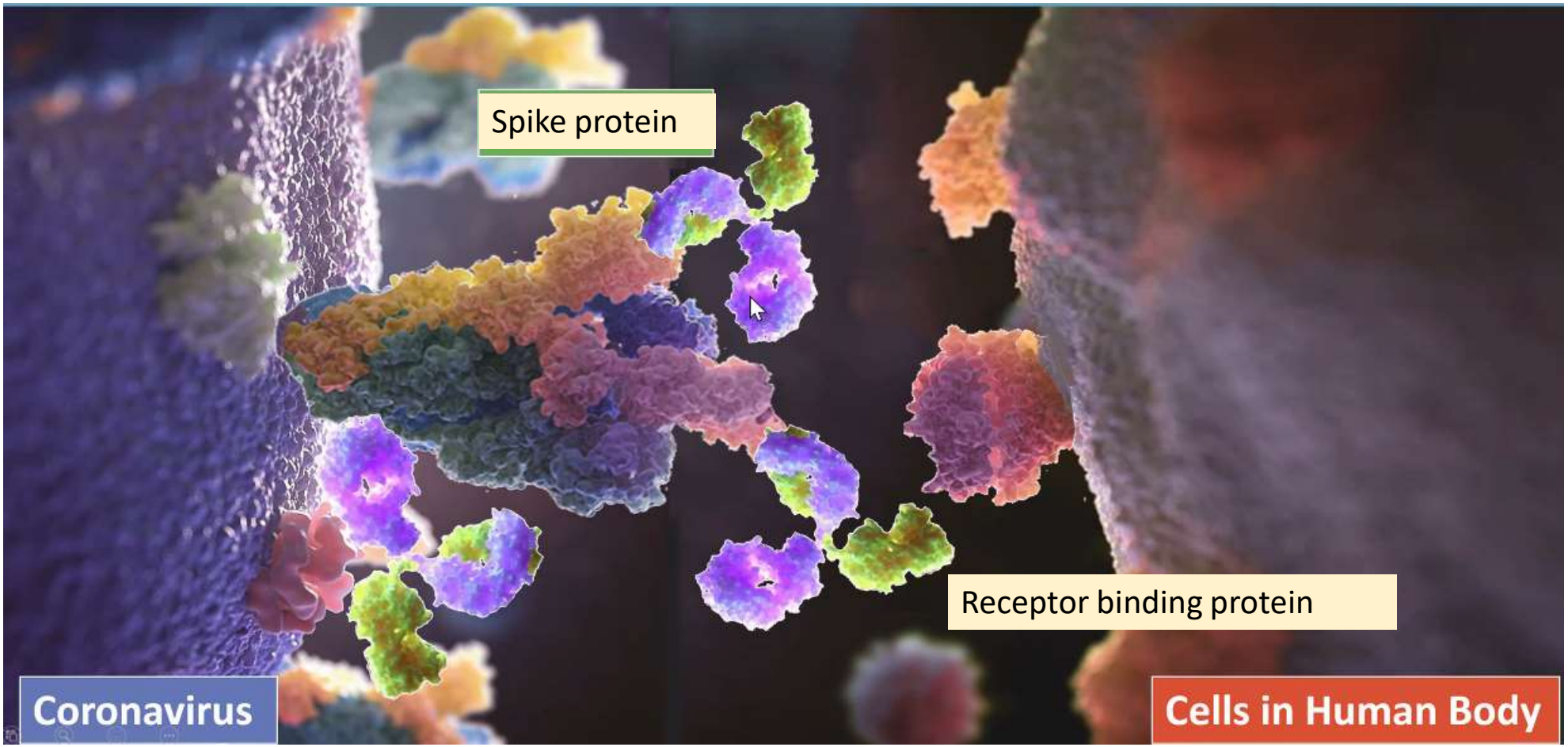
Monica Gandhi MD, MPH
Professor of Medicine, Division of HIV, Infectious Diseases and Global Medicine
Medical Director, Ward 86 and Director, UCSF Center for AIDS Research
October 18, 2021

LA CITY HEALTH COMMISSION

Company or name	Form of publication for phase 3 data/ type of vaccine	Reference
moderna	Peer reviewed publication/ mRNA	Baden NEJM, Feb 4, 2021
Pfizer	Peer reviewed publication/ mRNA	Polack NEJM, December 31, 2020
Johnson & Johnson	Press release only/ adenovirus + DNA	J&J press release January 29, 2021; FDA document Feb 24
AstraZeneca	Two peer-reviewed publications but ongoing (adenovirus + DNA)	Voysey Lancet December 8, 2020; Preprint Feb 1, 2021
NOVAVAX Creating Tomorrow's Vaccines Today	Press release, abstract, press release (phase 3 UK; phase 2b S. Africa; phase 3 US/Mexico)	Novavax press release June 14; Novavax NEJM June 30, 2021
Sputnik V	Peer-reviewed publication (DNA plus adenovirus)	Logunov Lancet, February 2, 2021
sinovac	Publication (whole inactivated)	Sinopharm, JAMA, May 28, 2021
SINOPHARM	Publication (whole inactivated)	Sinovac, JAMA May 28, 2021
BHARAT	Press release (whole inactivated)	Bharat Covaxin, April 21, 2021

There are actually 9 vaccines out there for COVID-19, three authorized in U.S.

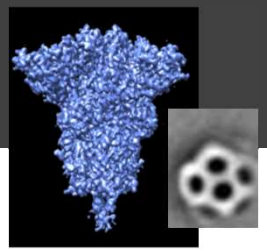
6 vaccine candidates to date involve spike protein and receptor binding domain of SARS-CoV-2 - either mRNA or adenoviral-vector DNA vaccines or protein adjuvant itself; 3 inactivated virus



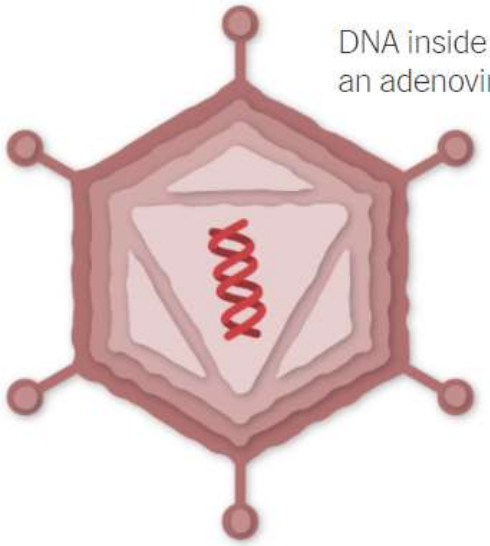
Three types of vaccines involving spike protein

- mRNA vaccines (2)
- Adenoviral vector DNA vaccines (3)
- Spike protein + M-adjuvant vaccine (1)

Three vaccines whole inactivated virions



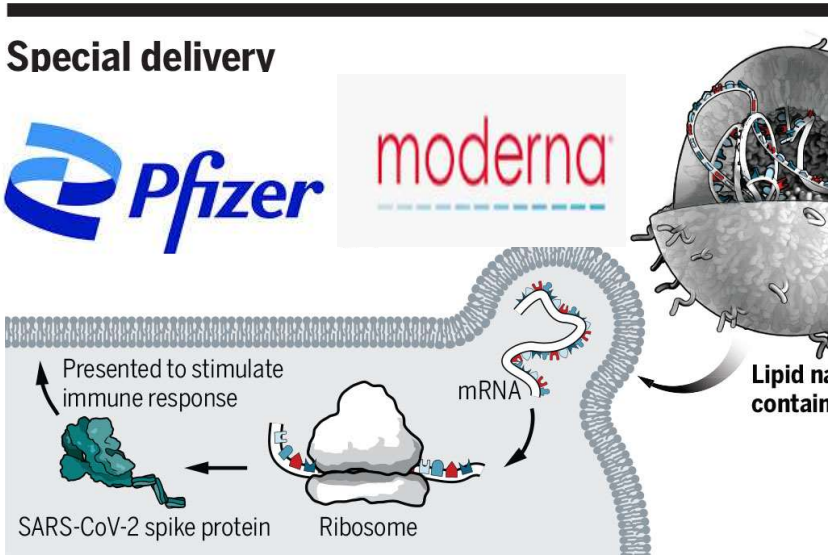
NOVAVAX
Creating Tomorrow's Vaccines Today



Johnson & Johnson

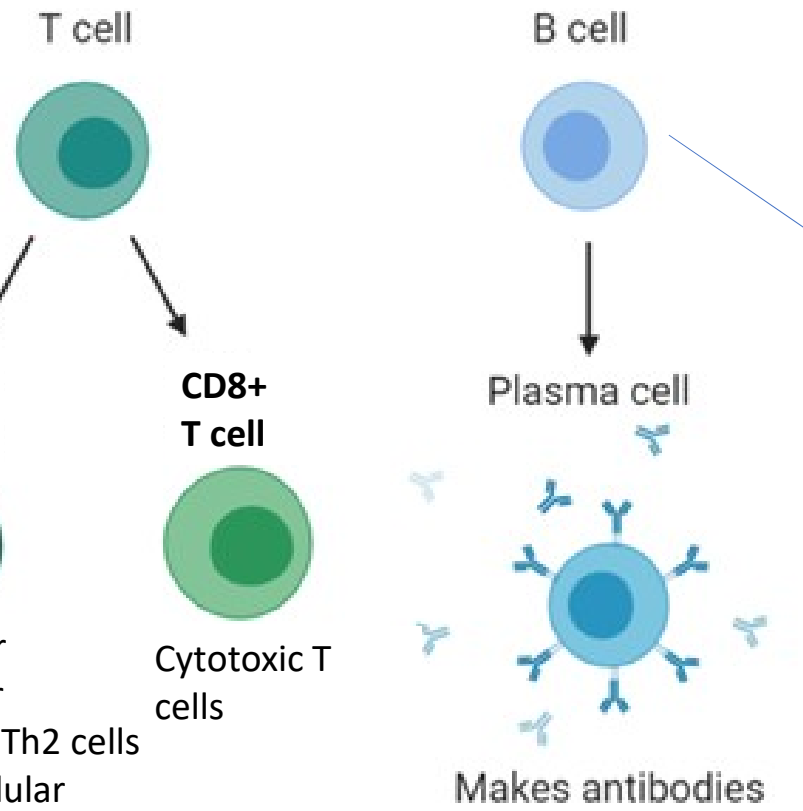
AstraZeneca

Sputnik V



Remember immunity -antibodies and cell-mediated

T cells are the major immune defense against viruses; preserved



Memory T cells

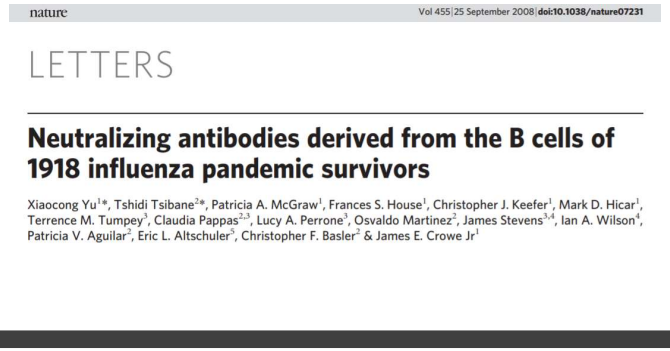
Th1 cells for intracellular pathogens; Th2 cells for extracellular pathogens

