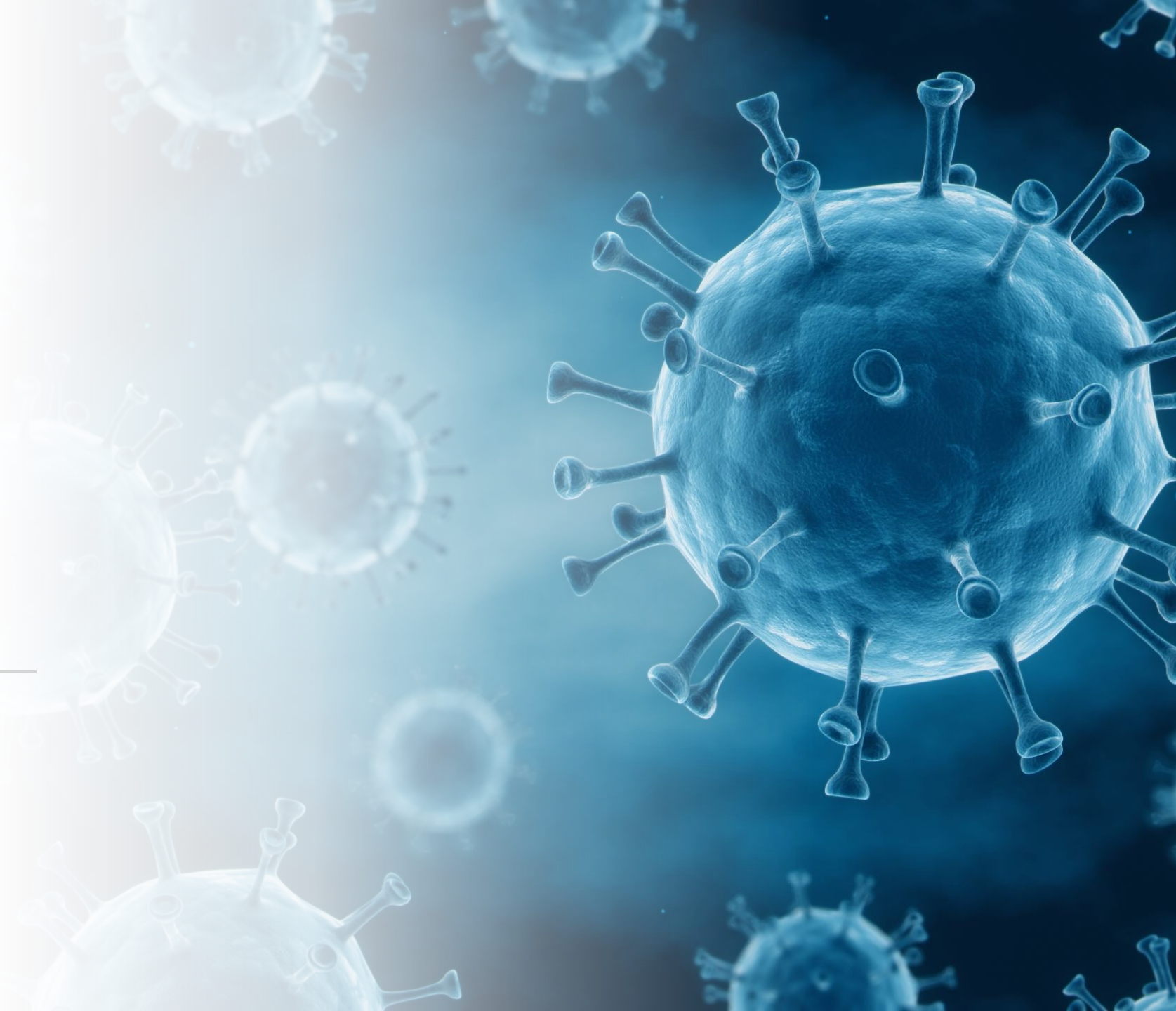




Infectious Disease News

Jorge Mera, MD



Outline

COVID-19

- Stats and new variants
- Vaccines Updates
- Treatment Updates
- Interesting manuscripts

RSV

STIs

COVID-19 STATS for the USA

August 14, 2023

Data Update for the United States

Hospitalizations

Hospital Admissions

10,320

(July 30 to August 5, 2023)

Trend in Hospital Admissions

+14.3% in most recent week



Jul 7, 2023 Aug 5, 2023

Deaths

% Due to COVID-19

1.1%

(July 30 to August 5, 2023)

Trend in % COVID-19 Deaths

+10% in most recent week



Jun 17, 2023 Aug 5, 2023

Vaccinations

Total Updated (Bivalent) Vaccine Doses Distributed

152,508,460

(through August 9, 2023)

