

## **Learning Objectives**

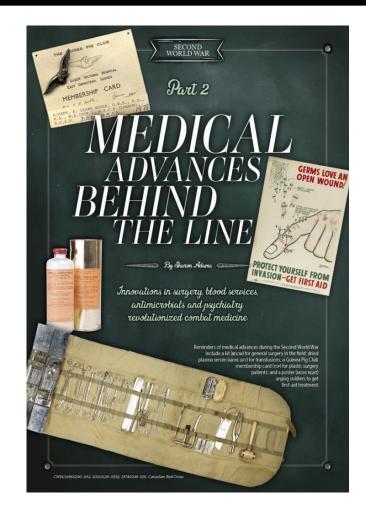
- Learning Objectives:
- 1. Appreciate the scientific/medical definition of Long COVID
- 2. Be familiar with the known frequency of occurrence of Long COVID
- 3. Understand the wide-ranging clinical presentations of people experiencing Long COVID
- 4. Appreciate the impact of Long COVID on physical performance/functional abilities.
- 5. Recognize the value of physical rehabilitation on improving physical performance and functional ability in people with Long COVID
- 6. Understand the appropriate strategies that should be used to adapt exercise prescription to serve people with Long COVID





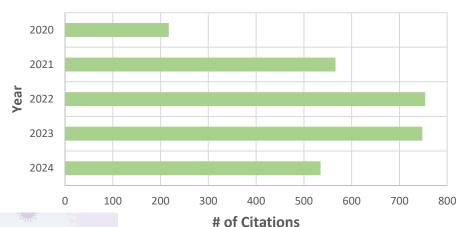
# Medical Advances Caused by WWII

- Penicillin
- Blood Transfusions
- Advancement in Surgery
- Dental Health
- Mobile Medical Units
- Amputation Techniques & Prosthetics



## Long COVID on PubMed

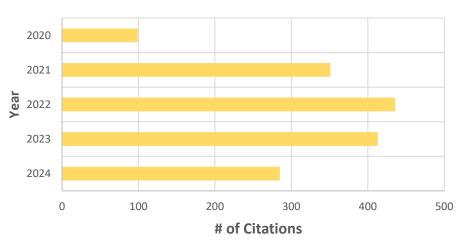
#### **Long COVID Rehabilitation**







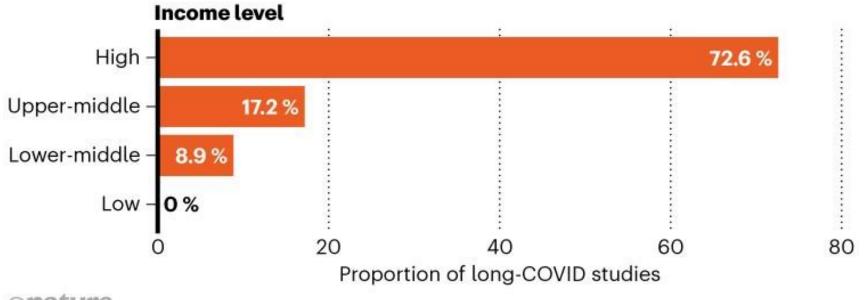
#### **Long COVID Exercise**

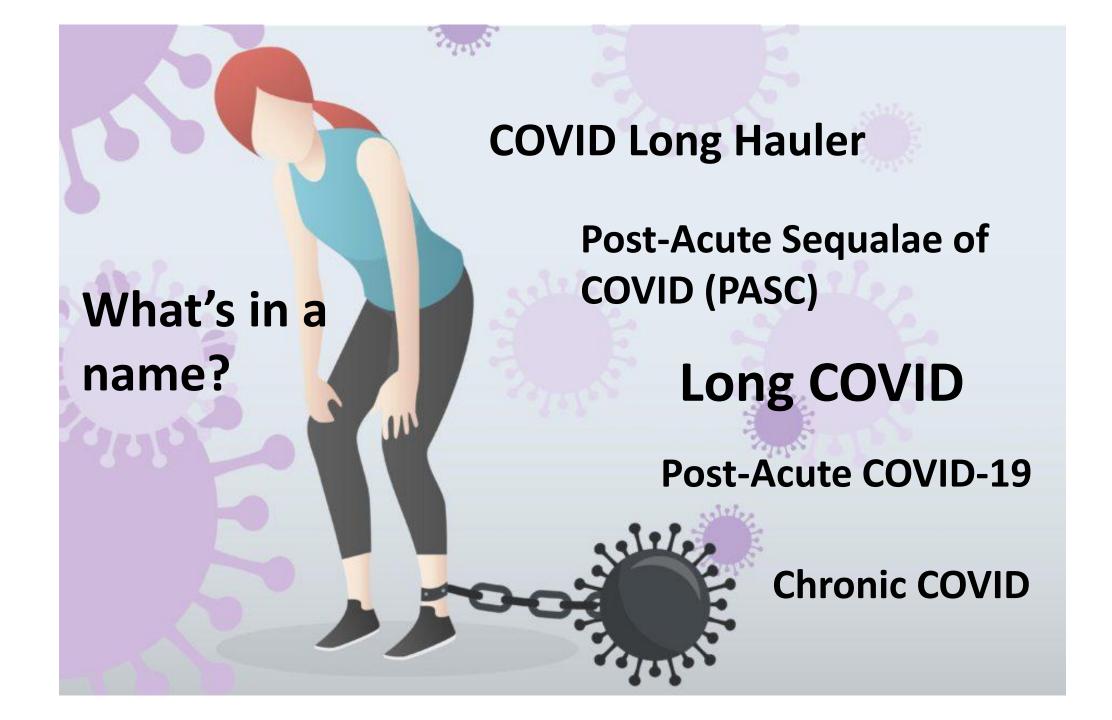


# Long COVID is a Double Curse in Low-Income Nations

### DEARTH OF RESEARCH

Studies of long COVID are uncommon in lower-income countries. In an analysis of more than 500 such studies, almost 90% were conducted in high- and upper-middle-income nations.





