

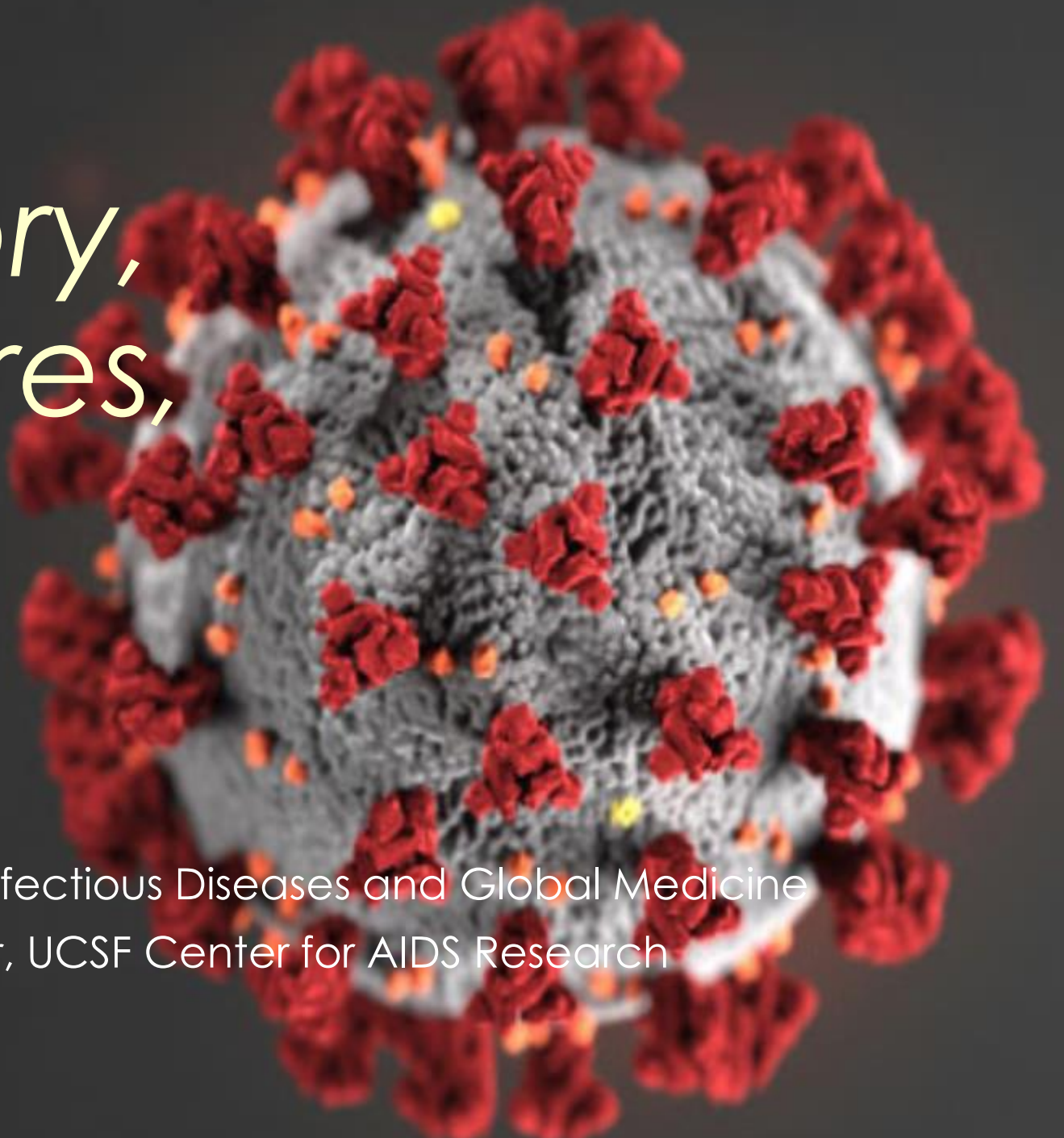
# *Updates on COVID: History, school closures, vaccines, endemicity*

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Medical Director, Ward 86 and Director, UCSF Center for AIDS Research

May 12, 2022



# Disclosure

- Neither I nor any member of my immediate family has a financial relationship or interest (currently or within the past 24 months) with any proprietary entity producing health care goods or services consumed by, or used on, patients related to the content of this CME activity.
- I do not intend to discuss an unapproved/investigative use of a commercial product/device.







# Objectives of talk

- History of COVID
- Pandemic playbooks and school closures
- COVID vaccines including child vaccines
- COVID variants/Omicron
- What defines endemicity?
- Masks



# HISTORY OF COVID

# How do new infectious diseases “emerge” or enter human populations?

Activity	Consequence
 <p><b>Global Warming</b></p>	<ul style="list-style-type: none"> <li>• Pathogens can go to new niches, have access to new hosts</li> </ul>
 <p><b>Interaction with animals (hunting, eating, pets)</b></p>	<ul style="list-style-type: none"> <li>• Zoonoses is when a microbe jumps from nonhuman to human hosts</li> </ul>
 <p><b>Changes in agriculture</b></p>	<p>New crops attract new pests</p>
 <p><b>Encroachment on animal habitats</b></p>	<ul style="list-style-type: none"> <li>• Other animals crowded, microbes can mutate, mix</li> <li>• Destruction of rain forests bring humans into contact with unfamiliar microbes</li> </ul>
 <p><b>Urbanization</b></p>	<ul style="list-style-type: none"> <li>• People more crowded together, contagious diseases</li> </ul>
 <p><b>Other</b></p>	<ul style="list-style-type: none"> <li>• Jet travel spreads diseases even when asymptomatic</li> <li>• Ships can carry “unintended passengers”</li> <li>• Breakdown of public health measures, poverty, war, famine, intent to harm</li> </ul>



# SARS 2002-2003 more limited

- In 2002, there was another virus (identified in China) called “SARS” - Severe Acute Respiratory Syndrome (SARS-CoV-1)
- Lasted about 9 months in the world until 2003; 8098 cases, 29 countries, 774 deaths
- 29 cases in U.S. but 0 deaths, more in Canada
- Horseshoe bat, then cat-like mammal called palm civet → human → human to human



# Middle East respiratory syndrome coronavirus in 2012 (MERS-CoV)



- First came out in Saudi Arabia in 2012; all cases linked to Middle East
- Went around world from 2012-2019: 27 countries, 2494 cases, 858 deaths
- United States: 2 cases in May 2014 (Indiana, Florida) – both health care workers from Saudi Arabia
- Was originally in camel and then went to humans then human to human



# SARS-CoV-2 history

- Illness with fever, cough, pneumonia reported from Wuhan, China on New Years' Eve to WHO (December 31, 2019)
- January 7, 2020: Identified etiology a new coronavirus
- Has been spreading around world since then
- January 30, 2020: WHO - "global health emergency"
- March 11, 2020: WHO – "Pandemic"
- March 26, 2020 – US becomes epicenter of pandemic (not for first time)
- December 11, 2020: First EUA from FDA for COVID-19 vaccine in US (Pfizer)
- 6.15 million deaths

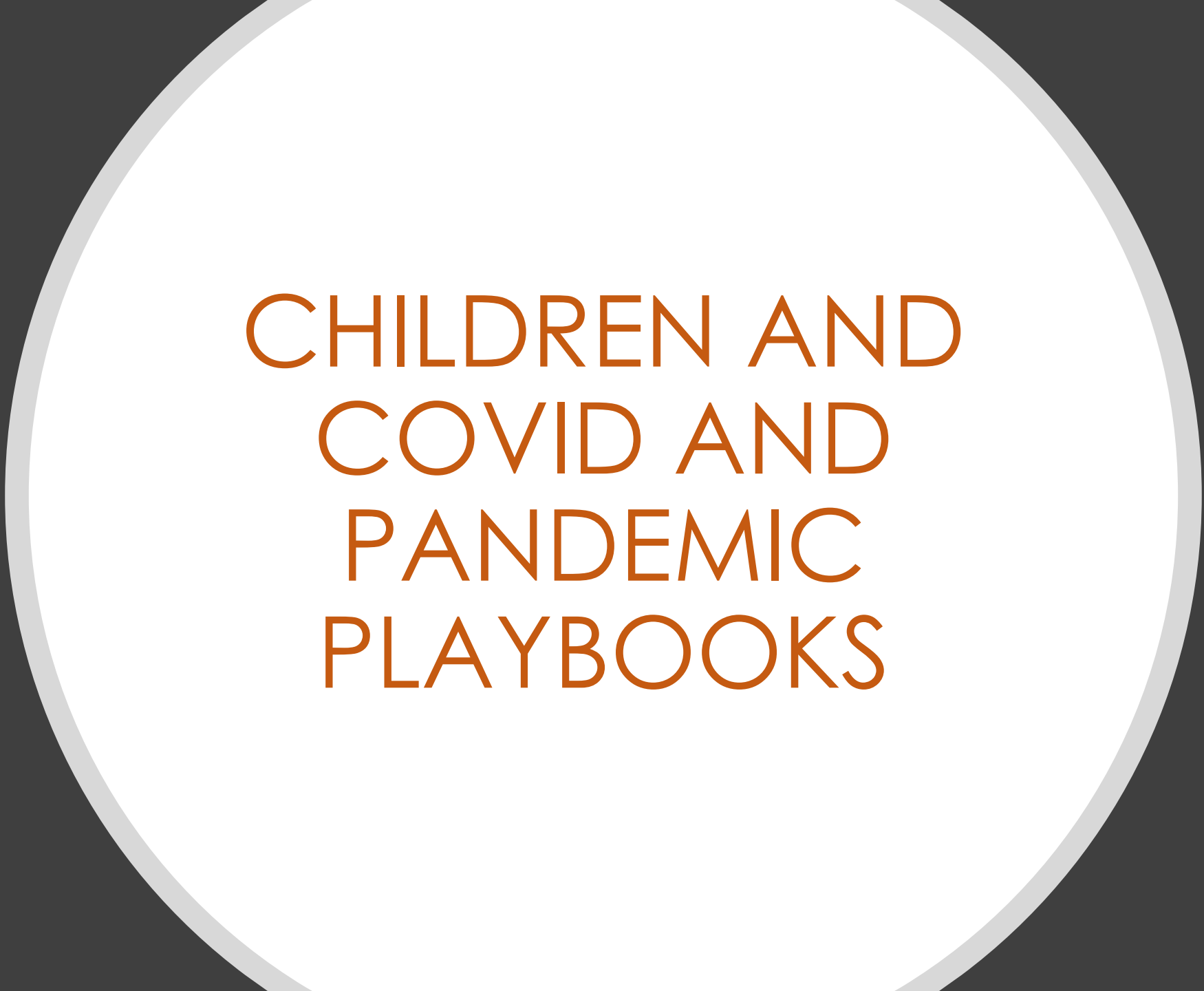




# HIV and COVID-19, something to do with animal treatment

Jane Goodall: COVID-19 is a product of our unhealthy relationship with animals and the environment (commentary)





CHILDREN AND  
COVID AND  
PANDEMIC  
PLAYBOOKS

# Children much less at risk for severe disease than adults

## nature medicine

Article | [Published: 11 November 2021](#)

### Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year

[Clare Smith](#) , [David Odd](#), [Rachel Harwood](#), [Joseph Ward](#), [Mike Linney](#), [Matthew Clark](#), [Dougal](#)

- From March 2020-February 2021, ~12 million children <18 in England
- 3105 died during this time of all causes, 25 from SARS-CoV-2 (0.8%): 22 due to COVID & 3 due to pediatric MISIC
- 99.995% of children 18 with a positive COVID test survived
- In contrast, 99% adults before vaccines survived but that is high mortality rate (100K deaths in England among adults during same period)

# In US

## Widespread vaccination of adults helps protect unvaccinated children,

The New York Times



- Also <0.1% deaths in children from COVID in US <18
- CDC from coding error had overestimated but just removed 25% of pediatric deaths from tracker
- Delta surge in US- we had fewer unvaccinated adults than UK
- Vaccinated adults protect kids

Age Group	COVID-19 Deaths	Total Deaths
All Ages	983,409	7,638,997
Under 1 year	248	42,516
0-17 years	962	75,444
1-4 years	121	7,931
5-14 years	303	12,627
15-24 years	2,592	81,010
18-29 years	6,129	143,041
25-34 years	10,936	171,262
30-39 years	17,807	212,192
35-44 years	27,244	253,771
40-49 years	42,366	318,113
45-54 years	65,639	450,584
50-64 years	184,388	1,291,294
55-64 years	144,569	1,020,383
65-74 years	226,178	1,563,066
75-84 years	253,601	1,852,728
85 years and o	251,978	2,183,119

thebmj covid-19 Research ▾ Education ▾ News & Views

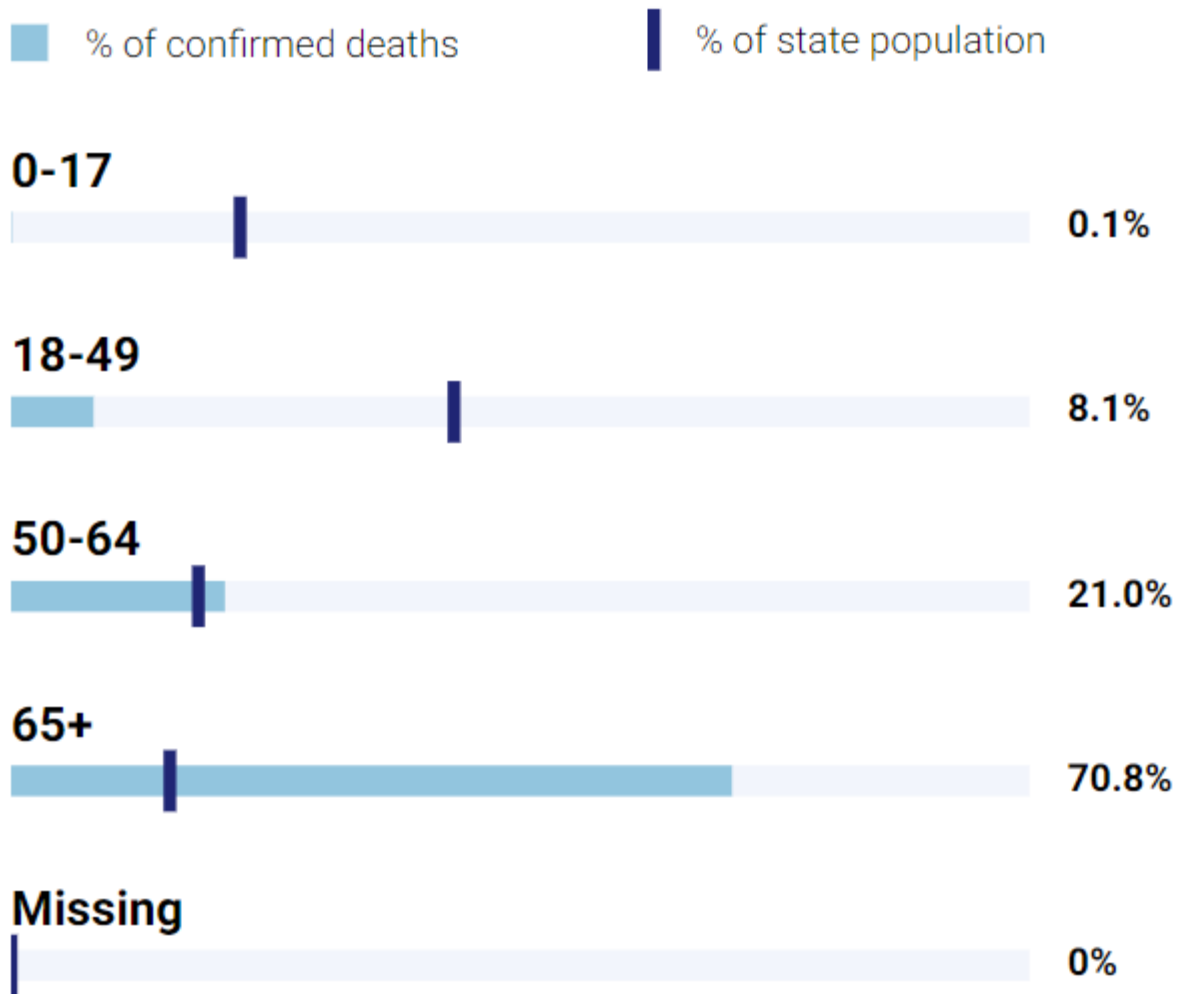
### News

#### Covid-19: US tracker overestimated deaths among children

BMJ 2022 ; 376 doi: <https://doi.org/10.1136/bmj.o831> (Published 29 March 2022)