Total Hospitalizations

6,244,216

Total Deaths

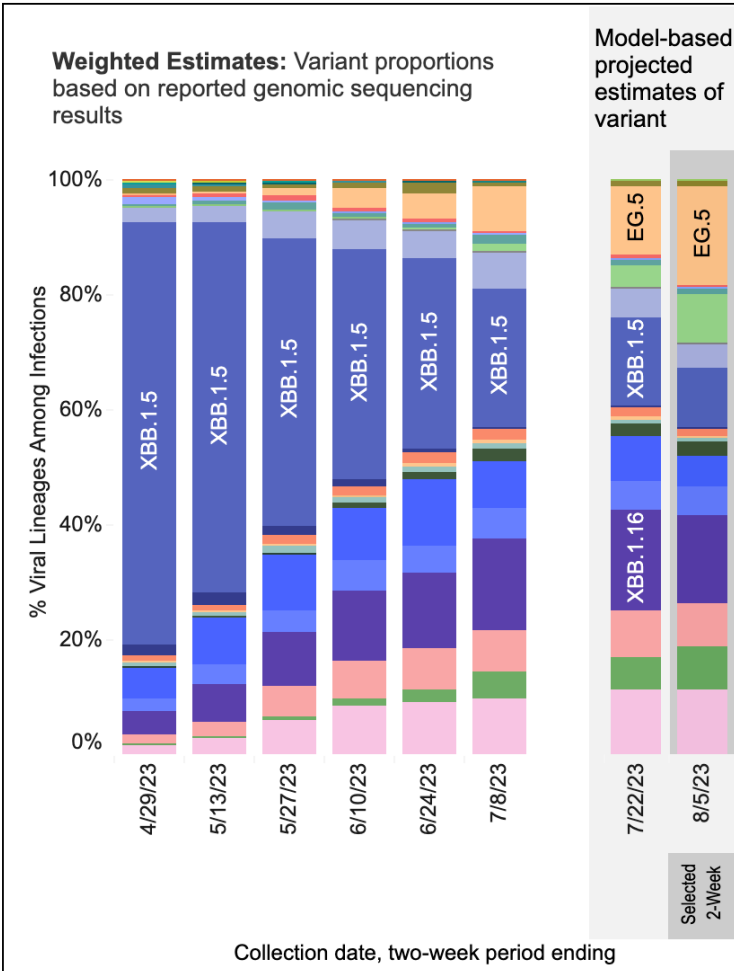
1,137,057

US COVID-19 Stats

Weighted and Nowcast Estimates in United States for 2-Week Periods in 4/16/2023 – 8/5..



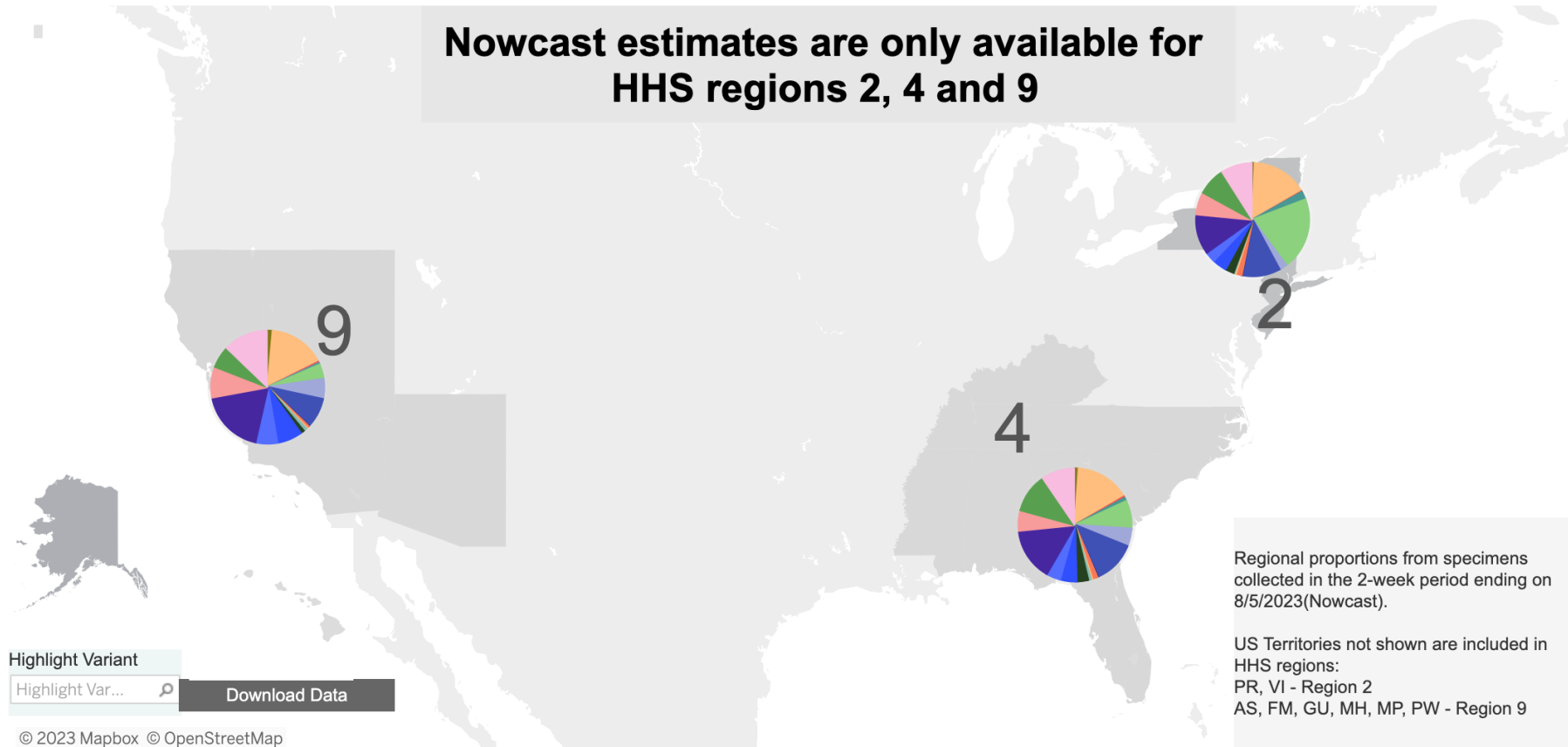
Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.



Nowcast Estimates in United States for 7/23/2023 – 8/5/2023

USA			
WHO label	Lineage #	%Total	95%PI
Omicron	EG.5	17.3%	14.1-21.0%
	XBB.1.16	15.6%	12.5-19.2%
	XBB.2.3	11.2%	9.5-13.1%
	XBB.1.5	10.3%	8.6-12.3%
	FL.1.5.1	8.6%	4.2-16.1%
	XBB.1.16.6	7.7%	5.6-10.6%
	XBB.1.16.1	7.2%	6.0-8.7%
	XBB.1.9.1	5.4%	4.5-6.5%
	XBB.1.9.2	4.8%	3.5-6.6%
	XBB	4.4%	3.1-6.1%
	XBB.1.5.72	2.4%	1.6-3.7%
	XBB.1.5.10	1.2%	0.7-1.9%
	FE.1.1	1.1%	0.6-2.1%
	CH.1.1	1.1%	0.6-1.9%
	XBB.1.5.68	0.6%	0.4-1.0%
	XBB.1.5.59	0.4%	0.2-0.8%
	EU.1.1	0.3%	0.2-0.6%
	XBB.1.5.1	0.2%	0.1-0.2%
	BA.2	0.0%	0.0-0.1%
	BA.2.12.1	0.0%	0.0-0.1%
	FD.2	0.0%	0.0-0.0%
	BA.5	0.0%	0.0-0.0%
	BQ.1.1	0.0%	0.0-0.0%
	BQ.1	0.0%	0.0-0.0%
Other	Other*	0.1%	0.0-0.1%

