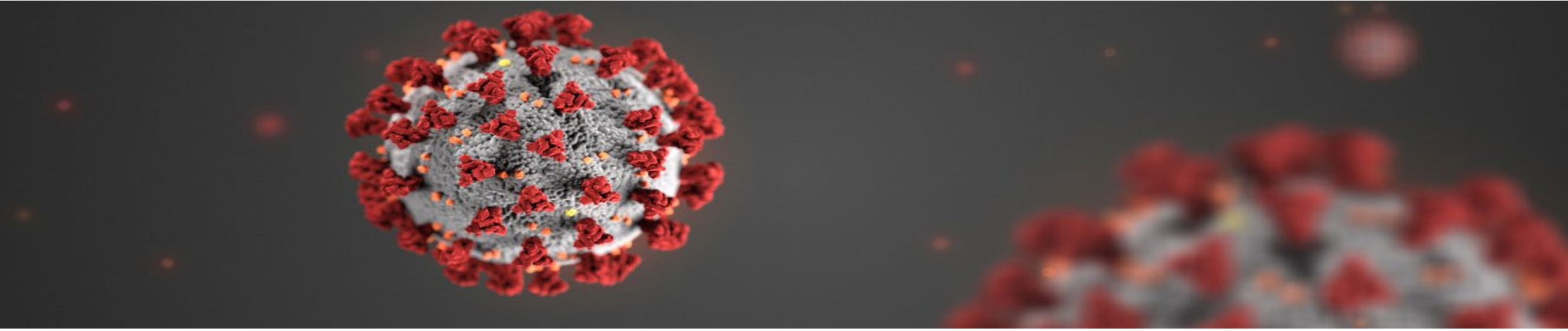

The COVID-19 Pandemic and Long-term Consequences

Dale W. Bratzler, DO, MPH, MACOI, FIDSA
Chief COVID Officer – University of Oklahoma
Professor Colleges of Medicine and Public Health
Chief Quality Officer – OU Health
Interim Dean - Hudson College of Public Health
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September 9, 2022

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Relevant Disclosure and Resolution

Under Accreditation Council for Continuing Medical Education guidelines disclosure must be made regarding relevant financial relationships with commercial interests within the last 12 months.

Dale W. Bratzler

I have no relevant financial relationships or affiliations with commercial interests to disclose.

Learning Objectives

Upon completion of this session, participants will improve their competence and performance by being able to:

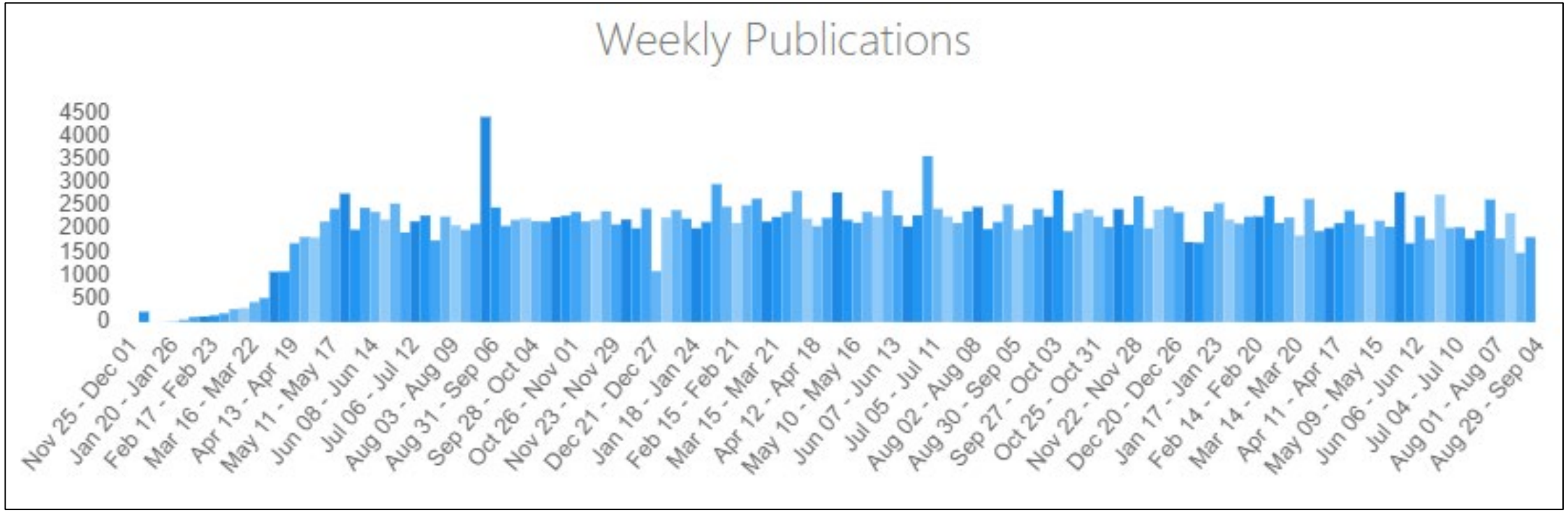
1. Describe the impact of the COVID pandemic in the US.

2. Understand some of the long-term consequences of COVID infection.

3. Describe proposed mechanisms for the development of long-haul symptoms.

4. Discuss the impact of COVID-19 on the opioid crisis in the US.

No one can keep up with the literature….



283,396 articles on COVID published in 8,000 journals and counting…..

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https://www.ncbi.nlm.nih.gov/research/coronavirus/
Updated August 29, 2022

Public Health Messages from COVID:

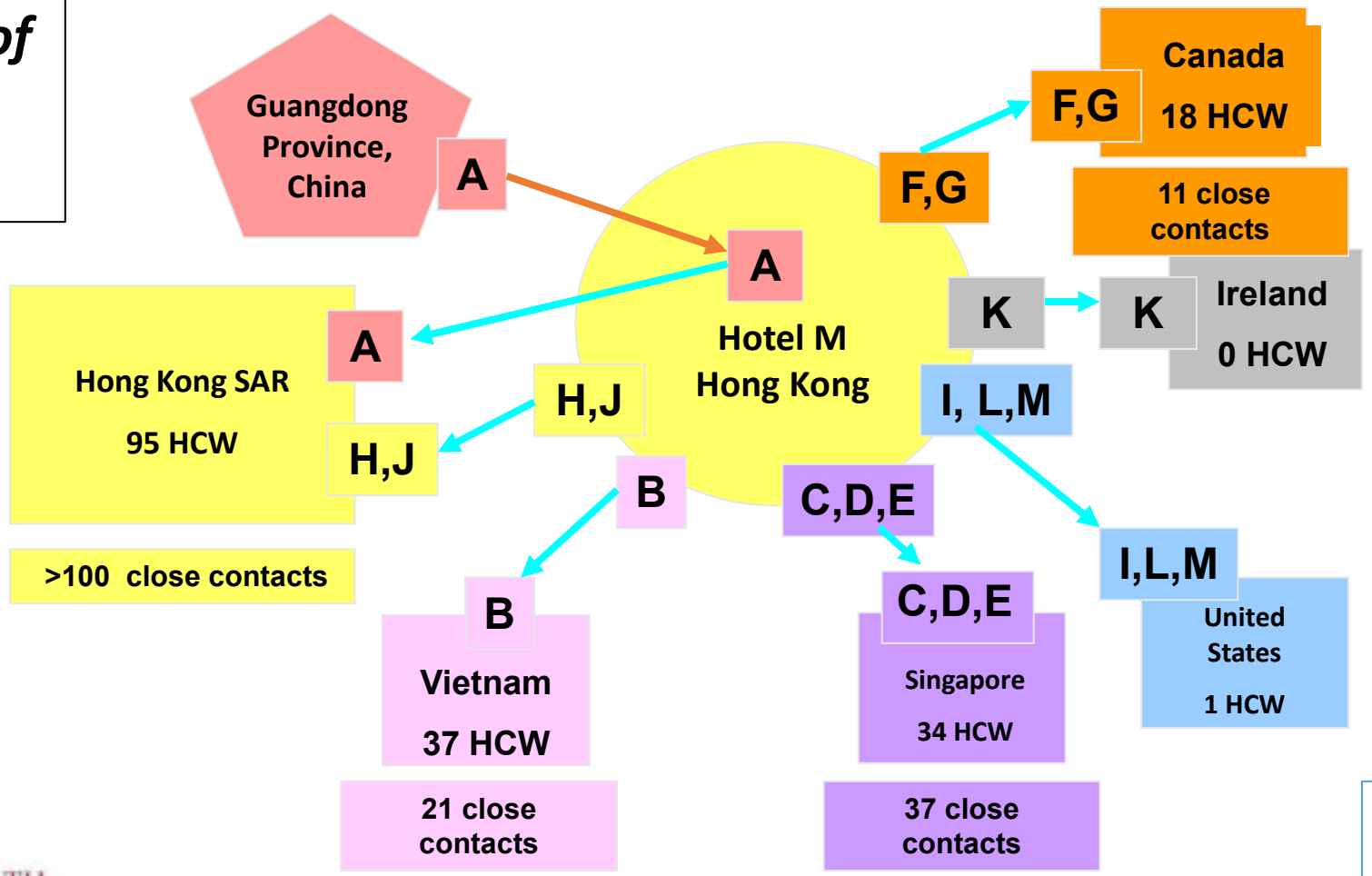
We live in a global community!

This disease cannot be eliminated based on current science!

The SARS Epidemic (SARS-CoV-1)

Patient "Zero"

Locking down borders does not stop the spread of respiratory viruses!



2003

Table 7.3: Eradication of Human Diseases: Smallpox (now COVID)

	Smallpox	COVID
Disease is limited to humans, i.e., no animal reservoir		**No**
Limited persistence in the environment?	Yes	**Yes**
Absence of long-term carrier state?	Yes	**??**
Long-term immunity results from infection?	Yes	**No**
Vaccination confers long-term immunity?	Yes	**??**
Herd immunity prevents perpetuation of an epidemic?	Yes	**No**
Easily diagnosed disease?	Yes	**No**
Vaccination effective postexposure?	Yes	**No**

We will not eliminate COVID!

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Slide from my Introduction to Public Health course.

One of my final slides from a November 2021 Presentation:

What could go wrong???? Variants.

More than 50 countries have missed the World Health Organization's (WHO) target for 10% of their populations to be fully vaccinated against COVID-19 by the end of September.