Cite this as: BMJ 2022;376:o831

## Confirmed deaths by age in California



Ages 0-17 =  
0.1% of COVID  
deaths (23%  
pop) in CA

# Potential mechanism: lower expression of ACE-2 receptors?

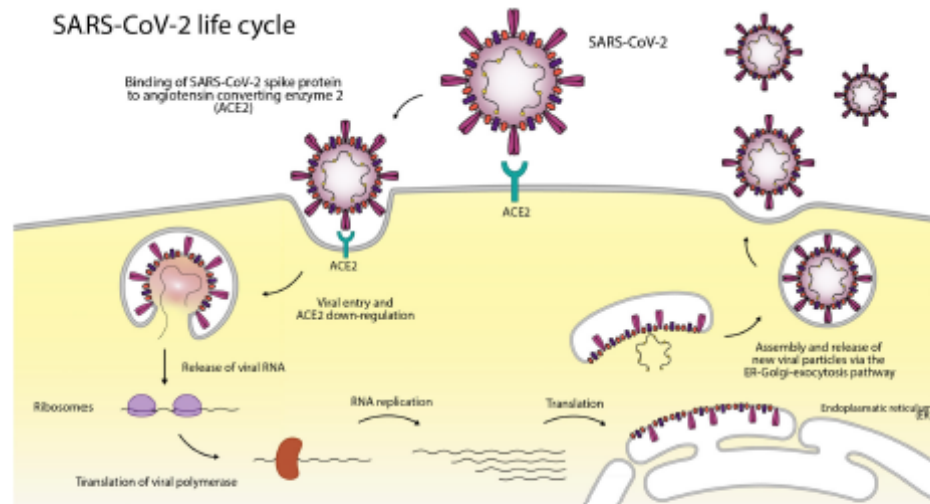
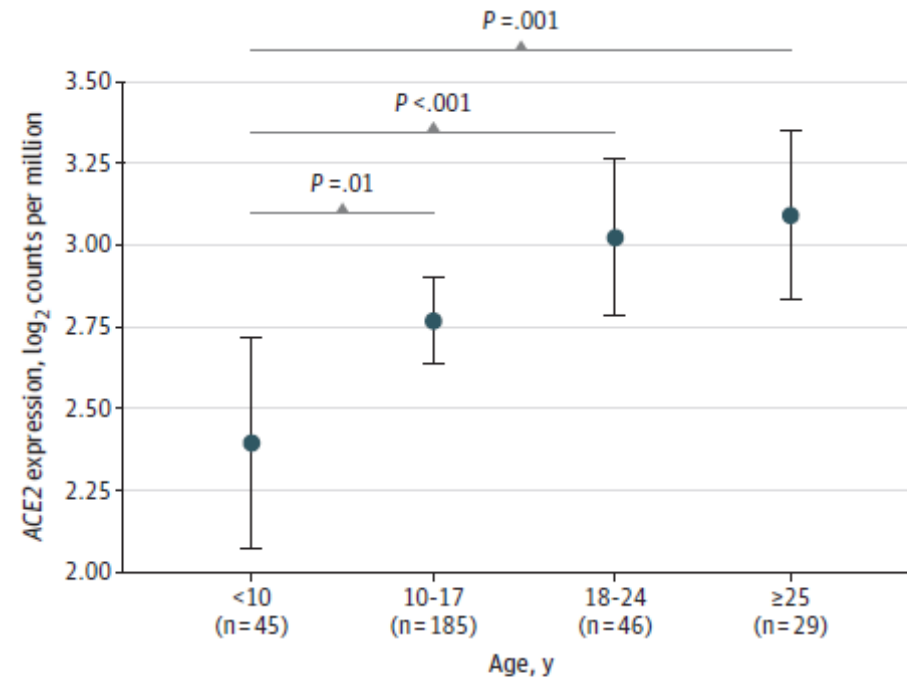


Fig. 1 SARS-CoV-2 life cycle: from binding to ACE2 receptor to shedding

Figure. Nasal Gene Expression of ACE2 in Different Age Groups



## **Kids and COVID: why young immune systems are still on top**

Innate immunity might be the key to why children have fared better with the virus.

By contrast, the children in the study had higher levels of the signalling proteins interferon- $\gamma$  and interleukin-17, which alert the immune system to the arrival of a pathogen. These were probably produced by cells that line the airways, and are involved in mediating innate immunity. Herold suspected that

Innate immune system seems to help children with COVID-19 (72% of children who died of COVID-19 had immune defects or other medical conditions)

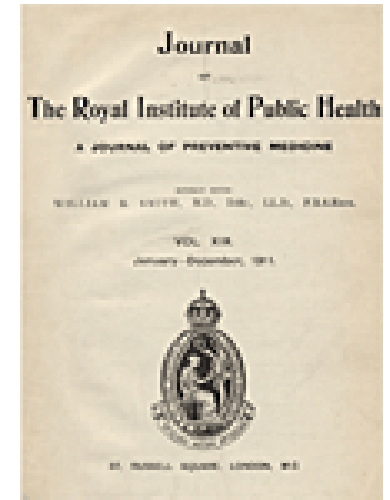
In some pandemics, schools initially closed then opened as no other options for learning- “last resort”

# THE LANCET

Volume 140, Issue 3612, 19 November 1892, Page 1180

## MEASLES AND SCHOOL CLOSURE.

MEASLES is rife just now in many parts of the country, as at Motherwell in Scotland and Tipton in Staffordshire. The absentees from school at the former place number 27 per cent. of the scholars, at the latter about 50 per cent. In face of this, the question of closing the schools at Dalziel has been adjourned for a week by the Motherwell authorities; whilst at Tipton nothing has been done beyond characterising the report of the school attendance officer as “exaggerated.” School authorities seem to be still slow to learn that it is the wisest plan to allow their schools to be closed in the early beginnings of an epidemic, before widespread prevalence has rendered their tardy acquiescence in closure a futile and nugatory step. \_\_\_\_\_



18

*The Control of Diphtheria in Schools*

## THE CONTROL OF DIPHTHERIA IN SCHOOLS.

BY

THOMAS ORR, M.D., B.Sc.

Assistant County Medical Officer to the West Riding of Yorkshire.

THERE is little doubt that intercourse at school is an important factor in the spread of diphtheria. A child may become infected at school, carry the infection to other members of his family, and by them the infection may be carried to other families and to other schools, and even to other districts. Infection at school and at the home are thus intimately related, and therefore the means of controlling the disease must be employed concurrently at both places. Diphtheria is essentially a disease of the early years of life,



ID pandemics and  
school closures-  
Influenza doesn't  
differentially spare  
younger children

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NATIONAL STRATEGY FOR  
**PANDEMIC  
INFLUENZA**

IMPLEMENTATION PLAN



HOMELAND SECURITY COUNCIL

MAY 2006

In 1918 influenza  
pandemic,  
schools closed for  
4 months at most

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**3 lessons from how schools  
responded to the 1918 pandemic  
worth heeding today**



AUG 5, 2020

# At Height of the 1918 Pandemic, NYC and Chicago Schools Stayed Open. Here's Why

Amid fierce controversy, public health officials in both cities decided children would be better off in classrooms.

# By 1918, high public school attendance and mandatory attendance laws in each state; schools were place for food, learning and safety

As the second wave of the Spanish flu hit in September 1918, Dr. Royal S. Copeland, a homeopathic physician and the city's health commissioner, initially considered school closures as a way of limiting the pandemic's spread. But Dr. S. Josephine Baker, director of the Department of Health Bureau of Child Hygiene and a leading Progressive reformer, persuaded Copeland to keep the city's schools open, according to [a 2010 article co-authored by Dr. Alexandra Stern](#). Baker argued that kids were better off contained in schools, and that regular medical inspections could identify sick students and keep healthy ones safe.

At the time, New York City's public school system contained close to 1 million children, and 750,000 of those lived in crowded and often unsanitary tenement homes. In an [article headlined "Epidemic Lessons Against Next Time,"](#) published in the *New York Times* in November 1918, after the worst of the pandemic had passed, Copeland described the advantages in keeping the schools open: "[Children] leave their often unsanitary homes for large, clean, airy school buildings, where there is always a system of inspection and examination enforced," he said.



# “Better Off in School”: School Medical Inspection as a Public Health Strategy During the 1918–1919 Influenza Pandemic in the United States

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ALEXANDRA MINNA STERN, PhD<sup>a</sup>

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## SYNOPSIS

During the 1918–1919 influenza pandemic in the United States, most cities responded by implementing community mitigation strategies, such as school closure. However, three cities—New York City, Chicago, and New Haven, Connecticut—diverged from the dominant pattern by keeping their public schools open while the pandemic raged. This article situates the experiences of these three cities in the broader context of the Progressive era, when officials and experts put great faith in expanding public programs in health and education. It adds an important dimension to the historical understanding of the

## GUARD AGAINST INFLUENZA

Influenza is spread by drop-lets sprayed from the nose and throat.

Cover each cough and sneeze with handkerchief.

Avoid crowds.

Get plenty of fresh air.

Do not spit on the floor or on the sidewalk.

Do not use common drinking cups and common towels.

Avoid excessive fatigue.

If taken ill, go to bed and send for a doctor.

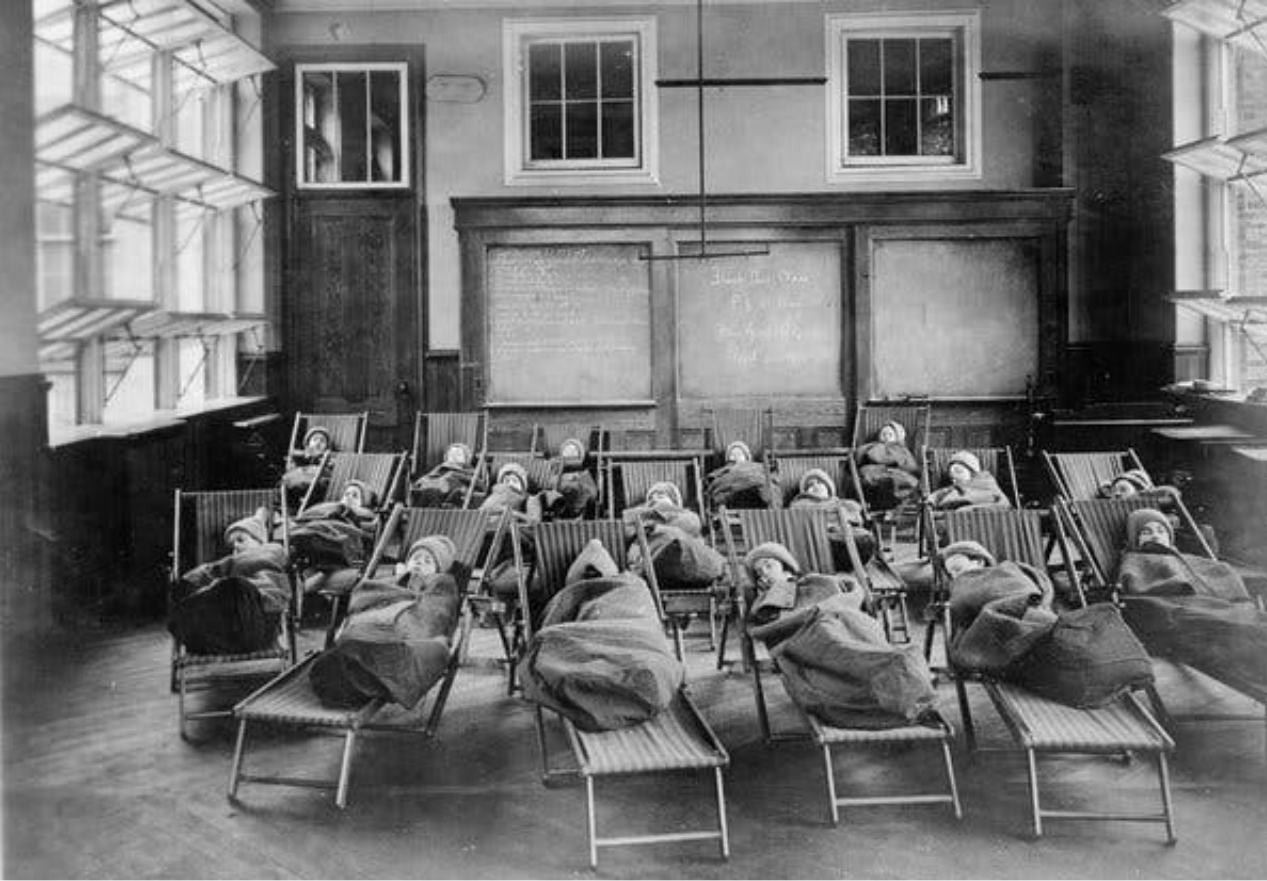
Walk to work, if possible.