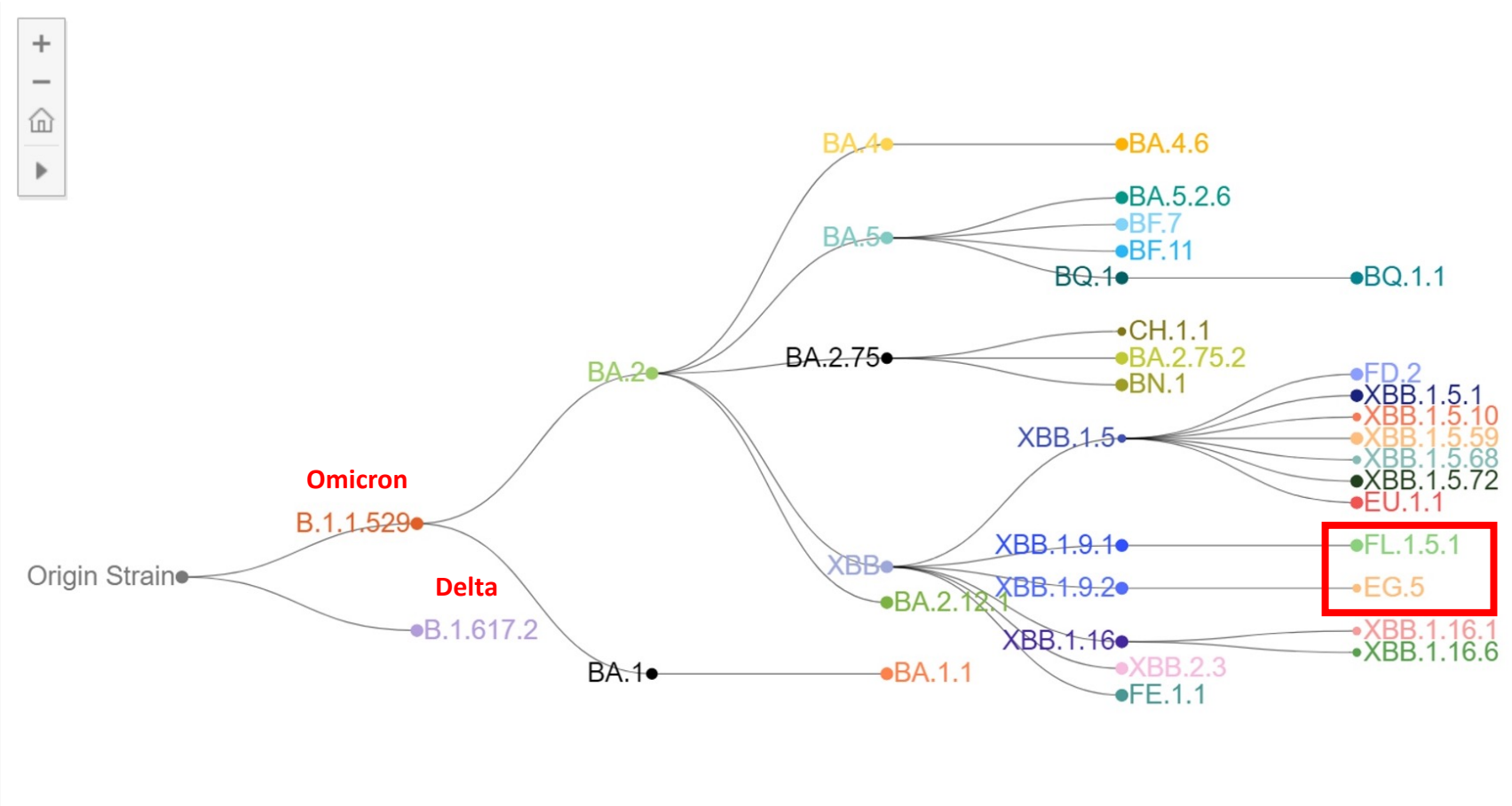
Variants by HHS Regions



Lineages called using pangolin v4.3.1, pangolin-data v1.21 and usher v0.6.2.

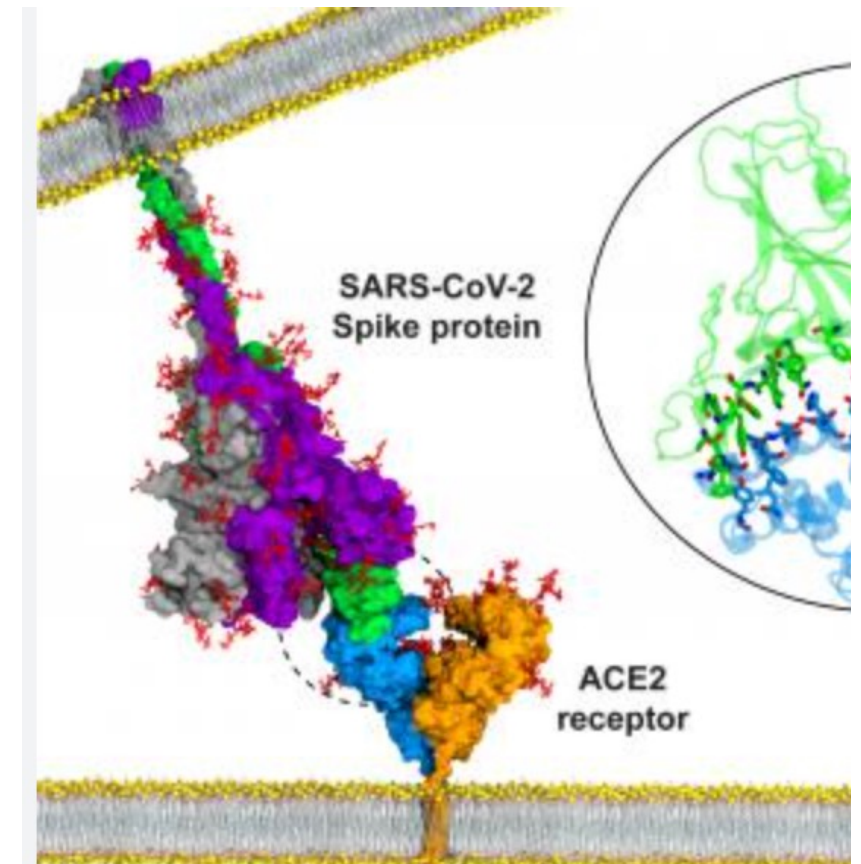
Updated August 4, 2023

SARS-CoV-2 Strain Relationship



EG.5.1 and FL.1.5.1: Should We Be Worried?