### How and why patients made Long Covid

Felicity Callard a,\*, Elisa Perego

Social Science & Medicine 268 (2021) 113426



- Driven by population and not the medical community
- Challenges Time Course
- Challenges theories around impact of initial severity
- Provides for large umbrella
- Reflects the lived experience

a University of Glasgow School of Geographical and Earth Sciences, University of Glasgow, United Kingdom

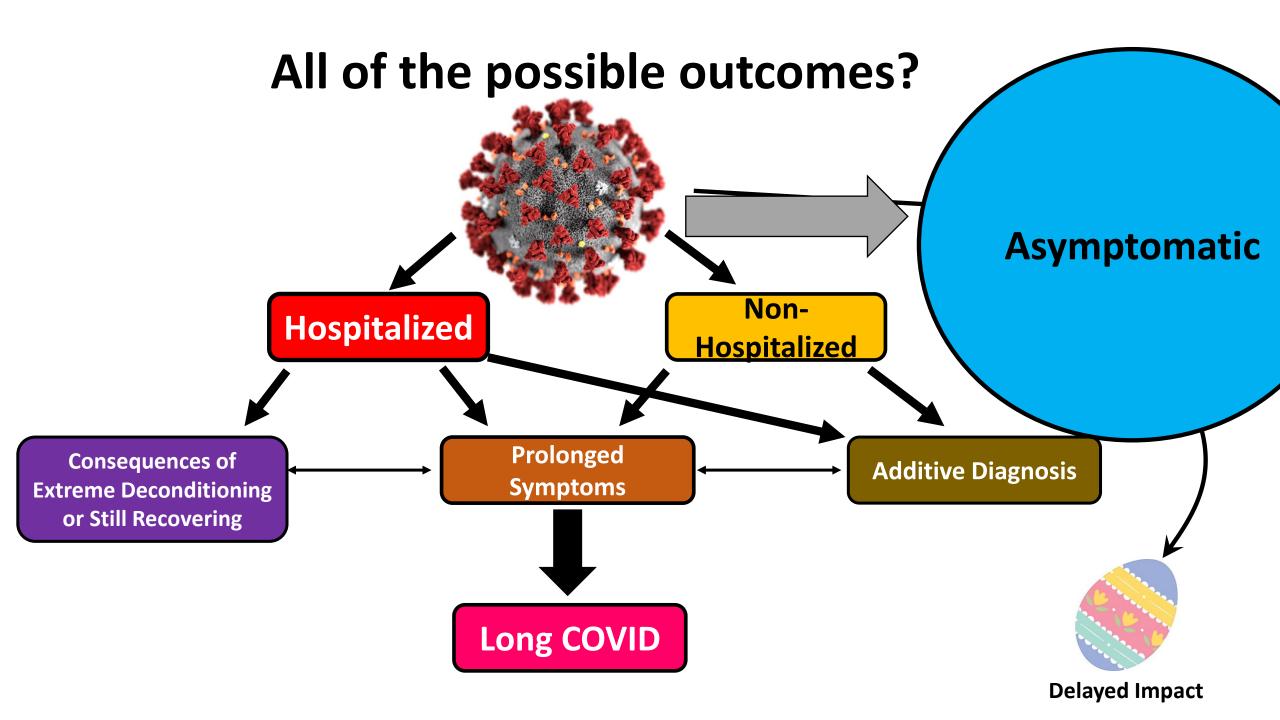
b University College London Institute of Archaeology, UCL, United Kingdom

## Ty Goodwin

- Felt like he has COVID-19, shortness of breath, malaise, fevers, headaches and fatigue for the last year.
- "I was a marathon runner and a triathlete before this," he said. "I've had nights where I wake up out of breath."
- "After 60 some doctors appointments, they eliminated all pre-2020 kind of traditional medical diagnoses, meaning they couldn't explain why I was running out of breath,"

The symptoms aren't just physical. There's also mental and emotional trauma

Long COVID is diagnosed by Exclusion



#### Post-acute COVID-19 syndrome

Ani Nalbandian 1.24, Kartik Sehgal 2.3.4.24 A Aakriti Gupta 1.56, Mahesh V. Madhavan 1.5, Claire McGroder 7, Jacob S. Stevens<sup>8</sup>, Joshua R. Cook 9, Anna S. Nordvig 10, Daniel Shalev 1, Tejasav S. Sehrawat 12, Neha Ahluwalia 13, Behnood Bikdeli 4.5.6.14, Donald Dietz 15, Caroline Der-Nigoghossian 16, Nadia Liyanage-Don 17, Gregg F. Rosner 1, Elana J. Bernstein 18, Sumit Mohan 8, Akinpelumi A. Beckley 19, David S. Seres 20, Toni K. Choueiri 2.3.4, Nir Uriel 1, John C. Ausiello 9, Domenico Accili 9, Daniel E. Freedberg 21, Matthew Baldwin 27, Allan Schwartz 1, Daniel Brodie 7, Christine Kim Garcia 7, Mitchell S. V. Elkind 10.22, Jean M. Connors 4.23, John P. Bilezikian 9, Donald W. Landry 8 and Elaine Y. Wan 15

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601-615 | www.nature.com/naturemedicine

