

Antiviral Treatment of Non-hospitalized Adults with COVID-19

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Disclosures

Dale W. Bratzler, DO, MPH

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

Learning Objectives

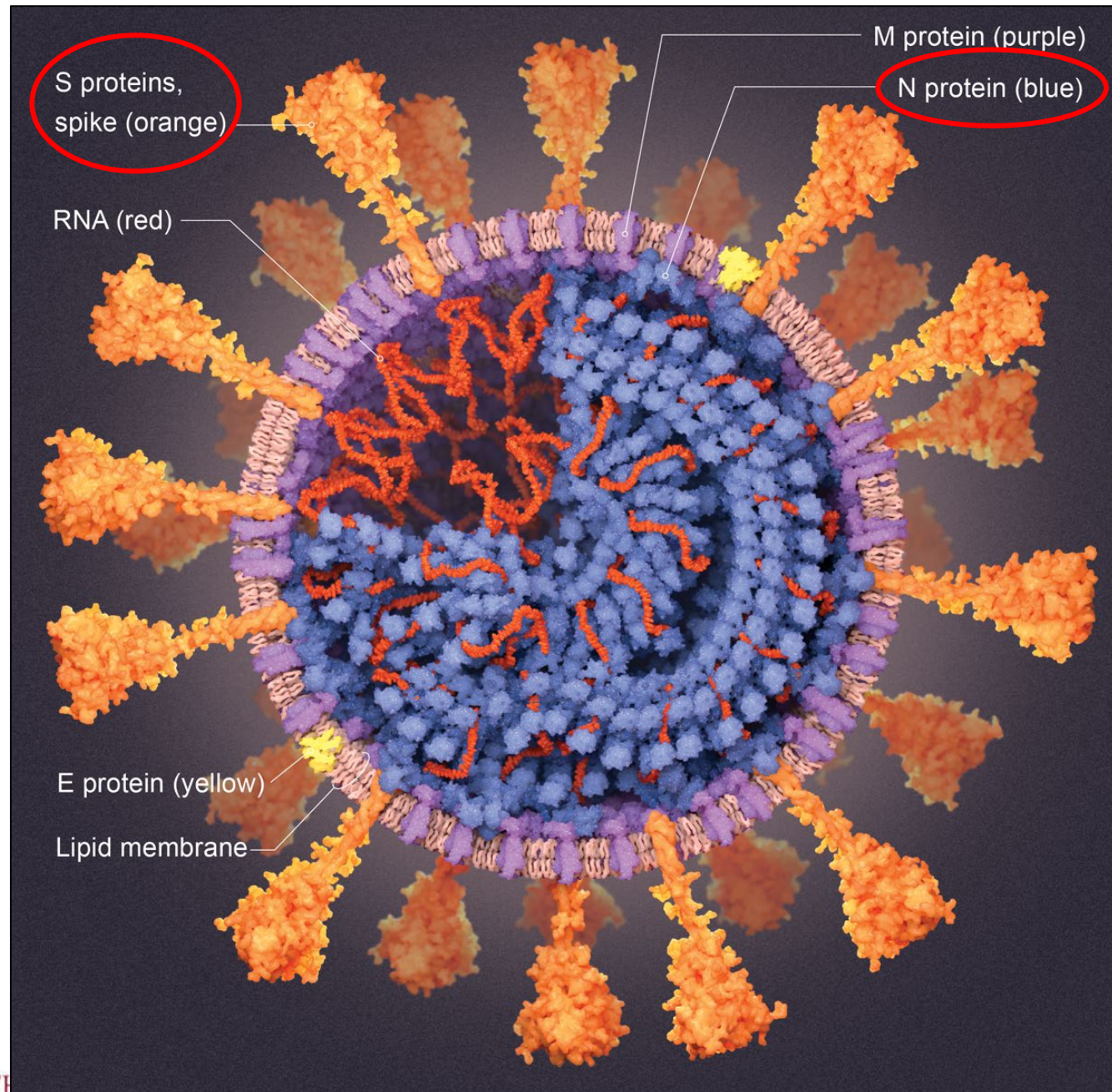
- Review the epidemiology of COVID-19 – where are we at now?
- Understand the at-risk populations for complications.
- Discuss the benefits and side-effects of taking antiviral medications for COVID-19.
- Briefly review long COVID as a disease.
- Virus protection for our seniors

Spike protein (S)

- Target of the mRNA and protein-based COVID vaccines

Anti-S antibodies from vaccination.

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



Structural proteins N, M, and E

Nucleocapsid protein (N)

- Many rapid antigen tests detect this protein

Anti-N antibodies from prior infection.

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

JHU Has Stopped Collecting Data As of **03 / 10 / 2023**

After three years of around-the-clock tracking of COVID-19 data from...

by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

Total Cases

676,609,951

Total Deaths

6,881,951

Total Vaccine Doses Administered

13,338,833,191

28-Day Cases

4,035,254

28-Day Deaths

28,018

28-Day Vaccine Doses Administered

28,156,730

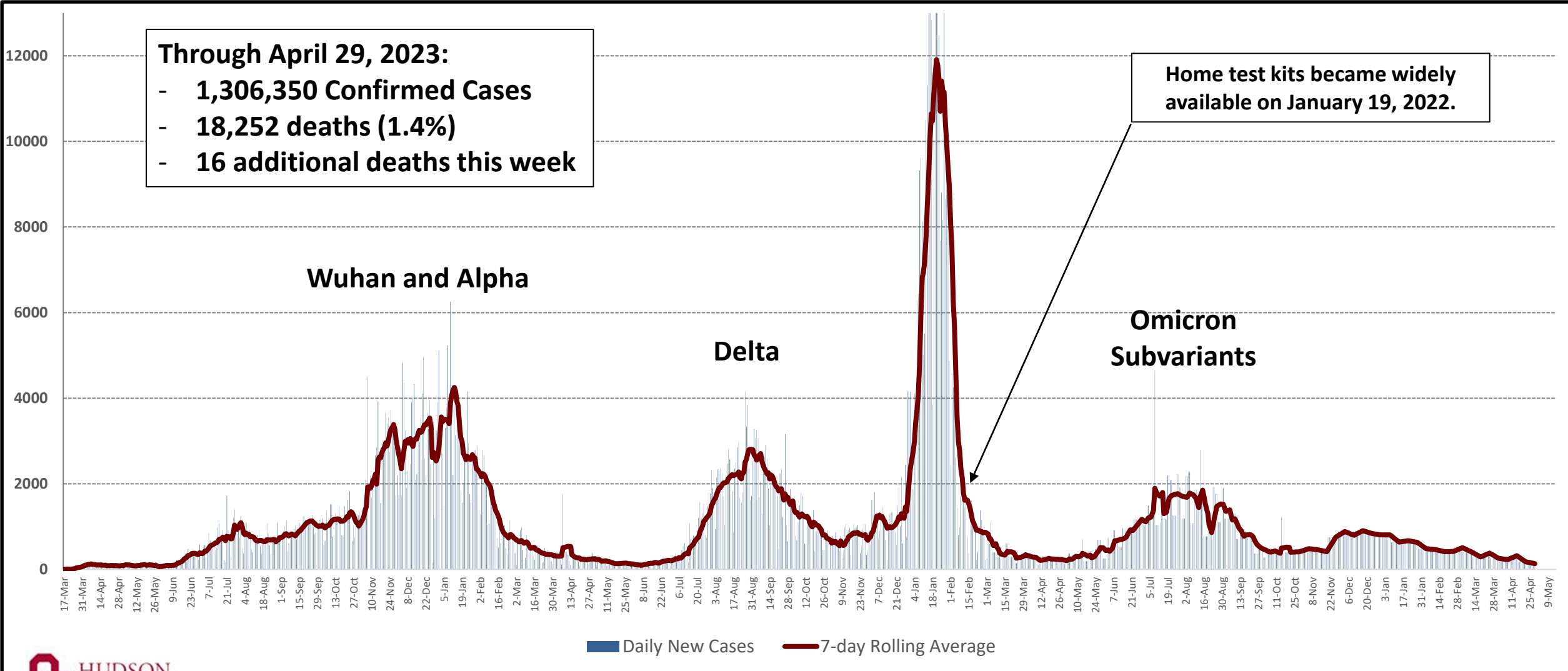
United States:

- 107,107,491 Cases
- 1,165,317 Deaths
- 675,024,615 Vaccine doses

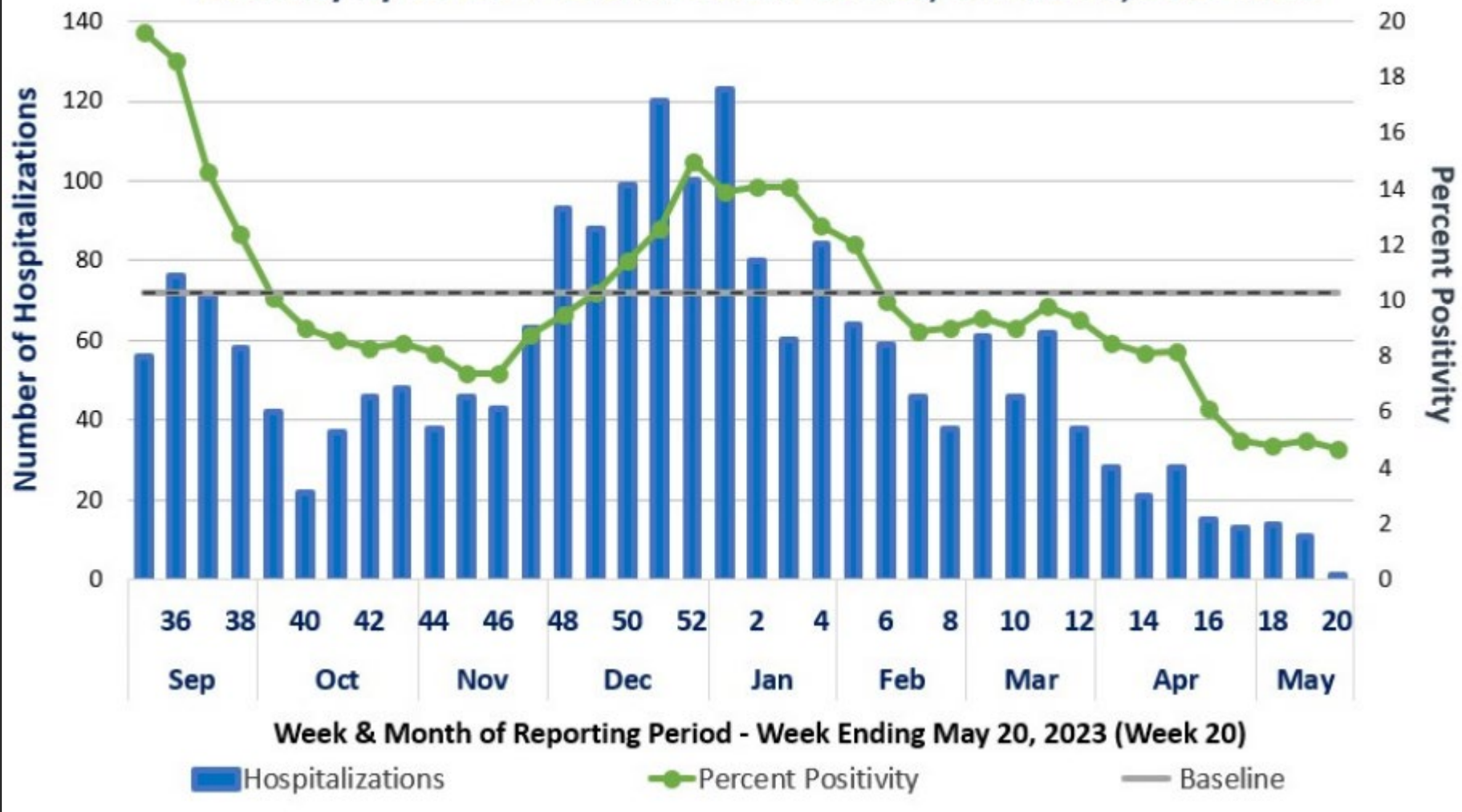
Daily New Cases with 7-day Rolling Average