- EG.51. and FL.1.5.1 continue to rise at a higher speed than the XBB precursors, almost doubling over the past few weeks
- It is also spreading in Asia and Europe
- The main new mutation is F456L, which causes a decrease in plasma neutralizing activity.
- These mutations cause a greater avidity of the spike protein to the ACE2 receptor
- No evidence yet that they cause increase morbidity or mortality



<https://www.sciencemuseumgroup.org.uk/blog/coronavirus-the-spike/>

COVID-19 Vaccines

- **The first new updated COVID-19 vaccines are expected to be available by the end of September**
 - Pending FDA and CDC approval and ACIP recommendation
- The vaccine is designed to target the XBB variants
 - Which descended from the original Omicron variant
- **Have a single component, targeting the XBB.1.5**
 - Moderna, Pfizer and Novavax are expected to offer the new vaccine
- Teens and adults, would have their pick of any of the three updated vaccines.
- **For children**
 - As young as 2 years old, CDC recommendations would allow for a single new shot from either Pfizer or Moderna
 - Children down to 6 months still might be recommended to get two or three doses.



COVID Treatment Updates



EUA for Vilobelimab (anti C5a monoclonal Ab)

To use within 48 hours of intubation or ECMO (28-day mortality benefit HR. 0.67 [0.48-0.96] P=0.027)

No omicron variant patients included

NIH panel does not recommend either for or against this drug



Immunocompromised patients with symptoms and viral replication

NIH now recommends three strategies:

- Longer courses of Nirmatrelvir/r or longer courses of Remdesivir
- High titer convalescent plasma from vaccinated recently recovered donor



Paxlovid

FDA approved and on IHS core formulary

Dose decrease of calcium channel blocker may be needed



Remdesivir

FDA and NIH allow Rx without dose adjustment for GFR <30 or dialysis

<https://www.covid19treatmentguidelines.nih.gov/therapies/immunomodulators/vilobelimab>

Do You Pick Your Nose?

- a. Never
- b. Occasionally
- c. Every week
- d. Every day
- e. Prefer not to answer



Why not to pick your nose: Association between nose picking and SARS-CoV-2 incidence, a cohort study in hospital health care workers

Background

- Hospital health care workers (HCW) are at increased risk of contracting SARS-CoV-2
- This study investigated whether certain behaviors and physical features, e.g. nose picking and wearing glasses, are associated with infection risk.

Aim

- To assess the association between nose picking and related behavioral or physical features (nail biting, wearing glasses, and having a beard) and the incidence of SARS-CoV-2- infection.

Methods

- Cohort study among 404 HCW in two university medical centers in the Netherlands.
- SARS-CoV-2-specific antibodies were prospectively measured during the first phase of the pandemic.
- HCW received an additional retrospective survey regarding behavior and physical features.

Why not to pick your nose: Association between nose picking and SARS-CoV-2 incidence, a cohort study in hospital health care workers

