

# A ROOT-CAUSE APPROACH TO LONG COVID IN THE POST-PANDEMIC ERA



# LONG COVID PREVALENCE <sup>1</sup>

- ❖ Greater than 80% of Americans have had acute COVID
- ❖ Most Long COVID cases occur in people with mild acute illness
- ❖ 1/3 of people with Long COVID have **no identified pre-existing conditions**

- ❖ 15-30% people have persistent symptoms @ 1 month
- ❖ 6-10% people have persistent symptoms @ 3 months
- ❖ 1-2% people have persistent symptoms @ 12 months

## Long COVID Incidence Estimate

- ❖ ~ 30 million people with Post-COVID @ 1 month
- ❖ ~ 10 million people with Post-COVID @ 3 months
- ❖ ~ 2 -4 million people with Post-COVID @ 12 months

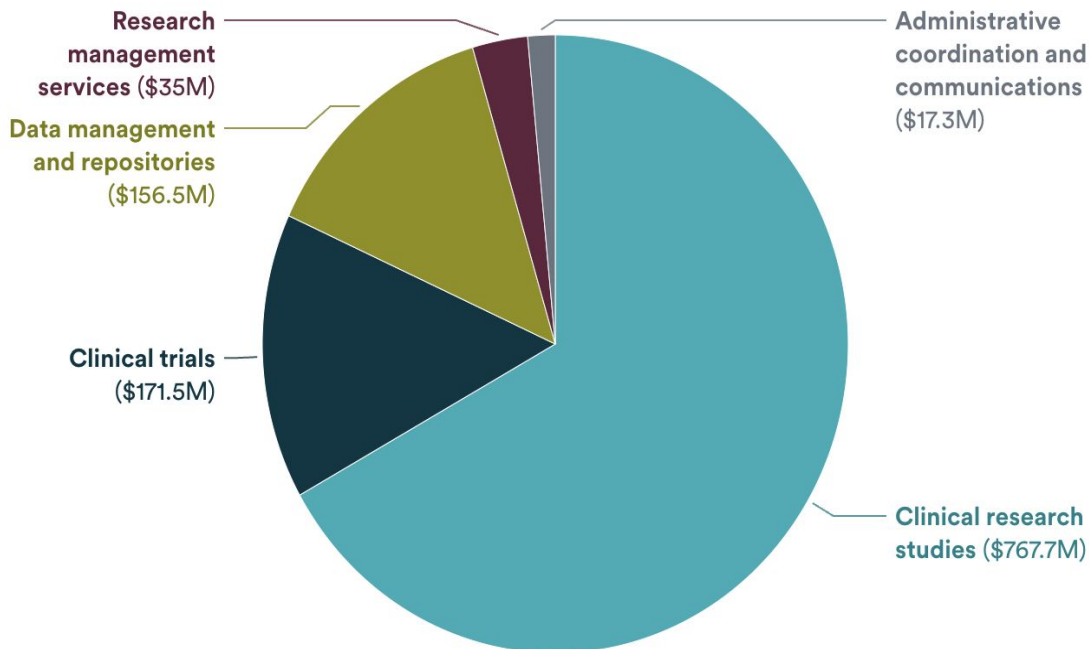
# Current Landscape:

## NIH RECOVER's spending has primarily gone to observational research

Cohrs, R., & Ladyzhets, B. (2023, July 25). The NIH has poured \$1 billion into long Covid research — with little to show for it. STAT.  
<https://www.statnews.com/2023/04/20/long-covid-nih-billion/>

### NIH RECOVER's spending

The NIH has spent the majority of its funding for long Covid research on observational studies of patient symptoms, with a smaller amount going to clinical trials.



# Focus Areas of RECOVER's Clinical Trials



## Autonomic Dysfunction

Dizziness, fast heart rate, shortness of breath, upset stomach, or other changes in body functions that happen automatically



## Cognitive Dysfunction

Brain fog, trouble thinking clearly, memory changes, slowed attention, and other symptoms related to brain function



## Viral Persistence

When the virus that causes COVID-19 stays in the body and causes damage to organs or the immune system to not function properly



