Rehabilitation of Post-COVI Conditions: a Path to Recovery

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UW Medicine

Disclosures

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The University of Washington acknowledges the Coast Salish peoples of this land, the land which touches the shared waters of all tribes and bands within the Suquamish, Tulalip and Muckleshoot nations.

https://www.realrentduwamish.org/land-acknowledgement.html

Objectives

- Describe the landscape and context of post-COVID conditions ("long-COVID" or PASC)
- Describe the prevalence and trajectory of PASC
- Explore diagnosis and rehabilitation strategies for PASC

CAVEATS

- Long COVID is a long-term public health issue.
- We *know* a lot less than we *believe*.
- We know even less about how long COVID affects many underserved

MY PERSPECTIVE.

Patient
Rehab Doctor
Researcher
Editor

Janna Friedly

is vice chair for Clinical Affairs, Department of Rehabilitation Medicine, UW School of Medicine.

August 9, 2021 at 2:20 pm

I'm a doctor yet struggled with long-term COVID symptoms | Op-Ed

After seeming to recover from the initial COVID infection, I began to experience headaches like never before, sleeplessness, muscle aches, nerve pains in my legs...

OPINION | SEATTLE TIMES OP-EDS

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CLEAR center

Putting the Evidence in Evidence-based Medicine

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Landscape/Context

BE BOUNDLESS

Landscape/Context of PASC

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American Academy of PM&R Multidisciplinary PASC Collaborative Led by:

Benjamin Abramoff, MD, MS – UPenn – PM&R
Eric Herman, MD – OHSU – Chief Primary Care and Population Health Officer
Jason Maley, MD – Mass General– Pulmonary & Critical Care

40+ Post COVID clinics participating with practitioners from multiple medical specialties and healthcare disciplines, as well as federal representation and patient organization representation.

https://www.aapmr.org/members-publications/covid-19/multidisciplinary-quality-improvement-initiative

How Common is Long COVID?

https://pascdashboard.aapmr.org

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FIND A PM&R PHYSICIAN | ABOUT PM&R | COVID-19 RESOURCE CENTER

FILTERS
(reset to default)
Select Est. PASC %
30%
Select a State
All
Select a County
All

MODEL ASSUMPTIONS AND SOURCES
(see all)

1. Model assumes 30% of COVID-19 surviving cases in the U.S. result in PASC.

2. COVID-19 surviving cases are confirmed cases less deaths.

3. U.S. case data is pulled nightly from JHU CSSE COVID-19 Data. U.S. Census data uses 2019 1-year estimates.

Powered by ASSOCIATION ANALYTICS

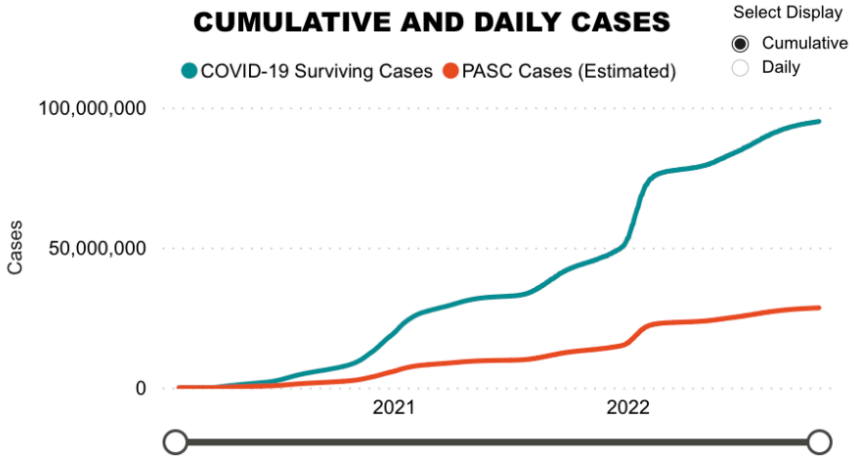
COVID-19 SURVIVING CASES (TOTAL)
96,204,592

PASC CASES (ESTIMATED)
28,861,3…

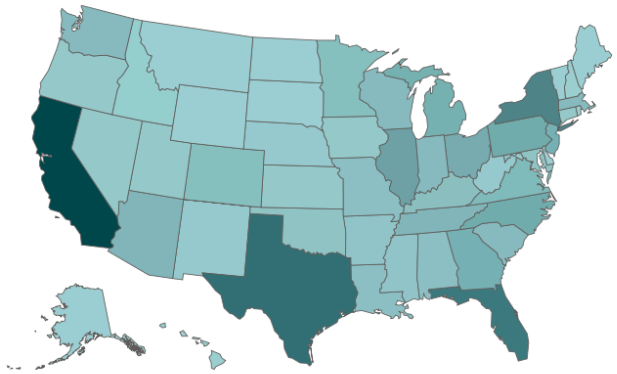
ESTIMATED PASC CASES PER STATE

State	PASC Cases (Estimated)
California	3,373,821
Texas	2,352,932
Florida	2,132,864
New York	1,845,555
Illinois	1,130,096
Pennsylvania	973,637
North Carolina	958,192
Ohio	939,981
Michigan	839,151
Georgia	831,120
New Jersey	824,555
Arizona	675,468
Tennessee	667,837
Virginia	625,297
Indiana	572,518
Wisconsin	562,875

CUMULATIVE AND DAILY CASES



PASC CASES (ESTIMATED)



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Terminology

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Many names for “long COVID”, inconsistent definitions

Long Haulers
Long-COVID
Long-term COVID
Longer term symptoms of COVID
Persisting symptoms post COVID
Post-acute COVID-19
Chronic COVID-19
Post-COVID Syndrome
Post COVID Conditions
Post Acute Sequelae of COVID (PASC)