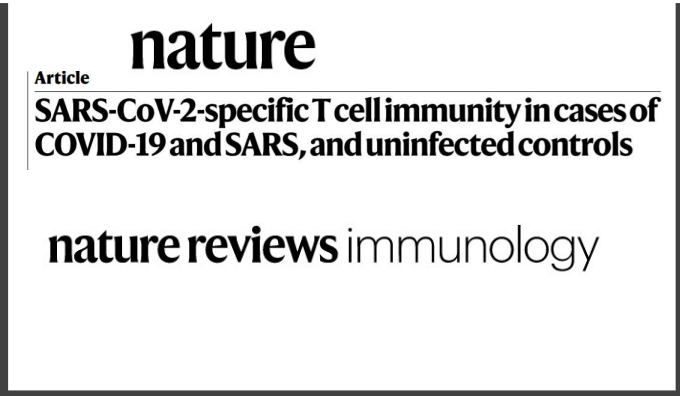
Cytotoxic T cells

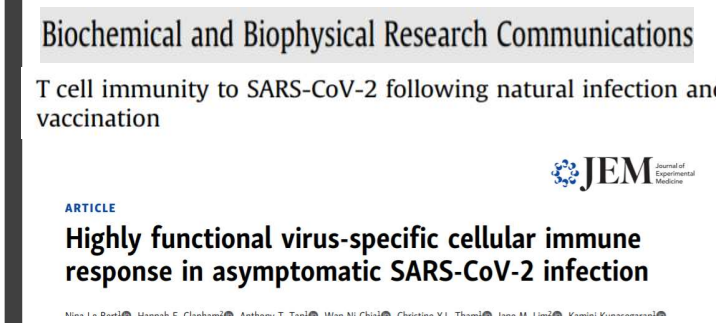
Of note, want Th1:Th2 ratio >>1 for viruses; Th2 CD4s block antiviral Th1-CD4s and CD8s

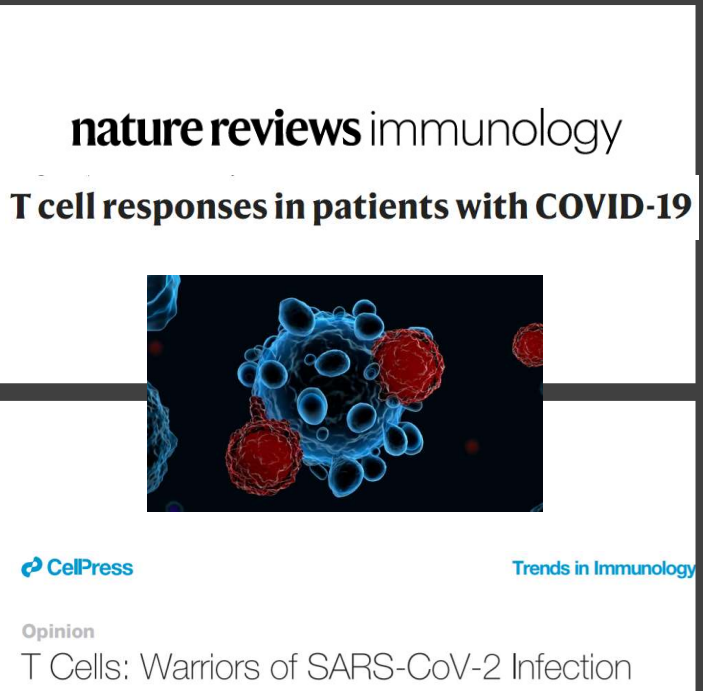
Memory B cells produce antibodies (remember antibodies will wane with time, but memory B cells are blueprint to make more)

Most vaccine trials measured antibodies and T cell responses









How does functional T-cell response modulate severity of disease?

- T cell responses modulate the severity of disease
- Strong T cell responses in all of these trials seem to have led to prevention of severe disease
- JEM study shows us that those with asymptomatic infection mounted good T cell responses to COVID-19
- If you get re-infected after natural infection or vaccine (rare), should be mild if mounted good T-cell response
- Fun fact: Study from 1918 survivors of influenza pandemic show durable B cell immunity (memory B- Ab) 90 years later!

Company	Platform	Doses	Non-clinical results	# with vaccine (same placebo)	Protection from COVID-19 hospitalization	Protection from COVID severe dz (some at home)	Efficacy against milder COVID
moderna	mRNA-1273 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+ protection from challenge (macaques)	~15,000	90% (1 in vaccine arm after 2nd dose hospitalized)	97% (30 cases in placebo arm; 0 in vaccine reported but 1 severe per FDA)	94.1%
Pfizer	BNT162b2 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+, CD8+; protection from challenge (macaques)	~18,600	100%	100% (9 cases in placebo arm; 0 in vaccine- 1 initially severe but not)	95%
Johnson & Johnson	JNJ-78436725 Non-replicating human adenovirus/DNA	1	Neutralizing Abs; Strong Th1 CD4+ > Th2; CD8+; challenge protection (macaque)	~22,000 US, Latin America, S. Africa	100%	85.4% across 3 sites (7 deaths, 16 hospitalizations, all in placebo arm)	72% US; 61% Latin America; 64% S. Africa (95% B1.351)
AstraZeneca	AZD 1222 Non-replicating Chimp Adenovirus-DNA	2	Neutralizing Abs; Strong Th1 CD4+ > Th2; CD8+; protection from challenge (macaques)	~28,588 (UK, SA, US/Peru/ Chili)	100%	100% (UK, 15 placebo arm hospitalized, 0 in vaccine; US, 8 severe in placebo, 0 vaccine)	76% US (85% in >65 yrs); 70% UK; S. Africa halted for mild
NOVAVAX Creating Tomorrow's Vaccines Today	NVX-CoV2373 Spike protein/RBD + Matrix M adjuvant	2	Neutralizing Abs; Strong Th1 CD4 > Th2; macaque challenge protection	8833 (Phase 3 UK; 2b SA); 12.5K (Φ 3)	100%	100% (24 severe placebo in UK/SA/US /MX; 0 vaccine)	90.4% US/MX; 100% severe; 93.2% variants
Sputnik V	Ad26 and Ad5 adenovirus/DNA	2	NAbs; IFN-γ secretion PMBCs, cellular response	~14964	100%	100% (20 in placebo; 0 vaccine)	91.6%

Company	Platform	Doses	Non-clinical results	# with vaccine (same placebo)	Protection from COVID-19 hospitalization	Efficacy against milder COVID
BHARAT	Inactivated whole virus	2	Neutralizing Abs; Strong Th1 CD4 responses in phase II trial (Lancet)	11,000 (press release 4/21)	100%	78%
sinovac	Whole inactivated virion	2	Neutralizing Abs; IFN-gamma assays T cell responses	13,068	100%	72.8%
SINOPHARM	Whole inactivated virion	2	Neutralizing Abs; IFN-gamma assays T cell responses	13,068	100%	78.1%

Will vaccines work against variants and all against severe disease?
Short answer: yes because of T cells

New names proposed for Covid variants

Country/region	Scientific name	WHO name
Kent, UK	B.1.1.7	Alpha
South Africa	B.1.351	Beta
Brazil	P.1	Gamma
India	B.1.617.2	Delta

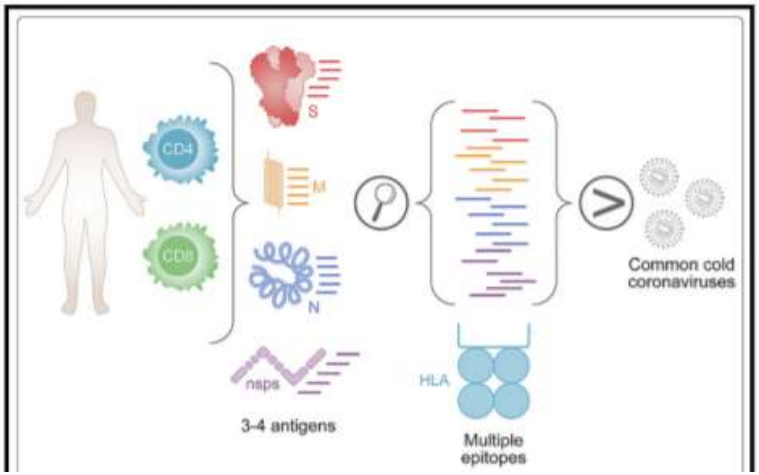
Why T cell response will work against variants? First look at natural infection

Cell Reports
Medicine

Article

Comprehensive analysis of T cell immunodominance and immunoprevalence of SARS-CoV-2 epitopes in COVID-19 cases

Graphical Abstract



Authors

Alison Tarke, John Sidney, Conner K. Kidd, ..., Daniela Weiskopf, Alba Grifoni, Alessandro Sette

Correspondence

agrifoni@lji.org (A.G.), alex@lji.org (A.S.)

