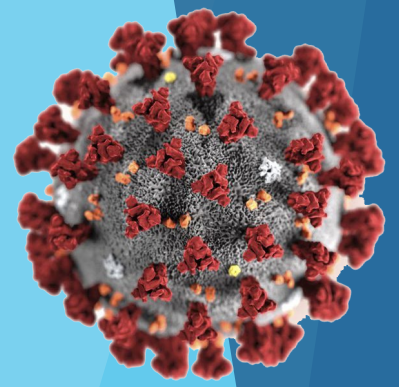
Long COVID's Impact on Patients, Workers & Society

Webinar Nov. 1st, 2023

https://healthconference.org

USA Health Watch



Post COVID Condition: The Clinical Lens

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Mayo Clinic

OUTLINE

Clinical presentation

Risk and prevalence

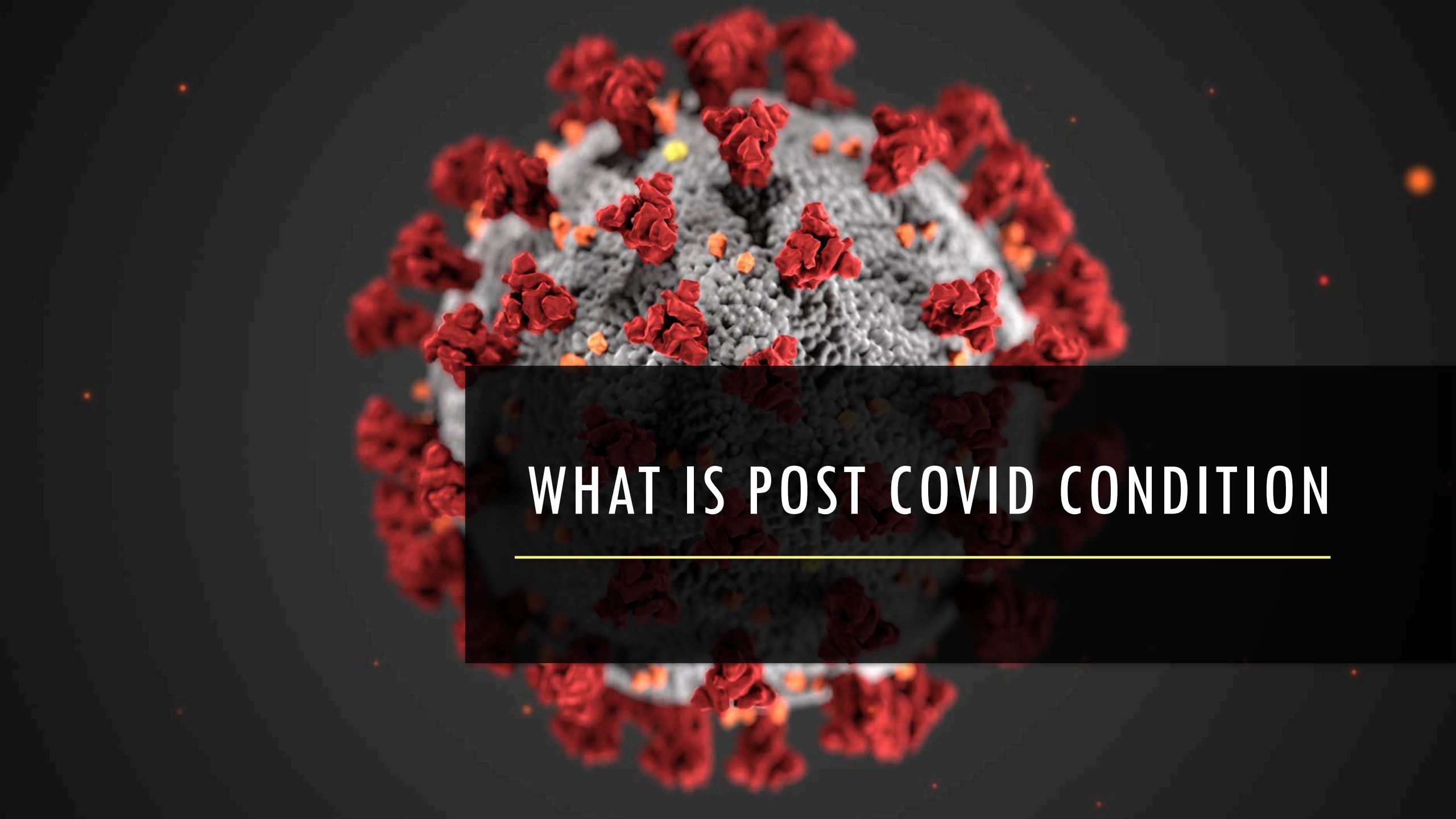
Biological plausibility

Treatment pearls

MAYO CLINIC POST COVID RECOVERY

COVID Activity Rehabilitation Program

- CARP
- Formalized June 2020
- 600-700 patients



WHAT IS POST COVID CONDITION

WHAT IS POST COVID CONDITION?