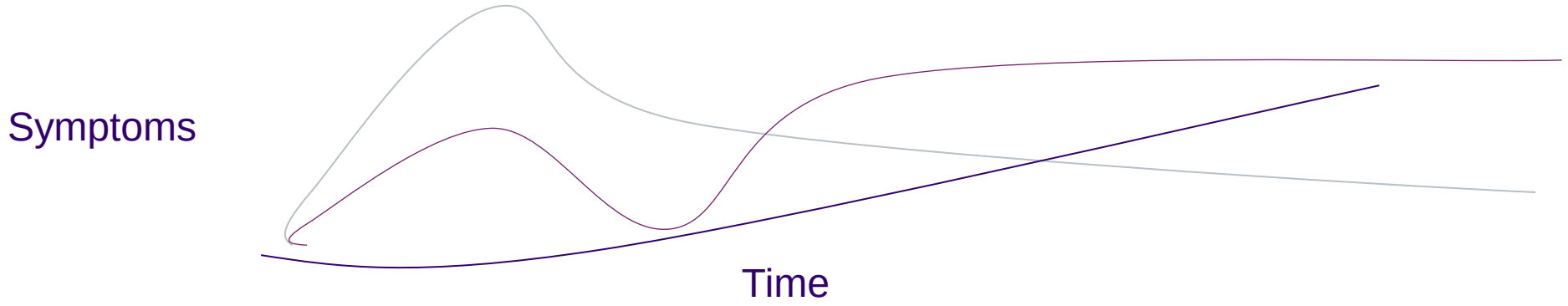
Del Rio C, Malani PN. COVID-19-New Insights on a Rapidly Changing Epidemic. JAMA 2020; 323:1339.
Greenhalgh T, Knight M, A'Court C, et al. Management of post-acute covid-19 in primary care. BMJ 2020; 370:m3026
Rubin R. As Their nNumbers Grow, COVID-19 “Long Haulers” Stump Experts. JAMA 2020.

What is Long COVID or PASC?

World Health Organization (WHO) and CDC definitions

Persisting symptoms 3 months after initial COVID infection that aren't explained by other medical conditions.

- Symptoms can be **new** after recovering from acute COVID or **persist** from the initial illness.
- Symptoms may fluctuate or relapse over time.
- *Lack of laboratory or imaging abnormalities doesn't invalidate the existence, severity, or importance of a patient's symptoms or conditions.*



Terminology

- Caution with "Long Hauler" and "Post-COVID Patient"
- Can shape self-identity and culture
- Patient first language
  - Patient with PASC
  - Person with longer term symptoms post COVID
- Allows for possibility of recovery

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6371927/
https://www.cdc.gov/ncbddd/disabilityandhealth/materials/factsheets/fs-communicating-with-people.html

Tips	Use	Do not use
Emphasize abilities, not limitations	Person who uses a wheelchair	Confined or restricted to a wheelchair, wheelchair bound
	Person who uses a device to speak	Can't talk, mute
Do not use language that suggests the lack of something	Person with a disability	Disabled, handicapped
	Person of short stature	Midget
	Person with cerebral palsy	Cerebral palsy victim
	Person with epilepsy or seizure disorder	Epileptic
	Person with multiple sclerosis	Afflicted by multiple sclerosis
Emphasize the need for accessibility, not the disability	Accessible parking or bathroom	Handicapped parking or bathroom
Do not use offensive language	Person with a physical disability	Crippled, lame, deformed, invalid, spastic
	Person with an intellectual, cognitive, developmental disability	Slow, simple, moronic, defective, afflicted, special person
	Person with and emotional or behavioral disability, a mental health impairment, or a psychiatric disability	Insane, crazy, psycho, maniac, nuts
Avoid language that implies negative stereotypes	Person without a disability	Normal person, healthy person
Do not portray people with disabilities as inspirational only because of their disability	Person who is successful, productive	Has overcome his/her disability, is courageous

Defining and Diagnosing PASC: *Addressing Disparities*

- Evolving post-COVID definitions may be influenced by symptoms reported by patients seen in clinics and enrolling in research studies.
- Due to inequities in access to diagnostics & care, PASC may be under-documented in vulnerable populations.
- PASC clinical care and research studies must address inequities.

Wisk LE, et al. *Annals of Internal Medicine* 2022.

Symptoms/Presentation of PASC

BE BOUNDLESS

Who is at higher risk for Long COVID?

