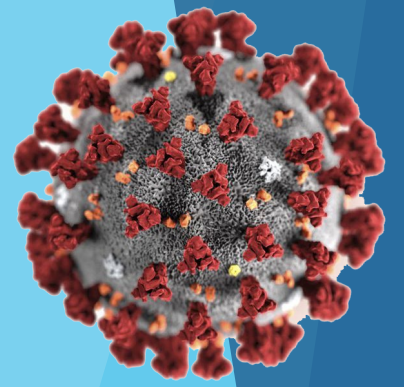
Long COVID's Impact on Patients, Workers & Society

Webinar Nov. 1st, 2023

https://healthconference.org

USA Health Watch



Impact of Long COVID on the United States

Ambassador Deborah Birx, MD

We continue to ignore the delayed consequences of COVID
Mild disease can lead to LONG COVID – maybe the immune response or could be pockets of ongoing infection

- Medium COVID
- Long COVD
- Brain inflammation of microglia cells
- Late cardiovascular events - strokes – heart attacks - these are not increasing due to just missed appointments but the very clear linkage to post COVID events
- This is not just about the acute COVID infection but the long term consequences that we continue to ignore

Excellent patient introduction and trials on the NIH site

What We Know About Long COVID

What causes Long COVID?

Scientists don't know for sure what causes Long COVID, but research is providing some clues.

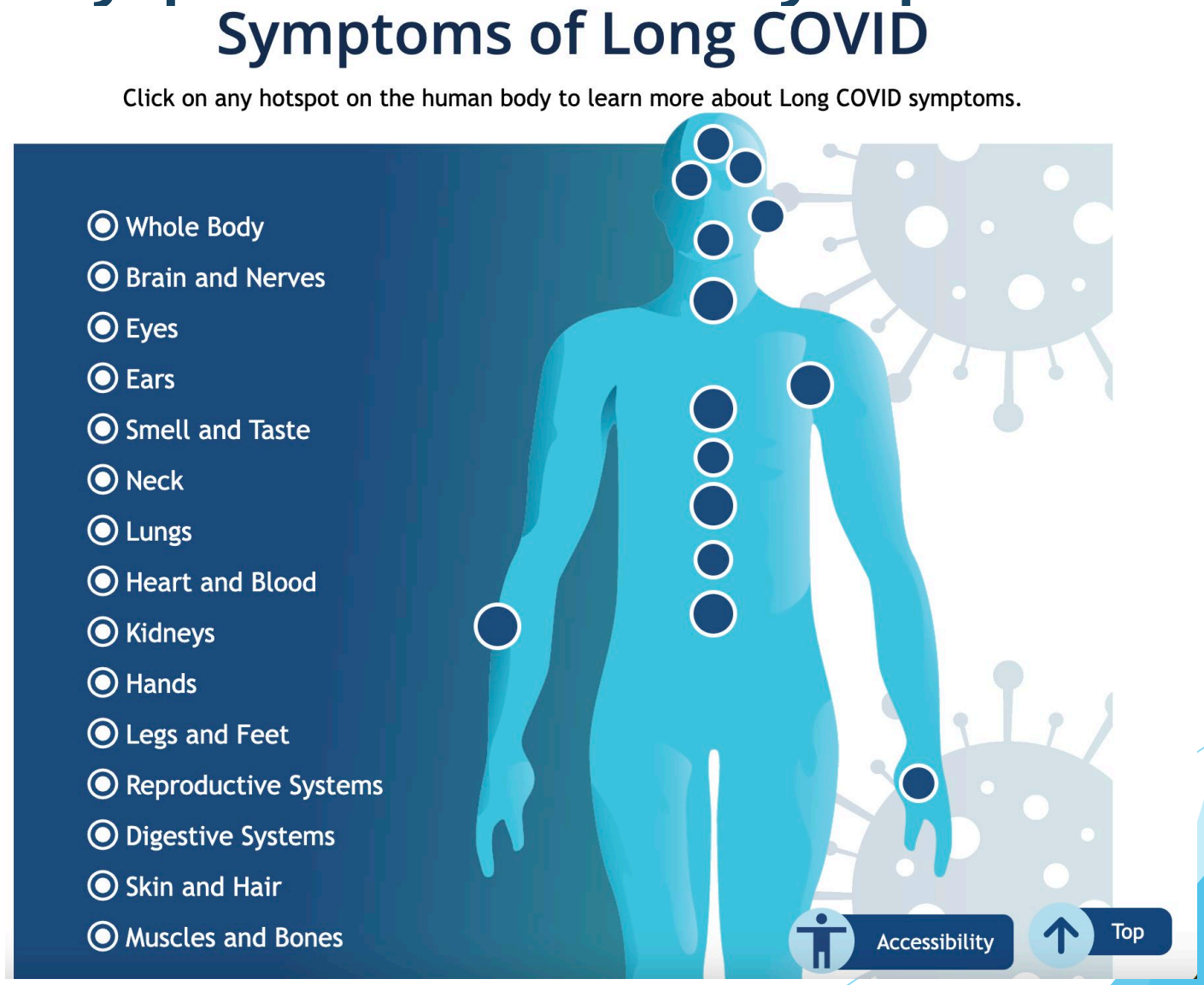
- SARS-CoV-2 particles may become active again, causing symptoms to reappear.
- Overactive immune cells may release high levels of inflammatory substances that can injure organs and tissues.
- The infection may cause the immune system to start making autoantibodies that attack a person's own organs and tissues.

Symptoms may also be caused by a combination of these and other factors. Research into these factors is ongoing.

Can children get Long COVID?

Children and teenagers can get Long COVID, whether they had COVID-19 symptoms or not.

NIH site is interactive with ability to scroll over different body parts to show symptoms



Clinical Infectious Diseases

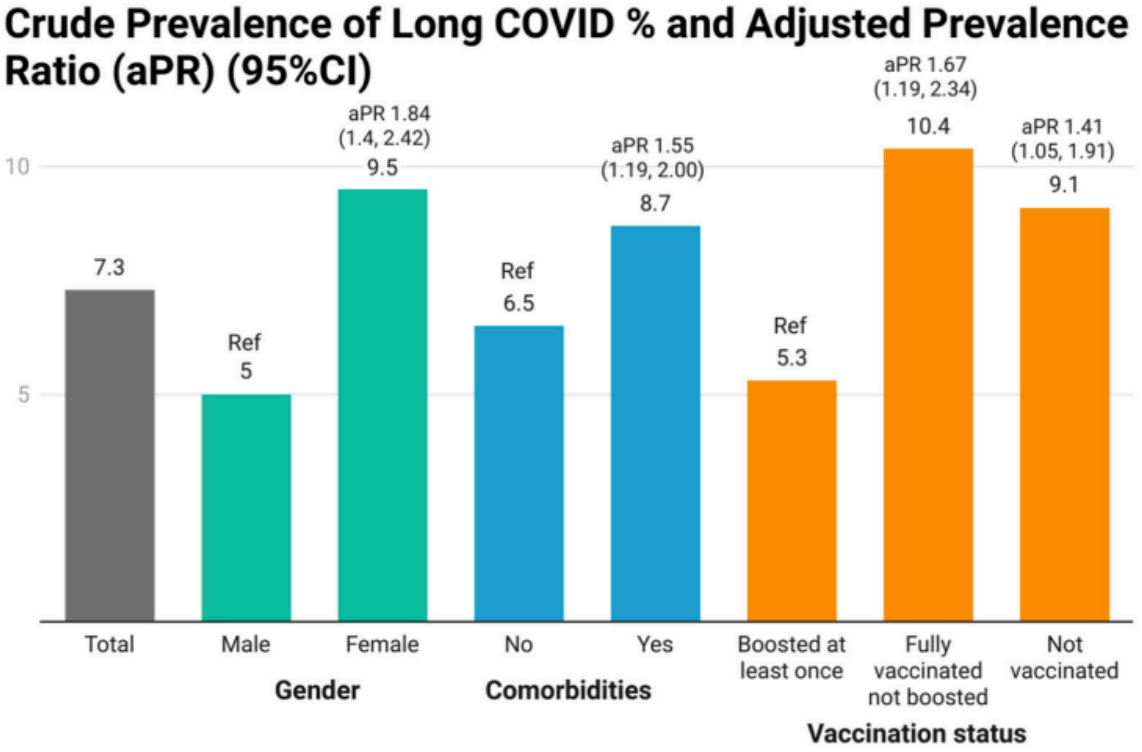
MAJOR ARTICLE

The Epidemiology of Long Coronavirus Disease in US Adults

McKaylee M. Robertson,[1,2] Saba A. Qasmieh,[1,2] Sarah G. Kulkarni,[1] Chloe A. Teasdale,[1,2] Heidi E. Jones,[1,2] Margaret McNairy,[1,3] Luisa N. Borrell,[2] and Denis Nash[1,2]

[1]Institute for Implementation Science in Population Health (ISPH), City University of New York (CUNY), New York, New York, USA; [2]Department of Epidemiology and Biostatistics, Graduate School of Public Health and Health Policy, City University of New York (CUNY), New York, New York, USA; and [3]Center for Global Health and Division of General Internal Medicine, Weill Cornell Medicine, New York, New York, USA

In a population-representative sample, we estimated **7.3%** of US adults, **approximately 18 million adults,** had symptoms of long COVID during the two-week study period ending July 2, 2022.



Long COVID prevalence and impact on quality of life 2 years after acute COVID-19

Yoonjung Kim, Sohyun Bae, Hyun-Ha Chang & Shin-Woo Kim

From: Long COVID prevalence and impact on quality of life 2 years after acute COVID-19

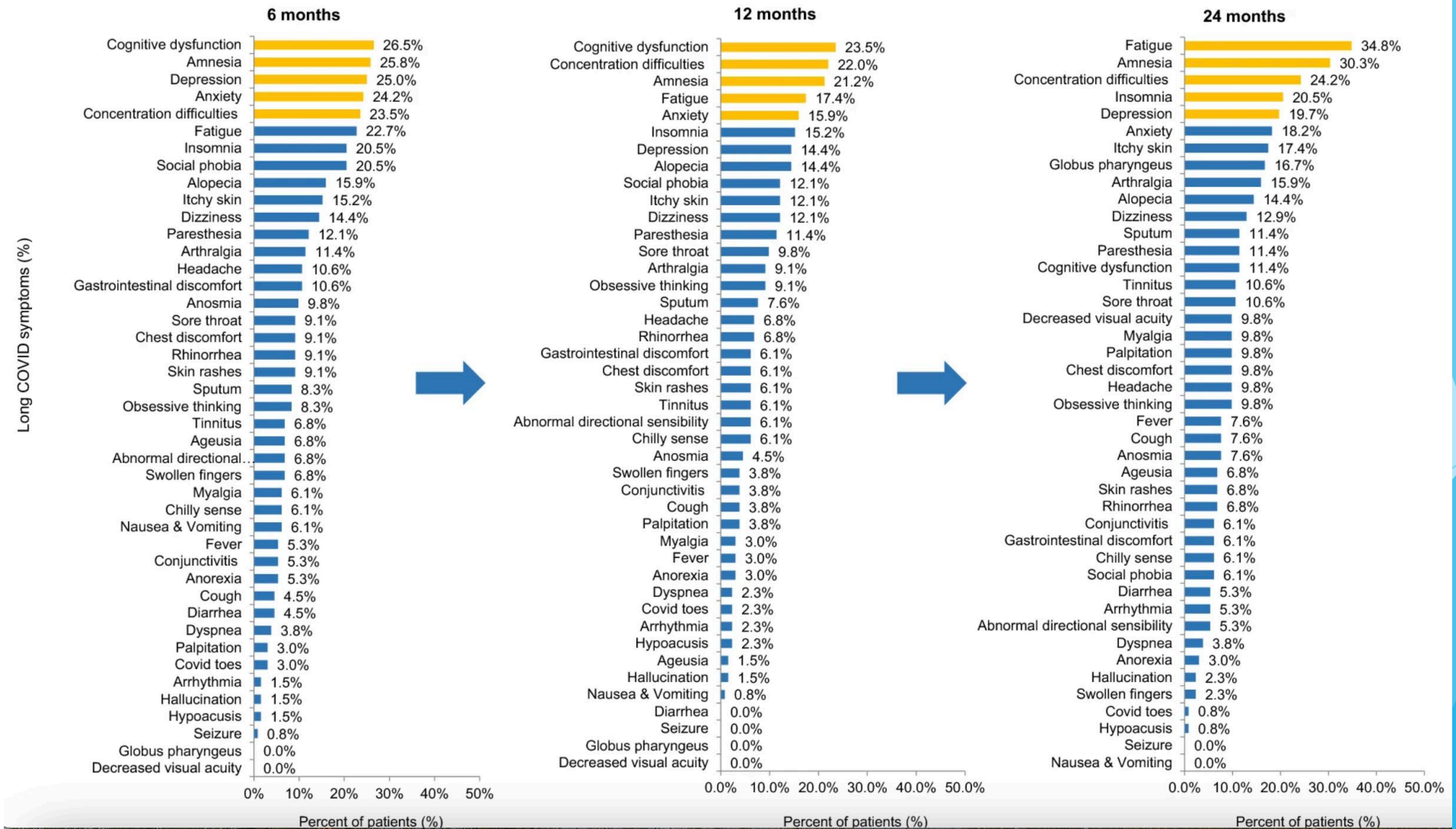
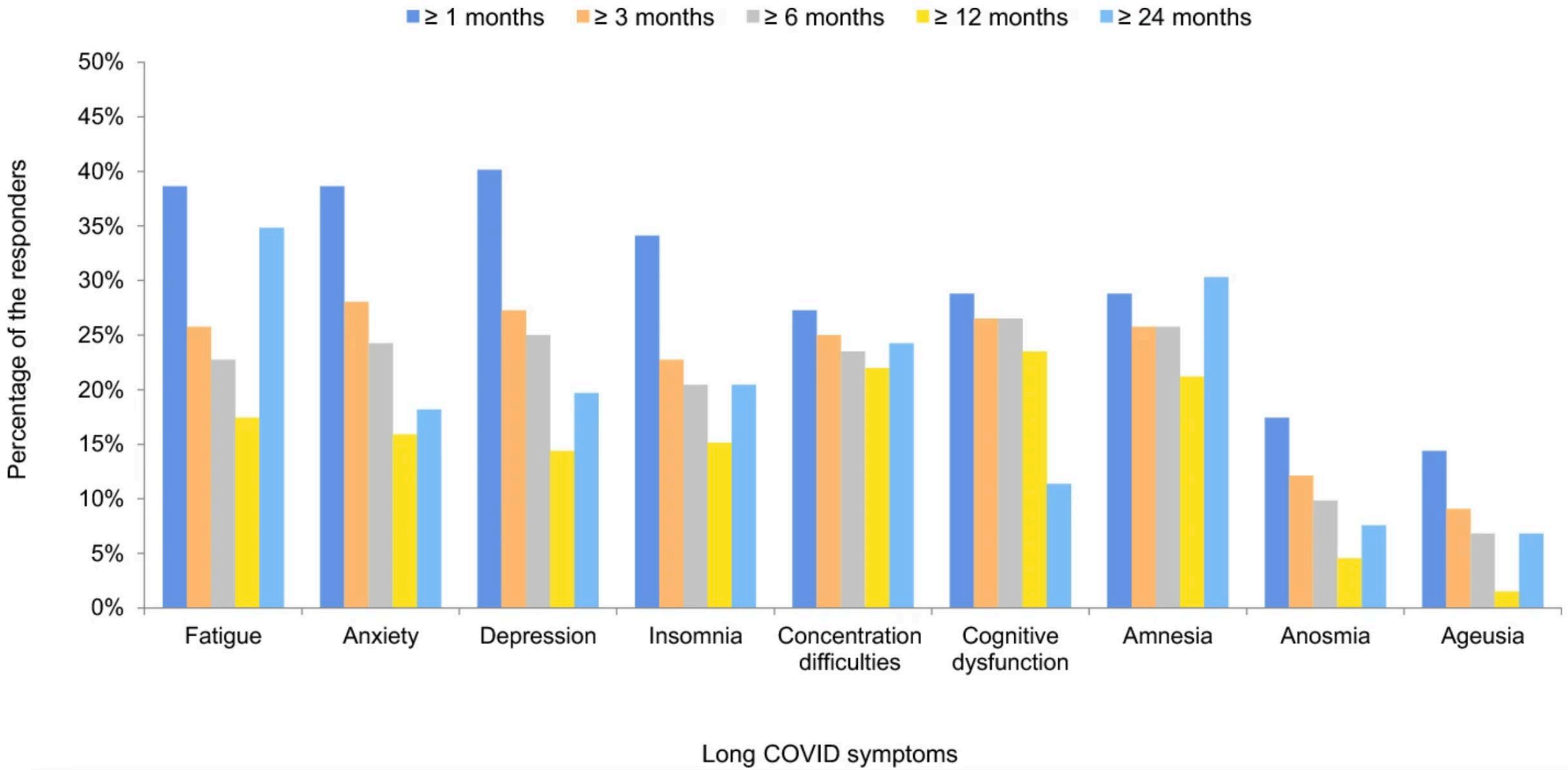