Oklahoma

Omicron



COVID-19 Associated Hospitalizations and Laboratory Testing Percent Positivity by Week of Positive COVID-19 Test, Oklahoma, 2022-2023



COVID-19 Has Become a Disease of the Elderly

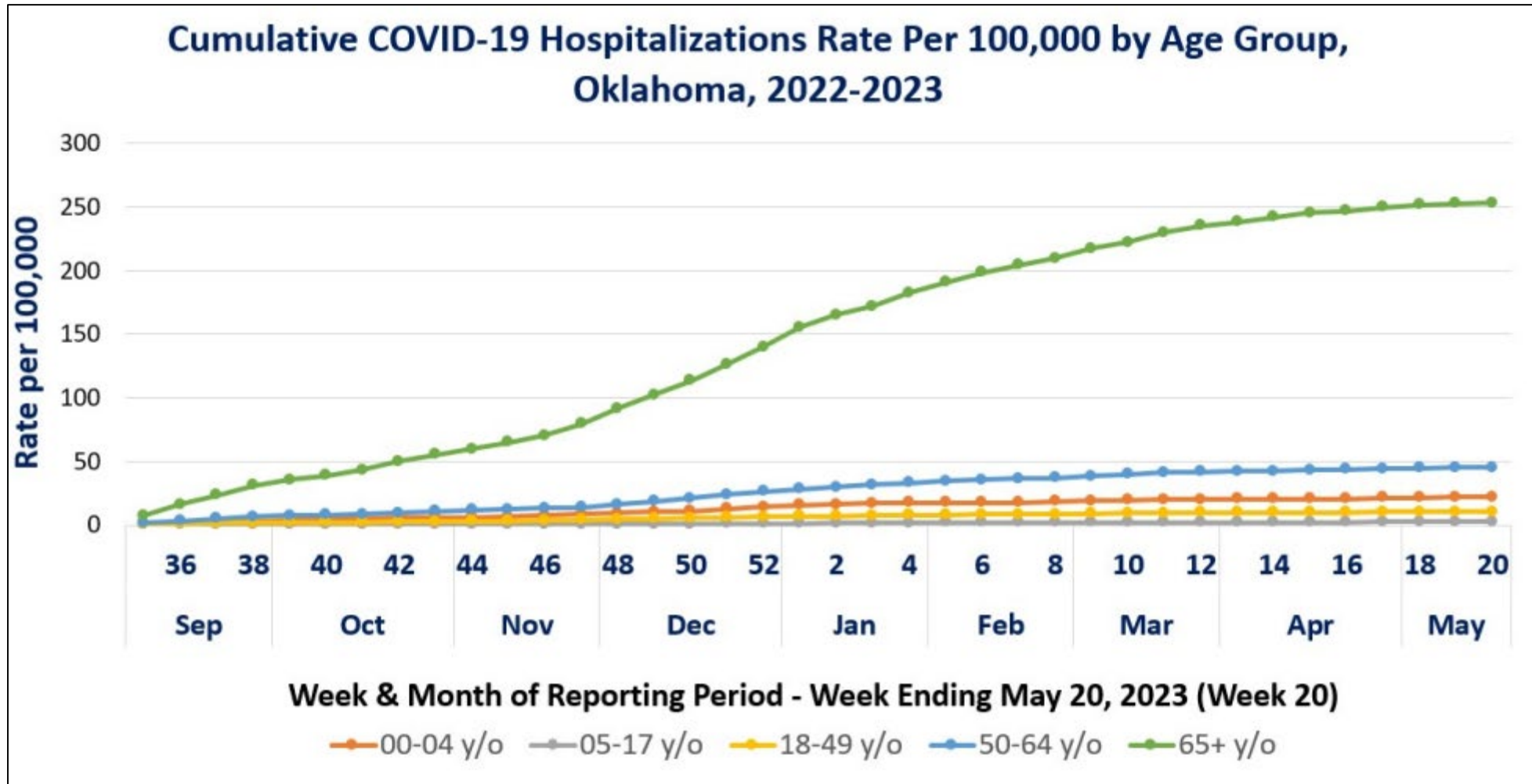
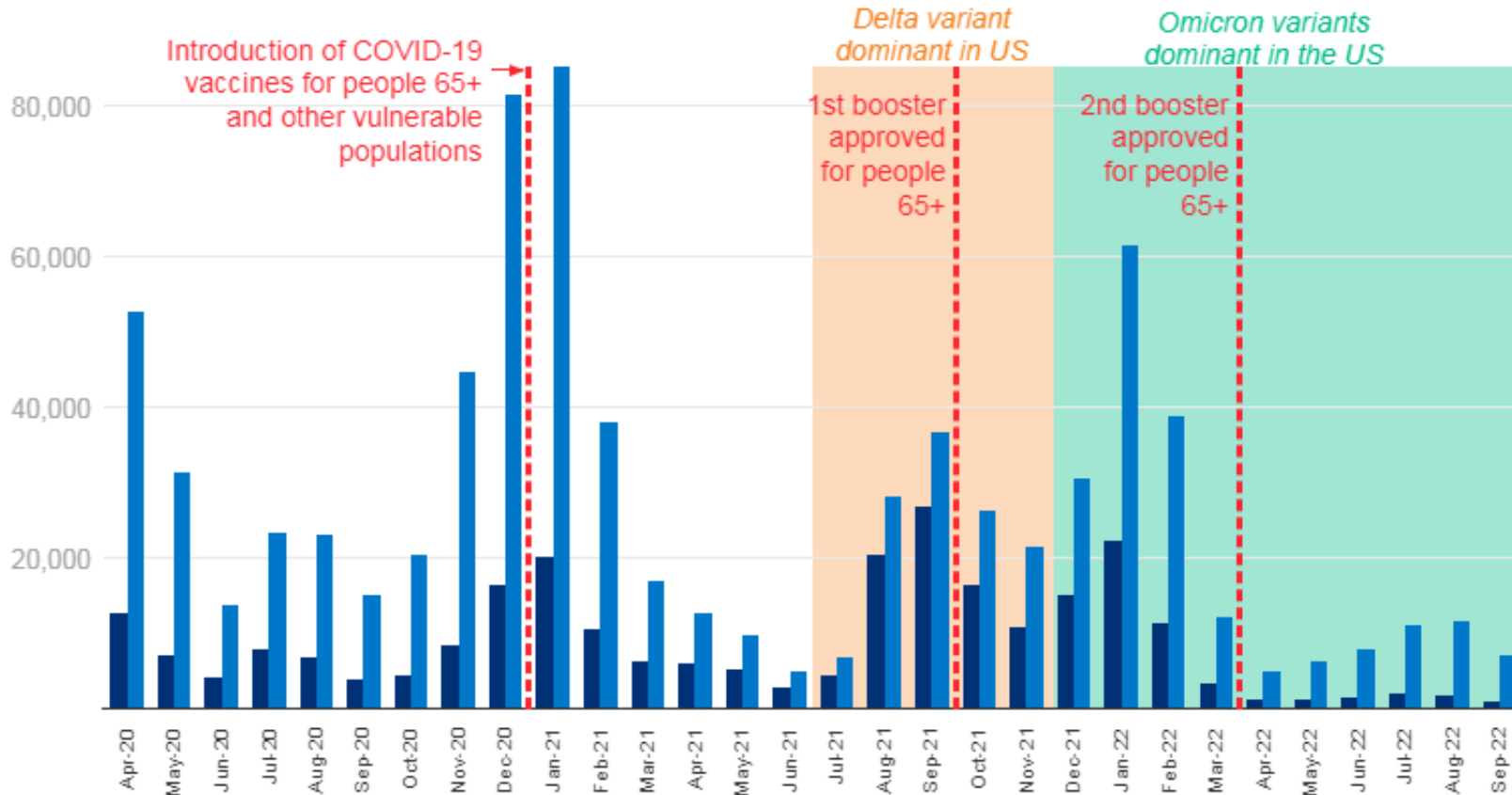


Figure 1

Deaths Due to COVID-19 Rose Faster for Older than Younger Adults in the Summer of 2022

■ COVID-19 Deaths Under 65 ■ COVID-19 Deaths 65 and Older



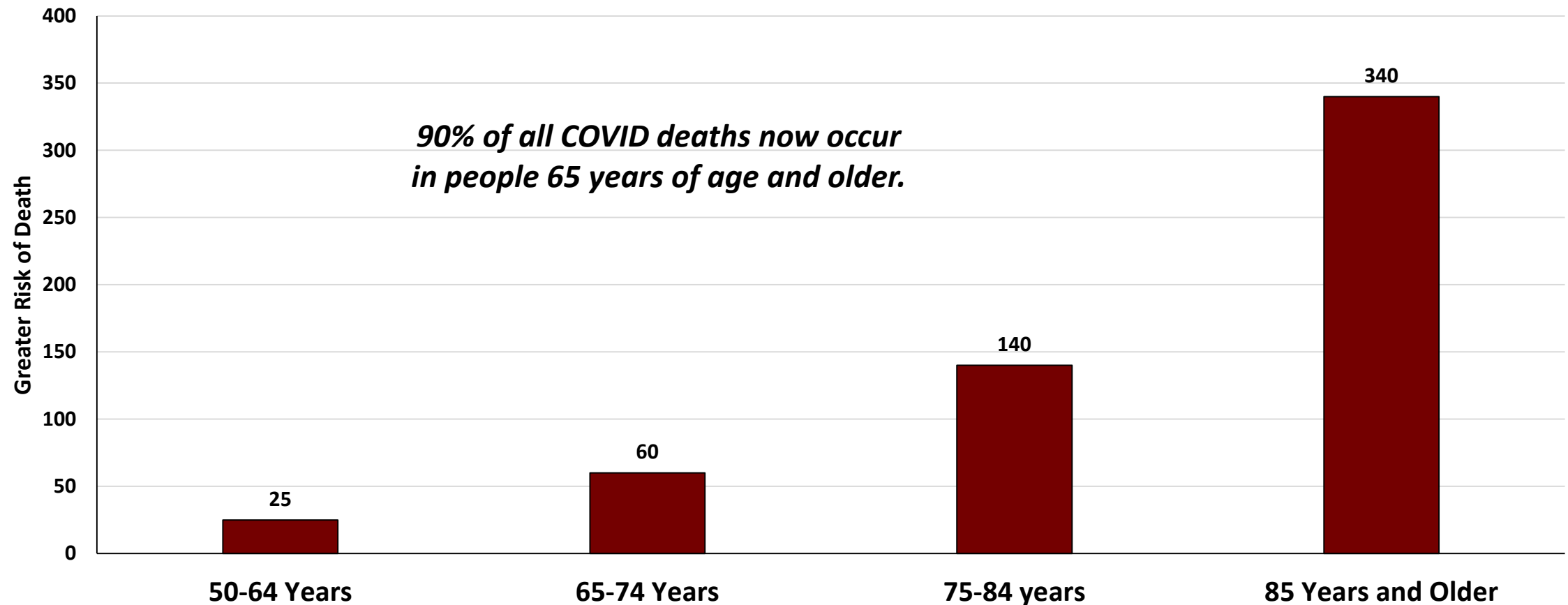
SOURCE: KFF analysis of CDC Provisional COVID-19 Death Counts by Sex and Age, as of the week ending October 1, 2022. • PNG

KFF

Risk of Death From COVID-19

As compared to people ages 18-29 years....