-No universal definition

World Health Organization – 10/6/2021

- A history of probable or confirmed SARS COV-2 infection
- Sx $\geq$ 3 months from onset of infection
- Sx $\geq$ 2 months
- Can't be explained by an alternative diagnosis

CDC Definition

- Call it "Post-COVID Conditions"
- $\geq$ 4 weeks from acute infection start (symptoms or test)

1. Organization WH. A clinical case definition of post COVID-19 condition by a Delphi consensus. Accessed 10/6, 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1
2. @CDCgov. Post-COVID Conditions: Information for Healthcare Providers. @CDCgov. Updated 2021-09-10T04:38:34Z. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/post-covid-conditions.html

CARP POPULATION

- Fatigue 80%
- Respiratory 59%
- Neurologic 59%
- Cognitive impairment 45%
- Sleep disturbance 30%
- Mental health sx 26%

Vanichkachorn G, Vanichkachorn.greg@mayo.edu, Newcomb R, et al. Post COVID-19 Syndrome (Long Haul Syndrome): Description of a Multidisciplinary Clinic at the Mayo Clinic and Characteristics of the Initial Patient Cohort. *Mayo Clinic Proceedings*. 2021;0(0)doi:10.1016/j.mayocp.2021.04.02

CARP POPULATION UNIQUE SX

- Tinnitus
- Prolonged loss of taste and smell
- Hair shedding (telogen effluvium)
- Syncope
- Sinus discomfort
- GI Symptoms

RISK FACTORS

Aug 2023

3094 patients

Severe/very severe acute COVID

Hospitalization

Female gender

Psychological stress

1. Munipalli B, Ma Y, Li Z, et al. Risk factors for post-acute sequelae of COVID-19: survey results from a tertiary care hospital. *J Investig Med. Aug 12 2023:10815589231190560. doi:10.1177/10815589231190560*

RISK FACTORS

August 2022

732 Patients

56% reported mild or asymptomatic acute infection

MAYO: 75% not hospitalized

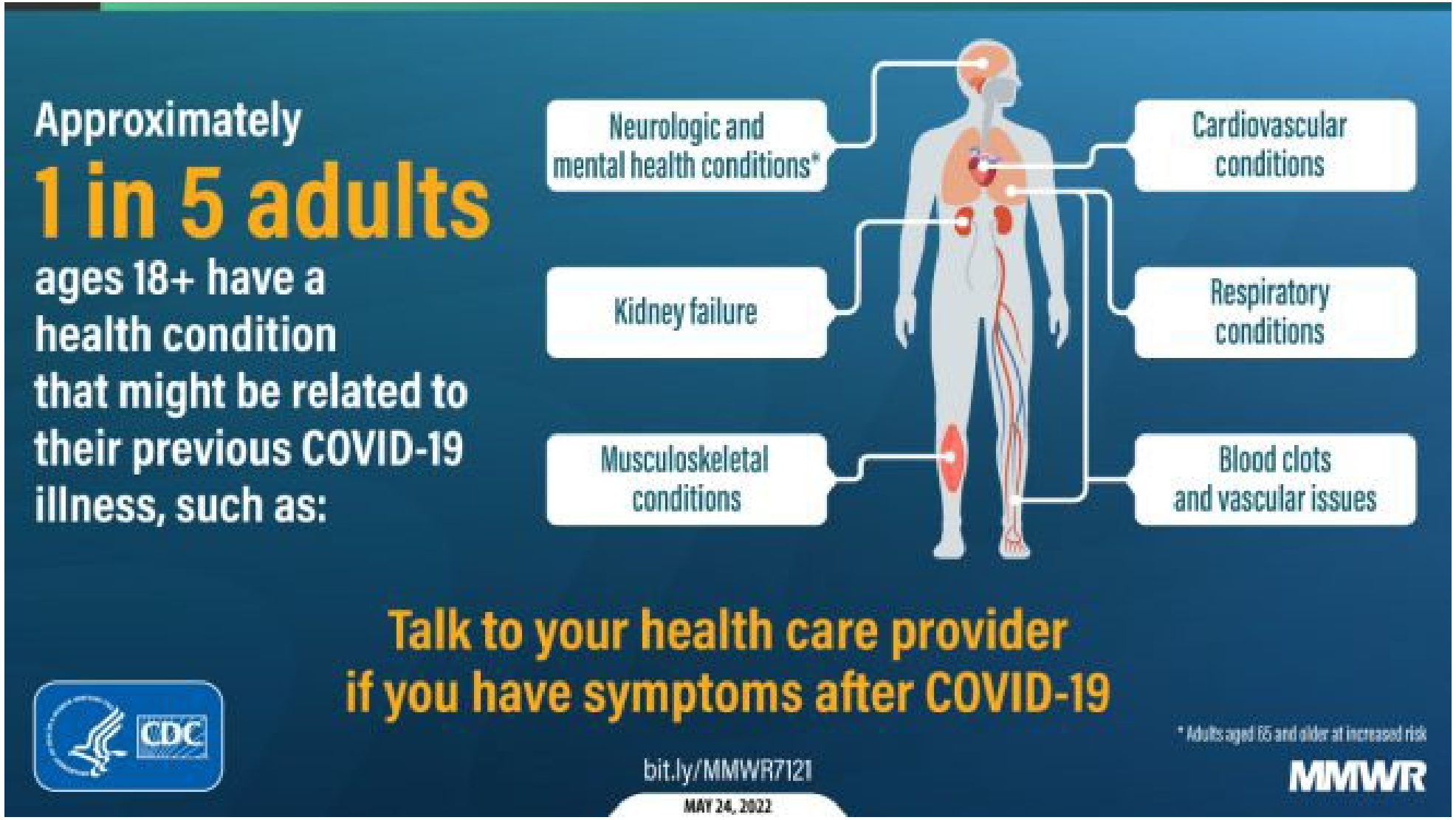
Group	Odds of Long COVID
Moderate infection	3.01 (95% CI 1.21, 7.47)
Severe infection	3.62 (95% CI 1.31, 10.03)