Figure 2

From: Long COVID prevalence and impact on quality of life 2 years after acute COVID-19



Review article

Long COVID: major findings, mechanisms and recommendations

Hannah E. Davis[1], Lisa McCorkell[2], Julia Moore Vogel[3] & Eric J. Topol[3]

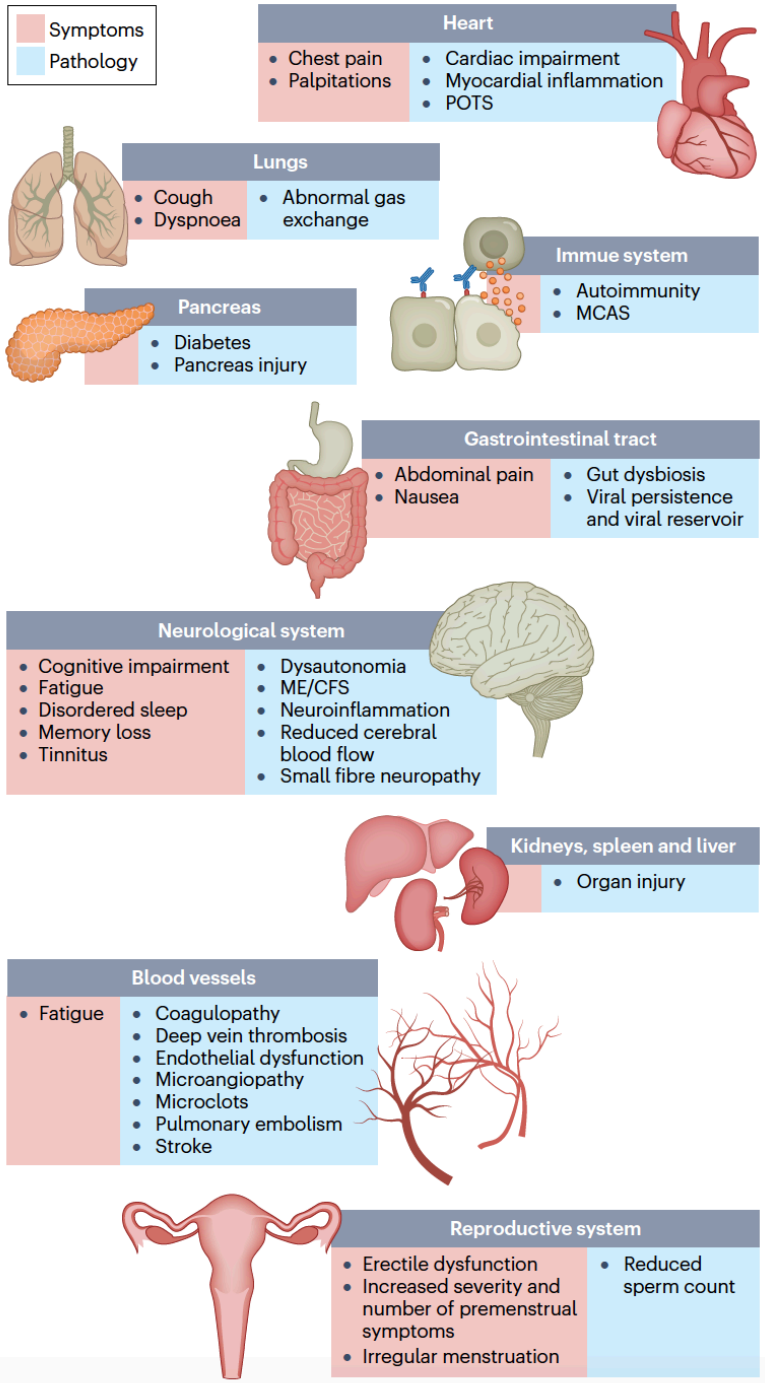


Fig. 1 | Long COVID symptoms and the impacts on numerous organs with

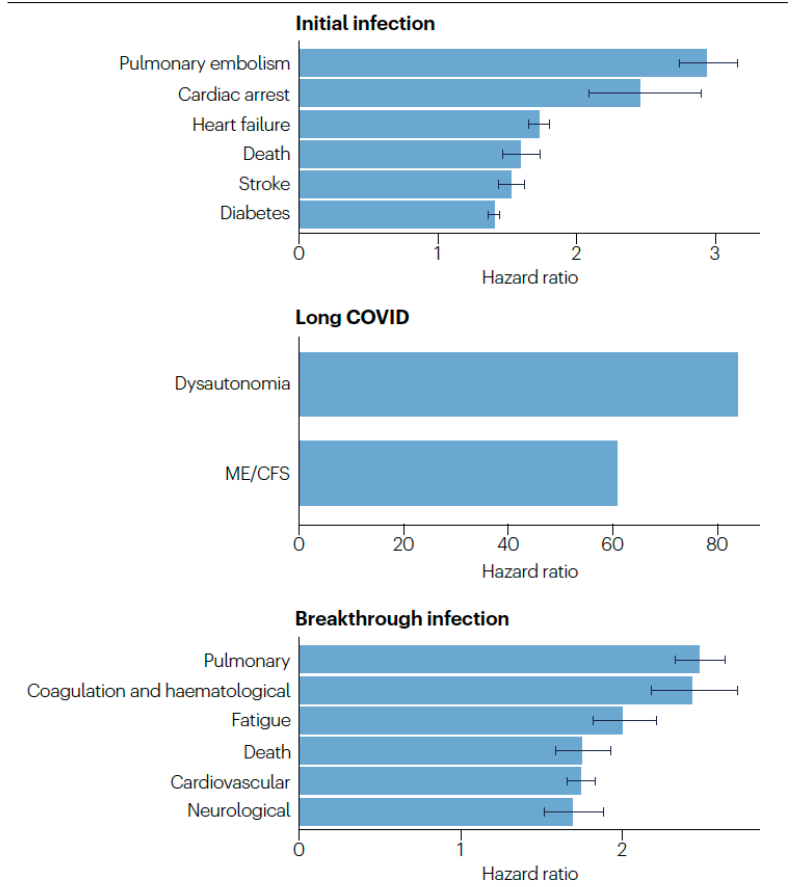


Fig. 2 | SARS-CoV-2 infection, COVID-19 and long COVID increases the risk of several medical conditions. Because diagnosis-specific data on large populations with long COVID are sparse, outcomes from general infections are included and a large proportion of medical conditions are expected to result from long COVID, although the precise proportion cannot be determined. One year after the initial infection, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections increased the risk of cardiac arrest, death, diabetes, heart failure, pulmonary embolism and stroke, as studied with use of US Department of Veterans Affairs databases. Additionally, there is clear increased risk of developing myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and dysautonomia. Six months after breakthrough infection, increased risks were observed for cardiovascular conditions, coagulation and haematological conditions, death, fatigue, neurological conditions and pulmonary conditions in the same cohort. The hazard ratio is the ratio of how often an event occurs in one group relative to another; in this case people who have had COVID-19 compared with those who have not. Data sources are as follows: diabetes[9], cardiovascular outcomes[8], dysautonomia[12,201], ME/CFS[10,202] and breakthrough infections[4].

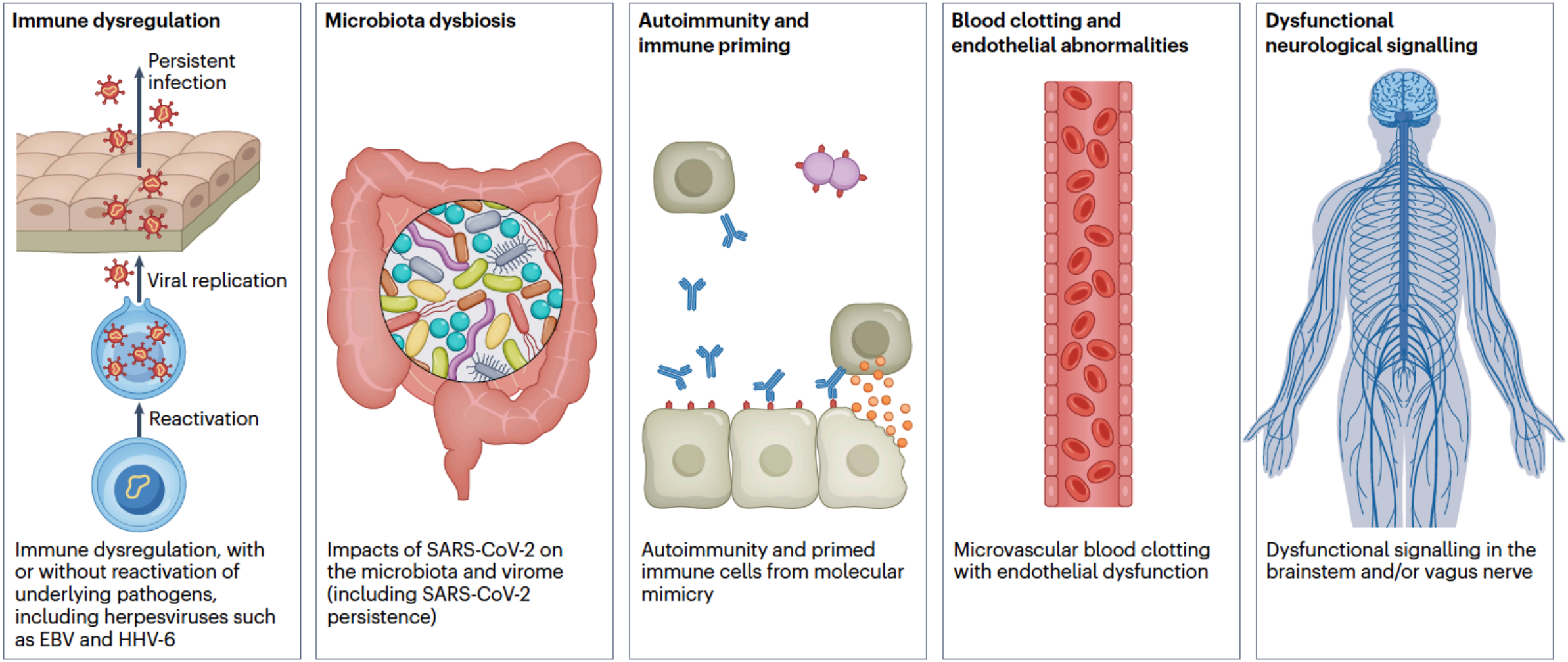


Fig. 3 | Hypothesized mechanisms of long COVID pathogenesis. There are several hypothesized mechanisms for long COVID pathogenesis, including immune dysregulation, microbiota disruption, autoimmunity, clotting and endothelial abnormality, and dysfunctional neurological signalling. EBV, Epstein–Barr virus; HHV-6, human herpesvirus 6; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 1 | Summary of candidate treatments and supporting evidence