### 4 weeks or 12 weeks

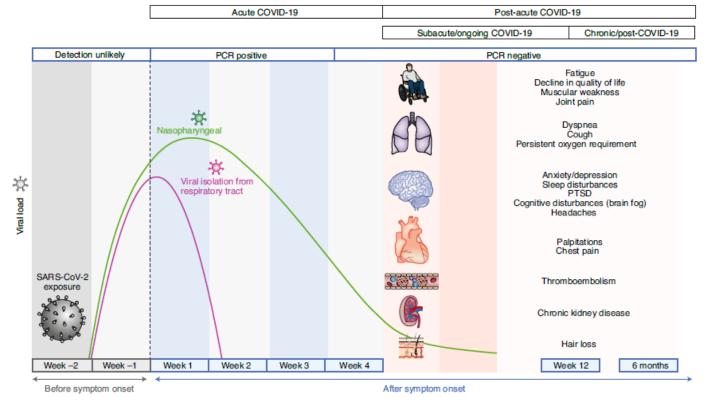
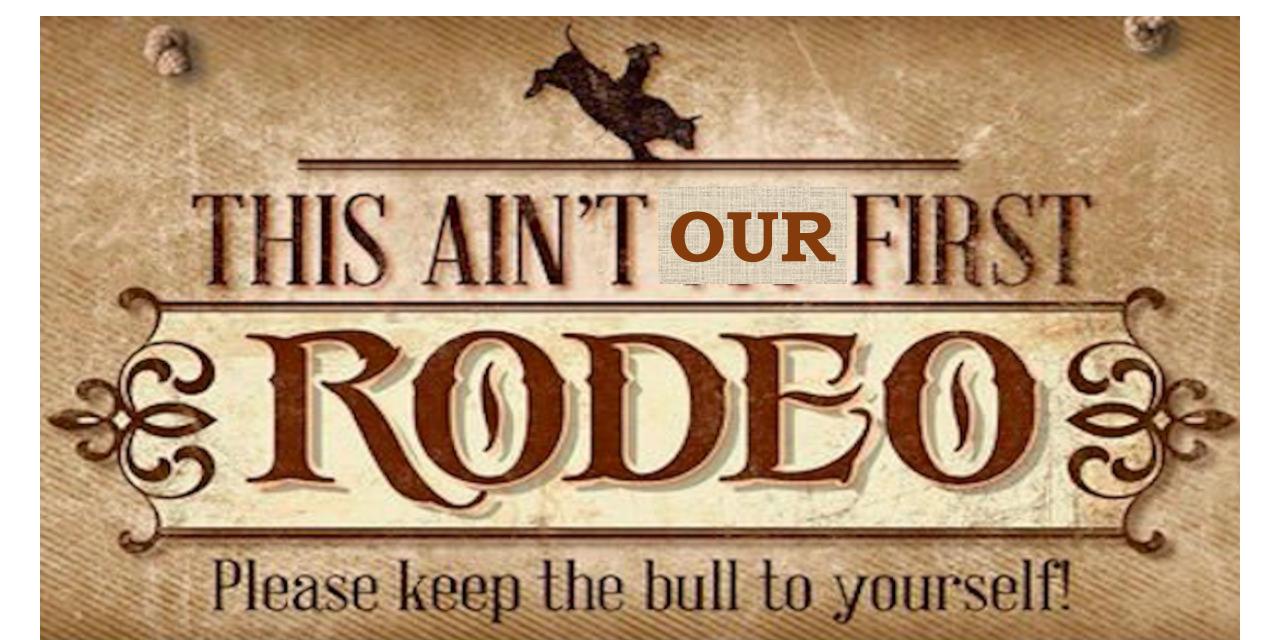
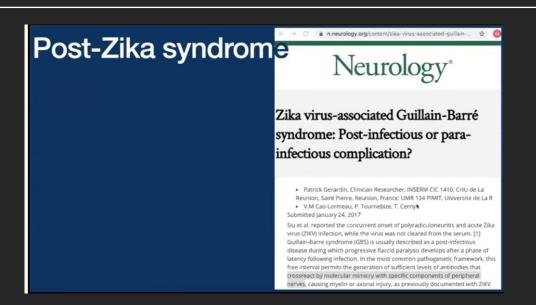
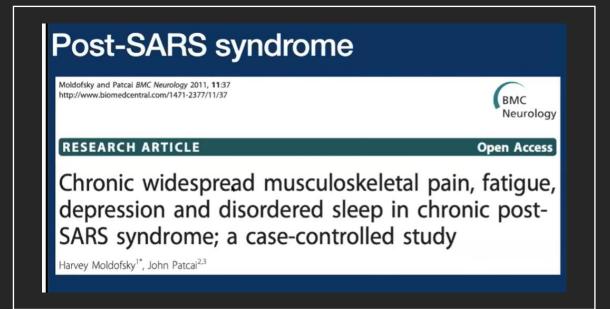
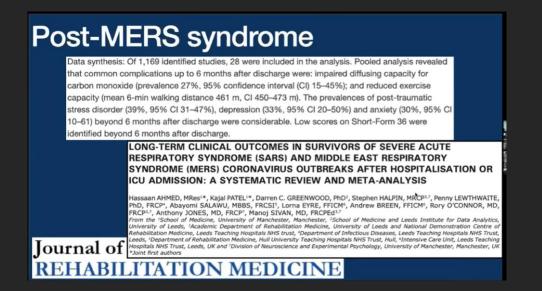


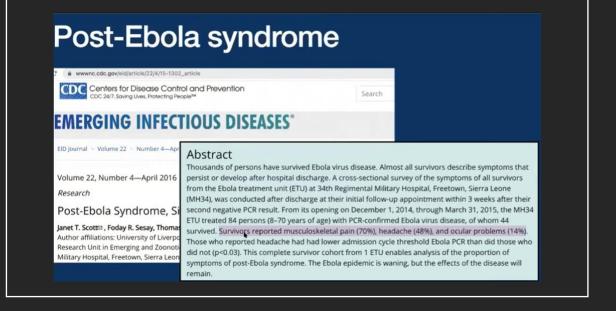
Fig. 1 | Timeline of post-acute COVID-19. Acute COVID-19 usually lasts until 4 weeks from the onset of symptoms, beyond which replication-competent SARS-CoV-2 has not been isolated. Post-acute COVID-19 is defined as persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms. The common symptoms observed in post-acute COVID-19 are summarized.











## So how many people are we talking about?

# Sort of kind of official numbers (at this moment)

- 25% have symptoms for at least a month
- 1 in 10 remain unwell after 12-weeks (or 6 months)

# 472,253,085 cases documented in the world (so far)

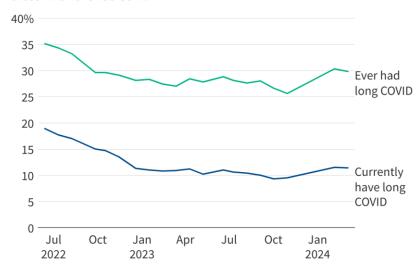
- So around 47 million people worldwide may be defined as having Long COVID
- 7.9 Million in the US

## Frequency of Long COVID

Figure 1

### Around 3 in 10 Adults Who Have Had COVID Report Getting Long COVID

Percentage of adults reporting they currently or ever had long COVID among those who have had COVID



Note: The Pulse Survey, an experimental survey conducted by the Census Bureau and National Center for Health Statistics, asked respondents whether they had any symptoms of COVID that had lasted longer than 3 months. This figure reports the findings between 6/13/2022 and March 4, 2024.

Source: National Center for Health Statistics. Post-COVID Conditions. Data accessed March 28

KFF

Figure 2

### Most Adults with Long COVID Report that it Limits Their Activities at Least a Little

Percentage of adults reporting that they have activity limitations from long COVID as of March 4, 2024

■ Long COVID Limits Activities "a Lot" ■ Long COVID Limits Activities "a Little"

Of all adults



6%

Of adults who currently have long COVD

25%

**54**%

79%

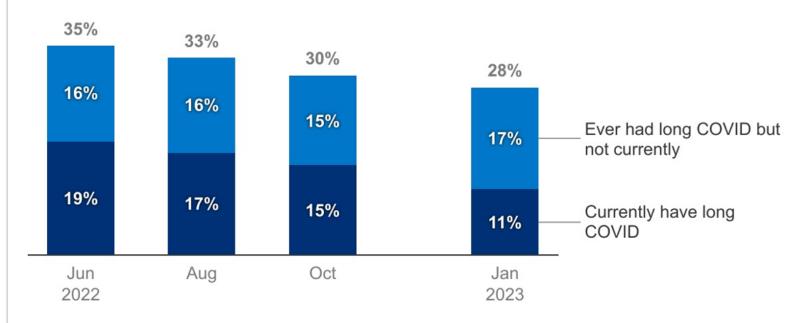
Note: The Pulse Survey, an experimental survey conducted by the Census Bureau and National Center for Health Statistics, asked respondents whether they had any symptoms of COVID that had lasted longer than 3 months and among adults who respond "yes," whether the symptoms limit their day-to-day activities "a lot," "a little," or "not at all." The survey characterizies "a lot" responses as "significant" activity limitations.

Source: National Center for Health Statistics. Post-COVID Conditions. Data accessed March 28, 2024.