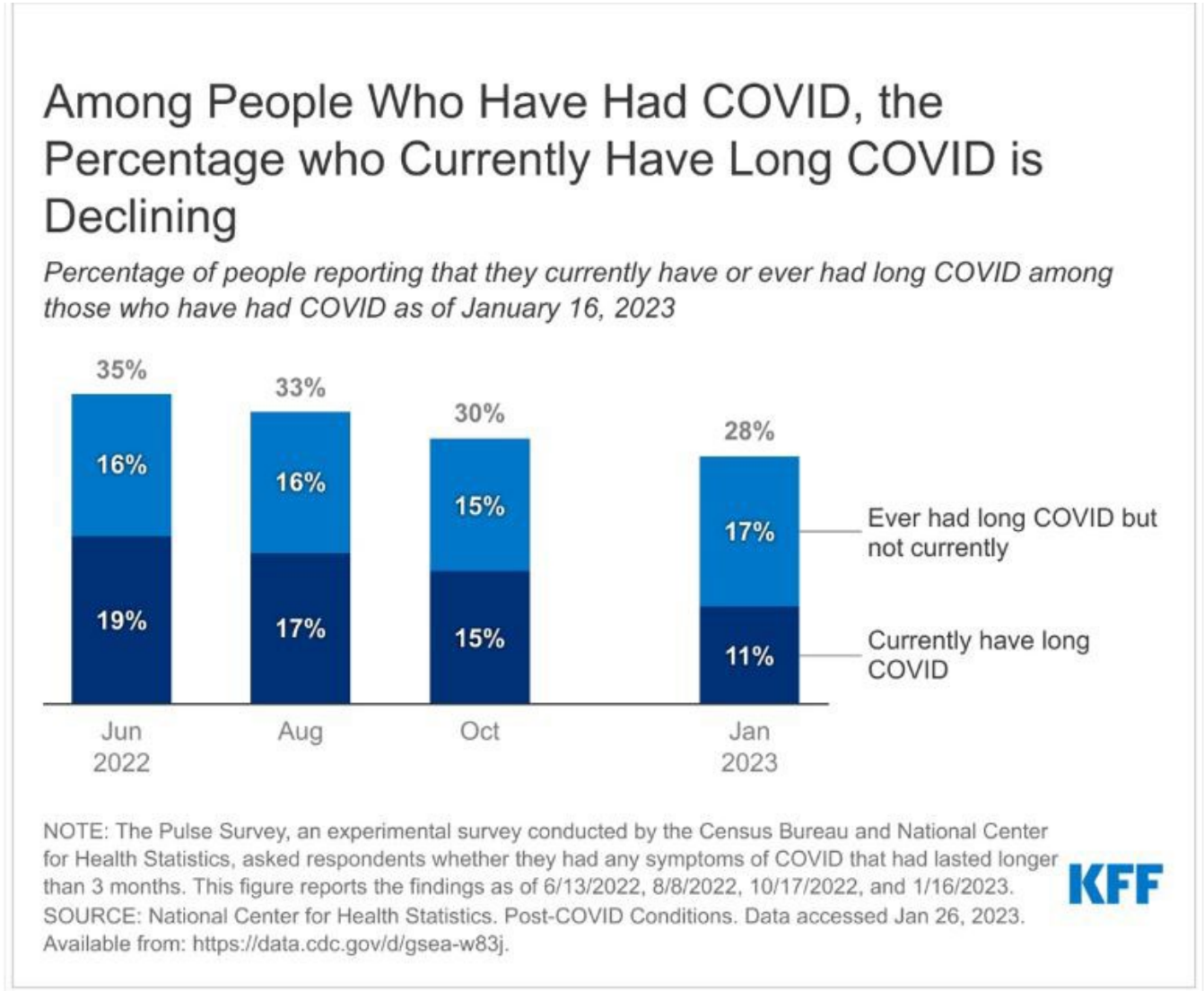
Moy FM, Hairi NN, Lim ERJ, Bulgiba A. Long COVID and its associated factors among COVID survivors in the community from a middle-income country-An online cross-sectional study. *PLoS One.* 2022;17(8):e0273364.

DOES VACCINATION MAKE A DIFFERENCE?

Symptom	Not vaccinated	Vaccinated	P-value
Abdominal pain*	77 (33.2%)	46 (18.8%)	**0.0003**
Anosmia	64 (27.6%)	44 (18.0%)	**0.0120**
Parosmia	70 (30.2%)	56 (22.9%)	**0.0701**
Chest pain/tightness	130 (56.0%)	105 (42.9%)	**0.0040**
Dizziness when standing	129 (55.6%)	108 (44.1%)	**0.0119**
Numbness & tingling	109 (47.0%)	84 (34.3%)	**0.0047**
Shortness of breath	142 (61.2%)	122 (49.8%)	**0.0122**
Spells/tremors	64 (27.6%)	48 (19.6%)	**0.0395**
Weakness	146 (62.9%)	123 (50.2%)	**0.0051**

1.Vanichkachorn G, Gilman E, Ganesh R, et al. Potential reduction of post-acute sequelae of SARS-CoV-2 symptoms via vaccination. *J Investig Med. Aug 23 2023:10815589231191812. doi:10.1177/10815589231191812*


Approximately
1 in 5 adults
ages 18+ have a health condition that might be related to their previous COVID-19 illness, such as:
Neurologic and mental health conditions*
Kidney failure
Musculoskeletal conditions
Cardiovascular conditions
Respiratory conditions
Blood clots and vascular issues
Talk to your health care provider if you have symptoms after COVID-19
CDC
* Adults aged 65 and older at increased risk
bit.ly/MMWR7121
MAY 24, 2022
MMWR



1.KFF. Rates of Long COVID in the U.S. Have Declined Since June of 2022 | KFF. https://www.kff.org/coronavirus-covid-19/press-release/rates-of-long-covid-in-the-u-s-have-declined-since-june-of-2022/

34% impaired ADLS

82% impaired IADLS

63% returned to work in some form

- Average time to between infection and presentation was 3 months
- 46% (29/63) were back at baseline work