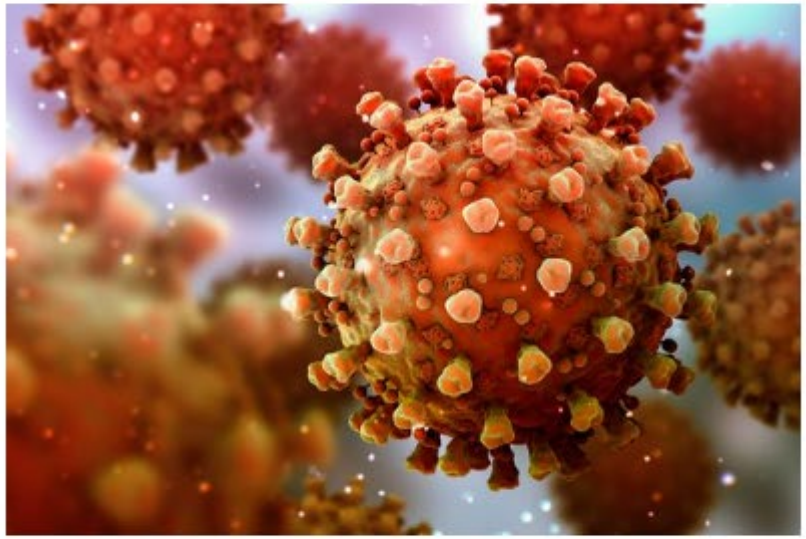
Most are in **Africa**, where the WHO's overall figure for those fully vaccinated is currently 4.4%. (*Omicron subsequently identified in Botswana and South Africa*)

Is there an animal reservoir where the virus could mutate?

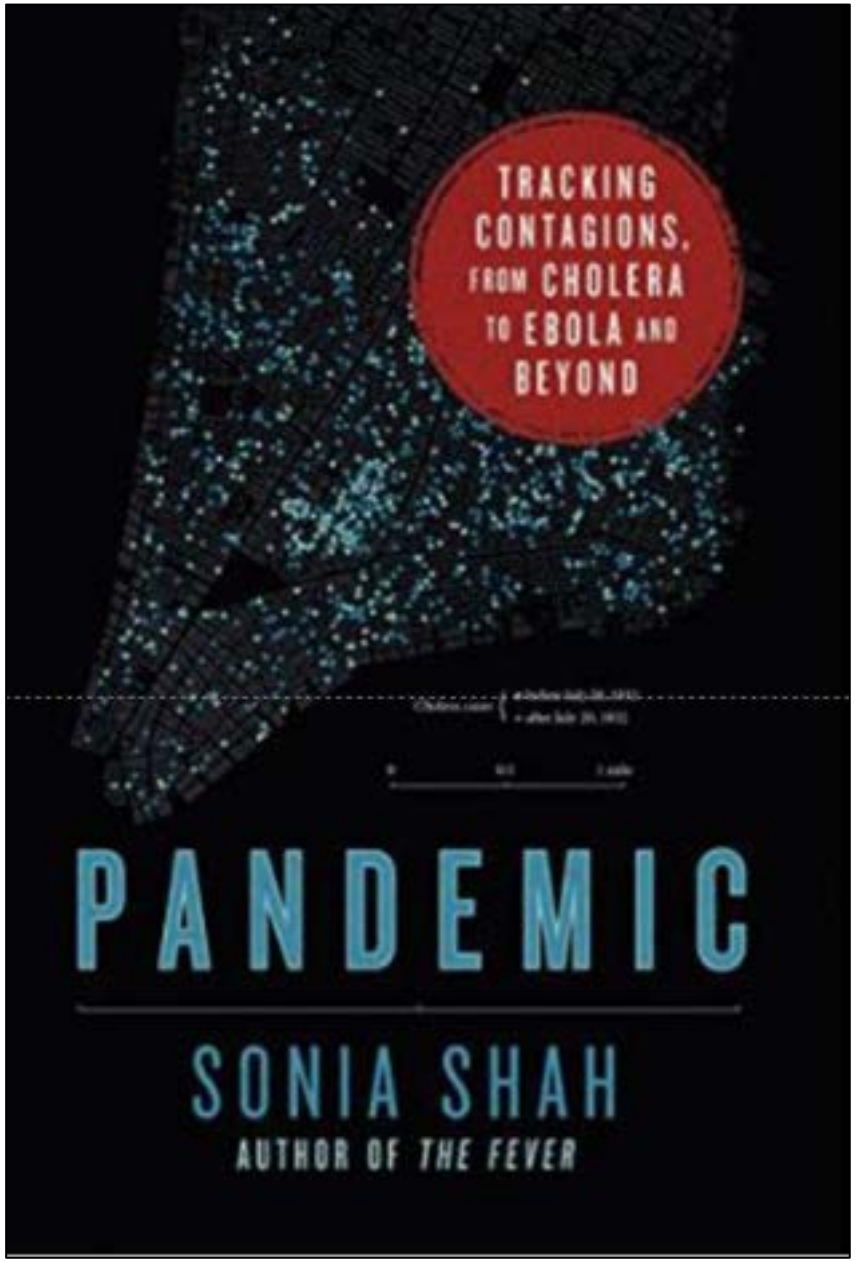
[WEBMD NEWS BRIEF]

First Possible Case of Deer-to-Human COVID Transmission Identified

By Carolyn Crist



March 1, 2022. https://www.webmd.com/lung/news/20220301/deer-to-human-covid-transmission-first-possible-case



"The disease-causing microbe, or pathogen, that will cause the world's next pandemic lurks among us today. We don't know its name or where it comes from."

Sonia Shah 2016

Remember when……..

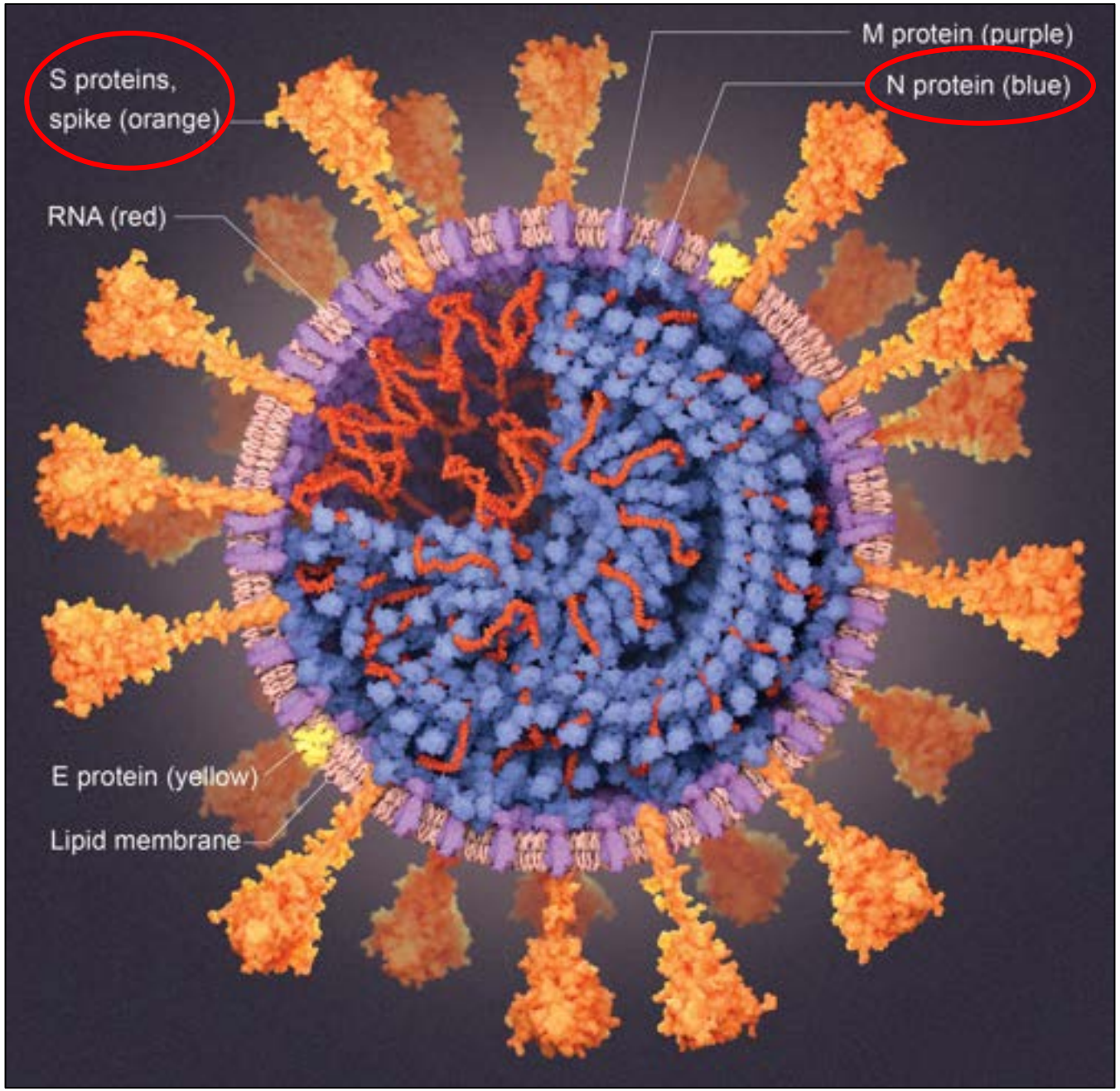
- On 31 December 2019, the WHO China Country Office was informed of cases of pneumonia of unknown etiology (unknown cause) detected in Wuhan City, Hubei Province of China.
  - First case confirmed in US on January 20, 2020

Spike protein (S)

- Target of the mRNA and Novavax COVID vaccines

Anti-S antibodies from vaccination.

PCR tests are very sensitive and detect fragments of the RNA in the virus.



Nucleocapsid protein (N)

- Many rapid antigen tests detect this protein

Anti-N antibodies from prior infection.