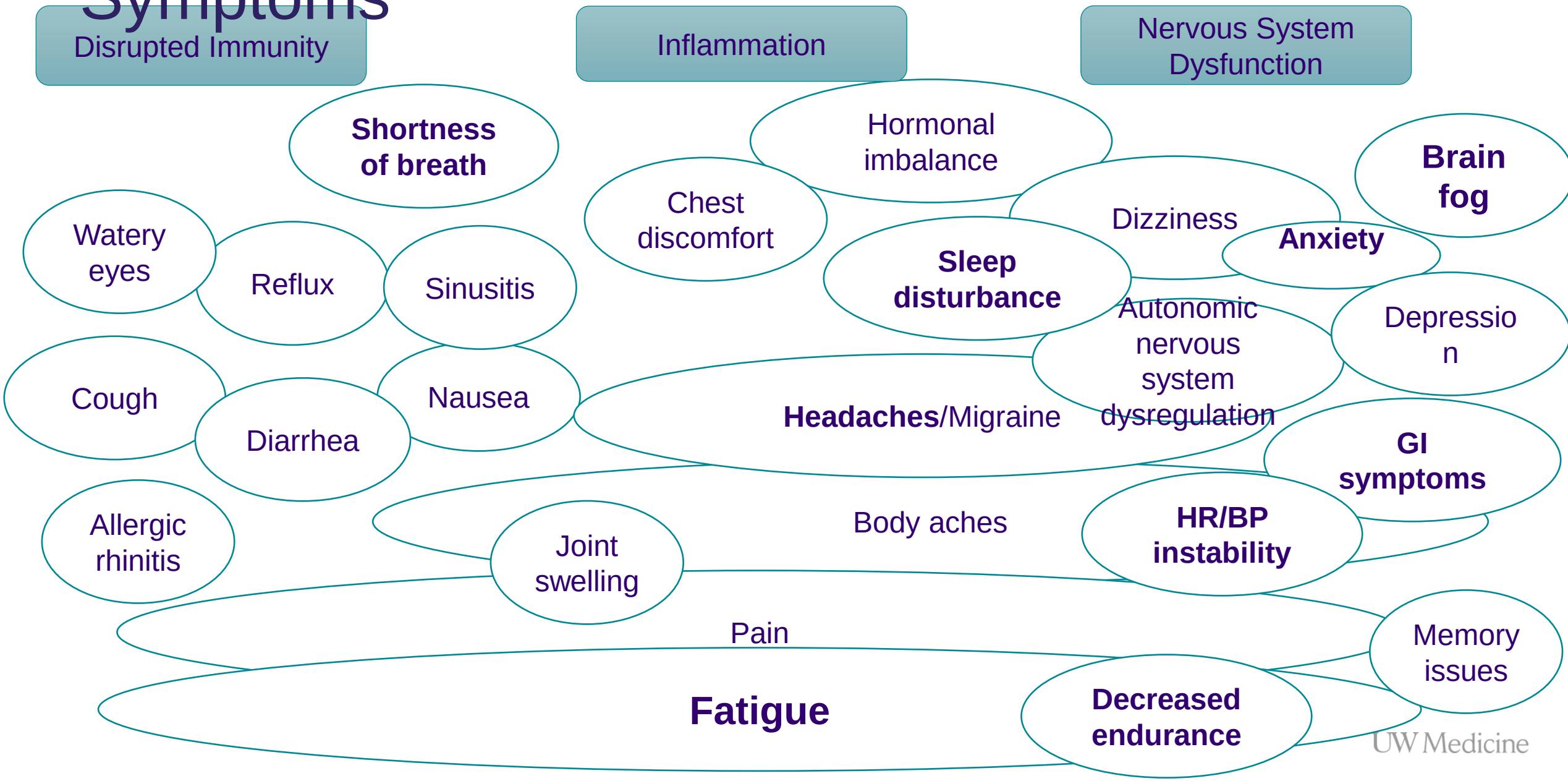
- Unvaccinated
- Women
- Ethnic Minorities
- Smokers
- Socioeconomically disadvantaged
- People with other medical conditions: obesity, diabetes, COPD, prostate disease, fibromyalgia, anxiety, depression, migraine, multiple sclerosis, celiac disease and learning disabilities

Subramanian, A., Nirantharakumar, K., Hughes, S. et al. Symptoms and risk factors for long COVID in non-hospitalized adults. Nat Med 28, 1706–1714 (2022)

A Common Outpatient Clinic Case

- 35 yo M, previously healthy fitness instructor w/ COVID approx. 1 yr ago.
- Initial infection was mild - fever x1 day, cough, SOB (normal SpO2), anosmia, fatigue x2 weeks. Symptoms initially improved, then worsened over the 3 months.
- Now with 9 months of fatigue and myalgias (constant, but worse after exertion), tachycardia (HR up to 130 when walking to the kitchen), SOB, headaches, intermittent tingling and allodynia in extremities, brain fog, insomnia, and new food sensitivities.
- Feels anxious and hopeless - worried he will never recover. Unable to return to work.
- **Says previous clinicians didn't believe his symptoms were real.**

Post-Acute Sequelae of COVID (PASC) Symptoms



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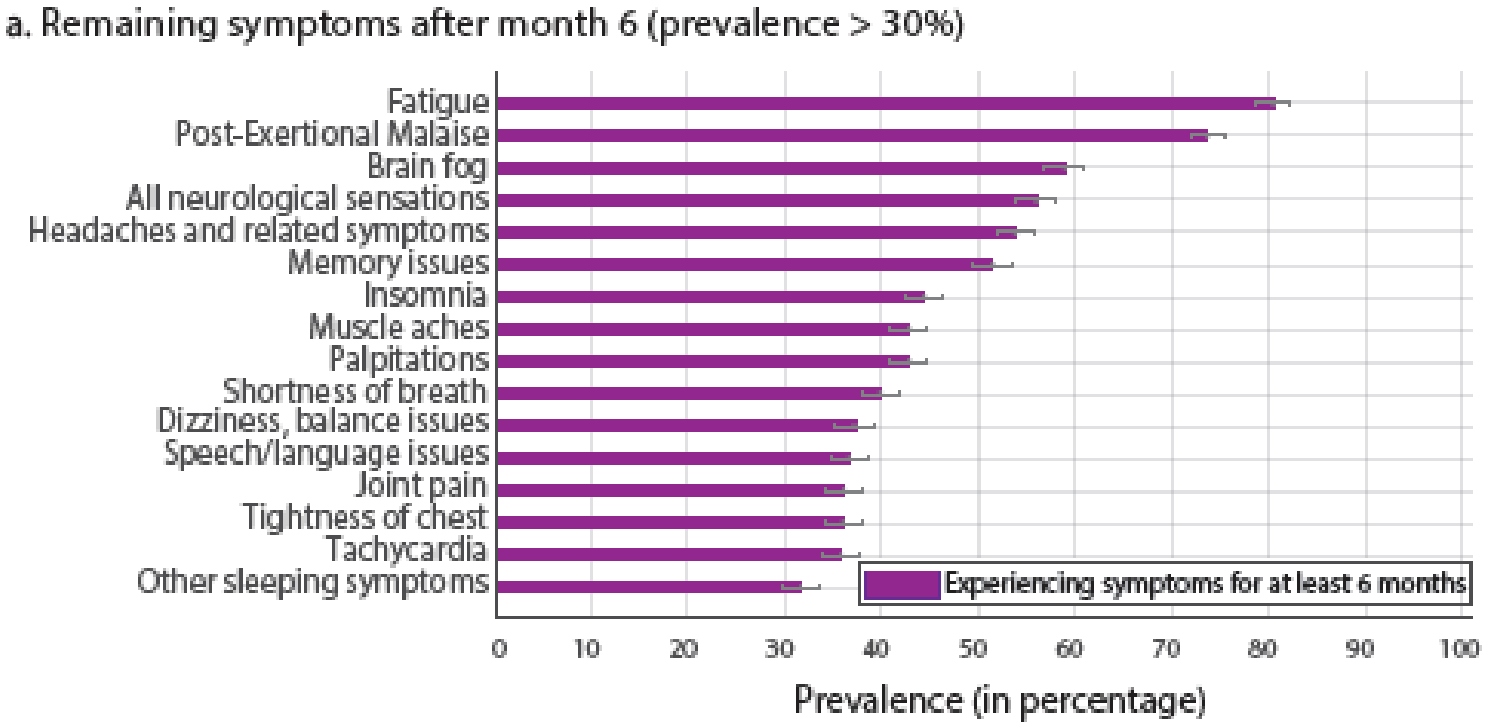
PASC Symptoms