CARP POPULATION FUNCTION

PROGNOSIS

-530 patients at Weil Cornell Medicine

-Follow up at12 months

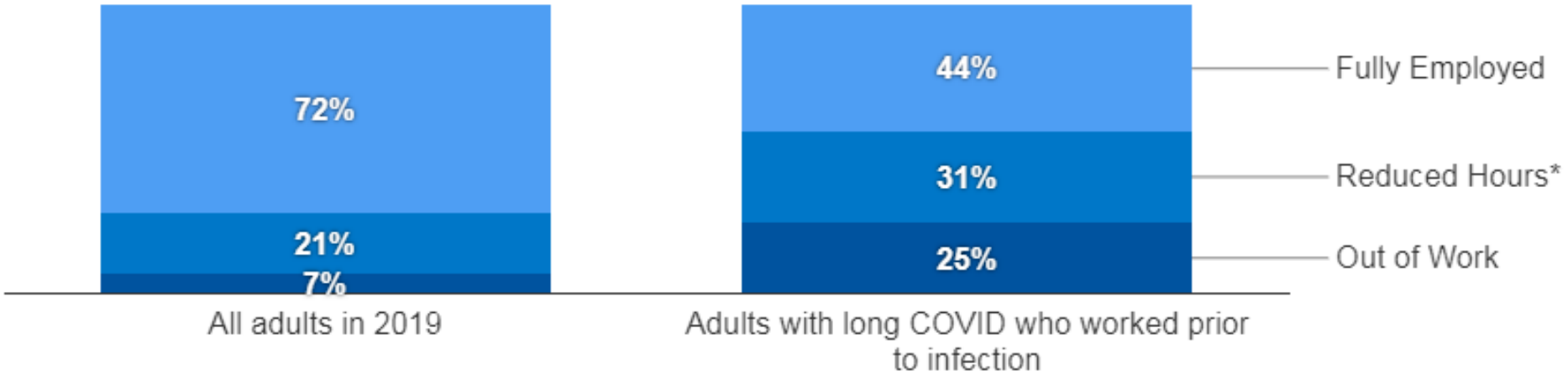
	12 months
Worse health	41.5%
Persistent symptoms	44.2%
Trouble lifting/carrying groceries	36.5%
Limited ability to climb a flight of stairs	38.1%
Troubles walking one block	22.1%

Adapted from Huang L, Yao Q, Gu X, et al. 1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study. *The Lancet*. 08/28/2021 2021;398(10302):747-758. doi:10.1016/s0140-6736(21)01755-4

Figure 2

Fewer than Half of Working Age Adults with Long COVID Who Worked Prior to Infection Work Full-Time After Infection

Employment status of working age adults (percent of population) for all adults in 2019 (Current Population Survey) and for survey respondents who worked prior to COVID infection (average of two surveys)



NOTE: KFF Analysis of: Katie Bach, "Is 'Long COVID' Worsening the Labor Shortage?" Brookings (Jan 1, 2022); Hannah E. Davis and others, "Characterizing Long COVID in an International Cohort: 7 Months of Symptoms and Their Impact, The Lancet, v. 38 (August 1, 2021); Workers' Experiences of Long COVID: A TUC Report (June 2021); and US BLS Labor Force Statistics from the Current Population Survey (2019).

PNG

KFF

DEJA VU

1918 Spanish Flu

- 1000 patients, 20% had ongoing symptoms

2016 Ebolavirus

- Fatigue in 28%

Epstein-Barr virus

- Fatigue 38% at 2 months

SARS 2003

- Fatigue in 60% at 12 months

1. Post-viral fatigue and COVID-19: lessons from past epidemics
2. Post-COVID-19 fatigue as a major health problem: a cross-sectional study from Missouri, USA

PERSISTENT VIRAL PROTEINS

Feb 2023

+/-PASC (n=33/14)

Absent in controls

PASC+ levels similar to acute infection

No difference in vaccination status

	PASC-	PASC+
Viral RNA	28%	59%
Spike Protein	28%	64%
Both present?	0%	33%

1.Craddock V, Mahajan A, Spikes L, et al. Persistent circulation of soluble and extracellular vesicle-linked Spike protein in individuals with postacute sequelae of COVID-19. *J Med Virol. Feb 2023;95(2):e28568. doi:10.1002/jmv.28568*

LACTATE DEHYDROGENASE

Sep 2023 Meta analysis

46 studies/8289 participants

Inflammatory marker

Associated with pulmonary fibrosis

Elevated LDH associated with:

- Respiratory PCC
- Cardiac PCC

1.Udeh R, Utrero-Rico A, Dolja-Gore X, Rahmati M, Mc EM, Kenna T. Lactate dehydrogenase contribution to symptom persistence in long COVID: A pooled analysis. *Rev Med Virol. Sep 14 2023:e2477. doi:10.1002/rmv.2477*