## Sleep Disturbances

Changes in sleep patterns or ability to sleep



## Exercise Intolerance and Fatigue

Exhaustion or low energy that interferes with daily activities



## RECOVER-VITAL Clinical Trial



## RECOVER-NEURO Clinical Trial



# Ziyad Al-Aly, Clinical Epidemiologist Washington University, St Louis

*Long COVID does not appear to be self-resolving, in the sense of spontaneous recovery or recovery in the absence of a cure or a treatment that has been validated. It further raises the importance of finding treatment because this is not going to go away.*

STAT Health Tech, 9/20/2023

[https://www.statnews.com/2023/09/20/do-long-covid-odds-increase-with-second-infection/?utm\\_campaign=breaking\\_news&utm\\_medium=email&\\_hsmi=275130536&\\_hsenc=p2ANqtz-\\_Fz5sQzp45OzS1UyaREko82SfD8HXld2tVTahbKLPYeT\\_IzbsU0EZCjEYEIU-qBJptPUPhyCM\\_6OqMlbAfcKQeCUgpWQ&utm\\_content=275130536&utm\\_source=hs\\_email](https://www.statnews.com/2023/09/20/do-long-covid-odds-increase-with-second-infection/?utm_campaign=breaking_news&utm_medium=email&_hsmi=275130536&_hsenc=p2ANqtz-_Fz5sQzp45OzS1UyaREko82SfD8HXld2tVTahbKLPYeT_IzbsU0EZCjEYEIU-qBJptPUPhyCM_6OqMlbAfcKQeCUgpWQ&utm_content=275130536&utm_source=hs_email)

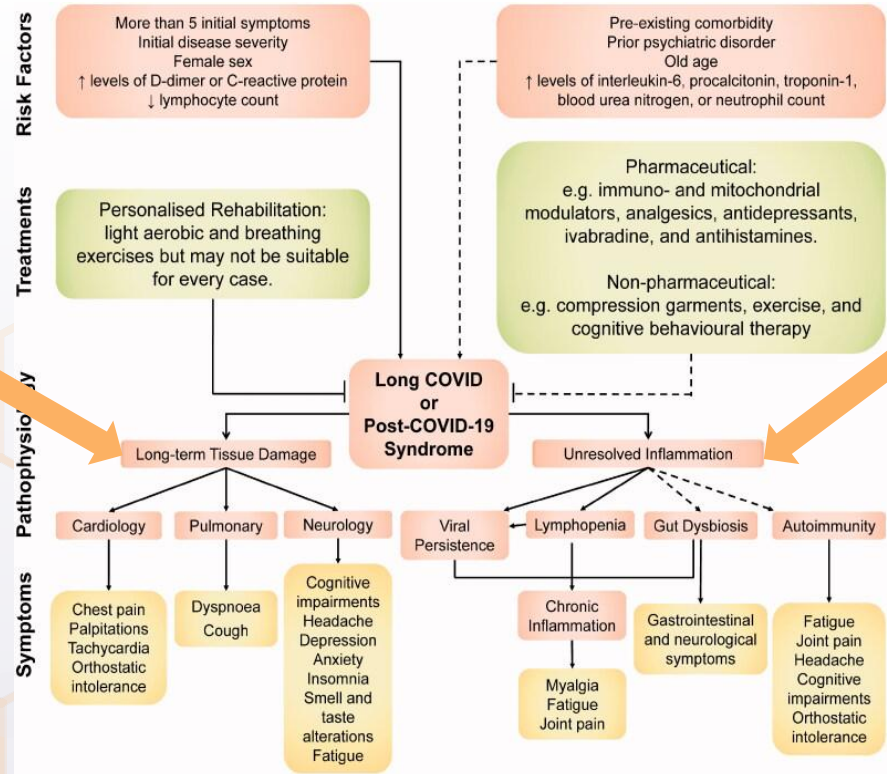
# LONG COVID IN THE POST-PANDEMIC ERA

ASSESSING PROGRESSION AND  
PERSONALIZING TREATMENT USING A  
ROOT-CAUSE APPROACH



# Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments

Yong, SS (2021). Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. *Infectious Diseases*, 53(10), 737–754. <https://doi.org/10.1080/23744235.2021.1924397>