- International Cohort Study, n= 3,762, >30 days from infection
- 203 symptoms in 10 organ systems prevalent
- Avg: 14.5 symptoms in 9.1 organ systems
- The most frequent symptoms reported after month 6 were:
  - fatigue (78%)
  - post-exertional malaise (72%)
  - cognitive dysfunction (55%)

Data collection period: 9/6/2020 -11/25/2020



Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact Patient-Led Research Collaborative Davis, et al, 2021 https://doi.org/10.1101/2020.12.24.20248802

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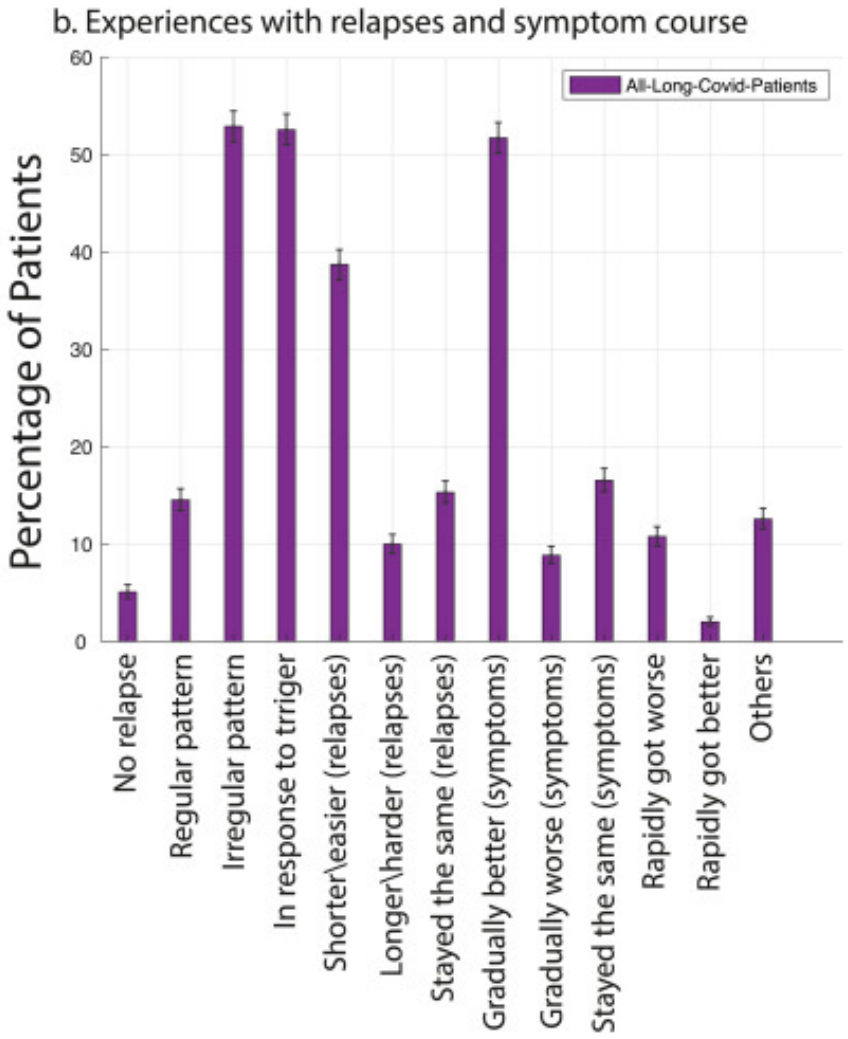
Most Common Relapse Triggers