People 85 and older are 340 times more likely to die if they get COVID compared to the 18–29-year-old person!



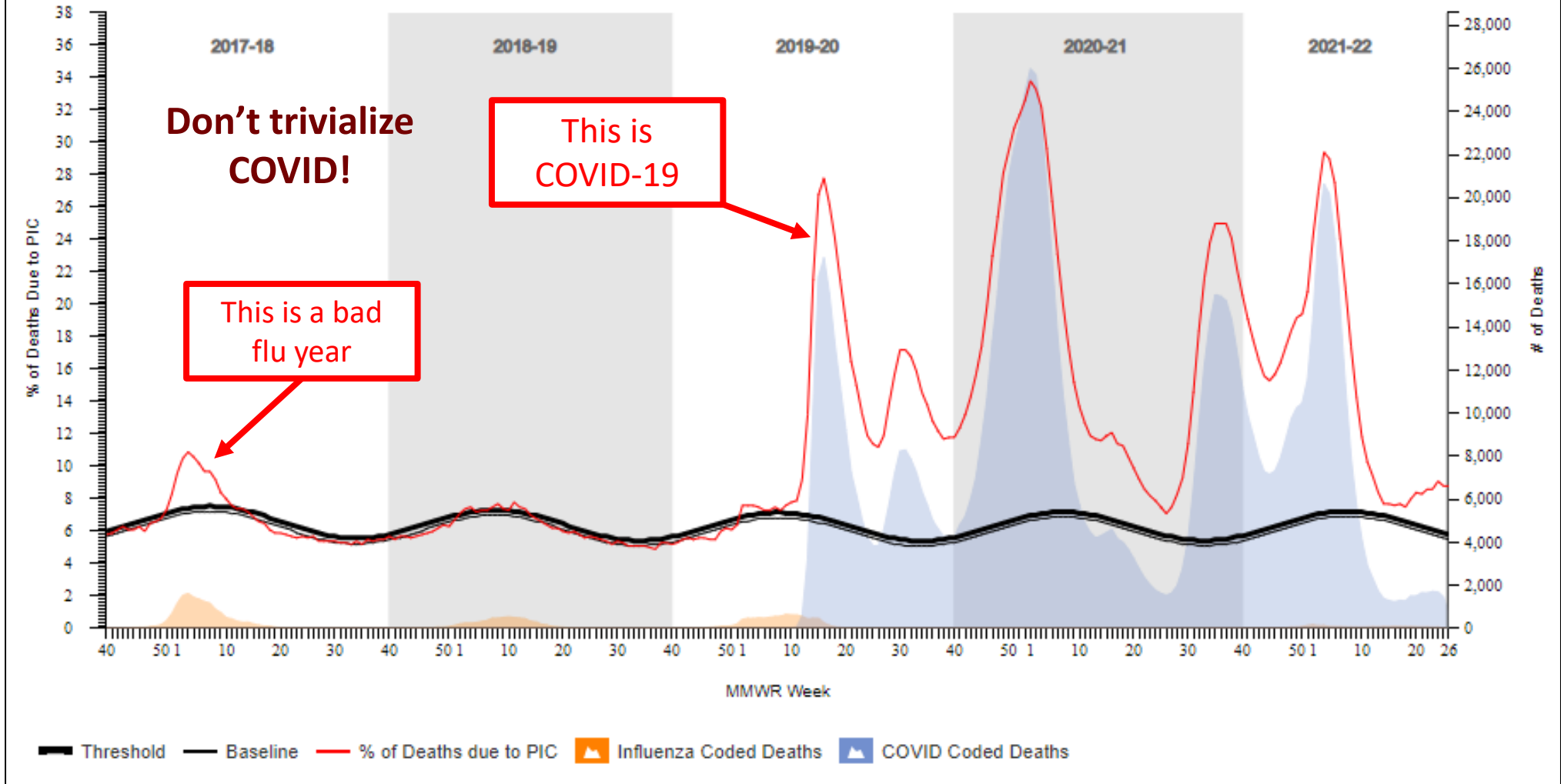
Percentage of all deaths due to pneumonia, influenza, and COVID-19, National Summary

[Download Image](#)

2017-22

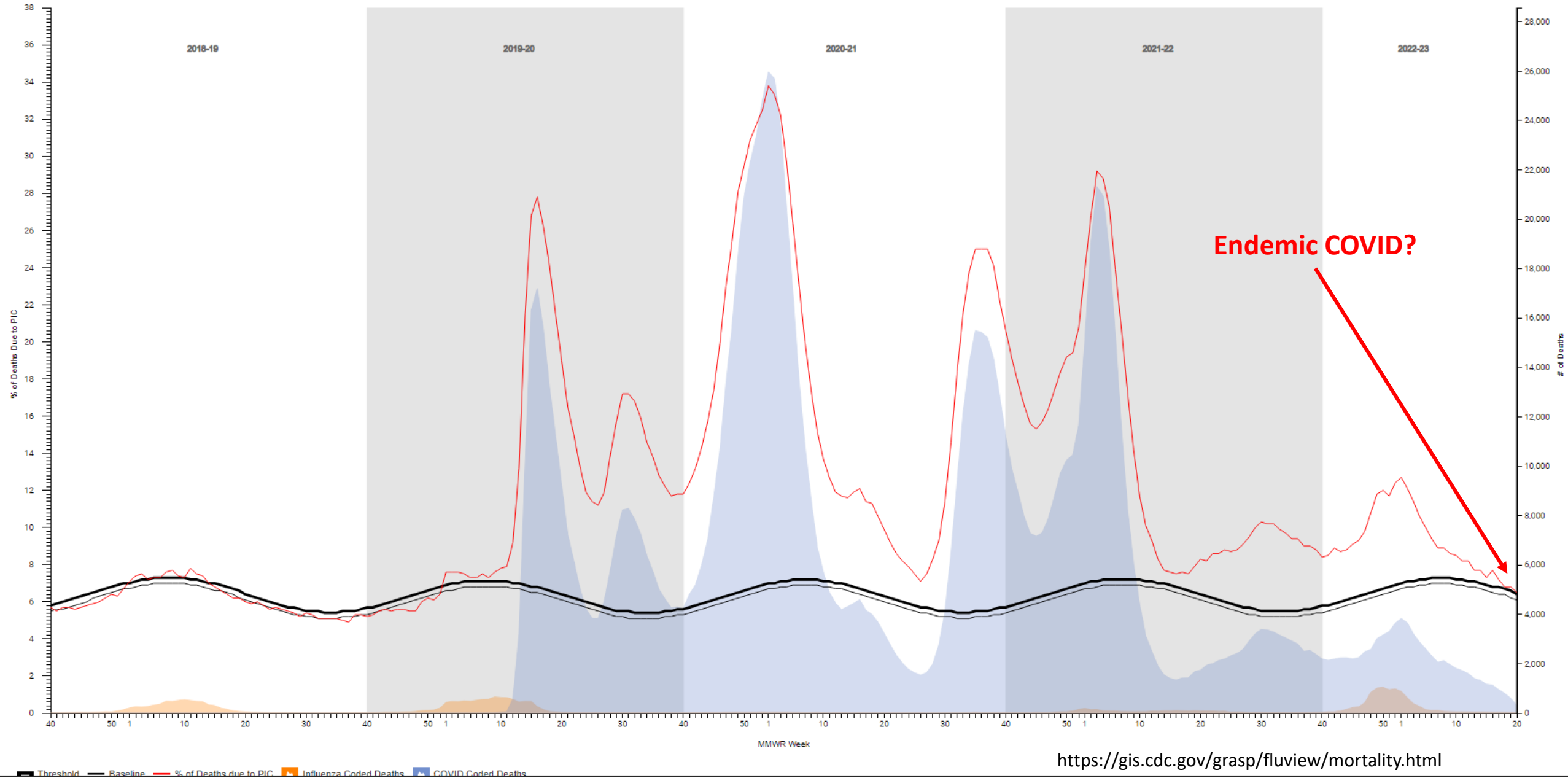
Show Number of Influenza Deaths and COVID Deaths

COVID-19 was the 3rd leading cause of death in the United States in 2020 and in 2021!



2018-23

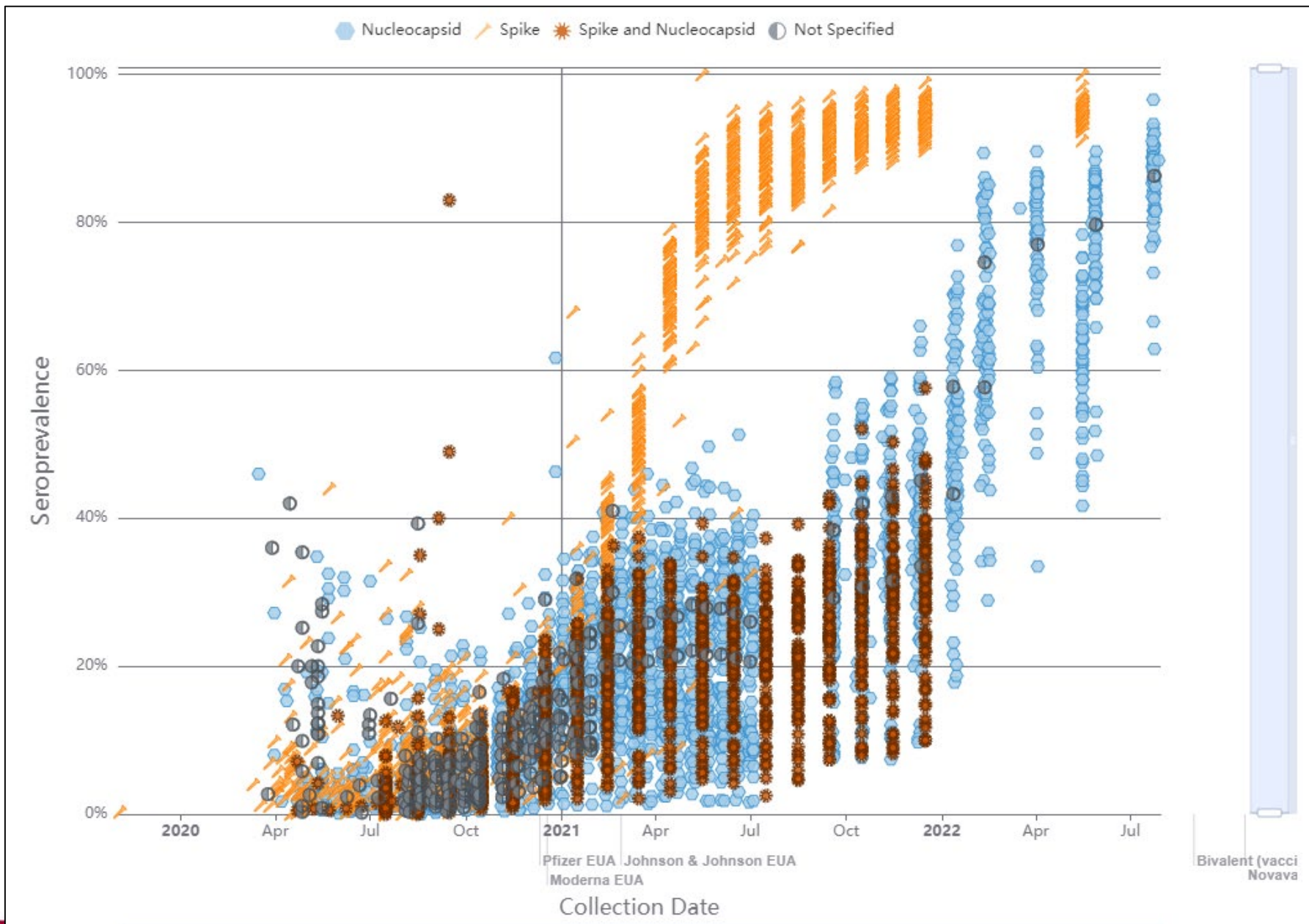
Show Number of Influenza Deaths and COVID Deaths



That's where we've been – what's different now??