SARS-CoV-2

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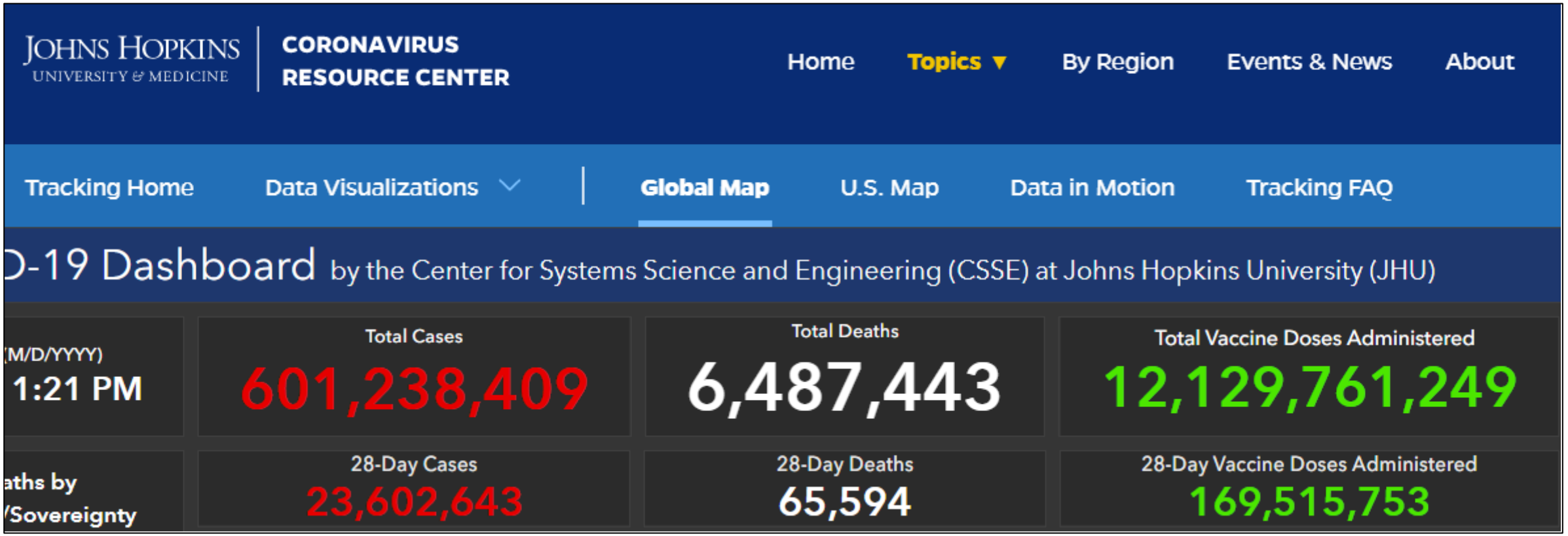
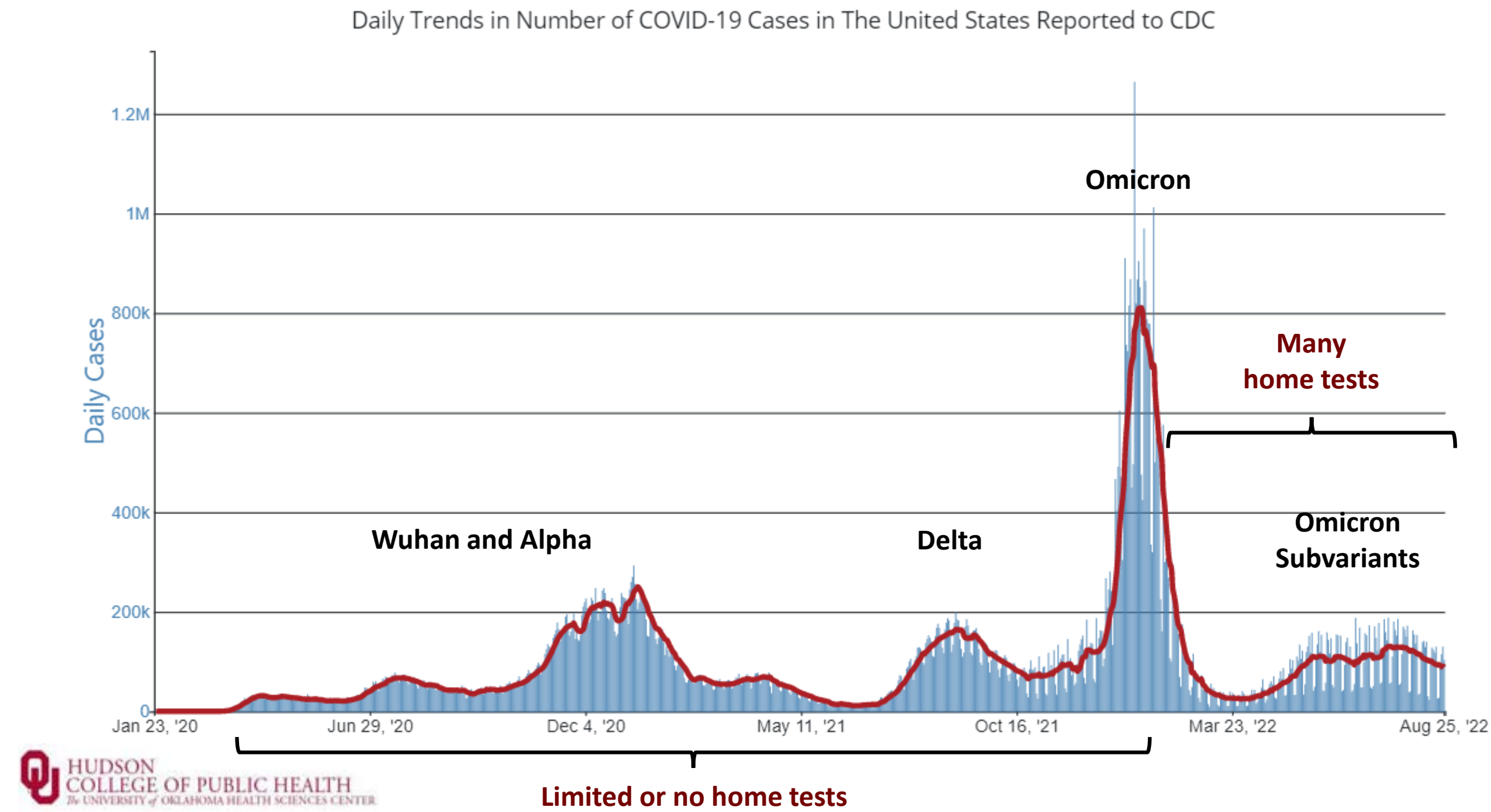
https://www.scientificamerican.com/article/a-visual-guide-to-the-sars-cov-2-coronavirus/



United States:

- 94,220,216 Cases
- 1,043,951 Deaths
- 604,656,326 Vaccine doses

Data as of August 29, 2022.
https://coronavirus.jhu.edu/map.html



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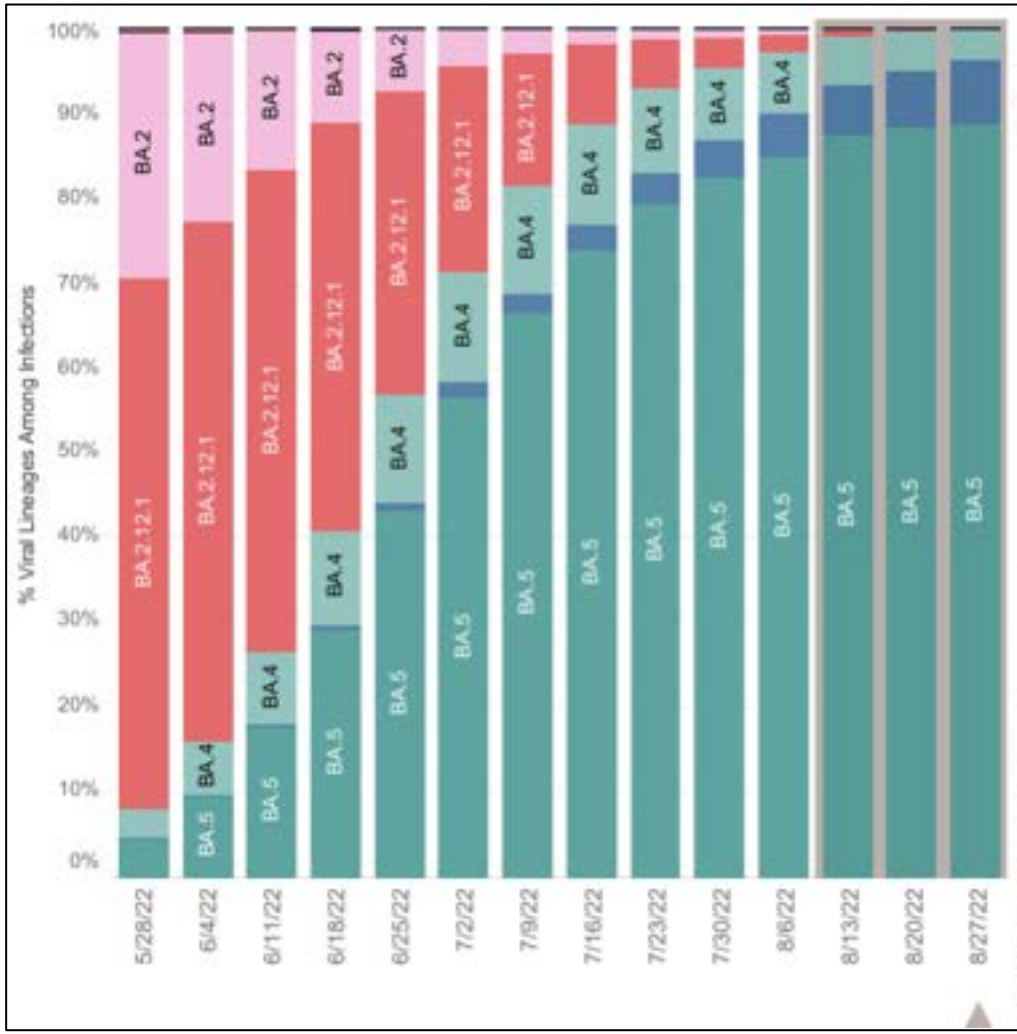
BA.2.12.1, BA.4, BA.5 all have the "delta mutation" which evades protection from prior Omicron infection. All are more contagious than the original Omicron variant



USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	88.7%	87.3-89.8%
	BA.4.6	VOC	7.5%	6.4-8.8%
	BA.4	VOC	3.6%	3.3-3.8%
	BA.2.12.1	VOC	0.2%	0.2-0.3%
	BA.2	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Sublineages of BA.5 are aggregated to BA.5.

BA.2.12.1, BA.4, and BA.5 now represent 100% of our cases.

