Long COVID - 2022 Updates

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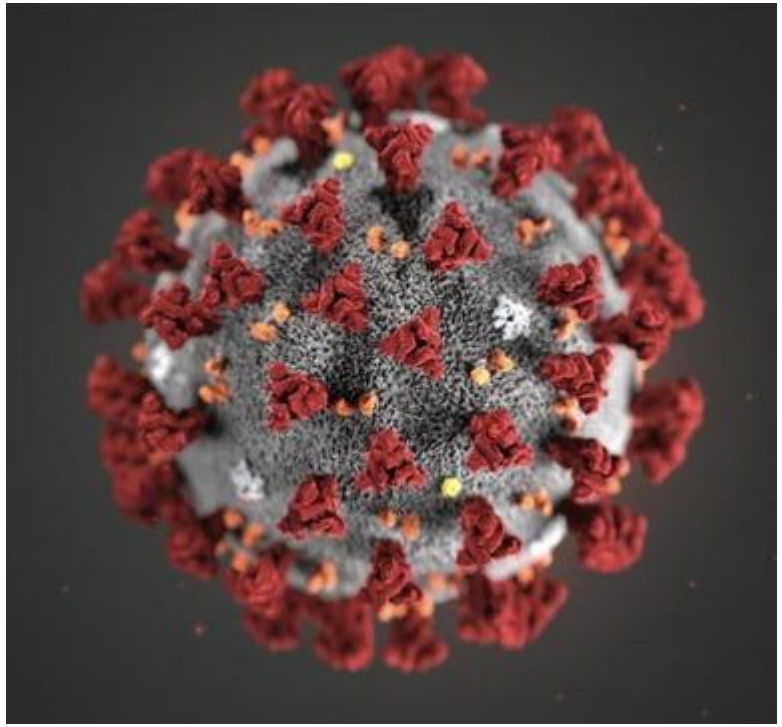
Objectives



- Define Long COVID and its pathophysiology
- Identify adverse impacts of COVID-19 on patients
- Appraise the current literature related to post-COVID syndrome and how to evaluate and treat these conditions

Disclosures:

- Been consultant or done research with Allergan, Merz, Ipsen, Piramal

- Honoraria to discuss PASC

- Co-PI RECOVER Trial with NIH

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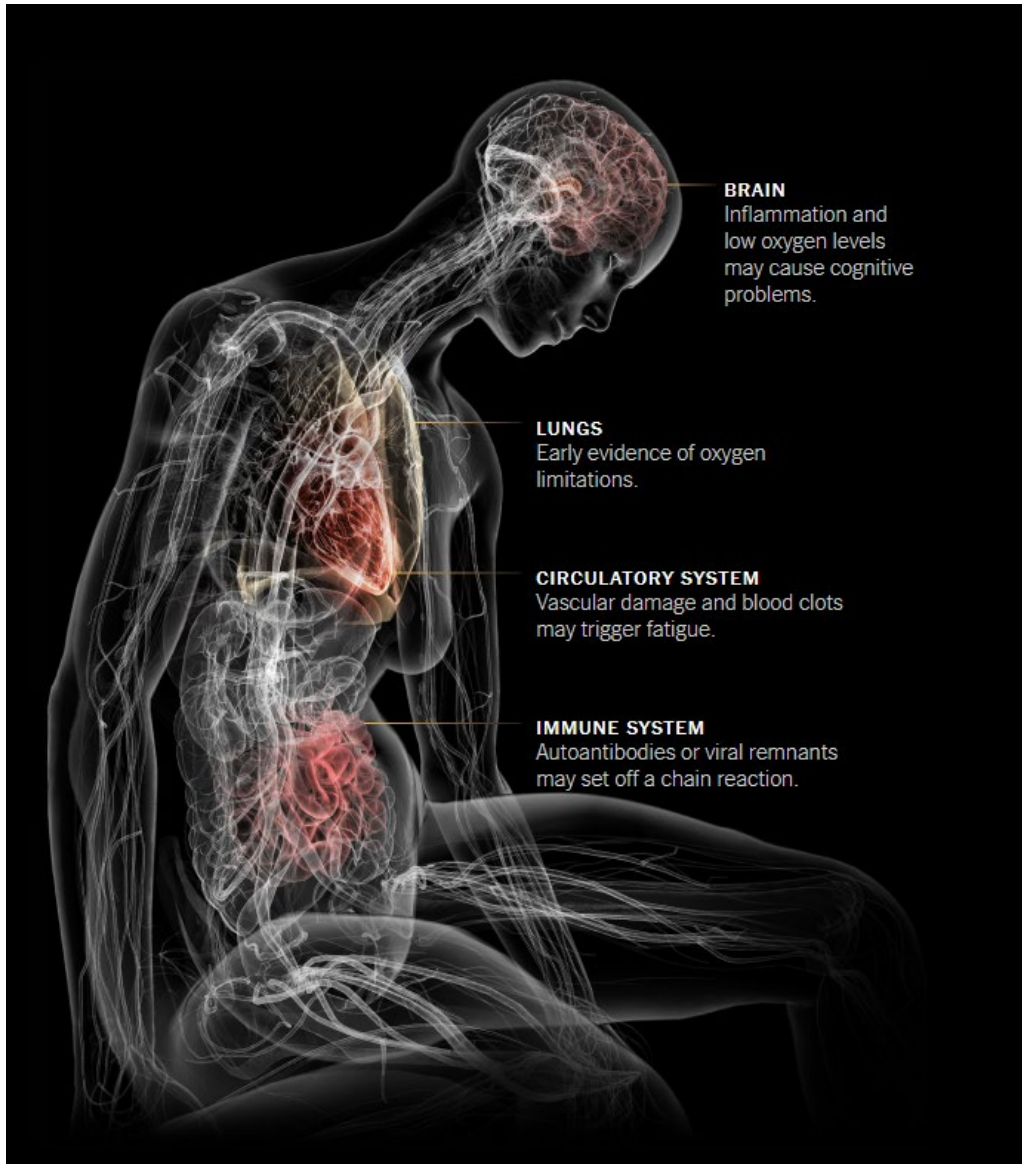
Review of Terminology

Long COVID – Syndrome characterized by varied persistent symptoms and health effects after resolution of the initial infection (lasting for weeks, months, or longer).

Long Hauler – COVID-19 survivor with lingering effects after resolution of infection.

Post-Acute Sequelae of SARS-CoV-2 infection (PASC) – New syndrome name announced by the National Institutes of Health in February 2021.



New York Times, Josh Keller

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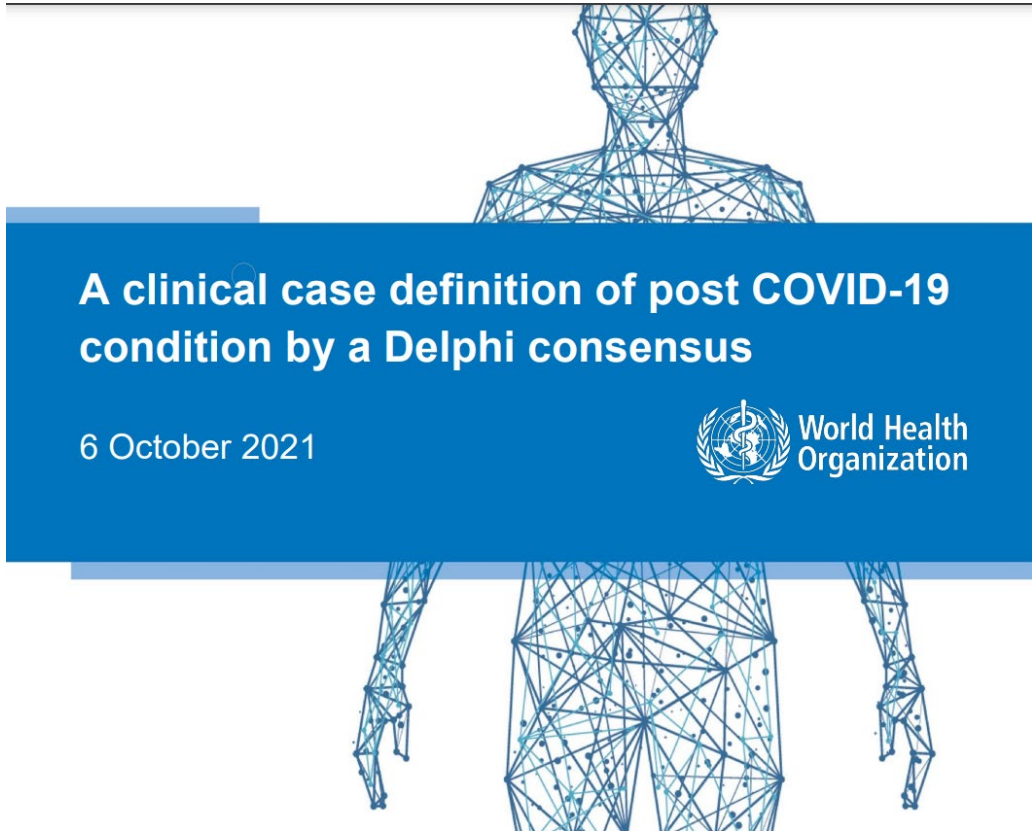
WHO

*Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for **at least 2 months** and cannot be explained by an alternative diagnosis.*

Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time.



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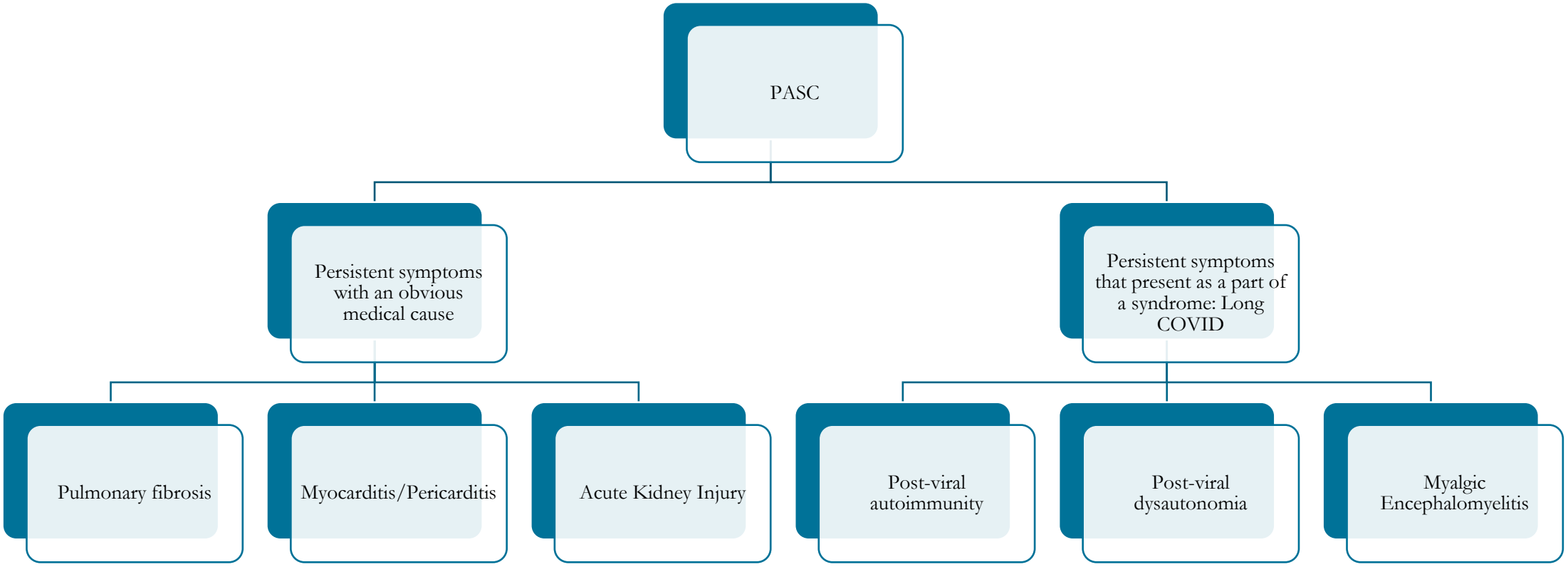
Nuance to PASC diagnosis



PASC is not always Long COVID

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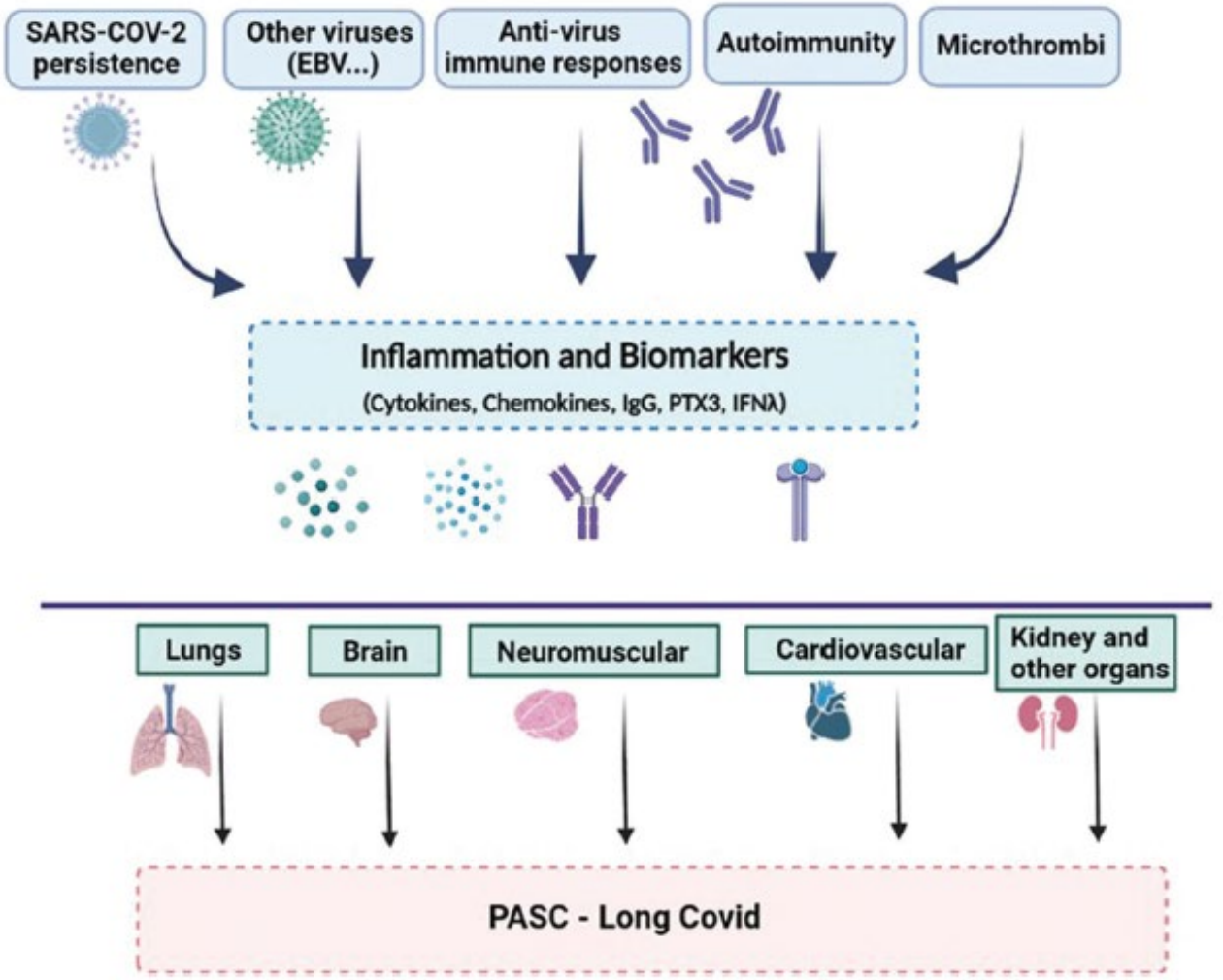
Pathogenesis and Targets of PASC



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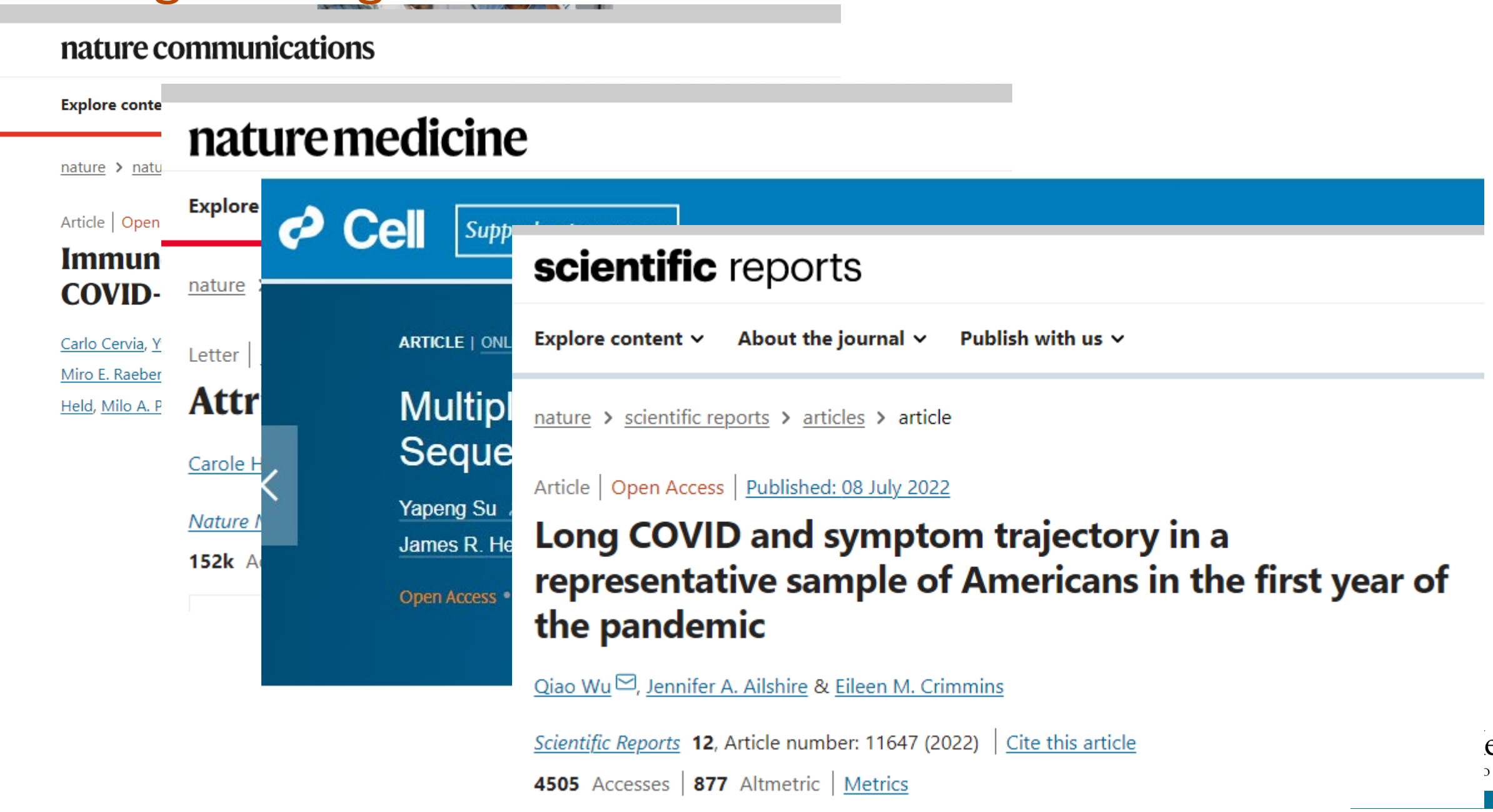
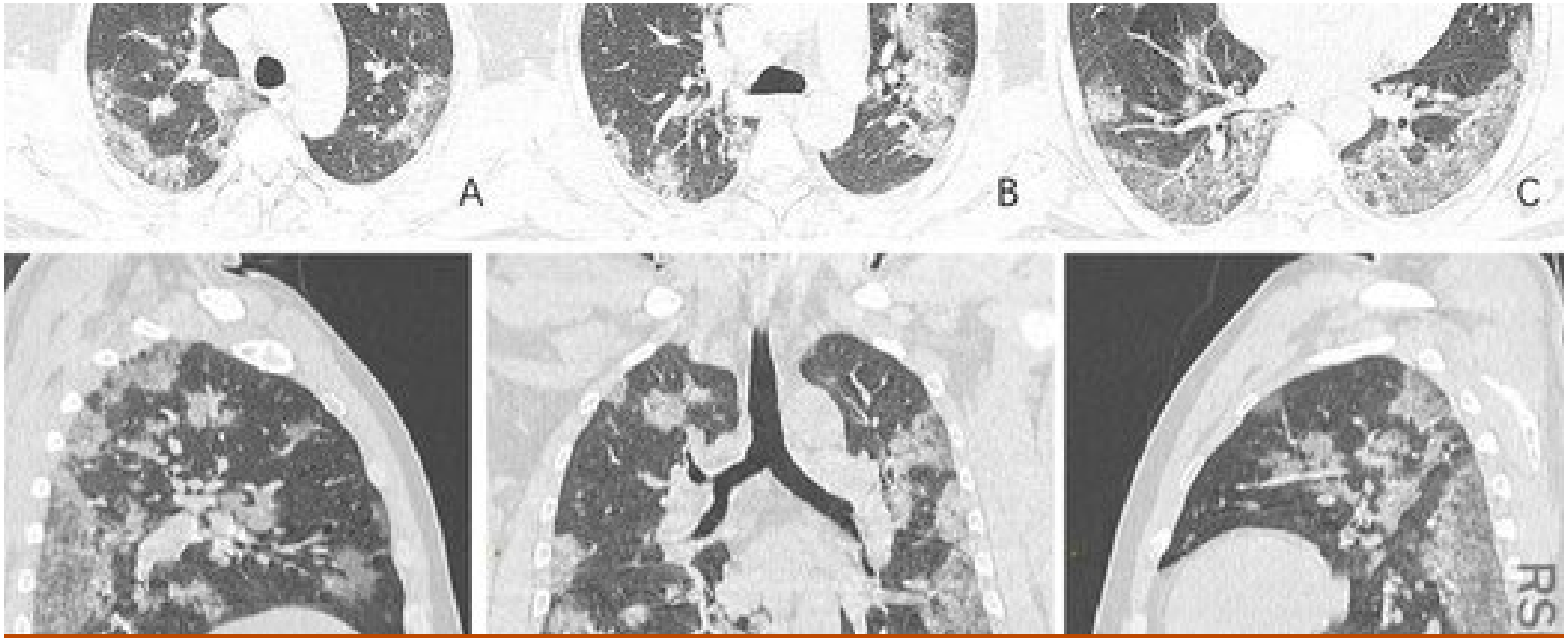
Who gets Long COVID?