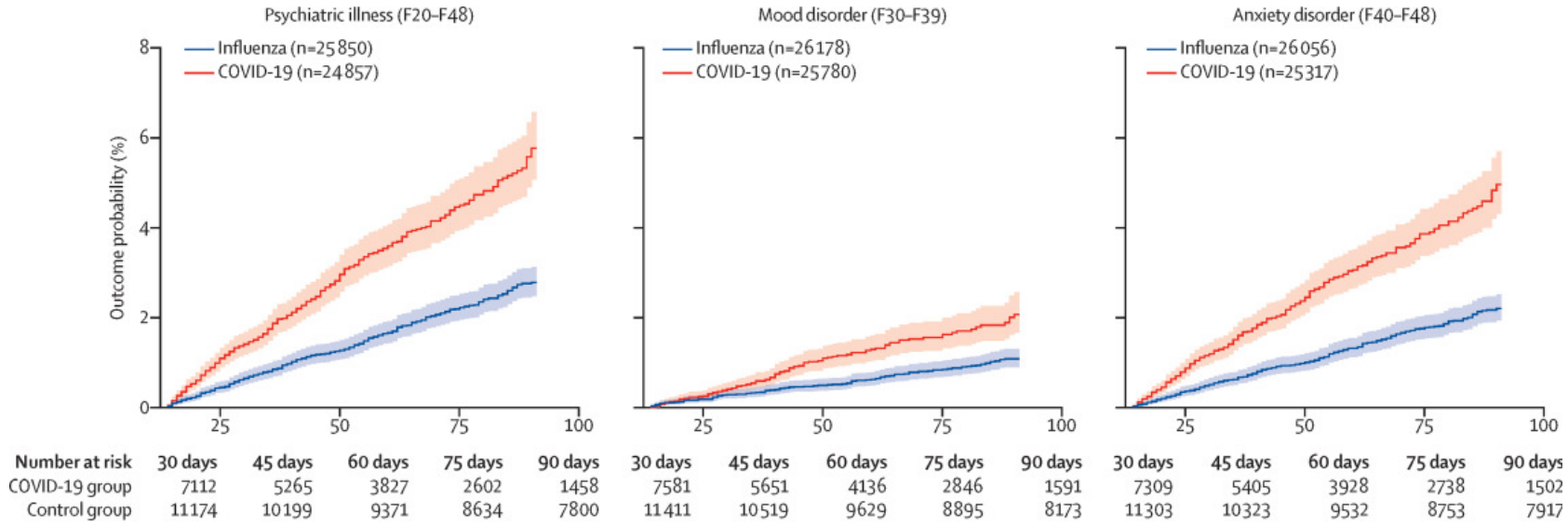
- Physical or cognitive exertion (86%)
- Stress (69%)
- Dehydration (49%)
- Weather changes (37%)
- Consuming large meals (28%)
- Premenstrual period (22%)
- Alcohol consumption (22%)



Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact
Patient-Led Research Collaborative Davis, et al, 2021 https://doi.org/10.1101/2020.12.24.20248802

Mental Health

First time MH diagnoses increase after COVID-19 Infection



Number at risk	30 days	45 days	60 days	75 days	90 days	30 days	45 days	60 days	75 days	90 days	30 days	45 days	60 days	75 days	90 days
COVID-19 group	7112	5265	3827	2602	1458	7581	5651	4136	2846	1591	7309	5405	3928	2738	1502
Control group	11174	10199	9371	8634	7800	11411	10519	9629	8895	8173	11303	10323	9532	8753	7917

- Taquet M, The Lancet Psychiatry VOLUME 8, ISSUE 2, P130-140, FEBRUARY 01, 2021 https://doi.org/10.1016/S2215-0366(20)30462-4

Does long COVID cause anxiety?

Yes!

- Things that are most related to worse anxiety in long COVID are:
  - Impact of Long COVID on health
  - Financial concerns
  - Interpersonal conflict within the home or with other family members

Long COVID is NOT caused by anxiety or depression, although anxiety and depression are risk factors for long COVID and can make recovery more difficult. Assessment and treatment is a critical part of holistic care.

Does Long COVID affect people's ability to work?

Yes!

In one international study (and many others):

- 45.2% required a reduced work schedule compared to pre-COVID
- 22.3% were not working 7+ months after COVID.

Impacts of COVID-19 on ability to return to work:

- $$$ impact
- Stress
- Anxiety
- Family/Relationships

Treatment must address return to work plans.

Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact
Patient-Led Research Collaborative Davis, et al, 2021 https://doi.org/10.1101/2020.12.24.20248802

Evaluation and Management

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Remember…. Common Clinic Case

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- Feels anxious and hopeless - worried that he will never recover. Unable to return to work.
- **Says previous clinicians did not believe his symptoms were real.**

Common Outpatient Clinic Case

Physical Exam

- BP 130/80, P 101, RR 18, T 37, SpO2 99%
- Orthostatic vitals
  - Supine: BP 130/80, P 85
  - Sitting: BP 125/75, P 100
  - Standing: BP 120/70, P 120; reports feeling "dizzy"
- Gen: tired-appearing, NAD
- Pulm: CTAB
- Cardiac: slightly tachycardic at rest, normal S1 & S2, no m/r/g
- Ext: trace edema
- Psych: slightly anxious, PHQ 10, GAD 12
- Remainder of exam unremarkable

Broad Differential Diagnosis:

Cardiac / Pulmonary: CHF, COPD, Sleep Apnea

Endocrine/Metabolic: Hypo/hyper thyroid, adrenal insufficiency, renal disease, liver disease, electrolyte abnormalities, vitamin deficiencies (B12, folate, thiamine)

Gastrointestinal: malnutrition, food sensitivities

Heme/Onc: Anemia, malignancy

Infectious Disease: mononucleosis, lyme disease, HIV, HCV etc.

Immunologic / Rheumatologic: PMR, systemic lupus erythematosus, rheumatoid arthritis, other autoimmune conditions, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), etc.

MSK: fibromyalgia, chronic pain

Neurological: insomnia/circadian rhythm disturbance, autonomic dysfunction/postural orthostatic tachycardia syndrome (POTS), CIDP, stroke

Psychological: depression, anxiety, PTSD, social isolation

Medications/Substances: benzodiazepines, antidepressants, muscle relaxants, antihistamines, beta-blockers, opioids, alcohol, marijuana, opioids, stimulants

Broad Differential Diagnosis:

Cardiac / Pulmonary – CHF, COPD, Sleep Apnea

Endocrine/Metabolic – Hypo/hyper thyroid, adrenal insufficiency, Renal disease, Liver disease, electrolyte abnormalities, vitamin deficiencies (B12, folate, thiamine)

Caution: Do NOT formally diagnose PASC without ruling out other etiologies

Neurological – insomnia/circadian rhythm disturbance, autonomic dysfunction/postural orthostatic tachycardia syndrome (POTS), CIDP, stroke

Psychological – Depression, anxiety, PTSD, Social isolation

Medications/Substances – Benzodiazepines, antidepressants, muscle relaxants, antihistamines, beta-blockers, opioids, alcohol, marijuana, opioids, stimulants

Postural Orthostatic Tachycardia Syndrome

Caution with labeling people post COVID with “POTS” and entering the “downward spiral” of decreasing activity, deconditioning and worsening symptoms.