These rules apply also to colds, bronchitis, pneumonia, and tuberculosis.



Ontario schools practiced  
blowing noses but stayed open

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Other cities (like Berkeley) closed schools but for 4 months at most as no other option; others held school outside



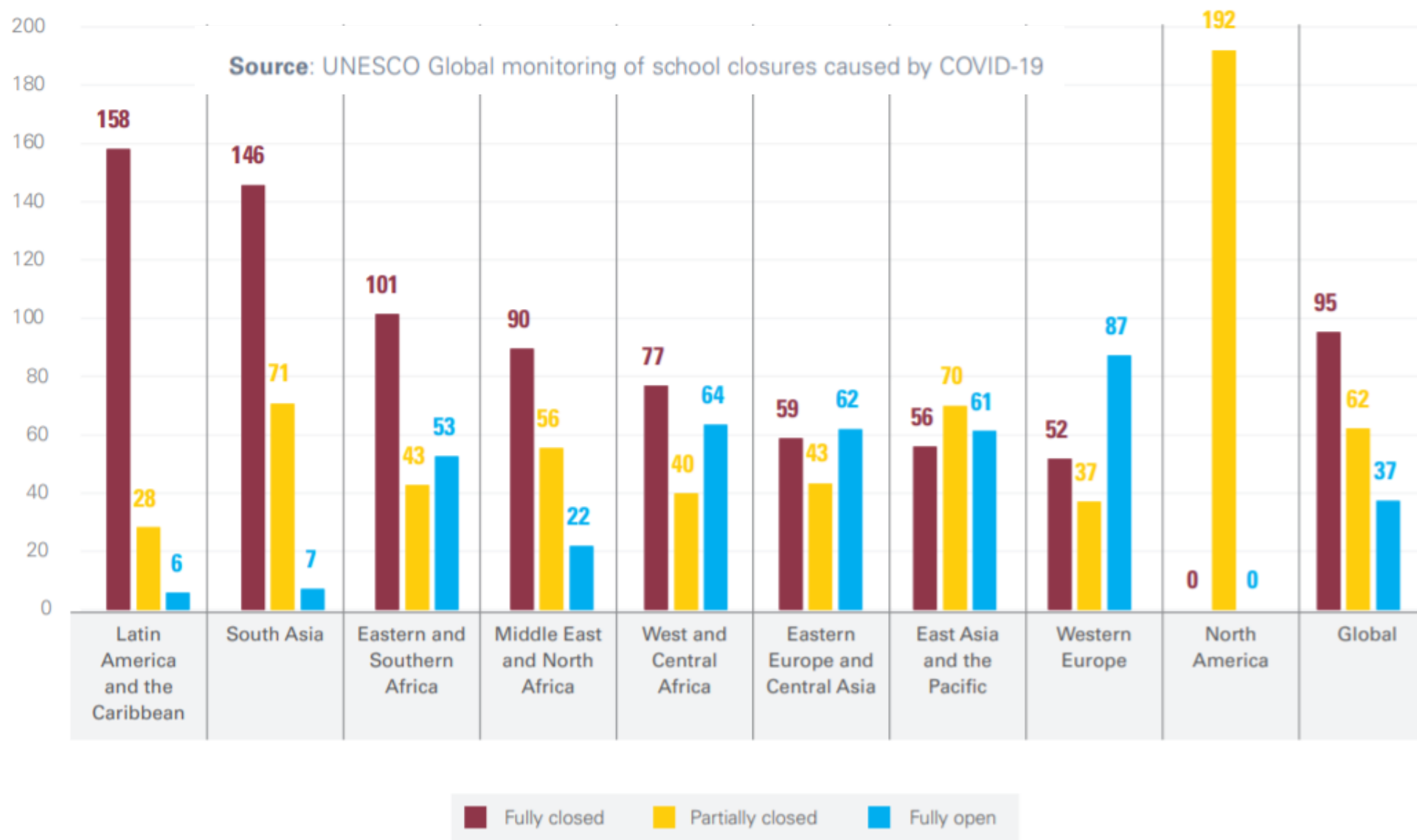
Schools re-opened in  
US in 1918 with  
following:

- Sometimes masks, not universally
- Outside work
- Wide open windows for ventilation
- School nurses
- Stay home when sick
- Wash hands
- School lunch programs



FIGURE 2

School closure status in number of days and by region, from March 2020 to February 2021 (weighted average)



Despite overwhelming evidence of the impact of school closures on children, and despite increasing evidence that schools are not drivers of the pandemic, too many countries have opted to keep schools closed, some for nearly a year.

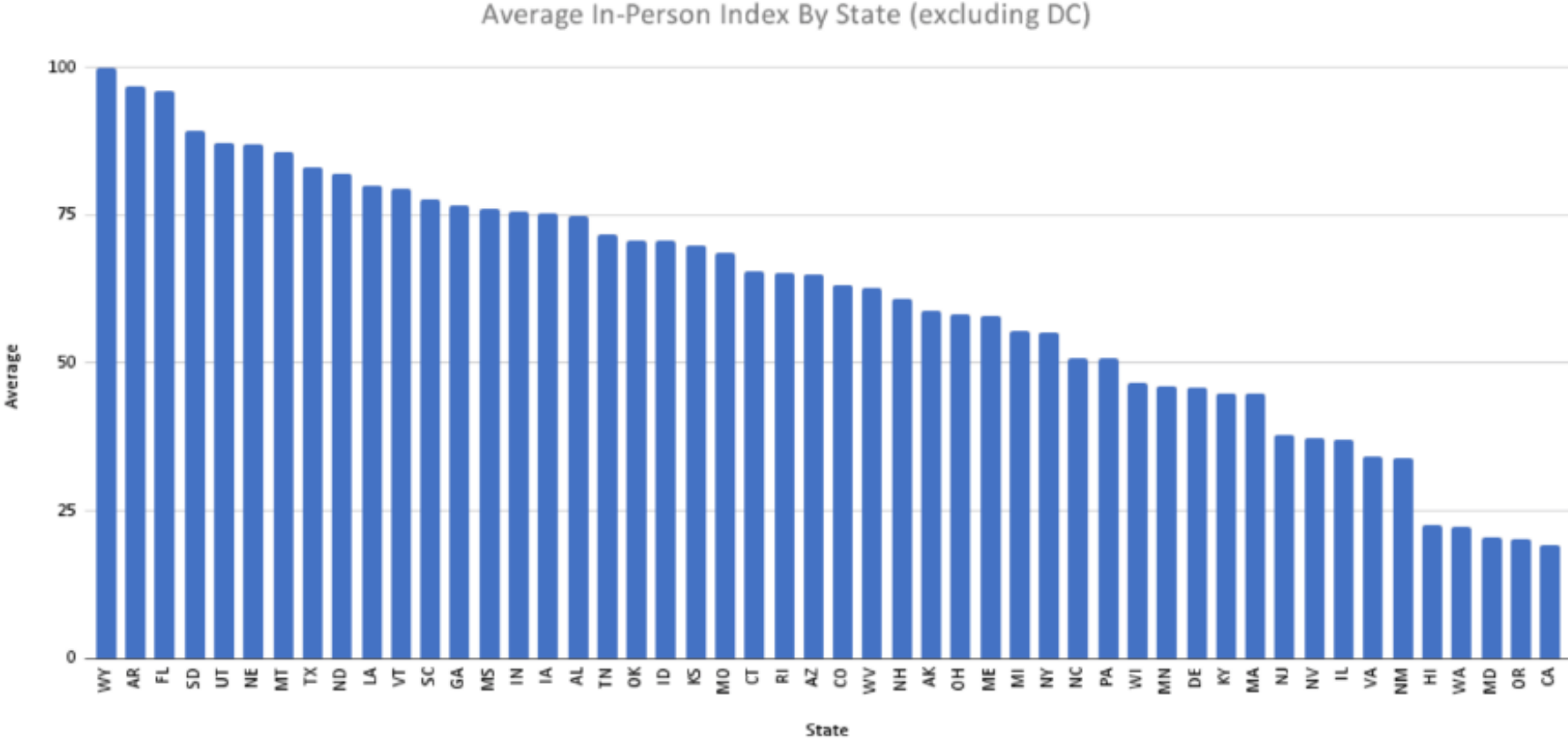
Schools are essential for children's learning, health, safety and well-being. For the most vulnerable children, school closures have deprived them of their one nutritious meal a day; children living in violent or dysfunctional family settings who rely on school to provide a safe, nurturing environment have also been cut off from this safety net (Borkowski *et al*, 2020; WHO, 2020). In many countries, schools also play essential role in immunization and health support.



CLASS ATTENDANCE

ABSENT: 168 MILLION CHILDREN

# Mixed re-opening in the United States 2020-2021 School Year



Source: <https://cai.burbio.com/school-opening-tracker/>

# Fall 2020: Transmission in school settings < community

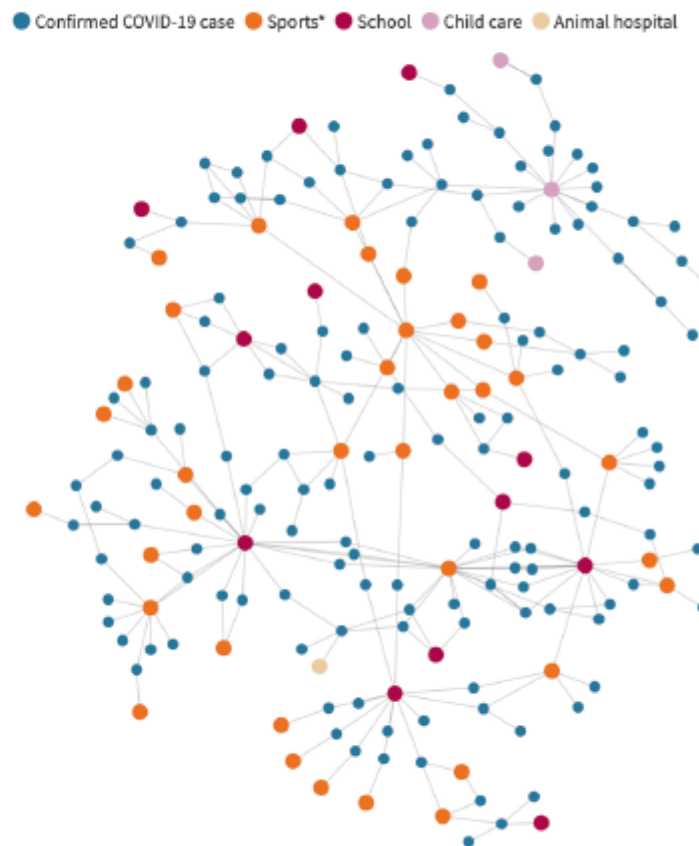
Setting	Time Period	# Students/Staff	Community Spread (per 100K/week)	Masks	Distance	Ventilation	Other	In School Transmission
Chicago Parochial Schools	Aug - Oct 2020	19,500/2,750	65 - 93 cases	Yes	6ft	Not described	Handwashing Symptom screening & Temp checks	3 clusters (2 staff -> staff, 1 staff -> student)
North Carolina Public Schools	Aug - Oct 2020	~100,000	100 - 200 cases	Yes	6ft	No	Handwashing Symptom screening & Temp checks	32 cases (no student -> staff)
NYC Public Schools	Oct - Nov 2020	~288,000/80,000	89 - 297 cases	Yes	6ft	Open windows/upgrades (where)	Hybrid Surveillance testing	0.5% secondary attack rate (staff index 78% of cases)
Wisconsin Public Schools	Sep - Nov 2020	4,876/654	~420 cases	Yes	6 ft	Not described	Cohorting	7 cases
Georgia Public Schools	Dec 2020 - Jan 2021	2,600/700	194 - 704 cases	Yes	<3ft + plexiglass	Not described	Cohorting	9 clusters of ≥3 cases (13 staff/32 students)
Utah Public Schools	Dec 2020 - Jan 2021	10,171/1,214	290 - 670 cases	Yes (86%)	3ft	Open doors/windows (80%) Air Filtration	Enhanced hand hygiene/disinfection	5 cases (secondary attack rate 0.7%)

Fricchione et al, *J Public Health Practice and Management*, 2020; Zimmerman et al, *Pediatrics* 2021; Varma et al, *Pediatrics* 2021; Falk et al, *MMWR* 1/26/21; Gold et al, *MMWR* 2/22/21; Hershov et al, *MMWR* 3/19/21

Slide courtesy of Lillian Brown MD, PhD

# Schools not major source of infection for youth

- Cases in schools highly correlated to case rates in the community<sup>1,2</sup>
- Close contact with a known case, social gatherings most likely to be associated with infection in school age children<sup>2</sup>
- Activities associated with youth sports emerged as source of outbreaks/transmission<sup>3,4</sup>



*\*Sports includes 10 high school teams, 10 club teams, 12 teams in a sports association, and three fitness/rec centers.*

1. Doyle et al, MMWR 2021; 2. Hobbs et al, MMWR 2021; 3. Siegel et al, MMWR 2021; 4. Minnesota Department of Public Health

# PROTECTING YOUTH MENTAL HEALTH

*The U.S. Surgeon General's Advisory*

December 2021



**AAP, AACAP, CHA declare national emergency in children's mental health**

October 19, 2021

# Large test-to-stay program in MA winter 21-22



## 'In-school transmission extremely rare' as Mass. starts new COVID-19 at home tests for students, teachers

1/18/2022

- Large test to stay program launched fall-winter 2021
- As of Jan. 9, 2022: 503,312 Test and Stay tests had been conducted; 496,440 of them were negative (almost 99%)
- Formed basis of Policy Lab recommendation CHOP on testing

Nearly half of LAUSD students have been chronically absent this year, data show

MARCH 31, 2022 **Los Angeles Times**

**The Washington Post**

LAUSD has asymptomatic surveillance testing; SFUSD does not in 2021-2022 school year



# School quarantines keep too many kids at home — with barely any effect on covid

Some states and school districts are shifting — against the CDC's advice — to a sensible 'test and stay' approach

By Jeffrey Vergales and Monica Gandhi

October 5, 2021 at 6:00 a.m. EDT





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

## EMERGING INFECTIOUS DISEASES®

### Lessons from the History of Quarantine, from Plague to Influenza A

Eugenia Tognotti✉

surveillance proved effective in containing the global threat in just over 3 months. For centuries, these practices have been the cornerstone of organized responses to infectious disease outbreaks. However, the use of quarantine and other measures for controlling epidemic diseases has always been controversial because such strategies raise political, ethical, and socioeconomic issues and require a careful balance between public interest and individual rights. In a globalized world that is becoming ever more vulnerable to communicable diseases, a historical perspective can help clarify the use and implications of a still-valid public health strategy.