Why are cases and deaths down so much now?

- Largely assumed that almost every American has either had COVID or has been vaccinated.
 - 81.3 % of US population has had at least one COVID vaccine dose
 - 69.4% have completed the primary series, but
 - Only 16.7% have received the updated bivalent booster.
 - Up to 95% + of the US population has antibodies against either the spike protein and/or the nucleocapsid proteins.

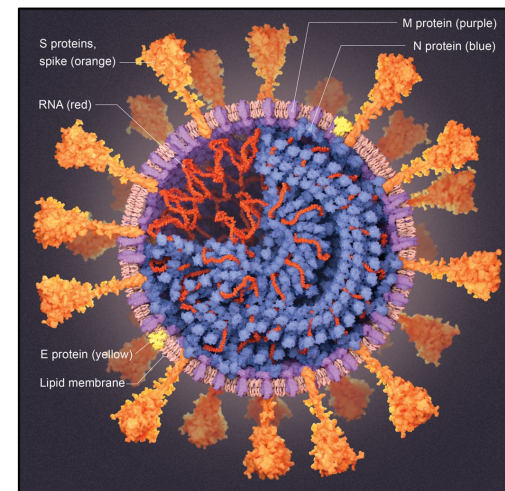


Antibodies to:

Spike glycoprotein

Nucleocapsid proteins

To both....



Vaccination is, by far, the most important thing we can do for our patients!

- Vaccination prevents COVID-19 infection.
- Vaccination dramatically reduces the risk of severe complications, hospitalization, and death from COVID-19.
- Vaccination reduces viral burden and likely reduces spread of the disease.
- Vaccination reduces the likelihood of long-COVID (PASC syndrome).

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, MD³; Junfeng Sun, PhD¹; Stacey Adjei, MPH³; Alex Mancera, MS¹; Benjamin J. Silk, PhD³; Adi V. Gundlapalli, MD, PhD³; Aaron M. Harris, MD³; Tegan K. Boehmer, PhD³; Sameer S. Kadri, MD¹ ([View author affiliations](#))

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

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.

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.

CORONAVIRUS

Prior SARS-CoV-2 infection enhances and reshapes spike protein–specific memory induced by vaccination

Véronique Barateau^{1†}, Loïc Peyrot^{1†}, Carla Saade^{1†}, Bruno Pozzetto^{1,2†}, Karen Brengel-Pesce^{3†}, Mad-Hélénie Elsensohn^{4,5}, Omran Allatif¹, Nicolas Guibert⁶, Christelle Compagnon³, Natacha Mariano⁷, Julie Chaix⁷, Sophia Djebali¹, Jean-Baptiste Fassier⁶, Bruno Lina^{1,8}, Katia Lefsihane¹, Maxime Espi¹, Olivier Thauinat¹, Jacqueline Marvel¹, Manuel Rosa-Calatrava¹, Andres Pizzorno¹, Delphine Maucort-Boulch^{4,5}, Laetitia Henaff^{1,9}, Mitra Saadatian-Elahi^{1,9}, Philippe Vanhems^{1,9}, Stéphane Paul^{1,2*‡}, Thierry Walzer^{1*‡}, Sophie Trouillet-Assant^{1,3*‡}, Thierry Defrance^{1*‡}

“.....our data suggest that prior SARS-CoV-2 infection increases the titers of SARS-CoV-2 spike protein–specific antibody responses elicited by subsequent vaccination and induces modifications in the composition of the spike protein–specific memory B cell pool that are compatible with enhanced functional protection at mucosal sites.”

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

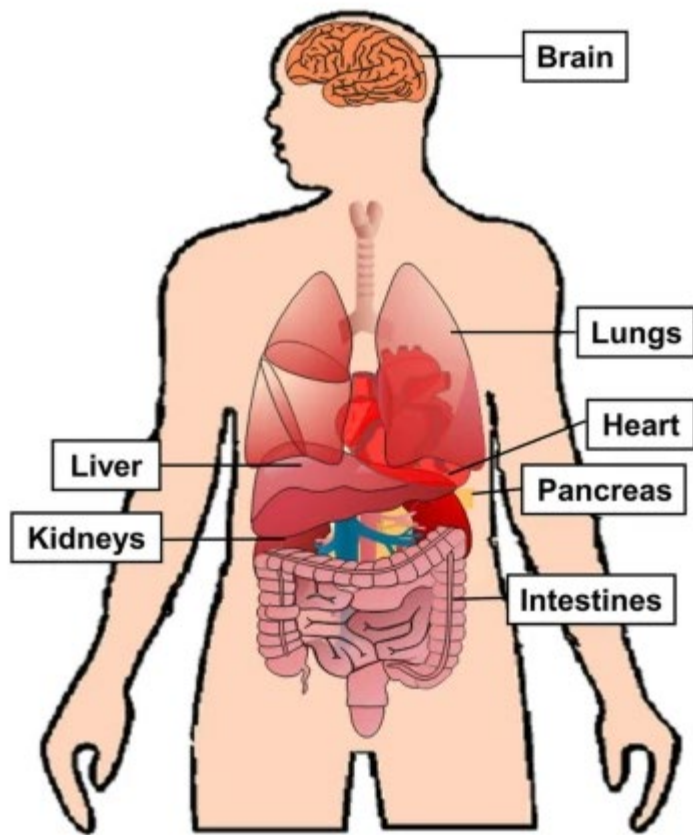
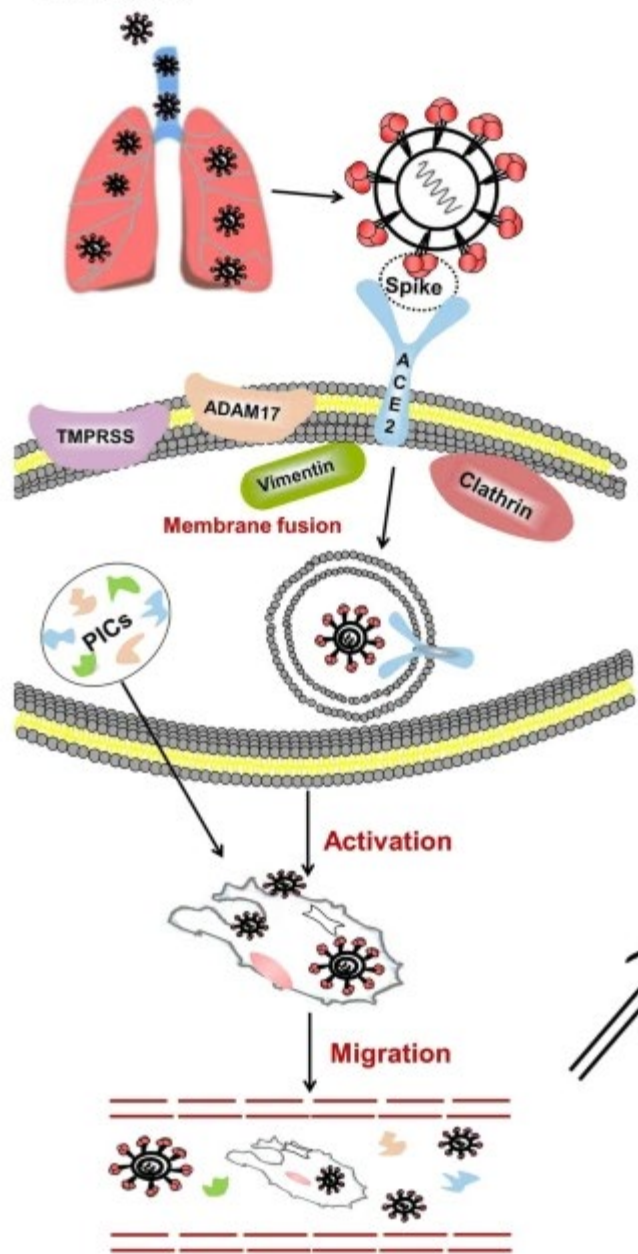
	OR (95% CI)	P value
Male sex	0.65 (0.44-0.98)	.04
Age ^b	1.23 (1.01-1.49)	.04
BMI ^b	1.10 (0.92-1.31)	.30
Allergies	1.50 (1.06-2.11)	.02
No. of comorbidities ^c	1.32 (1.04-1.68)	.03
COVID-19 wave		
2	0.72 (0.48-1.08)	.11
3	1.34 (0.26-7.01)	.73
Vaccine dose ^d		
1	0.86 (0.21-3.49)	.83
2	0.25 (0.07-0.87)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

**Despite of all of the progress, some of our patients
will still get infected with SARS-CoV-2**

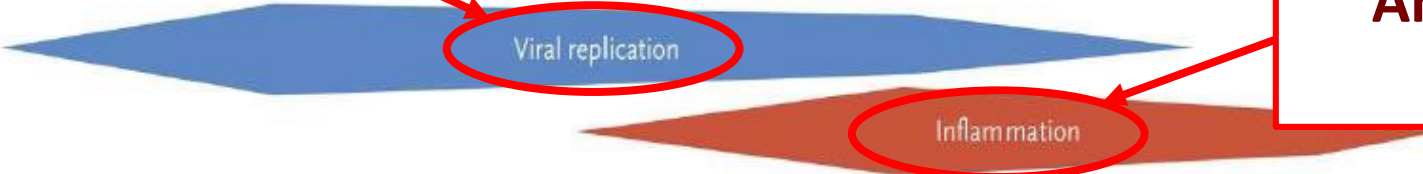
**So, what can we do to reduce the consequences of
that infection?**

SARS-CoV-2



Multi-organ injury in COVID-19

COVID Disease Progression

	Asymptomatic or Presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical Illness
Features	Positive SARS-CoV-2 test; no symptoms	Mild symptoms (e.g., fever, cough, or change in taste or smell); no dyspnea	Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation $\geq 94\%$	Oxygen saturation $< 94\%$; respiratory rate ≥ 30 breaths/min; lung infiltrates $> 50\%$	Respiratory failure, shock, and multiorgan dysfunction or failure
Testing	Screening testing; if patient has known exposure, diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing
Isolation	Yes	Yes	Yes	Yes	Yes
Proposed Disease Pathogenesis					
Potential Treatment	Antiviral therapy			Antibody therapy	
		Antibody therapy		Antiinflammatory therapy	
Management Considerations	Monitoring for symptoms	Clinical monitoring and supportive care	Clinical monitoring; if patient is hospitalized and at high risk for deterioration, possibly remdesivir	Hospitalization, oxygen therapy, and specific therapy (remdesivir, dexamethasone)	Critical care and specific therapy (dexamethasone, possibly remdesivir)

Don't use corticosteroids in early treatment!

Antivirals less effective!



Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid



Mortality and risk factors of vaccinated and unvaccinated frail patients with COVID-19 treated with anti-SARS-CoV-2 monoclonal antibodies: A real-world study



Riccardo Nevola¹, Giovanni Feola², Rachele Ruocco¹, Antonio Russo³, Angela Villani¹, Raffaele Fusco², Stefania De Pascalis³, Micol Del Core¹, Giovanna Cirigliano¹, Mariantonietta Pisaturo³, Giuseppe Loffredo¹, Luca Rinaldi¹, Aldo Marrone¹, Mario Starace³, Pellegrino De Lucia Sposito², Domenico Cozzolino¹, Teresa Salvatore¹, Miriam Lettieri⁴, Raffaele Marfella¹, Ferdinando Carlo Sasso¹, Nicola Coppola², Luigi Elio Adinolfi^{1,*}

“The data from our study show that the use of corticosteroids in the early phase of SARS-CoV-2 infection is associated with a deleterious effect on mortality. To optimize the treatment of frail patients, we suggest that corticosteroids should be avoided in the early phase of mild-moderate infection, when viral replication is at its highest and the immunological response has not yet adequately developed.”

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

PATIENT DISPOSITION

Does Not Require
Hospitalization or
Supplemental Oxygen

Viral Replication Phase

PANEL'S RECOMMENDATIONS

All patients should be offered symptomatic management **(AIII)**.

For patients who are at high risk of progressing to severe COVID-19,^a use 1 of the following treatment options:

Preferred Therapies

Listed in order of preference:

- Ritonavir-boosted nirmatrelvir (Paxlovid)^{b,c} **(AIIa)**
- Remdesivir^{c,d} **(BIIa)**

Alternative Therapies

For use *ONLY* when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order:

- ~~Bebtelovimab^e (CIII)~~
- Molnupiravir^{c,f} **(CIIa)**

The Panel **recommends against** the use of **dexamethasone^g** or **other systemic corticosteroids** in the absence of another indication **(AIII)**.

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

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ESTABLISHED IN 1812

APRIL 14, 2022

VOL. 386 NO. 15

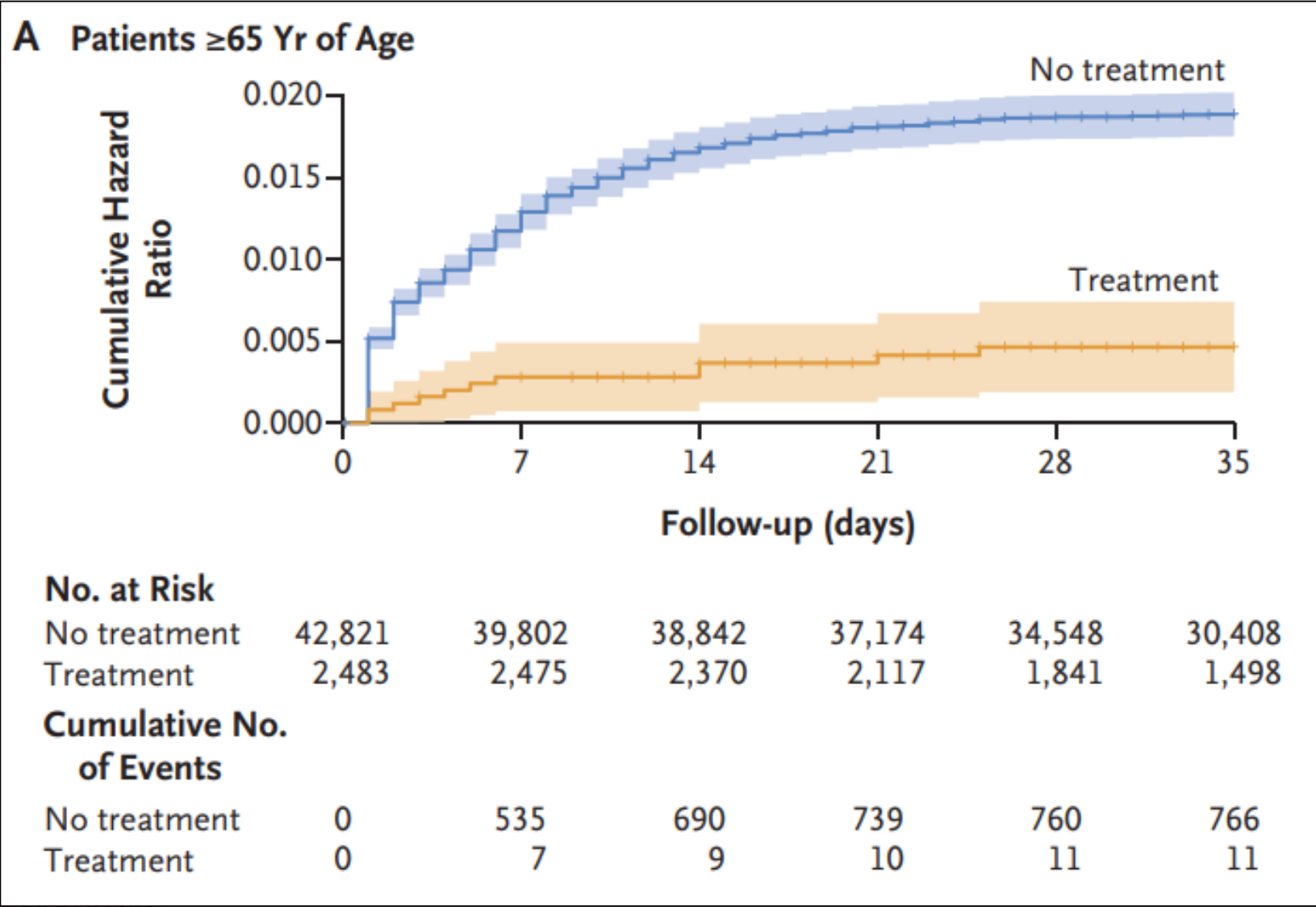
Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19

Jennifer Hammond, Ph.D., Heidi Leister-Tebbe, B.S.N., Annie Gardner, M.P.H., M.S.P.T., Paula Abreu, Ph.D.,
Weihang Bao, Ph.D., Wayne Wisemandle, M.A., MaryLynn Baniecki, Ph.D., Victoria M. Hendrick, B.Sc.,
Bharat Damle, Ph.D., Abraham Simón-Campos, M.D., Rienk Pypstra, M.D., and James M. Rusnak, M.D., Ph.D.,
for the EPIC-HR Investigators*

CONCLUSIONS:

Treatment of symptomatic Covid-19 with nirmatrelvir plus ritonavir resulted in a risk of progression to severe Covid-19 that was 89% lower than the risk with placebo, without evident safety concerns.

During the Omicron surge.. Paxlovid was highly effective!



Drug interactions – example from FDA table

Drug	Drug Class	Interaction Code
abemaciclib	Anticancer drug	***
alfuzosin	Alpha 1-adrenoreceptor antagonist	XXX
aliskiren	Cardiovascular agent	***
amiodarone	Antiarrhythmic	XXX
amlodipine	Calcium channel blocker	***
apalutamide	Anticancer drug	XXX
apixaban	Anticoagulant	***
aripiprazole	Neuropsychiatric agent	***
avanafil	PDE5 inhibitor	***
bedaquiline	Antimycobacterial	***
betamethasone	Systemic corticosteroid	***
brexpiprazole	Neuropsychiatric agent	***
bosentan	Endothelin receptor antagonist	***
budesonide	Systemic corticosteroid	***
bupropion	Antidepressant	***

Remdesivir (Veklury) – second drug of choice

- Intravenous remdesivir is approved by the Food and Drug Administration (FDA) for the treatment of COVID-19 in adults and pediatric patients aged ≥ 28 days and weighing ≥ 3 kg.
- In high-risk, non-hospitalized patients with mild to moderate COVID-19, remdesivir should be started within 7 days of symptom onset and administered for 3 days.