IMMUNE SYSTEM CHANGES AND BRAIN FOG

October 2023

Compared NC- and NC+

1642 patients

60% reported NC+

Noted Risk Factors

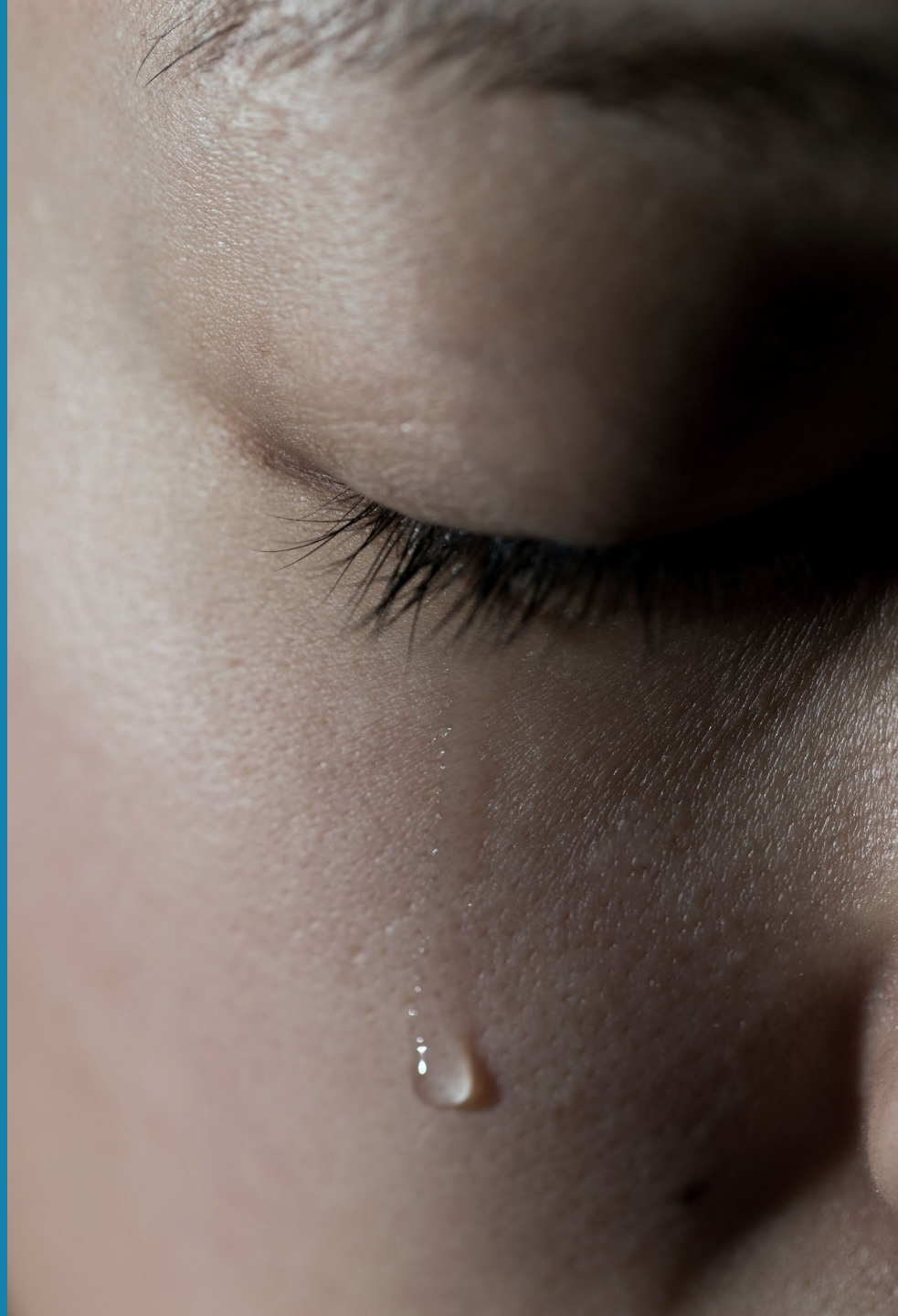
- Preexisting mental health conditions
- Female gender
- 45-65 age

	Without BF	With BF	P value
IgG	10.91	10.05	**<0.0001**
IgG1	5.9	5.3	**<0.0001**
IgG3	0.73	0.54	**0.006**
CRP	4.8	4.6	0.7

1.Lam GY, Damant RW, Ferrara G, et al. Characterizing long-COVID brain fog: a retrospective cohort study. *J Neurol. Oct 2023;270(10):4640-4646. doi:10.1007/s00415-023-11913-w*

COUNTER EVIDENCE

- Aug 2022
- 171 patients
- Rare objective evidence
- Elevated levels of somatization
- Associated with pre-existing psychiatric conditions



TREATMENT PROCESS OVERVIEW

Post Acute Phase (0-4 weeks post infection)

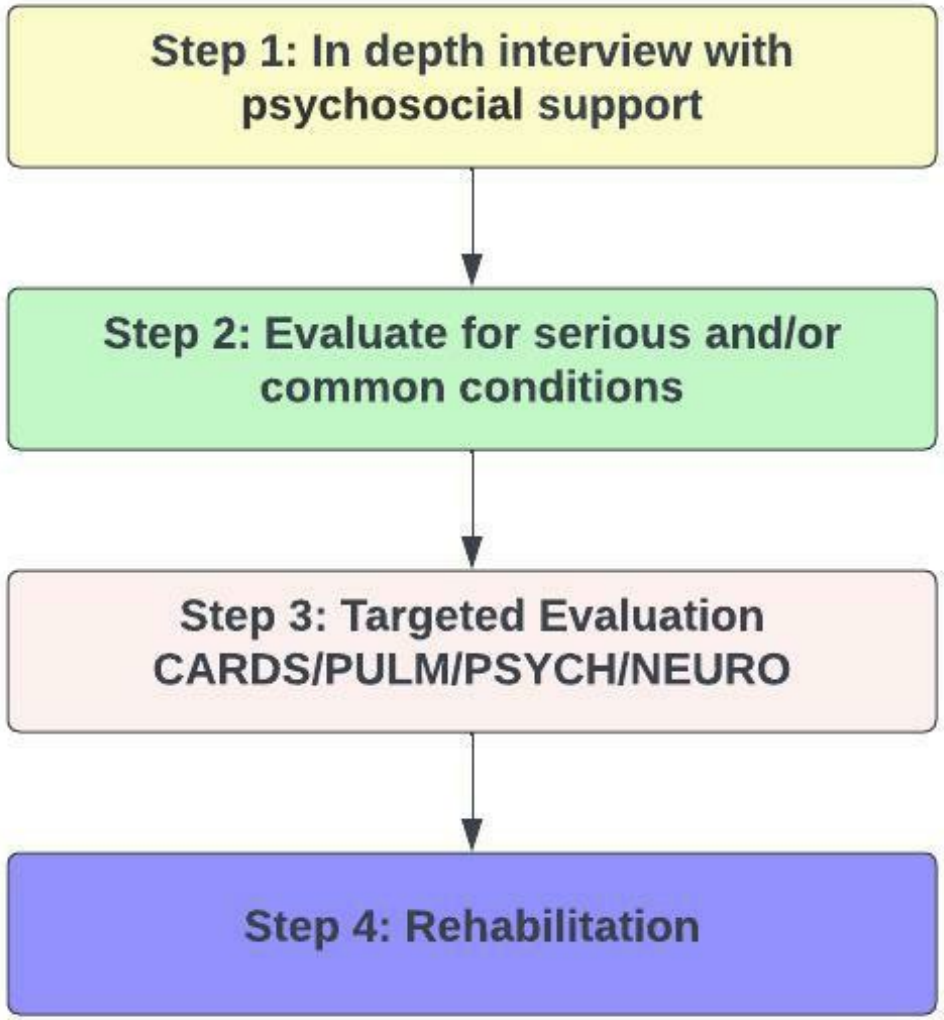
-Check for complications
-Ensure hydration and nutrition
-Educate on paced activity
-Address return to work