Symptoms and/or biological mechanism	Treatments	Supporting evidence	Comments
Postexertional malaise	Pacing	ME/CFS literature	Exercise, cognitive behavioural therapy and graded exercise therapy are contraindicated
POTS	Pharmacological: β-blockers, pyridostigmine, fludrocortisone, midodrine	POTS and ME/CFS literature	Options can be prioritized on the basis of a specific constellation of symptoms
	Non-pharmacological: increase salt and fluid intake, intravenously administered salt, compression stockings	POTS and ME/CFS literature	–
Immune dysfunction	Intravenous immunoglobulin	ME/CFS literature	Consider consulting an immunologist on implementation
Cognitive dysfunction	Cognitive pacing	ME/CFS literature	Consider implementation alongside pacing physical exertion
Cognitive dysfunction	Postconcussion syndrome protocols	ME/CFS and postconcussion syndrome literature	–
Fatigue	Coenzyme Q_{10}, D-ribose	ME/CFS literature	–
Pain, fatigue, neurological symptoms	Low-dose naltrexone	ME/CFS and other literature	Substantial anecdotal reports of success within the patient community
Fatigue, unrefreshing sleep, brain fog	Low-dose aripiprazole	ME/CFS literature	–
Autoimmunity	BC007	Long COVID case report	Neutralizes G protein-coupled receptor autoantibodies
Abnormal clotting	Anticoagulants	Long COVID pilot study	Additional trials in progress
Abnormal clotting	Apheresis	ME/CFS literature, long COVID pilot study	–
Viral persistence and antivirals (COVID-19)	Paxlovid	Long COVID case reports	No active trials, despite strong evidence for viral persistence
Viral persistence and antivirals (reactivations such as of EBV, HCMV and VZV)	Valaciclovir, famciclovir, valganciclovir and other antivirals	ME/CFS literature	–
Endothelial dysfunction	Sulodexide	Long COVID pilot study	–
Gastrointestinal symptoms	Probiotics	Long COVID pilot study	Resolved gastrointestinal and other symptoms
Dysautonomia	Stellate ganglion block	Long COVID case report	Effects may wane over time and require repeated procedures
Endothelial function, microcirculation, inflammatory markers and oxidative stress	Pycnogenol	COVID-19 pilot study	–
MCAS	H_1 and H_2 antihistamines, particularly famotidine	Long COVID case reports, MCAS literature	Expected to treat symptoms, not underlying mechanism
Autonomic dysfunction	Transcutaneous vagal stimulation	Long COVID pilot study	–

EBV, Epstein–Barr virus; HCMV, human cytomegalovirus; MCAS, mast cell activation syndrome; ME/CFS, myalgic encephalomyelitis/chronic fatigue syndrome; POTS, postural orthostatic tachycardia syndrome; VZV, varicella zoster virus.

REVIEW ARTICLE OPEN

Long-term effects of SARS-CoV-2 infection on human brain and memory

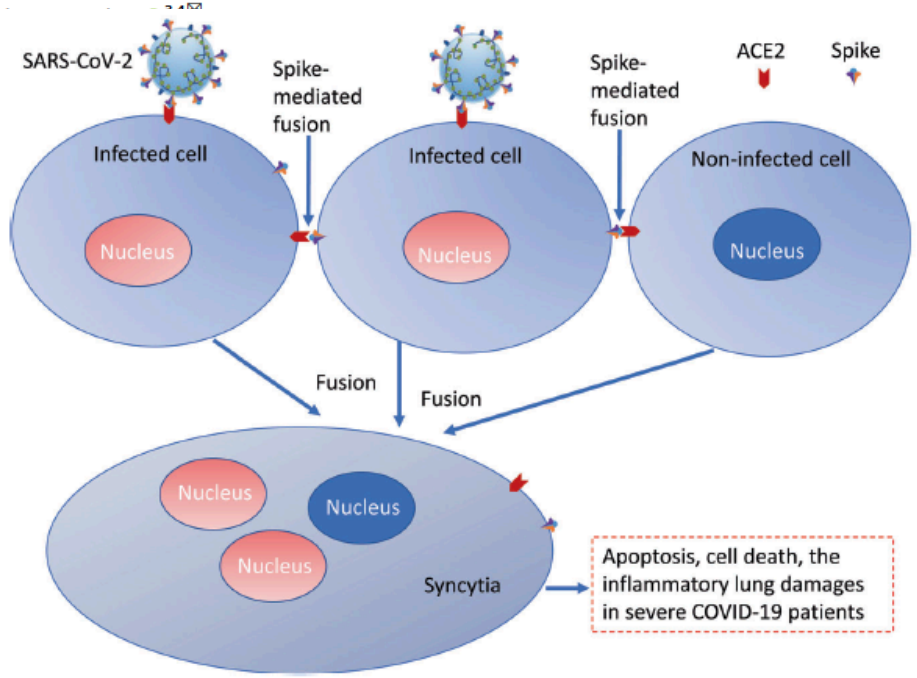
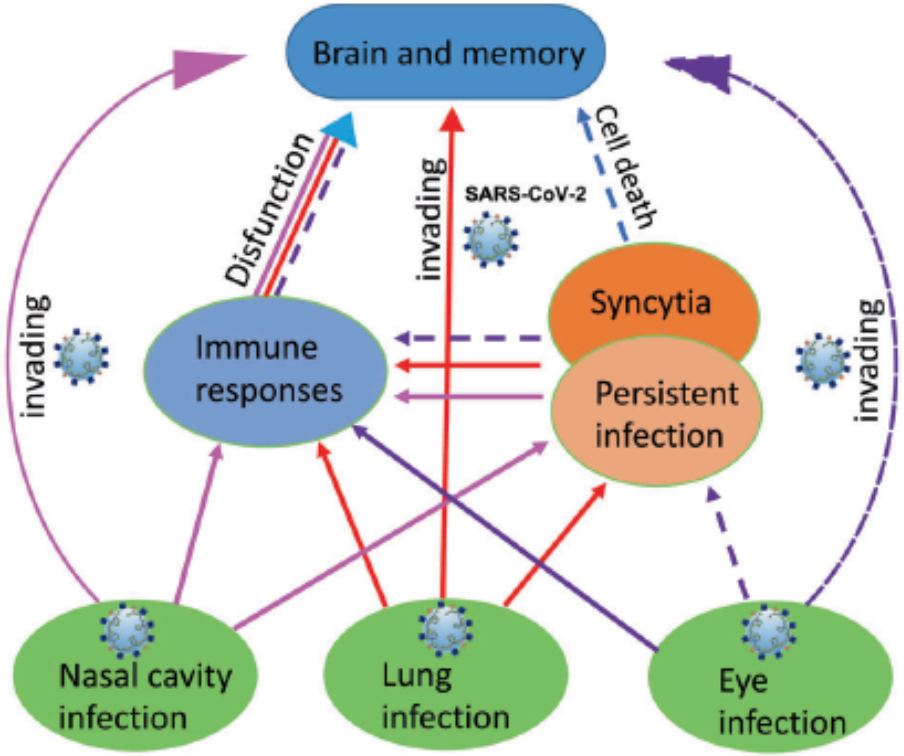


Fig. 2 The model of SARS-CoV-2 infection causing syncytia and cell death. Cells infected with SARS-CoV-2 could express spike protein on the cell surface, which can interact with ACE2 on the surface of infected or non-infected cells and then trigger the cell-cell fusion to form syncytia. The syncytia could induce apoptosis and cause inflammatory damages in different organs.

Table 1. The host receptors for SARS-CoV-2 infection based on current data.

Receptors	Cells and organs expressing the receptors	Reference
Angiotensin-converting enzyme 2 (ACE2)	Multiple organs including respiratory tract, heart, liver, brain, kidney, intestine, and other organs express ACE2. It is a critical receptor for SARS-CoV-2.	[23, 101]
CD147 (Basigin or extracellular matrix metalloproteinase inducer)	Megakaryocytes, human bronchial epithelial cells, the brain tissues, and many other organs express CD147. It is an alternative receptor for SARS-CoV-2.	[102, 103]
Tyrosine-protein kinase receptor UFO (ALX)	Pulmonary, marrow stromal cells, bronchial epithelial cells, and most human organs express ALX. It is an alternative receptor for SARS-CoV-2.	[32, 104]
Neuropilin 1 (NRP1)	Olfactory, cerebral area, and respiratory epithelial cells express NRP1. It is an alternative receptor for SARS-CoV-2.	[33, 34]
C-Type Lectins	Dendritic cells, macrophages, endothelial cells of lungs, lives, and renal vessels express C-Type lectins. They are alternative receptor or co-receptor for SARS-CoV-2.	[105, 106]



g. 1 The schematic map of SARS-CoV-2 infecting human brain nd affecting human memory. SARS-CoV-2 could directly infect the asal cavity, lungs and eyes. High viral titers could be detected in ne nasal cavity and lungs, which are likely to cause the direct viral ıvasion to brains through olfactory sensory neurons and the lood–brain barrier. The efficient viral replication in multiple organs an cause the exposure of these organs to high titers of SARS-CoV-2 and stimulate host immune responses and neuroinflammation to induce neurological symptoms. Persistent viral replication and syncytia formation can stimulate the production of cytokines and autoantibodies to affect the brain and memory with the long-term dysfunction. The eye infection with low viral replication is a potential route to affect the brain and memory. Color lines indicate the corresponding routes. Solid lines indicate the direct effects and dot lines indicate the routes of the potential effects.

COVID19 is not FLU

Long term and medium term disability and increase incidence of Diabetes and Heart Disease

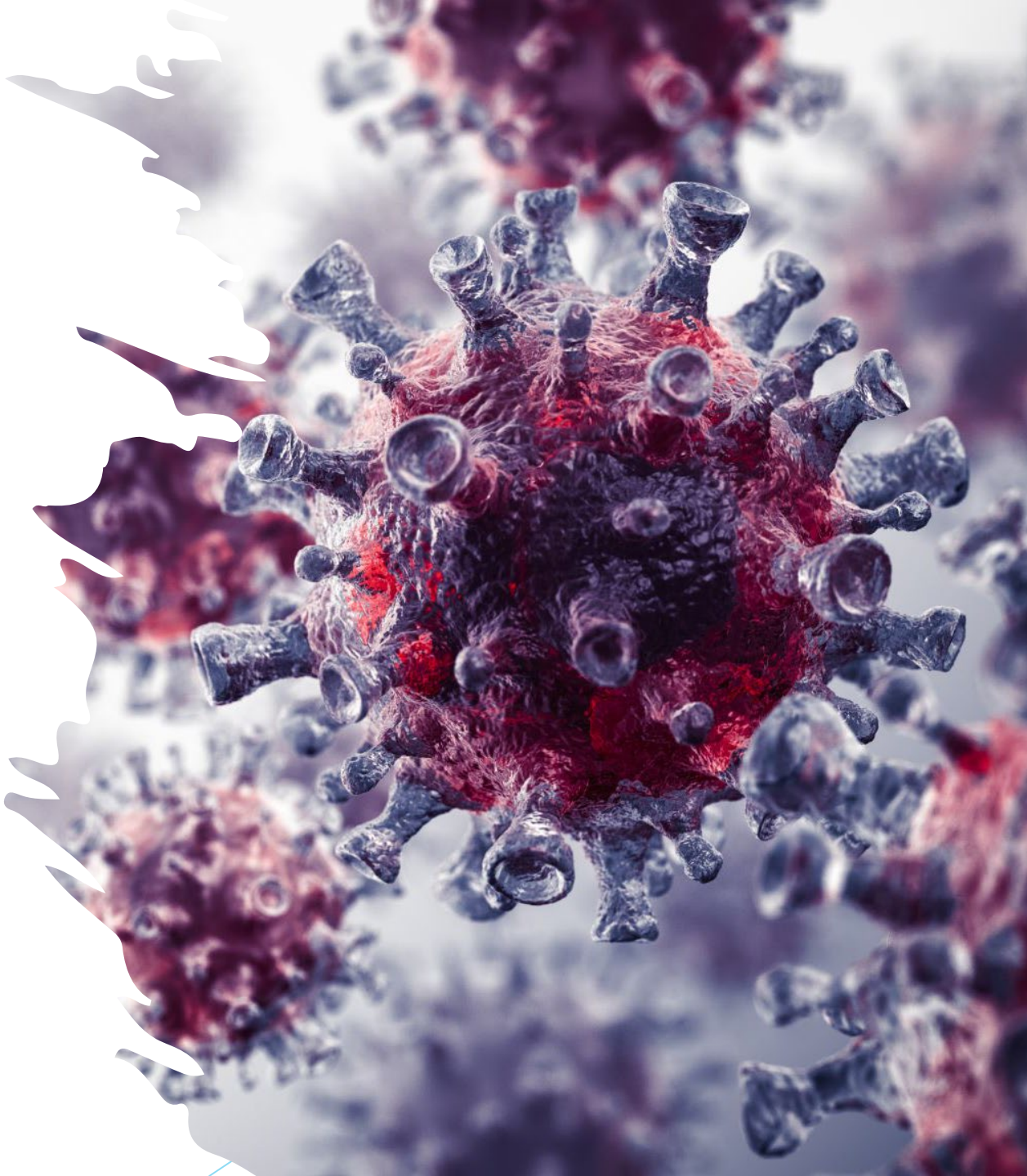
What about 10 years in?