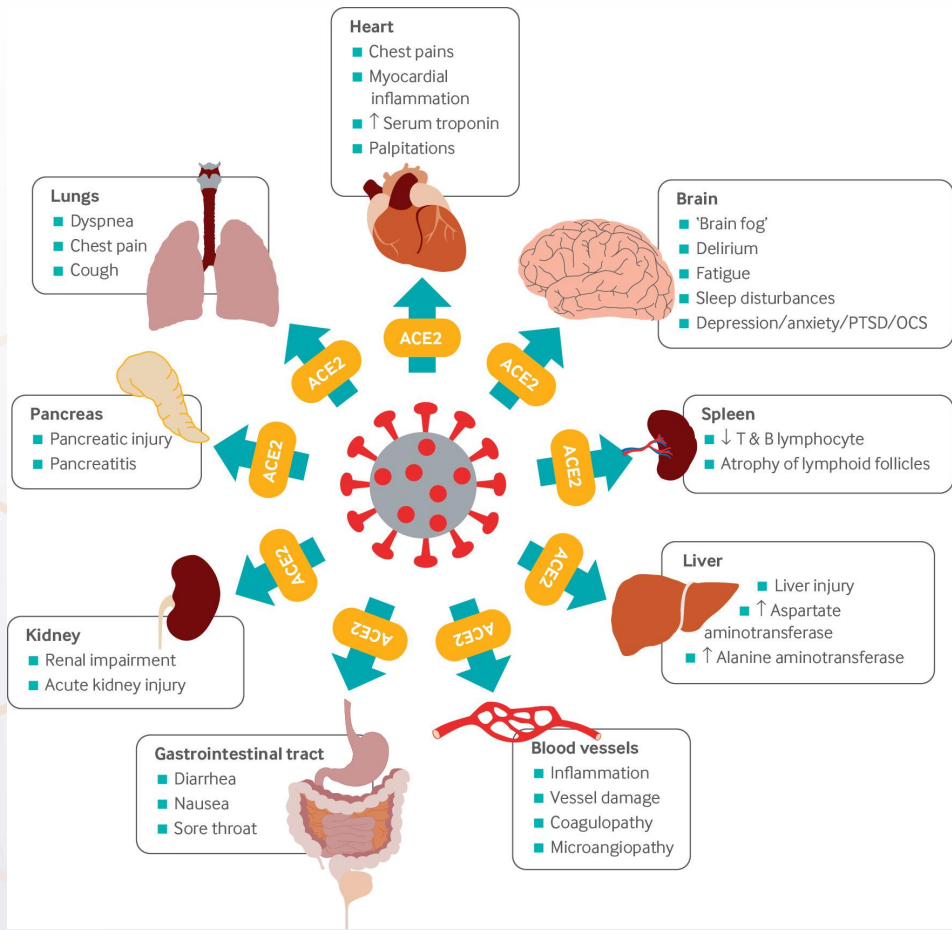


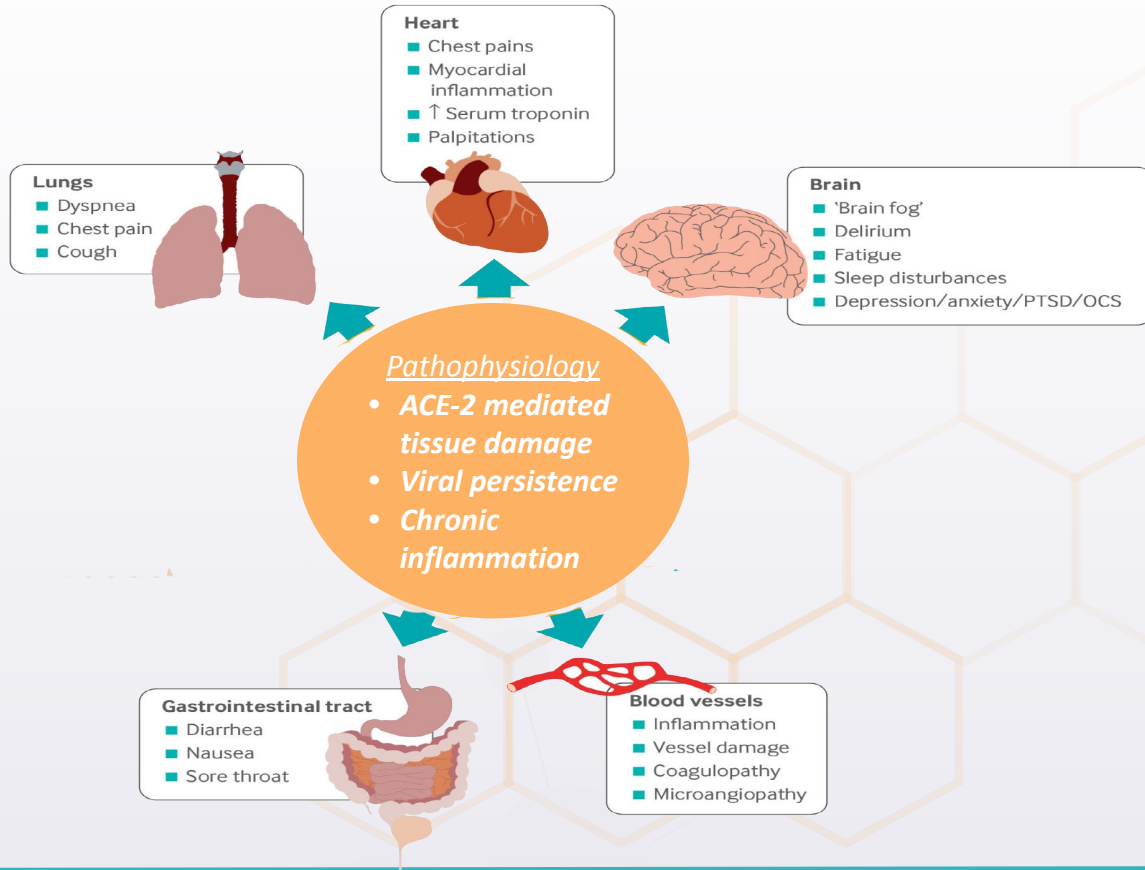
An overview of the symptoms, putative pathophysiology, associated risk factors, and potential treatments involved in long COVID. Note: Dashed lines represent areas where evidence is relatively lacking compared to non-dashed lines. (Color online only).

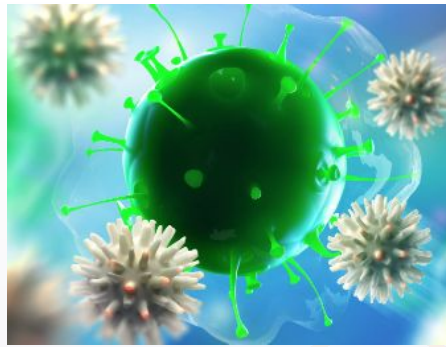
# Long Covid: mechanisms, risk factors, and management

Crook, H, Raza, S, Nowell, J, Young, MK, Edison, P (2021). Long covid—mechanisms, risk factors, and management. *BMJ*, n1648. <https://doi.org/10.1136/bmj.n1648>

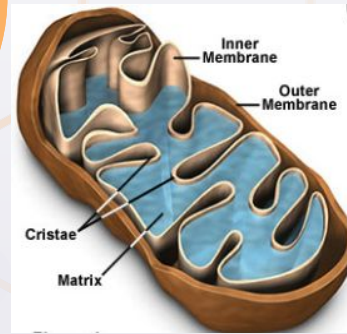
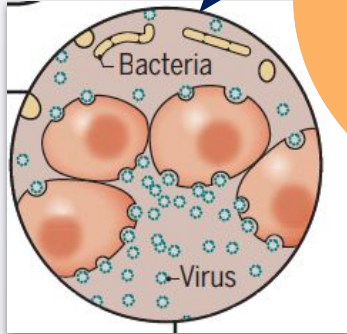
Multi-organ complications of covid-19 and long covid. The SARS-CoV-2 virus gains entry into the cells of multiple organs via the ACE2 receptor. Once these cells have been invaded, the virus can cause a multitude of damage ultimately leading to numerous persistent symptoms.