Early PCS/PASC Phase 5-12 weeks

-Continue graded activity increases, minimizing post exertional malaise
-Addtional testing and treatment as needed
-Monitor functional improvements
-Address return to work

PCS/PASC Phase >12 weeks

-Possible longer recovery course, up to a year
-Develop coping skills
-Education on central sensitization
-Uses experts in chronic fatigue and fibromyalgia


Step 1: In depth interview with psychosocial support
Step 2: Evaluate for serious and/or common conditions
Step 3: Targeted Evaluation CARDS/PULM/PSYCH/NEURO
Step 4: Rehabilitation

STEP 1: PSYCHOSOCIAL SUPPORT

-Patients feel “lost”

-Guilt/self doubt/fear

-Clinical depression/anxiety/PTSD

LISTEN AND VALIDATE

Li Z, Zheng C, Duan C, et al. Rehabilitation needs of the first cohort of post-acute COVID-19 patients in Hubei, China. *Eur J Phys Rehabil Med.* 2020;56(3):339-344

STEP 2: INITIAL DIAGNOSTICS

CBC

CMP

Thyroid

Iron studies

Vitamin B12

HgbA1c

First 100 patients

Tests performed	Abnormal tests
29 echocardiograms	13.8% (n=4)
28 pulmonary function tests	25.0% (n=7)
35 chest x-rays	2.9% (n=1)
21 autonomic reflex test (tilt and QSART)	57.1% (n=12)

DIAGNOSTICS

STEP 3: TARGETED EVALUATIONS

COMMON CONDITIONS WITH LONG COVID

Cardiovascular

- myocarditis/ pericarditis
- high blood pressure

Respiratory

- shortness of breath
- pulmonary fibrosis

Neurological

- headaches
- prolonged loss of taste and smell
- autonomic dysfunction such as postural tachycardia syndrome

Mental health

- anxiety
- depression
- PTSD

TARGETED EVALUATION: CARDIAC

Evaluation

- ECG
- Echocardiogram
- Cardiac MRI
- CPET (caution)

Most Common:

- Myocarditis
- New HTN
- Pericarditis

Have not seen more serious cardiac conditions

TARGETED EVALUATION: PULMONARY

Dyspnea can occur for months after coronavirus

Delay evaluation until 12 weeks

Earlier if pre-existing lung disease

Evaluation

- Chest CT
- Pulmonary function test
- Dec DLCO and pulmonary fibrosis

Tx with inhalers and pulmonary rehab

Barker-Davies RM, O'Sullivan O, Senaratne KPP, et al. The Stanford Hall consensus statement for post-COVID-19 rehabilitation. *Br J Sports Med*. Aug 2020;54(16):949-959. doi:10.1136/bjsports-2020-102596

TARGETED EVALUATION: PSYCH

Psychiatry (Mind AND Body)

- Therapy
- Psychiatry consult
- SNRIs – Duloxetine, Venlafaxine
- SSRISs – Sertaline, Fluvoxamine, Prozac
- Anti-anxiety – Hydroxyzine

Sleep

- Sleep hygiene
- Melatonin 5mg
- Overnight sleep study
- CPA

THE BIG BUCKET TARGETED EVALUATION: NEURO - GENERAL

Headaches

- Usual headache tactics
- Optimize sleep
- Appetite/hydration
- Medications
- Headache consult

Tremor

- Propranolol

Taste/Smell difficulties

- Dysfunction in 36.6%
- 5% still having sx at 6 months
- Rec olfactory retraining

-KH W, GCY L, KCF P, et al. Ocular surface disturbance in patients after acute COVID-19. *Clinical & experimental ophthalmology*. 02/26/2022 2022;doi:10.1111/ceo.14066
-JR L, CM C-E, E B, et al. Prevalence and 6-month recovery of olfactory dysfunction: a multicentre study of 1363 COVID-19 patients. *Journal of internal medicine*. 2021 Aug 2021;290(2)doi:10.1111/joim.13209