In Brief

Tarke et al. show a broad T cell repertoire, suggesting that viral escape of T cell immunity is unlikely. CD4 immunodominant regions correlate with

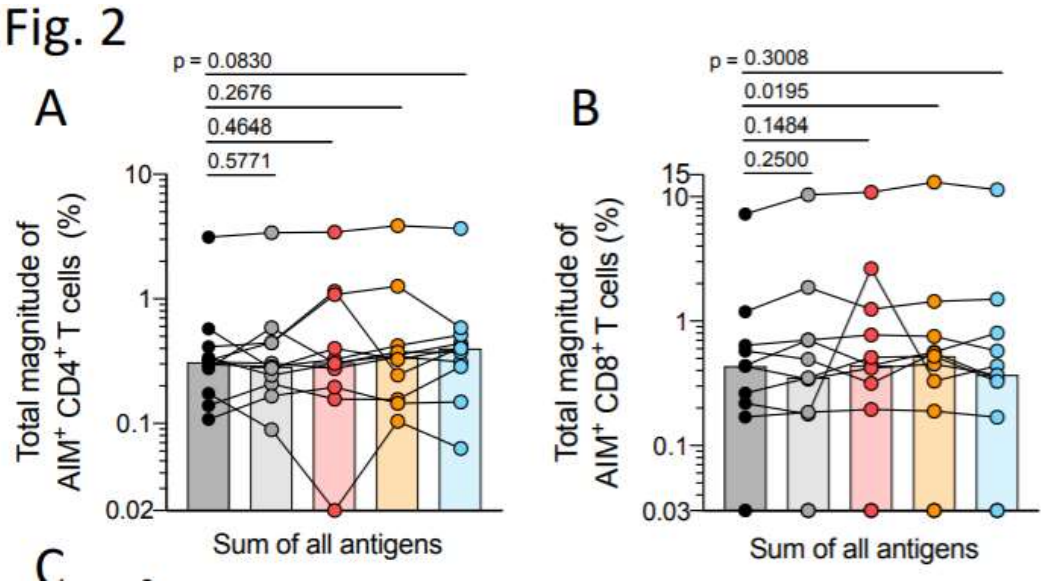
Broad T cell repertoire (100s of T cells across spike protein) after infection. Means viral escape of T cell-immunity (from both natural infection and vaccination) unlikely, re-infection if happens mild

Then look at T-cell response to variants after vaccines- still intact

bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+T cell reactivity in COVID-19 exposed donors and vaccinees.

Alison Tarke, John Sidney, Nils Methot, Yun Zhang, Jennifer M Dan, Benjamin Goodwin, Paul Rubiro,



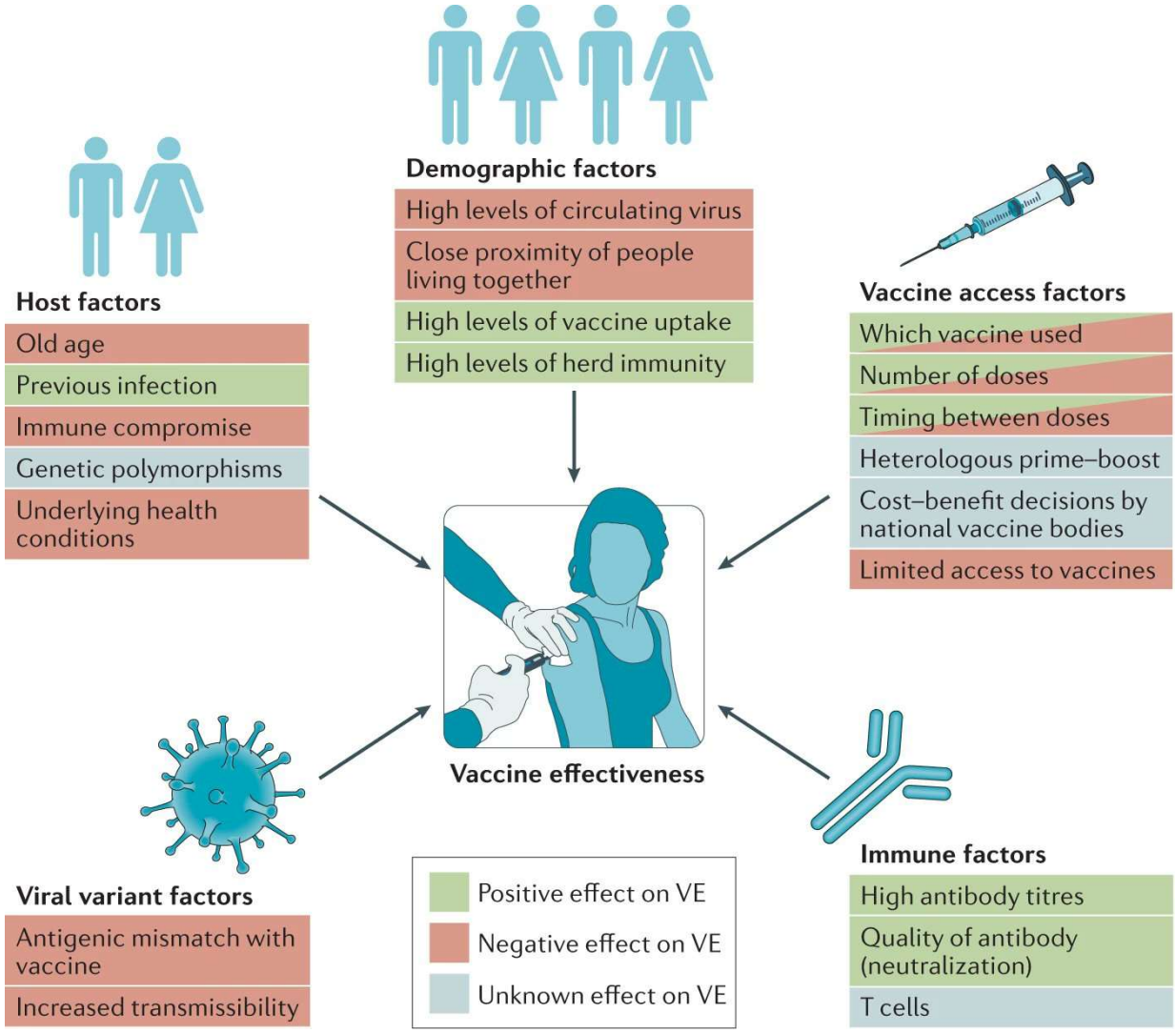
- Looked at SARS-CoV-2-specific CD4+ & CD8+ T cell responses from those with natural infection with non-variant & examined activity against alpha, beta, gamma variants
- T cell reactivity against those variants remained intact if you had natural infection or mRNA vaccination (Pfizer/Moderna)
- Same finding from UCSF paper- after vaccines, T cell response intact against alpha, beta variants

[1]Madhi. NEJM. March 16, 2021; Ma. Biorxiv April 29, 2021

Are vaccines waning in effectiveness with delta?

We need to first discuss B versus T cells!

Vaccine effectiveness – depends on many factors



Courtesy of Muge Cevik MD

Efficacy of mRNA vaccines against severe disease in settings where Delta variant is circulating, Sept 2021

Study Location (reference)	Vaccine	Effectiveness vs. severe disease or hospitalization	Lower limit of 95% CI	Upper limit of 95% CI
USA, Southern California KPSC (1)	BNT162b2 or mRNA-1273	93	84	96
USA, Minnesota (2)	BNT162b2	75	24	94
	mRNA-1273	81	33	96
USA, New York (3)	BNT162b2; mRNA-1273; Ad26.COV2.S	94.4	92.7	95.7
USA 13 jurisdictions (5)	BNT162b2; mRNA-1273; Ad26.COV2.S	90.4	87.7	92.5
USA, 7 locations VISION network (7)	BNT162b2	87	85	90
	mRNA-1273	91	83	93
USA, 9 States VISION network (8)	BNT162b2	80	73	85
	mRNA-1273	95	92	97
USA, 5 VA Medical Centers (9)	mRNA-1273	89	80	94
USA (14)	mRNA-1273	96	91	98
Israel, (4)	BNT162b2	88	94	91
Qatar (10)	BNT162b2	89.7	61	98.1
Qatar (11)	mRNA-1273	100	41.2	100
Singapore (12)	BNT162b2 or mRNA-1273	93	66	98
UK (13)	BNT162b2	96	86	99

[illegible]

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (*MMWR*)

SARS-CoV-2 Infections and Hospitalizations Among Persons Aged ≥16 Years, by Vaccination Status — Los Angeles County, California, May 1–July 25, 2021

Weekly / August 27, 2021 / 70(34);1170–1176

You are 29.2 times more likely to get hospitalized if unvaccinated than vaccinated in time of delta

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (*MMWR*)

Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions — United States, March–August 2021

Weekly / September 24, 2021 / 70(38);1337–1343

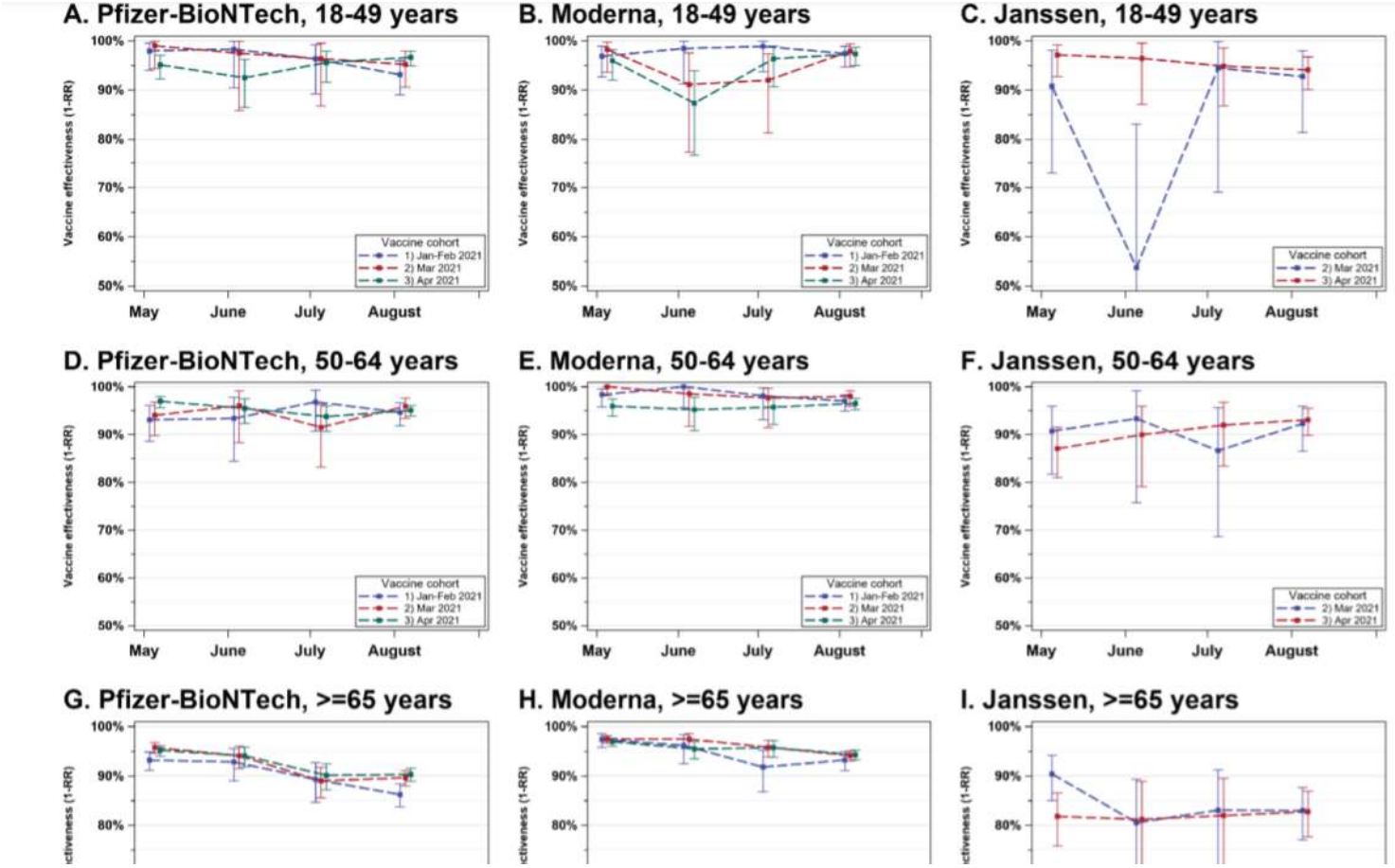
Protection against hospitalization with delta: 18 states