HR and BP instability after COVID tend to improve and often resolve with time.

Meredith Bryarly et al. *J Am Coll Cardiol* 2019; 73:1207-1228.

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Clinical Guidance | Free Access

Multi-disciplinary collaborative consensus guidance statement on the assessment and treatment of autonomic dysfunction in patients with post-acute sequelae of SARS-CoV-2 infection (PASC)

Svetlana Blitshteyn MD, Jonathan H. Whiteson MD, Benjamin Abramoff MD, MS, Alba Azola MD, Matthew N. Bartels MD, MPH ... See all authors

First published: 28 September 2022 | https://doi.org/10.1002/pmrj.12894

Funding information: American Academy of Physical Medicine and Rehabilitation

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Svetlana Blitshteyn MD, Jonathan
Alba Azola MD, Matthew N. Barte

First published: 28 September 20

Funding information: American

No.	Autonomic dysfunction assessment statement
1	Clinicians should conduct a full patient history including a review of predisposing comorbidities, prior autonomic symptoms or disorders, relevant hospitalizations, and timeline of symptom evolution The patient history should address: • Most disabling symptoms/signs that may be autonomic in nature: dizziness, lightheadedness, palpitations, presyncope, syncope, orthostatic intolerance, exercise intolerance, cognitive dysfunction, and fatigue (see Table 2) • Medication history: evaluate for medications that may impact symptoms, signs or assessment parameters (i.e., medications with side effects, such as orthostatic intolerance, orthostatic hypotension, or resting or postural tachycardia; these may include anti-hypertensive, anti-cholinergic, and stimulant medications) • Social history of previous and current substance use, current diet, fluid and salt intake, exercise routine, if any, employment status, and psychological stressors • Family history of autonomic, autoimmune and post-COVID complications
2	Clinicians should characterize symptoms including onset (new acute or chronic), frequency, intensity, aggravating and alleviating factors, and impact on function and activities
3	Clinicians should conduct a neurologic exam, including sensory exam to look for signs of small fiber neuropathy (particularly the loss of pinprick or temperature sensation)

No.	Autonomic dysfunction assessment statement
	To evaluate for autonomic dysfunction, clinicians should perform a 10-min stand test recording heart rate and blood pressure while patients is supine and after standing 3, 5, 7 and 10 min. Consider obtaining a tilt table test in symptomatic individuals with a negative 10-min stand test
4	Recommended initial laboratory tests in individuals with suspected autonomic dysfunction including: CBC, CMP, TFT, vitamin B12, ferritin, morning cortisol, ANA, ESR, CRP • Consider obtaining a D-dimer to assess for pulmonary embolism in the appropriate clinical setting
5	Clinicians should consider obtaining a pulse oximetry at rest and with exertion/activity to rule out persistent hypoxemia, ECG, echocardiogram, and ambulatory cardiac monitoring with: • Holter monitor for palpitations and tachycardia occurring daily • Cardiac event monitor for recurrent palpitations, tachycardia, or syncope occurring less than daily Further cardiac evaluation may be warranted as per the PASC Collaborative Cardiovascular Complications Consensus Guidance Statement[18]
6	Where diagnosis is uncertain or symptoms are progressing, consider a referral to an autonomic specialist for more detailed assessment including autonomic function tests such as Valsalva maneuver, deep breathing test, quantitative sudomotor axon reflex test (QSART), and a skin biopsy for evaluation of small fiber neuropathy

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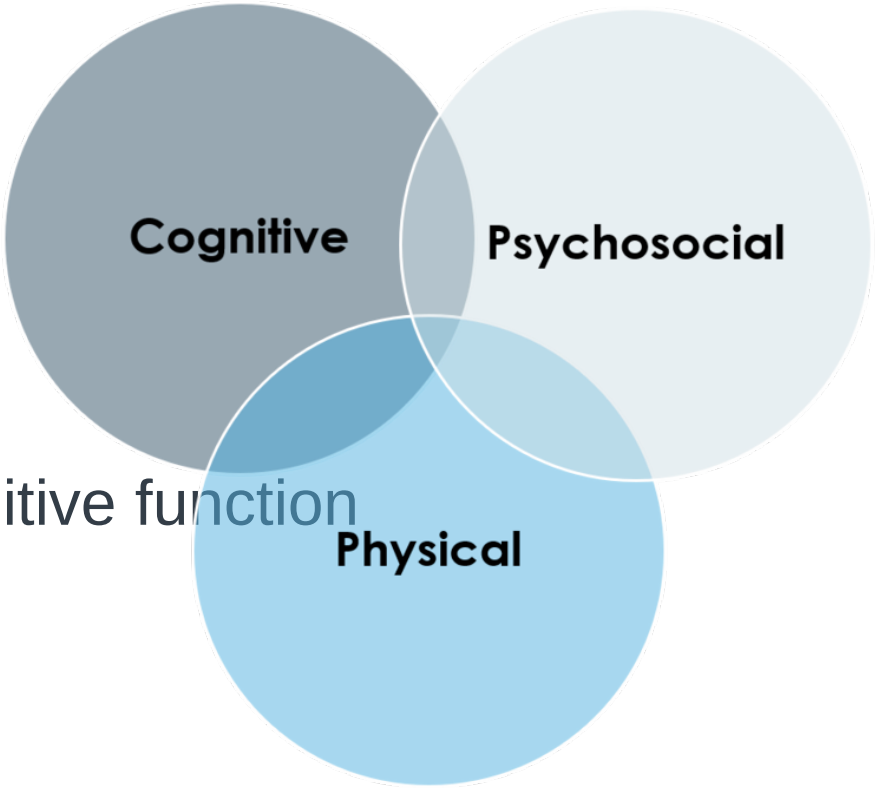
Funding information: American Academy of Physical Medicine and Rehabilitation