15h •

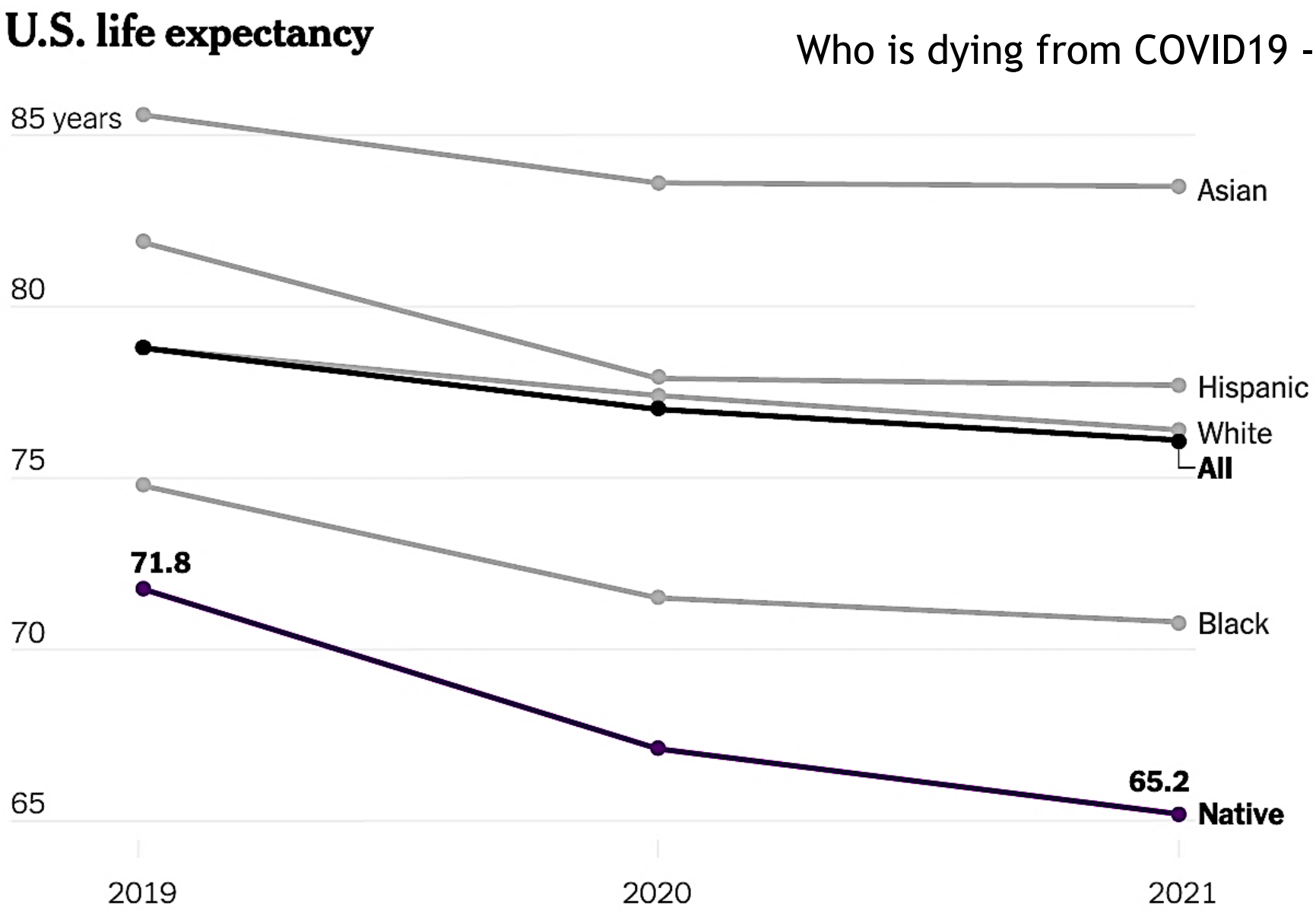
SARS-CoV-2 can directly infect the arteries of the heart and cause the fatty plaque inside arteries to become highly inflamed, increasing the risk of heart attack and stroke, according to an NIH-funded study. https://bit.ly/48AVxLR #SARSCoV2 #COVID19 #HeartAttack #heart #stroke #research #NHLBI #NIH

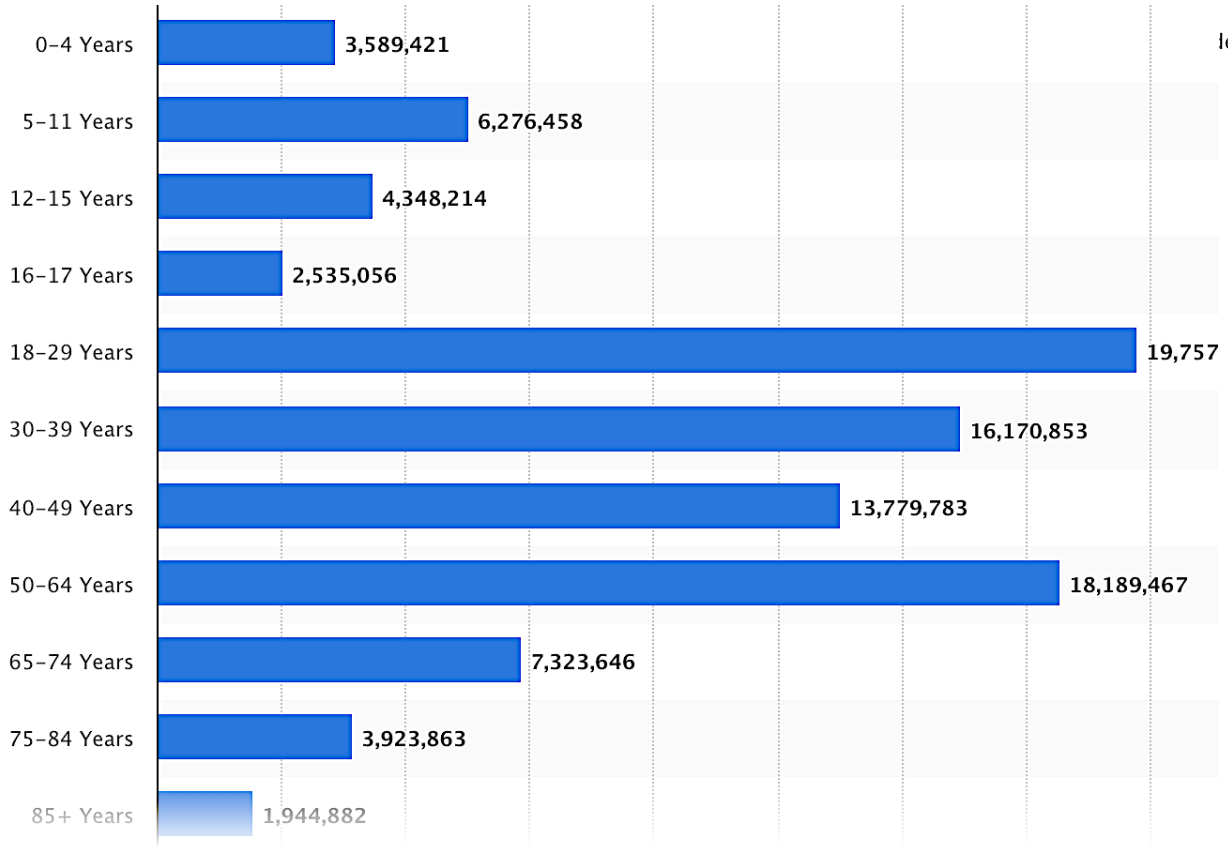
SARS-CoV-2 infects coronary

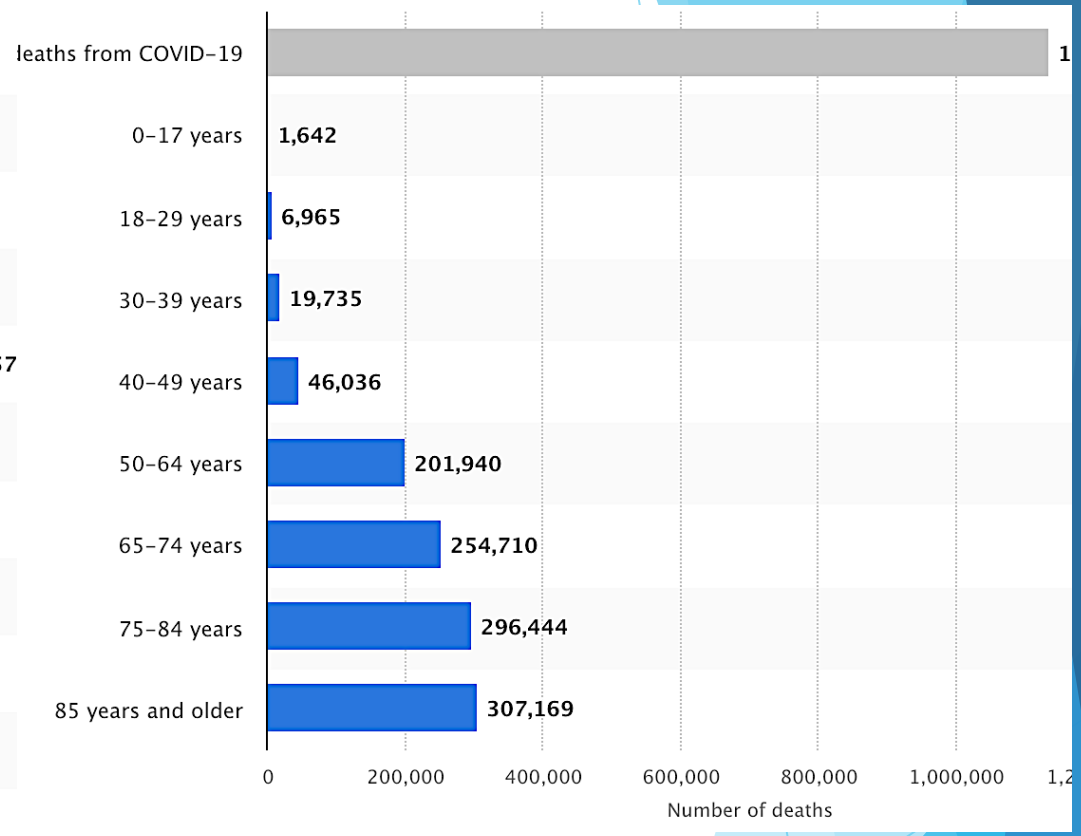
Who was dying and who is still dying from COVID19 and respiratory infectious diseases – we can change this outcome with testing and treatment