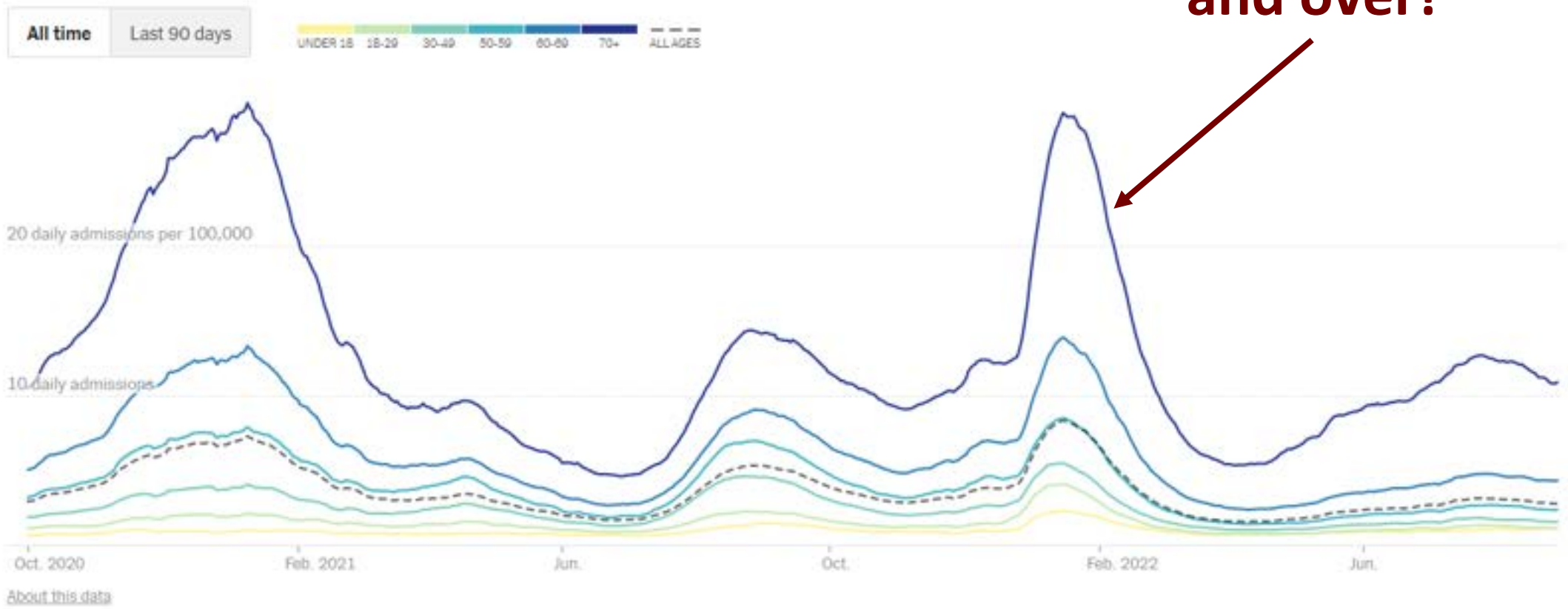
https://covid.cdc.gov/covid-data-tracker/#variant-proportions

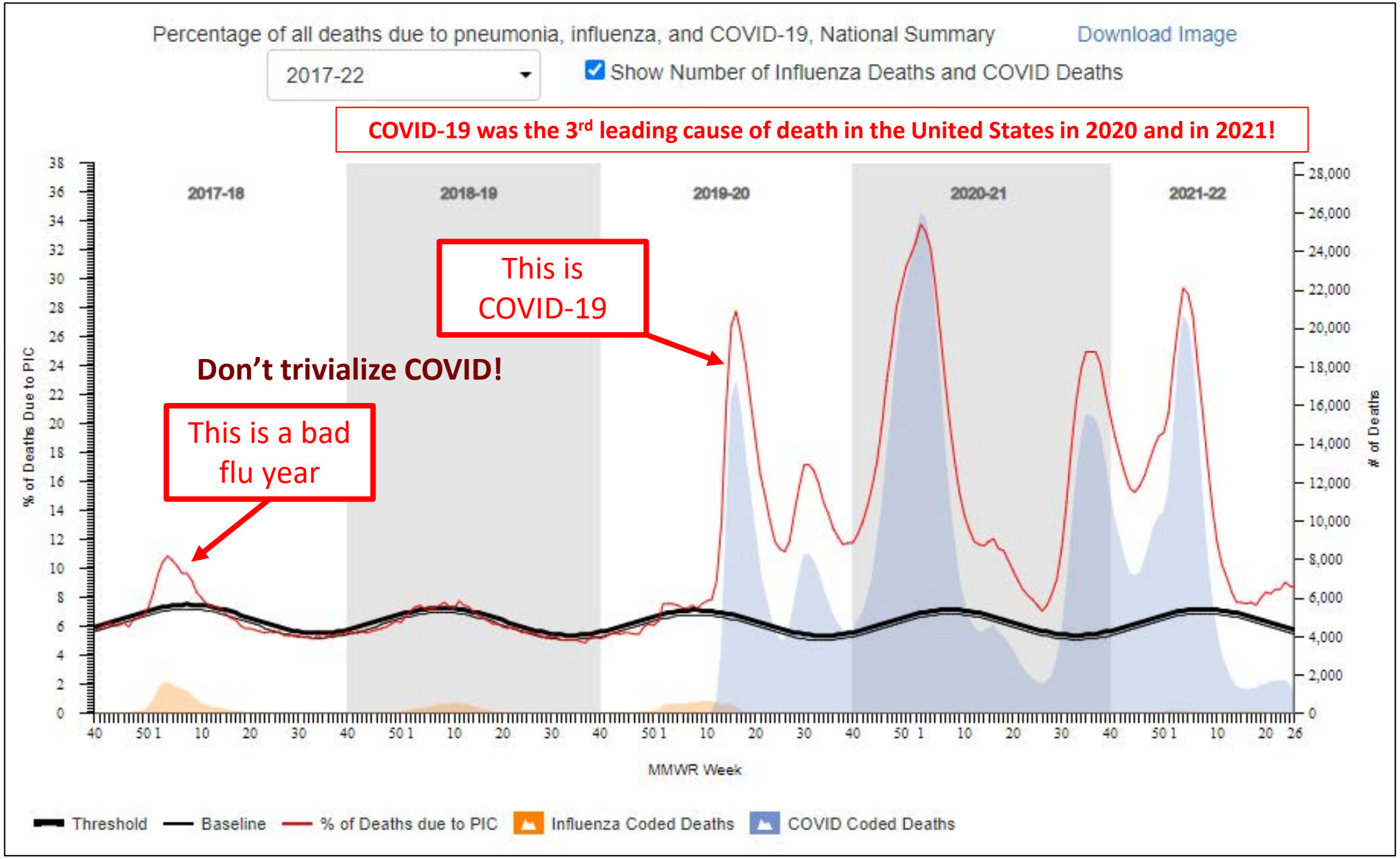
Through August 27, 2022.

Daily new hospital admissions by age

This chart shows for each age group the number of people per 100,000 that were newly admitted to a hospital with Covid-19 each day, according to data reported by hospitals to the U.S. Department of Health and Human Services.

Age 70 years and over!





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https://gis.cdc.gov/grasp/fluview/mortality.html

How is the disease spread?

BA.5 is the most contagious variant of the SARS-CoV-2 virus to date!

The virus is transmitted on droplets and fine aerosols that surround all of us.

Journal of Exposure Science & Environmental Epidemiology

www.nature.com/jes

ARTICLE

Check for updates

Monitoring SARS-CoV-2 in air and on surfaces and estimating infection risk in buildings and buses on a university campus

Xin Zhang[1,2], Jianfeng Wu[1,2], Lauren M. Smith[1], Xin Li[1], Olivia Yancey[1], Alfred Franzblau[1], J. Timothy Dvonch[1], Chuanwu Xi[1]✉ and Richard L. Neitzel[1]✉

The estimated probability of infection was about 1 per 100 exposures to SARS-CoV-2-laden aerosols through inhalation and as high as 1 per 100,000 exposures from contacting contaminated surfaces in simulated scenarios.

Risk from breathing was 10,000 times more likely than a contaminated surface.

What's different now??? Vaccines and Medications

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

A-Z Index
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Morbidity and Mortality Weekly Report (*MMWR*)

CDC

Risk Factors for Severe COVID-19 Outcomes Among Persons Aged ≥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

Christina Yek, MD[1,2,*]; Sarah Warner, MPH[1,*]; Jennifer L. Wiltz, MD[3]; Junfeng Sun, PhD[1]; Stacey Adjei, MPH[3]; Alex Mancera, MS[1]; Benjamin J. Silk, PhD[3]; Adi V. Gundlapalli, MD, PhD[3]; Aaron M. Harris, MD[3]; Tegan K. Boehmer, PhD[3]; Sameer S. Kadri, MD[1] (View author affiliations)

Very large study of 1.2 million people who had completed the primary COVID vaccinations between December 2020 and October 2021.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7101a4.htm

Bottom Line Findings

- **Fully vaccinated** persons were protected from most complications:
  - Risk of severe COVID-19-associated outcomes – 0.015%
  - Risk of death – 0.0033%

- All persons with severe outcomes had at least one (out of eight) underlying risk factor for poor outcomes

- **Of those who died, 78% had four or more risk factors.**

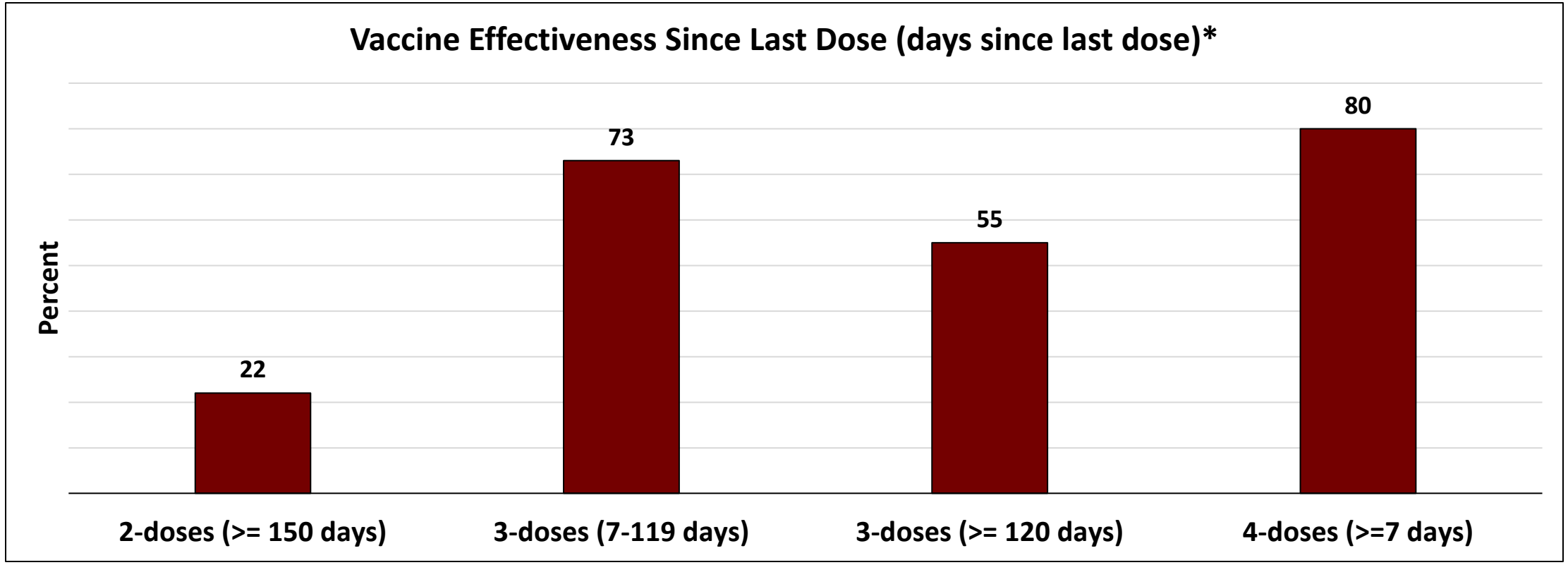
Severe COVID-19 outcomes were defined as hospitalization with a diagnosis of acute respiratory failure, need for noninvasive ventilation (NIV), admission to an intensive care unit (ICU) including all persons requiring invasive mechanical ventilation, or death (including discharge to hospice)
https://www.cdc.gov/mmwr/volumes/71/wr/mm7101a4.htm