No.	Autonomic dysfunction in PASC treatment recommendations
1	For individuals diagnosed with autonomic dysfunction, provide education on etiology and management including identification of exacerbating and remitting factors
2	For individuals presenting with autonomic dysfunction and no evidence of post-COVID cardiovascular complications or other contraindications such as congestive heart failure, pericarditis, myocarditis, coronary artery disease or hypertension, start non-pharmacologic management including: • Increased fluid/salt intake: >3 L of fluid and >10 g of salt (4 mg of sodium) daily • Compression garments (waist-high stockings and/or abdominal binder) • Lifestyle management to include recognizing and avoiding symptom triggers and physical counterpressure maneuvers to mitigate orthostatic intolerance • Patient education, psychological support and coping skills • Consideration of discontinuation of medications or substances that may cause or exacerbate orthostatic intolerance, tachycardia or hypotension
3	For individuals with severe or persistent symptoms after a trial of non-pharmacologic measures, consider pharmacologic interventions • First-line medications: low-dose beta blockers (e.g. propranolol or atenolol); fludrocortisone; midodrine • Second-line medications: pyridostigmine; ivabradine; clonidine; methyldopa; modafinil, methylphenidate; selective serotonin reuptake inhibitors (SSRIs); serotonin and norepinephrine reuptake inhibitors (SNRIs); bupropion; droxidopa
4	Individuals with autonomic dysfunction may benefit from personalized autonomic rehabilitation program interventions to reduce fatigue and gradually improve exertional

UW MEDICINE REHABILITATION AND RECOVERY APPROACH

"WE FOCUS PATIENTS ON A PATH TO RECOVERY RATHER THAN A PATH TO LONG-LASTING DISABLEMENT"

- Achieve medical and emotional stability
- Help patients manage symptoms
- Help patients cope with changes in physical and cognitive function
- Focus on lifestyle changes to support recovery
- Engage patients in structured activity program to improve function and prevent relapses



A Very Brief (!) Overview of Rehabilitation Strategy

- **No universal treatment of post-COVID symptoms (yet!)**
  - Patients present very differently, so treatment must be tailored
  - Treatment should be symptom-based and holistic
  - Focus on safe and effective rehabilitation strategies for symptoms: self-management, behavioral strategies

- **Keep in mind alternative diagnoses/co-morbidities that can contribute to symptoms**

- **Validate concerns**
  - Acknowledge what we don't yet know
  - Encourage participation in research

A Very Brief (!) Overview of Rehabilitation Treatments

Reassurance and Hope

- Some symptoms existing up to 12 weeks is not unexpected
- Recovery continues for most after 12 weeks

Continuity of Care

- Generally follow-up every 1 to 2 months
- Contact point for post-COVID symptoms
- Try to minimize over-use of specialists and costly, ineffective treatments

Beware… Expansive $$ lab panels and work-ups, vitamins, support groups/social media

- It is not known if OTC vitamins/supplements and many other treatments are helpful, harmful, or have no effect on symptoms
- Positive and negatives of support groups: moderated groups preferable

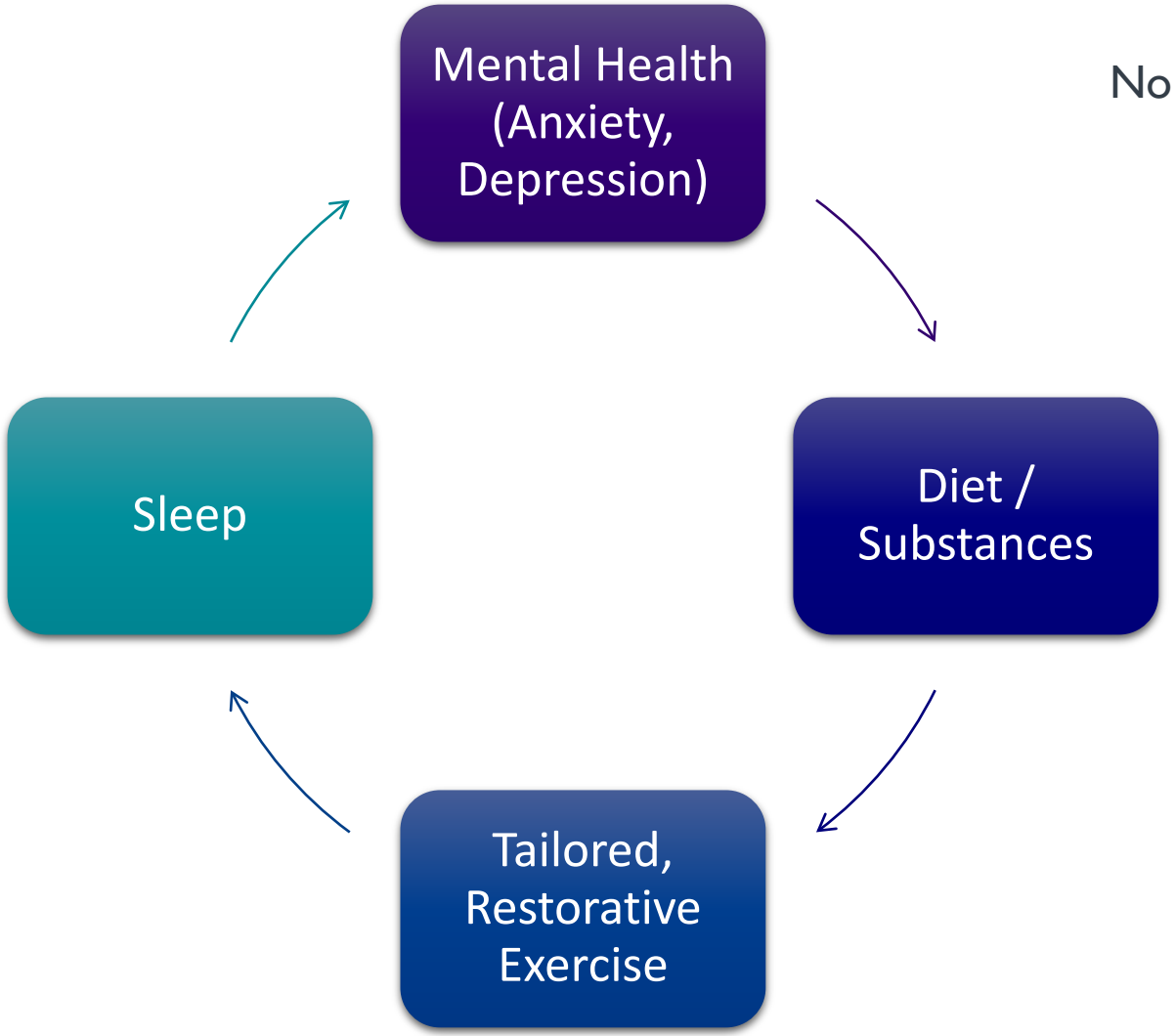
Long-Haul Covid Patients Put Hope in Experimental Drugs