# Roadmap – Policy Lab Children’s Hospital of Pennsylvania

- **Vaccinate:** Down to 5 now but 6 months-6 years coming (Moderna 25 micrograms x 2)
- **Masks:** Mask mandates for all release on hospitalization metrics in community (e.g. <10/100K COVID hospitalizations)- CDC did this on February 24, 2022
- **Testing:** No more asymptomatic testing in schools per Policy Lab, CHOP
- **Symptoms:** Symptom based management, stay home when sick
- **Ventilation**
- **No quarantines (wear mask if exposed)**
- School nurses
- Restore joy to school










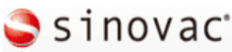

## SMERCONISH

*for Independent Minds*

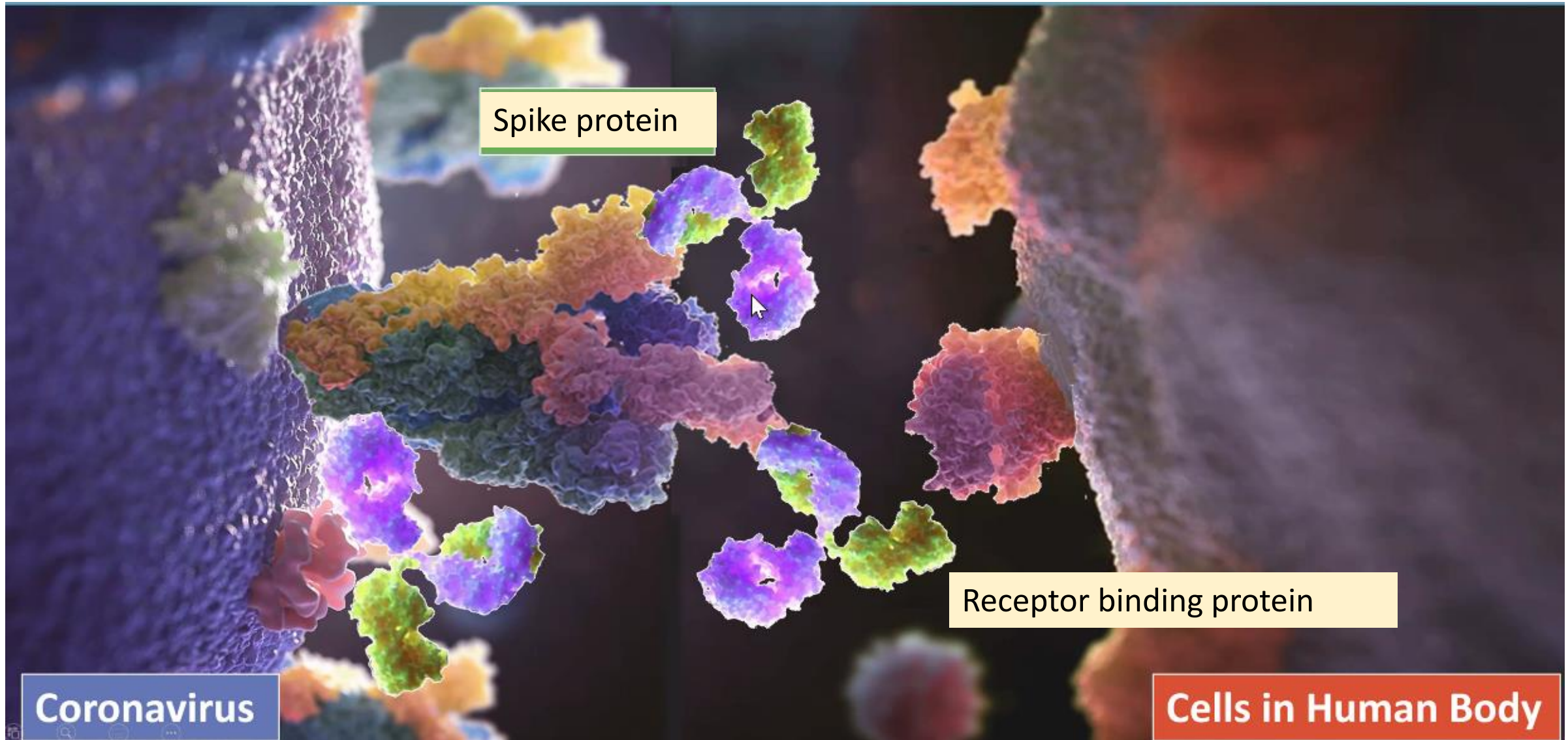
**A Roadmap to COVID-19 Endemicity  
in Schools**

# COVID VACCINES AND VARIANTS

There are actually 8 unique vaccines approved by WHO for COVID-19 (Sputnik V pending), three authorized in U.S.

Company or name	Type of vaccine	Reference
	mRNA vaccine	<a href="#">Baden NEJM</a> , Feb 4, 2021
	mRNA vaccine	<a href="#">Polack NEJM</a> , December 31, 2020
	Adenovirus + DNA vaccine	J&J <a href="#">press release</a> January 29, 2021; <a href="#">FDA document</a> Feb 24
 AstraZeneca	Adenovirus + DNA vaccine	<a href="#">Voysey Lancet</a> December 8, 2020; <a href="#">Preprint</a> Feb 1, 2021
 NOVAVAX Creating Tomorrow's Vaccines Today	Spike protein + an adjuvant	Novavax <a href="#">press release</a> June 14; Novavax <a href="#">NEJM</a> June 30, 2021
	Adenovirus + DNA vaccine	<a href="#">Logunov Lancet</a> , February 2, 2021
	Whole inactivated virion	<a href="#">Sinopharm</a> , JAMA, May 28, 2021
	Whole inactivated virion	<a href="#">Sinovac</a> , JAMA May 28, 2021
	Whole inactivated virion	<a href="#">Bharat Covaxin</a> , April 21, 2021

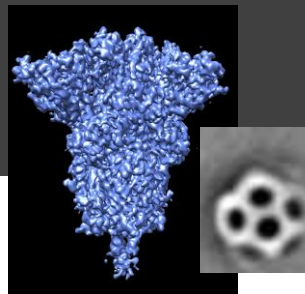
6 vaccine candidates to date involve spike protein and receptor binding domain of SARS-CoV-2 - either mRNA or adenoviral-vector DNA vaccines or protein adjuvant itself; 3 inactivated virus



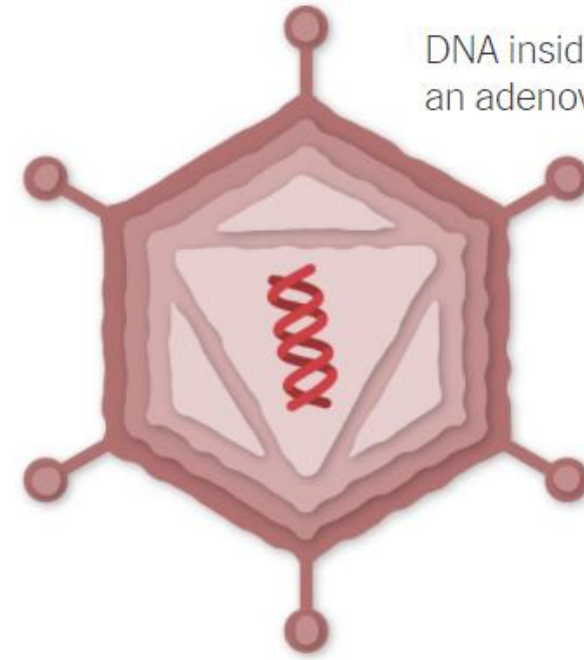
# Three types of vaccines involving spike protein

- 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



DNA inside  
an adenovirus

Johnson & Johnson

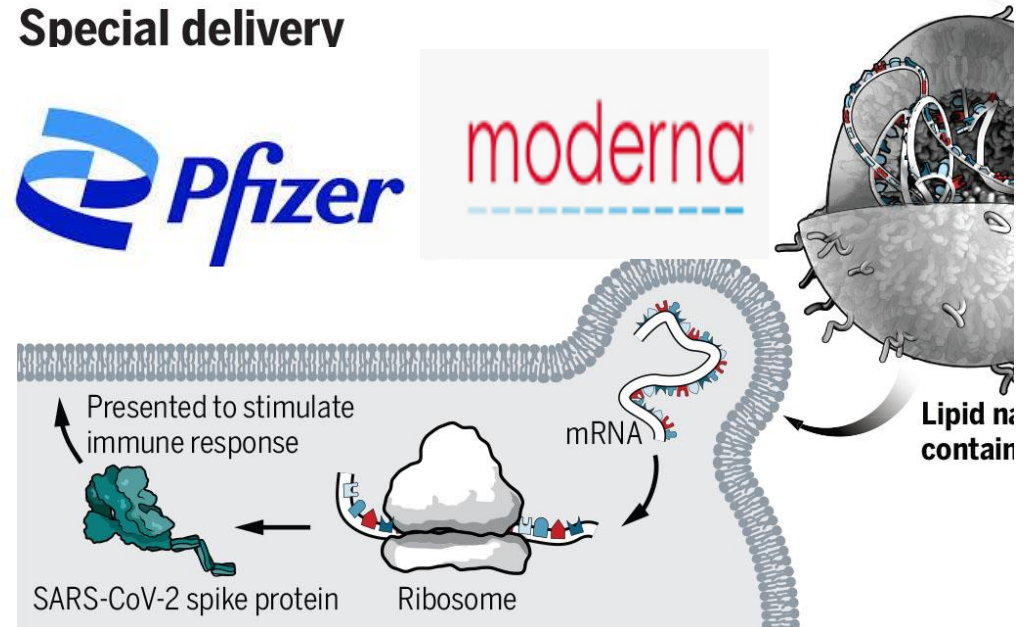
AstraZeneca

Sputnik V

## Special delivery

Pfizer

moderna



Presented to stimulate  
immune response

SARS-CoV-2 spike protein

Ribosome

mRNA

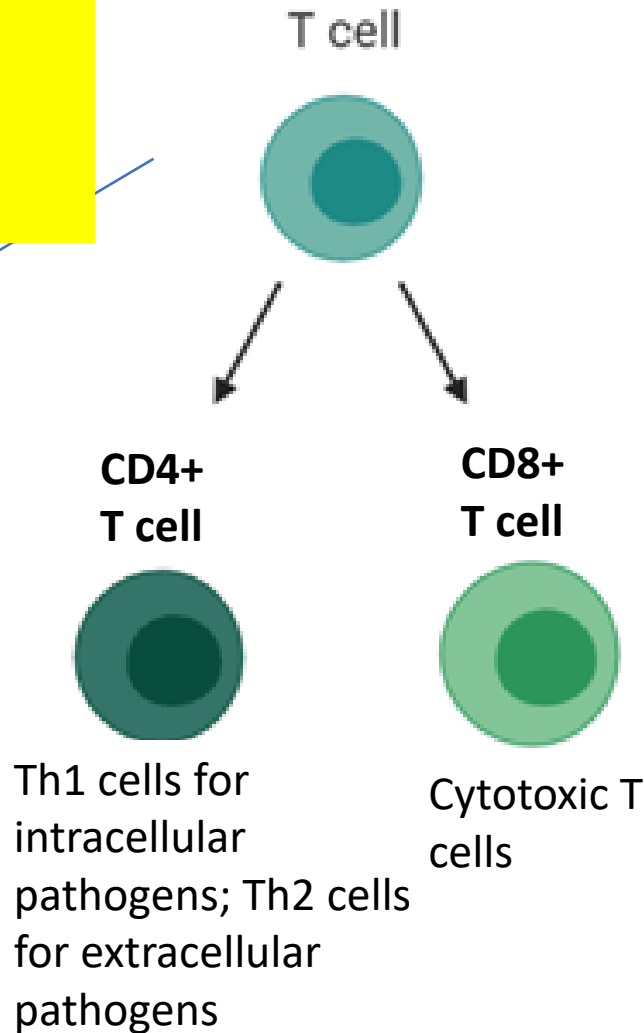
Lipid nanoparticles contain

# Remember immunity -antibodies and cell-mediated

**T cells are the major immune defense against viruses; preserved**

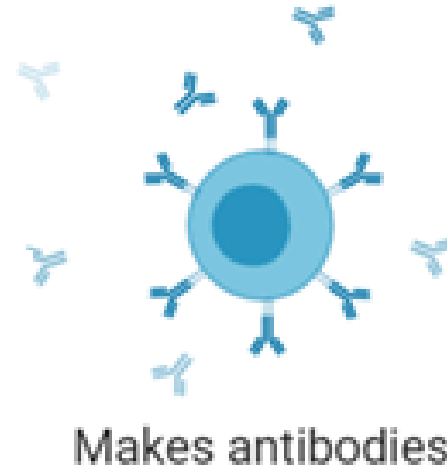
Memory T cells

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









B cell

Plasma cell






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

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
	mRNA-1273 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+ protection from challenge (macaques)	~15,000	90% (1 in vaccine arm <a href="#">after 2nd dose hospitalized</a> )	97% (30 cases in placebo arm; 0 in vaccine reported but 1 severe per FDA)	94.1%
	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- <a href="#">1 initially severe but not</a> )	95%
	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)
	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
	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
	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 ( <a href="#">Lancet</a> )	11,000 ( <a href="#">press release</a> 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%