OLFACTORY RETRAINING

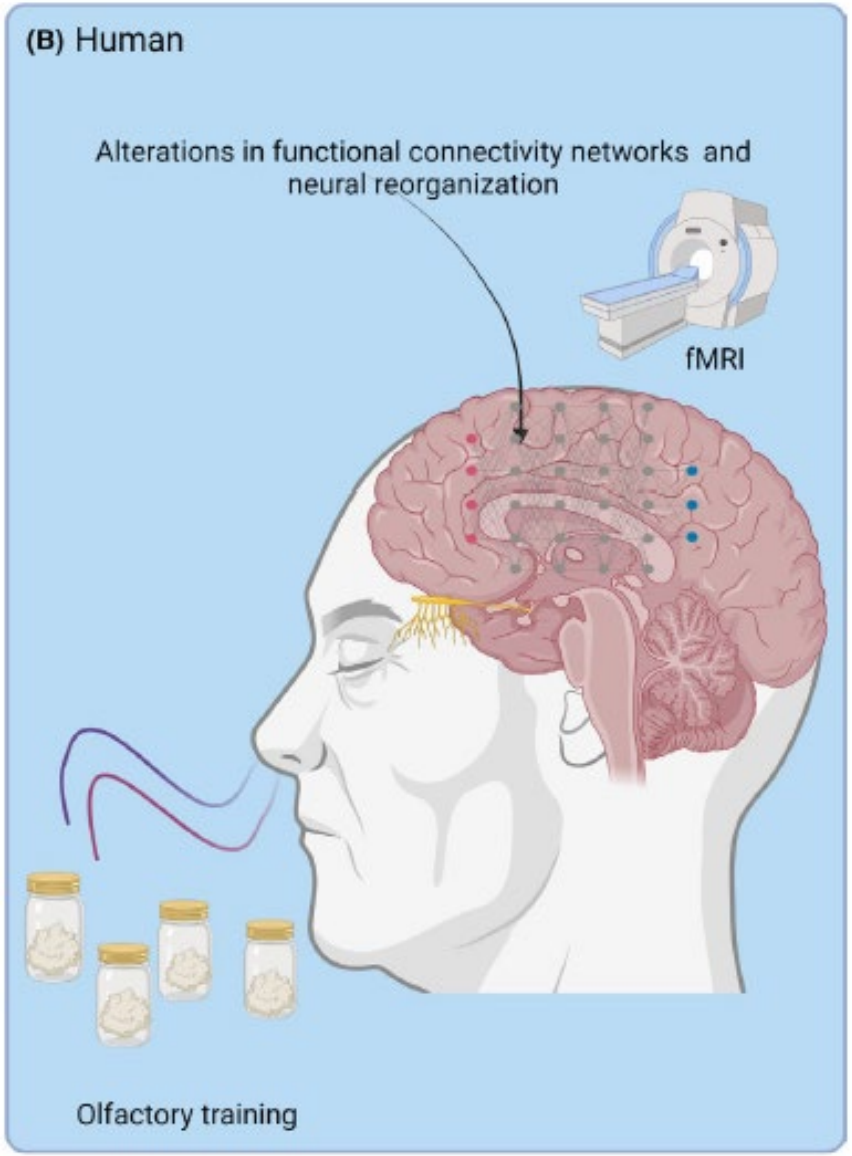
Rose, eucalyptus, lemon, clove

20 seconds

Twice a day – morning and before bed

Three months

Also improve cognition?



Ojha P, Dixit A. Olfactory training for olfactory dysfunction in COVID-19: A promising mitigation amidst looming neurocognitive sequelae of the pandemic. *Clin Exp Pharmacol Physiol. 2022;49(4):462-473.*

TARGETED EVALUATION: NEURO - DYSAUTONOMIA


Balance issues/Dizziness


Tachycardia


Pain


Brain fog


Shortness of breath


Exercise intolerance


Sleeping problems


Mood swings

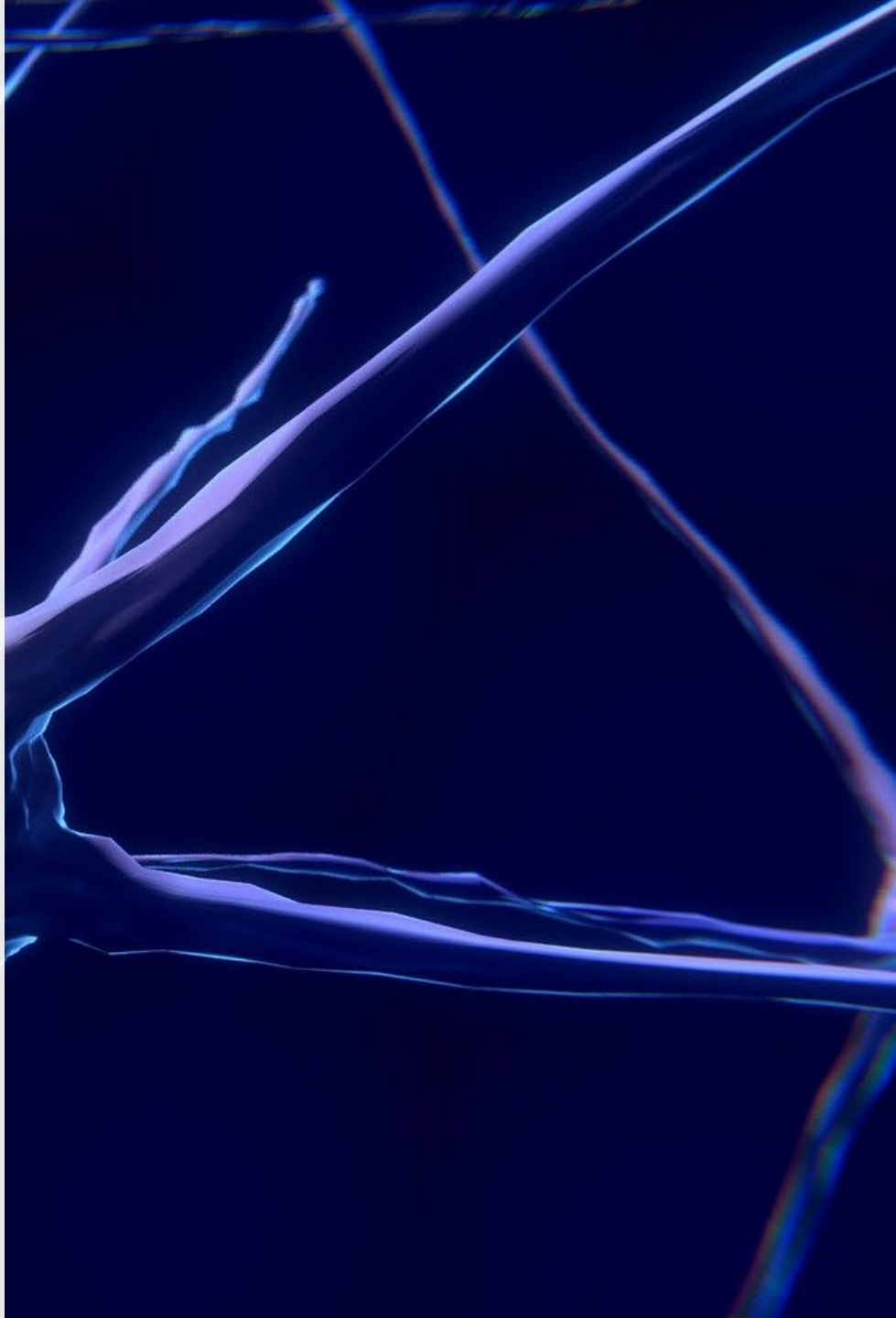

Etc…..