Eight Risk Factors for Severe Disease in the Fully Vaccinated

Risk Factor	Increased Risk of Severe Disease or Death*
≥ 65 years	3.2-fold higher risk
Immunosuppressed	1.9-fold higher risk
Diabetes	1.5-fold higher risk
Chronic kidney disease	1.6-fold higher risk
Chronic neurologic disease	1.5-fold higher risk
Chronic cardiac disease	1.4-fold higher risk
Chronic pulmonary disease	1.7-fold higher risk
Chronic liver disease	1.7-fold higher risk

*In fully vaccinated individuals.

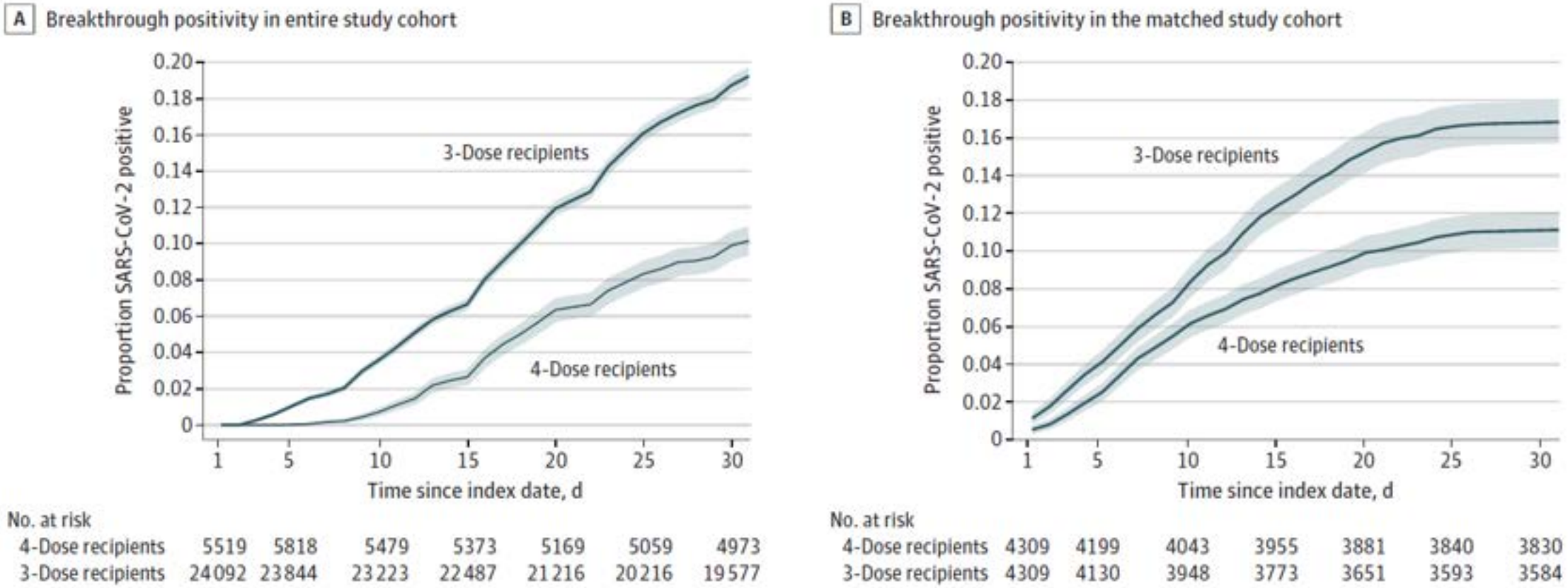
mRNA Vaccine Effectiveness against laboratory-confirmed COVID-19 hospitalization (Age 50 and over)



*During the Omicron BA.2/BA.2.12.1–predominant period.

Link-Gelles R, Levy ME, Gaglani M, et al. Effectiveness of 2, 3, and 4 COVID-19 mRNA Vaccine Doses Among Immunocompetent Adults During Periods when SARS-CoV-2 Omicron BA.1 and BA.2/BA.2.12.1 Sublineages Predominated — VISION Network, 10 States, December 2021–June 2022. MMWR Morb Mortal Wkly Rep. ePub: 15 July 2022. DOI: http://dx.doi.org/10.15585/mmwr.mm7129e1

Figure 2. Morbidity Curves of the Cumulative SARS-CoV-2 Positivity Rate Estimate Among Health Care Workers Who Received 4 Vaccine Doses vs 3 Vaccine Doses



For each matched pair, the index date was the day the worker received the fourth vaccine dose ($P < .001$). Gray shading indicates 95% CIs.

44% Reduction in Breakthrough Infections in matched recipients.

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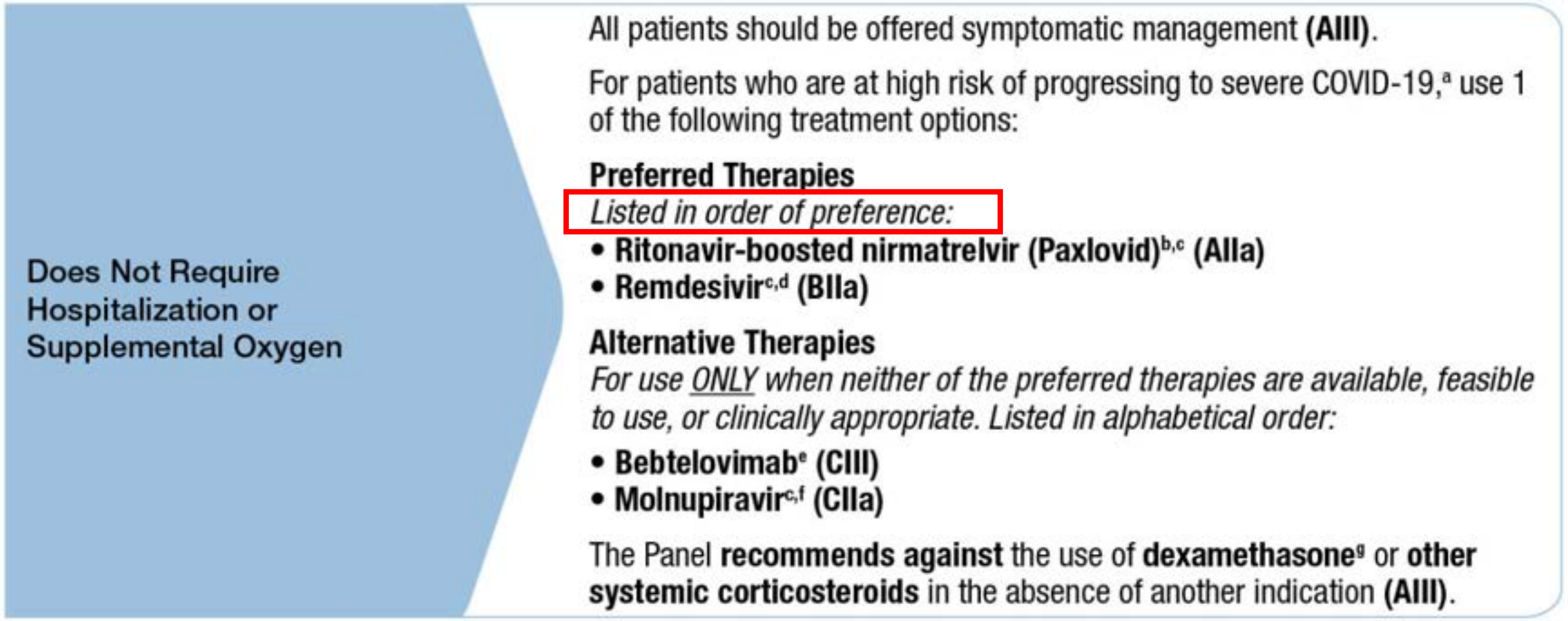
JAMA Network Open. 2022;5(8):e2224657. doi:10.1001/jamanetworkopen.2022.24657

Figure 1. Therapeutic Management of Nonhospitalized Adults With COVID-19



https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/

What do we know about long-term consequences of COVID-19?