What does recovery look like?

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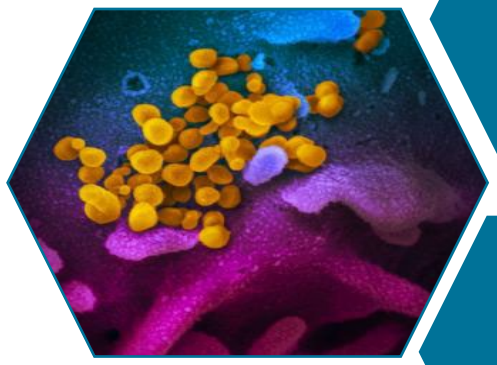
COVID-19 Outcomes

Mild
Mod

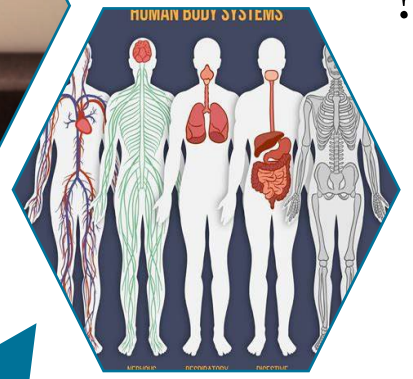


Severe

Silent

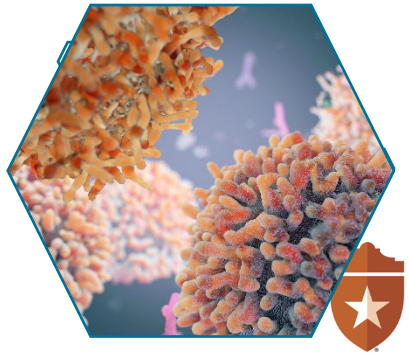
Long-COVID
10% - 50%

?



Recover

More
Sx



?

Death
17%

End
organ
damage

2020 2nd qtr, 240 pts

Vehar. Cleve Clin J Med. 2021.

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NCHS Pressroom

Weekly COVID-19 Mortality Overview

2022 Release Schedule

Nearly One in Five American Adults Who Have Had COVID-19 Still Have "Long COVID"

New data from the Household Pulse Survey show that more than 40% of adults in the United States reported having COVID-19 in the past, and nearly one in five of those (19%) are currently still having symptoms of "long COVID."

- Overall, 1 in 13 adults in the U.S. (7.5%) have "long COVID" symptoms, defined as symptoms lasting three or more months after first contracting the virus, and that they didn't have prior to their COVID-19 infection.
- Older adults are less likely to have long COVID than younger adults. Nearly three times as many adults ages 50-59 currently have long COVID than those age 80 and older.
- Women are more likely than men to currently have long COVID (9.4% vs. 5.5%).
- Nearly 9% of Hispanic adults currently have long COVID, higher than non-Hispanic White (7.5%) and Black (6.8%) adults, and over twice the percentage of non-Hispanic Asian adults (3.7%).

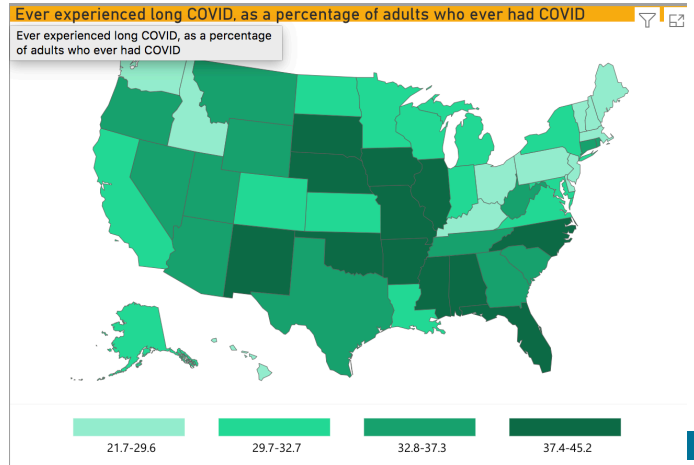
National Center for Health Statistics

Ever experienced long COVID, as a percentage of adults who ever had COVID

Phase	Jul 27 - Aug 8, 2022		Jun 29 - Jul 11, 2022		Jun 1 - Jun 13, 2022	
Time Period						
Group	Percent	95% CI	Percent	95% CI	Percent	95% CI
National Estimate						
United States	33.2	32.1 - 34.3	34.3	33.0 - 35.6	35.1	34.1 - 36.0
By Age						
18 - 29 years	30.3	27.2 - 33.5	30.9	28.2 - 33.8	36.1	32.3 - 40.1
30 - 39 years	34.0	31.3 - 36.7	33.7	30.9 - 36.6	32.3	30.4 - 34.2
40 - 49 years	36.3	33.8 - 38.8	36.5	33.9 - 39.2	36.7	34.3 - 39.1
50 - 59 years	37.6	34.5 - 40.7	35.6	32.8 - 38.5	38.2	35.7 - 40.8
60 - 69 years	31.1	27.9 - 34.5	33.9	30.8 - 37.2	34.4	31.7 - 37.3
70 - 79 years	23.9	20.0 - 28.1	37.7	32.6 - 42.9	31.1	26.4 - 36.1
80 years and above	25.0	15.8 - 36.1	28.8	19.6 - 39.5	23.3	18.0 - 29.3
By Sex						
Female	38.6	36.9 - 40.4	39.4	37.9 - 41.0	41.5	39.9 - 43.0
Male	26.8	25.0 - 28.7	28.4	26.4 - 30.6	27.6	26.1 - 29.2

Ever experienced long COVID, as a percentage of adults who ever had COVID

Phase	Jul 27 - Aug 8, 2022		Jun 29 - Jul 11, 2022		Jun 1 - Jun 13, 2022	
Time Period						
Group	Percent	95% CI	Percent	95% CI	Percent	95% CI
By Race/Hispanic ethnicity						
Hispanic or Latino	38.5	34.8 - 42.3	37.6	33.7 - 41.6	39.6	36.7 - 42.5
Non-Hispanic Asian, single race	20.5	16.7 - 24.6	26.9	20.8 - 33.7	25.4	21.0 - 30.2
Non-Hispanic Black, single race	33.5	29.3 - 37.9	33.5	29.0 - 38.2	37.8	33.5 - 42.2
Non-Hispanic White, single race	31.8	30.5 - 33.2	33.5	32.0 - 35.1	33.8	32.6 - 35.0
Non-Hispanic, other races and multiple races	42.5	36.3 - 48.8	39.8	34.2 - 45.6	35.7	31.0 - 40.6
By Education						
Less than a high school diploma	45.1	39.5 - 50.9	42.8	35.8 - 50.0	40.3	33.5 - 47.5
High school diploma or GED	34.9	32.1 - 37.8	39.6	37.2 - 42.0	38.5	36.2 - 40.8
Some college/Associate's degree	37.0	35.3 - 38.8	37.0	35.4 - 38.6	39.0	37.4 - 40.7
Bachelor's degree or higher	25.2	23.7 - 26.7	24.5	23.2 - 25.8	26.2	25.0 - 27.4
By Disability status						
With disability	53.6	50.3 - 56.9	58.2	54.9 - 61.5	57.7	54.1 - 61.2
Without disability	30.6	29.3 - 32.0	30.4	28.8 - 32.0	30.8	29.7 - 31.9



BA.5 variant

The prevalence of SARS-CoV-2 infection and long COVID in US adults during the BA.5 surge, June-July 2022

Saba A Qasmieh, McKaylee M Robertson, Chloe A Teasdale, Sarah G Kulkarni, Heidi Jones, Margaret McNairy, Luisa N. Borrell, Denis Nash

doi: https://doi.org/10.1101/2022.09.04.22279588

Table 3. Prevalence and characteristics of U.S. adults with long COVID, July 202

	Had COVID more than one month ago	Long COVID	Crude Prevalence of Long COVID	Age and sex direct-standardized prevalence of long COVID*	pre ra	
	N (%)	N (%)	% (95% CI)	% (95% CI)	PR (95% CI)	aPR (95% CI)
Total	1036 (100.0)	222 (100.0)	21.5 (18.2, 24.7)			
Age						
18-24	70 (6.8)	17 (7.8)	24.8 (7.5, 42.0)	18.6 (8.8, 35.2)	1.1 (0.7, 1.7)	1.2 (0.7, 1.9)
25-34	250 (24.2)	58 (26.1)	23.2 (15.2, 31.2)	22.3 (15.2, 31.5)	Ref	Ref
35-44	178 (17.2)	43 (19.1)	23.9 (15.5, 32.3)	27.6 (19.3, 37.8)	1.0 (0.7, 1.5)	1.2 (0.9, 1.8)
45-54	171 (16.5)	37 (16.5)	21.6 (13.9, 29.3)	22.3 (15.6, 30.9)	0.9 (0.7, 1.3)	1.1 (0.7, 1.5)
55-64	185 (17.9)	41 (18.2)	21.9 (15.5, 28.3)	23.1 (17.2, 30.3)	0.9 (0.7, 1.4)	1.1 (0.8, 1.5)
65+	182 (17.6)	27 (12.2)	14.9 (10.5, 19.2)	14.8 (10.8, 19.9)	0.6 (0.4, 1.0)	0.7 (0.5, 1.1)
Gender						
Male	465 (44.9)	72 (32.4)	15.5 (11.6, 19.4)	15.5 (11.9, 20.2)	Ref	Ref
Female	528 (51.0)	144 (64.8)	27.3 (22.2, 32.4)	27.4 (22.8, 32.6)	1.8 (1.4, 2.3)	1.8 (1.4, 2.3)
Non-binary	43 (4.2)	6 (2.8)	14.2 (0.0, 31.8)	13.3 (4.8, 32.1)	0.9 (0.4, 1.9)	0.9 (0.4, 1.9)
Race/Ethnicity						
Black NH	75 (7.2)	19 (8.4)	24.9 (11.8, 38.1)	27.3 (17.0, 4		
White NH	690 (66.6)	148 (66.8)	21.5 (18.0, 25.1)	22.4 (18.9, 2		
Hispanic	129 (12.5)	22 (9.7)	16.8 (5.4, 28.1)	16.8 (9.0, 29		
Asian/Pacific Islander	41 (4.0)	7 (3.2)	17.6 (0.0, 37.5)	11.0 (3.4, 30		
Other	101 (9.8)	26 (11.8)	26.0 (13.1, 38.9)	29.0 (19.7, 4		
Vaccination status						
Boosted	448 (43.3)	86 (38.7)	19.2 (14.8, 23.5)	20.9 (16.4, 26.2)	Ref	Ref
Fully vaccinated not boosted	196 (18.9)	49 (22.2)	25.1 (16.9, 33.4)	24.9 (18.2, 33.0)	1.3 (1.0, 1.8)	1.2 (0.9, 1.6)
Not vaccinated	392 (37.8)	87 (39.2)	22.2 (16.6, 27.9)	22.8 (17.5, 29.1)	1.2 (0.9, 1.5)	1.1 (0.8, 1.4)
Comorbidities						
Yes	315 (30.4)	96 (43.3)	30.6 (24.5, 36.8)	32.8 (25.9, 40.5)	1.8 (1.4, 2.2)	1.8 (1.4, 2.3)
No	721 (69.6)	126 (56.7)	17.5 (13.7, 21.2)	17.5 (14.2, 21.4)	Ref	Ref

*Preprint

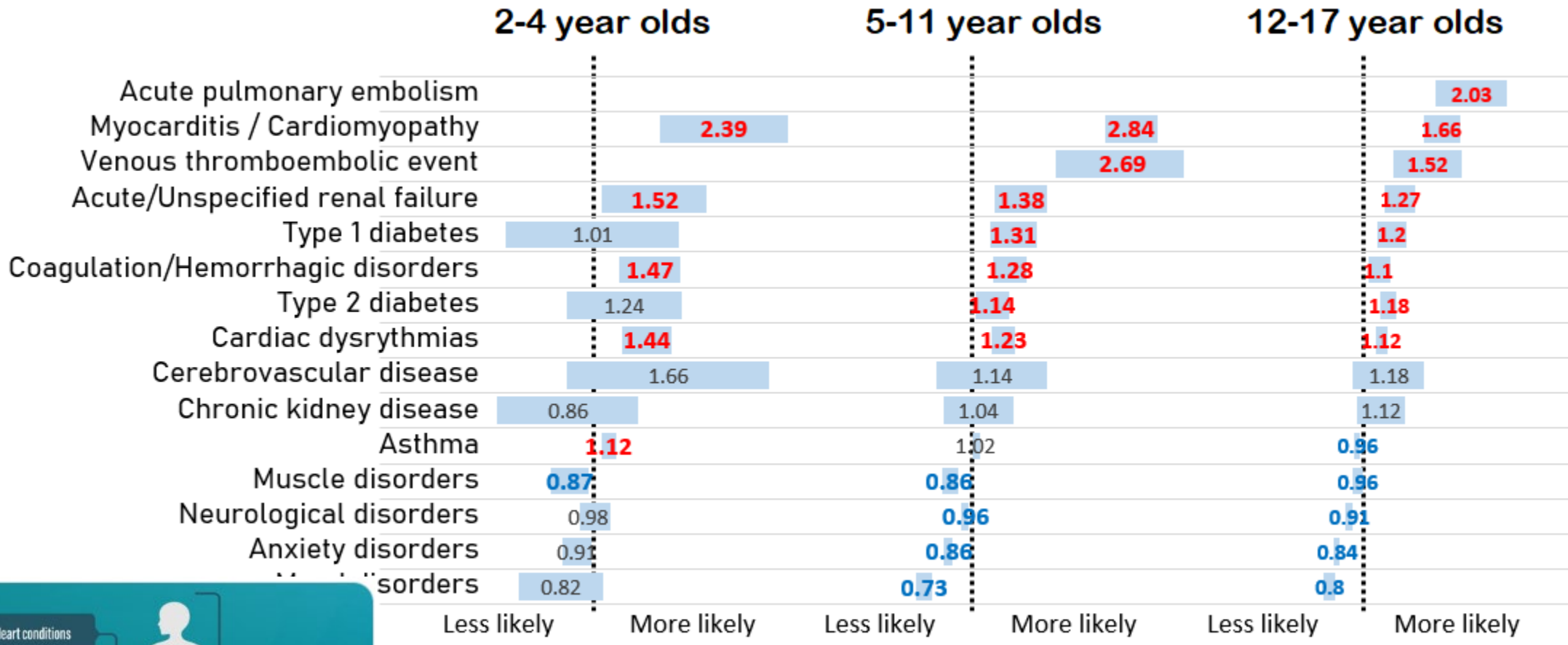
- 21.5% had symptoms >4 weeks

Long COVID in children?

- Early studies likely overestimated with reports of 8-52%
- Later studies estimated 0.8-2% of children develop PASC
- Younger children (0-5yo) are less frequently affected than adolescents

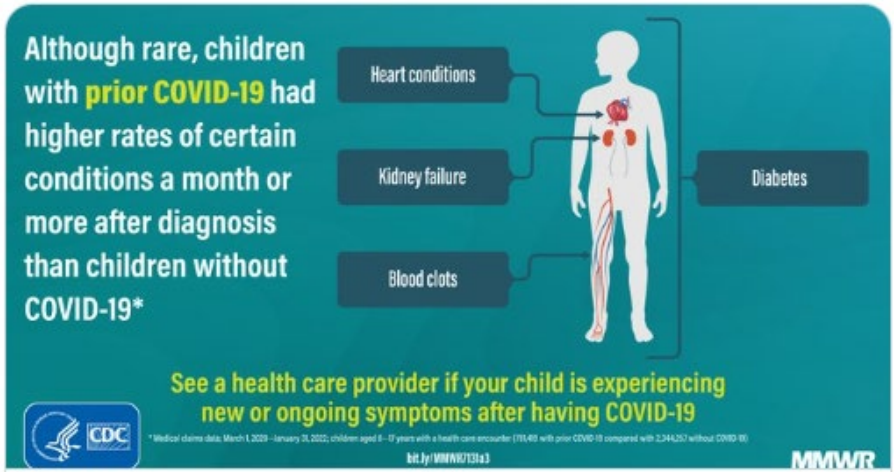
Hazard Ratio for Post-COVID-19 Diagnoses Among Children and Adolescents

Source: MMWR Morb Mortal Wkly Rep 2022;71:993–999.



Blue values represent that the diagnosis is less likely (p<0.05) after COVID-19 infection

Red values represent that the diagnosis is more likely (p<0.05) after COVID-19 infection



CDC report, Aug 2022

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JAMA Network Open

Original Investigation | Public Health

**Prevalence of Select New Symptoms and Conditions Among Pe
Younger Than 20 Years and 20 Years or Older at 31 to 150 Days A
Positive or Negative for SARS-CoV-2**

Alfonso C. Hernandez-Romieu, MD, MPH; Thomas W. Carton, PhD, MS; Sharon Saydah, PhD; Eduardo Azziz-Baumgartner, MD; Teg
Nedra Y. Garret, MS; L. Charles Bailey, MD, PhD; Lindsay G. Cowell, MS, PhD; Christine Draper, BS; Kenneth H. Mayer, MD; Kshema
Sonja A. Rasmussen, MD, MS; William E. Trick, MD; Valentine Wanga, PhD; Jennifer R. Chevinsky, MD, MPH; Brendan R. Jackson, MD
Jennifer R. Cope, MD, MPH; Adi V. Gundlapalli, MD, PhD; Jason P. Block, MD, MPH

40 systems' EHR data

Cohort study of:

338,024 persons younger than 20 years

1,790,886 persons 20 years or older who were tested for SARS-CoV-2 Mar-Dec 2020.

Looked at prevalence of new symptoms & conditions for those with med encounters between 31 and 150 days after testing.

168,701 (+) aged 20+

26,665 (+) aged <20

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4/ Some take home points 👉
The study says ≤11% prevalence of #PASC in nonventilated was "infrequent." (by the way, it was much higher in those hospitalized)

I still think 11% is high!
🦠 #COVID19 has impacted 75 million Americans.

#LongCOVID is real. More research needed!

Hov

>2C

In hospitalized: T2DM, Anxiety & depression, Ataxia or trouble walking.

<20: Change in bowel habits, fatigue, SOB. Most prevalent new diagnosis was anxiety & depression.

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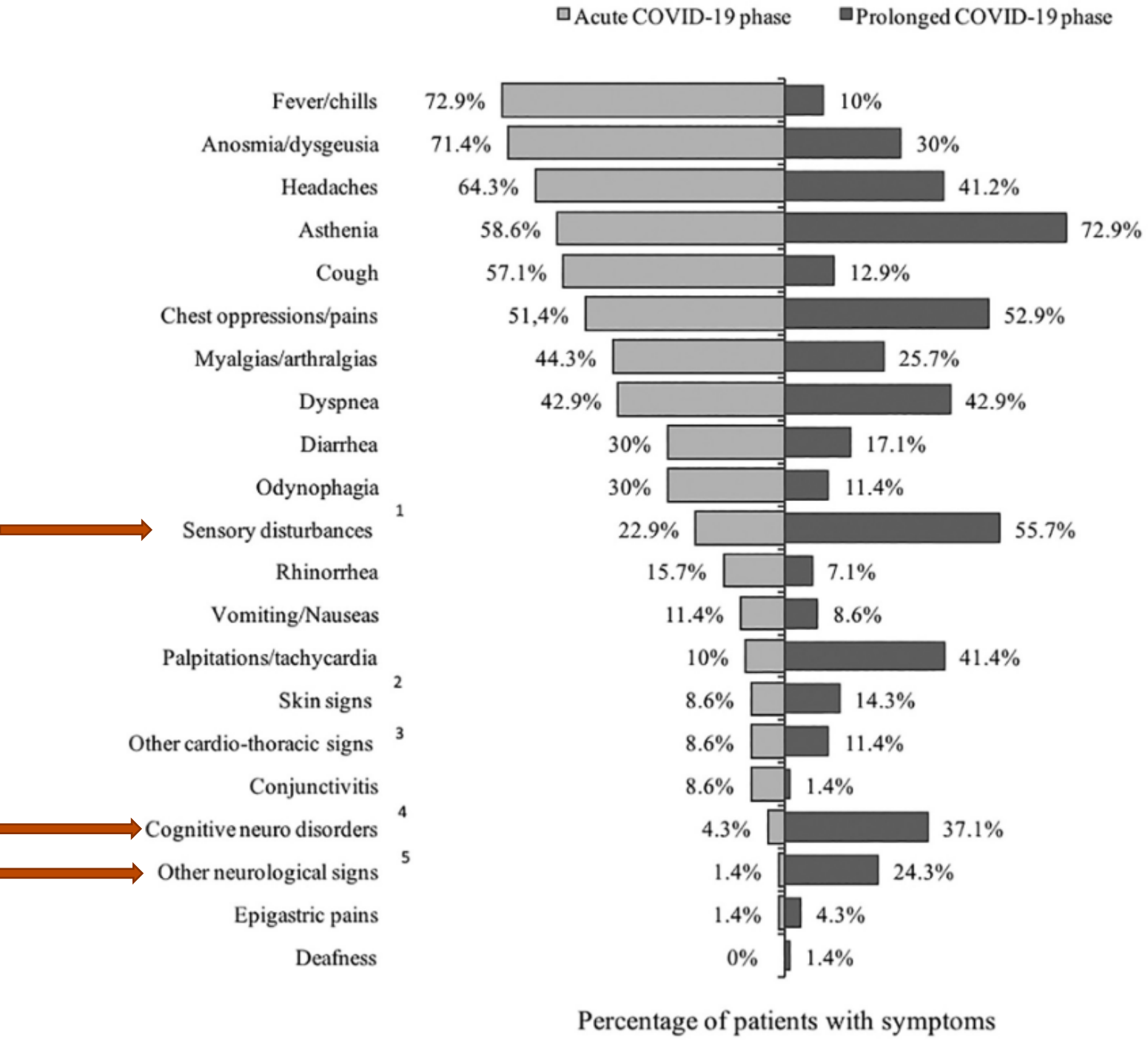