Who is dying from COVID19 - RACE



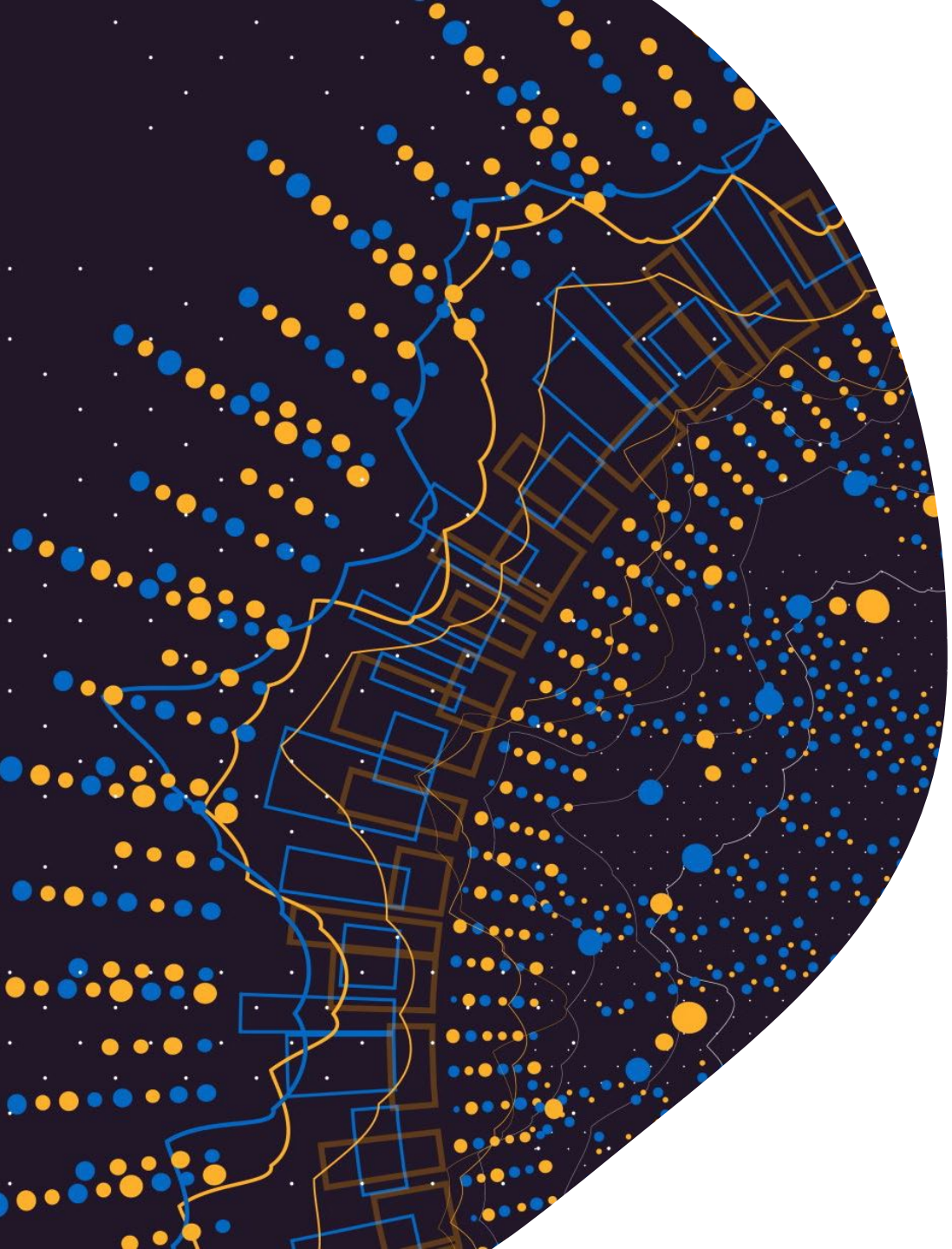




COVID 19 cases and deaths by age band

CFR (reported) cases and deaths

16% in Americans over 85

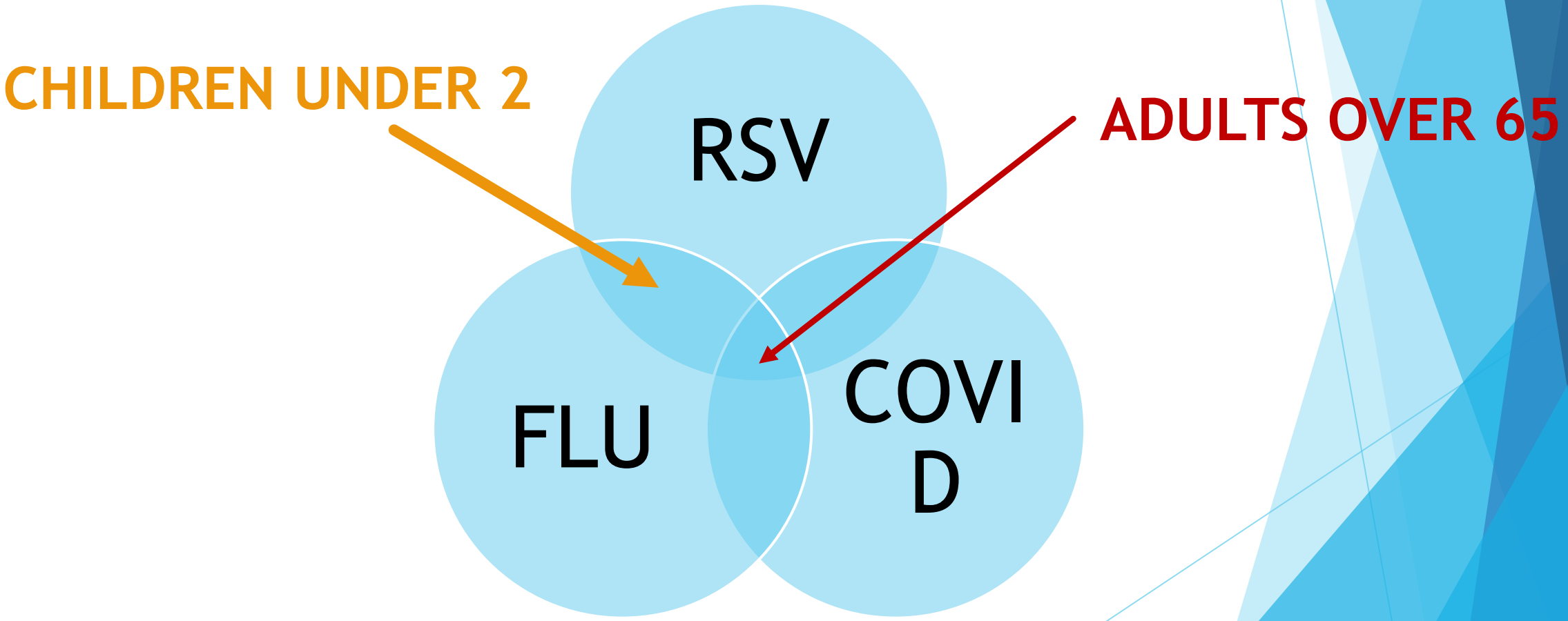


points

COVID has changed health care delivery forever giving us innovation and new tools – now we have to use them

1. New tests allowing at home diagnostic testing
2. New tests and equipment allowing for rapid definitive laboratory diagnosis of FLU, COVID, AND RSV from clinics to hospitals
3. Telehealth
4. Hospital without walls
5. Access to real time data to change outcomes
6. Rapid testing can dramatically decrease community spread – this has been demonstrated at universities, hospitals and LTCF

Overlapping respiratory diseases with overlapping symptoms and severe risk of hospitalization and death



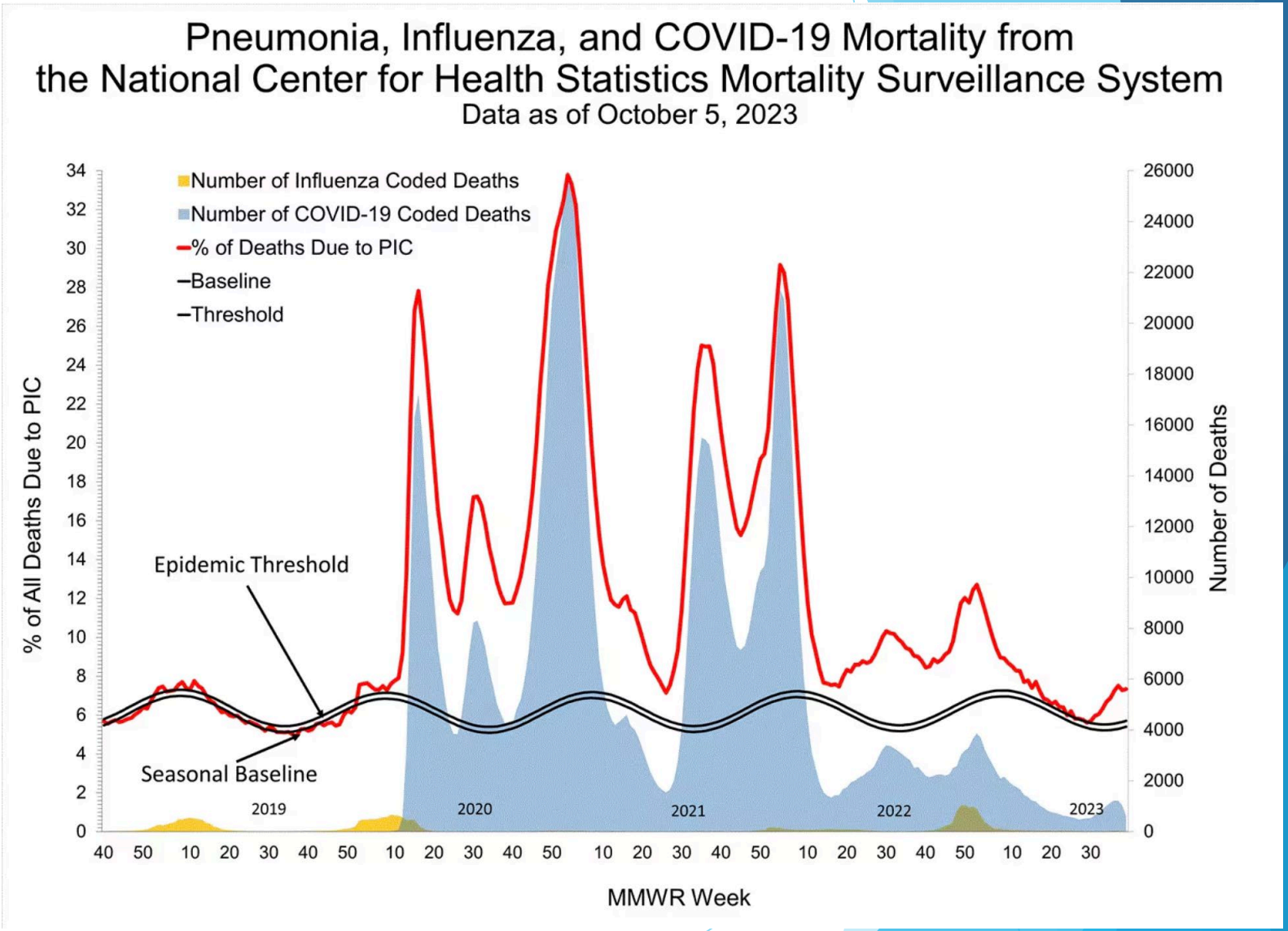
The problem of serial infectious surges – 4 months of serial infections and absenteeism

- **RSV November – December 2023 – impacts children under 2 and elderly severely**
- **FLU December – January 2024 – impacts children under 5, pregnant women and elderly with severe disease**
- **COVID19 – November 2023 in the upper Midwest, Northern Plain states peaking across the USA in the December 2023-January 2024**
- **The above led to continuous absenteeism of workers due to sick children, sick elderly and sick workers for nearly 4 months – how do we plan now for next year**
- Biggest risk to the workplace – continuous threat of medium and long COVID

Where are we today?

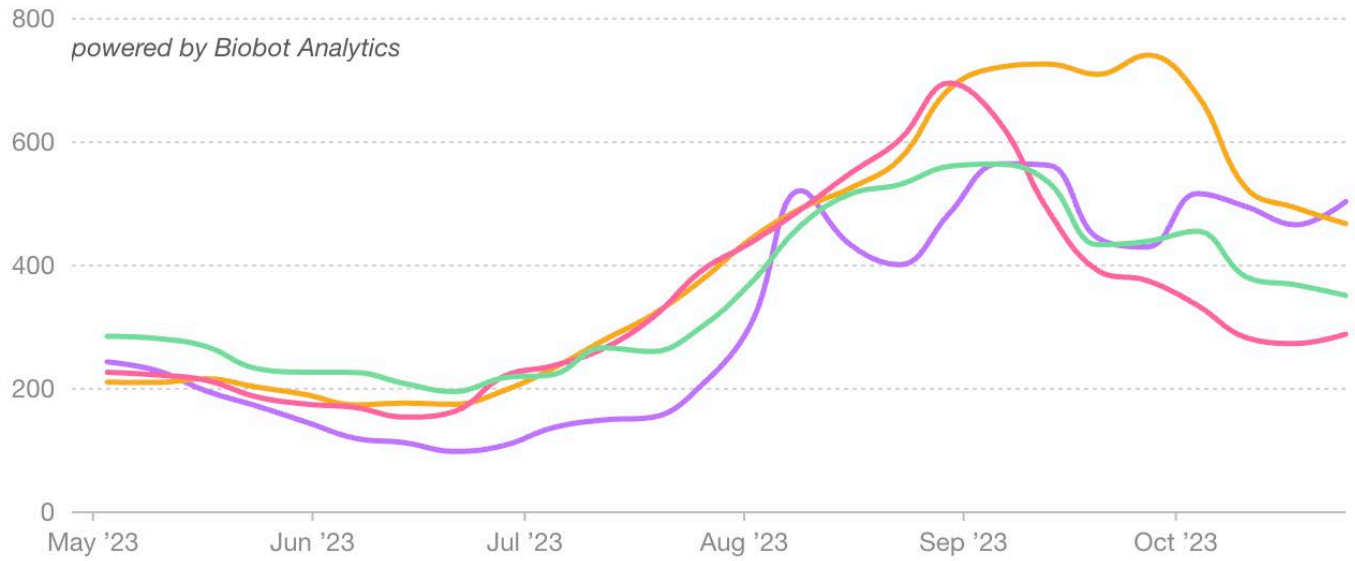
- First, we have lost nearly all reported data and across the globe it's the patient that needs to demand definitive diagnosis – its no longer acceptable to "guess" or say Flu-like illness as the treatments are vastly different
- We have lost COVID therapeutics that were essential to protecting vulnerable individuals - monoclonal antibodies
- Vaccines durability is very time limited to prevent severe disease and hospitalization as well as infection and boosting needs to be much more frequent for the most vulnerable
- We aren't using the limited data we have to decrease susceptibility of our vulnerable and elderly – need hospitals and clinics to post local testing data along with wastewater data so the public can understand their risks and are

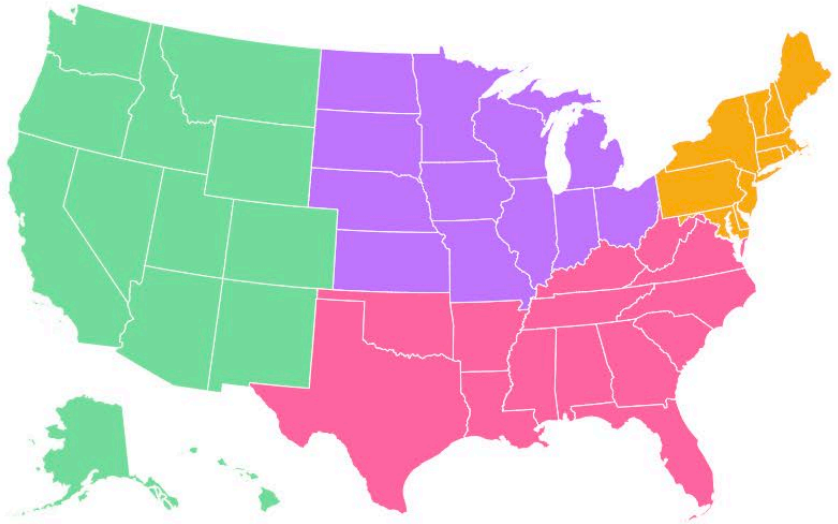
We have been above epidemic threshold for almost 4 years except for a few weeks this summer