Moderna 93%

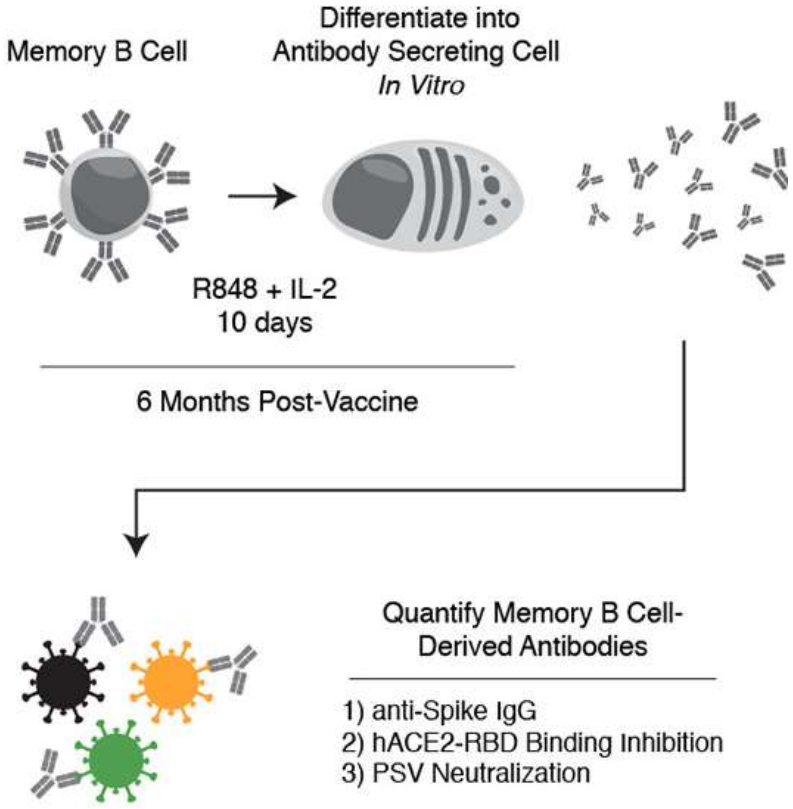
Pfizer 88%

Johnson and Johnson 71%

Recent data from NY shows that vaccine effectiveness not really waning for any group except >65 – J&J less effective



Memory B cells from vax or infection happily adapt to whatever variant they see



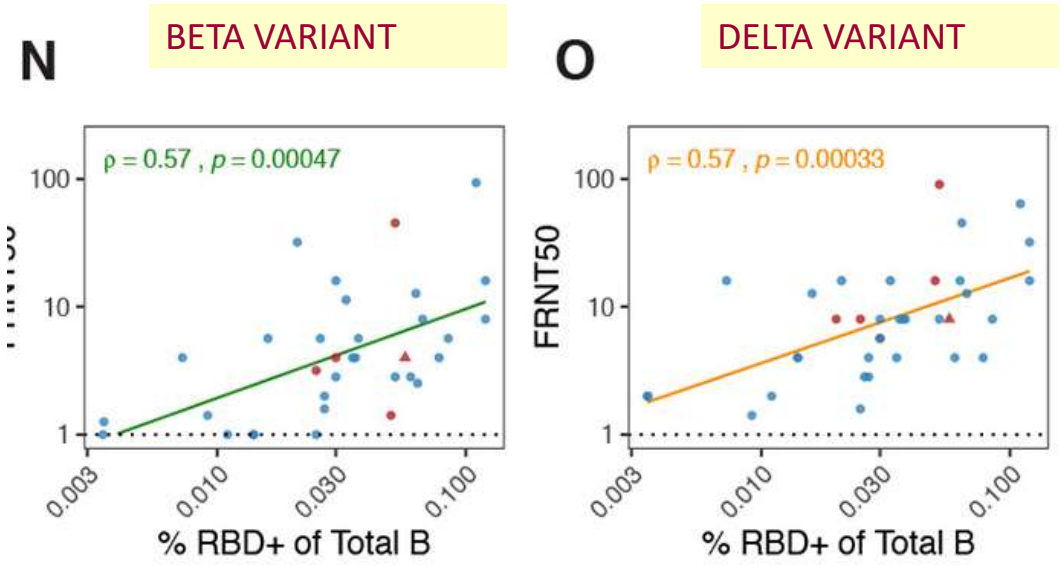
Science

RESEARCH ARTICLES

Cite as: R. R. Goel *et al.*, *Science* 10.1126/science.abm0829 (2021).

mRNA vaccines induce durable immune memory to SARS-CoV-2 and variants of concern

Rishi R. Goel[1,2†], Mark M. Painter[1,2†], Sokratis A. Apostolidis[1,2,3†], Divij Mathew[1,2†], Wenzhao Meng[1,4], Aaron M.

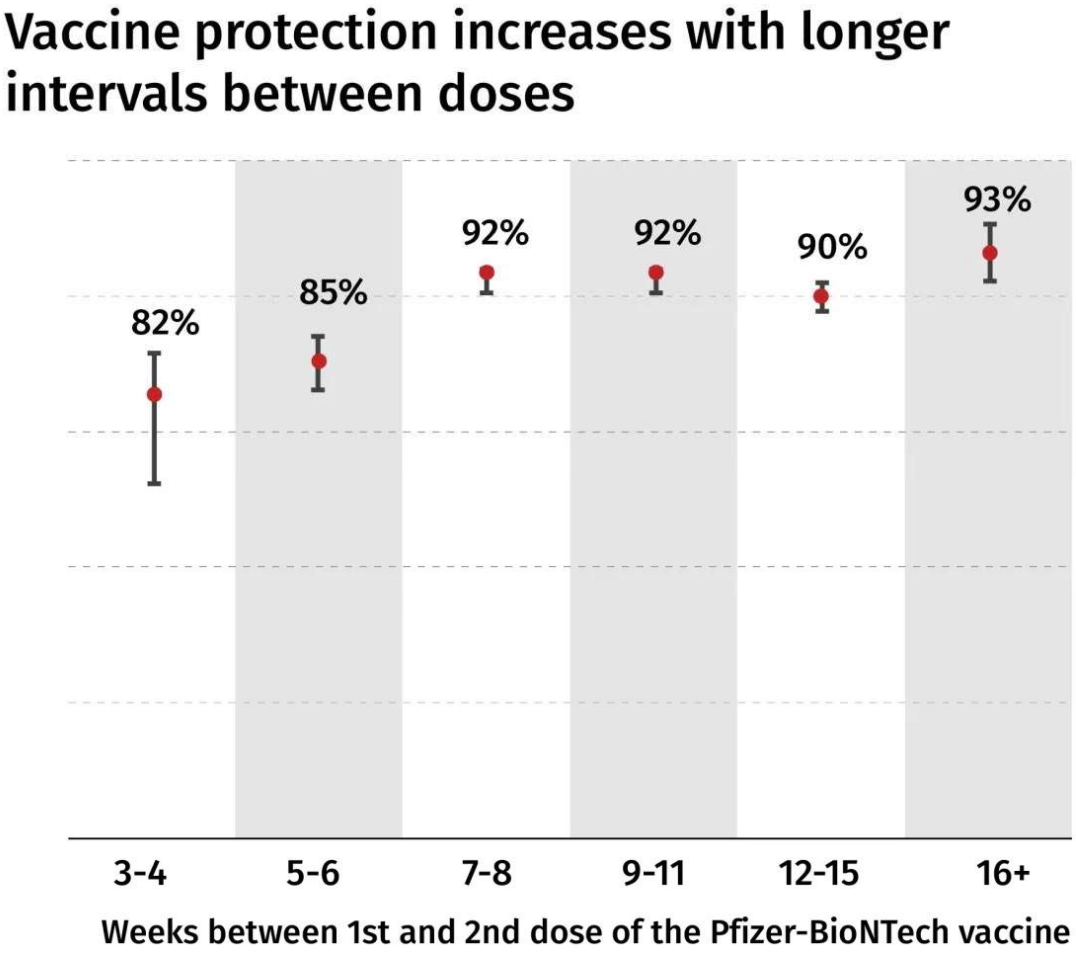


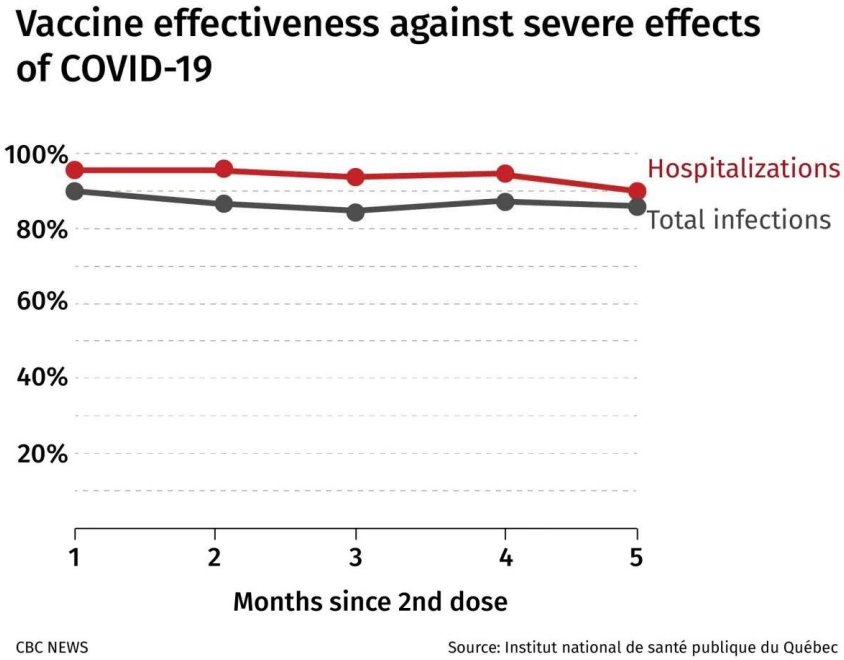
Why have we seen more symptomaticc breakthroughs with delta?