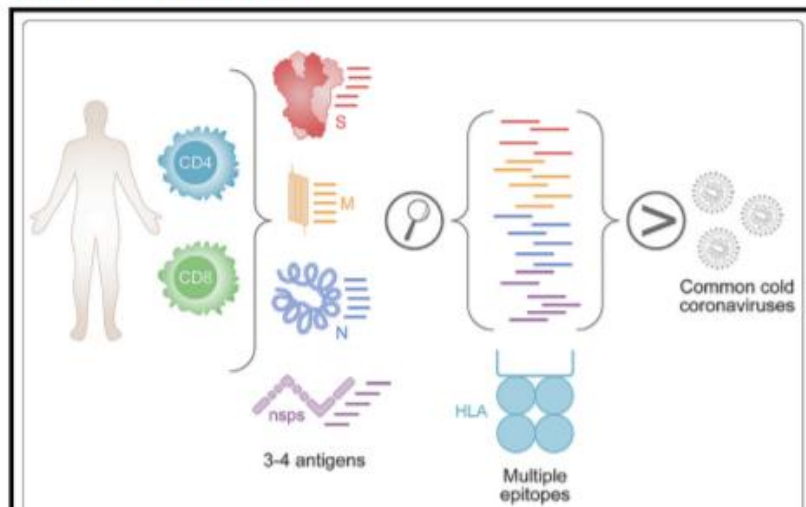
# T cells work against variants

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

COVID-19

nature reviews immunology

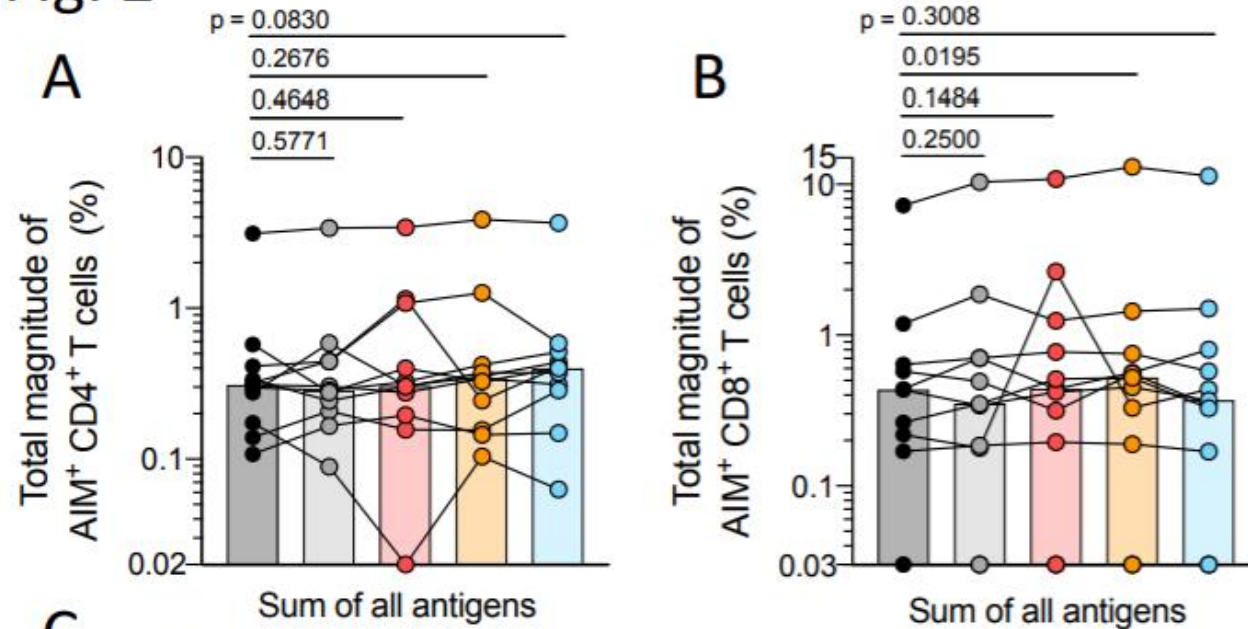
# Cross reactive T cells hold up against Omicron

# Then look at T-cell response to variants after vaccines- still intact- and expand with every exposure

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 Goodwiri 

Fig. 2



- T cell reactivity against variants remain intact if you had natural infection or mRNA vaccination from alpha to Omicron

Cell

Article

**SARS-CoV-2 vaccination induces immunological T cell memory able to cross-recognize variants from Alpha to Omicron**

Graphical abstract

Authors

Alison Tarke, Camila H. Coelho,

Article | Published: 05 April 2022

**SARS-CoV-2 antigen exposure history shapes phenotypes and specificity of memory CD8<sup>+</sup> T cells**

COVID-19

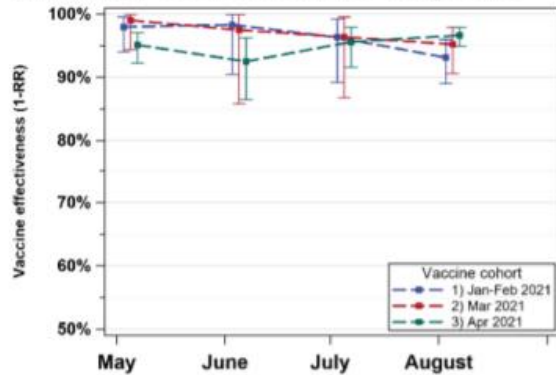
**Cross reactive T cells hold up against Omicron**

Anastasia A. Minervina, Mikhail V. Pogorelyy, Allison M. Kirk, Jeremy Chase Crawford, E. Kaitlynn Allen,

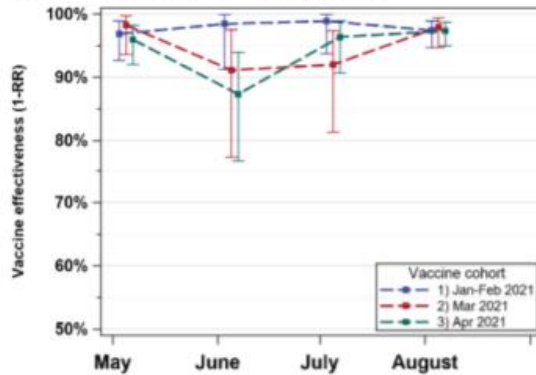
<sup>1</sup>Madhi. NEJM. March 16, 2021; Ma. Biorxiv April 29, 2021; deMarco. bioRxiv 2021.12.30.474453.

# Data from NY during delta shows that vaccine effectiveness AGAINST SEVERE DISEASE not waning except for older individuals

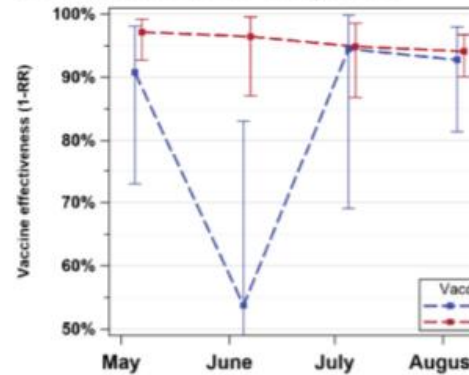
**A. Pfizer-BioNTech, 18-49 years**



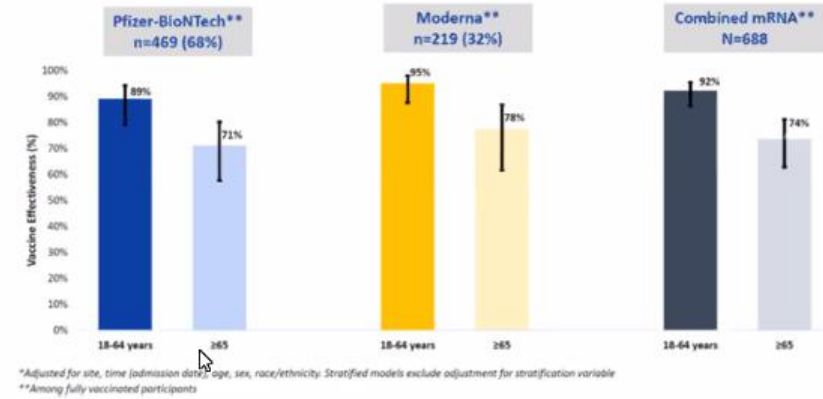
**B. Moderna, 18-49 years**



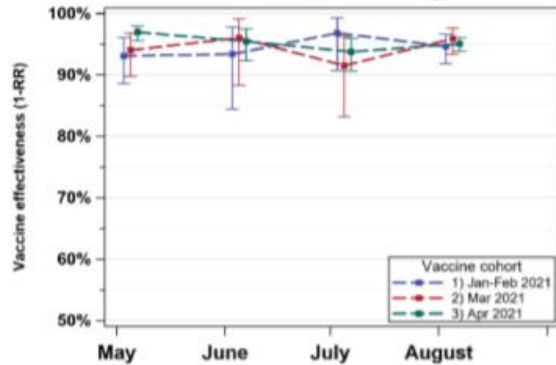
**C. Janssen, 18-49 years**



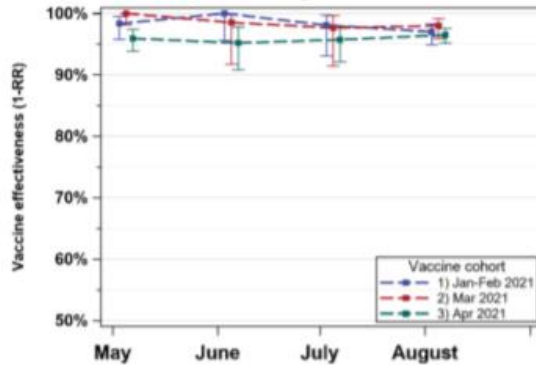
**VE\* against COVID-19-associated Hospitalization, by mRNA vaccine — SUPERNOVA Network, February 1–September 17, 2021**



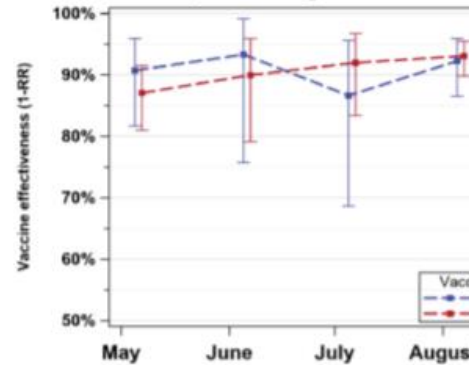
**D. Pfizer-BioNTech, 50-64 years**



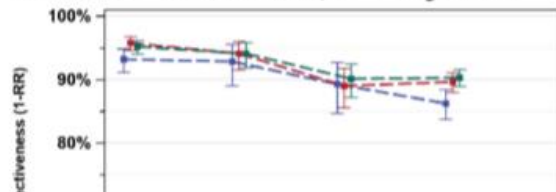
**E. Moderna, 50-64 years**



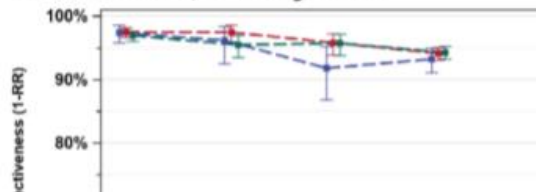
**F. Janssen, 50-64 years**



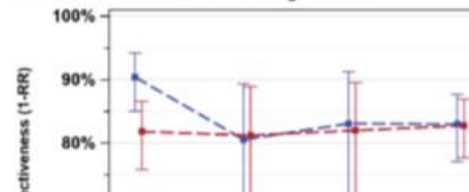
**G. Pfizer-BioNTech, >=65 years**



**H. Moderna, >=65 years**

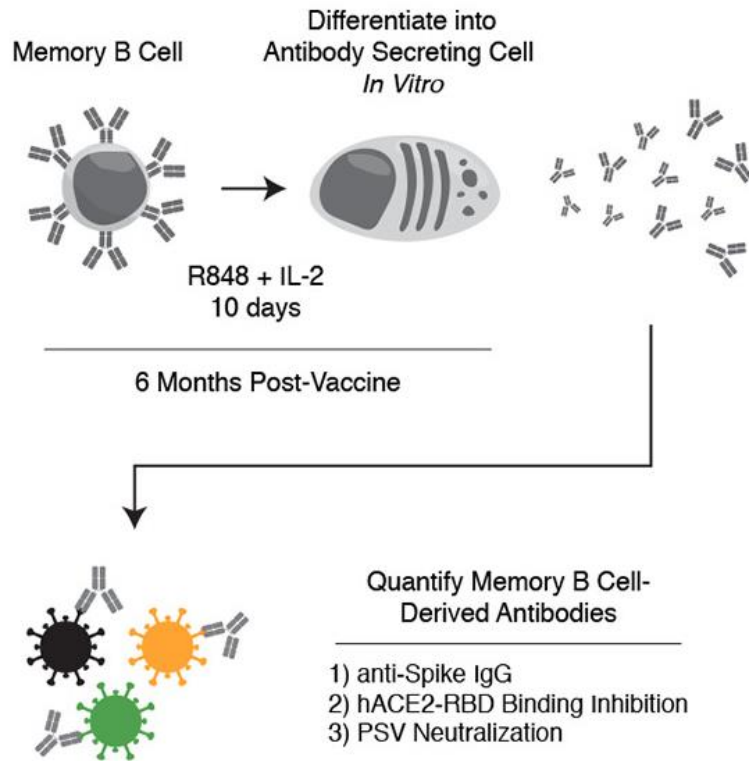


**I. Janssen, >=65 years**



<https://www.medrxiv.org/content/10.1101/2021.10.08.21264595v1.full.pdf>

# Memory B cells from vax or infection adapt to whatever variant they see; T cells cover any variant



Science

RESEARCH ARTICLES

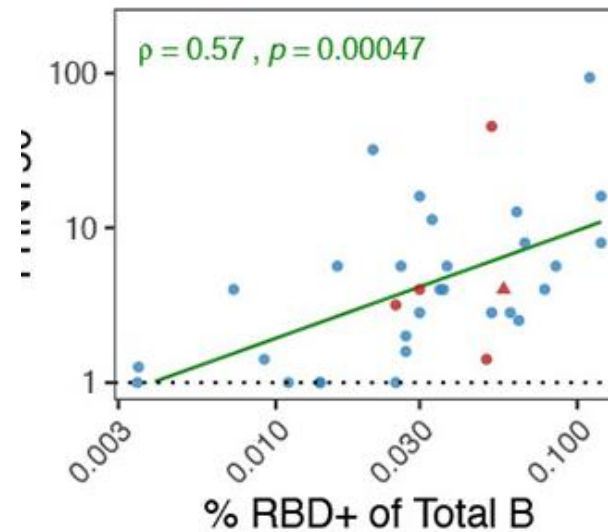
Cite as: R. R. Goel *et al.*, *Science* 10.1126/science.abm0829 (2021).

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

Rishi R. Goel<sup>1,2+</sup>, Mark M. Painter<sup>1,2+</sup>, Sokratis A. Anostolidis<sup>1,2,3+</sup>, Divii Mathew<sup>1,2+</sup>, Wenzhao Meng<sup>1,4</sup>, Aaron M.