# Among People Who Have Had COVID, the Percentage who Currently Have Long COVID is Declining

Percentage of people reporting that they currently have or ever had long COVID among those who have had COVID as of January 16, 2023



NOTE: The Pulse Survey, an experimental survey conducted by the Census Bureau and National Center for Health Statistics, asked respondents whether they had any symptoms of COVID that had lasted longer than 3 months. This figure reports the findings as of 6/13/2022, 8/8/2022, 10/17/2022, and 1/16/2023. SOURCE: National Center for Health Statistics. Post-COVID Conditions. Data accessed Jan 26, 2023. Available from: https://data.cdc.gov/d/gsea-w83j.

### How Common Is Long COVID in Children and Adolescents?

REVIEW ARTICLES

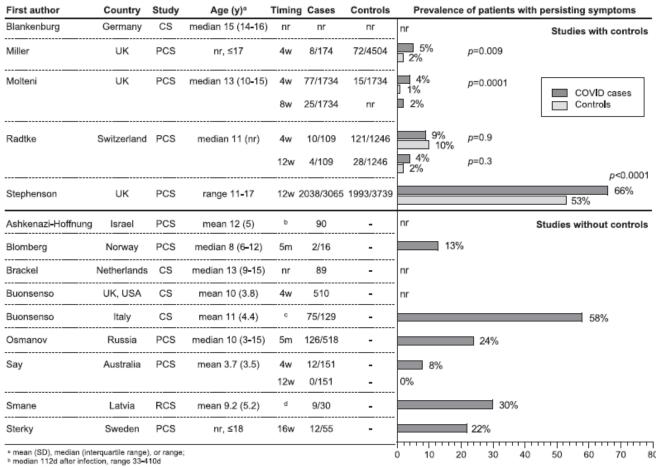
### How Common is Long COVID in Children and Adolescents?

Zimmermann, Petra MD, PhD\*,†,‡,\$; Pittet, Laure F. MD-PhD‡,\$,¶; Curtis, Nigel FRCPCH, PhD‡,\$,1

Author Information @

The Pediatric Infectious Disease Journal 40(12):p e482-e487, December 2021. | DOI: 10.1097/INF.000000000003328

- Risk is probably much lower that first reported
  - More like under 5% (or even lower) versus 25%
- 25-fold greater risk in children with obesity, kidney disease, cardiovascular disease, or immune disorder



e mean 163d after infection, SD 114d

CS, cross-sectional study; d, days; m, month; nr, not reported; PCS, prospective cohort study; RCS, retrospective cohort study; SD, standard deviation; w, weeks; y, years

d mean 101d after infection, SD 17d

## Why is PEM so important?

- Post-exercise malaise
- Made prominent by ME/CFS

SIMON DÉCARY, PT, PhD¹ • ISABELLE GABOURY, PhD² • SABRINA POIRIER³ • CHRISTIANE GARCIA⁴

SCOTT SIMPSON, BA, CWC⁵ • MICHELLE BULL, PhD⁶ • DARREN BROWN, MSc, MRes² • FRÉDÉRIQUE DAIGLE, MSc¹

Humility and Acceptance: Working Within Our Limits With Long COVID and Myalgic Encephalomyelitis/
Chronic Fatigue Syndrome

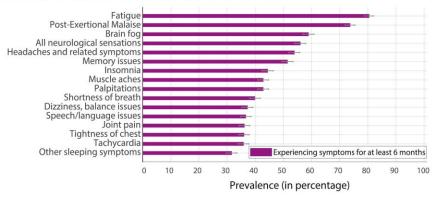


Characterizing long COVID in an international cohort: 7 months of symptoms and their impact

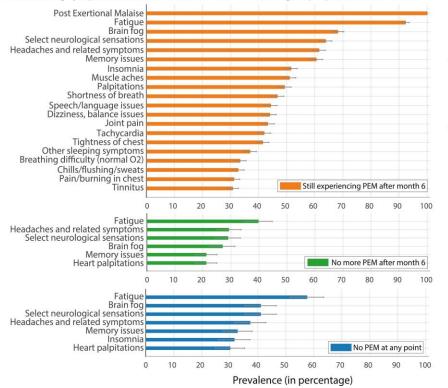
Hannah E. Davis<sup>a,1</sup>, Gina S. Assaf<sup>a,1</sup>, Lisa McCorkell<sup>a,1</sup>, Hannah Wei<sup>a,1</sup>, Ryan J. Low<sup>a,b,1</sup>, Yochai Re'em<sup>a,c,1</sup>, Signe Redfield<sup>a</sup>, Jared P. Austin<sup>a,d</sup>, Athena Akrami<sup>a,b,1,\*</sup>

## **Notice how present Fatigue** & PEM is a symptom

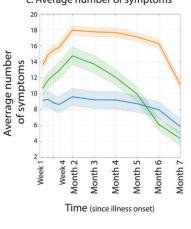
#### a. Remaining symptoms after month 6 (prevalence > 30%)

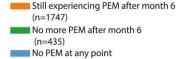


#### b. Remaining symptoms after month 6, for PEM vs No PEM groups (prevalence > 30%)



#### c. Average number of symptoms





(n=272)

a Patient-Led Research Collaborative

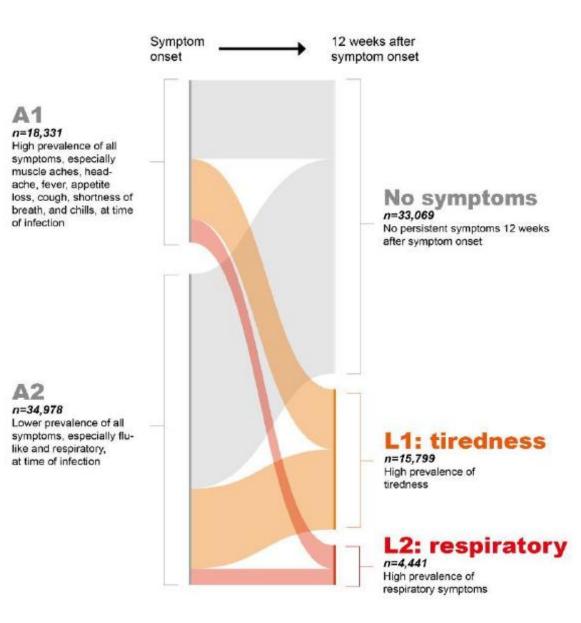
<sup>&</sup>lt;sup>b</sup> Sainsbury Wellcome Centre, University College London, London, United Kingdom