>25% New Neuro Symptoms

- 70 consecutive patients in post-acute clinic in Paris, France
  - Only 6 patients hospitalized
- Median age 45
- 78.6% female
- Symptom free interval in 32/65 cases (mean 25 days)
- Late symptoms in 7 categories
  - Major fatigue or exhaustion (72.9%)
  - Neurological symptoms (77.1%)
  - Cardiothoracic symptoms (71.4%)
  - MSK/articular pains (25.7%)
  - ENT symptoms (30%)
  - GI symptoms (24.3%)
  - Skin & vascular symptoms (14.4%)

Salmon-Ceron et al., J Infect. 2020

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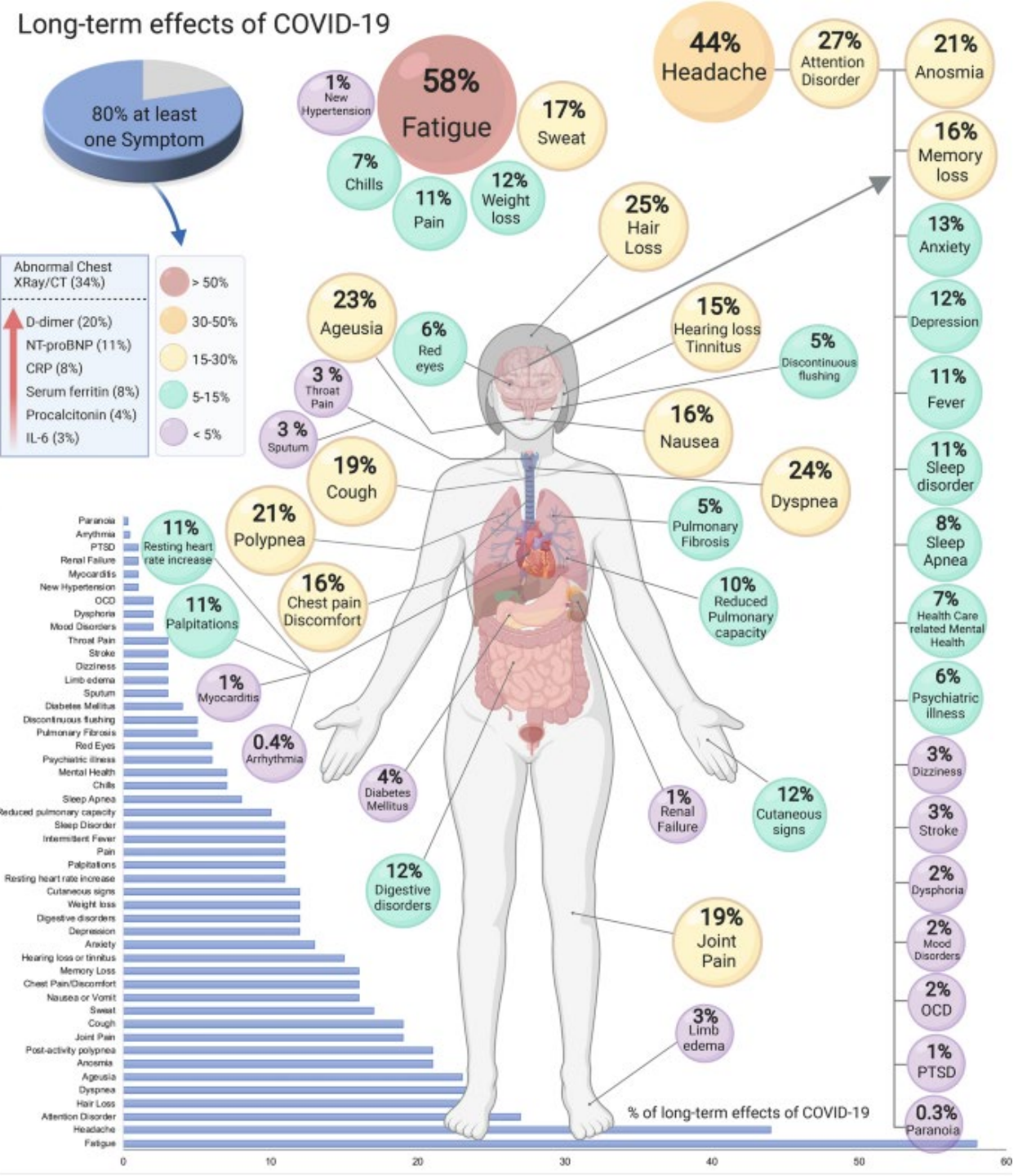

More than 50 long-term effects of COVID-19: a systematic review and meta-analysis

The prevalence of 55 long-term effects was estimated, 21 meta-analyses were performed, and 47,910 patients were included (age 17–87 years).

The five most common symptoms were:

- Fatigue (58%)
- Headache (44%)
- Attention disorder (27%)
- Hair loss (25%)
- Dyspnea (24%)

Lopez-Leon Scientific Reports 2021

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PATIENT-LED RESEARCH COLLABORATIVE

EClinicalMedicine
Published by THE LANCET
Volume 38, August 2021, 101019

Research paper

Characterizing long COVID in an international cohort: 7 months of symptoms and their impact

Hannah E. Davis [a, 1], Gina S. Assaf [a, 1], Lisa McCorkell [a, 1], Hannah Wei [a, 1], Ryan J. Low [a, b, 1], Yochai Re'em [a, c, 1], Signe Redfield [a], Jared P. Austin [a, d], Athena Akrami [a, b, 1]

International web-based eval. with Sx lasting over 28 d

Survey via COVID-19 support groups and social media

3,762 respondents from 56 countries

79% women

26% 30-39 yo, 34% 40-49 yo, 27% 50-59 yo

8.4% hospitalized. 27% lab-confirmation

96% reported symptoms beyond 90 days

206 symptoms queried

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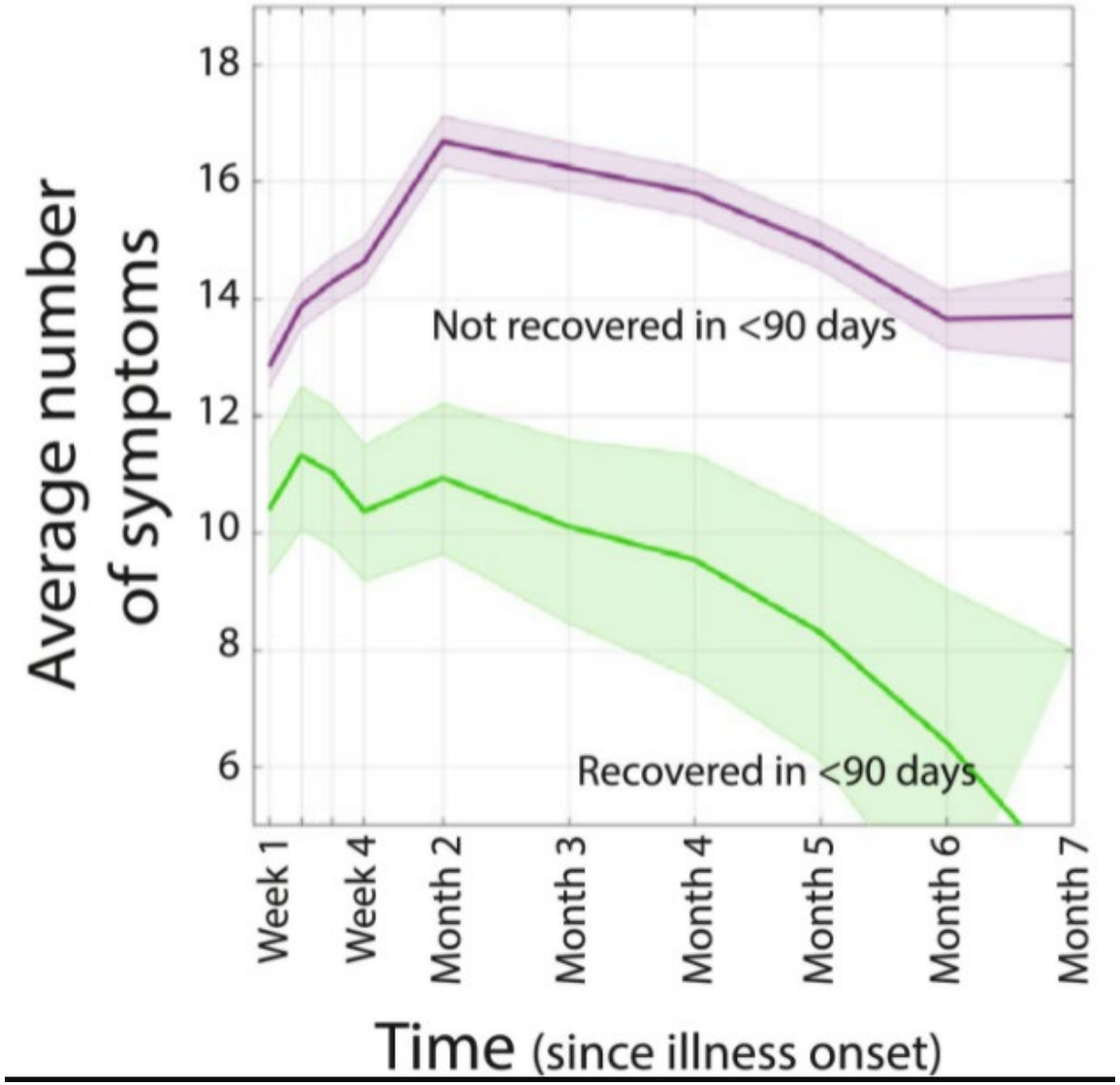
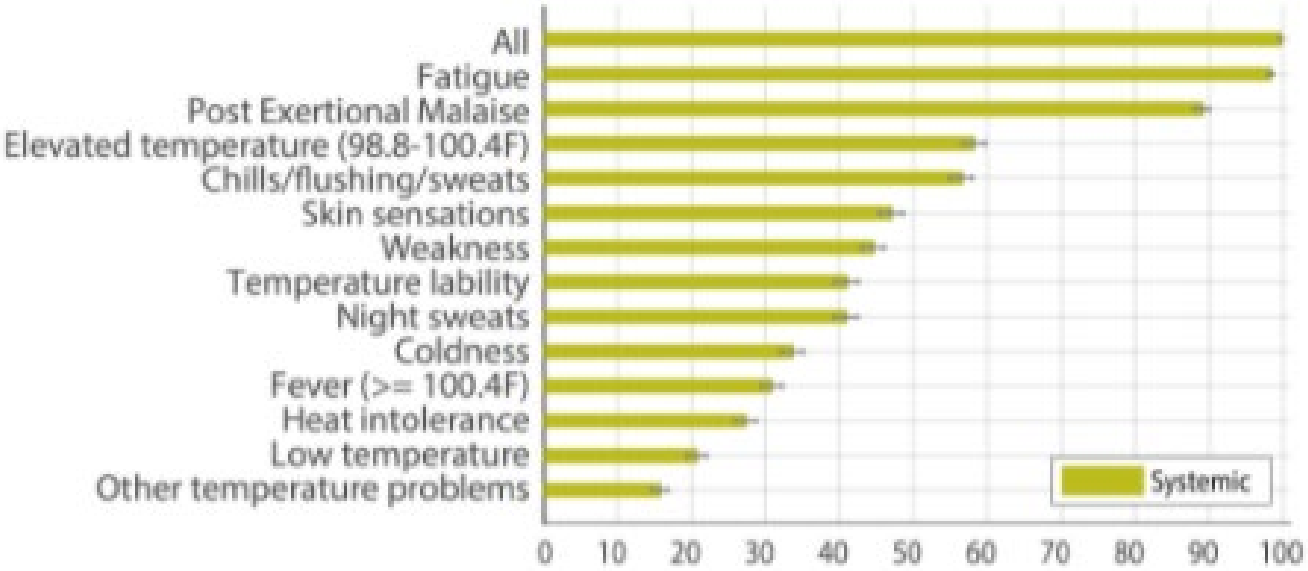
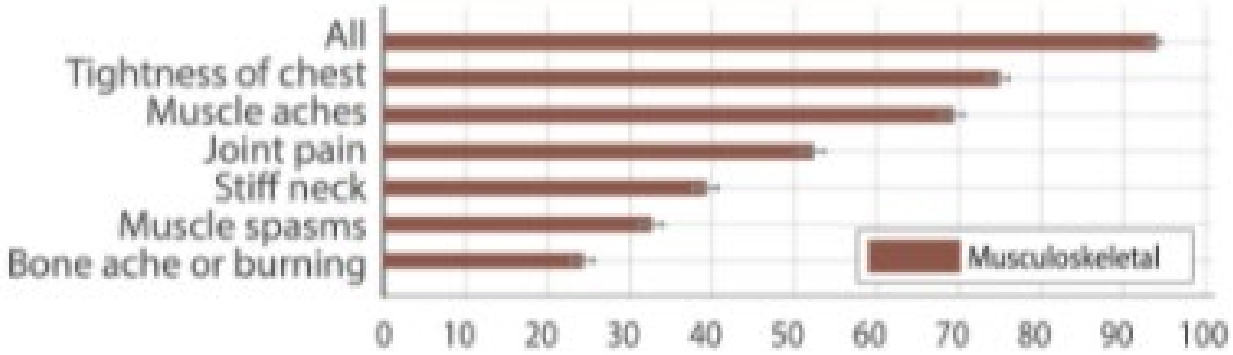
c. Average number of symptoms over time







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ComPaRe Long COVID Cohort

Tran et al., Nature Communications 2022

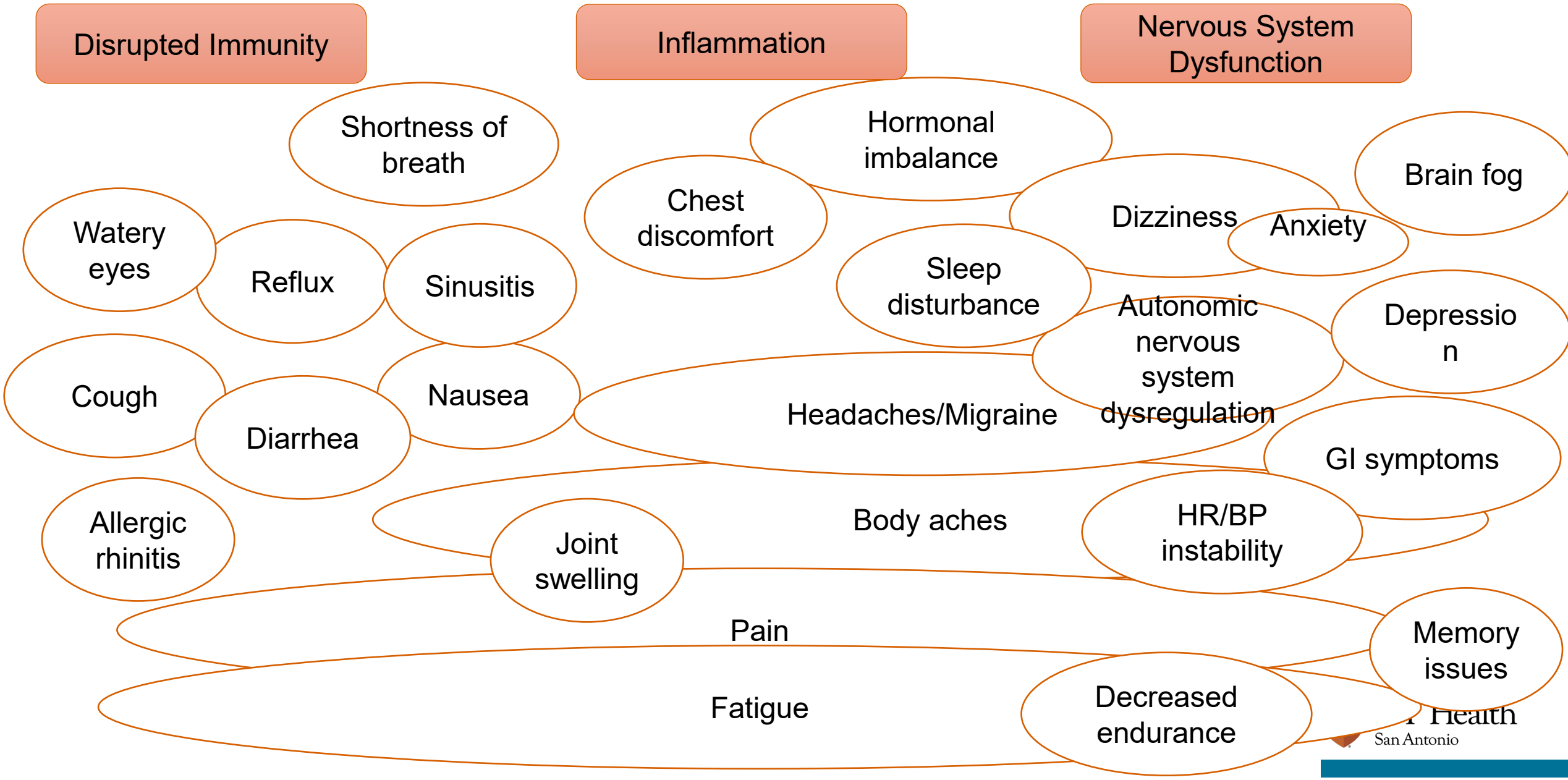
- 968 patients symptomatic after 2 months,

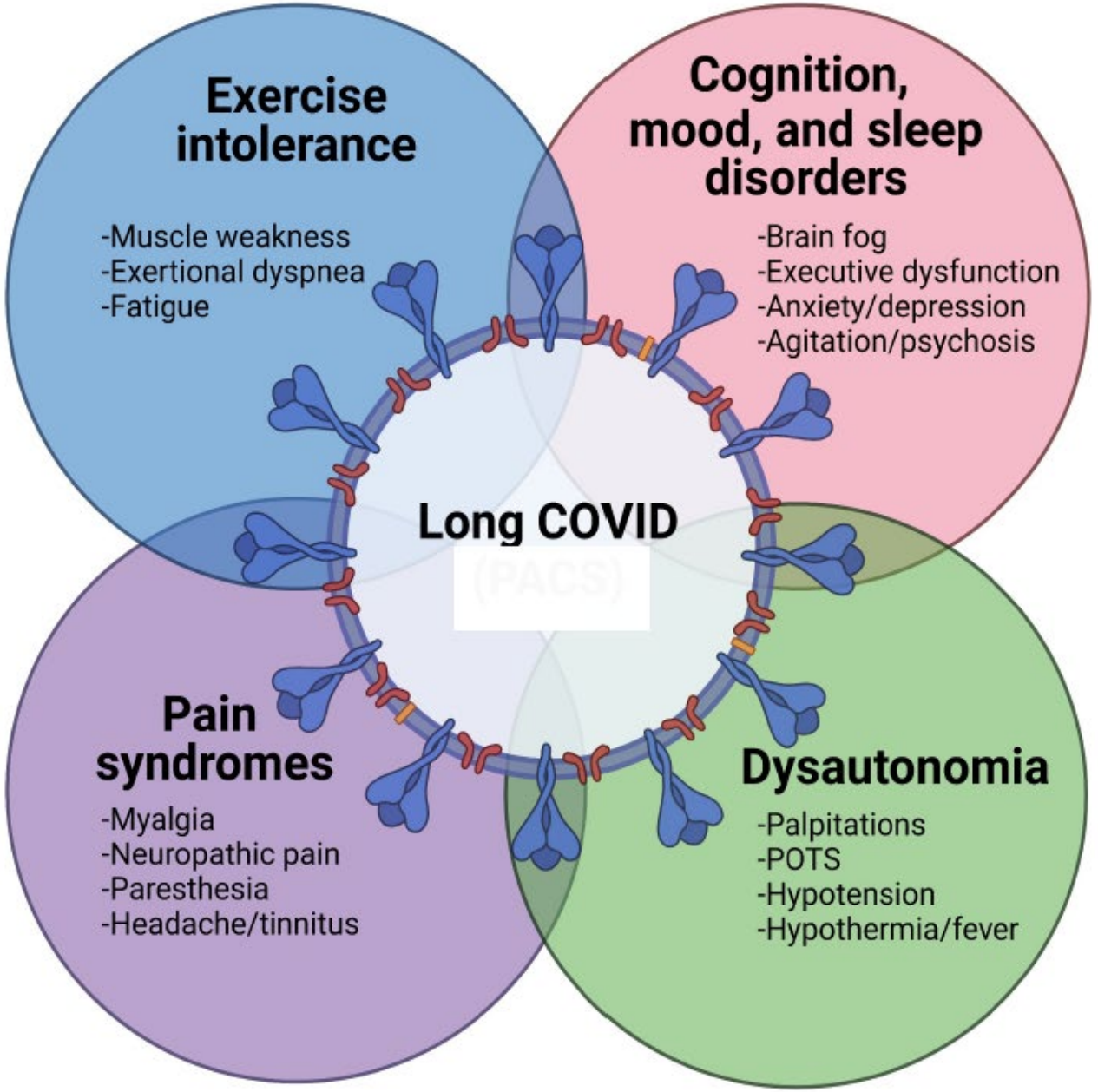
85% still reported symptoms at 1 year

- PASC is relapsing-remitting
- 8 symptoms had increase in prevalence over time

Discolouration/swelling of hands and feet	6.2	11.3	5.1
Heavy legs/swelling of the legs	14.3	19.8	5.5
Blurry vision	26.2	32	5.8
Hair loss	8.2	15.1	6.9
Bone and Joint Pain	32.2	41.4	9.2
Ear pain	5.2	16.9	11.7
Paraesthesia	21.1	33.7	12.6
Neck, back and low back pain	23.4	38.5	15.1

Post-Acute Sequelae of COVID (PASC) Symptoms





Balcom, et al., Brain 2021

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How to Diagnose Long COVID

- Listen to the timeline of events
- You don't need lab tests to rule it out
- It is NOT a diagnosis of exclusion

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Use validated measurements

Fatigue Severity Scale

Choose a number from 1 to 7 that indicates your degree of agreement with the following statements where **1 indicates strongly disagree** and **7 indicates strongly agree**. Please answer the questions with reference to how you have been feeling **on average over the last week**.