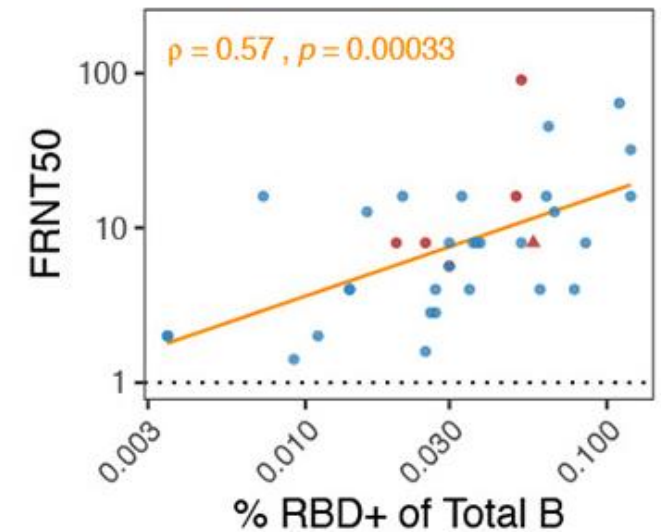
N

BETA VARIANT



O

DELTA VARIANT



ARTICLE | ONLINE NOW

PDF [37 MB] Figures





### Efficient recall of Omicron-reactive B cell memory after a third dose of SARS-CoV-2 mRNA vaccine

Rishi R. Goel<sup>†</sup> • Mark M. Painter<sup>†</sup> • Kendall A. Lundgreen • ... Paul Bates • Allison R. Greenplate • E. John Wherry

Published: April 07, 2022 • DOI: <https://doi.org/10.1016/j.cell.2022.04.009>

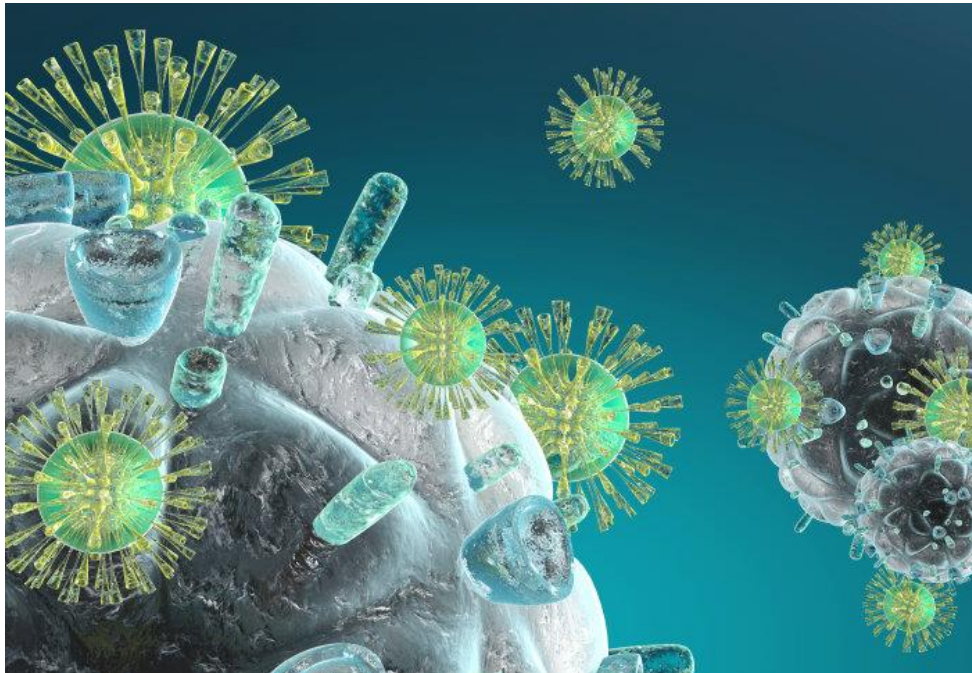


**World Health  
Organization**

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

## Omicron's feeble attack on the lungs could make it less dangerous

Mounting evidence from animal studies suggests that Omicron does not multiply readily in lung tissue, which can be badly damaged in people infected with other variants.



## Omicron- similarities to end of 1918 influenza pandemic?

- More and more immunity in the population – 60-75% of the world's population may be exposed to Omicron
- On top of an 80% seroprevalence in adults in S. Africa for instance (70% in children by NIH study in US)
- A less virulent influenza variant in 1918? (3<sup>rd</sup> wave)
- If you see Omicron, you get immunity across whole virus
- If not, a booster will help; older patients should get booster if infected prior- hybrid immunity
- In the future we may need whole inactivated virus vaccine as a booster (Covaxin, etc.)- to get immunity across whole virus to combat variants

# Whom did 1<sup>st</sup> booster benefit? And 4<sup>th</sup> shots?

- Data from CDC (February 18), Israel, and UK converged on the fact that boosters most benefitted those over 65 & some benefit over 50 (4/million deaths vs 1/million deaths)
- NEJM study December 23, 2021 showed no COVID-19 deaths in those 18-29 with two doses of the vaccine (0 deaths in 3 vs 2 doses)
- NEJM study looked at 4<sup>th</sup> shot in health care workers & found no benefit <60
- European CDC approved for >80; White House encouraging for >60

ORIGINAL ARTICLE

## Protection against Covid-19 by BNT162b2 Booster across Age Groups

Yinon M. Bar-On, M.Sc., Yair Goldberg, Ph.D., Micha Mandel, Ph.D., Omri Bodenheimer, M.Sc., Laurence Freedman, Ph.D., Sharon Alroy-Preis, M.D., Nachman Ash, M.D., Amit Huppert, Ph.D., and Ron Milo, Ph.D.

ABSTRACT

**44x Higher in Unvaccinated Adults Ages 18 Years and Older**

**30x Higher**  
in Unvaccinated Adults  
Ages 18-49 years

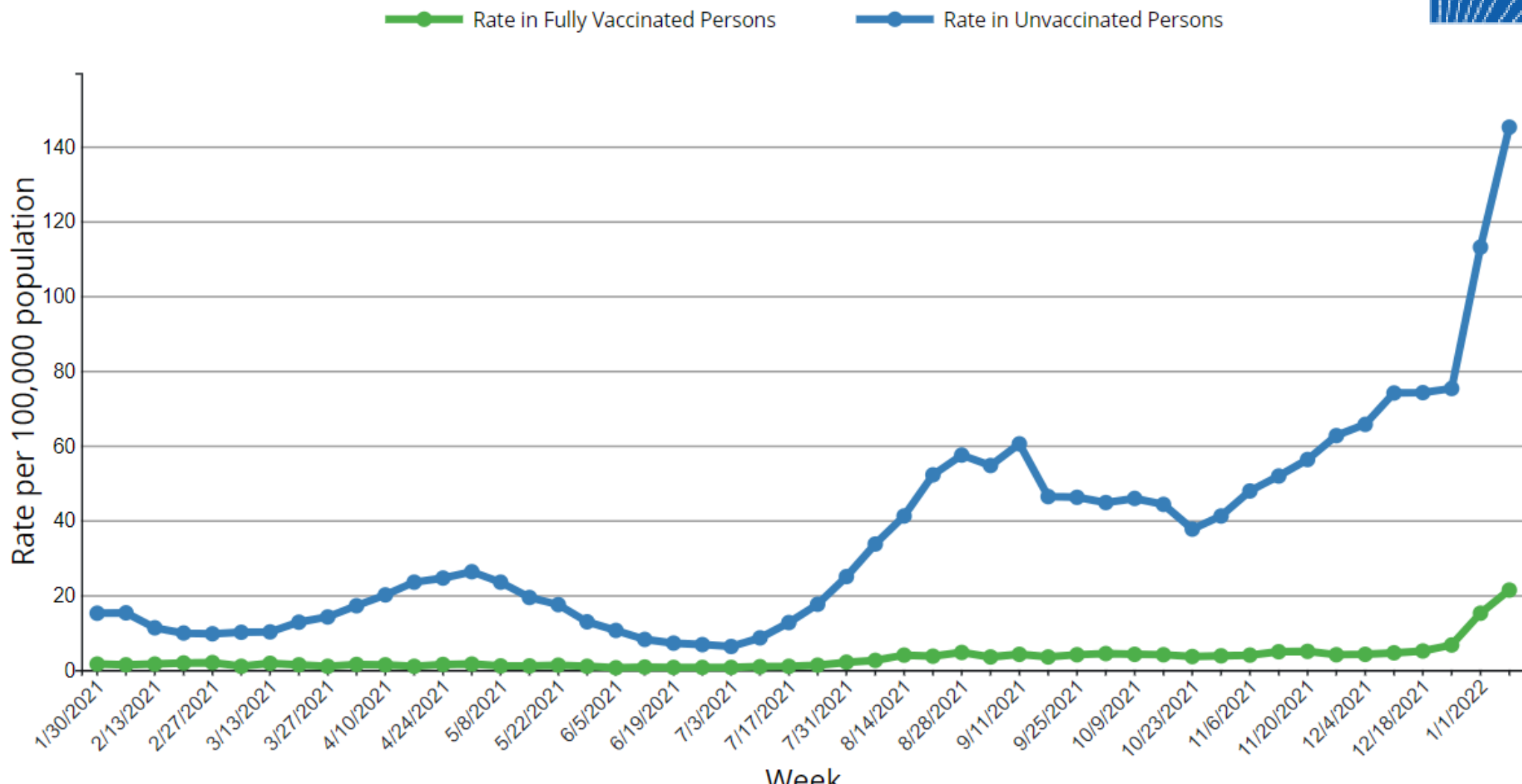
**45x Higher**  
in Unvaccinated Adults  
Ages 50-64 years

**51x Higher**  
in Unvaccinated Adults  
Ages 65 Years and Older



# Age-Adjusted Rates of COVID-19-Associated Hospitalizations by Vaccination Status in Adults Ages $\geq 18$ Years, January 2021–January 2022

During Omicron surge





# After 2-dose vaccination

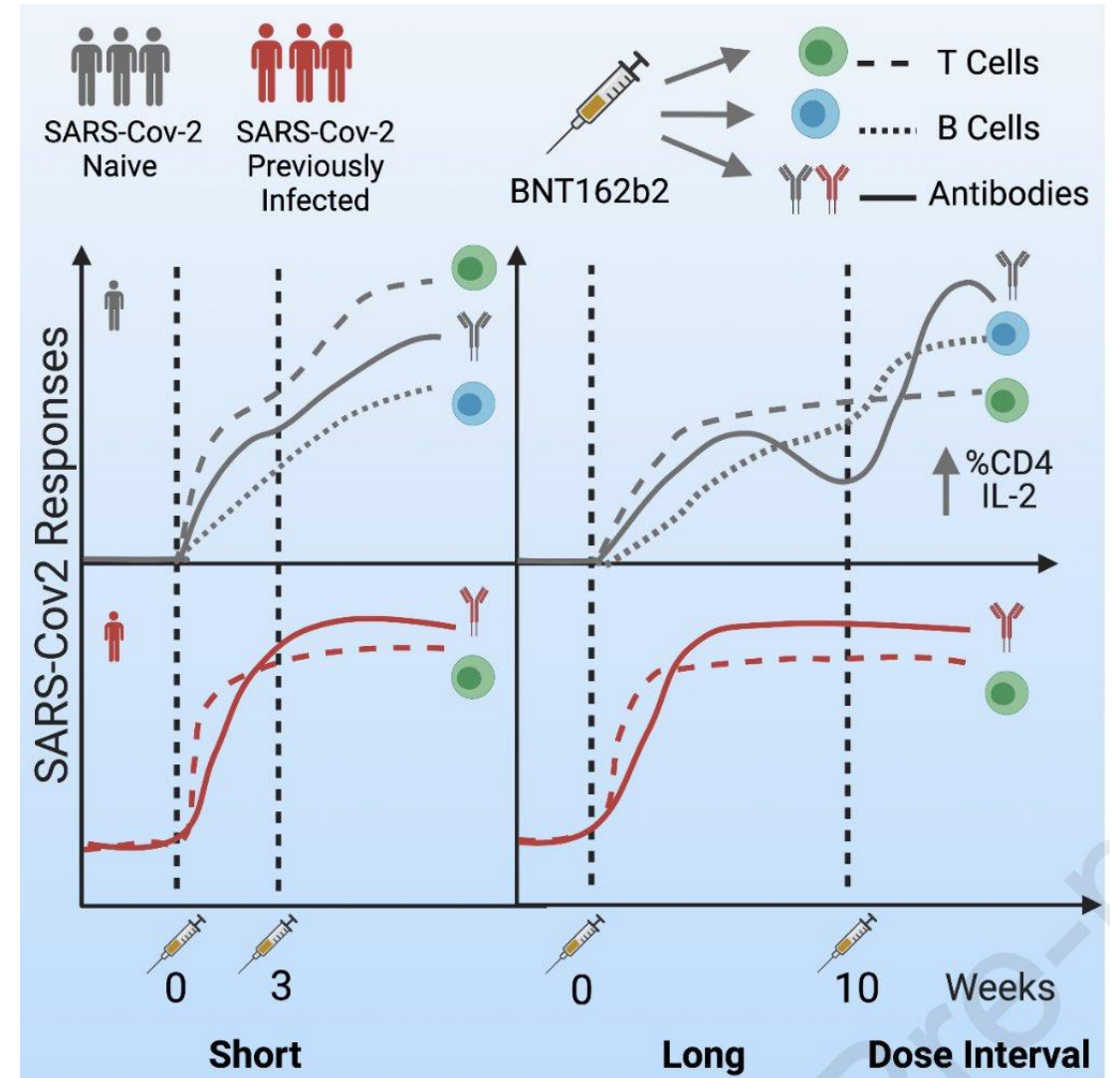
## Risk Factors for Severe COVID-19 Outcomes Among Persons Aged $\geq 18$ Years Who Completed a Primary COVID-19 Vaccination Series — 465 Health Care Facilities, United States, December 2020–October 2021

*Weekly* / January 7, 2022 / 71(1);19–25

- Even with 2 doses, risk of COVID-19 death 0.00003 after vaccination
- Risk factors for severe breakthrough (4<sup>th</sup> dose): severe immunocompromise, >75 with 4 comorbidities
- Explains who needs likely 4<sup>th</sup> booster; Paxlovid nearby