- Could be higher viral load
- **Think more likely waning antibodies with time** (protection in nose
- Increasing duration between doses leads to higher antibodies[1] (e.g. 8-12 weeks done in Canada and UK), less symptomatic breakthroughs in those two countries
- Less re-infection with Moderna than Pfizer[2] (Mayo Clinic study with delta) – Moderna given at 4 weeks, Pfizer at 3 weeks
- Luckily, waning antibodies NORMAL, not a GLITCH and are made anew by memory B cells – that is what they do

[1]https://www.nature.com/articles/d41586-021-01299;
[2]https://www.science.org/doi/10.1126/science.abm0829

Data from Canada shows Pfizer works better if extend interval to 7-8 weeks





Myocarditis (although mild/rare) more common with Pfizer q3 weeks (Israel) than longer intervals (usually 8)

Table 5. Rate Ratios for a Diagnosis of Myocarditis within 30 Days after the Second Dose of Vaccine, as Compared with Unvaccinated Persons (January 11 to May 31, 2021).

Age and Sex	Vaccinated Group		Unvaccinated Group		Rate Ratio (95% CI)
	Person-Days of Follow-up	Cases	Person-Days of Follow-up	Cases	
	number				
All recipients*	149,786,065	117	296,377,727	98	2.35 (1.10–5.02)
16–19 yr					
Male	6,018,541	31	19,135,706	11	8.96 (4.50–17.83)
Female	6,033,192	2	17,768,696	2	2.95 (0.42–20.91)
20–24 yr					
Male	7,088,335	27	20,926,320	13	6.13 (3.16–11.88)
Female	6,889,399	5	20,832,407	2	7.56 (1.47–38.96)
25–29 yr					
Male	6,590,263	18	20,944,595	16	3.58 (1.82–7.01)
Female	6,417,564	1	20,943,920	0	0
≥30 yr					
Male	53,577,403	26	82,419,957	40	1.00 (0.61–1.64)
Female	57,171,368	7	93,406,126	14	0.82 (0.33–2.02)

* Data for all vaccine recipients have been weighted according to age and sex.

The NEW ENGLAND JOURNAL of MEDICINE

Oct 6

ORIGINAL ARTICLE

Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel

D. Mevorach, E. Anis, N. Cedar, M. Bromberg, E.J. Haas, E. Nadir, S. Olsha-Castell,

Alberta

Office of the Chief Medical Officer of Health
Updated October 8, 2021

Myocarditis and/or Pericarditis following COVID-19 Vaccines

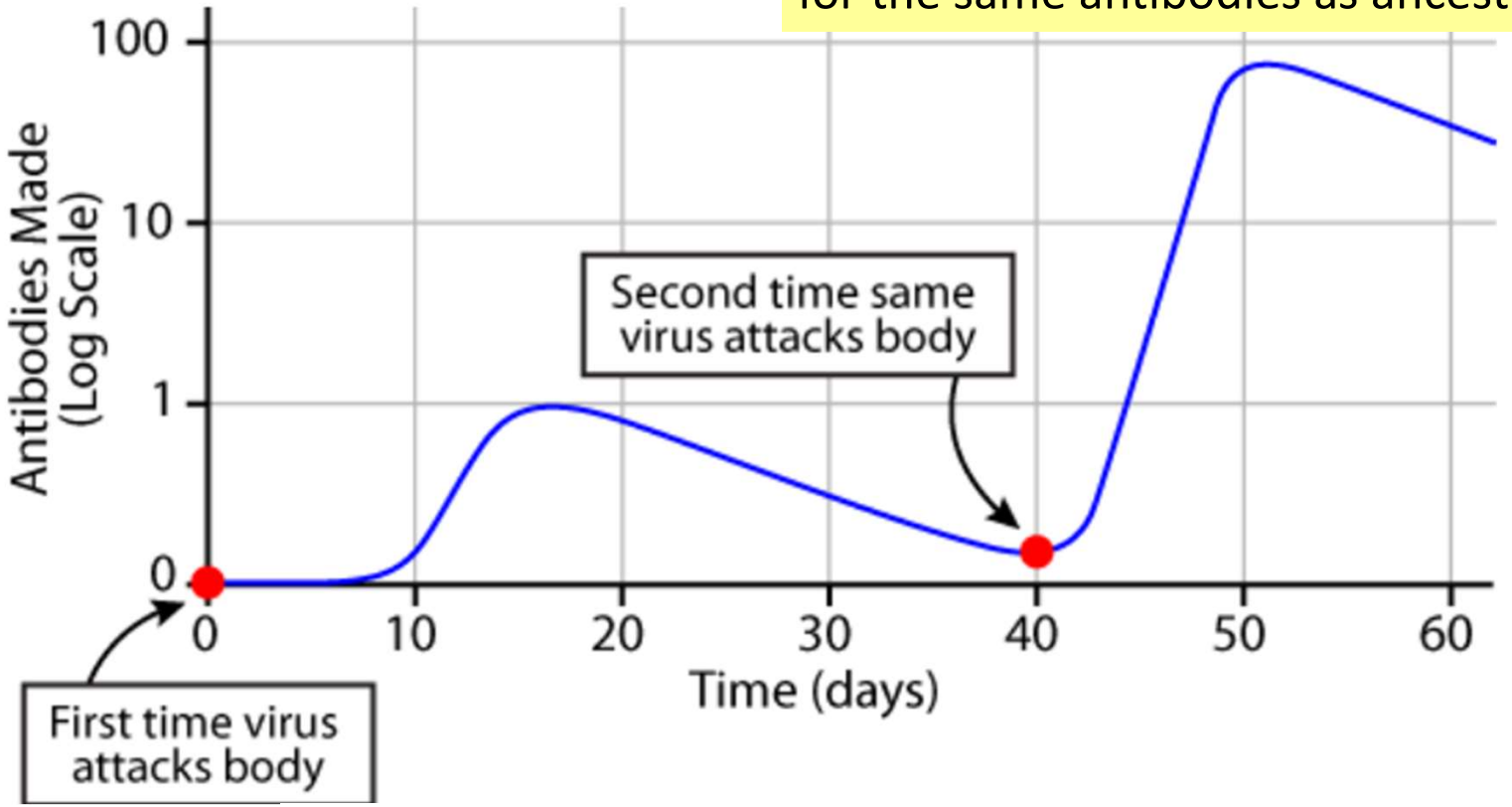
0.66/100,000 total myocarditis cases

Based on current Alberta AEFI data, all ages and both sexes combined, the rate of myocarditis after second dose of the Pfizer vaccine is 6.6 per million, while the rate after second dose of Moderna is 8.3 per million. Although the rate following the Moderna vaccination is slightly higher, occurrence of myocarditis is still very rare.

So, boosters for everyone or a tiered approach?

Antibodies come down naturally but memory B cells produce more if see virus again

Memory B cells ADAPT their antibodies they produce to cover variants; a booster will code for the same antibodies as ancestral strain



1https://www.science.org/doi/10.1126/science.abm0829
2https://www.medrxiv.org/content/10.1101/2021.05.28.21258025v1

Given J&J data from CDC, strong reason to boost J&J:
FDA MEETING DECIDED THIS ON OCTOBER 15