*ACE-2 mediated damage*  
*Viral persistence*  
*Chronic inflammation*  
*Gut/Microbiome dysbiosis*  
*Mitochondrial dysfunction*



# Distinguishing features of Long COVID identified through immune profiling

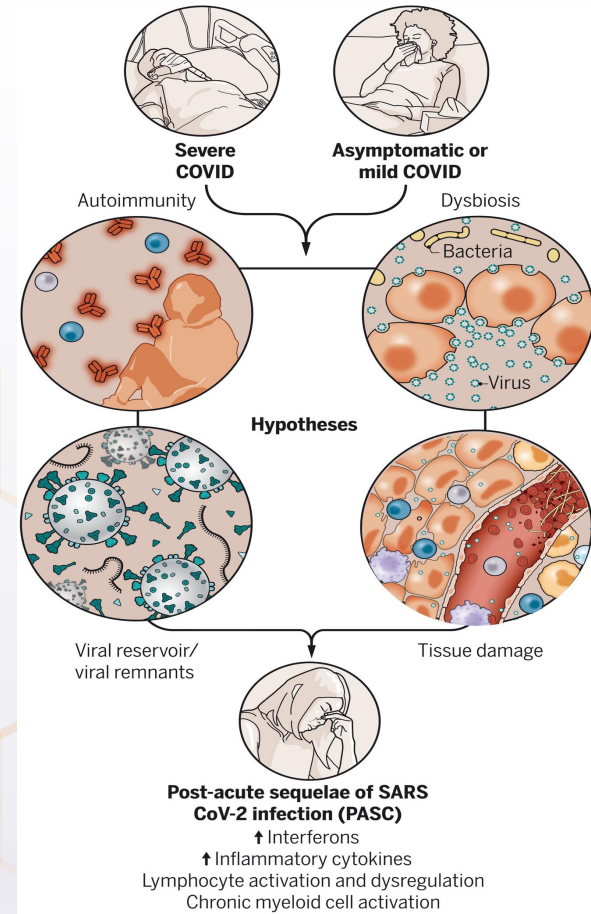
Klein, JB, Wood, JR, Iwasaki, A, et al. (2022).

Distinguishing features of Long COVID identified through immune profiling. medRxiv (Cold Spring Harbor Laboratory).

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

A fraction of COVID-19 patients with either severe or mild COVID-19 develop a variety of new, recurring, or ongoing symptoms and clinical findings 4 or more weeks after infection. Analyses of immune responses in people with PASC reveal key inflammatory cytokines and cellular activation phenotypes that are significantly elevated over nonPASC convalescent controls. Further studies are needed to identify the drivers of PASC pathophysiology.

Illustration: V. Altounian/Science





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

Proal, AD, VanElzakker, MB. (2021b). Long COVID or Post-acute Sequelae of COVID-19 (PASC): An Overview of Biological Factors That May Contribute to Persistent Symptoms. *Frontiers in Microbiology*, 12. <https://doi.org/10.3389/fmicb.2021.698169>

## Long COVID EndoTypes\*

- 1. Multi-Organ Tissue Damage, 2° to acute infection**
2. Persistent SARS-CoV-2 Infection
3. Reactivation of Neurotrophic Pathogens (e.g. HSV, HHV-6, EBV, etc.)
4. Microbiome/ Virome Dysregulation
5. Autoantibody Production with Molecular Mimicry
- 6. Dysregulated Brainstem & Vagal Nerve Signaling**
7. Activation of Primed Immune Cells [Hyperinflammation]
- 8. Clotting/ Coagulation Vascular Issues [ACE2]**