Current COVID Epidemiology in the USA

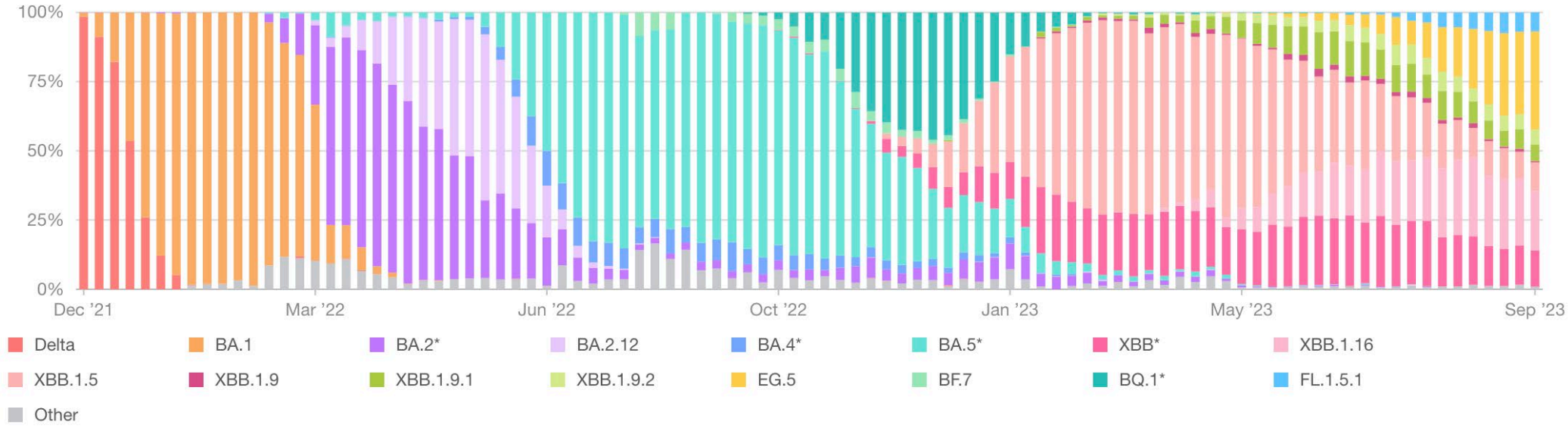
Wastewater: Effective SARS-CoV-2 virus concentration (copies / mL of sewage)



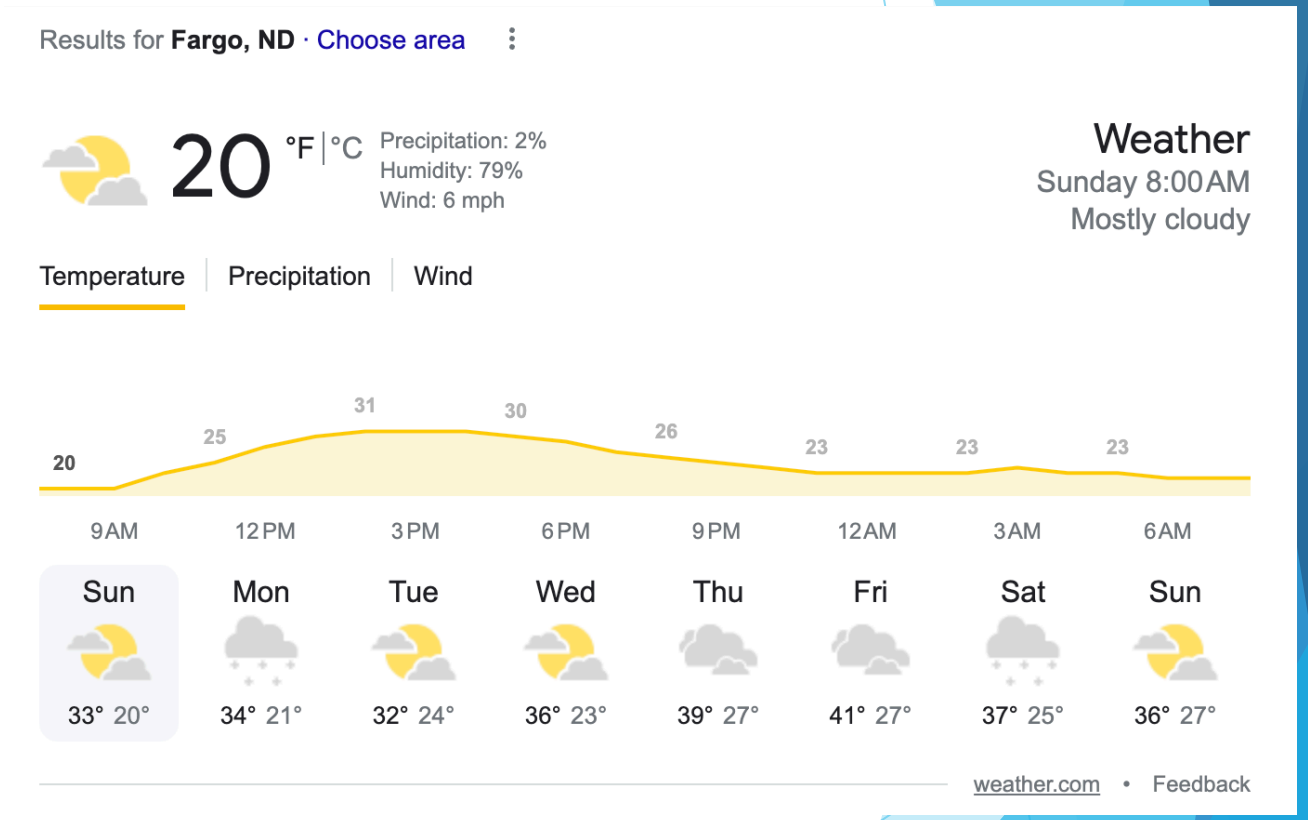


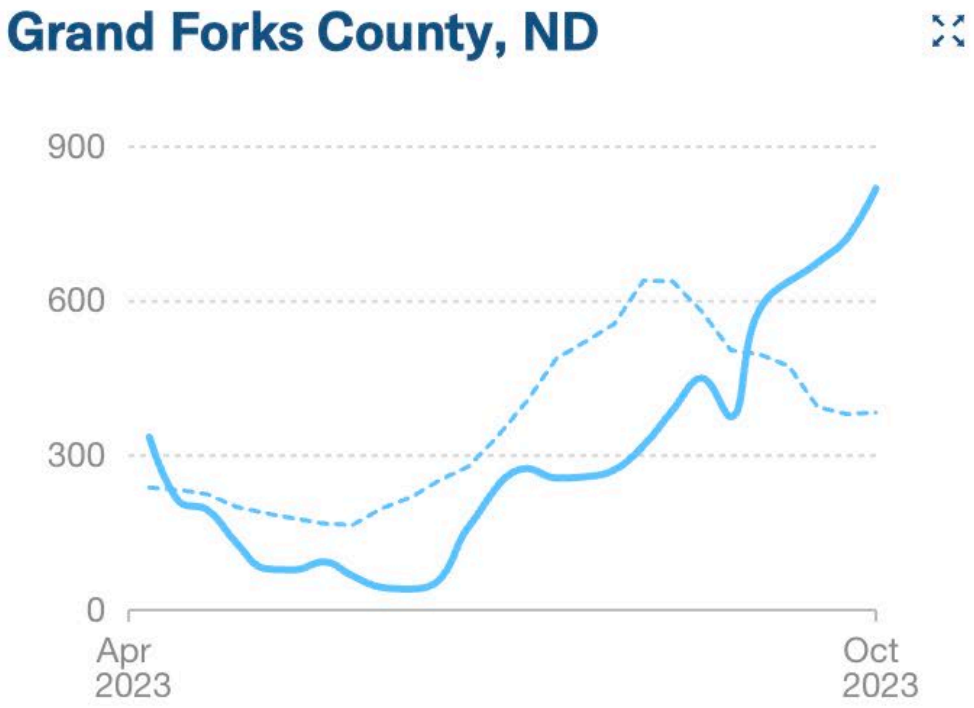
Source: Wastewater data from Biobot Analytics

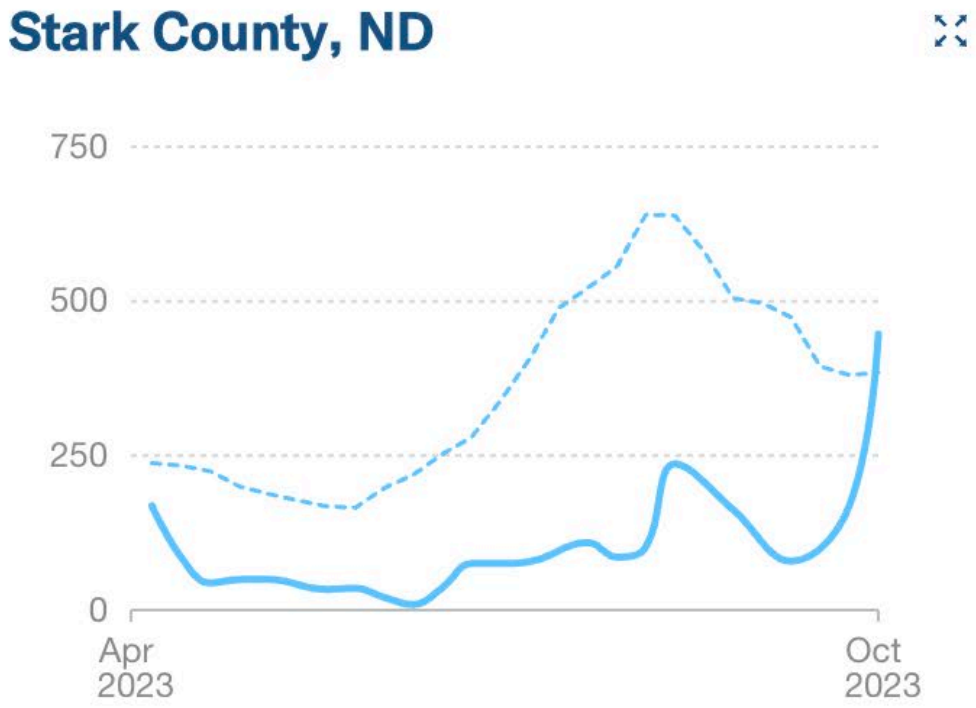
Variants: Percentage of variant lineage sequenced from SARS-CoV-2 genome found in wastewater



Cooling now in the Northern Areas will trigger and other COVID surge over the next 6-8 weeks







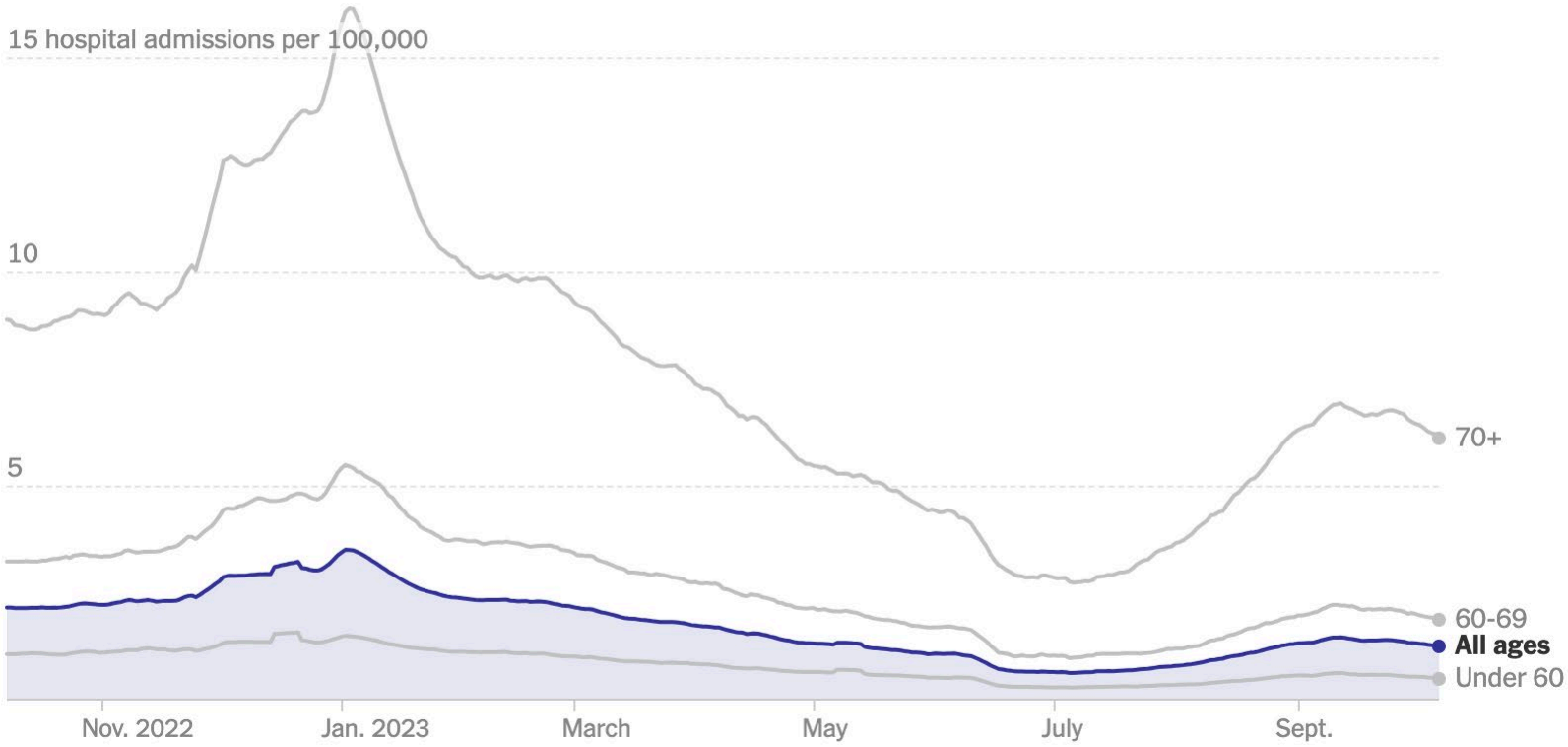
Wastewater is already beginning to rise in the Northern plains