<sup>&</sup>lt;sup>c</sup> Department of Psychiatry, NewYork-Presbyterian Hospital / Weill Cornell Medicine, NYC, United States

d Oregon Health and Science University, Portland, OR, United States

#### Early symptom clusters





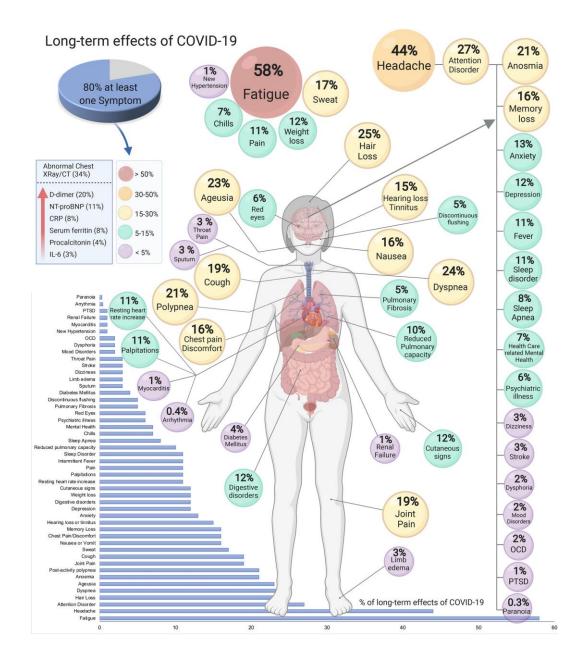
#### Symptom clusters at 12 weeks

7.1	9.0	Appetite loss
6.7	12.9	Severe fatigue
11.1	85.8	Shortness of breath
3.0	4.5	Chills
7.7	12.5	Heavy arms/legs
3.1	61.2	Tight chest
19.8	21.0	Difficulty sleeping
7.5	12.3	Dizziness
7.7	8.5	Blocked nose
7.2	6.0	Runny nose
3.6	3.7	Diarrhoea
3.0	20.9	Chest pain
2.0	3.2	Nausea/vomiting
5.0	9.1	Hoarse voice
7.5	9.1	Sore eyes
3.7	6.0	Abdominal pain / belly ache
5.7	5.0	Sneezing
5.1	7.9	Numbness/tingling
3.1	3.4	Red, itchy areas on skin
0.2	0.5	Sudden swelling to face or lips
0.8	0.9	Purple sores/blisters on feet
12.5	9.3	Loss or change of sense of taste
15.5	9.8	Loss or change of sense of sme
9,6	16.6	New persistent cough
7.7	8.8	Sore throat
50.8	29.1	Tiredness
18.7	23.7	Muscle aches
13.9	15.3	Headache
2.9	4.8	Fever
Cluster L1 n=15799	Cluster L2 n=4441	

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

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Sandra Lopez-Leon<sup>®</sup>, Talia Wegman-Ostrosky<sup>®</sup>, Carol Perelman<sup>®</sup>,
Rosalinda Sepulveda<sup>®</sup>, Paulina A. Rebolledo<sup>®</sup>, Angelica Cuapio<sup>®</sup> & Sonia Villapol<sup>®</sup>, Sania Villapol
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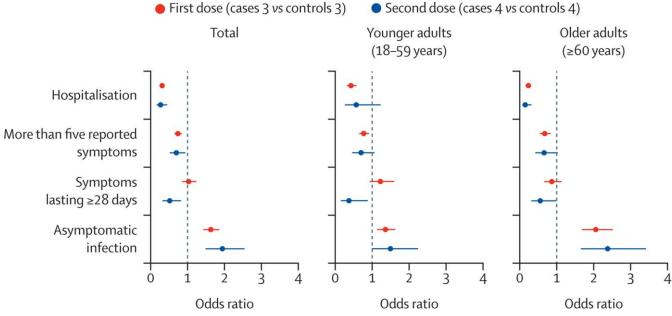
Scientific Reports | (2021) 11:16144



## What if you are vaccinated and get COVID-19?

Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study

 Risk seems to be reduced by half if fully vaccinated.



# Revisiting the Primary Targets for Rehab Intervention

- Fatigue PEM & general
- Cardiac Function (Tachycardia)
- Dysautonomia
- Brain Fog
- Oxygen Saturation/Ventilation Abnormalities
- Coughing/Hoarseness
- Psychosocial/Spiritual

## Potential Pathophysiologic Mechanisms

- Ability to infect many cells
- Viral Reservoirs
- Immunosuppressive activity of SARS-CoV-2
- "Dysbiosis" of microbiome

SARS-CoV-2's acute actions may inform the long-term impact

Long COVID or Post-acute Sequelae of COVID-19 (PASC): An Overview of Biological Factors That May Contribute to Persistent Symptoms

Amy D. Proal1 and Michael B. VanElzakker1,2\*

<sup>1</sup> PolyBio Research Foundation, Kenmore, WA, United States, <sup>2</sup> Division of Neurotherapeutics, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States

Frontiers in Microbiology | www.frontiersin.org

June 2021 | Volume 12 | Article 698169

## New Work Being Produced All the Time

Measurement of circulating viral antigens post-SARS-CoV-2 infection in a multicohort study Zoe Swank<sup>1),2),3),†</sup> · Ella Borberg<sup>1),2),3),†</sup> · Yulu Chen<sup>3),4)</sup>· ... · Elizabeth W. Karlson<sup>3),15),†</sup> · David R. Walt<sup>1),2),3),†</sup> dwalt@bwh.harvard.edu · RECOVER consortium authors... Show more

The team found evidence of persistent infection in 43 percent of participants with cardiopulmonary, musculoskeletal or neurologic symptoms of long COVID.

But only 21% of those who didn't report any long COVID symptoms tested positive for the SARS-CoV-2 biomarkers in this same period.