PUBLIC HEALTH

The Problem of 'Long Haul' COVID

More and more patients are dealing with major symptoms that linger for months

By Carolyn Barber on December 29, 2020

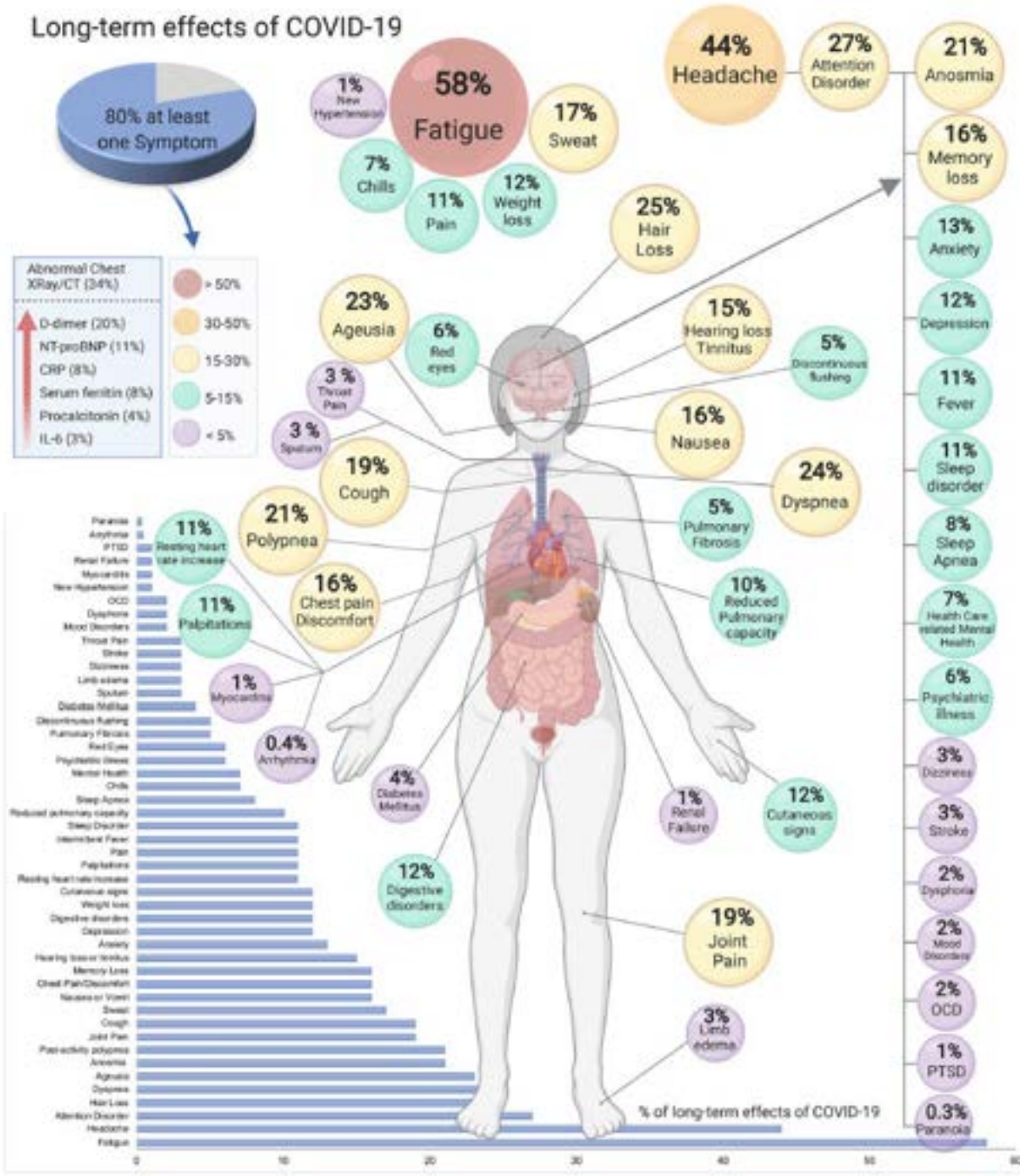
In some emergency departments, they said, their complaints were largely being dismissed—or at the very least diminished—by health care professionals…….

……. Each of the patients had already been infected with COVID-19 and presumably had recovered, yet each was still dealing with symptoms of the disease—sometimes vague, sometimes nonspecific—that simply would not go away.

https://www.scientificamerican.com/article/the-problem-of-long-haul-covid/

Post-acute Sequelae of SARS-CoV-2 Infection (PASC)

- "Long-haulers" who have symptoms for weeks to months (at least 28 days)
- Up to 25% of those who test positive – 60-80% are women
- Fatigue, shortness of breath, cough, joint pain, and chest pain most common
  - "Brain fog," depression, muscle pain, headache, intermittent fever, palpitations
  - In addition to myocardial damage, pulmonary scarring, strokes and VTE events



It was estimated that 80% of the infected patients with SARS-CoV-2 developed one or more long-term symptoms. The five most common symptoms were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), and dyspnea (24%).

https://doi.org/10.1038/s41598-021-95565-8

Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients

Maxime Taquet, Rebecca Sillett, Lena Zhu, Jacob Mendel, Isabella Camplisson, Quentin Dercon, Paul J Harrison

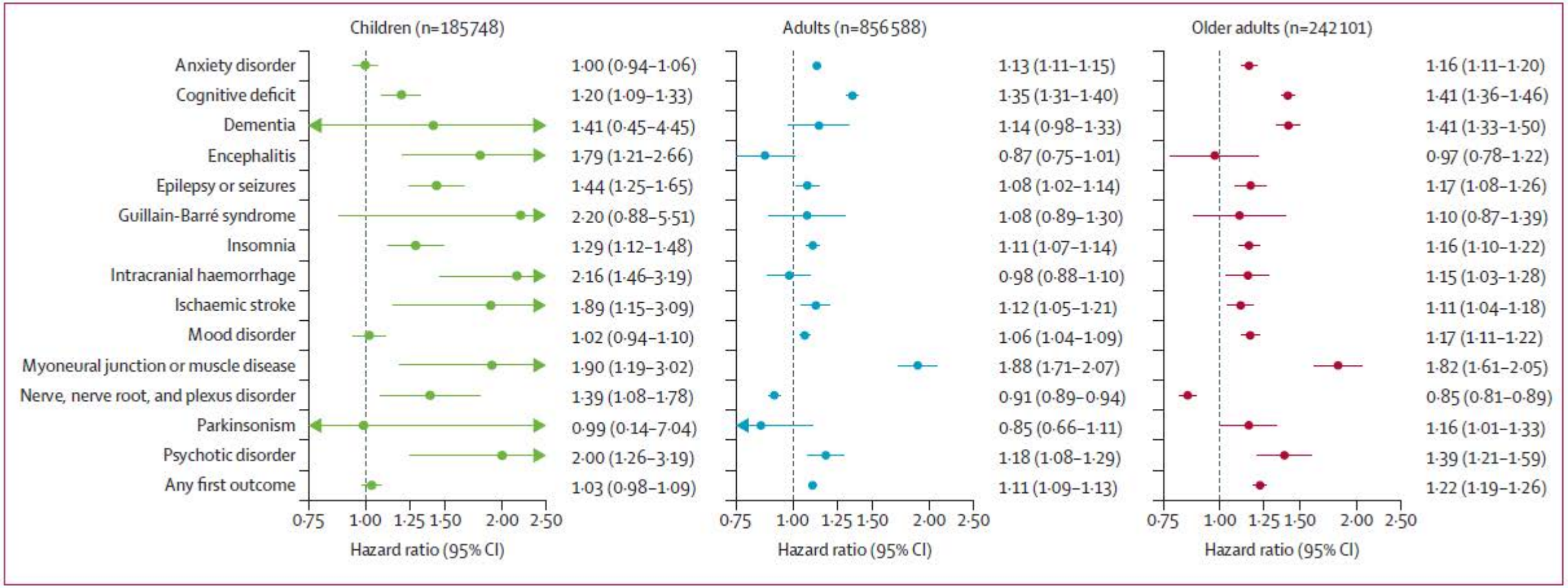
Summary

Background COVID-19 is associated with increased risks of neurological and psychiatric sequelae in the weeks and months thereafter. How long these risks remain, whether they affect children and adults similarly, and whether SARS-CoV-2 variants differ in their risk profiles remains unclear.

Methods In this analysis of 2-year retrospective cohort studies, we extracted data from the TriNetX electronic health

Lancet Psychiatry 2022

Published Online
August 17, 2022
https://doi.org/10.1016/S2215-0366(22)00260-7



This analysis of 2-year retrospective cohort studies of individuals diagnosed with COVID-19 showed that the increased incidence of mood and anxiety disorders was transient, with no overall excess of these diagnoses compared with other respiratory infections. In contrast, the increased risk of psychotic disorder, cognitive deficit, dementia, and epilepsy or seizures persisted throughout.

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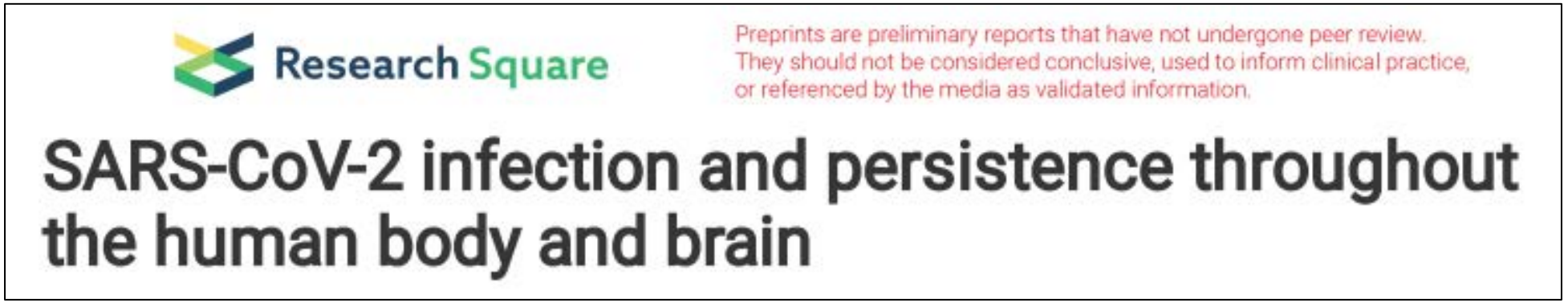
www.thelancet.com/psychiatry Published online August 17, 2022 https://doi.org/10.1016/S2215-0366(22)00260-7

How do we explain long-COVID symptoms?