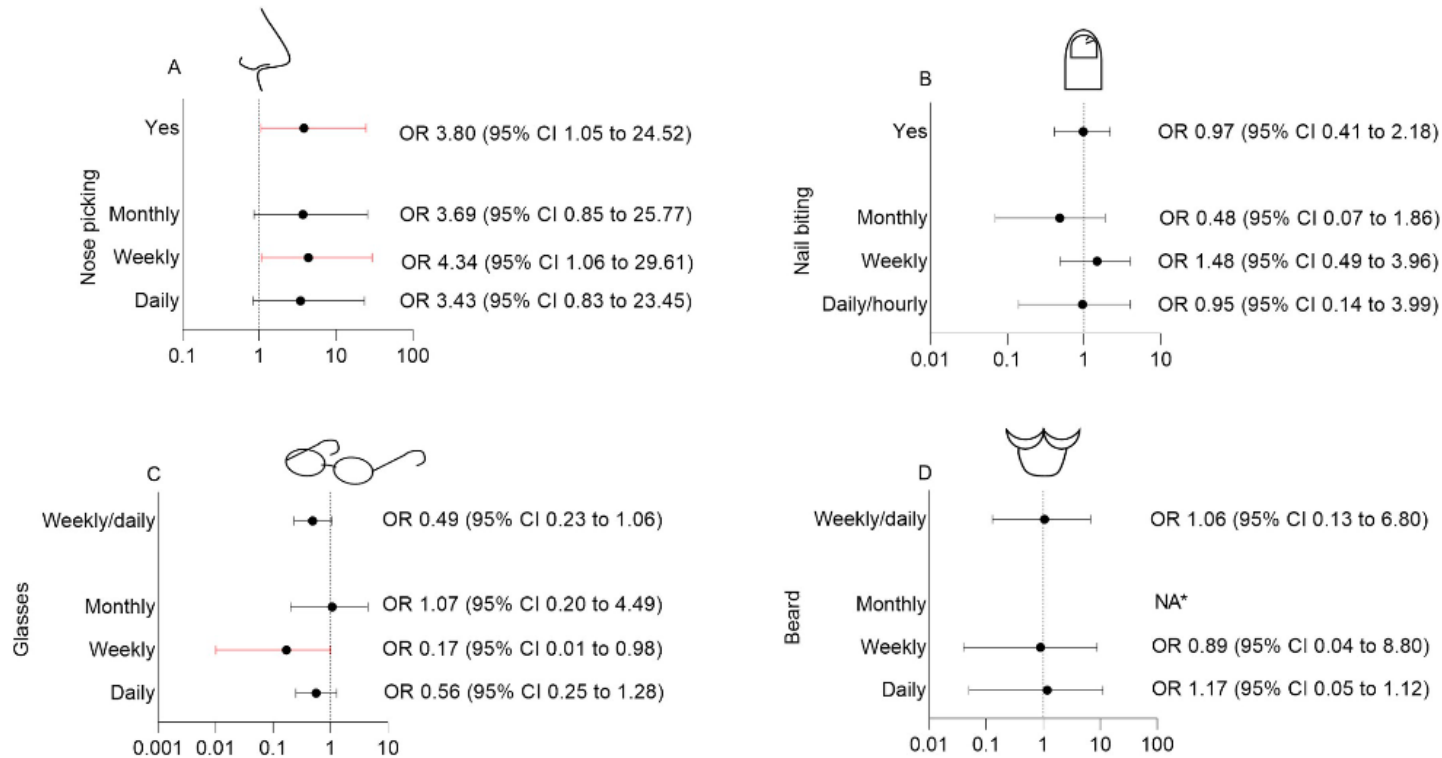
Results

- In total 219 HCW completed the survey (response rate 52%)
- The majority, 84.5% reported picking their nose at least incidentally, with frequency varying
- 15.5% of the 219 HCW became SARS-CoV-2 seropositive during follow-up
- SARS-CoV-2 incidence was 17.3% in nose pickers vs. 5.9% not nose pickers OR 3.80 (95% CI 1.05 to 24.52)
- No association between nail biting, wearing glasses, or having a beard

Conclusion

- Nose picking among HCW is associated with an increased risk of contracting a SARS-CoV-2 infection.
- Authors recommend health care facilities to create more awareness, e.g. by educational sessions or implementing recommendations against nose picking in infection prevention guidelines.

Association between nose picking and SARS-CoV-2 incidence, a cohort study in hospital health care workers



We are launching a
“Nose Picking Not Good
for Your Health”
Campaign

Need Campaign Ideas



Is There a Genetic Predisposition to COVID-19 Outcomes?

1 in 5 people with a SARS-CoV-2 infection are asymptomatic

- Advanced age and preexisting health conditions are important risk factors for severe infection.

Some healthy young adults have a serious infection and some older people with comorbidities only develop minor symptoms.

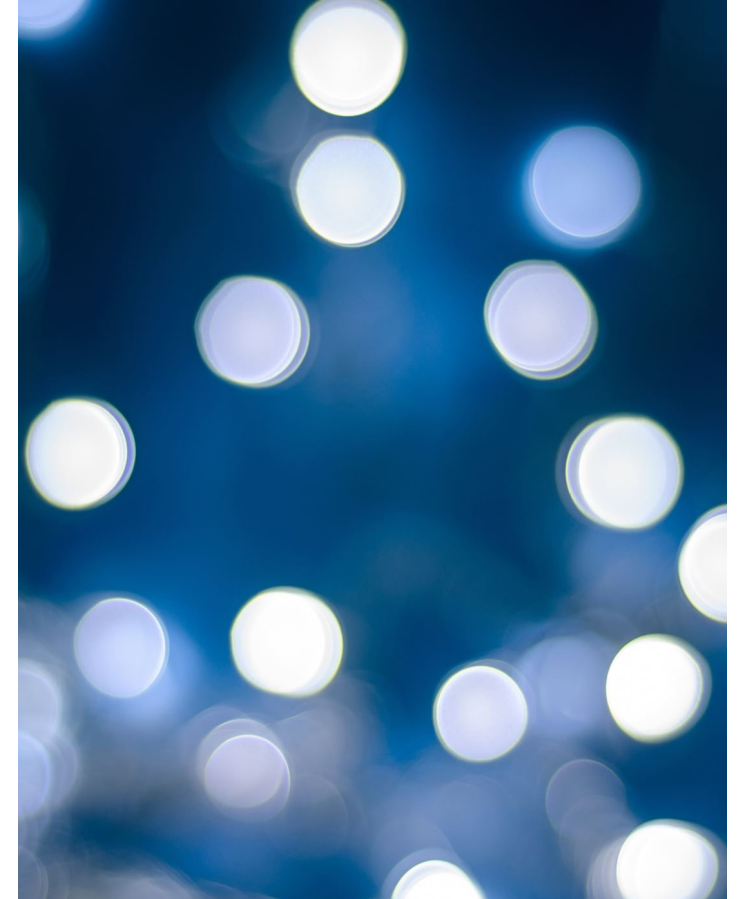
- Few studies have examined the why some people have a mild infection

Human leukocyte antigen (*HLA*) genes system were studied

- HLA molecules are essential to the immune response to pathogens

This study shows that people with a particular HLA appeared to have preexisting T cell immunity to the virus

- Probably due to remnant immunologic memory from previous bouts of the common cold.



A common allele of *HLA* is associated with asymptomatic SARS-CoV-2 infection: Methods



Participants: 30,000 potential bone marrow donors in US with detailed HLA region sequencing



Participants tracked COVID-19 symptoms on smartphones

Study focused on 1428 unvaccinated White individuals with positive COVID-19 tests



Investigated association between asymptomatic infection and 5 HLA genes

Findings validated in 2 independent European ancestry cohorts (UK, US)



Used immunology and structural biology for investigating genetic factor in asymptomatic infections

Analyzed pre-pandemic T cells from bone marrow donors with no coronavirus exposure

A common allele of *HLA* is associated with asymptomatic SARS-CoV-2 infection: Results



1292 participants had COVID-19 symptoms, 136 were asymptomatic



Common allele HLA-B*15:01:

Found in 20% asymptomatic, 9% symptomatic participants

2 copies linked to over 8x higher likelihood of no symptoms



Variant strongly associated with asymptomatic infection in 2 independent cohorts



Meta-analysis:

Variant carriers had over twice the rate of asymptomatic infections



T cell analysis:

Participants with variant had pre-pandemic killer T cells targeting SARS-CoV-2

A common allele of *HLA* is associated with asymptomatic SARS-CoV-2 infection:

Limitations

Lack of diversity in European ancestry cohorts

- HLA-B*15:01 allele common in European ancestry (1 in 10), less in other backgrounds
- Allele's role in asymptomatic infection in Black individuals was inconclusive
- Unclear trend in association for Asian and Hispanic people