Remdesivir (Veklury) for Non-hospitalized patients

The NEW ENGLAND JOURNAL of MEDICINE

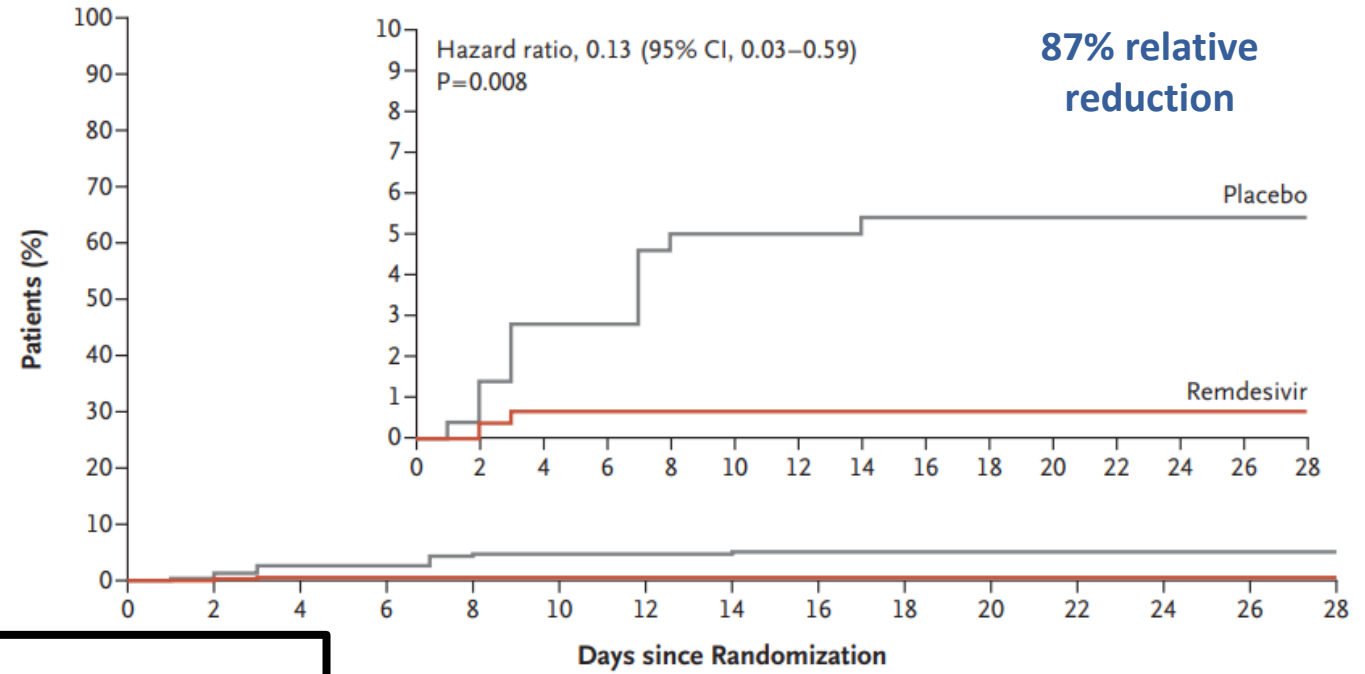
ORIGINAL ARTICLE

Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients

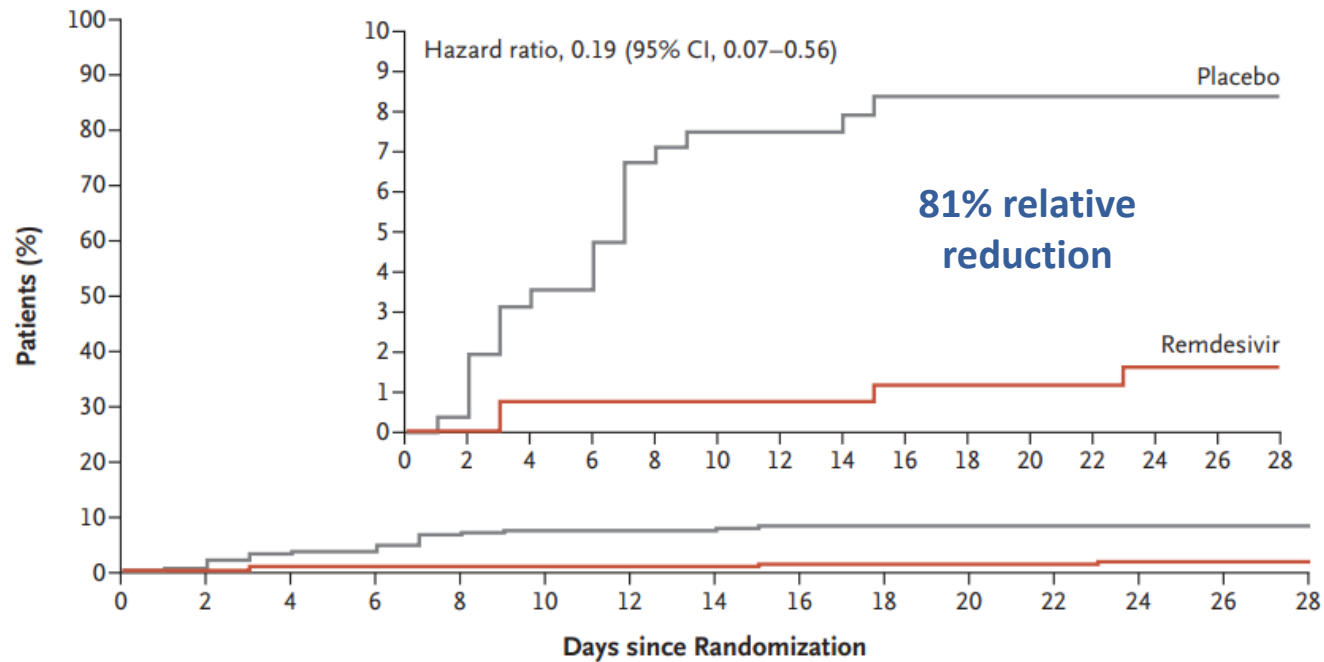
Among non-hospitalized patients who were at high risk for Covid-19 progression, a 3-day course of remdesivir had an acceptable safety profile and resulted in an 87% lower risk of hospitalization or death than placebo.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2116846>

A Covid-19–Related Hospitalization or Death from Any Cause



B Covid-19–Related Medically Attended Visit or Death from Any Cause



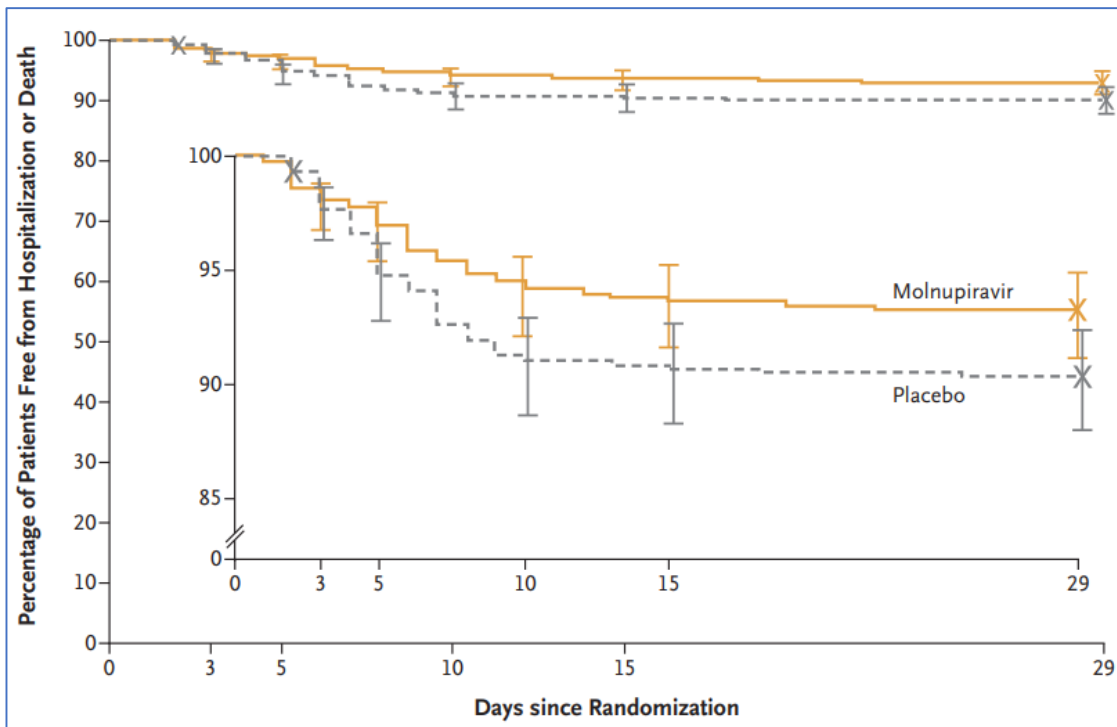
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

FEBRUARY 10, 2022

VOL. 386 NO. 6

Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients



By day 29, the use of molnupiravir reduced the risk of hospitalization or death by 31%, with 48 of 709 participants (6.8%) in the molnupiravir arm experiencing hospitalization or death compared with 68 of 699 participants (9.7%) in the placebo arm (-3.0% adjusted difference; 95% CI, -5.9% to -0.1%).

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

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Hospitalization or
Supplemental Oxygen

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The Panel **recommends against** the use of **dexamethasone^g** or **other systemic corticosteroids** in the absence of another indication **(AIII)**.

How do we explain long-COVID symptoms?

Research

JAMA | Original Investigation

Development of a Definition of Postacute Sequelae of SARS-CoV-2 Infection

Tanayott Thaweethai, PhD; Sarah E. Jolley, MD, MS; Elizabeth W. Karlson, MD, MS; Emily B. Levitan, ScD; Bruce Levy, MD; Grace A. McComsey, MD; Lisa McCorkell, MPP; Girish N. Nadkarni, MD, MPH; Sairam Parthasarathy, MD; Upinder Singh, MD; Tiffany A. Walker, MD; Caitlin A. Selvaggi, MS; Daniel J. Shinnick, MS; Carolin C. M. Schulte, PhD; Rachel Atchley-Challenner, PhD; RECOVER Consortium Authors; Leora I. Horwitz, MD; Andrea S. Foulkes, ScD; for the RECOVER Consortium

Table 2. Model-Selected Symptoms That Define PASC and Their Corresponding Scores^a

Symptom	Log odds ratio	Score
Smell/taste	0.776	8
Postexertional malaise	0.674	7
Chronic cough	0.438	4
Brain fog ^b	0.325	3
Thirst	0.255	3
Palpitations	0.238	2
Chest pain ^b	0.233	2
Fatigue ^b	0.148	1
Sexual desire or capacity	0.126	1
Dizzines	0.121	1
Gastrointestinal	0.085	1
Abnormal movements	0.072	1
Hair loss	0.049	0

SARS-CoV-2 infection and persistence throughout the human body and brain

- ***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***

Study Findings – are there viral reservoirs?

“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.”

EPIDEMIOLOGY

People with Long COVID May Still Have Spike Proteins in Their Blood

A possible biomarker for long COVID suggests some people with the condition never fully cleared the virus

By Sasha Warren on July 21, 2022

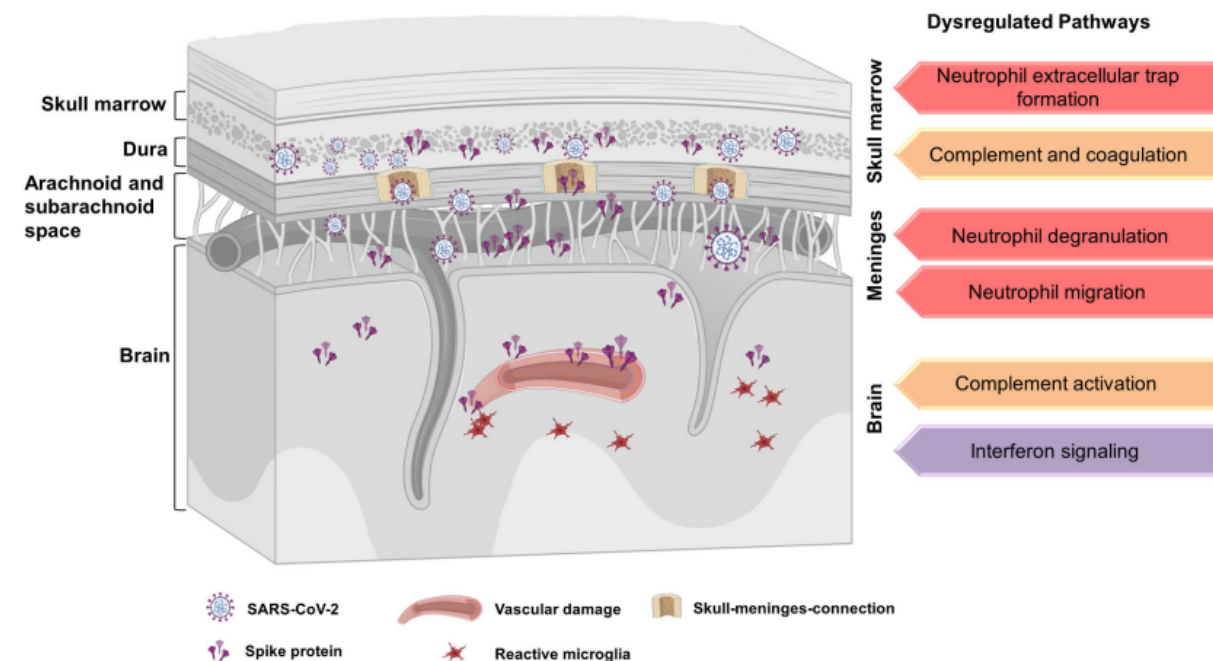
“.....researchers reported detecting a fragment of SARS-CoV-2 in blood samples from long COVID sufferers up to a year after their original infection.”

“.....we observed the presence of spike protein in the skull of deceased patients long after their COVID-19 infection, suggesting that the spike’s persistence may contribute to long-term neurological symptoms.”