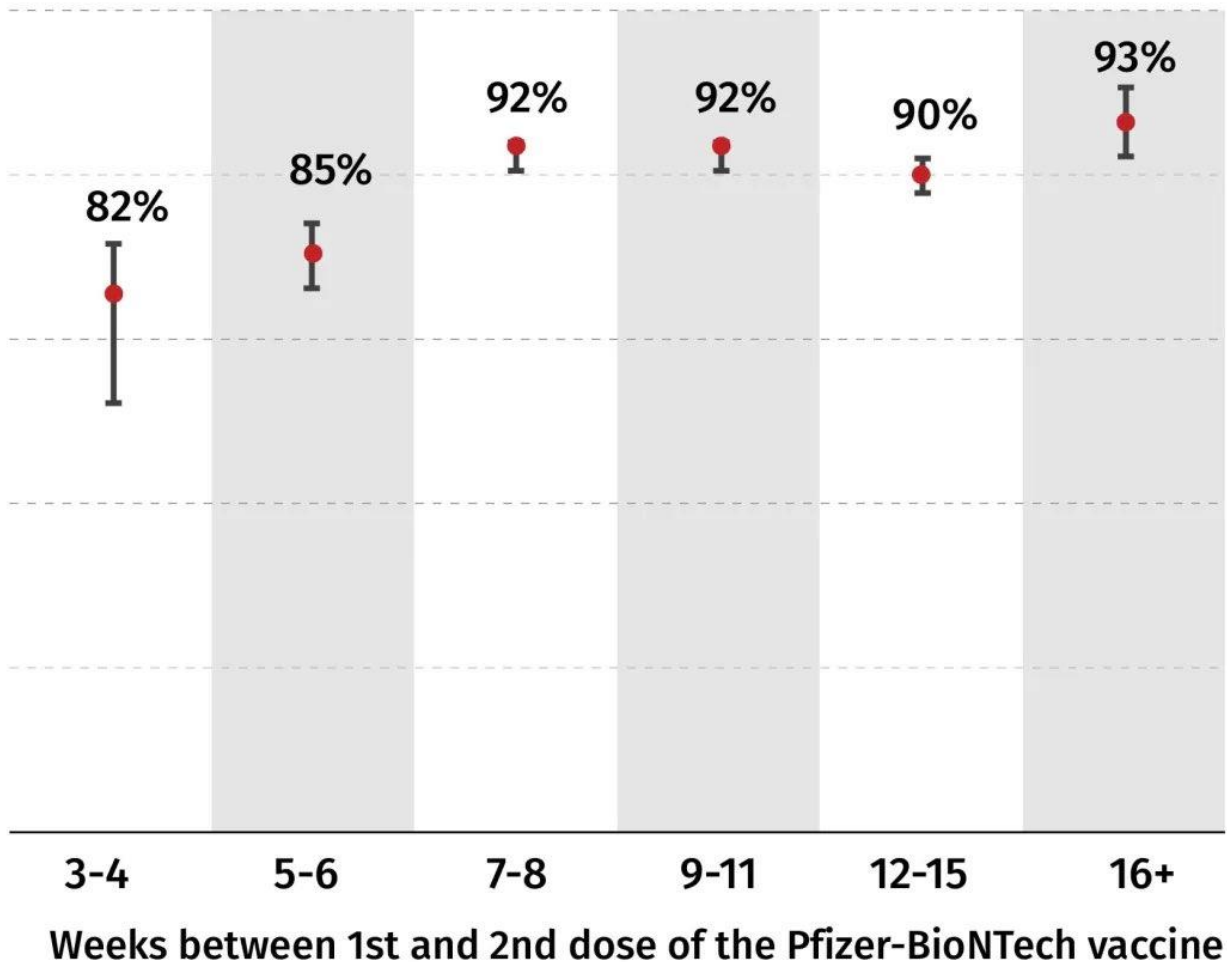
# Extending dosing interval increases T cell & antibody responses

Immunologic research shows better antibody response and importantly CD4 T cell responses if extend interval on Pfizer vaccine to 6-8 weeks instead of 3 weeks; October 15, 2021

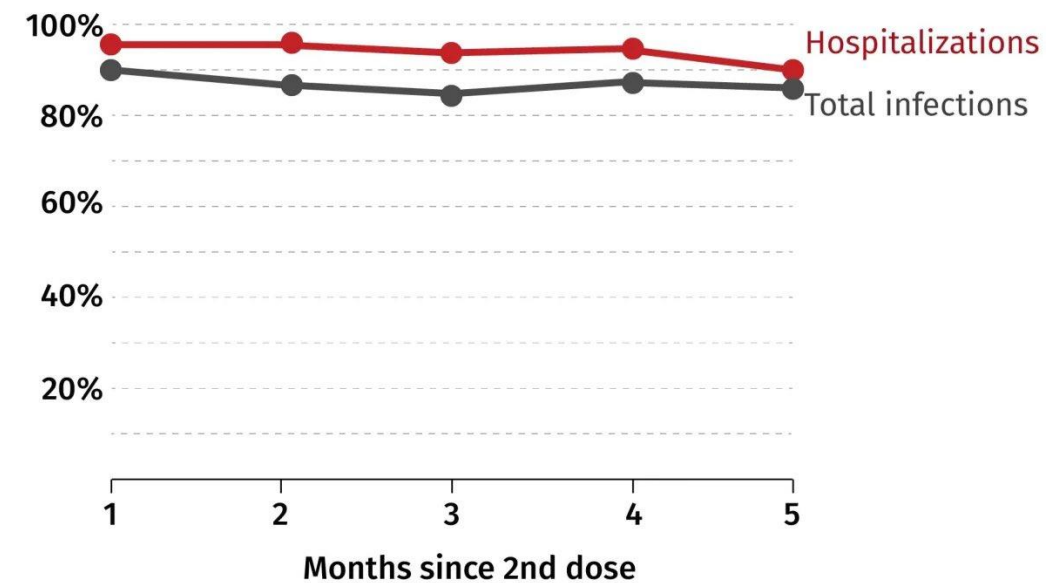


# Data from Canada shows Pfizer works better if extend interval to 7-8 weeks (both against infection and severe disease)- associated with more safety (myocarditis)s

Vaccine protection increases with longer intervals between doses



Vaccine effectiveness against severe effects of COVID-19



# CDC has only advertised interval to professionals, not public or media 2/22/22



## Extend the Interval Between COVID Vaccine Doses

— The safety and effectiveness data should prompt CDC to update its policy

TABLE 2. COVID-19 vaccination schedule for the primary series in the general population\*

Primary series vaccine manufacturer	Age group	Number of doses in primary series	Number of booster doses	Interval between 1st and 2nd dose	Interval between primary series and booster dose
Pfizer-BioNTech	5-11 years	2	NA	3 weeks	NA
Pfizer-BioNTech	≥12 years	2	1	3-8 weeks <sup>†</sup>	≥5 months
Moderna	≥18 years	2	1	4-8 weeks <sup>†</sup>	≥5 months
Janssen	≥18 years	1	1	NA	≥2 months

\*For the vaccination schedule for people who are moderately or severely immunocompromised, see [Table 3](#)

<sup>†</sup>An **8-week** interval may be optimal for some people ages 12 years and older, especially for males ages 12 to 39 years. A **shorter interval** (3 weeks for Pfizer-BioNTech; 4 weeks for Moderna) between the first and second doses remains the recommended interval for: people who are moderately to severely immunocompromised; adults ages 65 years and older; and others who need rapid protection due to increased concern about community transmission or risk of severe disease.

# Omicron created a lot of natural immunity

Centers for Disease Control and Prevention

**MMWR**

Morbidity and Mortality Weekly Report

Early Release / Vol. 71

April 26, 2022

## Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies — United States, September 2021–February 2022

Kristie E.N. Clarke, MD<sup>1</sup>; Jefferson M. Jones, MD<sup>1</sup>; Yangyang Deng, MS<sup>2</sup>; Elise Nycz, MHS<sup>1</sup>; Adam Lee, MS<sup>2</sup>; Ronaldo Iachan, PhD<sup>2</sup>;  
Adi V. Gundlapalli, MD, PhD<sup>1</sup>; Aron J. Hall, DVM<sup>1</sup>; Adam MacNeil, PhD<sup>1</sup>

**60% of adults and  
75% of children 0-  
18 in the US have  
had exposure to  
COVID-19**

# Hybrid immunity

SHANE CROTTY

Omicron seemed  
to show power of  
“hybrid immunity”

# Science

## Omicron reduced protection from either former infection or vaccines for mild (not severe) disease

- Qatar [study](#) showed that protection from re-infection after infection declined from ~90% with the Alpha, Beta and Delta variants to 56% [against Omicron](#)
- [Canada study](#) showed protection after two-dose vaccination declined from 89% against Delta to 36% against Omicron.
- Omicron variant [to evade antibodies](#), although the protection against severe disease [due to cellular immunity](#) from either vaccination or infection is more durable.
- A [study](#) among employees at the Cleveland Clinic verifies that one booster dose of the vaccine after either two-dose vaccination or natural infection protects against subsequent re-infection with Omicron.
- Single dose of the Pfizer COVID-19 [vaccine after recovery protected against re-infection](#) during the Delta surge by at least 3-fold, with two doses conferring no additional benefit
- Recovery immunity waned after a year [but was higher than 90%](#) in those with subsequent vaccination.

## Clinical Infectious Diseases

ACCEPTED MANUSCRIPT

### Immunity Against the Omicron Variant from Vaccination, Recovery or Both

Monica Gandhi, MD, MPH ✉

*Clinical Infectious Diseases*, ciac172, <https://doi.org/10.1093/cid/ciac172>

Published: 02 March 2022 [Article history](#) ▼



The NEW ENGLAND  
JOURNAL of MEDICINE



# Daily new confirmed COVID-19 deaths per million people

7-day rolling average. Due to varying protocols and challenges in the attribution of the cause of death, the number of confirmed deaths may not accurately represent the true number of deaths caused by COVID-19.



**LINEAR** LOG

**Deaths at lowest point in pandemic worldwide since beginning of pandemic**



World

# WHO Lays Out Plan to Emerge From Emergency Phase of Pandemic

March 30, 2022- Excess mortality from other medical conditions not being worked on – so this is plan for COVID

By Julie Steenhuisen and Mrinalika Roy

March 31, 2022



Added to Email Alerts



REUTERS

Base scenario



Vaccinate vulnerable groups every winter

Best case: Less virulent variant emerges



Most won't need re-vaccination

Worst case: More virulent variant emerges



Boost everyone & consider whole virus vaccine

ENDEMICITY

COVID-19 likely to be controlled not eradicated – so frequency of boosters will depend on variants



- **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.

# COVID-19 does not have features of an eradicable infectious diseases, can still be controlled

## Smallpox- eradicated

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



## COVID-19 – will get under control

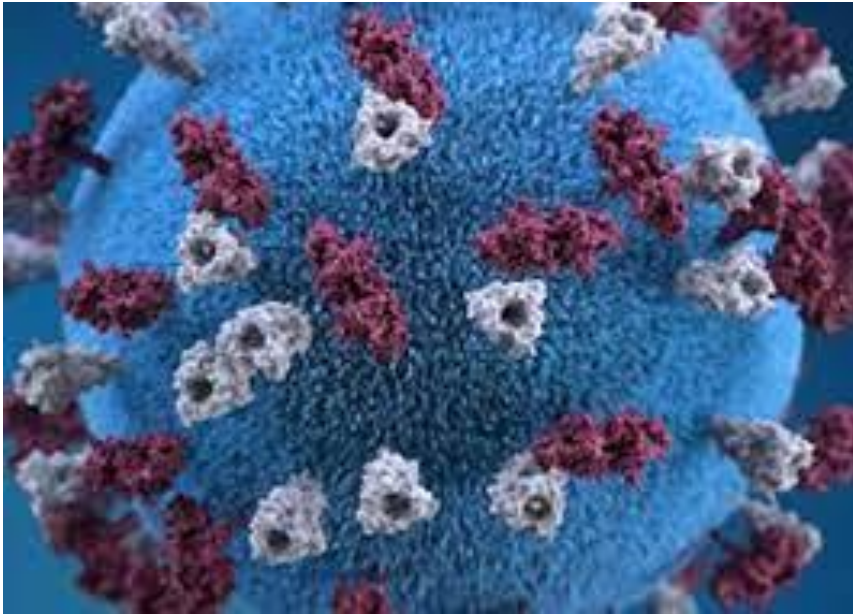
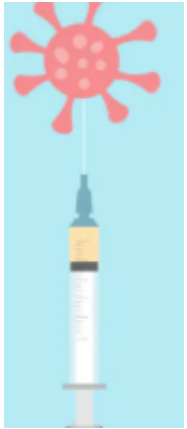
- COVID-19 looks like other respiratory illnesses
- Can spread when presymptomatic
- Found in animals
- Highly effective vaccine for severe disease; increasingly non-sterilizing with variants

**We won't eradicate covid. The pandemic will still end.**

By Monica Gandhi

September 21, 2021

**The Washington Post**



Measles



Pertussis

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

***COVID-19 has vaccines from age of 5 onwards now (prevention) and oral antivirals as of December 2021 (molnupiravir, Paxlovid)***

*The Atlantic*

IDEAS

# The New COVID Drugs Are a Bigger Deal Than People Realize

Vaccines are amazing, but people who become infected need effective treatments.