Self-reported COVID-19 test results and symptoms introduced potential error

Asymptomatic cases defined by clinicians in independent cohorts

Takeaway



Uncovered genetic factor explains around 20% of asymptomatic SARS-CoV-2 infections



Other factors, both genetic and non-genetic, are likely significant as well

COVID-19 outcomes result from a complex interplay of various influences



Study's findings to be translated into clinical applications

Potential impact on next-generation vaccines
Focus on understanding exceptional T cell effectiveness in managing infection

Discontinuation of Universal Admission Testing for SARS-CoV-2 and Hospital-Onset COVID-19 Infections in England and Scotland

England and Scotland discontinued universal admission testing for SARS-CoV-2

- Universal admission testing aimed to prevent transmission from asymptomatic or Presymptomatic patients
- Testing stopped due to resource constraints, care delays, and limited evidence of reduced infections

Researchers analyzed data to determine the impact of discontinuation

- Study used public datasets to track hospital-onset COVID-19 cases
- Weekly rates of hospital-onset infections per 1000 community infections calculated
- Study divided into Delta and Omicron dominance periods with and without testing

After testing ended, there were significant relative increases in hospital-onset infections

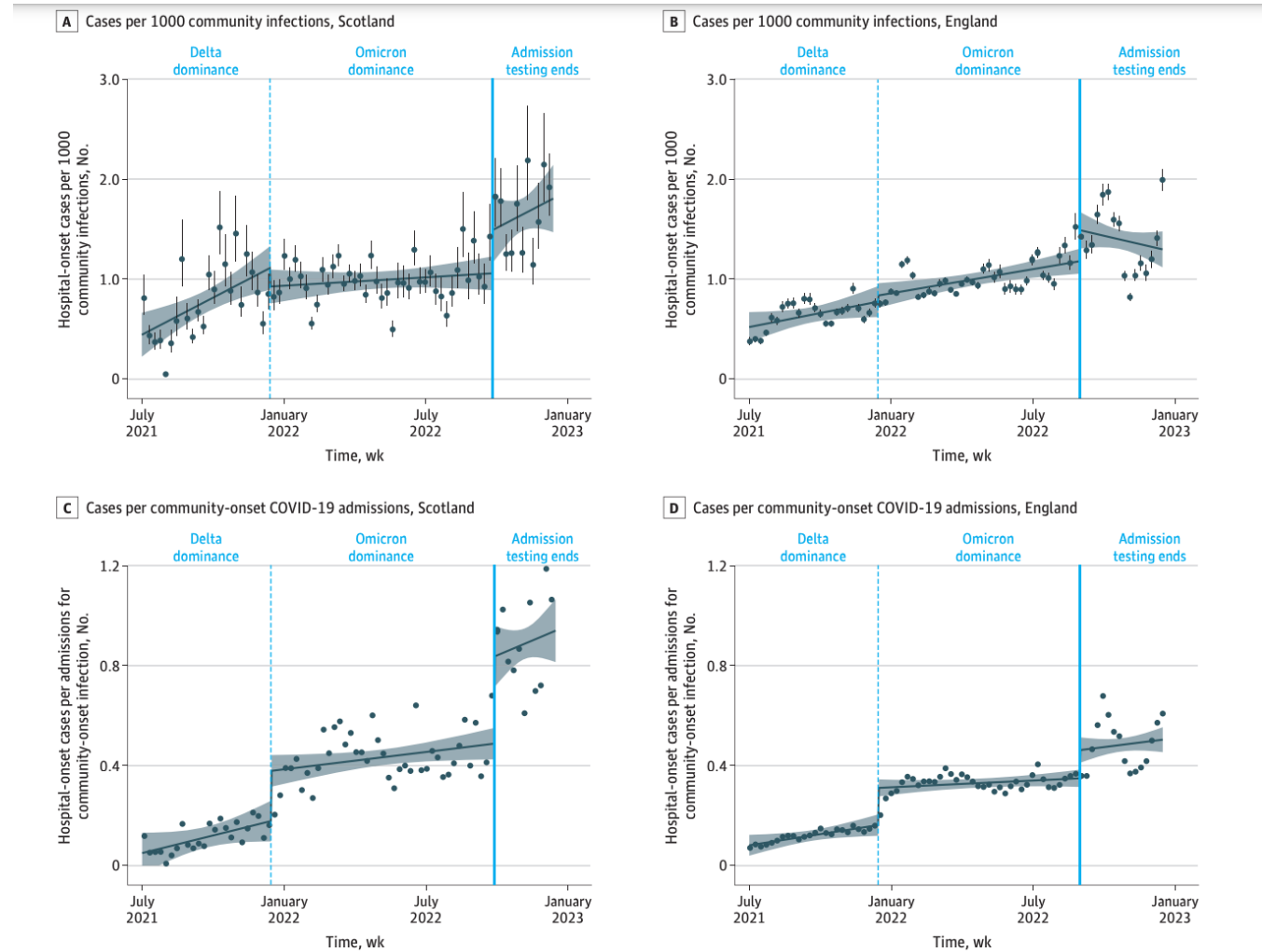
- Potential mechanisms include unrecognized infections spreading to staff and patients
- Study limitations include lack of concurrent controls and potential misclassification

Nosocomial SARS-CoV-2 Omicron infections remain common

- With crude mortality estimates ranging from 3% to 13%
- Hospitals should exercise caution before stopping universal admission testing for SARS-CoV-2 infections.

Weekly New Hospital-Onset COVID-19 Cases in Scotland and England per 1000 Estimated Community COVID-19 Infections and per New Admissions for Community-Onset COVID-19 Infection

- Hospital-onset infections were defined by the first positive test taken more than 7 days after admission, and community-onset infections by the first positive test at 7 days or less after admission.
- All regression lines are interrupted time series models.
- Dots represent weekly rates, and vertical lines in panels A and B represent 95% CIs for weekly rates
- The shaded area represents 95% CIs for the interrupted time series model.



Core mitochondrial genes are down-regulated during SARS-CoV-2 infection of rodent and human hosts

SARS-CoV-2 needs host cells to generate molecules for viral replication and propagation.