- ***Autopsy study of 44 people who died of COVID-19***
- ***Extensive tissue sampling from throughout the bodies looking for long-term persistent SARS-CoV-2 virus***

https://assets.researchsquare.com/files/rs-1139035/v1_covered.pdf?c=1640020576

Study Findings

"We show that SARS-CoV-2 is widely distributed, even among patients who died with asymptomatic to 76 mild COVID-19, and that virus replication is present in multiple pulmonary and extrapulmonary tissues early in infection. Further, we detected persistent SARS-CoV-2 RNA in multiple anatomic sites, including regions throughout the brain, for up to 230 days following symptom onset."

https://assets.researchsquare.com/files/rs-1139035/v1_covered.pdf?c=1640020576

COVID-19 Can Trigger Self-Attacking Antibodies – Even in People That Had No Symptoms of Infection

TOPICS: Antibodies Cedars-Sinai Medical Center COVID-19 Immunology Infectious Diseases Popular

By CEDARS-SINAI MEDICAL CENTER JANUARY 6, 2022

Cedars-Sinai Investigators Found Evidence of an Overactive Immune Response.

https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-021-03184-8

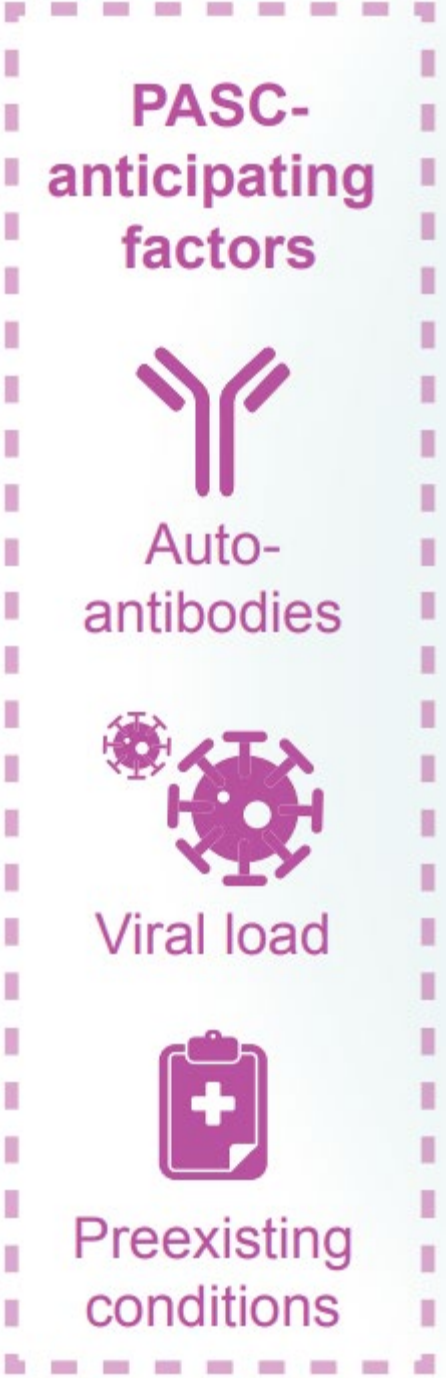
Persistent Autoimmune Response? Cause of Long-haul Symptoms?

- Infection with the virus that causes COVID-19 can trigger an immune response that lasts well beyond the initial infection and recovery—even among people who had mild symptoms or no symptoms at all….

- These patterns of immune dysregulation could be underlying the different types of persistent symptoms we see in people who go on to develop the condition now referred to as long COVID-19….

https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-021-03184-8

We identified four PASC-anticipating risk factors at the time of initial COVID-19 diagnosis: type 2 diabetes, SARS-CoV-2 RNAemia, Epstein-Barr virus viremia, and specific autoantibodies.



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Article

SARS-CoV-2 is associated with changes in brain structure in UK Biobank

https://doi.org/10.1038/s41586-022-04569-5

Received: 19 August 2021

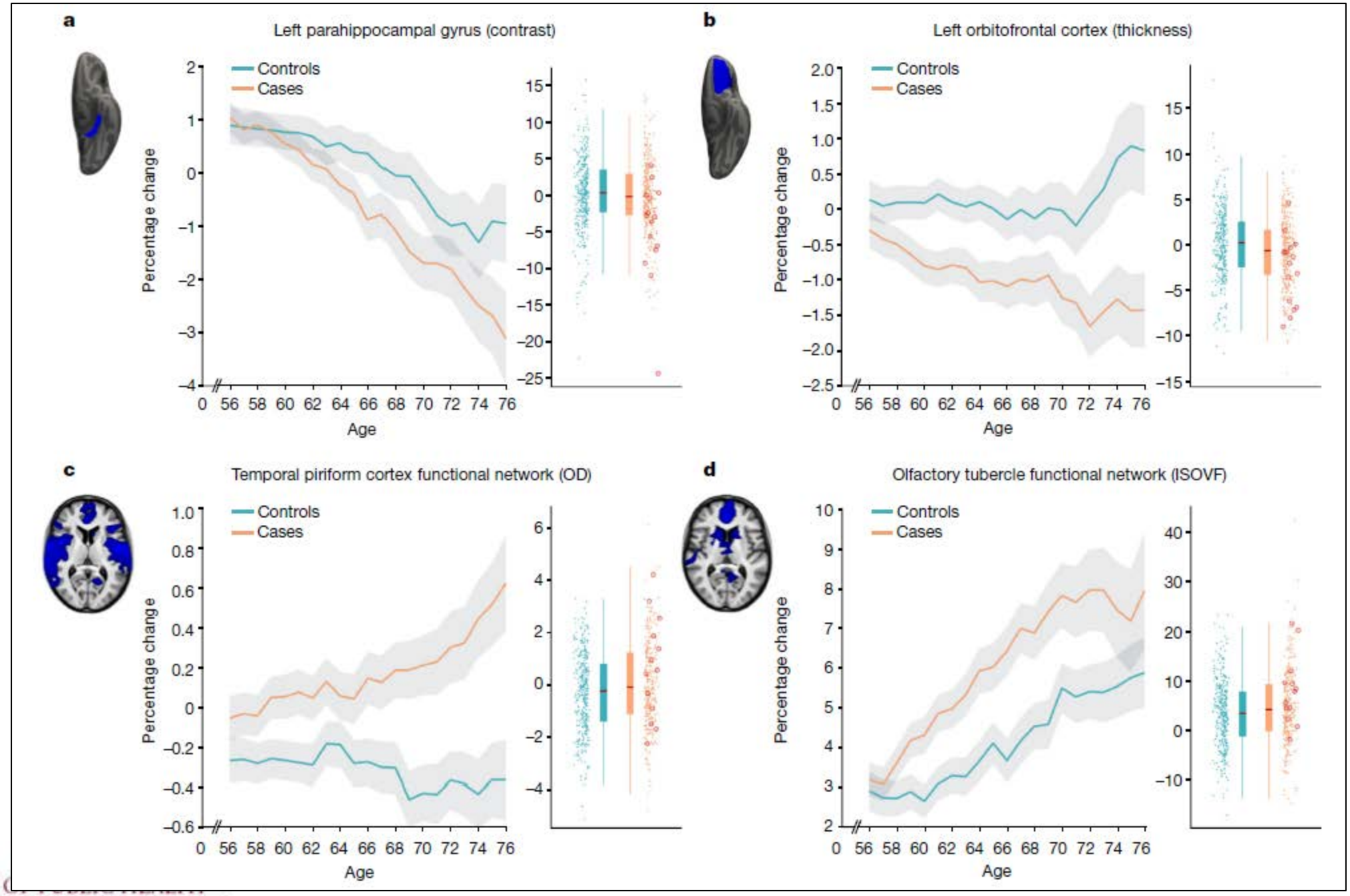
Accepted: 21 February 2022

Published online: 7 March 2022

Open access

Gwenaëlle Douaud[1]✉, Soojin Lee[1], Fidel Alfaro-Almagro[1], Christoph Arthofer[1], Chaoyue Wang[1], Paul McCarthy[1], Frederik Lange[1], Jesper L. R. Andersson[1], Ludovica Griffanti[1,2], Eugene Duff[1,3], Saad Jbabdi[1], Bernd Taschler[1], Peter Keating[4], Anderson M. Winkler[5], Rory Collins[6], Paul M. Matthews[7], Naomi Allen[6], Karla L. Miller[1], Thomas E. Nichols[8] & Stephen M. Smith[1]

Here we investigated brain changes in 785 participants of UK Biobank (aged 51–81 years) who were imaged twice using magnetic resonance imaging, including 401 cases who tested positive for infection with SARS-CoV-2 between their two scans—with 141 days on average separating their diagnosis and the second scan—as well as 384 controls.


a
Left parahippocampal gyrus (contrast)
Controls
Cases
Percentage change
Age
b
Left orbitofrontal cortex (thickness)
Controls
Cases
Percentage change
Age
c
Temporal piriform cortex functional network (OD)
Controls
Cases
Percentage change
Age
d
Olfactory tubercle functional network (ISOVF)
Controls
Cases
Percentage change
Age

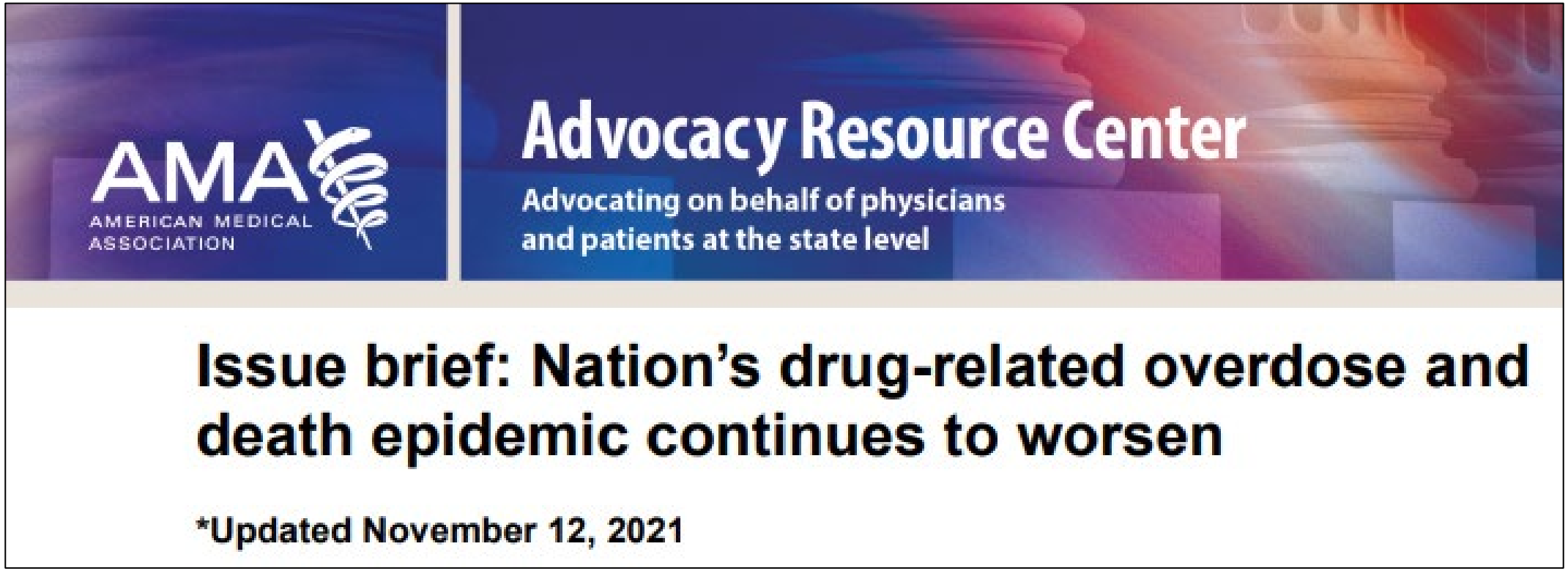
…….We identified significant longitudinal effects when comparing the two groups, including (1) a greater reduction in grey matter thickness and tissue contrast in the orbitofrontal cortex and parahippocampal gyrus; (2) greater changes in markers of tissue damage in regions that are functionally connected to the primary olfactory cortex; and (3) a greater reduction in global brain size in the SARS-CoV-2 cases. The participants who were infected with SARS-CoV-2 also showed on average a greater cognitive decline between the two time points.