USA

Daily Covid hospital admissions

Avg. on Oct. 7: 4,050

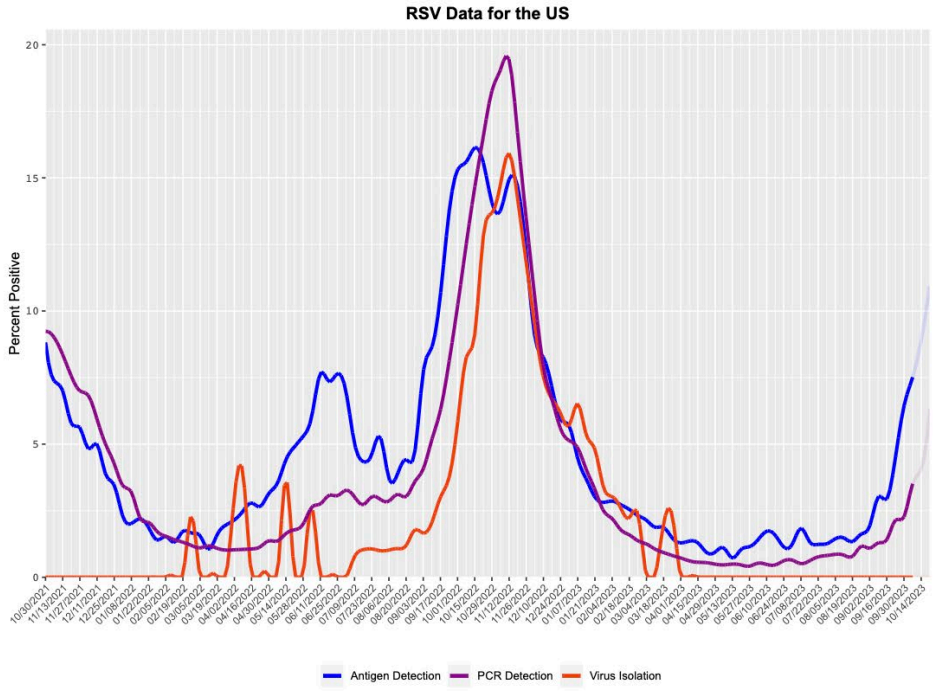
14-day change: −11%



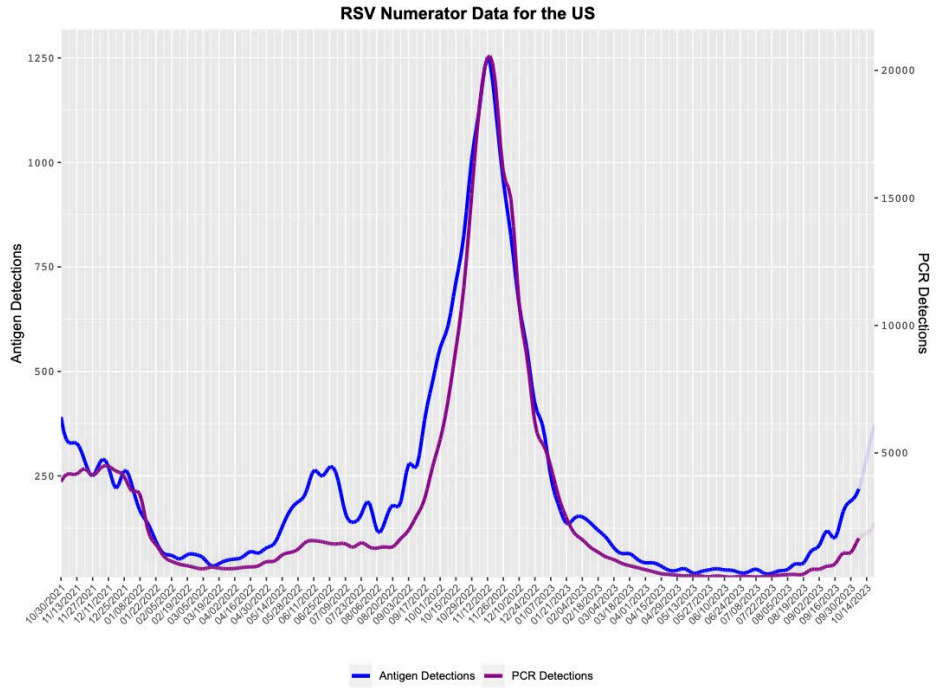
Current RSV Epidemiology in the USA

Respiratory Syncytial Virus (RSV)

Percent Positive



Detections



RSV USA – just starting – will peak in December

RSV is already increasing in the South and will impact the vulnerable in 6-8 weeks