**ACE-2 mediated  
tissue damage**

**Viral Persistence**

**Chronic  
Inflammation**

**Gut/Microbiome  
dysbiosis**

**Mitochondrial  
dysfunction**

# ACE2-Driven Tissue Damage AND/OR Inflammation/ Immune Dysregulation

## ACE2 TISSUE DAMAGE

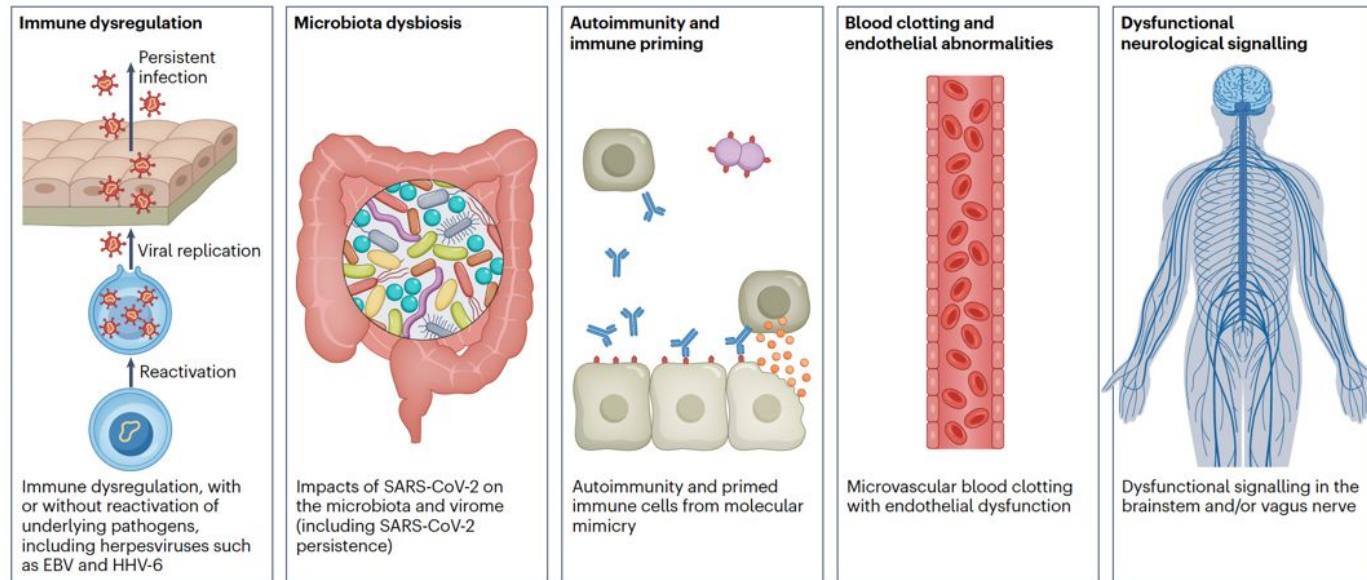
- ❖ **Tissue Damage**
  - ❖ Cardiac
  - ❖ Pulmonary
  - ❖ Endothelitis
  - ❖ Brain/Neural tissue
  - ❖ GI Tract
- ❖ Secondary dysfunction
  - ❖ Clotting/ Coagulation
  - ❖ Vagus nerve/ Brainstem
  - ❖ Cognitive & Mood Disorders

## IMMUNE DYSREGULATION

- ❖ Infection
  - ❖ **Persistent SARS-CoV-2 virus/ fragments**
  - ❖ EBV Reactivation
  - ❖ Reactivation of Neurotrophic Pathogens
- ❖ **Chronic Inflammation**
  - ❖ T-cell Dysregulation
  - ❖ MicroGlial Activation
  - ❖ Mast Cell Activation
  - ❖ **Gut/ Microbiome Dysbiosis**
  - ❖ **Mitochondrial Dysfunction**

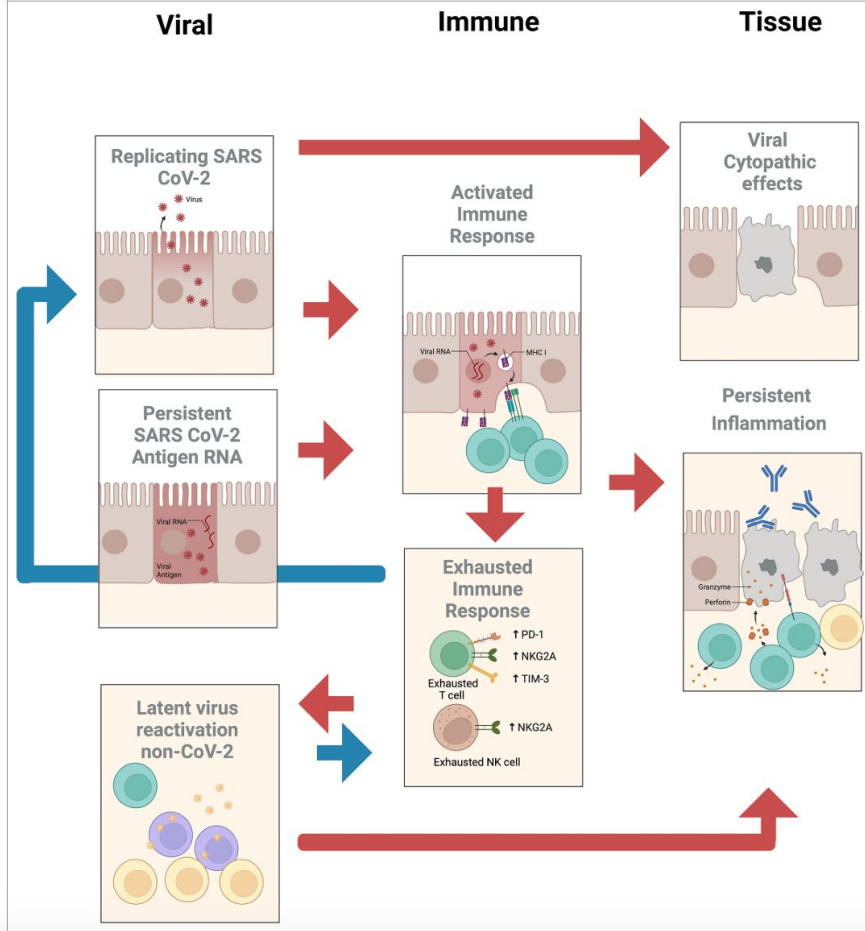
# Long COVID: major findings, mechanisms and recommendations