DYSAUTONOMIA

-Autonomic dysfunction was seen in SARS

-POTS preceded by viral illness in 21-40%

-Case reports of POTS in COVID-19



-Miglis MG, Prieto T, Shaik R, Muppidi S, Sinn DI, Jaradeh S. A case report of postural tachycardia syndrome after COVID-19. *Clin Auton Res*. 10 2020;30(5):449-451. doi:10.1007/s10286-020-00727-9

-Kanjwal K, Jamal S, Kichloo A, Grubb BP. New-onset Postural Orthostatic Tachycardia Syndrome Following Coronavirus Disease 2019 Infection. *J Innov Card Rhythm Manag.* 2020;11(11):4302-4304

DYSAUTONOMIA TESTING

-Autonomic Reflex Test

- Tilt Table
- QSART

-Additional Options

- COMPASS-31 Survey
- Epidermal nerve fiber biopsy
- Thermoregulatory sweat test

STEP 4: REHABILITATION

-COVID-19 Fatigue

- 41% reduced exercise capacity
- Hard to walk any distance
- Trouble with stairs
- Limited lifting
- Limited screen tolerance

-Rooney S, Webster A, Paul L. Systematic Review of Changes and Recovery in Physical Function and Fitness After Severe Acute Respiratory Syndrome-Related Coronavirus Infection: Implications for COVID-19 Rehabilitation. *Phys Ther.* 2020;100(10):1717-1729

-George PM, Barratt SL, Condliffe R, et al. Respiratory follow-up of patients with COVID-19 pneumonia. *Thorax*. Aug 2020;doi:10.1136/thoraxjnl-2020-215314

REHABILITATION

Post Exertional Malaise

Also seen in ME/CFS

After physical stress

- 30% reported fatigue, flu like sx, muscle pain

Graded exercise

- Negative effect in 54-74% of patients

-Geraghty K, Hann M, Kurtev S. Myalgic encephalomyelitis/chronic fatigue syndrome patients' reports of symptom changes following cognitive behavioural therapy, graded exercise therapy and pacing treatments: Analysis of a primary survey compared with secondary surveys. *J Health Psychol.* 2019;24(10):1318-1333

-Chu L, Valencia IJ, Garvert DW, Montoya JG. Deconstructing post-exertional malaise in myalgic encephalomyelitis/ chronic fatigue syndrome: A patient-centered, cross-sectional survey. *PLoS One.* 2018;13(6):e0197811.

REHABILITATION

-Rehabilitation ≠ exercise

-Use Adaptive Paced Therapy

"START LOW AND GO SLOW"

Individualized

- **Use personal experiences**
- Gradual increases (i.e., 10 min to 13 min of walking)
- Applies to both physical and mental activities

Not simply "stop when it hurts"

TABLE 2. Treatment of Post-COVID Conditions[a]

Categories	Examples	Comments	Indications	Doses
Medications	Duloxetine	Serotonin-norepinephrine reuptake inhibitor	Useful for treating headaches, neuropathic symptoms, mood disorders, and poor sleep	Start 20 mg by mouth daily for 1 week, then 40 mg daily for 1 week, then 60 mg daily
	Nortriptyline	Tricyclic antidepressant	Useful for treating neuropathic symptoms, low mood, and poor sleep	Start 25 mg by mouth at bedtime and titrate to effect
	Trazadone	Antagonizes serotonin 5-HT2A/C and α_1-adrenergic receptors; inhibits serotonin reuptake	Useful for treating poor sleep	25-50 mg by mouth at bedtime
	Gabapentin	Blocks voltage-dependent calcium channels, modulating excitatory neurotransmitter release	Useful for treating neuropathic symptoms and poor sleep	Start 300 mg by mouth for 1 day, then 300 mg twice daily for 1 day, then 300 mg 3 times daily, then titrate to effect
	Naltrexone[b]	Antagonizes various opioid receptors	Has demonstrated some success for treating postviral fatigue at a dose of 4.5 mg	3-6 mg by mouth at bedtime
	Aripiprazole[b]	Antagonizes D2 and serotonin 5-HT1A/5-HT2A receptors	Has demonstrated some success for treating postviral fatigue	1-2 mg by mouth daily

1. M, R G, RT H, TJ B. Post-COVID Conditions. *Mayo Clinic proceedings. 2023 Jul 2023;98(7)doi:10.1016/j.mayocp.2023.04.007*

NALTREXONE

Low dose

Impacts immune system

- Chron's Disease
- Fibromyalgia
- Multiple Sclerosis

Ireland study

- 36 patients
- 1-3mg over three months
- Improvement in function, energy, sleep, concentration and **pain**

Limits

- No control
- Not blinded
- Small population

O'Kelly B, Vidal L, McHugh T, Woo J, Avramovic G, Lambert JS. Safety and efficacy of low dose naltrexone in a long covid cohort; an interventional pre-post study. *Brain Behav Immun Health.* 2022;24:100485.

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https://www.mayoclinic.org/appointments

Appointment number: 507-538-1377

https://connect.mayoclinic.org/blog/post-covid-recovery/