#### Long COVID: a clinical update

#### Trisha Greenhalgh, Manoj Sivan, Alice Perlowski, Janko Ž Nikolich

Lancet 2024; 404: 707–24

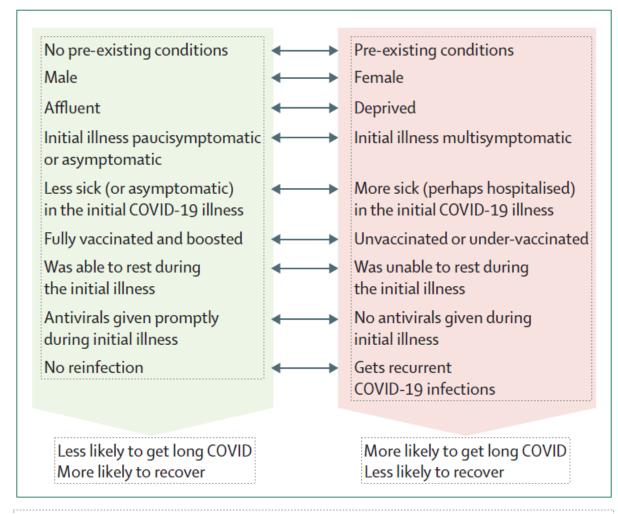


Figure 2: Summary of risk factors for long COVID

Long COVID: a clinical update

Trisha Greenhalgh, Manoj Sivan, Alice Perlowski, Janko Ž Nikolich

Lancet 2024; 404: 707-24

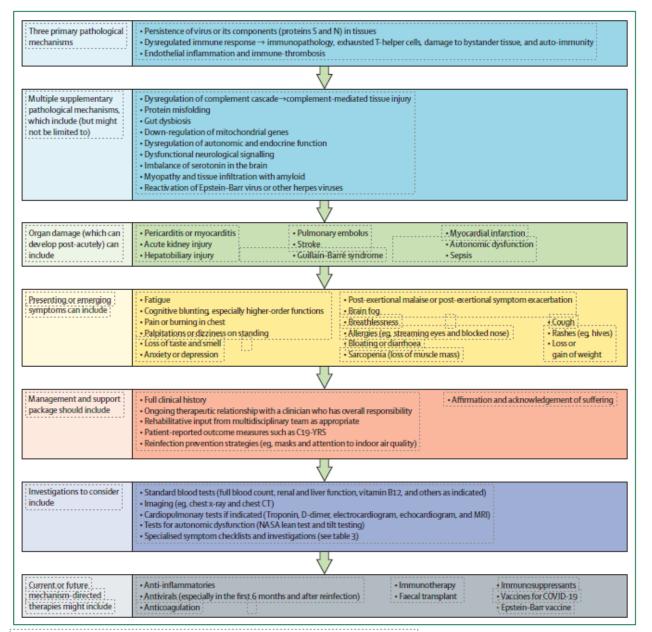
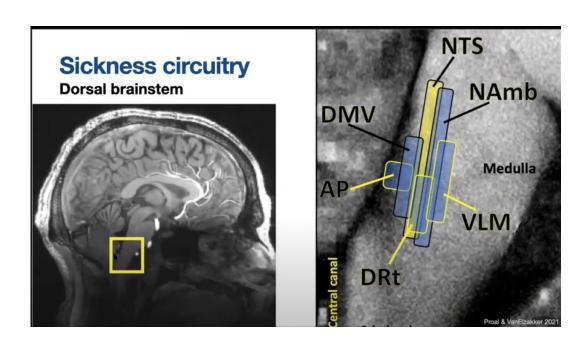
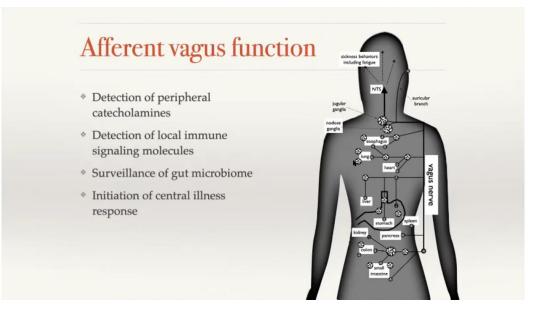


Figure 3: Summary of pathology, presentation, and management of long COVID
C19-YRS=COVID-19 Yorkshire Rehabilitation Scale, NASA=National Aeronautics and Space Administration.

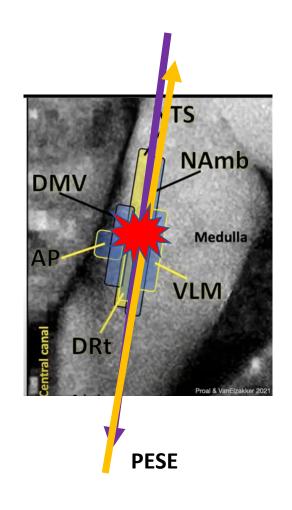
# How can these desperate problems drive similar symptoms?

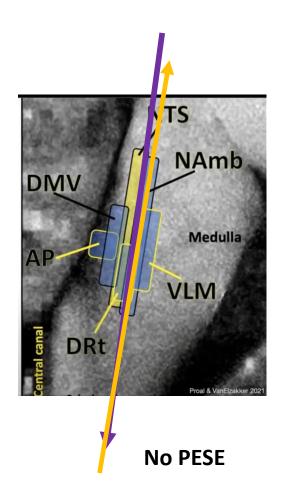
- The Neuroscience of Feeling Sick
- Vagus Nerve acts as diffuse sensory organ





# How could physical/mental activity be causing these outcomes?





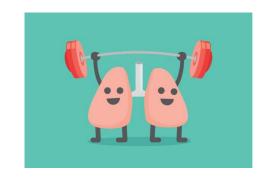
## Rehab Approach – Facilitated Adaptation

- Shared decision-making model
- Patient Centered
- Multidisciplinary

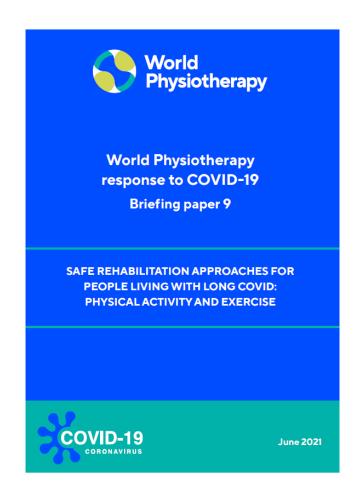








# Two Particularly Helpful Documents



Rehabilitation for Clients with Post COVID-19 Condition (Long COVID)

Guidance for Canadian Rehabilitation and Exercise Professionals

# Rehabilitation Approach



- Clinical complexity and uncertainty = patient-centered personalized approach
- Education about resuming daily activities at appropriate pace that is safe and manageable (avoid or minimize PEM)
- "Stop, Rest, Pace" and heart rate monitoring to manage symptoms
- Avoid O₂sat drop with exertion, ≥3% should be investigated
- Orthostatic Hypotension
  - Autonomic conditioning therapy
  - Non-upright exercise
  - Isometric exercise
  - Compression garments
  - Patient education



## DePaul Symptom Questionnaire (adapted)

	Frequency:					Severity: Throughout the past 6 months, how much has this							
	Throughout the past 6 months, how often have you had												
	this symptom?				symptom bothered you?								
	For each symptom listed below, circle a number from:  0 = none of the time  1 = a little of the time  2 = about half the time						For each symptom listed below, circle a number from:  0 = symptom not present  1 = mild  2 = moderate						
Symptoms													
	3 = most of the time 4 = all of the time							3 = severe 4= very severe					
1. Dead, heavy feeling after starting to exercise	0	1	Ź	2	3	4			0	1	2	3	4
2. Next day soreness or fatigue after non-strenuous, everyday activities	0	1	2	2	3	4			0	1	2	3	4
3. Mentally tired after the slightest effort	0	1	Ź	2	3	4			0	1	2	3	4
4. Minimum exercise makes you physically tired	0	1		2	3	4			0	1	2	3	4
5. Physically drained or sick after mild activity	0	1	-	2	3	4			0	1	2	3	4