# 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  $\geq$ 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 1443 patients of planned n=1550
- Latin America (55%), Europe (23%), Africa (15%) in addition to US
- 30% reduction in 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



# Protease inhibitor (Antiviral) for SARS-CoV-2: PF-07321332 ('332) + ritonavir= PAXLOVID

- Oral SARS CoV-2-3CL protease inhibitor (given with ritonavir)
- Phase 2/3 EPIC trial in **high-risk** non-hospitalized patients
- Randomized to receive '332/rtv (3 pills) every 12 h or placebo, 5 days
- Interim analysis of patients treated within 3 days of symptom onset (n=774)

Owen DR et al, Science, 2021  
<https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate>

	Hospitalization or death	% Reduction
<b>332/rtv</b>	<b>3/389 (0.8%) 0 deaths</b>	<b>89% P&lt;0.0001</b>
<b>Placebo</b>	<b>27/385 (7%) 7 deaths</b>	

- Similar reductions in hospitalization or death among people treated within 5 days of symptom onset (n=1219)
- Also being evaluated in lower risk patients and for post-exposure prophylaxis

# 3 trials for Paxlovid

EPIC-HR

Unvaccinated at  
high risk of →  
severe disease

89% protection from  
hospitalization/death

EPIC-SR

Unvaccinated at  
standard risk of →  
severe disease

(Interim results) – 70%  
protection from  
hospitalization/death

EPIC-PEP

Household  
members of →  
those infected

No efficacy in preventing infection

# Monoclonal antibodies for prophylaxis

## Fact Sheet for Patients, Parents And Caregivers Emergency Use Authorization (EUA) of EVUSHELD™ (tixagevimab co-packaged with cilgavimab) for Coronavirus Disease 2019 (COVID-19)



18 February 2022

Clinical Infectious Diseases

## Prospective evaluation of COVID-19 vaccine responses across a broad spectrum of immunocompromising conditions: the COVICS study FREE

Ghady Haidar, MD ✉, Mounzer Agha, MD, Andrew Bilderback, MS,

mRNA vaccines work well  
against range of  
immunocompromising  
conditions, but 6 month  
monoclonal antibody infusion  
protects

## 10 point plan

Mar 22 - Written By Drs. Jeanne Noble & Monica Gandhi

- 1) Stop mass asymptomatic testing, but focused testing of vulnerable & wastewater surveillance
- 2) Stop quarantines but isolation when sick (COVID 5 days & paid sick leave)
- 3) Invest heavily in test and treat program with oral antivirals
- 4) Stop vaccine passports
- 5) Space out initial doses of vaccine by 8 weeks in those <40
- 6) Rational approach to vax boosters in vulnerable; acknowledge hybrid immunity
- 7) Novavax and Covaxin approval in US along with mRNA vaccines
- 8) Long COVID and vaccination: Good studies showing vax brings to baseline
- 9) Ventilate indoor spaces
- 10) Retire mask mandates but recommend fit/filtered masks inside with high cases

# President's plan for endemic management March 2

1. Vaccines, decide on vaccine booster strategy, new vaccines
2. Prophylaxis with monoclonal antibodies for immunocompromised; Test and treat for those with COVID at high risk with oral antivirals
3. Wastewater surveillance to see if cases going up; pandemic recovery schools, offices
4. Vaccinate world

THE WHITE HOUSE



April 26

MENU



BRIEFING ROOM

**FACT SHEET: Biden Administration  
Increases Access to COVID-19  
Treatments and Boosts Patient and  
Provider Awareness**

APRIL 26, 2022 • STATEMENTS AND RELEASES



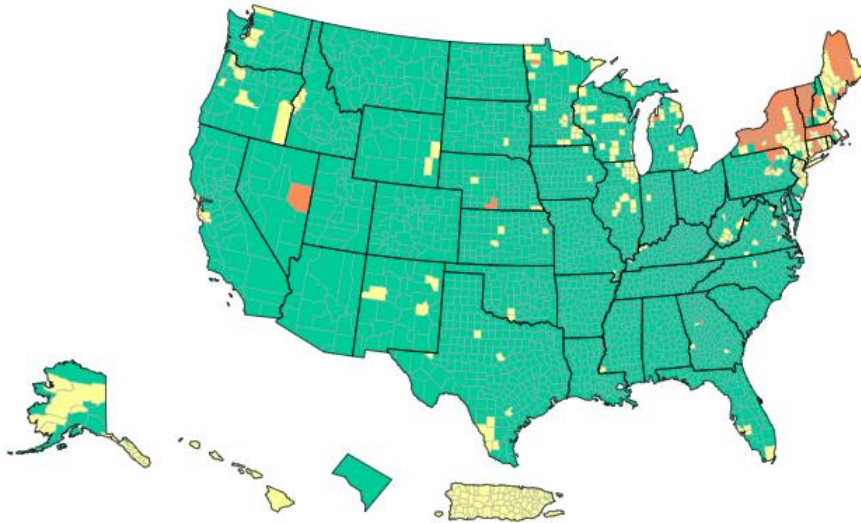
March 2

**NATIONAL COVID-19  
PREPAREDNESS PLAN**



# Centers for Disease Control and Prevention

CDC 24/7: Saving Lives, Protecting People™



## COVID-19 Community Levels in US by County

	Total	Percent	% Change
High	79	2.45%	0.71%
Medium	318	9.86%	1.86%
Low	2827	87.69%	- 2.57%

How are COVID-19 Community Levels calculated?



CDC changed criteria for masking guidance to be based on hospitalizations in your region Feb 24, 2022

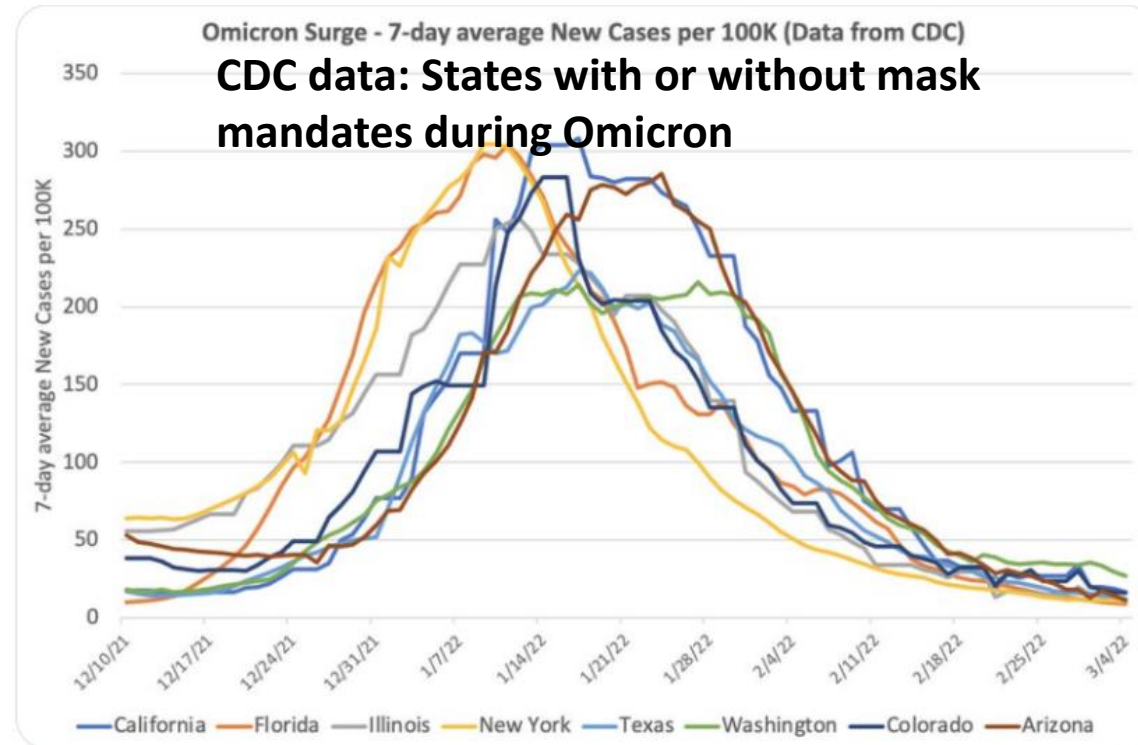
# Uniting Infectious Disease and Physical Science Principles on the Importance of Face Masks for COVID-19

Monica Gandhi<sup>1,\*</sup> and Linsey C. Marr<sup>2</sup>

January 2021

## Two major principles.. **FIT AND FILTRATION**

- N95
- FFP2
- KN95
- KF94
- Double mask
- Cloth mask with filter



With an endemic virus and vaccines- likely to be optional for personal protection

Analysis of mask “mandates” didn’t find changed spread much likely because type of masks, compliance

# How can medical providers help with public health response?

1. Harm reduction approach needed for any pandemic
2. Lancet report that strongest predictor of mortality from COVID - rates of vaccination & boosting in elderly
3. School closures did harm to the young & increased non-COVID related deaths in this population (overdoses, homicide, road-related injuries, alcohol)

PDF [5 MB] Fig  
Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21

March 10, 2022

THE LANCET

COVID-19 Excess Mortality Collaborators <sup>†</sup> • [Show footnotes](#)

[Open Access](#) • Published: March 10, 2022 • DOI: [https://doi.org/10.1016/S0140-6736\(21\)02796-3](https://doi.org/10.1016/S0140-6736(21)02796-3)



# Physician trust high – 1:1 interactions

- Trust in medical system (not public health) increased during the pandemic
- Patients trust their provider when advising on the vaccines
- Therapeutics now available
  - EVUSHELD for those who are immunosuppressed
  - Antivirals – Paxlovid and Molnupiravir



May 2021

Table 2. Public Ratings of the Nation's Public Health vs. Medical Systems, 2009 and 2020/2021

	Positive Rating (%)	
	2009	2020-2021
Nation's medical system <sup>a</sup>	36	51*
Nation's public health system <sup>b</sup>	43	34*

THE PUBLIC'S PERSPECTIVE  
ON THE UNITED STATES  
PUBLIC HEALTH SYSTEM

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

September 20, 2021

No severe disease in either group; 3 infections with vaccine, 16 with placebo (90.7% efficacy)

- 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

## *Pfizer Shot Is Far Less Effective in 5- to 11-Year-Olds Than in Older Kids, New Data Show*

February 28, 2022

While protection against hospitalization is still strong, the vaccine offered almost no protection against infection, even just a month after full vaccination.

- Much more immunity by then from exposures
- Doses not spaced out for 5-11 year olds (10 micrograms x 2 3 weeks apart)
- One dose after natural infection?
- During Omicron, less effective with antibodies, strong B/T cell immunity
- 28% US children 2-dose vaccine (34% 1-dose)

# Where are we with vaccines under 5?

Pfizer 3-micrograms doses (x 2 3 weeks apart) for those under 5 only appropriately generated an immune response for 6 months-2 years but not 2-4 yrs

Moderna 6 mo-6 (25 micrograms x 2 4 weeks apart) generated good antibodies but prevented 37, 44% of all infections although no hospitalizations (in either group) – to be reviewed in June

Ocugen (Covaxin) vaccine (whole inactivated) applied to FDA from ages 2 onwards on November 5 but not approved yet

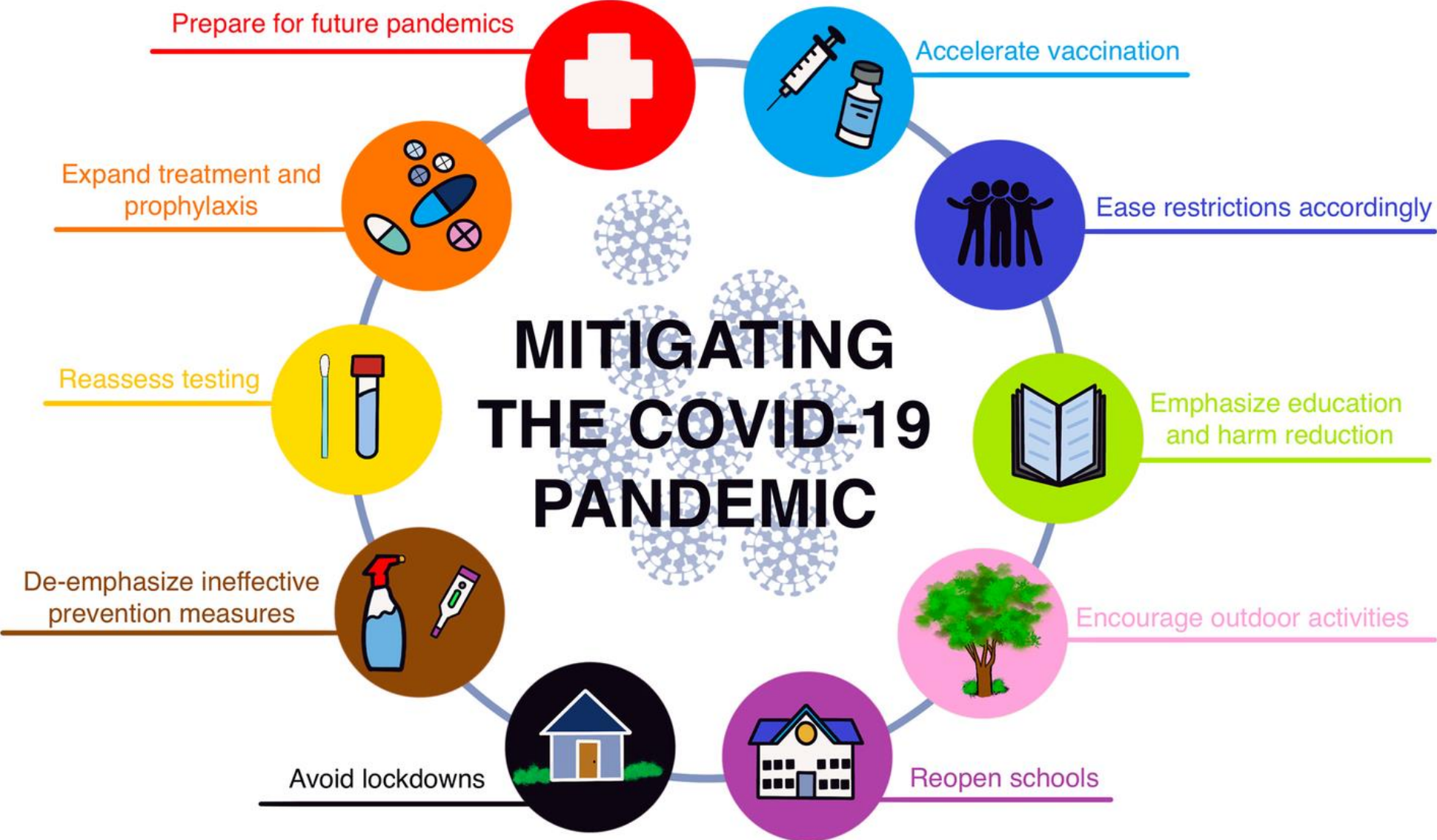
Pregnancy vaccination – 57% of infants still had SARS-CoV-2 antibodies at 6 months after vaccination in pregnancy

## RESEARCH LETTER

**Durability of Anti-Spike Antibodies in Infants After Maternal COVID-19 Vaccination or Natural Infection**

**JAMA Network™**

# Revisiting COVID-19 policies: 10 evidence-based recommendations for where to go from here



# Conclusion

- COVID-19 unfortunately not eradicable by its properties
- Goal is control
- Worldwide strategy is vaccination but US strategy is vaccination + therapeutics and latter should be made available worldwide too
- More treatments coming
- Will always be a medical problem for us (like influenza)

HEALTH

More uniformly infectious, more  
treatable, more genetically predictable:  
How coronavirus is getting closer to flu

STAT