	Strongly disagree						Strongly agree
1. My motivation is lower when I am fatigued	1	2	3	4	5	6	7
2. Exercise brings on my fatigue	1	2	3	4	5	6	7
3. I am easily fatigued	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities	1	2	3	4	5	6	7
8. Fatigue is among my three most disabling symptoms	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family or social life	1	2	3	4	5	6	7

- Neuro-QoL scale
- Health-related QoL
- Compass-31
- DePaul Symptom Questionnaire or DSQ-SF or DSQ-PEM

Symptom measurement can be the difference between getting disability coverage or being declined

Distinguishing features of Long COVID identified through immune profiling

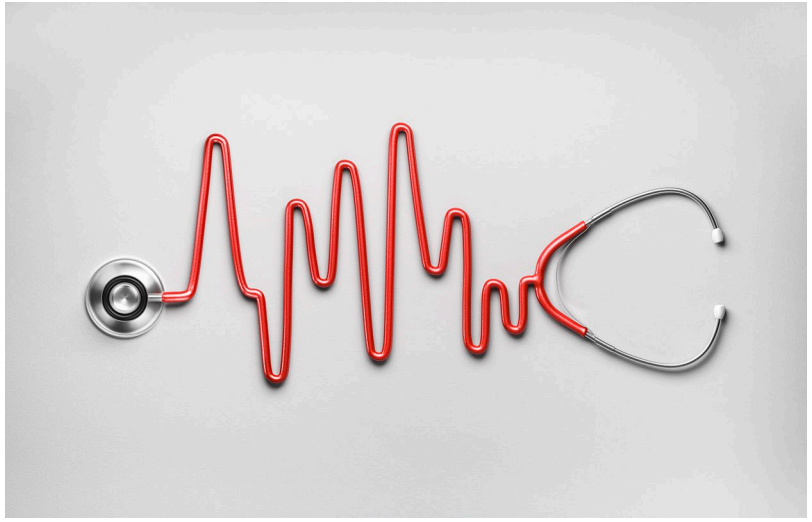
Jon Klein, Jamie Wood, Jillian Jaycox, Peiwen Lu, Rahul M. Dhodapkar, Jeff R. Gehlhausen, Alexandra Tabachnikova, Laura Tabacof, Amyn A. Malik, Kathy Kamath, Kerrie Greene, Valter Silva Monteiro, Mario Peña-Hernandez, Tianyang Mao, Bornali Bhattacharjee, Takehiro Takahashi, Carolina Lucas, Julio Silva, Dayna Mccarthy, Erica Breyman, Jenna Tosto-Mancuso, Yile Dai, Emily Perotti, Koray Akduman, Tiffany J. Tzeng, Lan Xu, Inci Yildirim, Harlan M. Krumholz, John Shon, Ruslan Medzhitov, Saad B. Omer, David van Dijk, Aaron M. Ring, David Putrino, Akiko Iwasaki

doi: https://doi.org/10.1101/2022.08.09.22278592

215 individuals including 99 with LC

Cross-sectional study

Immune profiling



Structural pathology is NOT correlating with Long COVID symptoms.

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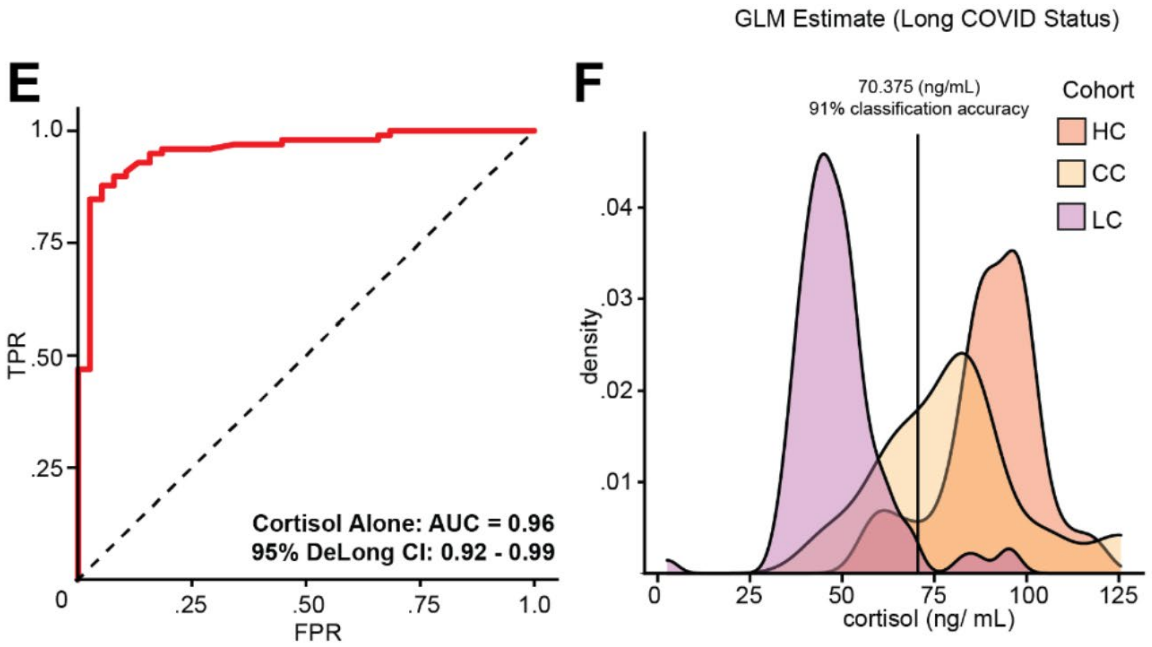
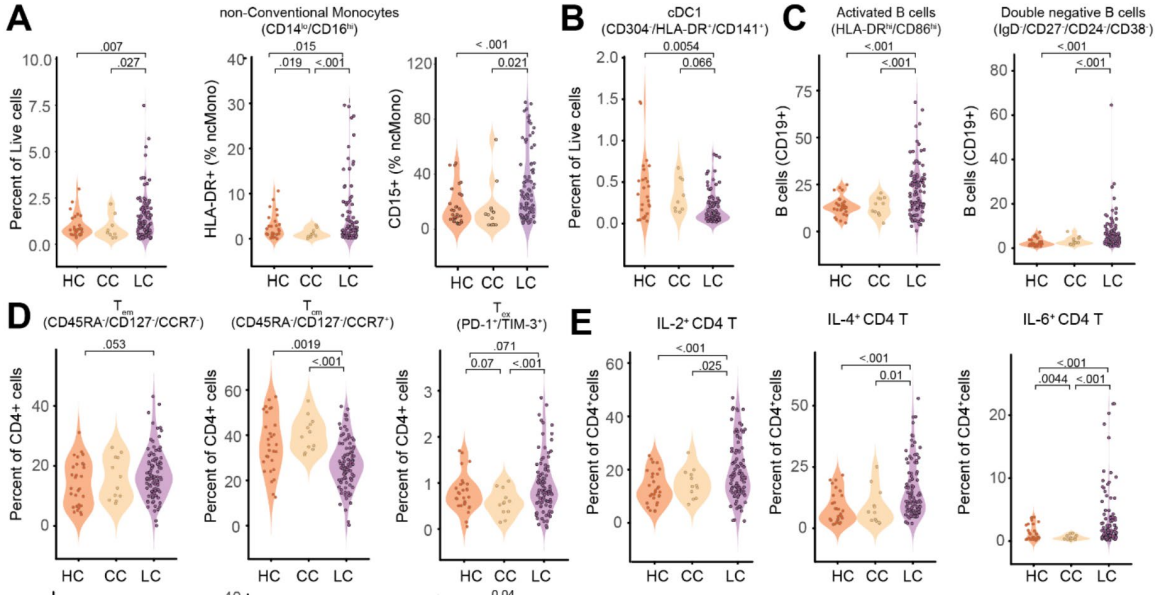
2 major findings

Low cortisol



Exhausted T-cells



UT Health San Antonio

UT Health San Antonio

UT Health San Antonio Rehab Medicine
Post COVID-19 Recovery Program

Mission

Our mission is to serve our diverse patient population - locally and regionally - who were diagnosed with COVID-19 and suffer from various physical, cognitive, and functional difficulties.

Our vision is to reflect the strength of the community we serve with professional, compassionate, and concierge type of Physical Medicine and Rehabilitation services.

UT Health San Antonio

Post COVID-19 Diagnosis Focus

Muscle weakness	Falls / balance issues	Neuropathy & myopathy
Unsteady gait	Pain	Dyspnea
Deconditioning	Cognitive changes	Stroke
Amputation	Pressure injury / wounds	Mood / mental health issues

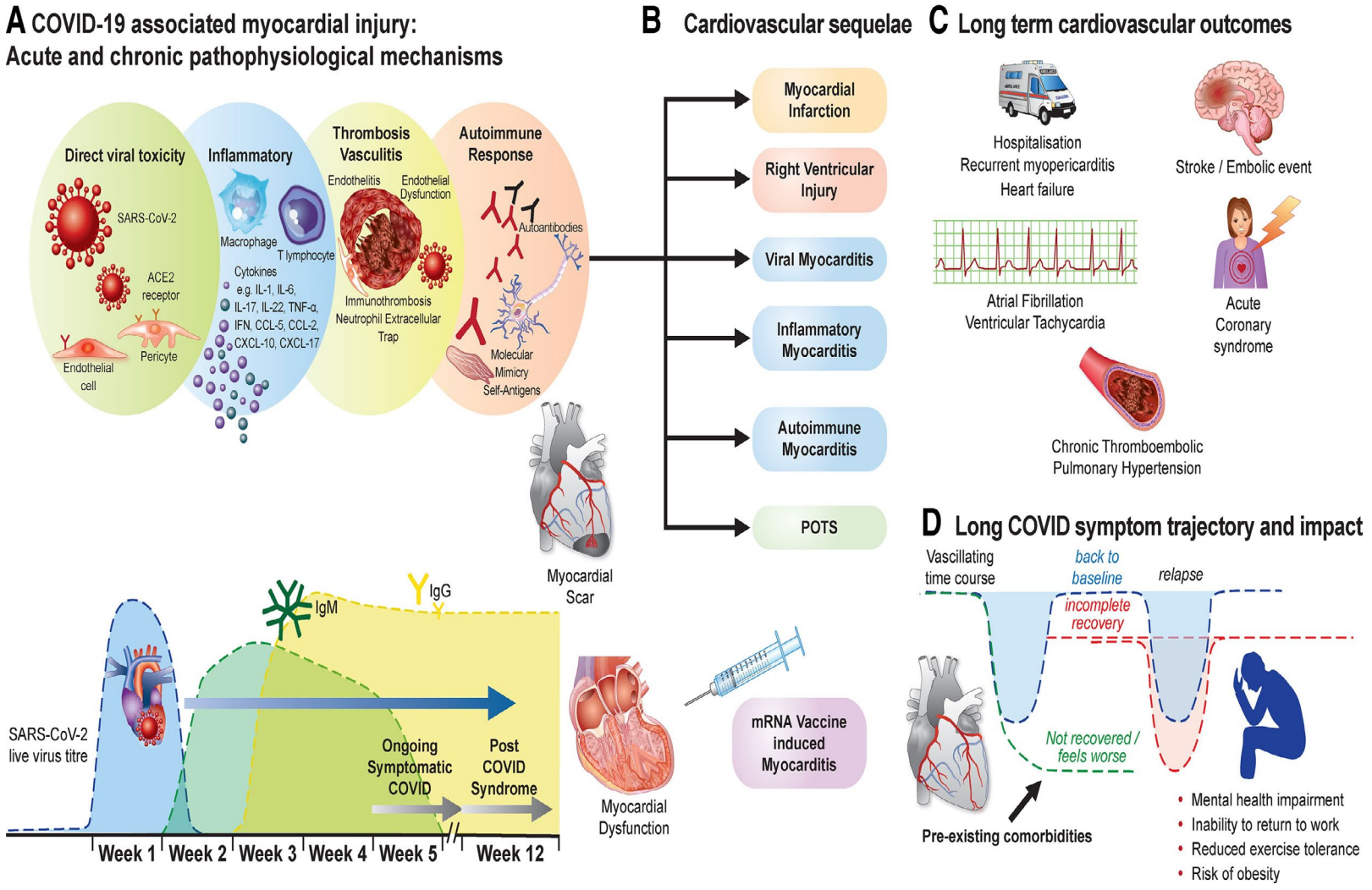
UT Health San Antonio

Long COVID and the Cardiovascular System

Cardiovascular manifestations:

Symptoms: chest pain, palpitations, breathlessness, syncome

- Myopericarditis
- Myocardial infarction
- Right ventricular dysfunction
- Vasculitis
- Aortic and arterial thrombosis
- Venous thrombosis



Eur Heart J, ehac031, https://doi.org/10.1093/eurheartj/ehac031

OXFORD UNIVERSITY PRESS

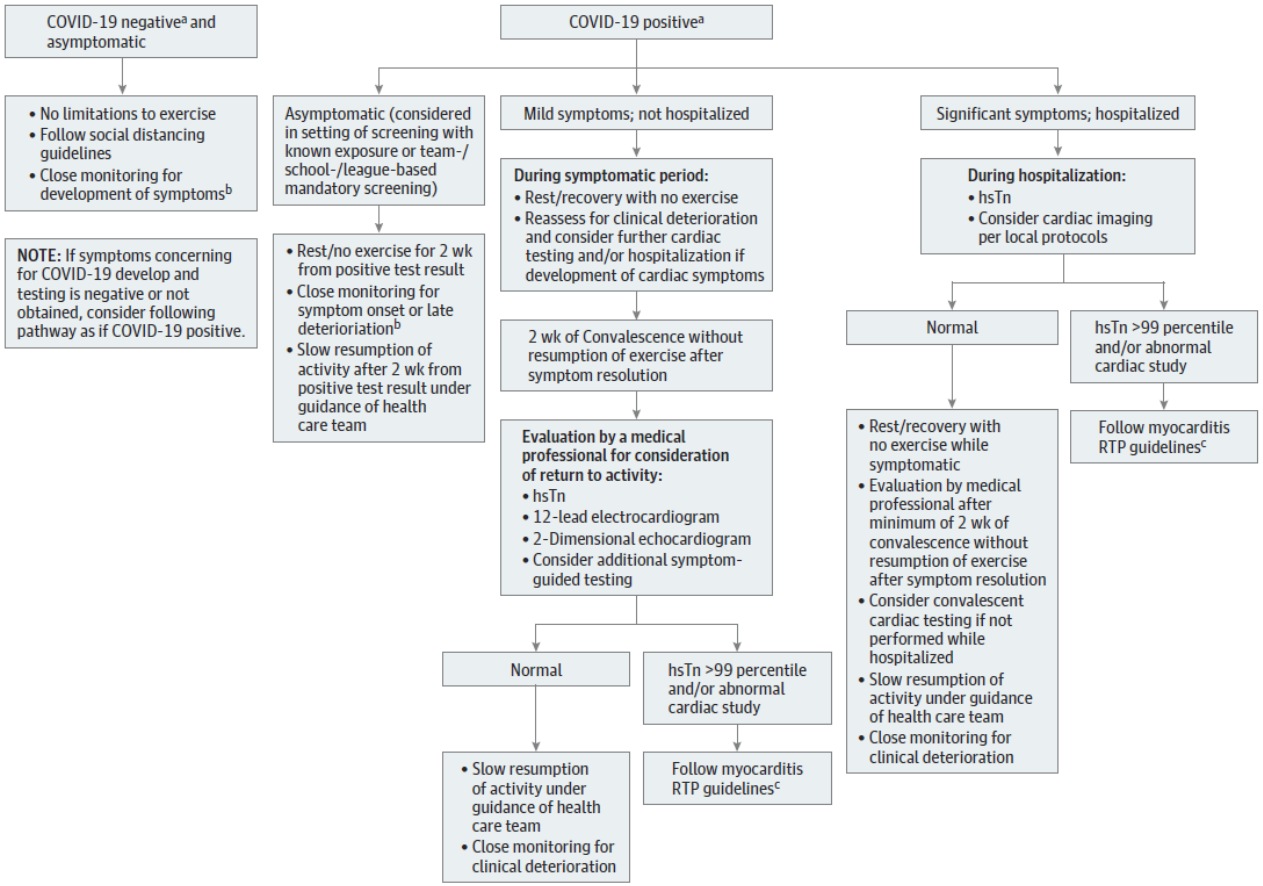
ESC European Society of Cardiology

UT Health San Antonio

Return-to-Play

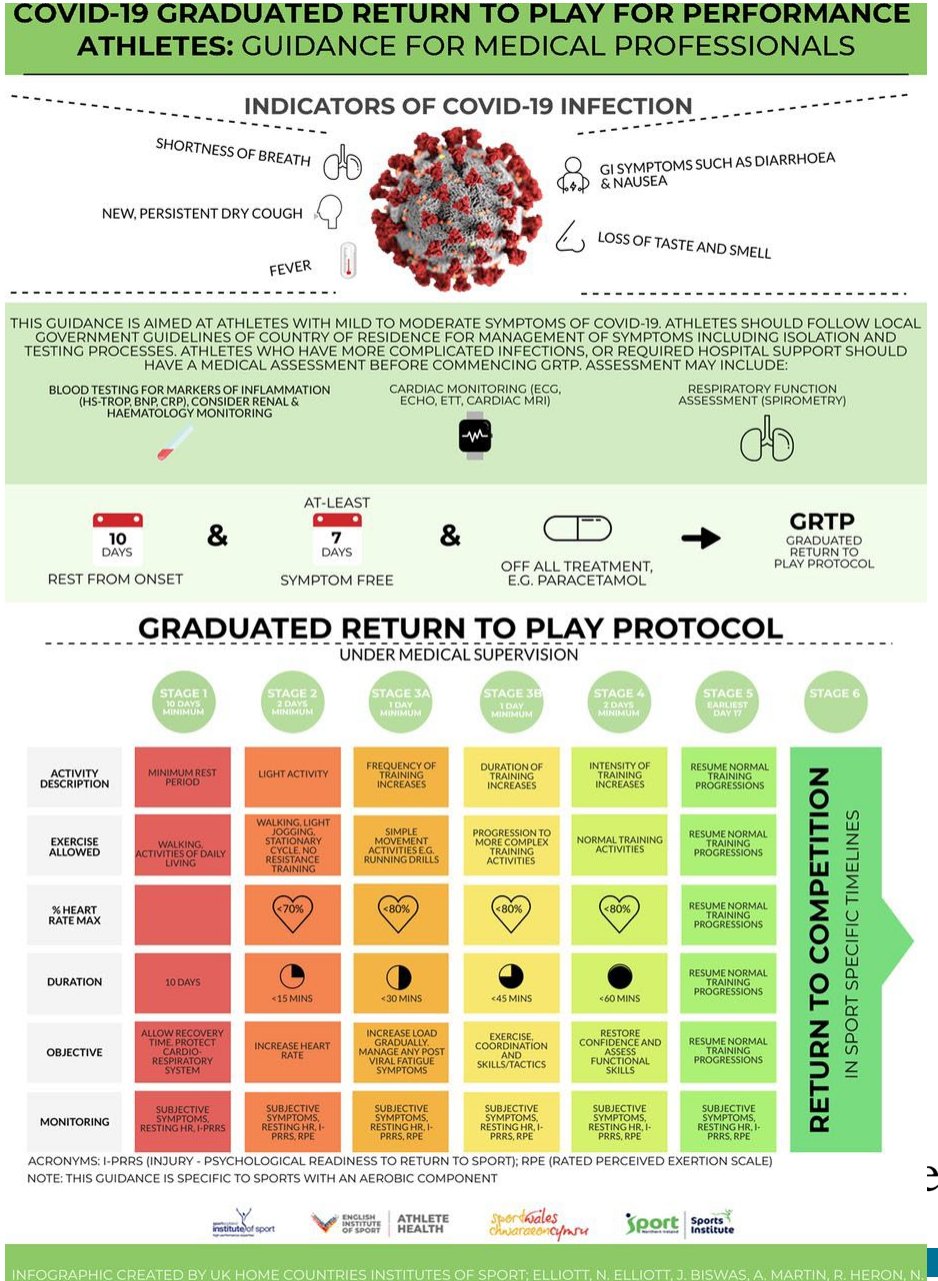
JAMA Cardiology, May 2020

Figure. COVID-19 Return-to-Play Algorithm for Competitive Athlete and Highly Active People

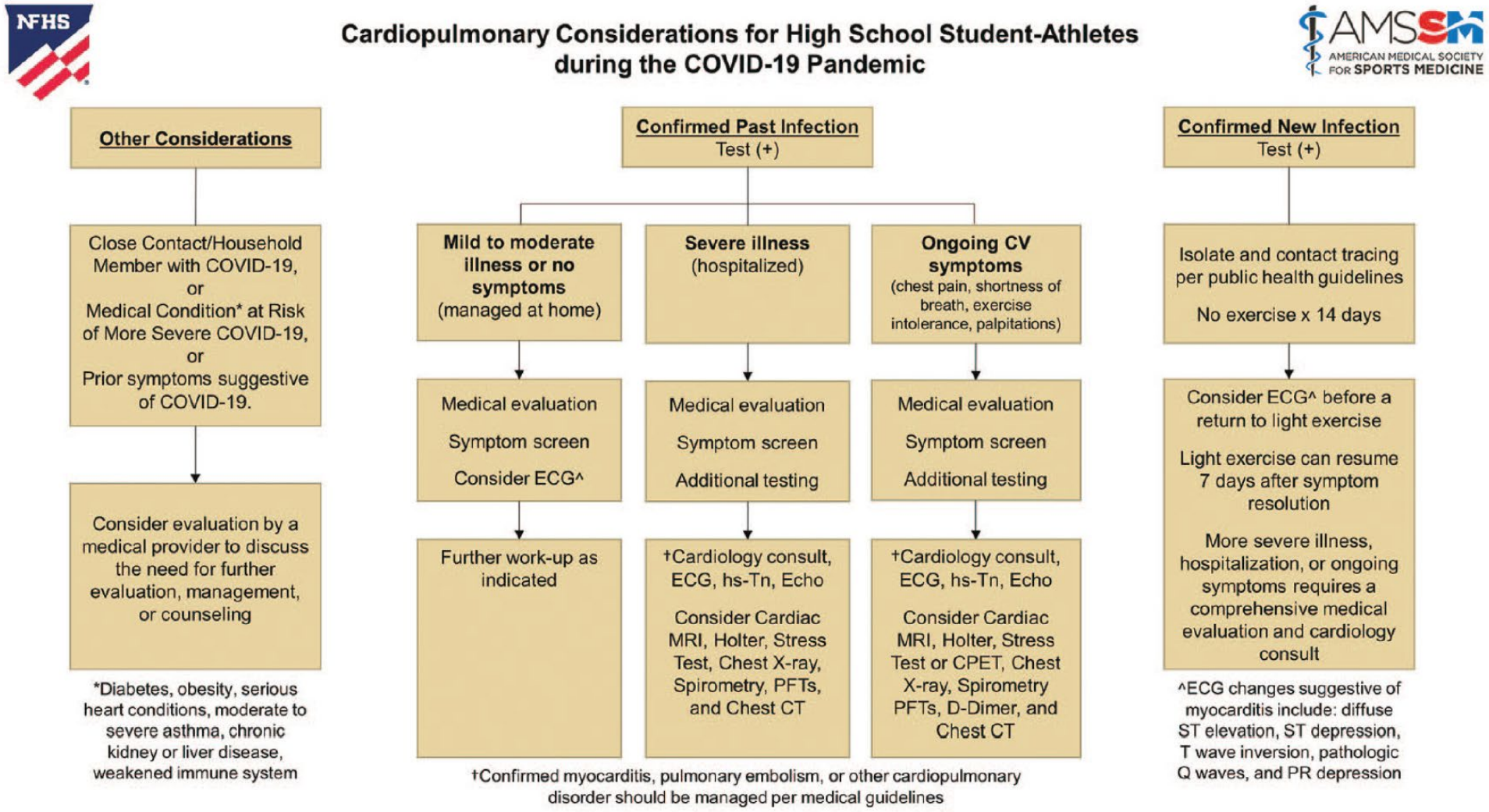


COVID-19 indicates coronavirus disease 2019; hsTn, high-sensitivity troponin I; RTP, return to play.