People suffering from debilitating symptoms for months after getting sick with Covid are searching for relief

PASC Holistic Treatment Approach

Sleep a major contributor to fatigue (~45% of patients report insomnia)

- Assessment: PROMIS Sleep, STOP-Bang
- Sleep hygiene
- Consider short-term pharmacotherapy
  - Melatonin, Trazodone first line in our clinic
  - Cognitive behavioral therapy for insomnia (CBT-I) if available



No evidence re: ideal diet

- Anti-inflammatory
  - Few processed foods
  - Fewer calories from animal fats
  - Liberal fruits, vegetables and high-quality oils
  - Low sugar / processed flour / "energy drinks"
  - Drink enough water
- Substances (Significant sleep and mental health impacts)
  - Low or no alcohol
  - Avoid caffeine after noon, limit overall intake
  - Address other substance dependence

TELEMEDICINE REHAB PSYCHOLOGY LED GROUPS TO ADDRESS THE MOST COMMON PSYCHOLOGICAL AND BEHAVIORAL NEEDS OF OUR PATIENTS

Session 1: COVID/biopsychosocial model/introduce-teach breathing & relaxation

Session 2: Fatigue, pacing, energy management

Session 3: Sleep/sleep hygiene, cognitive functioning, pain

Session 4: Managing your care: communicating with providers, media/detecting misinformation, stigma

Session 5: Stress management: sources of stress/communication with family-employer/stress-mood/behavioral activation/self-talk/vigilance about symptoms

Session 6: Anxiety - breathlessness, dealing with uncertainty, mindfulness techniques

Medications

Currently, none approved for treatment of PASC, but some options for symptom management include:

- NSAIDs, Tylenol (pain)
- H1+H2 blockers (GI and allergy sx, other)
- SSRI/SNRIs (depression, anxiety, pain, cognition)
- Beta-blockers (autonomic dysfunction, inappropriate tachycardia)
- Low dose naltrexone (pain, brain fog)
  - Expensive, ? insurance coverage, compounding pharmacy

Long-Haul Covid Patients Put Hope in Experimental Drugs

People suffering from debilitating symptoms for months after getting sick with Covid are searching for relief

Ongoing Treatment Studies: clinicaltrials.gov

Curcumin/Boswellia/Serrata/Ascorbic Acid
Monoclonal Ab tx
Paxlovid
Homeopathic tx
Prospekta
Lyt-100 - Deupirfenidone
TENS
tDCS
Vitamin C drops
Inspiratory muscle Training
Physical Training
Cardiopulmonary rehab
AXA1125 – oral amino acid mixture
CBDRA60 – cannabidiol/Gigartina red algae
COVI-MS – stem cell tx
ExoFlo – stem cell infusion
S-1226 – bronchodilator and synthetic surfactant
BREATHE – virtual self management
Mobile app for rehab
Mindfulness
HEARTLOC: HR variability biofeedback
Metoprolol
Vortioxetine – antidepressant
Omega 3 supplement

<u>UW Research:</u>
RSLV-132 – RNA immune modulator
Project ECHO vs MDR clinic
Rehab psychology group sessions

Support For Disability and Work Accommodations

- All patients need to time to recover
- Relapses are common
- Working, stress, pushing too hard is the most common trigger for relapses and post exertional malaise
- Facilitating respite and / or reasonable re-entry back to work is enormously beneficial for quality-of-life and faster recovery
- Energy conservation strategies can help get people back to work!

Work accommodations for fatigue & brain fog

- Limited hours/adjust 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

Things I've learned about treating patients with Long COVID

No two people have the same symptoms or same course

We must listen to the patient's story to understand how to best treat

There is no single treatment for long COVID….yet

We do have many effective treatment strategies already – patients are getting better. There is hope!

COVID-19 lights everything on fire – there are many associated psychosocial stressors and consequences of COVID

Patients feel relieved when they find a doctor who understands long COVID

UW Post COVID Rehabilitation and Recovery Clinic at Harborview Medical Center

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UW Medicine