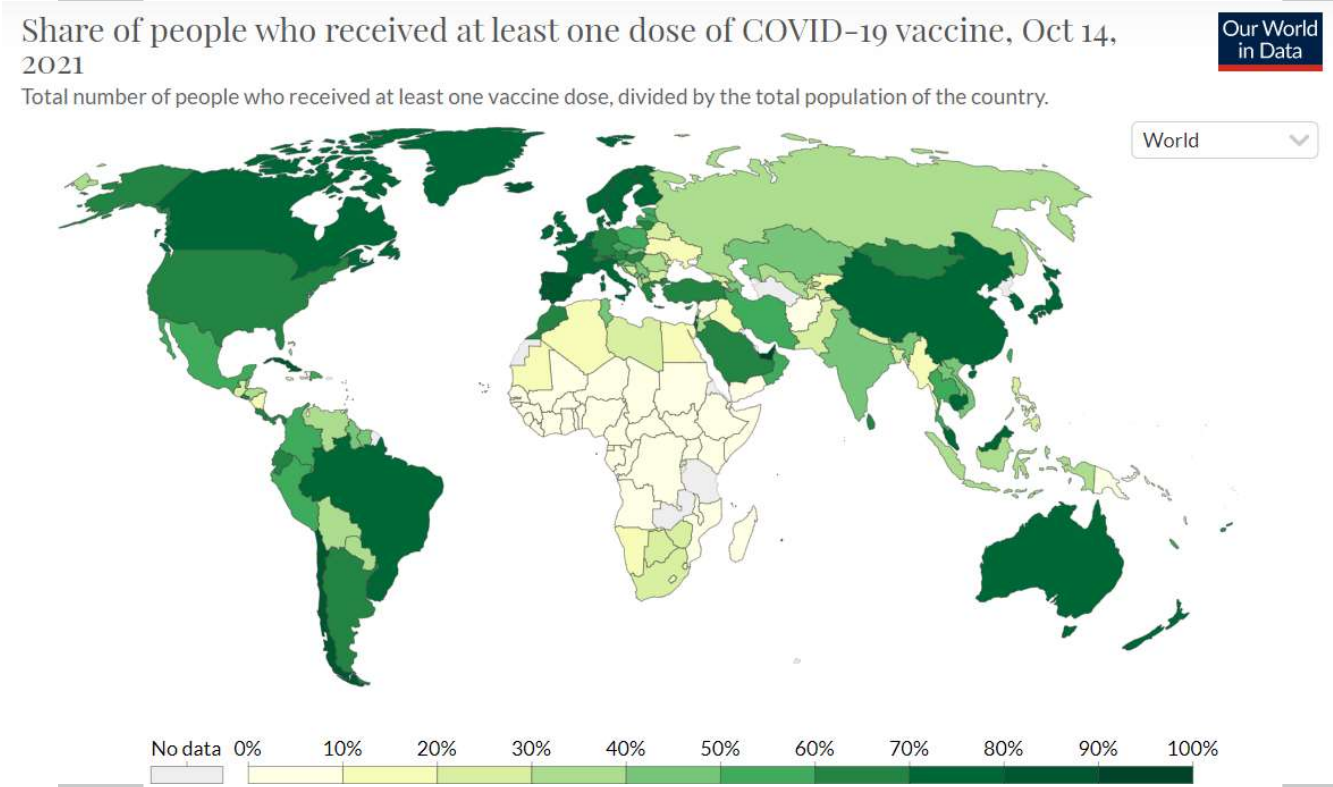
Boosters (Moderna/Pfizer) approved for

- Immunocompromised
- >65 years
- 18-64 with medical conditions
- Lots of exposure

- Received an organ transplant and are taking medicine to suppress the immune system
- Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
- Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids or other drugs that may suppress your immune response

6.6 billion doses administered worldwide

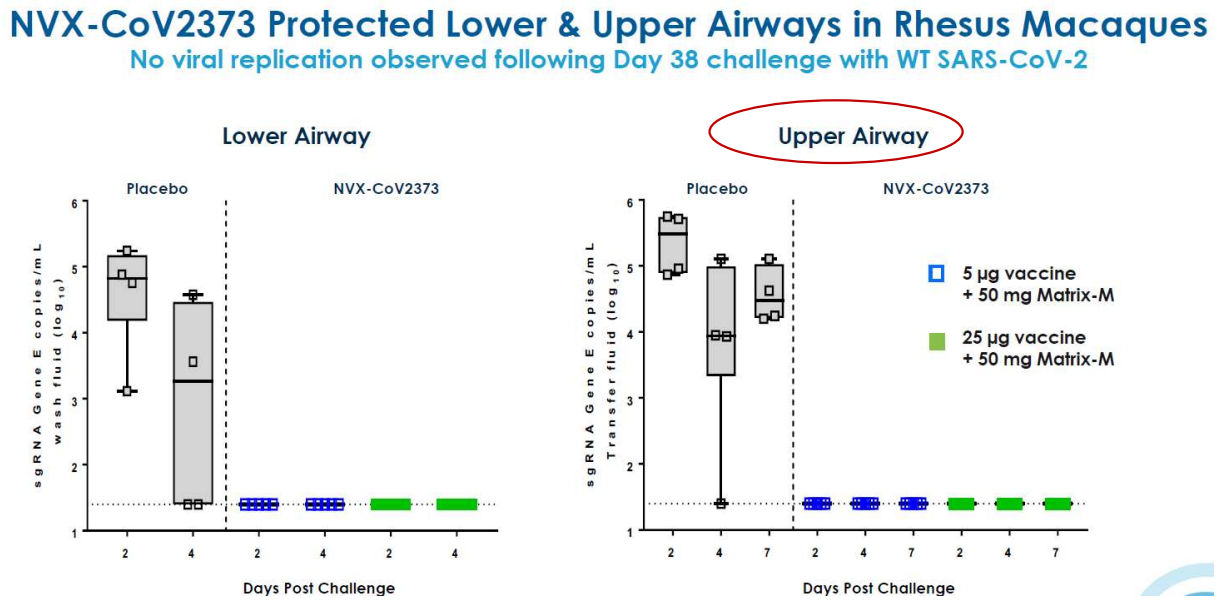
- **2.7% doses given to low-income counties?**
- **So, should we give boosters to immuncompetent?**
- **Or focus on global vaccine equity instead!**



Do vaccines reduce transmission?

Yes, but with delta less so

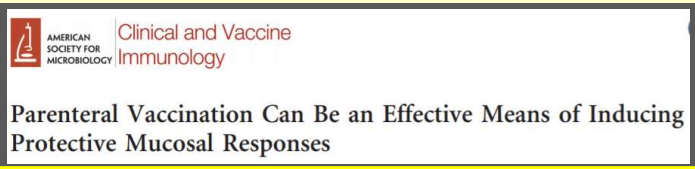
Will vaccines decrease transmission? Biological plausibility (4 main reasons)



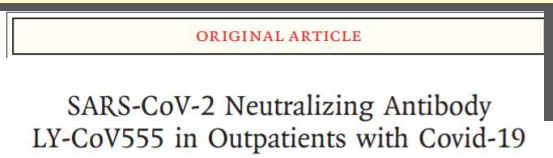
4. Challenge experiments with macaques in pre-clinical trials show blocking of viral replication (or no/low viral RNA) in BAL and nasal swabs (Mercado Nature J&J vax, 2020; Guebre-Xabier Vaccine Novavax 2020)

1. IgG antibodies measured in trials found in high levels in nasal mucosa

2. Systemic vaccines induce IgA (mucosal immunoglobulin) and recent study shows mRNA COVID-19 vaccines induce IgA



3. Monoclonal antibodies hasten viral clearance from airways



PRIOR TO THE DELTA VARIANT		
Setting	% reduction in asymptomatic infection or transmission	Reference
Healthcare workers in England	**85%**	Hall Lancet, April 23, 2021
Healthcare workers in Israel	**75% and 86%**	Amit, Lancet, March 6; Angel JAMA May 6
Patients in Mayo Clinic health system	**88.7%**	Pawlowski medRxiv, February 27, 2021
Israel Ministry of Health (nationwide) Israel general population (Pfizer)	**94% (largest study)** **90%**	Pfizer press release, March 11, 2021 (and Goldberg Medrxiv, April 24, 2021) Dagan NEJM, February 24, 2021
Pre-surgical patients in Mayo Clinic system swabbed asymptomatically	**80%**	Tande Clin Inf Dis, March 10, 2021
Healthcare workers in Cambridge University Hospitals	**75%**	Weekes Authorea, February 24, 2021
First-line responders and HCWs in US	**90%**	Thompson A. MMWR, March 30, 2021
Israel population (>16) with children unvaccinated	**For every 20-point increase in adult vaccination, rates of kids testing positive halves**	Milman O. Medrxiv. March 31, 2021
Long-term care facility, Spain	**90%**	Salazar P. Medrxiv. April 13, 2021
Nursing homes, U.S. (two studies)	**100%**	Cavanaugh MMWR, April 21 and Terran MMWR, April 30
Nasal viral load values most important determinant of transmissibility (Lancet study, Spain); Viral loads from post-vaccination exposures are low and likely noninfectious per CT values (use rapid antigen tests after vaccination if test symptomatic or incorporate CT)		

Health

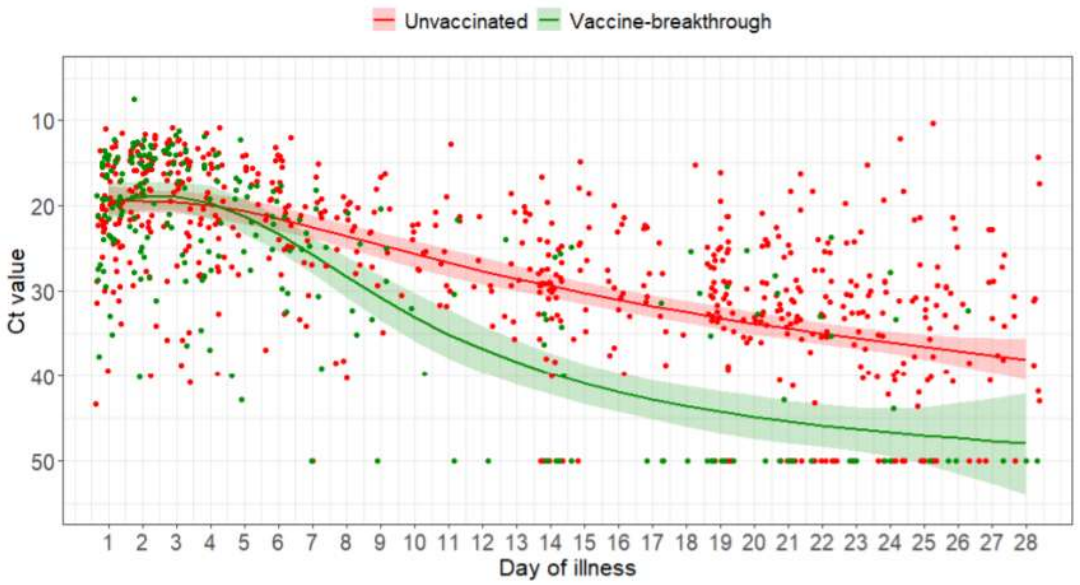
How Provincetown, Mass., stress-tested the coronavirus vaccine with summer partying and delta

Showed us that

1) Delta variant likely to transmit from symptomatic breakthroughs but less so – will explain (no evidence from asymptomatic)
2) lots of exposure, lots of mild breakthroughs “stress test’ but vaccines held up to their promise- prevented severe disease!