SARS-CoV-2 Spike Protein Accumulation in the Skull-Meninges-Brain Axis: Potential Implications for Long-Term Neurological Complications in post-COVID-19

Zhouyi Rong^{1,2,15†}, Hongcheng Mai^{1,2,15†}, Saketh Kapoor^{1†}, Victor G. Puelles^{3,4,13,14}, Jan Czogalla^{3,4}, Julia Schädler⁵, Jessica Vering⁵, Claire Delbridge⁶, Hanno Steinke⁷, Hannah Frenzel⁷, Katja Schmidt⁷, Özüm Sehnaz Caliskan⁹, Jochen Martin Wettengel¹⁰, Fatma Cherif¹¹, Mayar Ali^{1,16}, Zeynep Ilgin Kolabas^{1,2,16}, Selin Ulukaya¹, Izabela Horvath^{1,17}, Shan Zhao¹, Natalie Krahmer⁹, Sabina Tahirovic¹¹, Ali Önder Yildirim¹², Tobias B. Huber^{3,4}, Benjamin Ondruschka^{3,5}, Ingo Bechmann⁷, Gregor Ebert⁸, Ulrike Protzer¹⁰, Harsharan Singh Bhatia^{1,2}, Farida Hellal^{1,2}, Ali Ertürk^{1,2*}

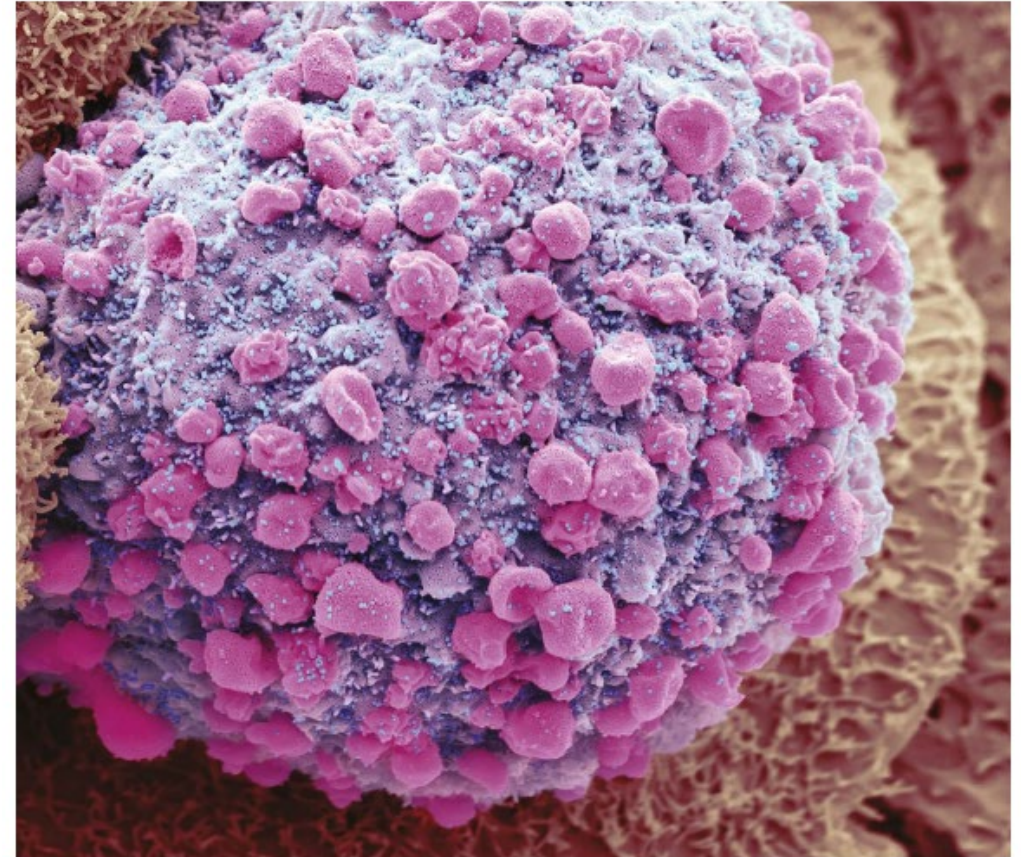
Graphical Summary



“.....both teams published results last month suggesting that pieces of SARS-CoV-2 can linger in the gut for months after an initial infection. The findings add to a growing pool of evidence supporting the hypothesis that persistent bits of virus — coronavirus “ghosts”, Bhatt has called them — could contribute to the mysterious condition called long COVID.”

Natarajan, A. et al. Med <https://doi.org/10.1016/j.medj.2022.04.001> (2022).

Zollner, A. et al. Gastroenterology <https://doi.org/10.1053/j.gastro.2022.04.037> (2022)



Particles of SARS-CoV-2 (blue; artificially coloured) bud from a dying intestinal cell.

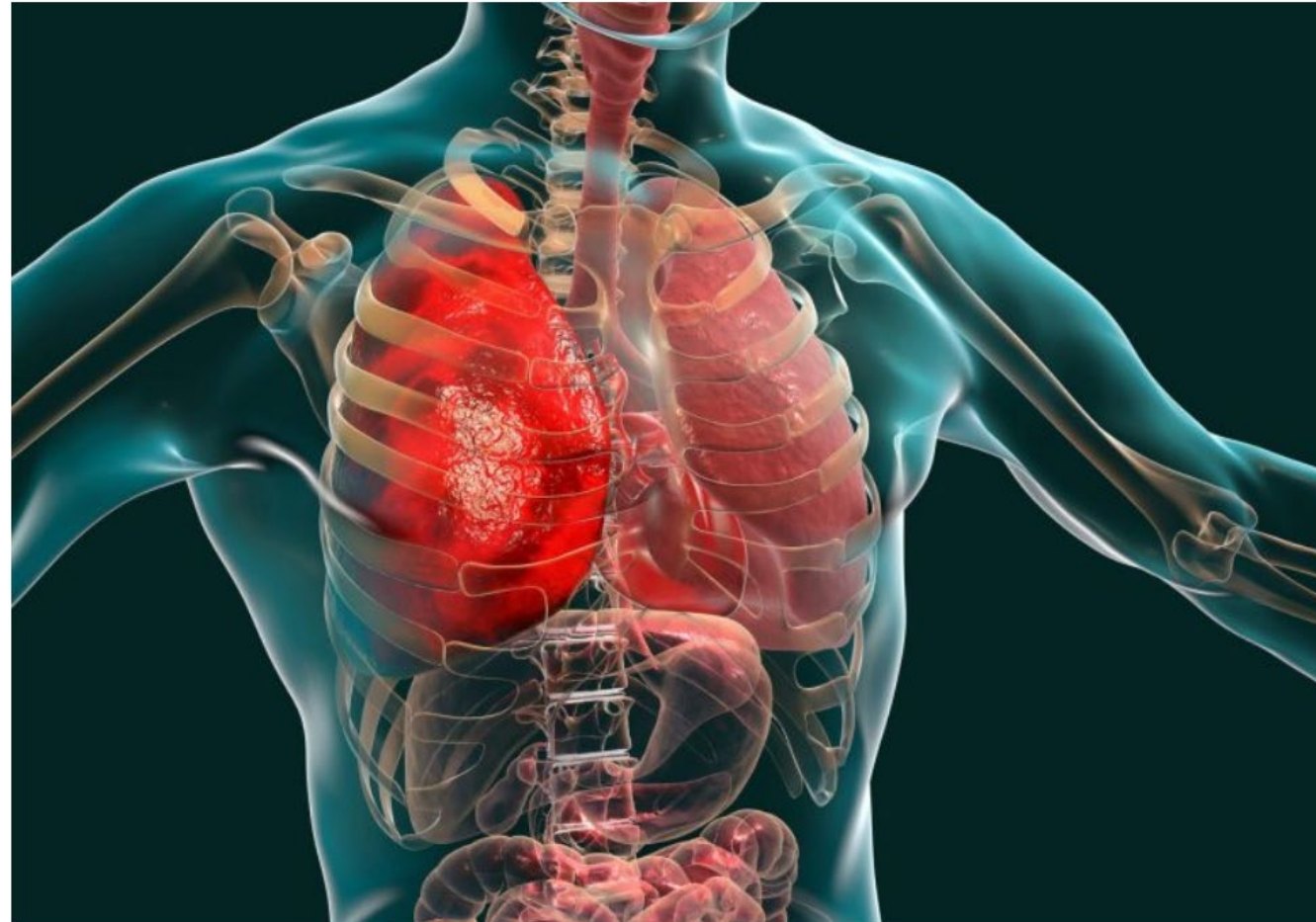
CORONAVIRUS ‘GHOSTS’ CAN LINGER FOR MONTHS IN THE GUT

Scientists are studying whether long COVID could be linked to viral fragments that persist in various tissues.

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



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

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

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....

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

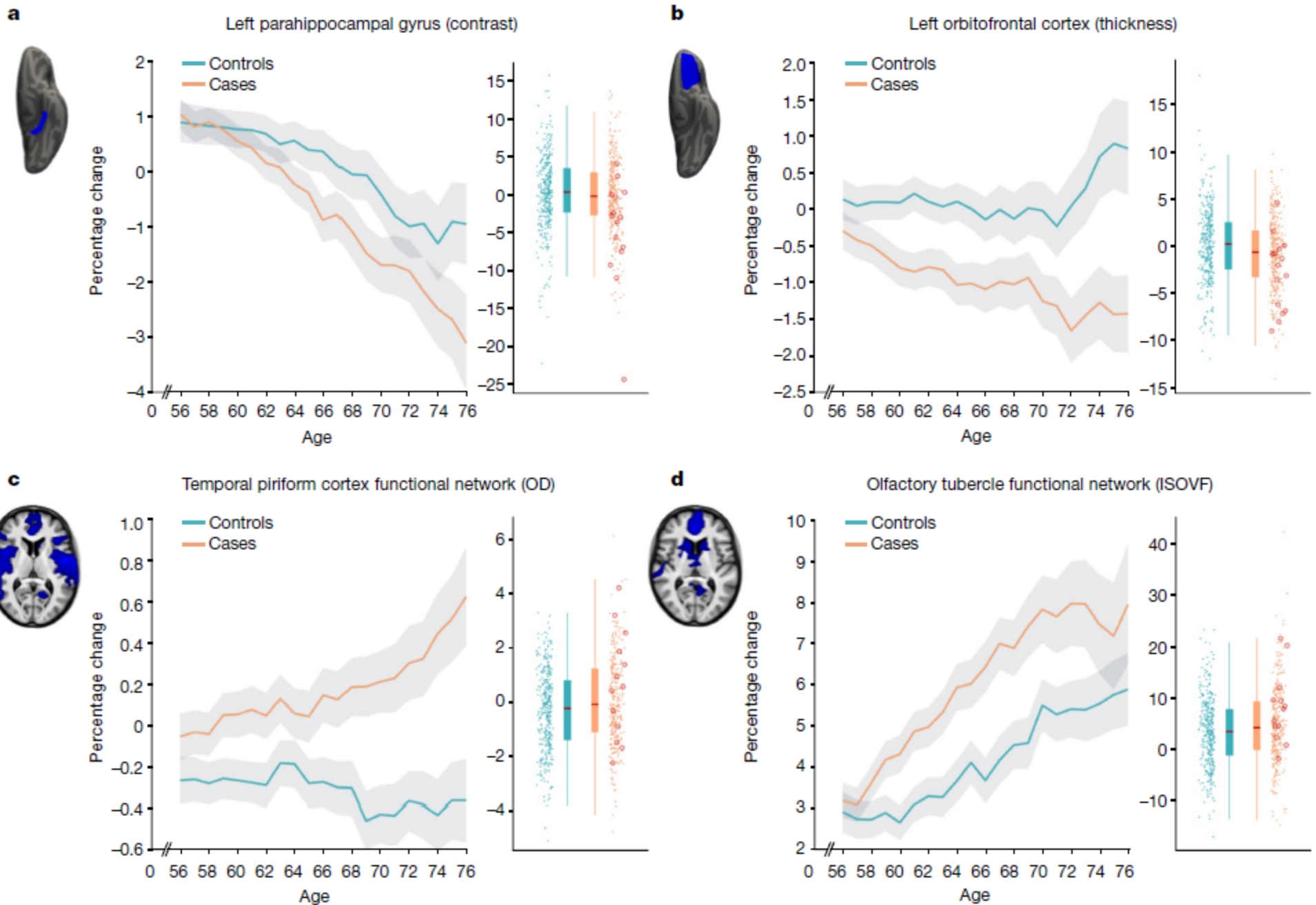
Accepted: 21 February 2022

Published online: 7 March 2022

Open access

Gwenaëlle Douaud¹✉, Soojin Lee¹, Fidel Alfaro-Almagro¹, Christoph Arthofer¹, Chaoyue Wang¹, Paul McCarthy¹, Frederik Lange¹, Jesper L. R. Andersson¹, Ludovica Griffanti^{1,2}, Eugene Duff^{1,3}, Saad Jbabdi¹, Bernd Taschler¹, Peter Keating⁴, Anderson M. Winkler⁵, Rory Collins⁶, Paul M. Matthews⁷, Naomi Allen⁶, Karla L. Miller¹, Thomas E. Nichols⁸ & Stephen M. Smith¹

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.