British Journal Sports Med



Return-to-Play



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Athletes and Long COVID

fastkate • Following

fastkate Lil post-Covid patient still just chilling over here. Long caption coming 😭

I don't really know how to talk about this, but I figure may as well share bc this is what's going on. January did not go great ha. After returning to workouts I had about three weeks that were a struggle. We thought it was just normal getting back into shape. But it became clear that I was just still not well (i really noticed it in sprints. I had a 200 workout where I could barely run faster than a 29. Which should never happen. Even if I'm out of shape. Ask @nikerunning shoe development from when they had me test spikes 3 weeks into my post season break 🤣).

Anyway, moral of the story is apparently I'm taking a longer time to get over the virus. I started to notice this collection of symptoms that I'm now learning are being seen in people with long Covid: out of breath quickly with any activity. Irregular/racing heart beat, lightheaded or dizzy and shaky after runs, excessively sweaty ha. I don't want to add to Covid fears with this post. I've learned that 1 similar symptoms are being documented in a small number of cases 2 this isn't necessarily new to this virus, there is always a chance of an adverse reaction when you get sick 3 they don't know for sure the mechanism or how to fix it but most people are recovering.

So, after pushing through for a few weeks we are trying a new tactic. I'm taking a break from structured training to go by feel and get fully better. Not at all what I had planned for this time of year lol, but it seems my personal growth opportunity for the moment is being okay with going off plan 🙂.

And that's me. I'll keep you updated, but I'm going to turn off anding if im not super d by this, and I want to with every person bc ice. Gotta protect that

CNN Sports Football Tennis Golf Olympics More Audio Live TV

Lionel Messi reveals his behind-the-scenes Covid-19 struggle

By Matt Foster, CNN

Updated 1:02 PM ET, Mon May 30, 2022

GLENN GERVOT/MOSON SPORTSWIRE/GETTY IMAGES

MORE FROM CNN

VIDEO: Uvalde dispatch a
informing officers that a
calling 911 in the room, 'f

Lisa Marie Riley, whose h
social media posts broug
during the pandemic, has

questions, Answered Long Covid's Toll

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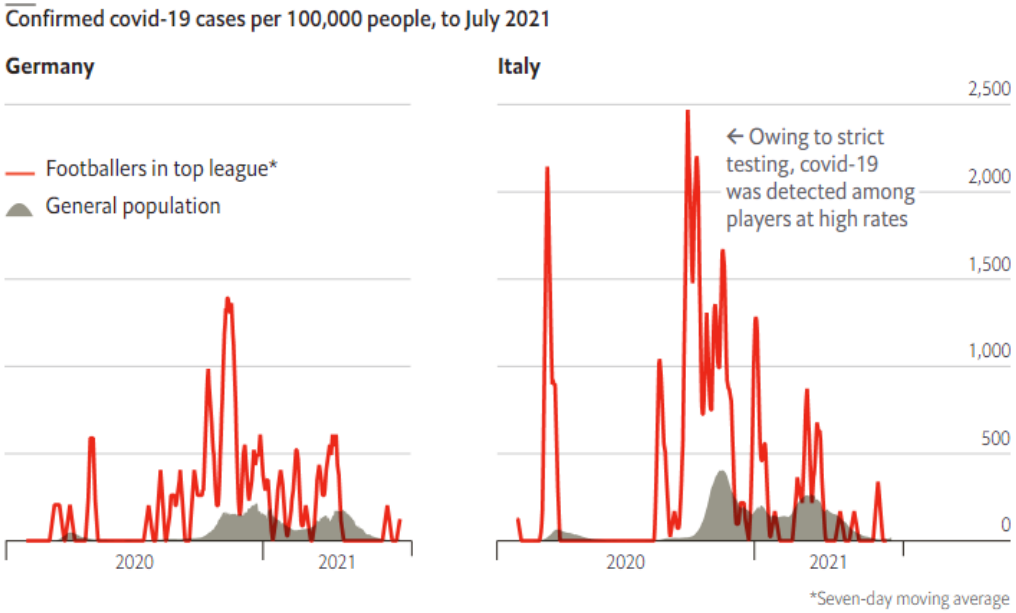
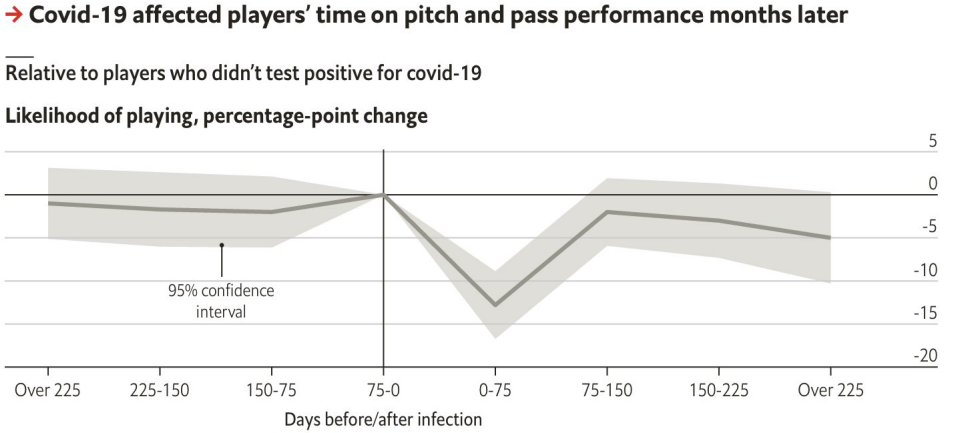
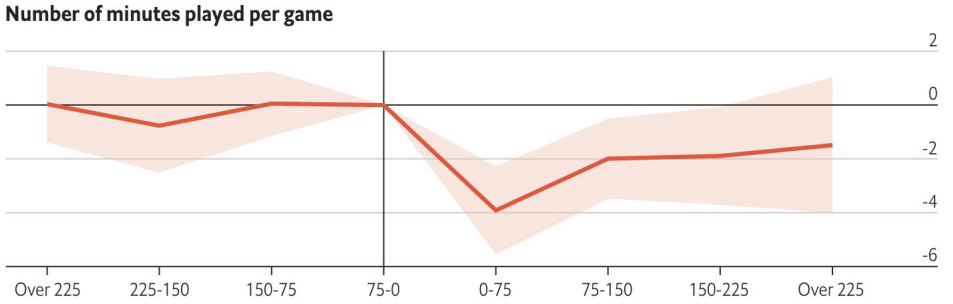
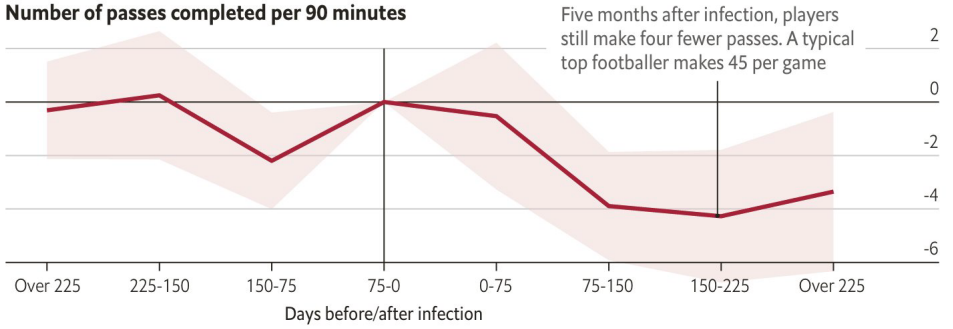
For elite footballers, the effects of Covid-19 linger for months

JAN 8TH 2022









COVID-19 affected players' time on pitch and pass performance months later.

Decline in 9% minutes played.

Passes completed fell by 6%.

Average drop in score of 0.14 SD (equivalent of average player dropping to 30th percentile)

[Chest Infections Original Research]

CHEST

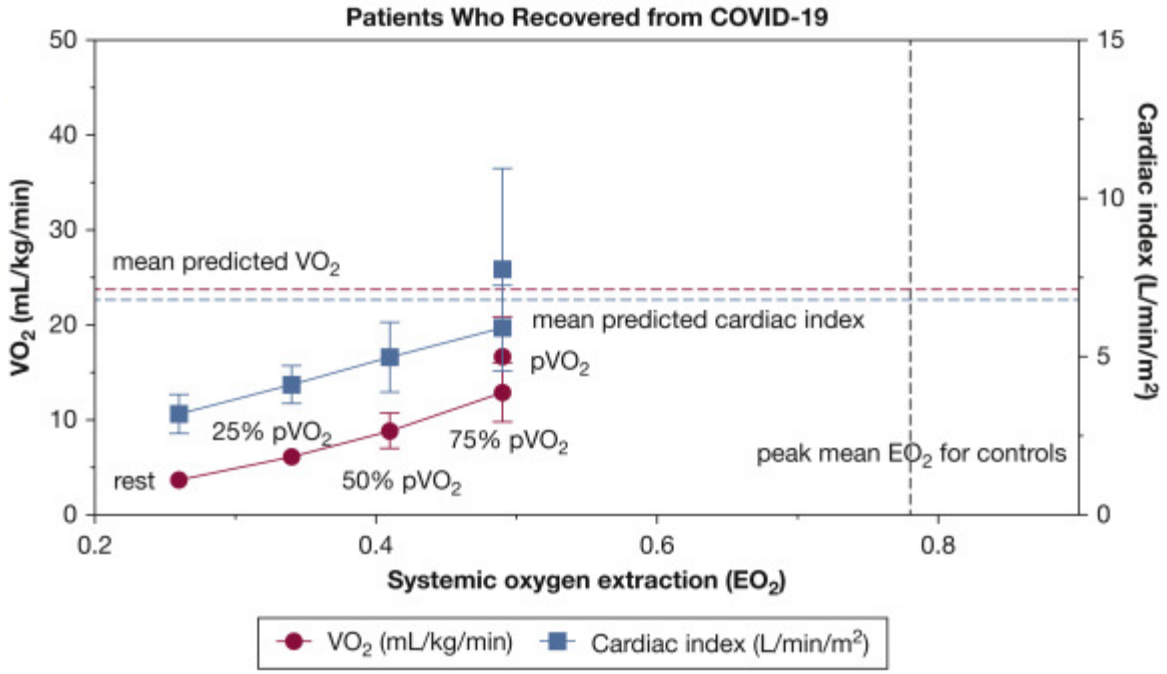
Persistent Exertional Intolerance After COVID-19

Insights From Invasive Cardiopulmonary Exercise Testing

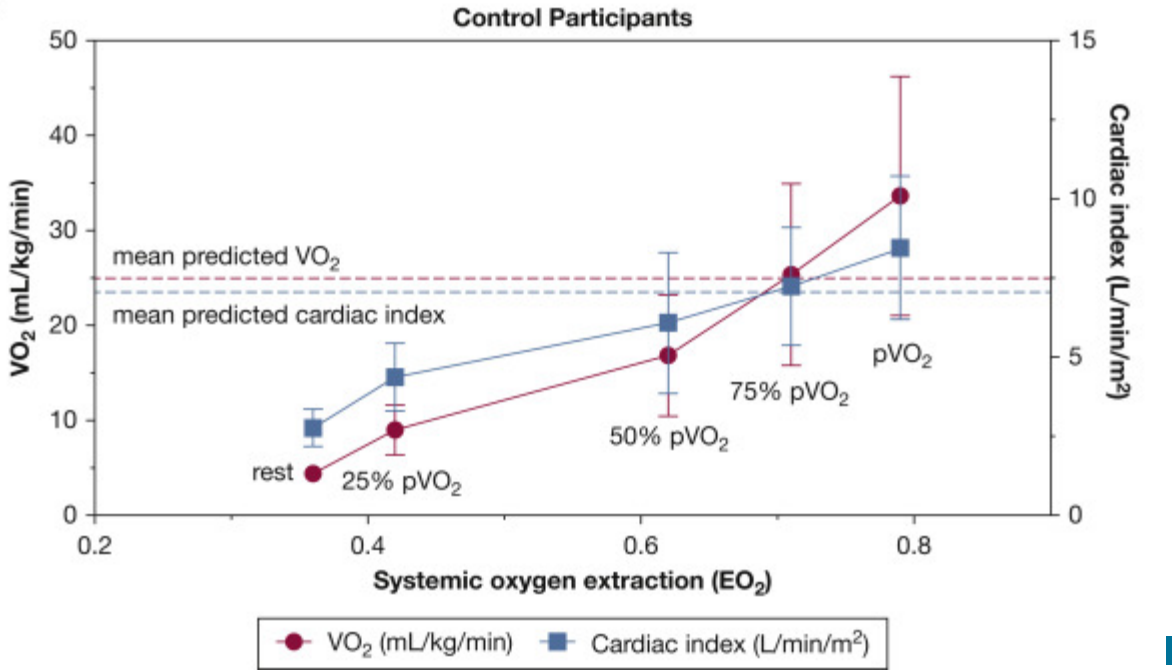
Inderjit Singh, MD; Phillip Joseph, MD; Paul M. Heerdt, MD, PhD; Marjorie Cullinan, RT; Denyse D. Lutchmansingh, MBBS; Mridu Gulati, MD, MPH; Jennifer D. Possick, MD; David M. Systrom, MD; and Aaron B. Waxman, MD, PhD

"If I don't have cardiopulmonary disease, why can't I exercise?"

Interpretation: Patients without cardiopulmonary disease who have recovered from COVID-19 demonstrate a marked reduction in peak oxygen consumption from a peripheral rather than a central cardiac limit, along with an exaggerated hyperventilatory response during exercise.



B



JACC: HEART FAILURE
VOL. 9, NO. 12, 2021

PUBLISHED BY ELSEVIER

Use of Cardiopulmonary Stress Testing for Patients With Unexplained Dyspnea Post-Coronavirus Disease

Donna M. Mancini, MD,[a,b] Danielle L. Brunjes, PHD,[a] Anuradha Lala, MD,[a,b] Maria Giovanna Trivieri, Johanna P. Contreras, MD, MSc,[a] Benjamin H. Natelson, MD[c]

41 patients with normal PFTs, CXR, CT chest.

(9 hospitalized. None intubated.) Average 45yo.

Only 2 had completely normal CPET tests.

CPET identified significant abnormalities.

Peak VO2 averaged 20.3 +/- 7 mL/kg/min, which was 77% +/- 21% of predicted.

15 of 17 with normal peak VO2 had vent abnormalities (peak **resp rate >55 or dysfunctional breathing**).

61% had hypocapnia PetCO2 <35.

46% met criteria for ME/CFS

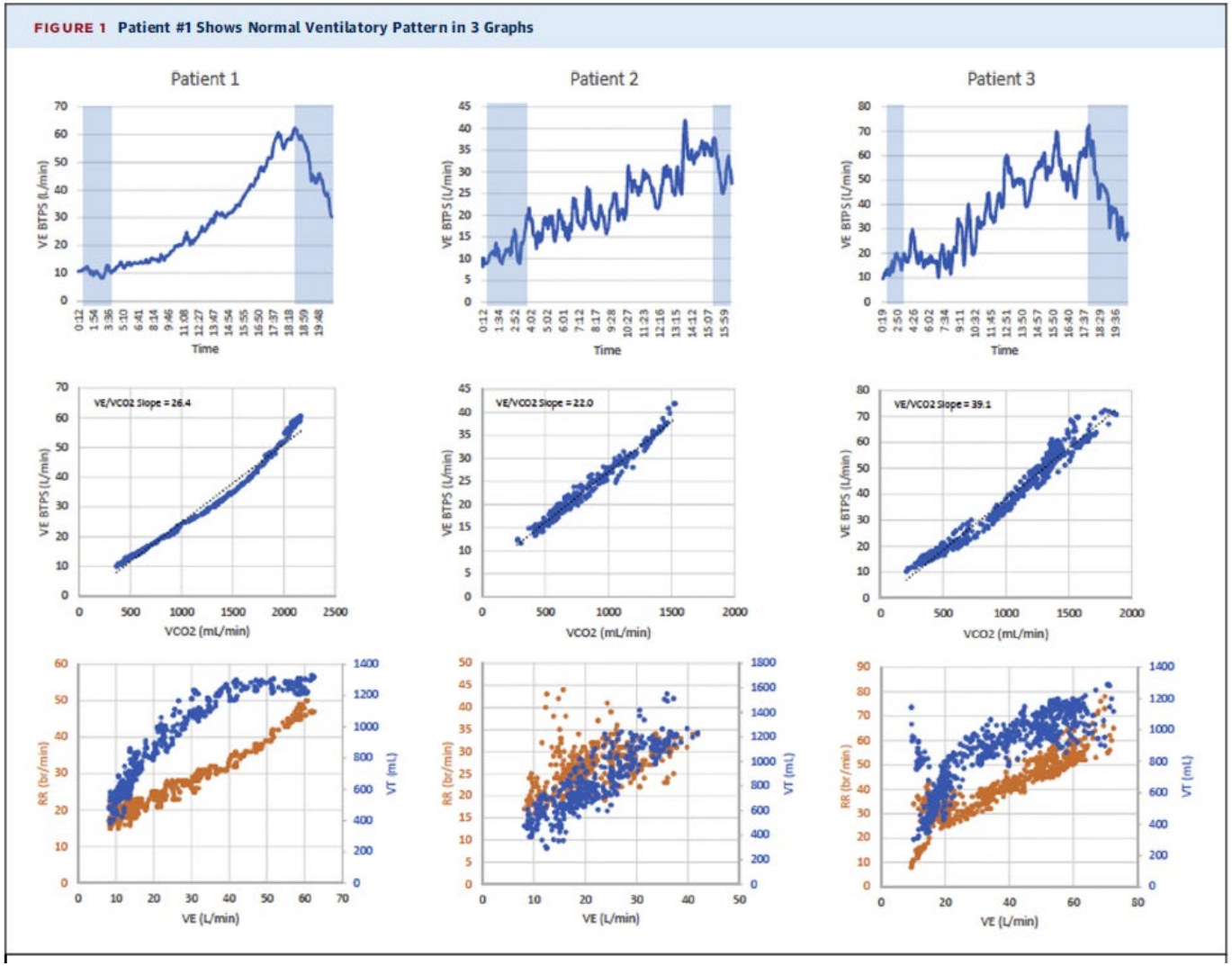


FIGURE 1 Patient #1 Shows Normal Ventilatory Pattern in 3 Graphs

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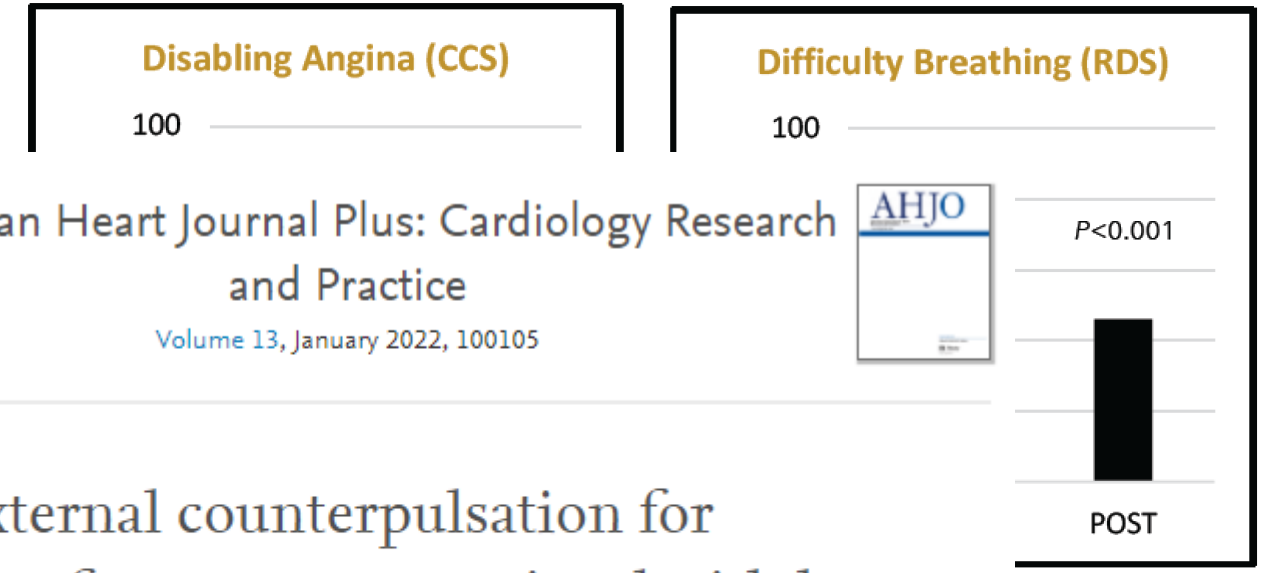
EECP Improves Long COVID Related Clinical Markers