Delta variant not as infectious in vaccinated as unvaccinated though

- More transmissible
- Likely not as infectious from vaccinated than unvaccinated (Provincetown outbreak data looked at one point in time of CT values of PCR tests in vaccinated & unvaccinated being same)
- Singapore study of delta breakthroughs **did serial testing** and found viral loads (by CT) drop more quickly among the vaccinated
- NPIs work against delta



Delta variant outbreak in Singapore: https://www.medrxiv.org/content/10.1101/2021.07.28.21261295v1.full.pdf

Looked at culture data from delta breakthroughs in vaccinated HCWs

Less likely to be infectious by culture data

Bottom line: Vaccinated people can likely spread if symptomatic with delta, but less than unvaccinated

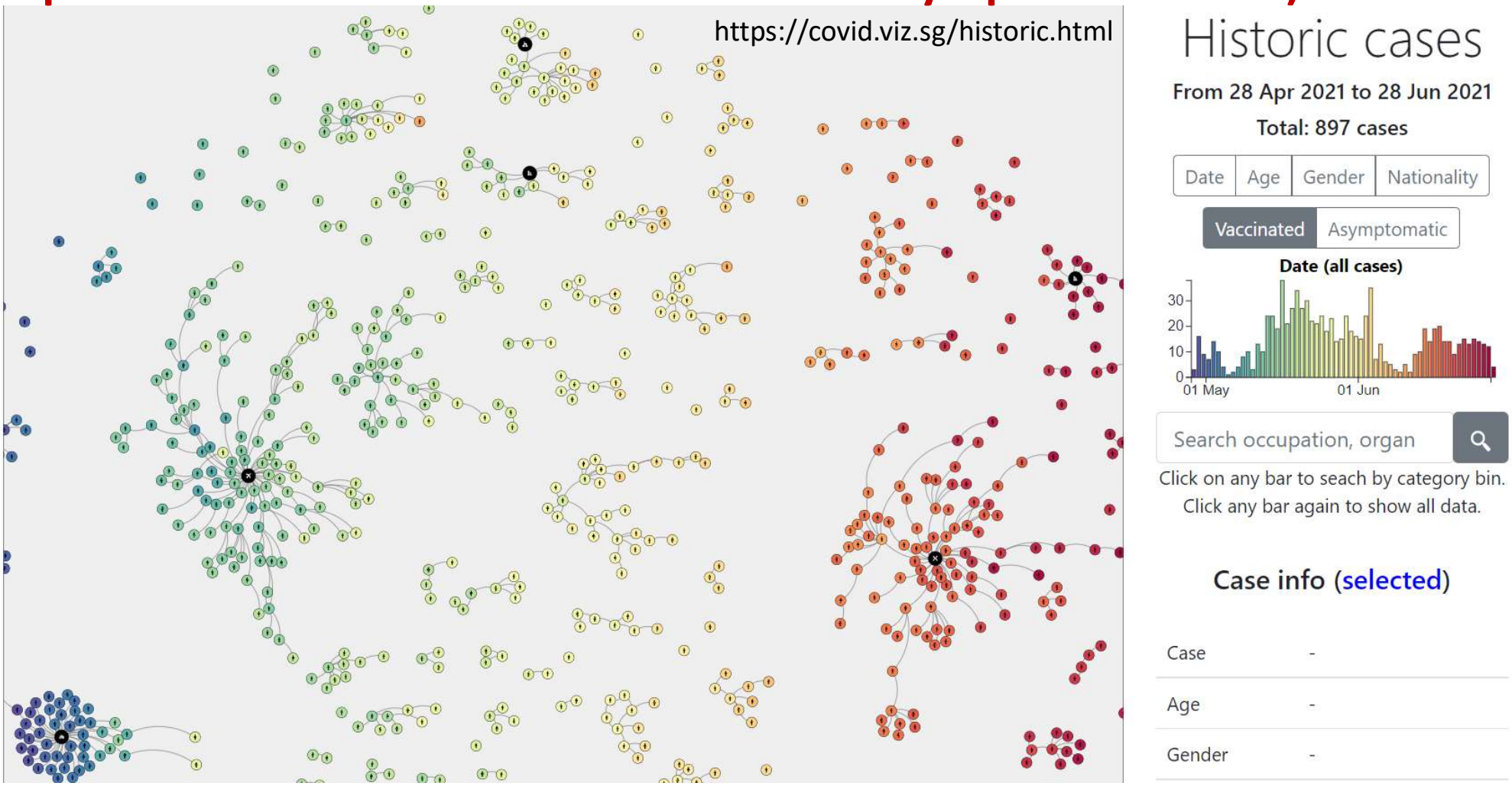
medRxiv
THE PREPRINT SERVER FOR HEALTH SCIENCES
CSH Cold Spring Harbor Laboratory BMJ Yale

Virological characteristics of SARS-CoV-2 vaccine breakthrough infections in health care workers

Marc C. Shamier, Alma Tostmann, Susanne Bogers, Janet de Wilde, Jeroen IJpelaar, Willemijn A. van
Herbert de Jager, Bart L. Haagmans, Richard Molenkamp, Bas. B. Oude Munnink, Carsten van Rossum,
Janette Rahamat-Langendoen, Nannet van der Geest, Chantal P. Bleeker-Rovers, Heiman Wertheim,
Marion P.G. Koopmans, Corine H. GeurtsvanKessel

doi: https://doi.org/10.1101/2021.08.20.21262158

Singapore tracing study showing asymptomatic vax'd spread rare (our post-doc counted 1 transmission from asympomatic vax'd)

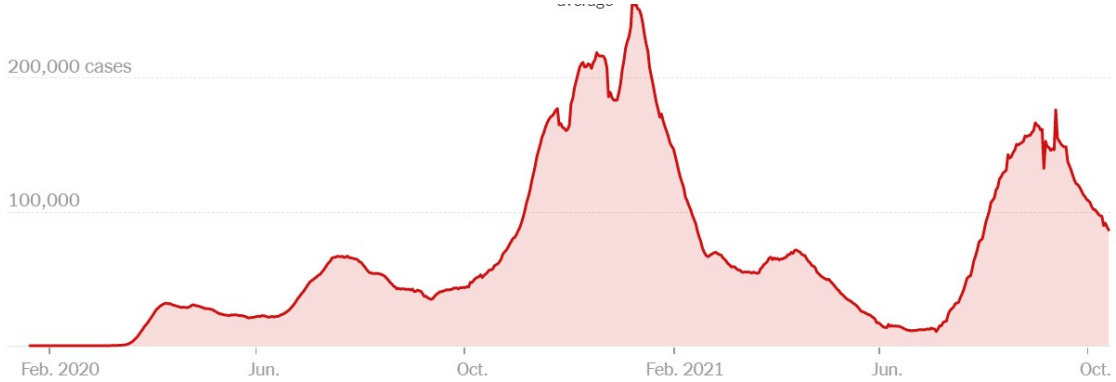


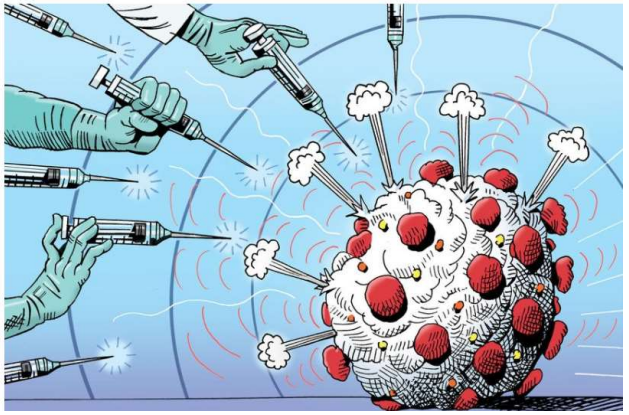
CDC breakthrough data

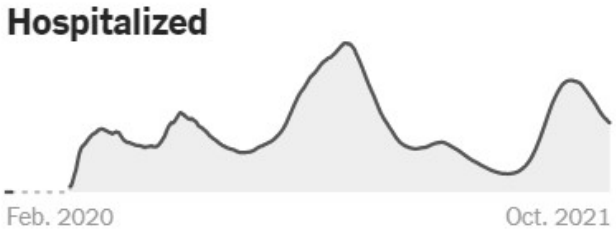
- CDC keeping track of breakthrough infections in U.S
- Out of >187 million Americans who are fully vaccinated against COVID-19
  - 13,775 hospitalized breakthroughs (0.01%) – 67% >65 years
  - Deaths 0.003% for COVID-19 (85% >65 years)

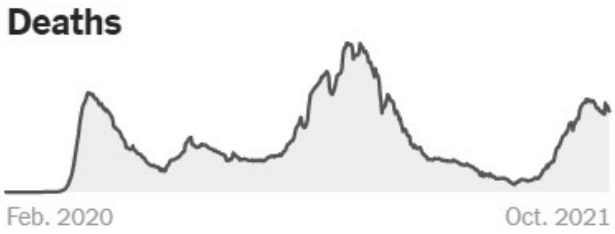
https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html

State of the pandemic









USA cases coming down but occurred fastest in states with high rates of vaccination

California Now Has Nation's Lowest Virus Transmission Rate

California is seeing lower coronavirus transmission than other U.S. states as virus cases and hospitalizations decline following a summer surge.

By Associated Press | Sept. 21, 2021, at 8:16 p.m.

NEWS | 14 October 2021

COVID super-immunity: one of the pandemic's great puzzles

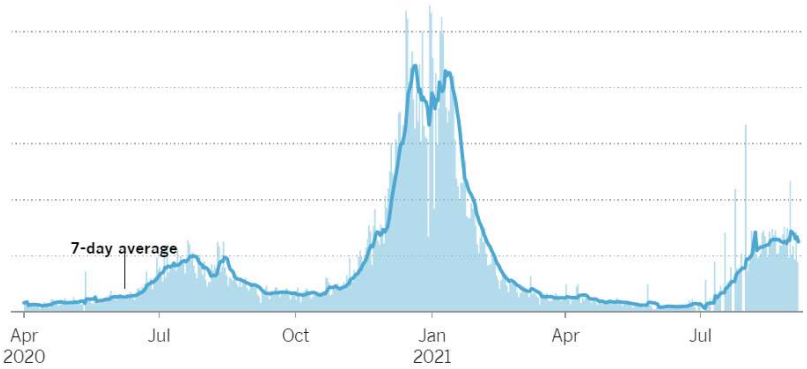
People who have previously recovered from COVID-19 have a stronger immune response after being vaccinated than those who have never been infected. Scientists are trying to find out why.

California's terrible winter surge and immunity prior to vaccine roll-out in general population

Coronavirus cases in California

The number of cases announced each day by local health officials.

New cases by day



Many Californians have some virus immunity

About 38% of Californians recently tested for antibodies appear to have some immunity against the coronavirus, according to estimates from state health officials.