Score of 2 on both frequency and severity = PEM

## DePaul Symptom Questionnaire (adapted)

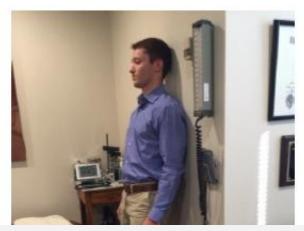
### **Supplementary Questions**

6. If you were to become exhausted after actively participating in extracurricular activities, sports, or outings with friends, would you recover within an hour or two after the activity ended?		Yes		No			
7. Do you experience a worsening of your fatigue/energy related illness after engaging in minimal physical effort?	Yes			No			
8. Do you experience a worsening of your fatigue/energy related illness after engaging in mental effort?		Yes			No		
9. If you feel worse after activities, how long does this last?	≤1 h	2–3 h	4–10 h	11–13 h	14–23 h	≥ 24 h	
10. If you do not exercise, is it because exercise makes your symptoms worse?		Yes			No		

## NASA 10 Minute Lean Test for OH

#### Orthostatic Vital Signs/The NASA 10-minute Lean Test

	Blood	Pressure (BP)	- 1		
	Systolic	Diastolic	Pulse	Comments	
Supine 1 minute					
Supine 2 minute					
Standing 0 minute					
Standing 1 minute					
Standing 2 minute					
Standing 3 minute					
Standing 4 minute				$oxed{oxed}$ Ortl	
Standing 5 minute				was	
Standing 6 minute					
Standing 7 minute				+ mor	
Standing 8 minute				mor	
Standing 9 minute				$oxed{oxed}$ Post	
Standing 10 minute				$\perp$	





**Orthostatic hypotension (OH)** (lowered blood pressure upon standing) was defined as a decrease in systolic blood pressure (SBP) 20 mm Hg or more, or a decrease in diastolic blood pressure (DBP) of 10 mm Hg or more in the first 3 minutes.

**Postural orthostatic tachycardia syndrome (POTS**) was defined as a heart rate increase of >30 beats per minute (bpm) upon standing or a heart rate of greater than 120 bpm.

## **Energy Envelope**

- Avoid "Pushing & Crashing" and Post-Exertional Malaise (PEM)
- Spread out activity with rest inbetween
- http://www.cfsselfhelp.org/pacing -tutorial
- Post-Exertional Symptom **Exacerbation (PESE)**
- Titration of Physical Activity vs **Graded Exercise**



## How to use pacing with your physiotherapist





Pacing is a self-management strategy during activity to avoid post-exertional symptom exacerbation (PESE). When pacing you do less activity than you have energy for, keeping activities short, and resting often.



#### Learn about your energy reserve/reservoir

Your energy reserve is how much energy you have each day - this will vary so it is best to find your baseline by using an activity and symptom diary. Your "baseline" is what you can do fairly easily on a good day and only just do on a bad day.



You should always aim to leave some energy at the end of the exercise - don't keep going until you feel tired.



### Learn how much energy you have

Your activity and symptom diary should start to show some patterns. You can now reduce or modify your activity levels so that you don't trigger PESE or "crash". This will help you find a level of activity you can maintain on both good and bad days, unless you have a relapse. Learn to recognise early signs of PESE and immediately initiate stop, rest, pace to avoid a crash.





### Learn how to use the 4 Ps to help you plan your activities

- · Prioritise what you really need to do in a day or week. Question whether all activities are necessary. Can someone else do it? Can I change the activity so it is easier for me?
- Plan in your main prioritised tasks for the day. Plan in your rest time so the day is paced.
- · Pacing break up your activity into smaller, more manageable tasks with rest breaks.
- Pleasure spend some energy on things you enjoy to help improve your quality of life.



### Learn how to save energy

- Avoid the temptation to "do just a little more".
   Take short cuts and ask for help.
- Modify your activities to use less energy.





- Rest means absolutely minimal activity and little or no mental stimulation.
- During rests avoid activities that can be stimulating, such as TV and social media.
- Try some meditation and/or breathing exercises instead.





### Can I ever do more?

- When your symptoms improve you will experience less weakness and fatigue. Work with your physiotherapist to find out how to increase your activity levels very gradually, such as carrying out some core strengthening exercise or increasing the amount you can walk by 10%.
- · Be realistic and stay flexible try to create a weekly routine, but accept that some days you will need more rest than others and avoid your triggers.
- Focus on your accomplishments instead of symptoms or what you have not achieved.

### Heart rate monitoring

Your physiotherapist can teach you how to take your heart rate. Then, take your heart rate every morning before getting out of bed. Keeping your heart rate within 15 beats per minute of your weekly average should reduce the risk of PESE.



Activity management or pacing is likely to be a safe and effective intervention for managing fatigue and post-exertional symptom exacerbation (PESE). Heart rate monitoring is likely to be a safe and effective intervention for managing fatigue and PESE.

Graded exercise therapy should not be used, particularly when post-exertional symptom exacerbation is present.



## **Evaluation of Aerobic Capacity**

- 6-MWT
- 2-MWT
- 2-minute step test
- Encouraged to Track Fatigue after test

## Example Case

- 58 yo, female
- 5'2", 196 lbs
- March 2021
- Meds
  - Telmisartan 40mg
  - Atenolol 25 mg
  - Synthyroid 200 mg

- Home Based Walking Program
  - Dizziness & Excessive Fatigue
- HR=78, O2sat=98, BP=178/94
- Modest 5 min Intervals
  - 2 to 2.5 mph, 0-3% grade
  - Mild Dyspnea, HR=111, O2sat=96, BP=192/92, RPE=3-4, Borg Breathlessness=4
  - Sudden onset of dizziness
    - BP=212/102
    - O2Sat=94
    - HR=94

## Example Case

- Retreat to sub PESE
- Avoid dizziness
- Everyday monitoring of fatigue
- Review med with Cardiologist
  - BP goal not met
  - Dizziness with elevated BP
  - SOB



# The Effect of Exercise Training on Long COVID-19

Brown M, Megurdichian M, Milgrom S, and Bailey S. *Elon University, Elon, NC.* 

# Methods

- Twelve participants (9 females, 3 males)
- Before and after the intervention participants were assessed for 6-minute walk distance (6MWD), 5-times sit to stand (5XSTS), gait speed, grip strength, perceived quality of life (SF-12), and general fatigue (visual analog fatigue scale, VAFS).
- Participants then completed a progressive, individualized exercise program (~8 weeks) designed to improve cardiovascular fitness, muscle strength, and endurance. Modes of exercise used to facilitate improvement in cardiorespiratory fitness included the treadmill, NuStep, semi-recumbent bike, semi-recumbent elliptical, stand-up elliptical.
- Heart rate, blood pressure, O<sub>2</sub> saturation, and rating of perceived exertion were regularly monitored during aerobic exercise. Dumbbell exercises targeted at large muscle groups were used to challenge muscular strength and endurance.
- Progression of exercise intensity and duration was based on symptom response to exercise.