EECP **improved validated markers** of fatigue, brain fog, shortness of breath, chest pain and function capacity (n=50)

Degree of Benefit after EECP (Summary)

Endpoint	Change from Baseline	*P*-Value
PROMIS Fatigue	-5.9 ± 3.8	
DASI	19.8 ± 15.5	
SAQ-7 Summary	25.9 ± 19.9	
6MWT (feet)	163.3 ± 207.5	



ELSEVIER
American Heart Journal Plus: Cardiology Research and Practice
Volume 13, January 2022, 100105
AHJO

Short Communication

Enhanced external counterpulsation for management of symptoms associated with long COVID

Mohanakrishnan Sathyamoorthy [a], Monica Verduzco-Gutierrez [b], Swathi Varanasi [c], Robyn Ward [d], John Spertus [e], Sachin Shah [c, f]

AMERICAN COLLEGE of CARDIOLOGY

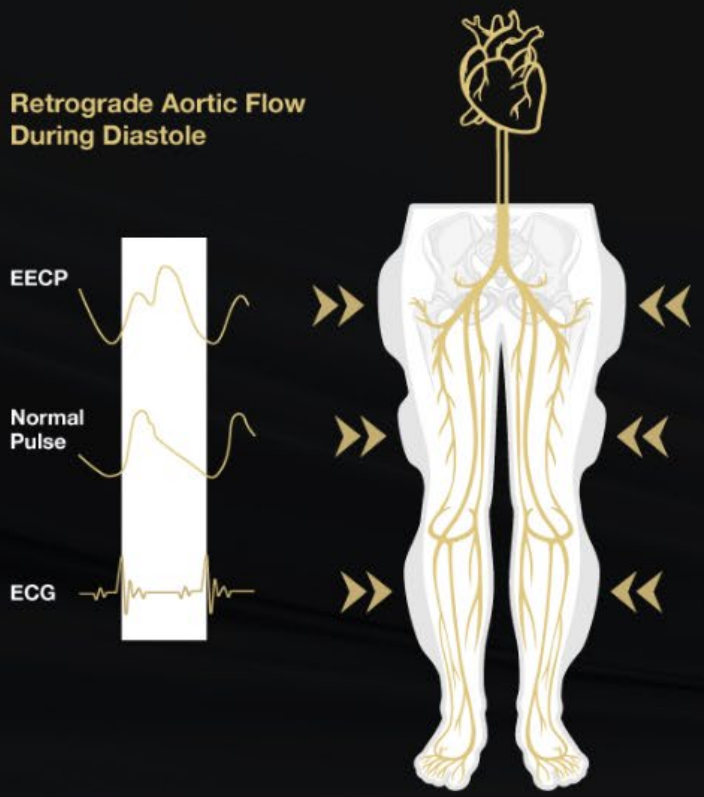
Presented at ACC CV Summit Feb 14, 2022

@MVGutierrezMD

UT Health San Antonio

Mechanism of Action

Mechanical Force



Physiologic / Biochemical Changes

PHYSIOLOGIC / HEMODYNAMIC

- ↑ Diastolic Augmentation
- ↑ Systolic Unloading
- ↑ Shear Stress
- ↑ Endothelial Progenitor Cells

BIOCHEMICAL / NEUROHOMONAL

- ↓ BNP, ANP, Angiotensin II
- ↓ Inf. Cytokines (TNF-a, MCP-1)
- ↑ Growth Factors (VEGF, HGF)

Cardiac / Systemic Benefits

CARDIAC

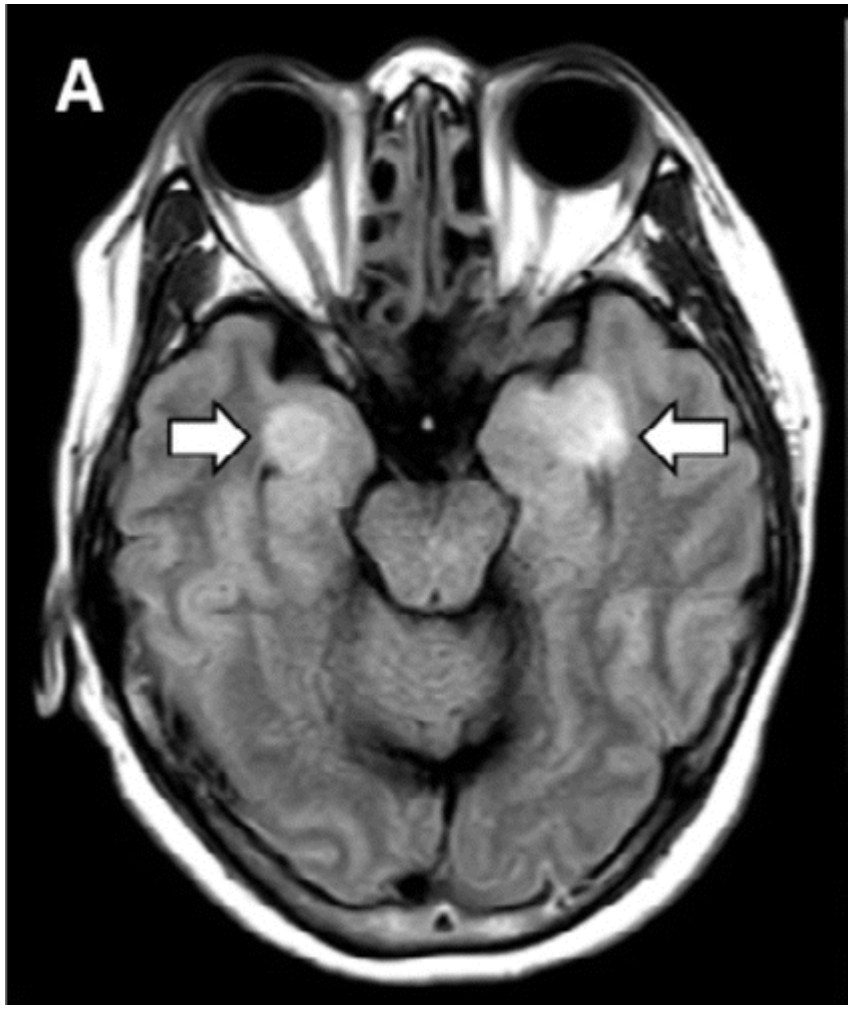
- ↓ Ischemia
- ↑ Coronary Blood Flow / Perfusion
- ↑ CO / Cardiac Efficiency
- ↑ Angiogenesis & Collateralization

SYSTEMIC

- ↓ Endothelial Dysfunction
- ↑ Vascular Tone & Stiffness
- ↑ Perfusion to Vital Organs

Neurologic Sequelae

- Headaches
- Disturbed consciousness
- Encephalopathy / delirium
- Seizures
- Anosmia/ Ageusia
- Stroke
- CIN/CIM
- Myasthenia gravis
- GBS
- FNS



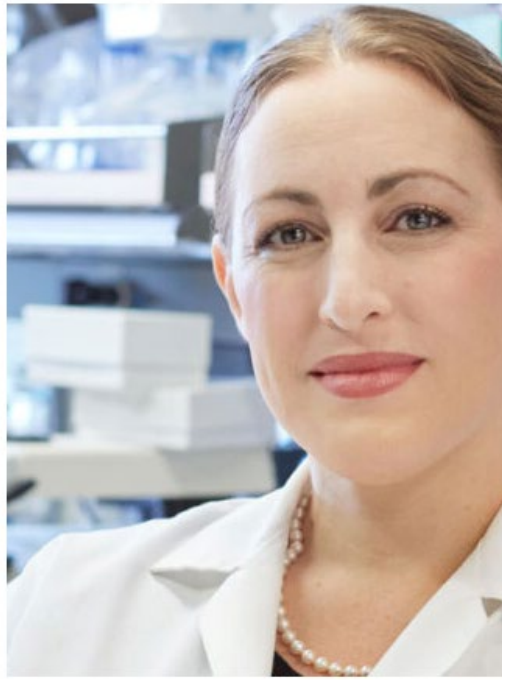
Acute Necrotizing Encephalopathy

What's happening in the brain?

HEALTH

In 'chemo brain,' researchers see clues to unravel long Covid's brain fog

By Elizabeth Cooney Jan. 28, 2022



Stanford neuro-oncologist Michelle Monje is study

Chemo Brain

Cold Spring Harbor Laboratory

bioRxiv

THE PREPRINT SERVER FOR BIOLOGY

bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

New Results

Follow this preprint

Mild respiratory SARS-CoV-2 infection can cause multi-lineage cellular dysregulation and myelin loss in the brain

Anthony Fernández-Castañeda, Peiwen Lu, Anna C. Geraghty, Eric Song, Myoung-Hwa Lee, Jamie Wood, Belgin Yalçın, Kathryn R. Taylor, Selena Dutton, Lehi Acosta-Alvarez, Lijun Ni, Daniel Contreras-Esquivel, Jeff R. Gehlhausen, Jon Klein, Carolina Lucas, Tianyang Mao, Julio Silva, Mario A. Peña-Hernández, Alexandra Tabachnikova, Takehiro Takahashi, Laura Tabacof, Jenna Tosto-Mancuso, Erica Breyman, Amy Kontorovich, Dayna McCarthy, Martha Quezado, Marco Hefti, Daniel Perl, Rebecca Folkerth, David Putrino, Avi Nath, Akiko Iwasaki, Michelle Monje

doi: https://doi.org/10.1101/2022.01.07.475453

White matter-selective microglia reactivity

Pro-inflammatory CSF cytokines with persistent elevation of CCL11

@MVGutierrezMD

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Abnormal CSF

ANNALS of Clinical and Translational Neurology
Open Access
AMERICAN NEUROLOGICAL ASSOCIATION

BRIEF COMMUNICATION

Risk factors and abnormal cerebrospinal fluid associate with cognitive symptoms after mild COVID-19

Alexandra C. Apple[1,2], Alexis Oddi[1,2], Michael J. Peluso[3], Breton M. Asken[1,2], Timothy J. Henrich[4], J. Daniel Kelly[5,6], Samuel J. Pleasure[2,7], Steven G. Deeks[3], Isabel Elaine Allen[5], Jeffrey N. Martin[5], Lishomwa C. Ndhlovu[8], Bruce L. Miller[1,2], Melanie L. Stephens[1,2] & Joanna Hellmuth[1,2]

CSF:
Elevated protein
Abnormal oligoclonal banding

LIINC study

- Cognitive symptoms (22) vs control (10)
- 43% delayed onset cognitive symptoms (1-6 months)
- 77% (10/13) of participants with cognitive PASC had a CSF abnormality compared with 0% (0/4) of cognitive controls

Cognitive Sequelae

PICS

Cognitive impairment can affect:

- 70%-100% of patients at discharge
- 46%-80% still have it one year later
- 20% still have it after 5 years

Memory/ cognitive deficits

- NeuroPsych eval
- Speech therapy
- Memory techniques
- Medications – Donepezil, Memantine, Amantadine, etc

Eur J Nucl Med Mol Imaging. 2021; 48(9): 2823–2833. PMCID: PMC7
Published online 2021 Jan 26. doi: 10.1007/s00259-021-05215-4 PMID: 33

^{18}F-FDG brain PET hypometabolism in patients with long COVID

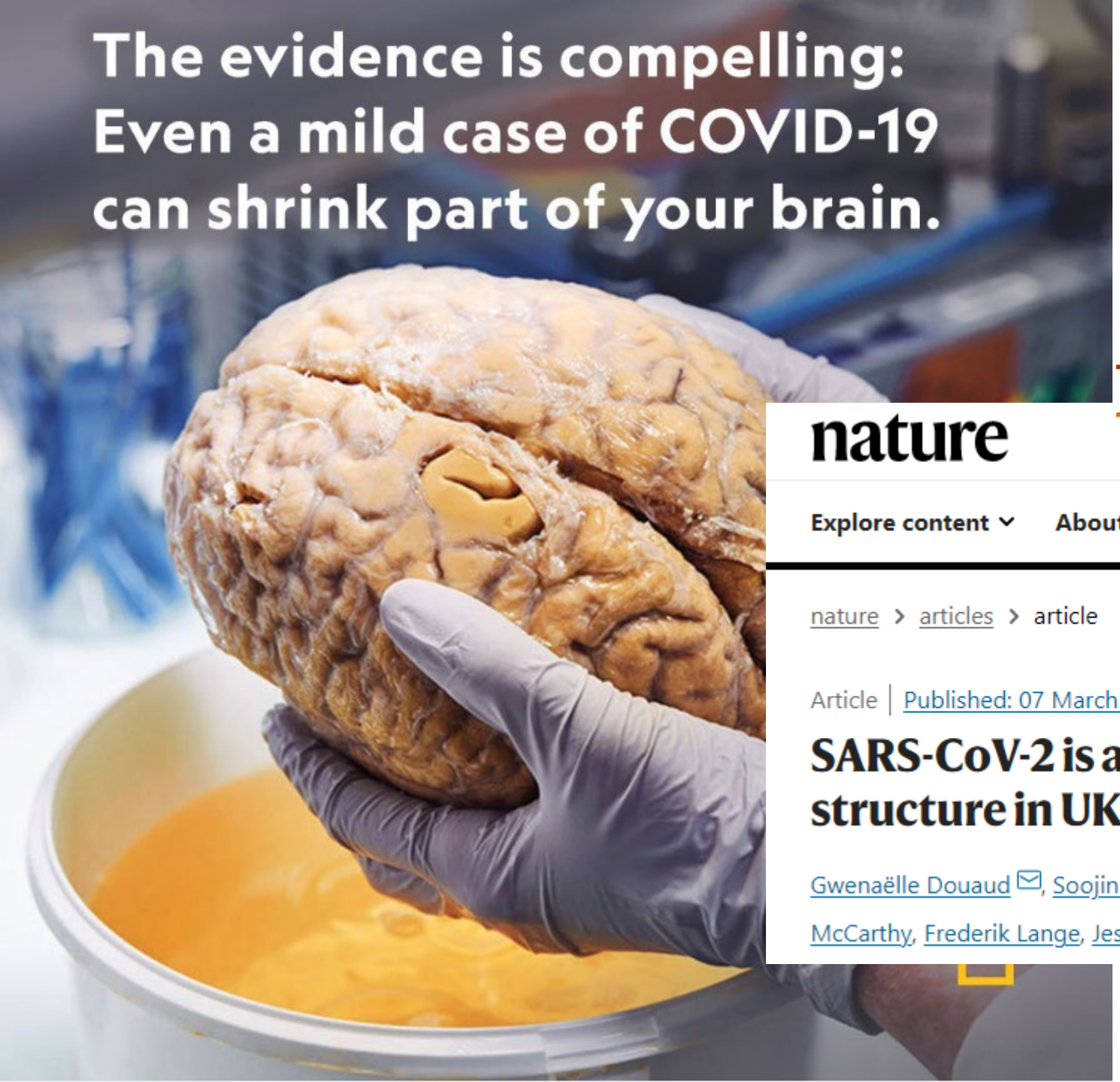
E. Guedj,[1] J. Y. Campion,[1] P. Dudouet,[2,3] E. Kaphan,[4] F. Bregeon,[2,3,5] H. Tissot-Dupont,[2] S. Guis,[6] F. Barthelemy,[1] P. Habert,[7,8] M. Ceccaldi,[9] M. Million,[2,3] D. Raoult,[2,3] S. Cammilleri,[1] and C. Eldin[2,10]

ALTERNATE FORMAT RESEARCH ARTICLE | Open Access

Alzheimer's-like signaling in brains of COVID-19 patients

Steve Reiken, Leah Sittenfeld, Haikel Dridi, Yang Liu, Xiaoping Liu, Andrew R. Marks

First published: 03 February 2022 | https://doi.org/10.1002/alz.12558



- Reduction in grey matter thickness
- Tissue damage in primary olfactory cortex
- Reduction in global brain size

10 years of aging

nature

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nature › articles › article

Article | Published: 07 March 2022

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

Gwenaëlle Douaud ✉, Soojin Lee, Fidel Alfaro-Almagro, Christoph Arthofer, Chaoyue Wang, Paul McCarthy, Frederik Lange, Jesper L. R. Andersson, Ludovica Griffanti, Eugene Duff, Saad Jbabdi, Bernd

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nature medicine

ARTICLES

https://doi.org/10.1038/s41591-022-02001-

Check for upda

OPEN

Long-term neurologic outcomes of COVID-19

Evan Xu[1], Yan Xie[1,2,3] and Ziyad Al-Aly[1,2,4,5,6] ✉

>150K patients with COVID & 11M patient controls

*VA study (older, white males)

42% increase of any neurologic sequelae 1 year later in Long COVID patients.

- even if not hospitalized

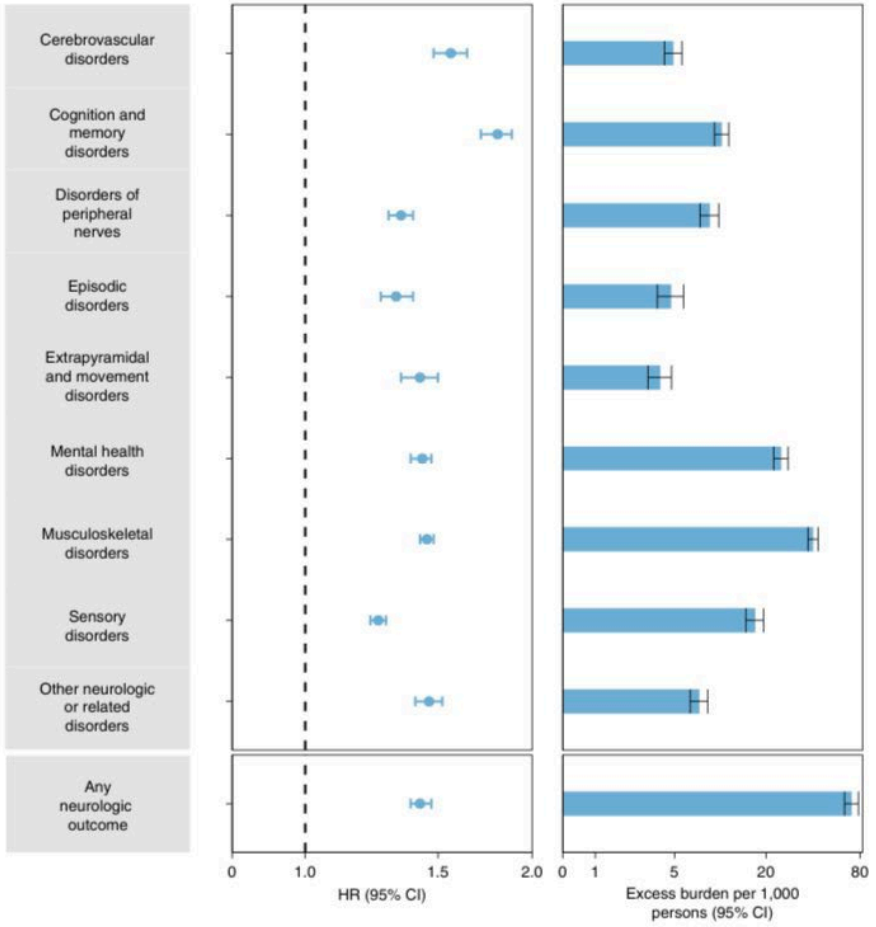

Fig. 3 | Risks and 12-month burdens of incident postacute COVID-19 composite neurologic outcomes compared with the contemporary control cohort. Composite outcomes consisted of cerebrovascular disorders (ischemic stroke, TIA, hemorrhagic stroke and cerebral venous thrombosis), cognition and memory (memory problems and Alzheimer's disease), disorders of the peripheral nerves (peripheral neuropathy, paresthesia, dysautonomia and Bell's palsy), episodic disorders (migraine, epilepsy and seizures and headache disorders), extrapyramidal and movement disorders (abnormal involuntary movements, tremor, Parkinson-like disease, dystonia, myoclonus), mental health disorders (major depressive disorders, stress and adjustment disorders, anxiety disorders, and psychotic disorders), musculoskeletal disorders (joint pain, myalgia and myopathy), sensory disorders (hearing abnormalities or tinnitus, vision abnormalities, loss of smell and loss of taste), other neurologic or related disorders (dizziness, somnolence, Guillain–Barré syndrome, encephalitis or encephalopathy and transverse myelitis) and any neurologic outcome (incident occurrence of any neurologic outcome studied). Outcomes were ascertained 30 days after the COVID-19-positive test until the end of follow up. The COVID-19 cohort had $n = 154,068$ and the contemporary control cohort had $n = 5,638,795$. Adjusted HRs (dots) and 95% (error bars) CIs are presented, as are estimated excess burdens (bars) and 95% CIs (error bars). Burdens are presented per 1,000 persons at 12 months of follow up. The dashed line marks a HR of 1.00; lower limits of 95% CIs with values greater than 1.00 indicate significantly increased risk.