This study analyzed human nasopharyngeal samples and autopsy tissues from patients with COVID-19 and tissues from hamsters and mice infected with SARS-CoV-2.

- The virus blocks expression of both nuclear-encoded and mitochondrial-encoded mitochondrial genes
- This results in impaired host mitochondrial function.
- Host cells attempt to compensate by activating innate immune defenses and mitochondrial gene expression

Chronically impaired mitochondrial function ultimately may result in serious COVID-19 sequelae such as organ failure.

Long COVID Pathogenesis

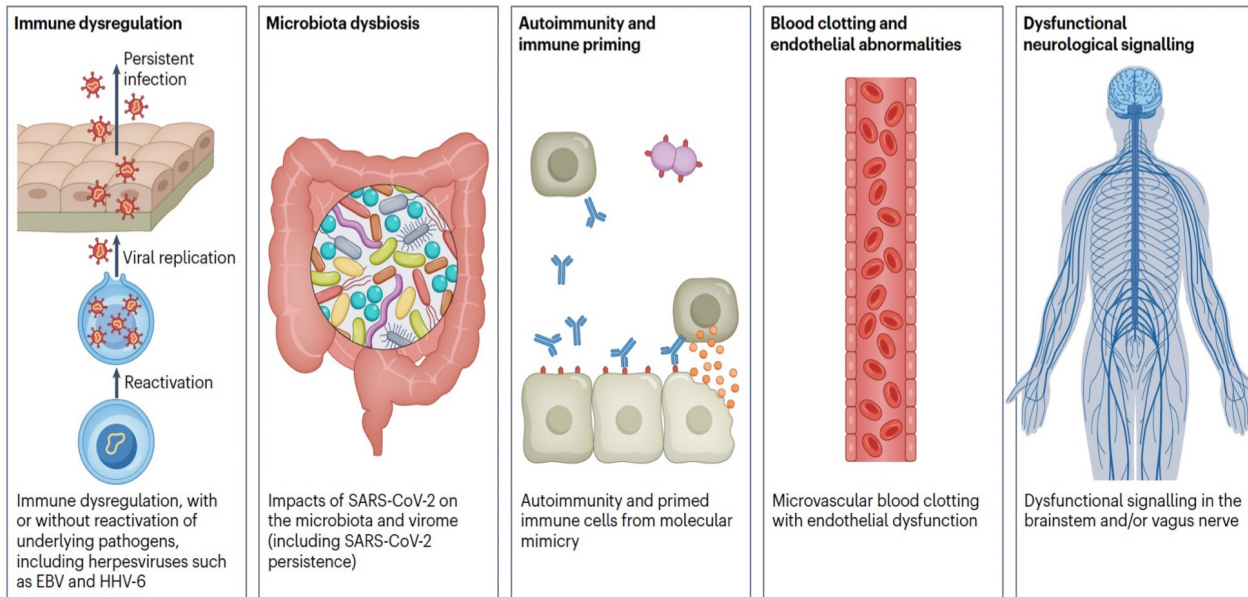


Fig. 3 | Hypothesized mechanisms of long COVID pathogenesis. There are several hypothesized mechanisms for long COVID pathogenesis, including immune dysregulation, microbiota disruption, autoimmunity, clotting

and endothelial abnormality, and dysfunctional neurological signalling. EBV, Epstein-Barr virus; HHV-6, human herpesvirus 6; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

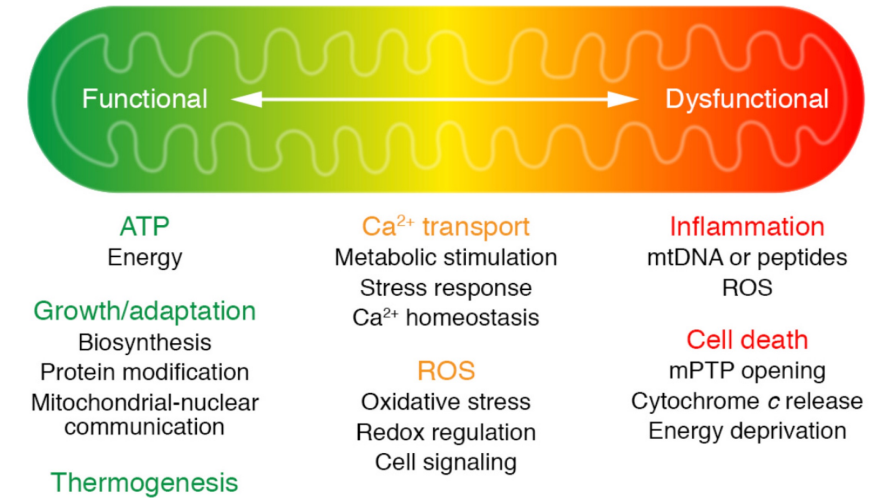


Figure 1. An overview of mitochondrial function in health and disease.

Persistent endothelial dysfunction in post-COVID-19 syndrome and its associations with symptom severity and chronic inflammation