Association Between BNT162b2 Vaccination and Long COVID After Infections Not Requiring Hospitalization in Health Care Workers

Table 2. Multivariable Logistic Regression Analysis of the Association of Long COVID (N = 229) With Patient Characteristics[a]

	OR (95% CI)	*P* value
Male sex	0.65 (0.44-0.98)	.04
Age[b]	1.23 (1.01-1.49)	.04
BMI[b]	1.10 (0.92-1.31)	.30
Allergies	1.50 (1.06-2.11)	.02
No. of comorbidities[c]	1.32 (1.04-1.68)	.03
COVID-19 wave		
2	0.72 (0.48-1.08)	.11
3	1.34 (0.26-7.01)	.73
Vaccine dose[d]		
1	0.86 (0.21-3.49)	.83
2	0.25 (0.07-0.87)	.03
3	0.16 (0.03-0.84)	.03

In this longitudinal observational study conducted among health care workers with SARS-CoV-2 infections not requiring hospitalization, 2 or 3 doses of vaccine, compared with no vaccination, were associated with lower long COVID prevalence.



The nation's COVID pandemic made the nation's drug overdose epidemic worse…… .. Every state has reported a spike or increase in overdose deaths or other problems during the COVID pandemic. One prevailing theme is the fact that the epidemic now is driven by illicit fentanyl, fentanyl analogs, methamphetamine, and cocaine, often in combination or in adulterated forms.

https://www.ama-assn.org/system/files/issue-brief-increases-in-opioid-related-overdose.pdf

News > Medscape Medical News

COVID Leaves Wake of Medical Debt Among US Adults

Jaleesa Baulkman

July 19, 2021

6 Read Comments

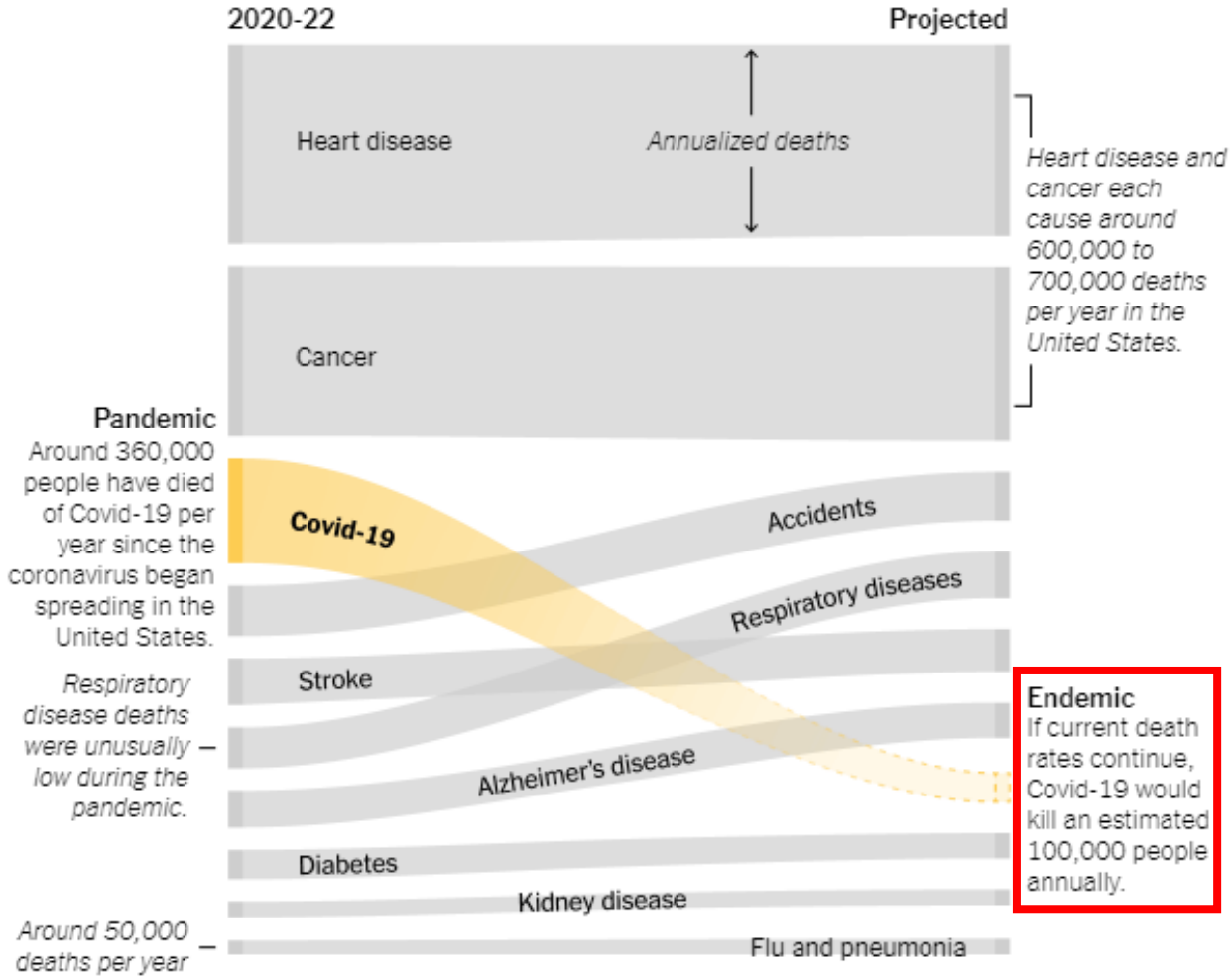
Add to Email Alerts

https://www.commonwealthfund.org/publications/issue-briefs/2021/jul/as-pandemic-eases-what-is-state-coverage-affordability-survey

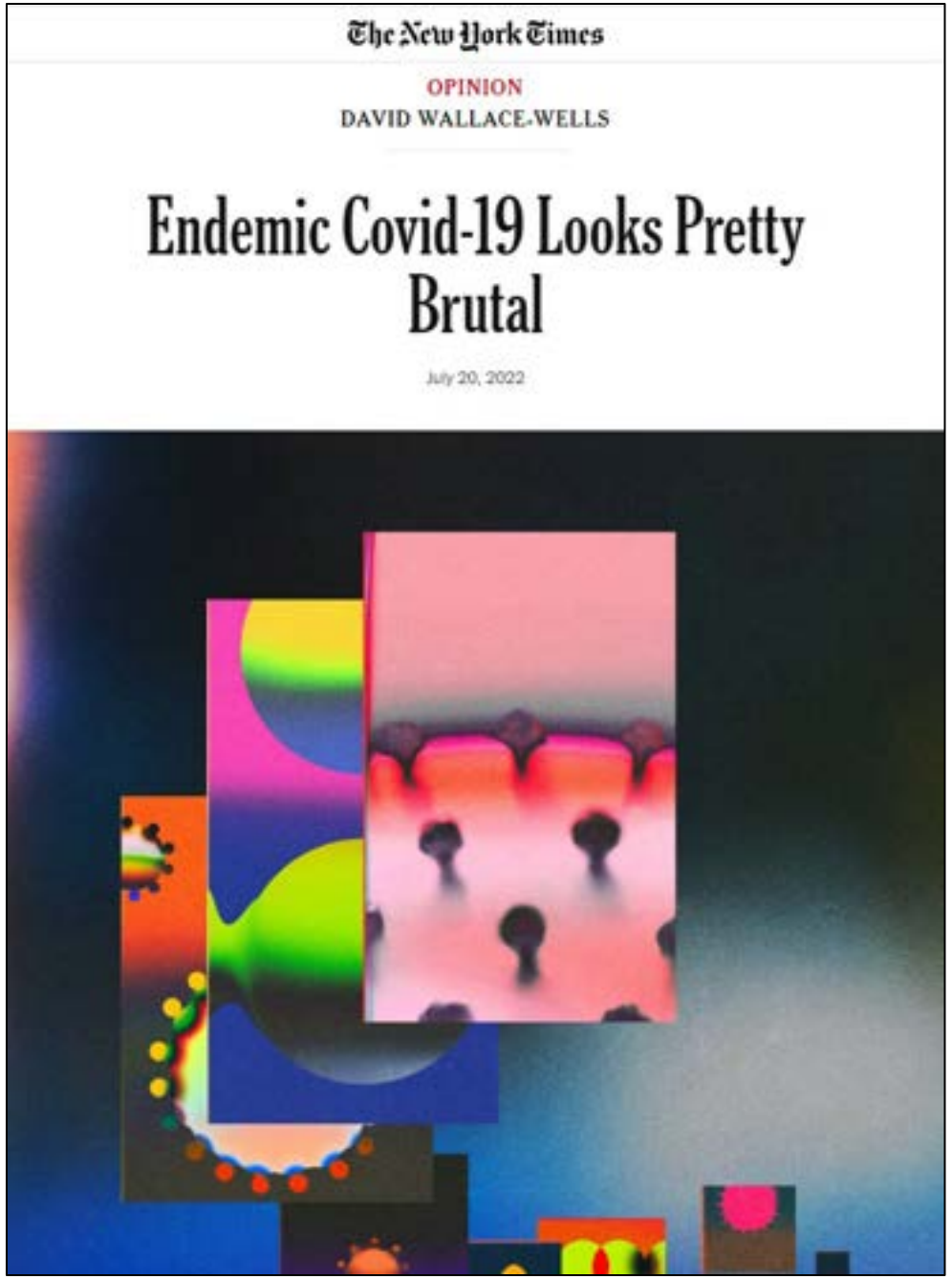
What might endemic COVID look like?

How Covid-19 might fit into the leading causes of death

Some of the most common causes of death in the United States, sized by number of deaths per year, shown during the pandemic and projected into the future.



Source: Mortality data for 2018 through June 2022 from CDC WONDER, provisional from 2021 onward. Future mortality estimated based on 2018 and 2019 data. • Note: Respiratory disease deaths were low during the pandemic due in part to lower circulation of respiratory viruses, and because some people with lung problems who could have died from respiratory disease died from Covid-19 infections instead. • Graphic by Sara Chodosh



So, when I am asked why people should be vaccinated against COVID

- The vaccines do reduce the likelihood of infection.
- Most importantly, they reduce your risk of hospitalization, complications (including AMI and stroke), and death from COVID
- They reduce the likelihood of long-COVID syndrome (PACS)
- If you do get infected, they may reduce the chance that you spread the disease to someone else.

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