## **Intervention Plan**

Week	Intervention
1	PT Eval
2	One Session
3	One Session
4	Two Sessions
5	Two Sessions
6	Three Sessions
7	Three Sessions
8	Three Sessions
9	Three Sessions

## **Evaluation of General Fatigue**

### VISUAL ANALOGUE FATIGUE SCALE (VAFS)

Please mark an "X" on the number line which describes your global fatigue with 0 being "no fatigue" and 10 being the worst.

0	1	2	3	4	5	6	7	8	9	10
No										Worst
Fatigue										Fatigue

Before Treatment, IP Treatment, 24 & 48 hours After Treatment

# 6MWD Distance before and after the Intervention \*

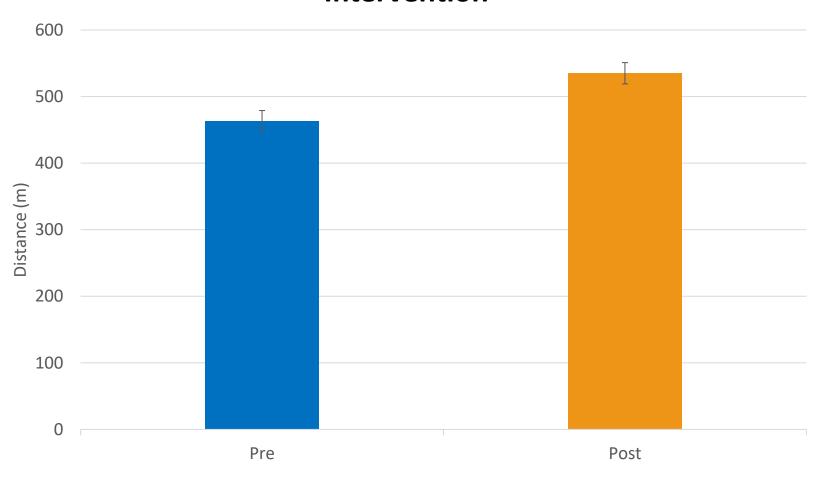


Figure 1. \* indicates significant difference between pre and post (p=0.001)

## Perceived Quality of Life (SF-12) before and after the intervention.

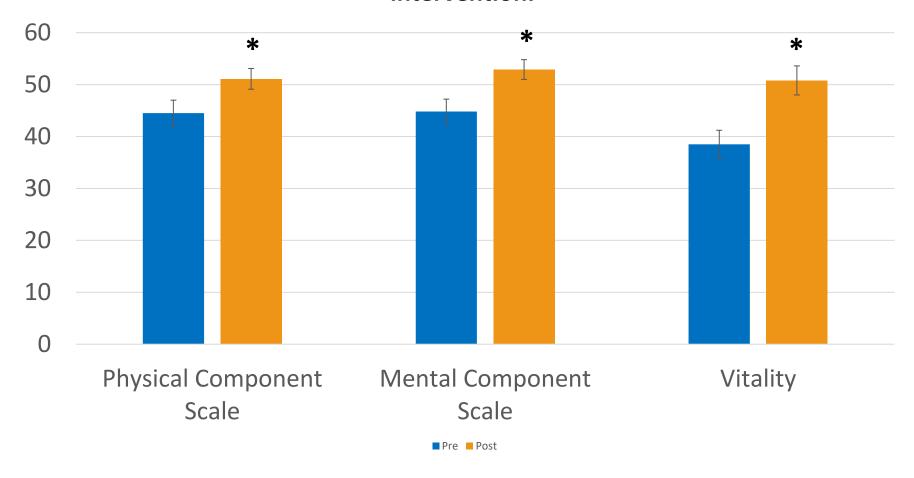


Figure 2. \* indicates significant difference between pre and post (p=0.006, 0.007, 0.013)

### **5TSTS** before and after the intervention

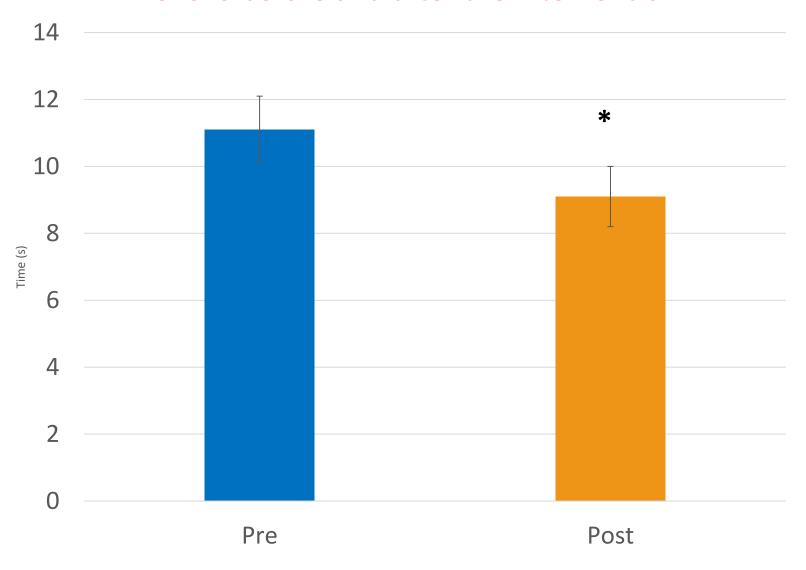
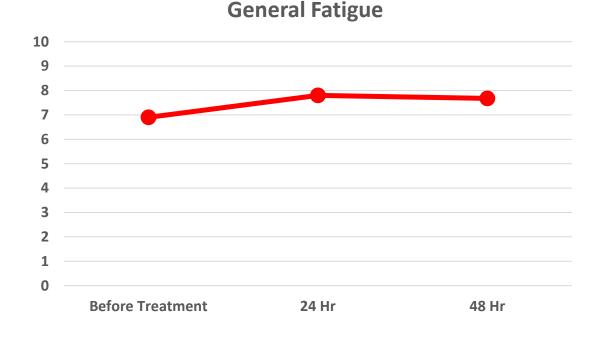


Figure 3. \* indicates significant difference between pre and post (p=0.027)

19-year-old male
3 years with Long COVID
Competitive Soccer Player
Fatigue & Brain Fog



14 visits over 3.5 months

Day 1: 10 minutes @ 2 mph & 0% grade

Most Recent Visit: 15 minutes @ 2.8 mph & 2.5% grade

5 minutes Nu-Step @ Level 4

Leg Press, Biceps Curl, Triceps Extension, Bench Press, & Lat Pull Down

## General Recommendations for Long COVID

- 1. Be Patient & Persistent
- 2. Monitor Post-Treatment Fatigue for 48 hours
- 3. Path away from Long COVID is not the path to Long COVID
- 4. Likely more than one cause of Long COVID

## Closing Thoughts & Opinions

- Probably operating on an unstable landscape for a while
- Wide diversity in time course and presentation
- The path to Long COVID is probably not the path to optimal function
- We can learn from pulmonary rehab, interventions for POTS, and ME/CFS
- Length of time between Dx and intervention may be important
- Tools are already available