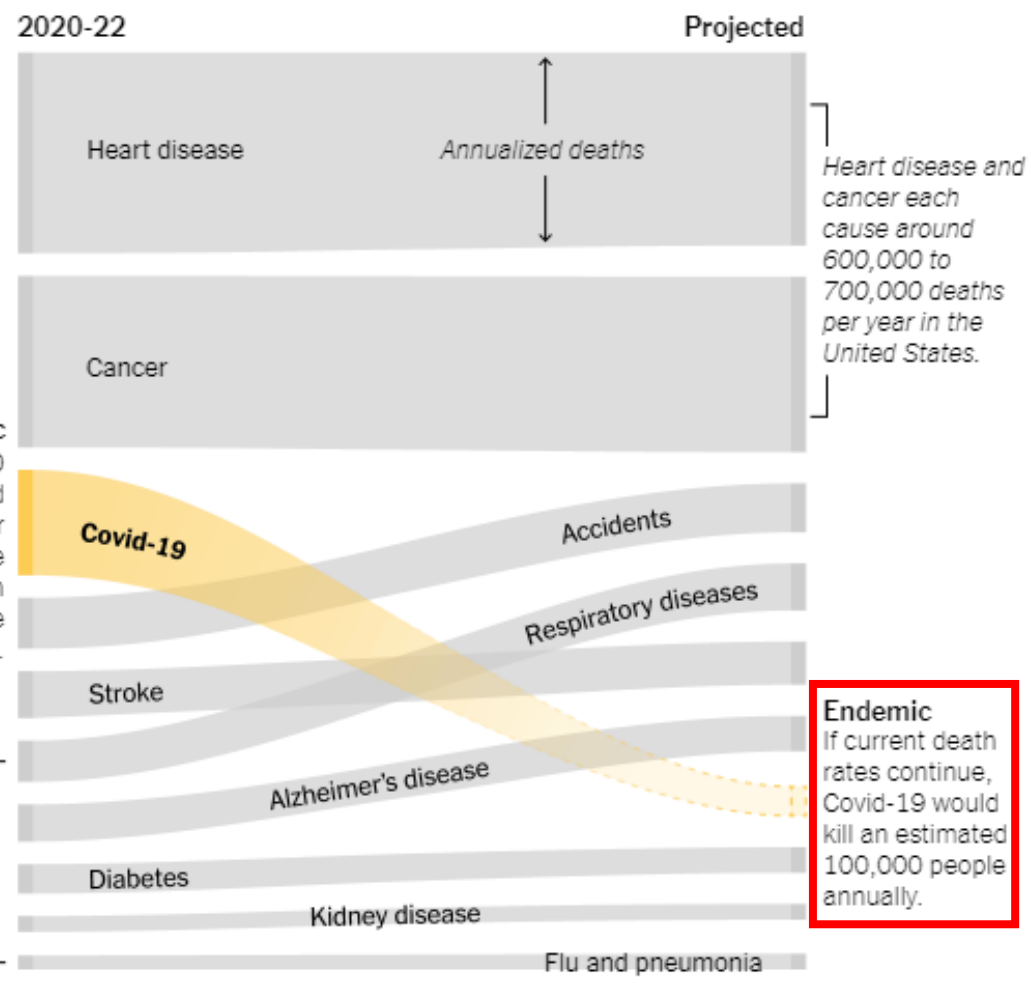


.....We identified significant longitudinal effects when comparing the two groups, including (1) a greater reduction in grey matter thickness and tissue contrast in the orbitofrontal cortex and parahippocampal gyrus; (2) greater changes in markers of tissue damage in regions that are functionally connected 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.

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

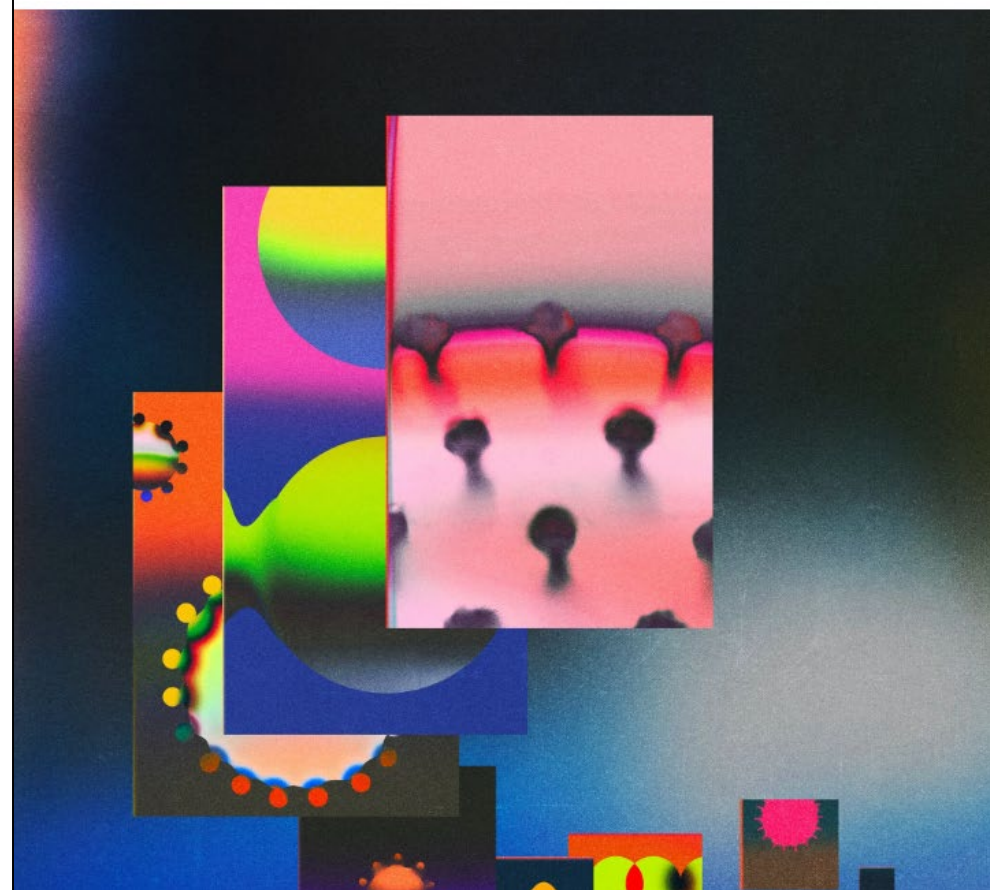
The New York Times

OPINION

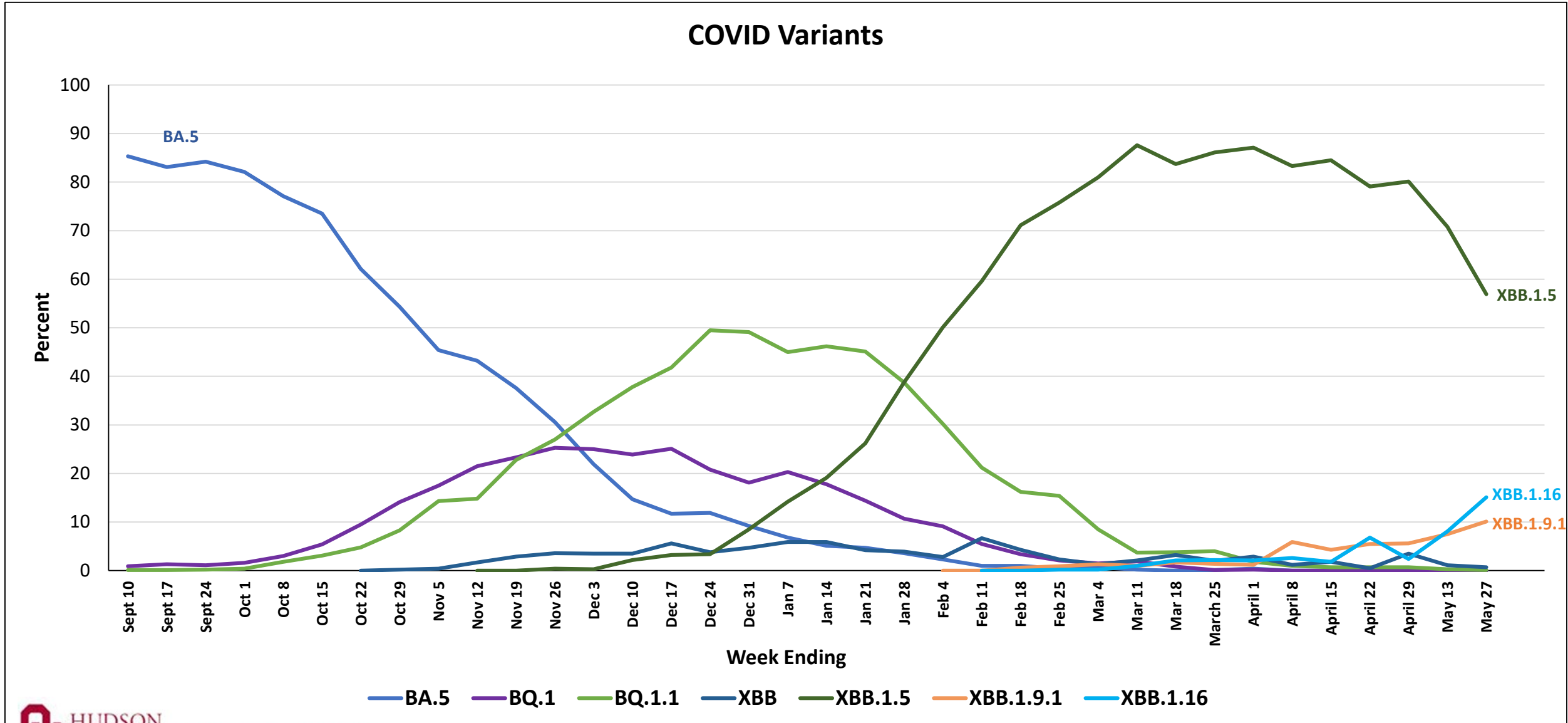
DAVID WALLACE-WELLS

Endemic Covid-19 Looks Pretty Brutal

July 20, 2022



COVID Variant Trends – US Region 6 (includes Oklahoma)



Protecting seniors during viral outbreaks

• Vaccines!!!

- Influenza (high-dose better than standard dose in the elderly)
- Pneumococcal vaccine – PCV-20 now available
- COVID-19 vaccine (may be a new omicron specific vaccine in the fall)
- RSV vaccine (RSV kills more adults than kids every year!)

Burden of Respiratory Syncytial Virus (RSV)

- RSV is a highly contagious virus that causes infections of the lungs and breathing passages in individuals of all age groups. RSV circulation is seasonal, typically starting during the fall and peaking in the winter. In older adults, RSV is a common cause of lower respiratory tract disease (LRTD), which affects the lungs and can cause life-threatening pneumonia and bronchiolitis (swelling of the small airway passages in the lungs). According to the U.S. Centers for Disease Control and Prevention, each year in the U.S., RSV leads to approximately 60,000-120,000 hospitalizations and 6,000-10,000 deaths among adults 65 years of age and older.

Final thoughts.....

- The nature of infection with SARS-CoV-2 has changed – the elderly and immunosuppressed are at greatest risk of complications and death!
- Vaccination remains the best option to prevent disease complications – antibody titers wane over time (particularly in the elderly)
 - At risk individuals who test positive for COVID-19 need to receive early antiviral treatment!
- Long COVID symptoms are common – the etiology is being studied but may include persistent viral reservoirs and immune response and inflammation
- Multiple clinical trials are ongoing to define treatments for long COVID symptoms

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