COVID Headache

- Headache is one c
  neurologic preser
- Prevalence of 6-7
- Limited data rega
  of headache

Uygun *et al. The Journal of Headache and Pain* (2020)
https://doi.org/10.1186/s10194-020-01188-1

RESEARCH ARTICLE

Headache characteri
pandemic-a survey s

Özge Uygun[1*], Mustafa Ertaş[1], Esme Ekizoğlu
Arif Atahan Çağatay[4] and Betül Baykan[1*]

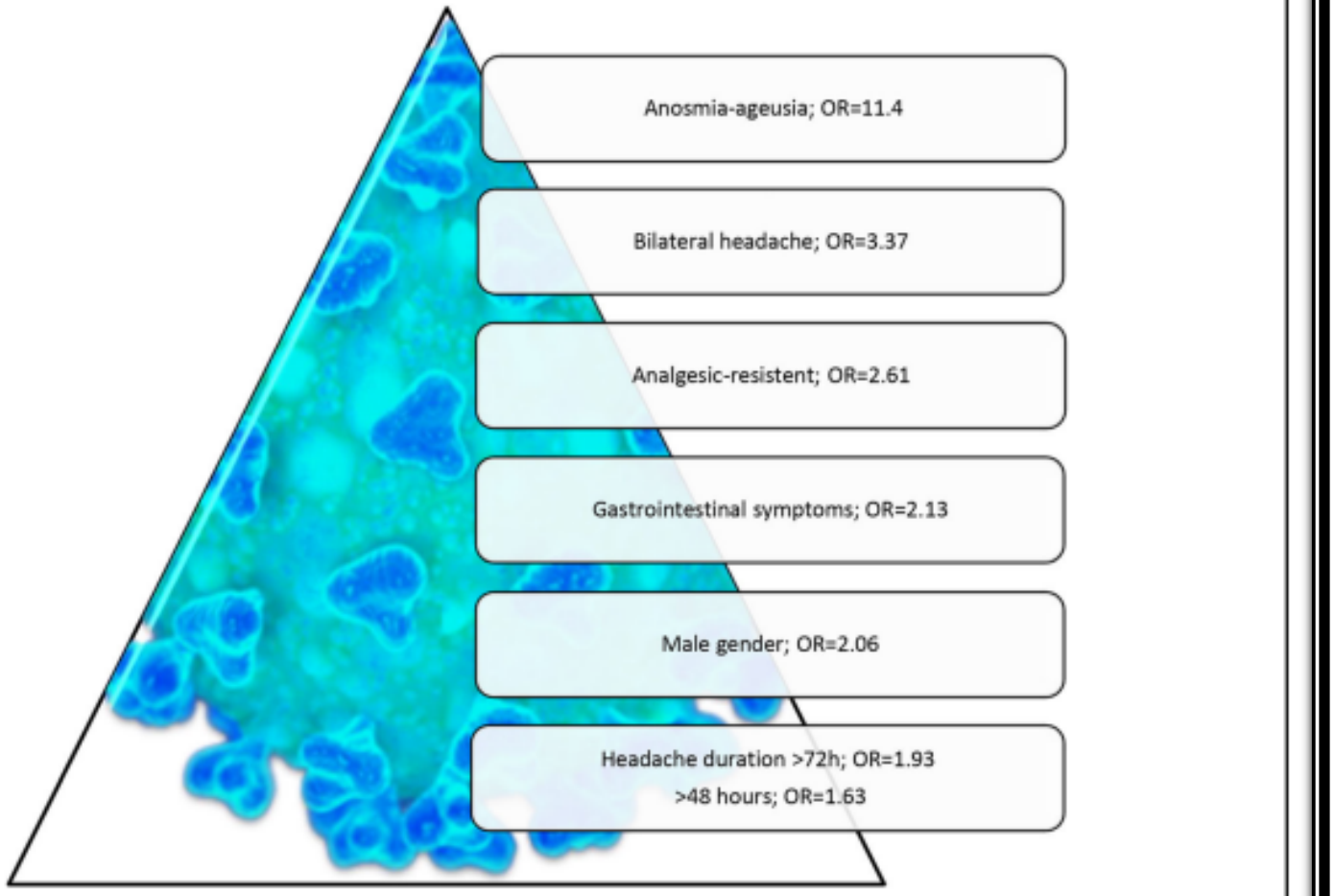

Fig. 4 Odds ratios of differentiating variables related to the presence of headache in patients with COVID-19 diagnosis reporting headache during the pandemic

Table 1

Demographic features of participants and characteristics of headache experienced during the p

	(*n* = 1968)	COVID-19 positive[a]		
			eadache (*n* = 87)	p
				.370
				.104
				.541
				.430
				.008
				.058
				.633
				.330
				.538
				.509
				.508
				.090
				–
				.479
				.152
				.481
				.257
				.227
				.530
				.231
Completely recovered with analgesics %	12.4	11.9		.568

Diagnosis & Treatment COVID-19 Headache

- Further evaluations should be considered to exclude secondary etiologies of headache
- Brain MRI with & without gadolinium should be considered to evaluate secondary causes of headache
- Symptomatic management of headache is the next step once secondary etiologies are ruled out
- Treatment according to the phenotype of headaches

Tension

- APAP, NSAIDs, massage/myofascial

Migraine

- Triptans, 5 HT1F receptor agonists, CGRP-antagonists
- Intravenous agents, such as magnesium and dopamine receptor antagonists and
- Peripheral nerve blocks (occipital, auriculotemporal, supraorbital, supratrochlear)
- SPG blocks

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Annals of NEUROLOGY
An Official Journal of the American Neurological Association and the Child Neurology Society
AMERICAN NEUROLOGICAL ASSOCIATION

Research Article | Free Access

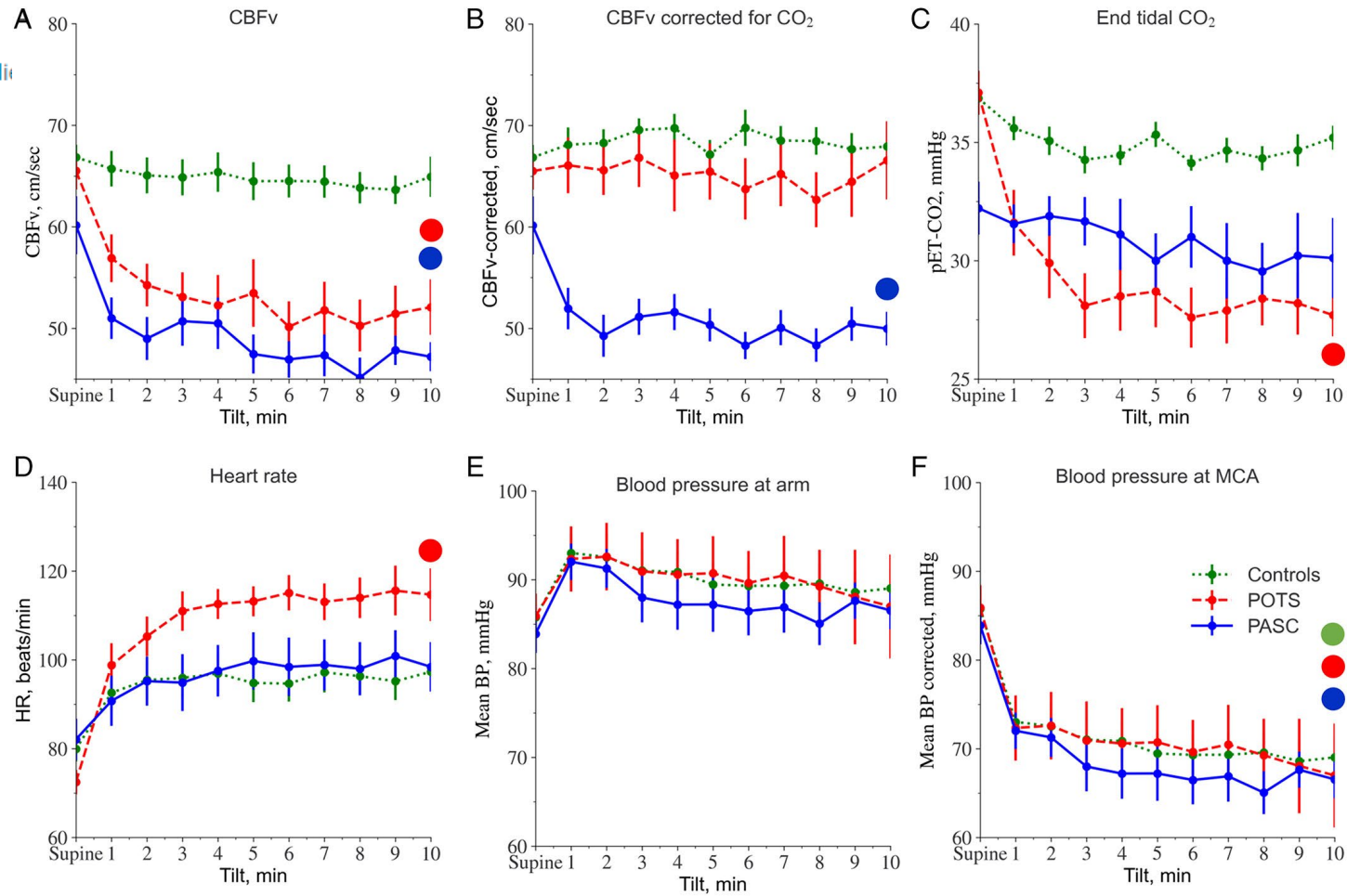
Multisystem Involvement in Post-Acute Sequelae of Coronavirus Disease 19

Peter Novak MD, PhD, Shibani S. Mukerji MD, PhD, Haitham S. Alabsi DO, David Systrom MD, Sadie Marciano PA-C, Donna Felsenstein MD, William J. Mullally MD, David M. Pilgrim MD

First published: 24 December 2021 | https://doi.org/10.1002/ana.26286

Mild COVID-19 is associated with **multisystem involvement**:

- Cerebral Blood Flow Dysregulation
- Hypocapnic Hyperventilation
- Small fiber neuropathy
- Dysautonomia
- Pain
- Inflammatory Markers



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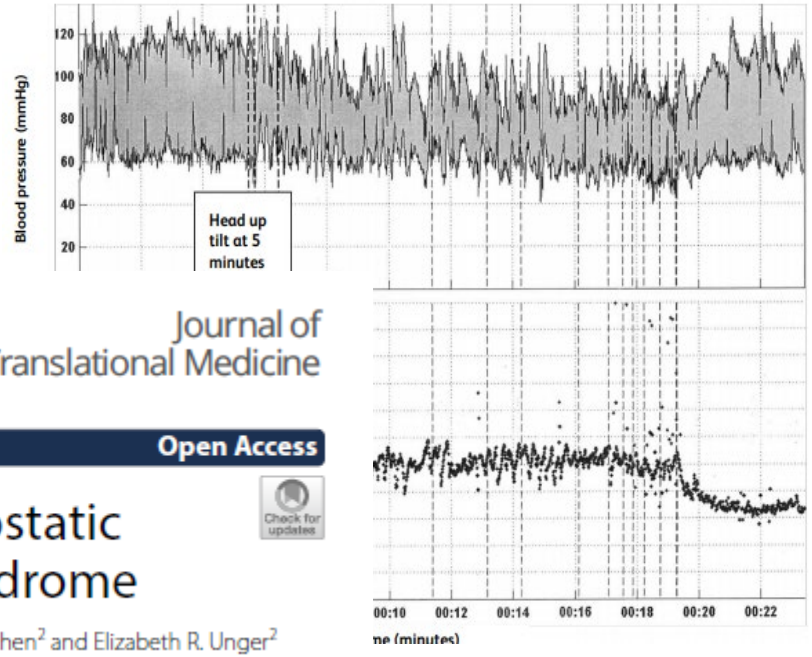
Autonomic Impairment

Postural Tachycardia Syndrome (PoTS)

- Sustained HR increment of 30 BPM within 10 min of standing or head-up lift in the absence of orthostatic hypotension
- Standing HR often > 120
- Symptoms of orthostatic intolerance



Natelson et al.
Journal of Translational Medicine (2022) 20:95
https://doi.org/10.1186/s12967-022-03289-8

Journal of Translational Medicine

RESEARCH Open Access

Physiological assessment of orthostatic intolerance in chronic fatigue syndrome

Benjamin H. Natelson[1*], Jin-Mann S. Lin[2], Michelle Blate[1], Sarah Khan[1], Yang Chen[2] and Elizabeth R. Unger[2]

Autonomic dysfunction in 'long COVID': rationale, physiology and management strategies

Authors: Melanie Dani,[A] Andreas Dirksen,[B] Patricia Taraborrelli,[B] Miriam Torocastro,[C] Dimitrios Panagopoulos,[D] Richard Sutton[E] and Phang Boon Lim[F]

Management

- Education
- Exercise
- Fluid and Salt repletion
- Avoiding exacerbating factors
- Isometic exercises
- Compression garments
- Pharmacologic

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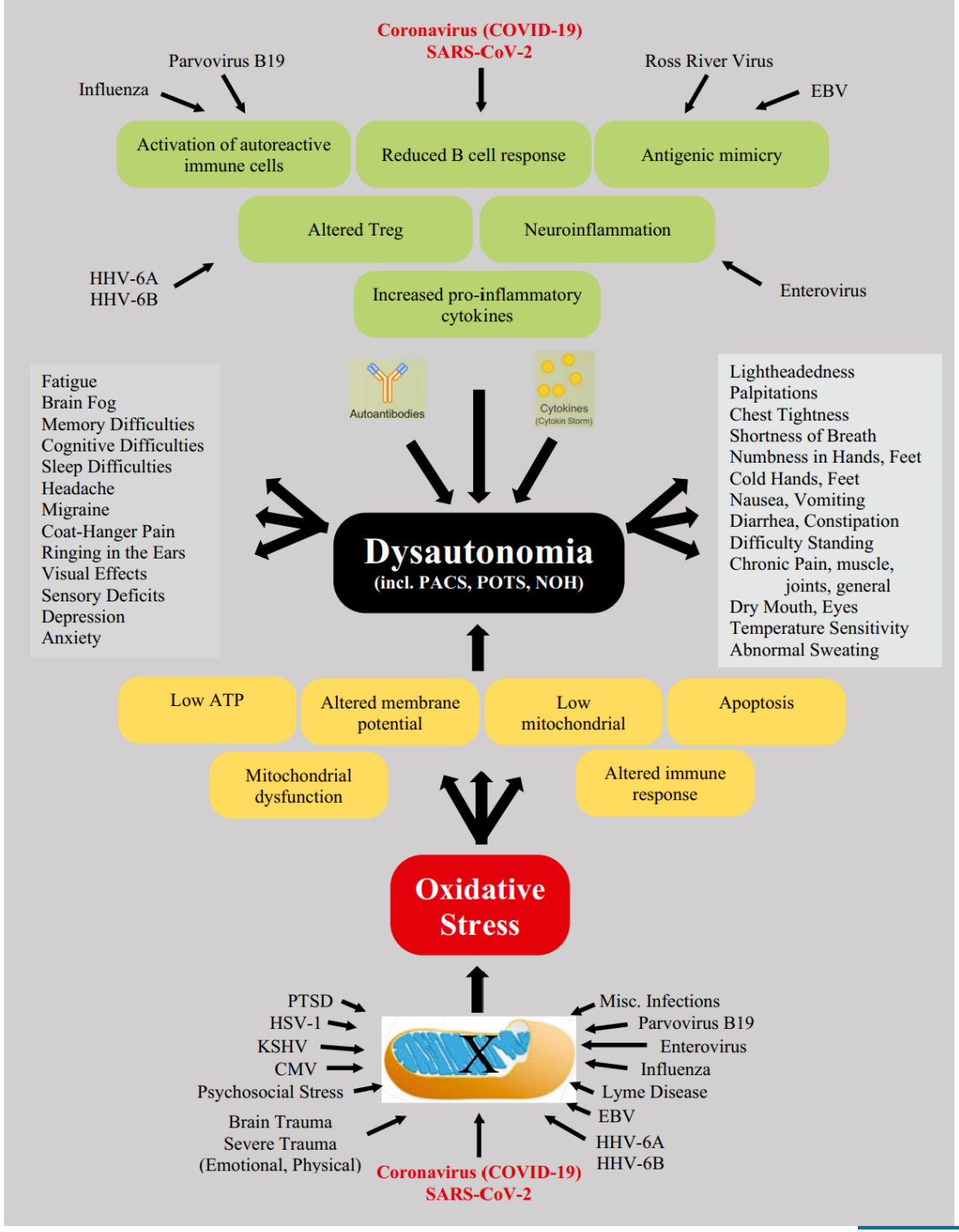
Dysautonomia

Neurocardiologic

- Fatigue
- Brain fog
- Memory Difficulties
- Cog difficulties
- Sleep difficulties
- Headache
- Migraine
- Coat-hanger pain
- Ringing in the ears
- Visual effects
- Sensory deficits
- Depression
- Anxiety
- Lightheadedness
- Palpitations
- Chest tightness
- SOB
- Nausea/vomiting
- Diarrhea/constipation
- Abnormal sweat
- Difficulty standing
- Dry mouth, eyes
- Chronic pain
- Temp sensitivity



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Post-COVID Postural Orthostatic Tachycardia Syndrome –
Retrospective Review of Experience at UT Health San Antonio

Results

40 patients who were diagnosed with Post-COVID POTS.
Mean age was 40.98 ± 11 years with a mean BMI of 32.32 ± 9.70.
Females comprised of 97.5% of the patients.
Symptoms began 4-6 weeks after COVID and included fatigue (75%), palpitations (70%), lightheadedness (47.5%), cognitive decline (50%), mental clouding (50%), dyspnea (50%), and memory loss (47.5%), and syncope (2.5%).
Patients were diagnosed with Post-COVID POTS an average of 219.9 ± 156.4 days after the diagnosis of COVID-19.
Tachycardia upon standing mean change in heart rate of 42.48 ± 29.37 bpm.
Initial management along with increased water and salt intake: beta blocker (30%), fludrocortisone (5%), midodrine (5%), rehabilitation, and lower body compression.
At 6 months, patients still had persistent symptoms with 65.52% of patients noting some improvement, 31.0% with stable symptoms, and 3.45% with worsening symptoms.
Physical therapy and rehabilitation were reported as the most effective treatment in the group that reported some improvement.

At 6 months disabling symptoms persisted in 100% of these high functioning women pre-COVID.
No patient had full recovery.

frontiers in Medicine

HYPOTHESIS AND THEORY
published: 07 May 2021
doi: 10.3389/fmed.2021.625836

Vagus Nerve Stimulation: A Potential Adjunct Therapy for COVID-19

Eric Azabou [1], Guillaume Bao [1], Rania Bounab [2], Nicholas Heming [2] and Djillali Annane [2]*

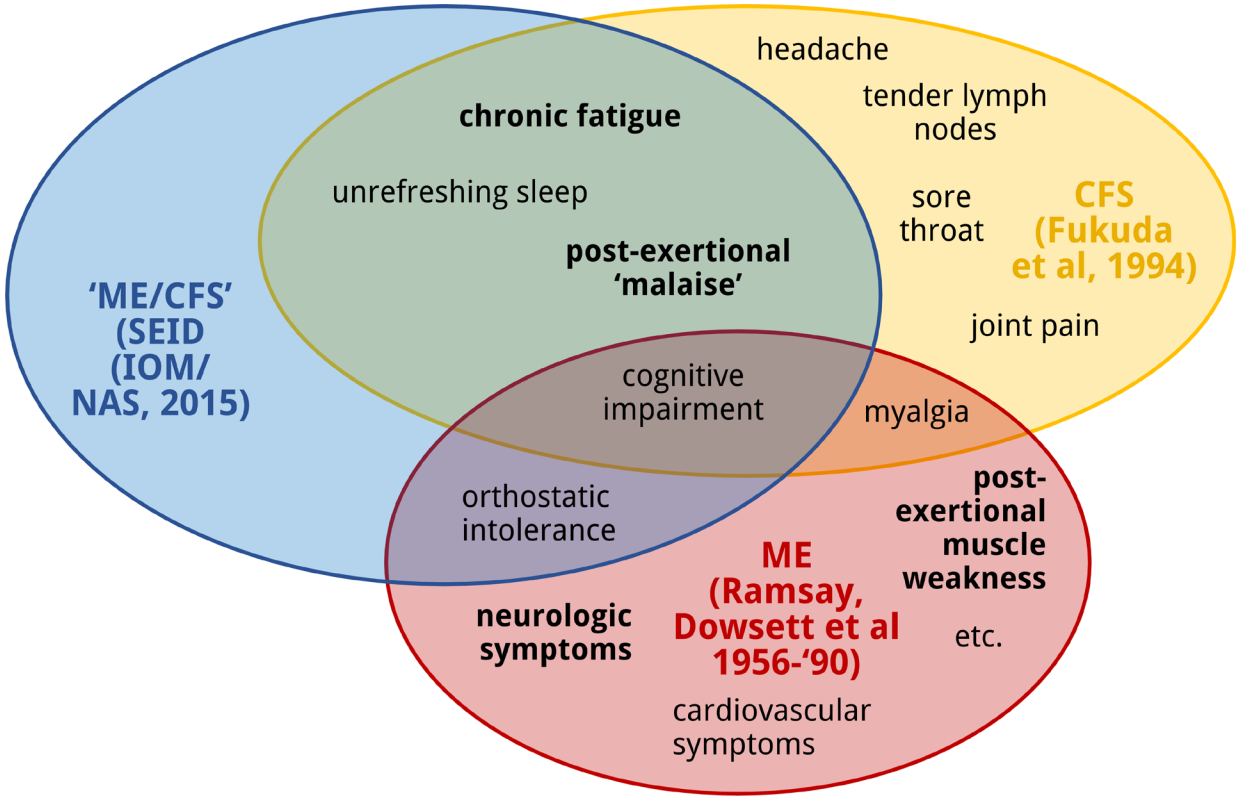
Vagus nerve stimulation attenuates inflammation both in experimental models and preliminary data in human. Modulating the activity of cholinergic anti-inflammatory pathways (CAPs)

Non-invasive transcutaneous vagal nerve stimulation (t-VNS), as a non-pharmacological adjuvant, may help reduce the burden of COVID-19 and deserve to be investigated.

Post-Viral Fatigue

Myalgic encephalomyelitis / CFS

- Pulm/ Cardiac screens
- Vitamin levels & Viral reactivation
- ME/CFS Tiered Testing Recommendations
- Check sleep
- Therapy, but **do not** exercise to fatigue (graded RTP)
- Other things: Melatonin, Omega-3, Iron, Magnesium, breathing/meditation, Vit D, duloxetine, stimulants (amantadine), Mast Cell protocol, EECP



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Brain, Behavior, and Immunity
Available online 29 December 2021
In Press, Journal Pre-proof

Review Article

Fatigue and Cognitive Impairment in Post-COVID-19 Syndrome: A Systematic Review and Meta-Analysis

Felicia Ceban [a, b, c], Susan Ling [a, d], Leanna M.W. Lui [a], Yena Lee [a, b, c], Hartej Gill [a], Kayla M. Teopiz [a], Nelson B. Rodrigues [a, c], Mehala Subramaniapillai [a, b, c], Joshua D. Di Vincenzo [a], Bing Cao [e], Kangguang Lin [f, g], Rodrigo B. Mansur [a, h], Roger C. Ho [i, j], Joshua D. Rosenblat [a, c, d, h], Kamilla W. Miskowiak [k, l], Maj Vinberg [m, n], Vladimir Maletic [o], Roger S. McIntyre [a, b, c, d, h]

Meta-analysis on 81 studies estimating Long COVID prevalence

Key findings:

32% of patients have fatigue at 12 weeks

31% at 6+ months

22% have cognitive impairment at 12 weeks

21% at 6+ months

A significant key finding is that fatigue and cognitive impairment were not statistically significantly different between hospitalized and non-hospitalized patients!