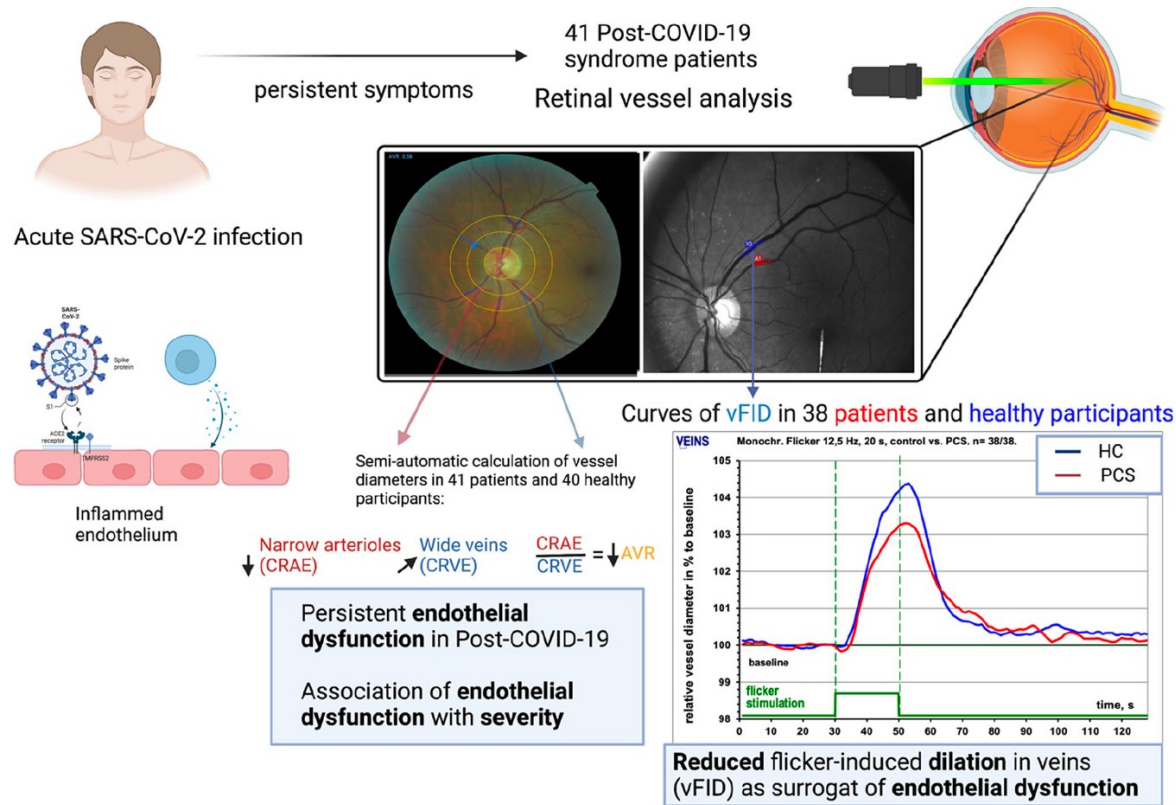
Background

- PCS is a public health priority, and the pathophysiology is not well understood

Methods

- Prospective observational cohort study
- Analyzed the retinal microcirculation using Retinal Vessel Analysis (RVA)
- Compared a cohort of patients with PCS to an age- and gender-matched healthy cohort ($n = 41$, matched out of $n = 204$).

Persistent endothelial dysfunction in post-COVID-19 syndrome and its associations with symptom severity and chronic inflammation



- Acute SARS-CoV-2 infection indirectly or directly causes endotheliitis in patients.
- $N = 41$ PCS patients were recruited, and retinal vessel analysis was performed to assess microvascular endothelial function.
 - Images of SVA and DVA are illustrative for RVA data analysis.
 - For each PCS patient and healthy cohort, venular vessel diameter of the three measurement cycles was calculated and plotted on a diameter-time curve.
- PCS patients exhibited:
 - Reduced flicker-induced dilation in veins (vFID)
 - Lower central retinal arteriolar equivalent (CRAE) and arteriolar-venular ratio (AVR)
 - Tendency towards higher central retinal venular equivalent (CRVE)
- Created with BioRender.com

Persistent endothelial dysfunction in post-COVID-19 syndrome and its associations with symptom severity and chronic inflammation

Conclusion

- These results demonstrate that prolonged endothelial dysfunction is a hallmark of PCS, and impairments of the microcirculation seem to explain ongoing symptoms in patients.
- As potential therapies for PCS emerge, RVA parameters may become relevant as clinical biomarkers for diagnosis and therapy management.

RSV vaccines for adults

Adults 60 and older may receive RSV vaccines

Efficacy

- GSK: Efficacy for LRTD was 82.8%
- Pfizer: Efficacy for LRTD was 88.9%
- Unpowered to show prevention in hospitalization or death

Inflammatory Neurologic disease occurred (GBS and ADEM) in 6 patients out of about 38,000

- Whether RSV vaccination increases the risk for inflammatory neurologic events is currently unknown

Vaccination in older adults should be targeted to those who are at highest risk for severe RSV disease

- The most likely to benefit from vaccination..

Shared clinical decision-making is recommended

- Intended to allow flexibility for providers and patients to consider individual risk for RSV disease, while taking into account patient preferences

<https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4htm>

LRTD: Lower Respiratory tract disease,
ADEM: Acute disseminated encephalomyelitis
GBS: Guillain-Barré syndrome (GBS)



RSV Monoclonal Ab for all infants

- Nirsevimab is a long-acting monoclonal antibody against RSV
 - It is given as a single IM injection
- Universally recommended for all infants younger than 8 months born during or entering their first RSV season (winter spring)
 - Also recommended for high-risk children ages 8-19 months entering their second RSV season
- Three trials show 70-75% efficacy in preventing medically attended lower respiratory tract disease



Doxycycline as STI PEP: Considerations for Individuals and Healthcare Providers of Gay or Bisexual Men or Transgender Women

As CDC and others work quickly to [evaluate data](#) to inform clinical guidance on the safe and effective use of post-exposure prophylaxis with doxycycline (also called doxy as PEP) to prevent gonorrhea, chlamydia, and syphilis, we acknowledge there are individuals and clinicians who are already engaged in the off-label use of doxycycline as bacterial STI post-exposure prophylaxis or considering it. As such, we are providing the following considerations to inform those decisions:

- [Current efficacy data](#)  only applies to gay and bisexual men and transgender women. Studies among heterosexual cis-gender women are ongoing.
- Doxycycline 200 mg administered within 24-72 hours of condomless sex was the regimen evaluated in this study. Other antibiotics should not be considered for PEP.
- In addition to informing patients about the potential STI prevention benefits of doxy as PEP, providers should also counsel patients about potential adverse side effects of doxycycline including phototoxicity, gastrointestinal symptoms, and more rarely esophageal ulceration.
- Providers should continue to screen, test, and treat for bacterial STIs in accordance with [CDC's STI Treatment Guidelines](#) and [CDC's PrEP for the Prevention of HIV guidelines](#) , even among people who may be using doxycycline as PEP or PrEP.

New addition to CDC STI guidelines

- <https://www.cdc.gov/std/treatment-guidelines/clinical-primary.htm#CautionsForDoxyPEP>

Questions