	Percentage of people who had confirmed infections	Percentage of people with antibody immunity
California (total)	8.7%	38.5%
Los Angeles	11%	45%
Southeast	10%	42.7%
San Joaquin Valley	9.1%	43.5%
Central Coast	7.8%	30%
Southern Border	7.8%	28.4%
Greater Sacramento	5.5%	30.9%
Bay Area*	5.2%	29.1%
Northern California	5%	32.7%

*State system also includes Monterey and Santa Cruz counties in Bay Area

Source: California Department of Public Health

John Blanchard / The Chronicle

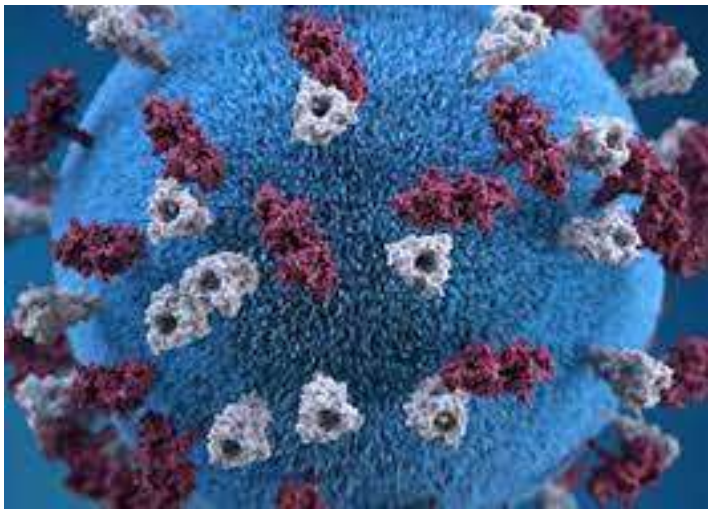
COVID-19 likely to be controlled not eradicated – so frequency of boosters will depend on if we tamp down transmission WORLDWIDE

- **Control:** Reduction of disease incidence to acceptable levels
- **Elimination**: Reduction to zero incidence in a defined geographical area
- **Eradication**: Permanent reduction to zero worldwide
- **Extinction:** Infectious agent no longer exists in nature or laboratories.

Features of eradicable infectious diseases – like smallpox

- No animal reservoir
- Clear pathogenic features
- Short period of infectiousness
- Immune for life and then highly effective vaccine

- (COVID-19 looks like other respiratory illnesses, can spread when presymptomatic, in animals, vaccine good)



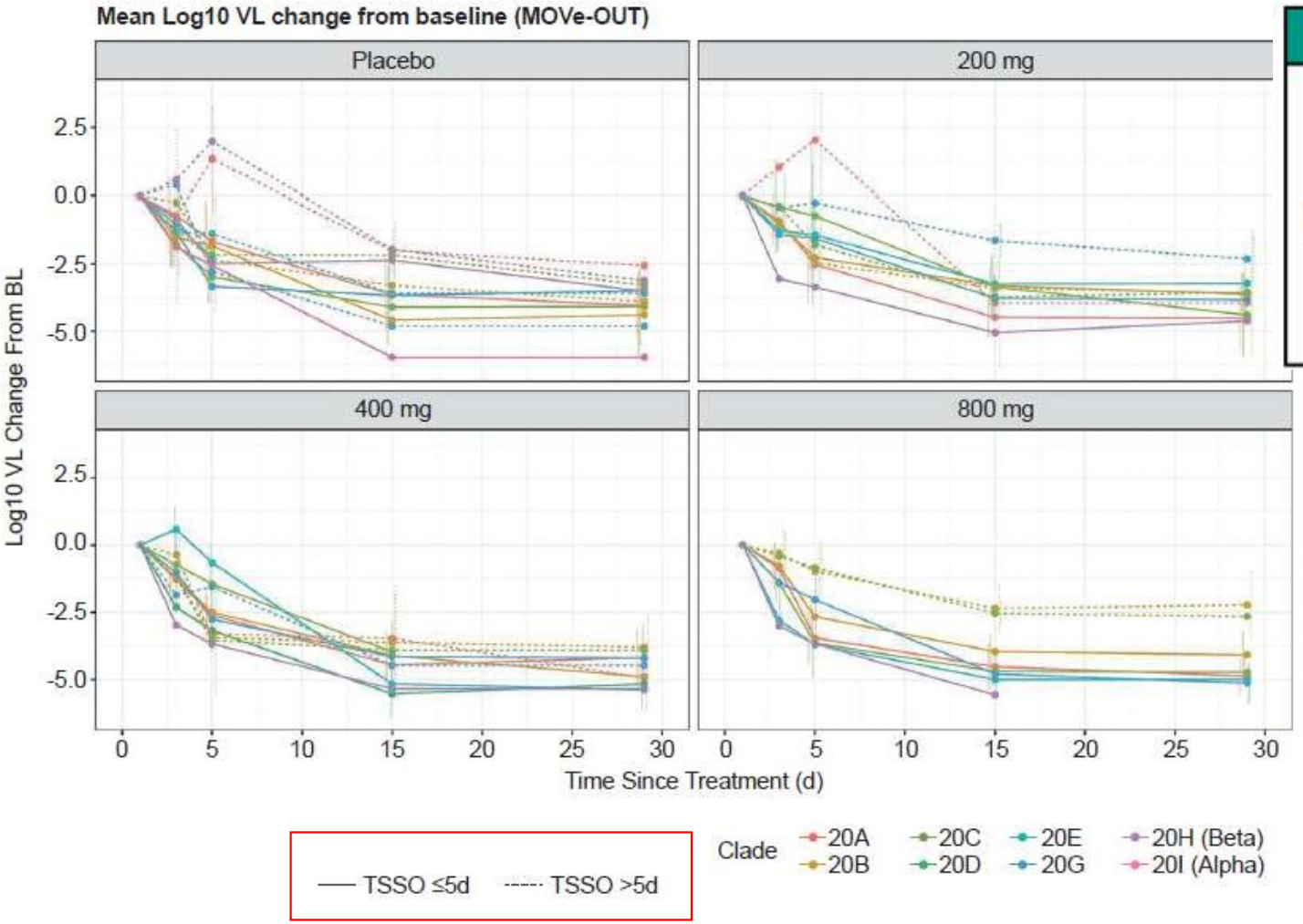
Measles

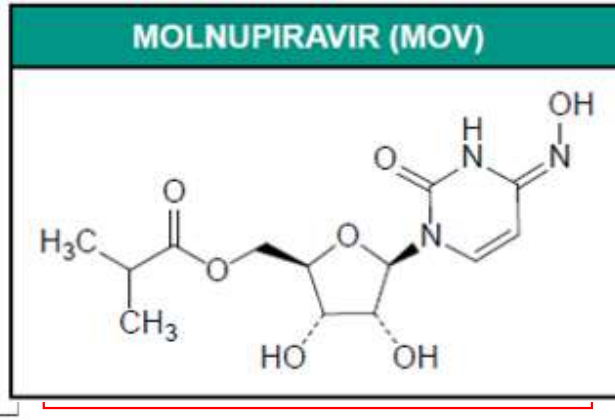
Pertussis

Comes under control/elimination with vaccines (measles) and vaccines/treatment (pertussis)

Figure 3. Virologic response is greater in participants with time since symptom onset ≤5 days

Virologic response by clade and TSSO





#543, Grobler IDWeek

NEWS RELEASE

Merck and Ridgeback's Investigational Oral Antiviral Molnupiravir Reduced the Risk of Hospitalization or Death by Approximately 50 Percent Compared to Placebo for Patients with Mild or Moderate COVID-19 in Positive Interim Analysis of Phase 3 Study

10/1/2021

"MOVe-OUT"

- Outpatients with mild-moderate COVID (O2 sat ≥93%)
  - Symptom onset w/in 5 days
  - One or more risk factors for severe COVID (including age>60, obesity, diabetes, CAD)
  - 800mg BID x 5 days vs Placebo
- Interim analysis of 775 patients of planned n=1550
- Latin America (55%), Europe (23%), Africa (15%) in addition to US
- 14.1%-> 7.3% reduction in 1º endpoint of all-cause hospitalization/death
  - No deaths in MOV vs 8 deaths PCBO
- Adverse events: 35% vs 40%, Drug related 12% vs 11%, D/c due to AE 1.3% vs 3.4%
- Viral sequencing in 40%: similar efficacy in Delta, Gamma &Mu

PFIZER AND BIONTECH ANNOUNCE POSITIVE TOPLINE RESULTS FROM PIVOTAL TRIAL OF COVID-19 VACCINE IN CHILDREN 5 TO 11 YEARS

September 20, 2021

- Results are the first from a pivotal trial of any COVID-19 vaccine in children under 12 years of age
- In participants 5 to 11 years of age, the vaccine was safe, well tolerated and showed robust neutralizing antibody responses
- Companies plan to submit these data to the FDA, EMA and other regulatory agencies around the world as soon as possible
- Results in children under 5 years of age are expected as soon as later this year

Denmark

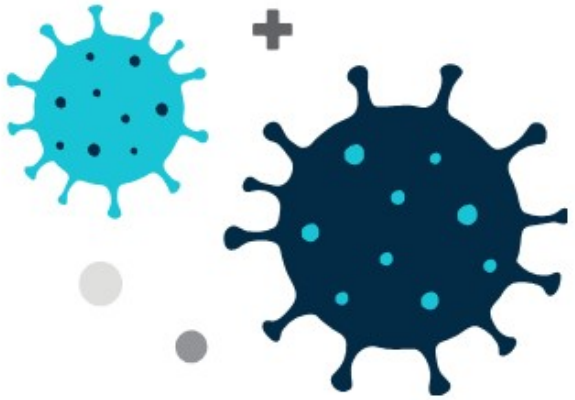
Science

30 SEP 2021

- Opened up at 74% vaccination rate for whole population (80% over 12- same as California)
- September 10 – no restrictions, not even masks
- Hospitalizations staying low

Life in Denmark now feels so much like it did before the pandemic that it can put visitors on edge, says Lone Simonsen, an epidemiologist at Roskilde University. The country lifted all of its remaining coronavirus restrictions on 10 September. Copenhagen clubs are buzzing, music lovers flock to festivals, and buses are packed with unmasked commuters. The government has given up its power to close schools and shut down the country. "When

Summary



- California lowest rate of transmission & Denmark opened up at this rate but no increased hospitalizations
- All vaccines reduce severe disease significantly, likely due to T-cell response
- Vaccines decrease transmission but more symptomatic and transmission with delta
- Variants can be managed - B cells
- Rare safety concerns – much more rare than COVID itself
- Molnupiravir, child vaccines coming – COVID getting under control