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PM&R

Consensus Guidance Statement

Multidisciplinary co
the assessment and
of SARS-CoV-2 infec

Joseph E. Herrera DO, William N
MD, MBA, Talya K. Fleming MD,
MD, Monica Verduzco Gutierrez
... See fewer authors

First published: 04 August 2021

TABLE 1 PASC fatigue assessment recommendations

#	Statement
1	Patients should be assessed for fatigue patterns throughout their normal day to guide activity recommendations.
1a	Patients should be assessed for their responses to initiating and escalating activity on their fatigue.
1b	Patients should be evaluated for changes in daily functioning and activity levels.
1c	Patients' physical functioning and endurance should be assessed to inform activity and therapy recommendations. (Examples of tests that can be chosen based on an individual's activity tolerance: 30 s sit to stand[55]; 2-min step (seated or standing)[56]; 6 min walk test[57]; 10 m walk test[58]).
2	Clinicians should assess for changes in activities of daily living, independent activities of daily living, school, work, and avocational (ie, hobbies)
3	A full patient history with review of preexisting conditions should be conducted
4	Patients should be evaluated for conditions that may exacerbate fatigue symptoms and warrant further testing and potential subspecialty referral (see Table 2). Particular areas include: • Sleep • Mood, including anxiety, depression and PTSD. Note: Patients often report dissatisfaction with their care because of their persistent symptoms being attributed to psychological factors. It is important to note that mood disorders may be secondary to persistent medical issues or one of many factors leading to fatigue. • Cardiopulmonary • Autoimmune • Endocrine
5	A medication review should be conducted to investigate medications that may be contributing to fatigue. Of note, antihistamine, anticholinergic, and antidepressant/anxiolytic medications can contribute to fatigue in patients with PASC.
6	The following basic lab workup should be considered in new patients or those without lab workup in the 3 months before visit including complete blood count with differential, chemistries including renal and hepatic function tests, thyroid stimulating hormone, c-reactive protein or erythrocyte sedimentation rate, and creatinine kinase. Other laboratory tests may be considered based on the results of these tests or if there is specific concern for comorbid conditions as outlined in Table 2.

Abbreviations: PASC, postacute sequelae of SARS-CoV-2 infection; PTSD, posttraumatic stress disorder.

Please learn about Post-Exertional Malaise:

TABLE 3 National Aademy of Sciences proposed diagnostic criteria for ME/CFS

Proposed Diagnostic Criteria for ME/CFS
Diagnosis requires that the patient has the following three symptoms:
1. A substantial reduction or impairment in the ability to engage in preillness levels of occupational, education, social, or personal activities that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest,
2. Postexertional malaise[a] and
3. Unrefreshing sleep[a]
At least one of the following manifestations is also required:
1. Cognitive impairment[a] or
2. Orthostatic intolerance

IOM Case Definition

- Cardinal symptom of myalgic encephalomyelitis / chronic fatigue syndrome, according to the National Academy of Medicine
- Definition: A prolonged exacerbation of a patient's baseline symptoms after physical/cognitive/orthostatic exertion or stress. It may be delayed relative to the trigger.

Guidance Statements:

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PASC Fatigue Treatment Recommendation #2: The Four Ps

Energy conservation strategies

- **Pacing.** Avoiding the push and crash cycle that is common in post-COVID recovery.

- **Prioritizing.** Encourages a patient to focus and decide on which activities need to get done and which activities can be postponed to avoid overexertion and crashing.

- **Positioning.** Modifying activities to make them easier to perform.

- **Planning.** Encourages the patient to plan the day or week to avoid overexertion and to recognize energy windows.

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Therapy Program: longcovid.physio

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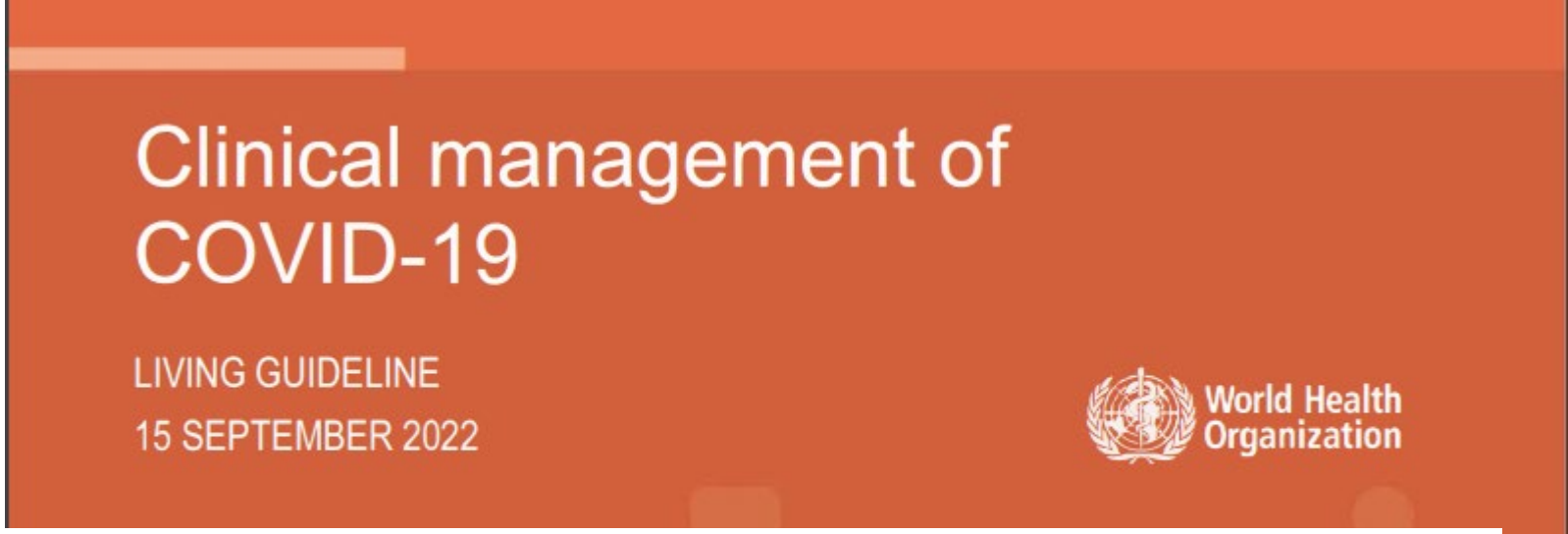
- Components and functions of rehab care
  - Multidisciplinary
  - Continuity & coordination of care
  - People-centered & shared decision-making

- Red flags for safe rehabilitation
  - Exertional desaturation & cardiac impairment should be ruled out before physical exercise

- Post-exertional symptom exacerbation
  - Assess PESE
  - Pacing/energy conservation
  - Graded exercise should NOT be offered

- Orthostatic intolerance
  - Screen
  - Self-management skills

- Return to everyday activities and work
  - Energy conservation, assist products
  - Prolonged & flexible phased RTW



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Topic 12 Olfactory impairment 116
Topic 13 Orthostatic intolerance 117
Topic 14 Swallowing impairment 118
Topic 15 Voice impairment 119
Topic 16 Return to everyday activities and work 120

Know/teach triggers

- Physical or cognitive exertion
- Stress
- Dehydration
- Weather changes
- Consuming large meals
- Alcohol consumption
- Premenstrual period

Long COVID: Psychiatric and Sleep Problems

Spanish multicenter study
7 months after discharge from hospital
n = 1142

50% had anxiety or depressive symptoms and/or poor sleep quality

Anxiety in 16.2%
Depressive in 19.7%
Poor sleep quality in 34.5%

Fernández-de-Las-Peñas et al. J *Infect*. 2021.

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NeuroPsychiatric Symptoms

TriNetX

The TriNetX Global Health Research Network

Image Source: trinetx.com

- Prevalence of neuropsych complaints in patient with acute COVID-19 = **22.5**%
- Incident psychiatric disorders in the first 3 months is **18**% (6% new onset)
- Pre-existing psychiatric » increased risk of infection, hospitalization, death

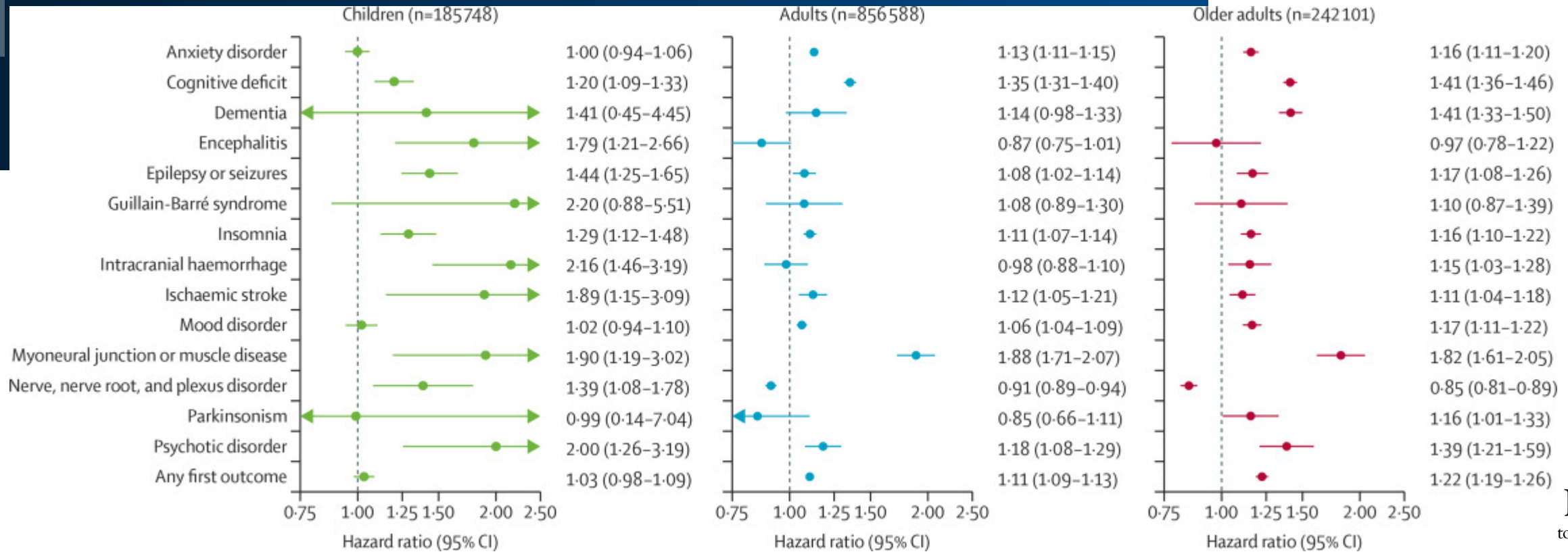
(Garcia-Azorin et al., 2020; Jeon et al., 2020; Li et al., 2020; Nalleballe et al., 2020; Taquet et al., 2020; Yang et al., 2020)

THE LANCET
Psychiatry

- Mental health conditions returned to normal over time
- Cognitive & neurological impacts did not & persisted for 2 years

ARTICLES | ONLINE FIRST

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



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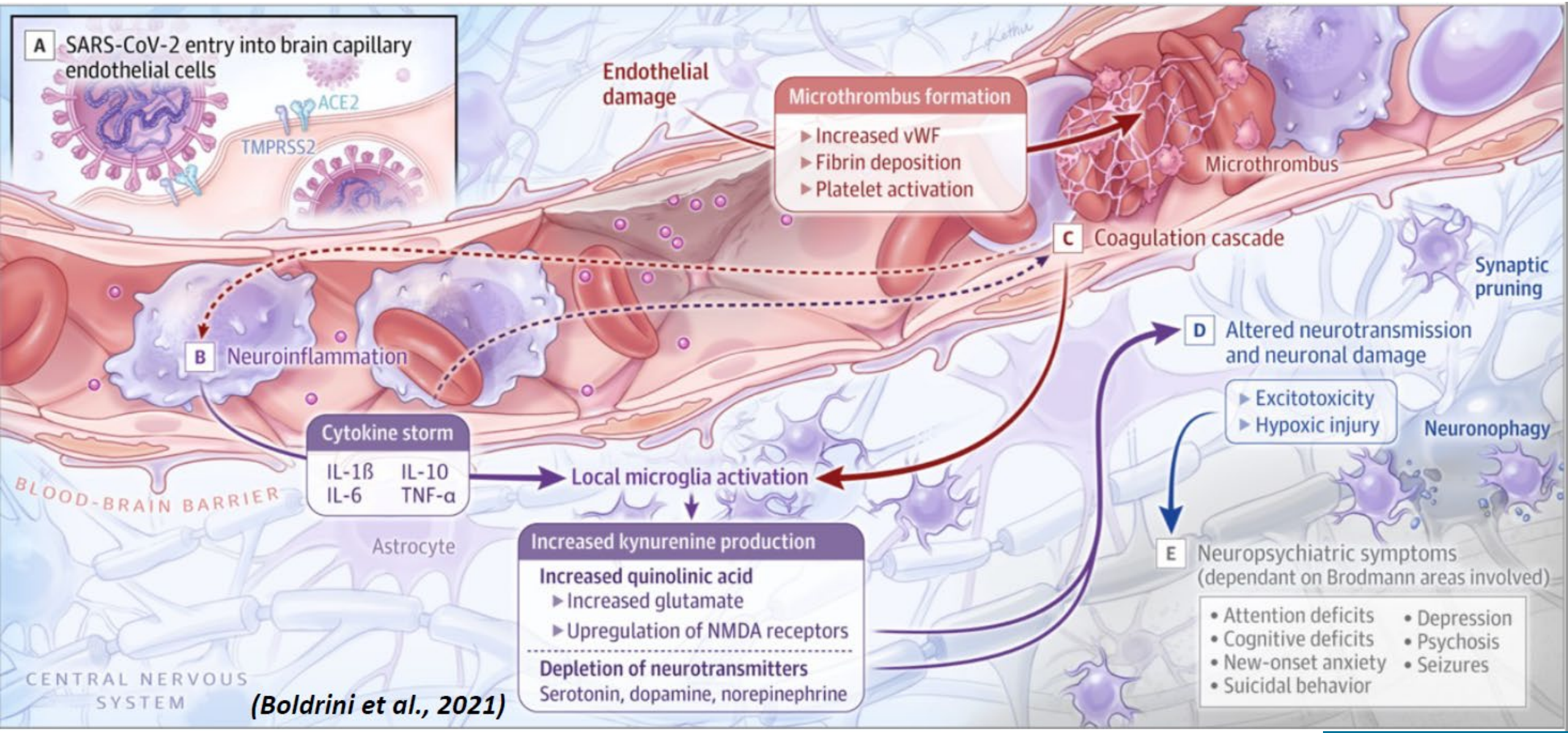
What is happening here?



PASC And COVID Vaccines

- Preliminary patient led observational study showed 56.7% of vaccinated showed overall improvement in PASC symptoms while 18.7% deteriorated and 24.6% were unchanged. (Strain et al. Lancet reg Health Eur. 2022;12:100265)
- Another study based on COVID symptom app showed that the odds of experiencing symptoms more that 28 days post-vaccination, were halved by two vaccinations in 906 participants (Antonelli et al. Lancet infectious Diseases. 2022;22:43-55)
- Study in Italy covering the omicron wave indicated strong protection against PASC after break through infection by vaccination with mRNA vaccines. (Azzolini Et al. JAMA 2022;328)

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Long COVID:
Mechanism & Possible Therapeutic Strategies

Pathogenesis	Potential Treatment
Persistent microclots/Microvascular disease/Endothelial dysfunction	Rivaroxaban, Triple therapy (clopidogrel, ASA, apixaban) EECP
Inflammation	Anti-inflammatories (steroids, colchicine), antihistamines
Viral reservoir/Persistent viral infection and ongoing tissue harm	Anti-virals (Paxlovid, molnupiravir, remdesivir) Virus monoclonal antibodies (ex. Evusheld) Therapeutic vaccine
Autoimmune/Autoantibodies	IVIg, B cell-directed therapies
Acute viral infection with irreversible tissue damage	Rehabilitation
Mitochondrial dysfunction	AXA1125, mito-directed therapies

Currently 75 Clinical Trials for Long COVID in ClinicalTrials.gov

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Long COVID:
Therapeutic Strategies for Autoimmunity

Monoclonal Antibody to IL-6

Anakirnra – IL-1 receptor antagonist

Infliximab – monoclonal anti-TNF-α

Abatacept – inhibits T-lymphocyte activation

JAK inhibitor DMARDs

Naltrexone

Systemic steroids

IVIg

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Low Dose Naltrexone in ME/CFS

Table 1. Mechanisms of action and clinical use in regard to different doses of naltrexone used.

Dose Range	Dose Specific Mechanism of Action	Clinical Use
Standard (50–100 mg)	Opioid receptor antagonism	Alcohol and opiate abuse
Low-dose (1–5 mg)	Toll-like receptor 4 antagonism, opioid growth factor antagonism	Fibromyalgia, multiple sclerosis, Crohn's disease, cancer, Hailey-Hailey disease, complex-regional pain syndrome
Very low-dose (0.001–1 mg)	Possibly same as low-dose	Aid in methadone detoxification taper
Ultra low-dose (<0.001 mg)	Binding to high affinity filamin-A (FLNA) site and reducingμ-opioid receptor associated Gs-coupling	Potentiating opioid analgesia

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LDN in PASC

Table 3
Incidence of reported symptoms at baseline and at 2 months.

Symptoms	Baseline n (%)	2 month follow up n(%)	P value (2 tailed <0.05)
Total	36	36	
Fatigue	33(91.7)	27(75)	.085
Fevers	6(16.7)	2(5.6)	.185
Sore throat	13(36.1)	8(22.2)	.136
Anosmia/dysgeusia	16(44.4)	11(30.6)	.171
Hair loss	11(30.6)	9(25)	.65
Tinnitus	17(47.2)	12(33.3)	.2
Chest pain/tightness	20(55.6)	12(33.3)	.047
Palpitations	22(61.1)	16(44.4)	.132
Cough	19(37.3)	5(13.9)	.016
Shortness of breath	25(69.4)	19(52.8)	.09
Headache	27(75)	24(63.9)	.314
Dizziness	17(47.2)	14(38.9)	.618
Brain fog	27(75)	20(55.6)	.072
Sleep disturbance	26(72.2)	16(44.4)	.058
Dysthesia	20(55.6)	13(36.1)	.056
Abdominal discomfort/ bloating	17(47.2)	14(38.9)	.449
Nausea/Vomiting	12(33.3)	6(16.7)	.083
Diarrhoea	14(38.9)	9(25)	.166
Joint pain	26(72.2)	13(36.1)	.008
Myalgia	20(55.6)	14(38.9)	.163
Low mood	28(77.8)	17(47.2)	.003
Anxiety	20(55.6)	16(44.4)	.337
Personality change	9(25)	0(0)	.001

O'Kelly, B et al. Brain, Behavior, & Immunity-Health 24 (2022)

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Some initial orders

- Multi-disciplinary rehab program:
  - Rehab Without Walls or Texas PT Specialists or Warm Springs
- Cognitive: Speech therapy
- Cognitive: amantadine, memantine, donepezil, montelukast
- Fatigue: EECP treatments (BCBS will cover, others is +/-), REST & pacing, Mast cell protocol (anti-histamines), anti-inflammatory diet, omega-3, vitamin &/or iron replacement. Look at sleep
- Mood: Consider Fluvoxamine
- Tinnitus: steroids early, check hearing
- Migraine: IV magnesium for migraine status, CGRPs
- Autonomic: Check orthostatics, 10-min stand test, tilt table &/or Cardiac MRI
  - Paresthesia: Neuro for skin biopsy for SFN
  - Mayo neurologic panel, ENCES panel, ganglionic AChR antibody, serum metanephrines
  - Tx: Propranolol, midodrine, pyridostigmine, clonidine, fludrocoritisone

Support For Disability & Work Accommodations

Likely the 2nd most important thing we can do!

- All patients need to time to recover
- Relapses are common
- Working, stress, pushing themselves too hard is the most common trigger for relapses and PEM
- Facilitating respite and / or reasonable reentry back to work is enormously beneficial for quality-of-life faster recovery

Accommodations & Disability for Fatigue & Brain Fog

Possible Disability Accommodations:

Limited hours

Frequent breaks

Avoid standing

Parking close to entry

Adjust work activities

Limit tasks with divided attention

Optimize range of movements

Limit environments with multiple sensory inputs

Return home if breathing rate is increased for more than a few minutes?

For Disability Applications, Document:

Activity levels pre/post infection

Symptoms that are remitting and relapsing

Specific work activities will result in physical and mental fatigue

Environmental settings that result in sensory overload (markets, etc)

Work-ups that rule out other associated causes including pre-existing conditions

Long COVID is a Disability Under the ADA

Guidance on "Long COVID" as a Disability Under the ADA, Section 504, and Section 1557

U.S. Department of Health Human Services
Office for Civil Rights

U.S. Department of Justice
Civil Rights Division
Disability Rights Section

Although many people with COVID-19 get better within weeks, some people continue to experience symptoms that can last months after first being infected, or may have new or recurring symptoms at a later time.[1] This can happen to anyone who has had COVID-19, even if the initial illness was mild. People with this condition are sometimes called "long-haulers." This condition is known as "long COVID."[2]

In light of the rise of long COVID as a persistent and significant health issue, the Office for Civil Rights of the Department of Health and Human Services and the Civil Rights Division of the Department of Justice have joined together to provide this guidance.

This guidance explains that long COVID can be a disability under Titles II (state and local government) and III (public accommodations) of the Americans with Disabilities Act (ADA),[3] Section 504 of the Rehabilitation Act of 1973 (Section 504),[4] and Section 1557 of the Patient Protection and Affordable Care Act (Section 1557).[5] Each of these federal laws protects people with disabilities from discrimination.[6] This guidance also provides resources for additional information and best practices. This document focuses solely on long COVID, and does not address when COVID-19 may meet the legal definition of disability.

The civil rights protections and responsibilities of these federal laws apply even during emergencies.[7] They cannot be waived.

1. **What is long COVID and what are its symptoms?**

/ 3

This is a game changer!

Health systems will need to rally our resources to support patients accordingly

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Get your patients enrolled in trials

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Post-COVID Rehab

Community-based approach

Early and often

Inpatient Rehab

Home-based Rehab

Respiratory Rehab / Breathing Program

Autonomic Reconditioning

Mobility and Functional Rehab

Education

Mental health services

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