Detections

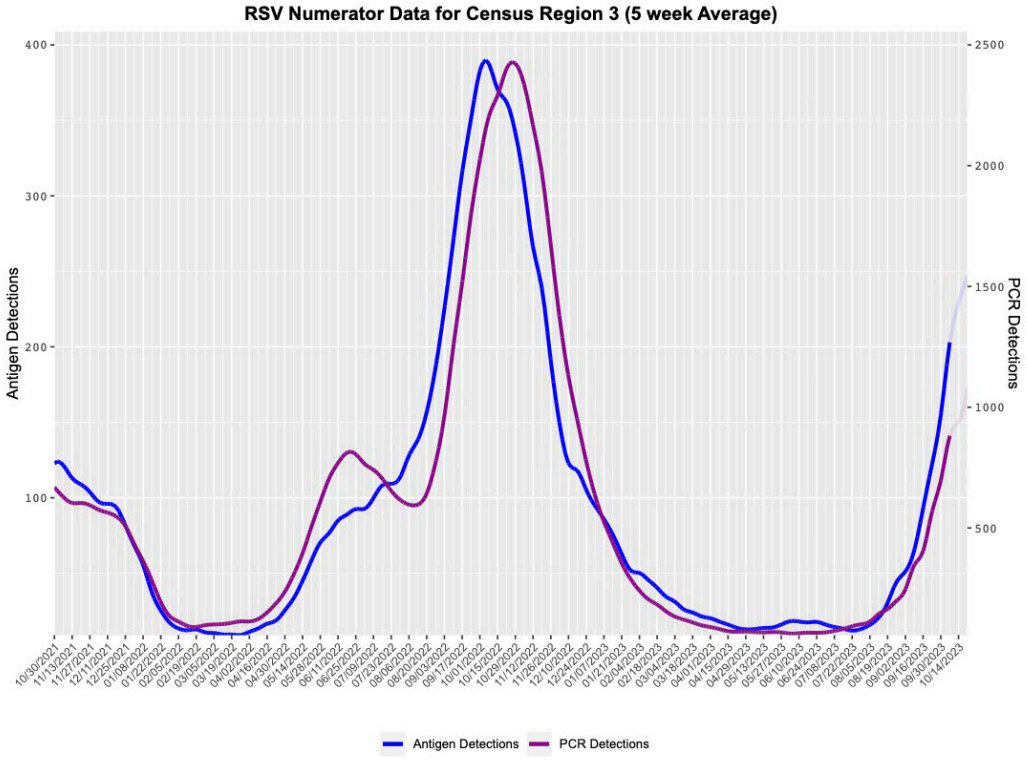


Table: South United States RSV detections, by week

Detections

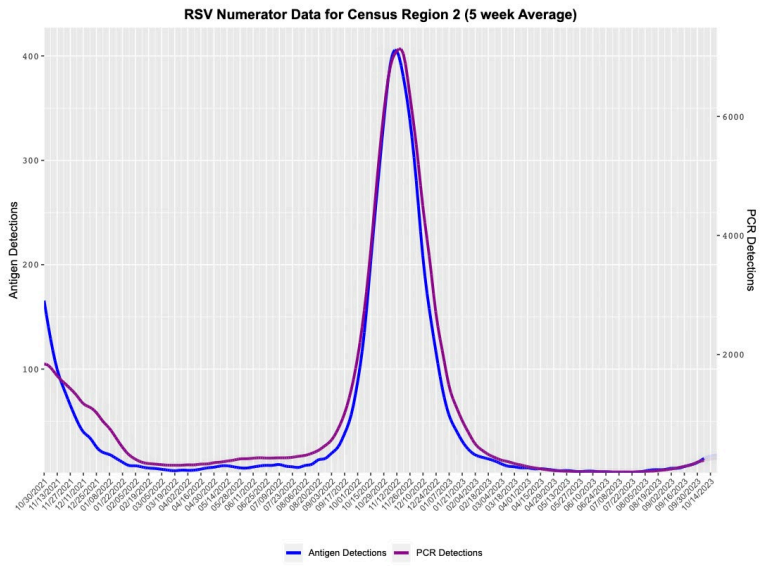


Table: Midwest United States RSV detections, by week

Detections

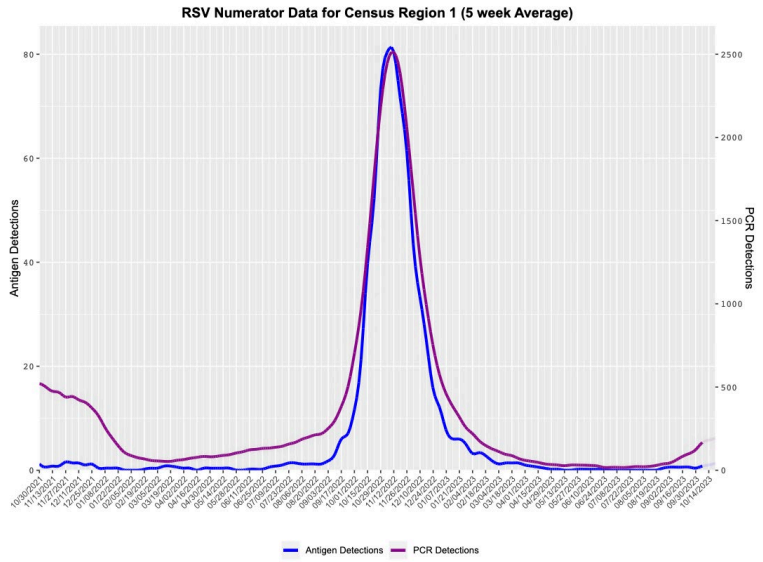


Table: Northeast United States RSV detections, by week

Detections

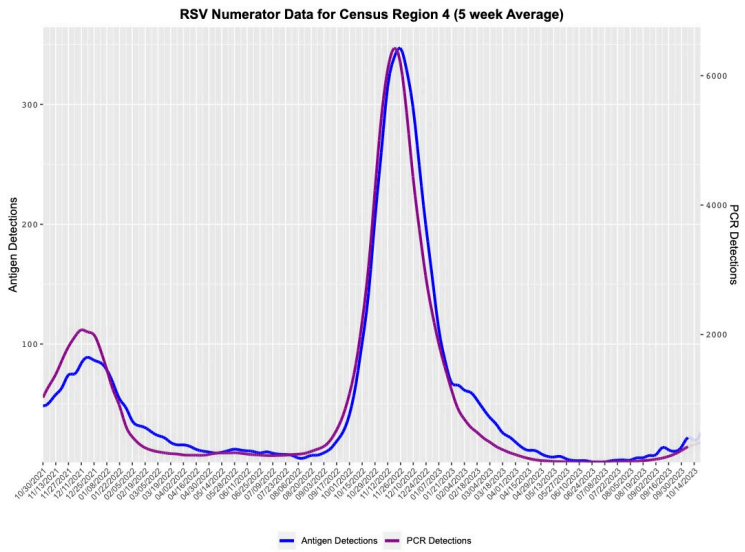
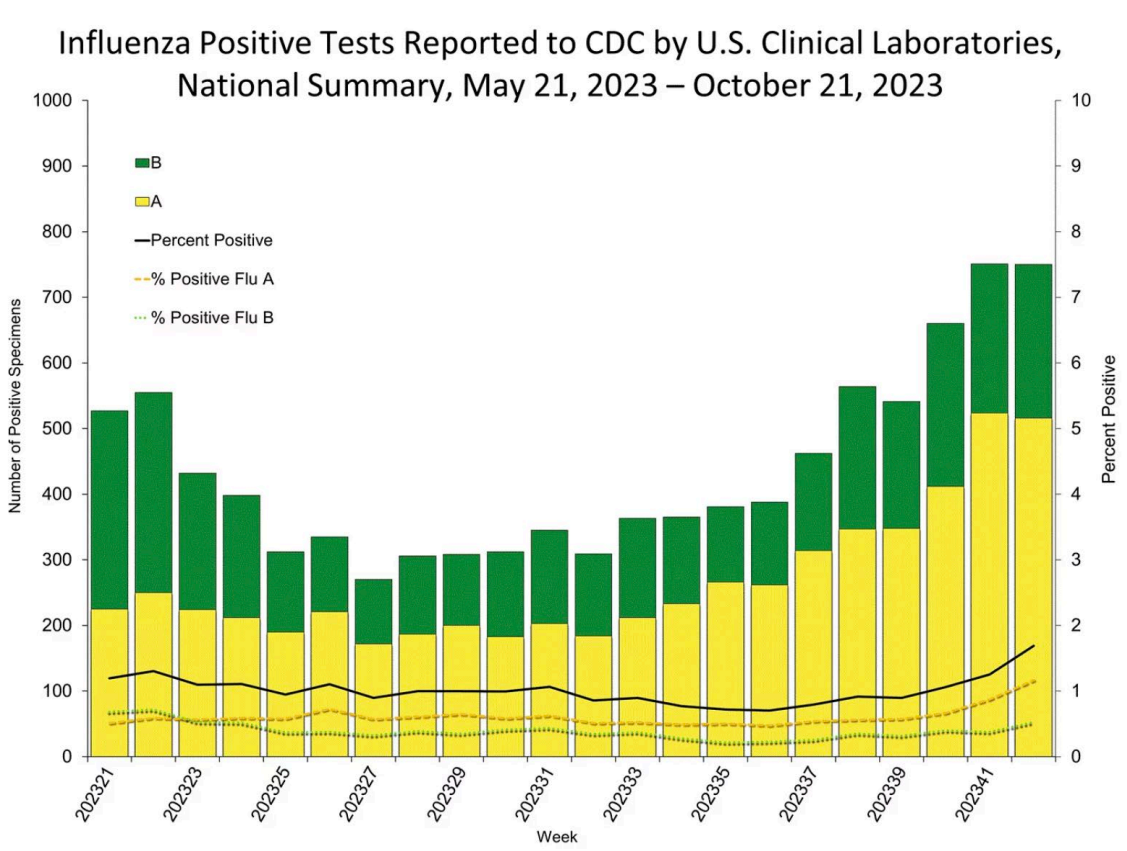
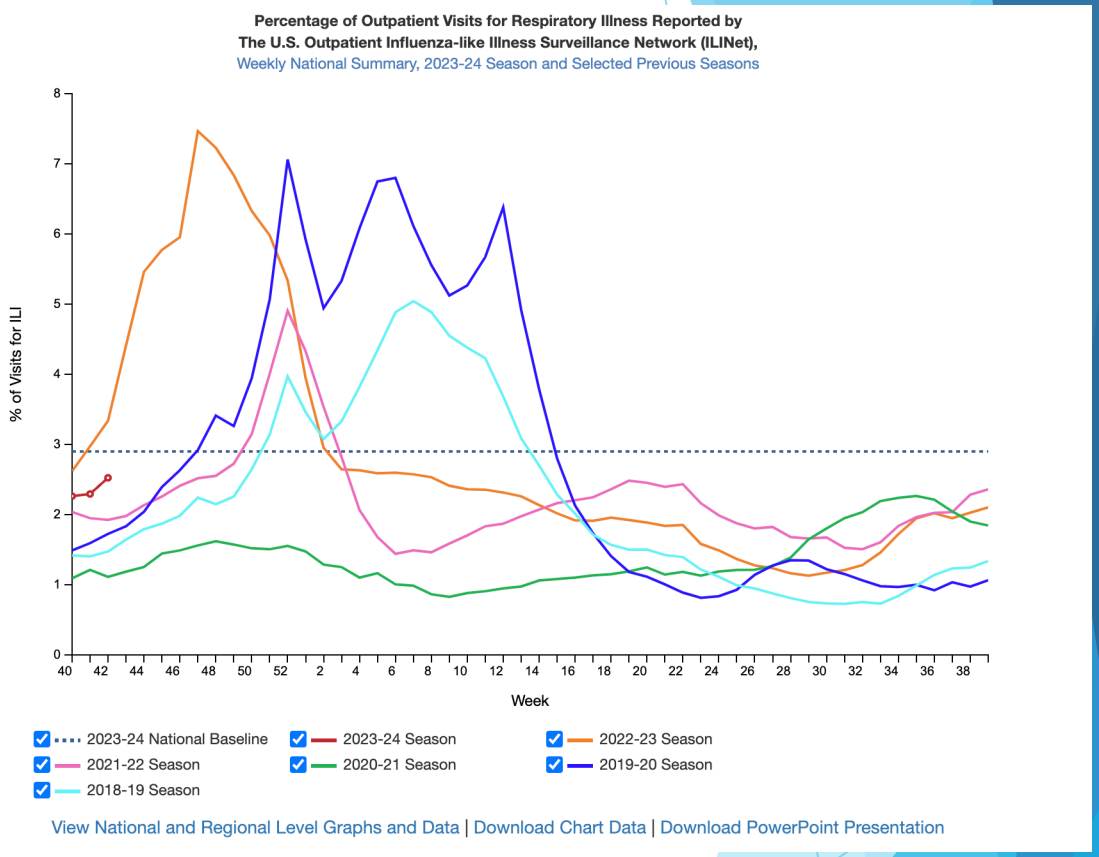


Table: West United States RSV detections, by week

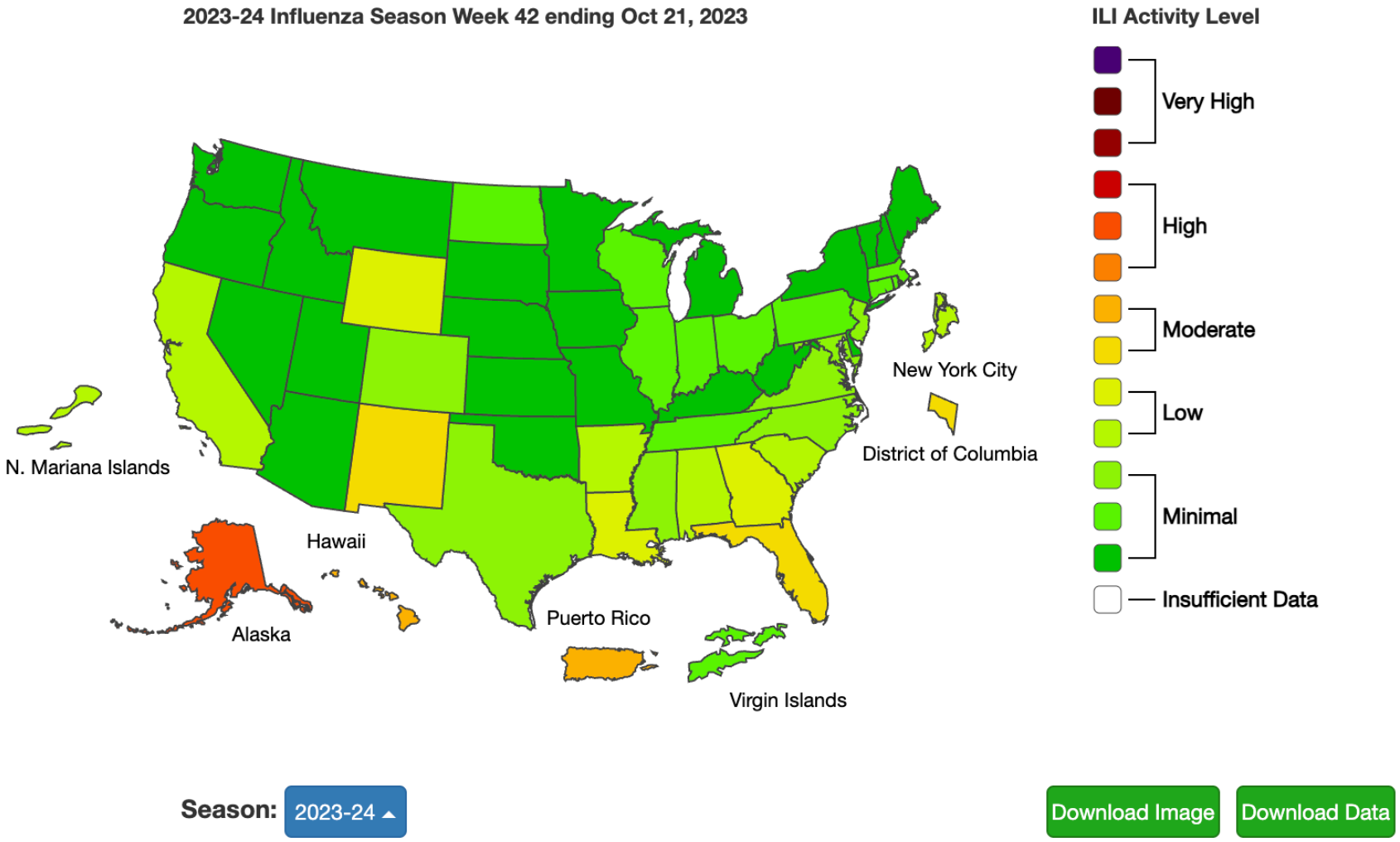
Current RSV Detection by Region

Current FLU epidemiology in the USA





US FLU profile – just beginning– predict cases rising post Halloween and peaking in late Nov early Dec



Flu like RSV and soon COVID is beginning with a potential overlap in the Nov-Jan Timeframe

Long-term symptom profiles after COVID-19 vs other acute respiratory infections: an analysis of data from the COVIDENCE UK study

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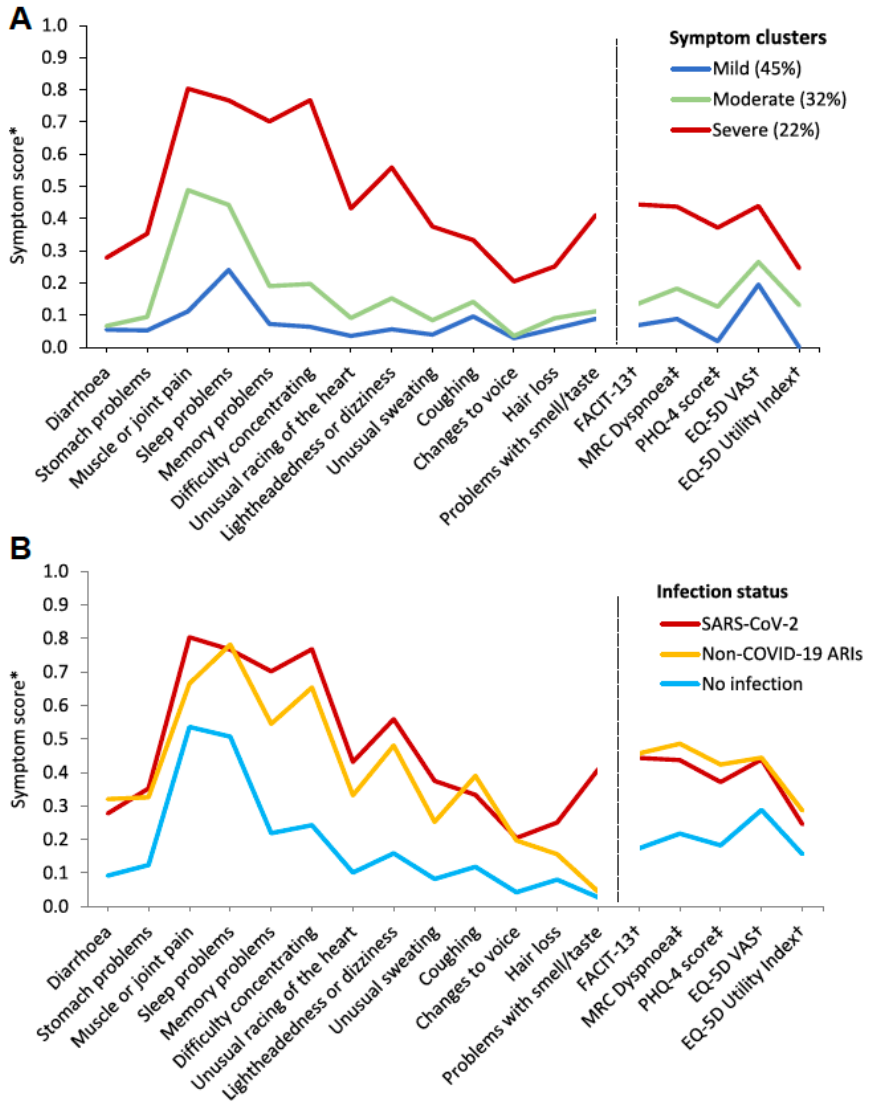

***Fig. 1:* Symptom profiles among all participant with previous SARS-CoV-2 infection (A) and among participants with the most severe symptoms, by infection status (B).** Figure shows the conditional probability (left of the dashed line) or mean severity (right of the dashed line) for all symptoms considered, adjusted for age and sex. Parallel lines between the classes indicate a fairly even increase in the probability or severity of the symptoms considered; disproportionate changes in symptom probability or severity are shown by deviations from the parallel. Displayed probabilities or scores are shown in Appendix Table S13. (A) Includes all participants with previous SARS-CoV-2. (B) Symptom profiles for participants with the most severe symptoms from the three separate latent class analyses are overlaid. MRC = Medical Research Council; VAS = visual analogue scale; PHQ = Patient Health Questionnaire. *Symptom score represents conditional probability for binary variables and mean severity for ordinal and continuous variables. †Continuous variables have been reversed to aid with interpretation, so that higher values indicate worse severity or health state. ‡Ordinal variable.

We have the 21st century tools and the knowledge to ensure every American is safe from hospitalization and death independent of age but we must expand testing and definitive diagnosis of respiratory infectious disease

- **Vaccination and Boosting** – but this is not enough to prevent infection and transmission to vulnerable family members : protection against hospitalization wanes
- **Proactive testing** through surges and immediate Paxlovid or FLU antivirals if at risk for significant disease
- **Using tests proactively to protect the vulnerable**
- **N95 and KN95 masking** for those at risk for serious disease during surges
- Communication and clarity with about what is happening, what is expected and tools to both survive and thrive
- **Next generation vaccines and therapeutics are needed**
- **Therapies for long covid are essential**