Davis, HE, McCorkell, L, Vogel, JM et al. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol 21, 133–146 (2023). <https://doi.org/10.1038/s41579-022-00846-2>



**Fig. 3 | Hypothesized mechanisms of long COVID pathogenesis.** There are several hypothesized mechanisms for long COVID pathogenesis, including immune dysregulation, microbiota disruption, autoimmunity, clotting

and endothelial abnormality, and dysfunctional neurological signalling. EBV, Epstein–Barr virus; HHV-6, human herpesvirus 6; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.



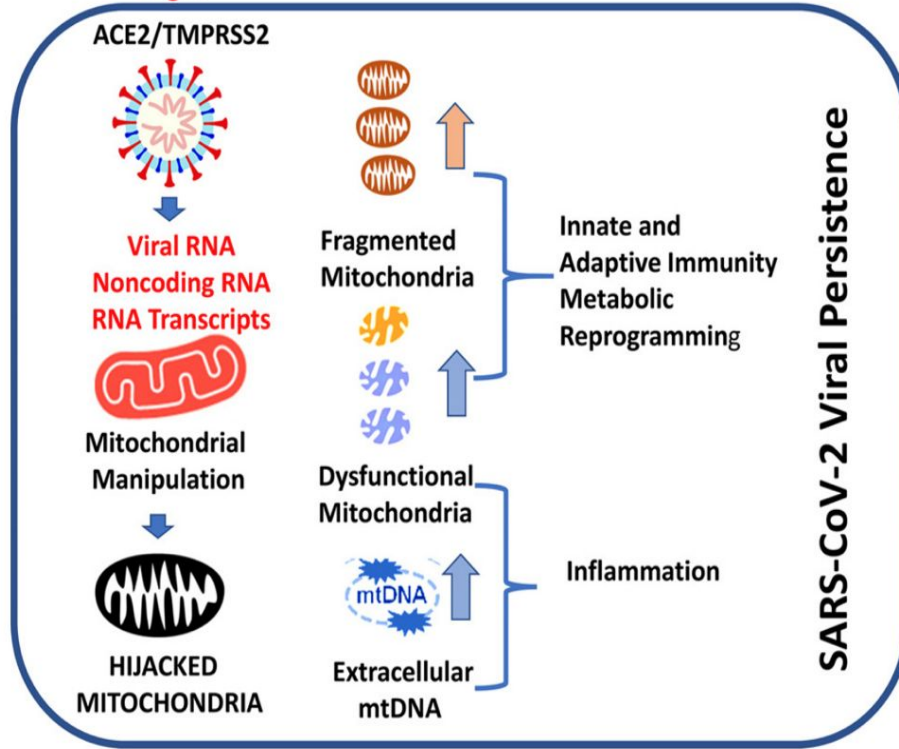
- Viral Persistence
  - SARS CoV-2 Virus
  - SARS CoV-2 RNA
  - SARS CoV-2 Fragments
- Tissue Damage
- Chronic Inflammation
- Immune Dysregulation
- Latent Viral Reactivation (e.g. EBV, HHV-6)

Chen, B, Julg, B. Mohandas, S, & Bradfute, SB (2023). Viral persistence, reactivation, and mechanisms of long COVID. eLife, 12. <https://doi.org/10.7554/elife.86015>

Figure 1. Summary of potential viral, immune, and tissue roles in post-acute sequelae of SARS CoV-2 infection (PASC).

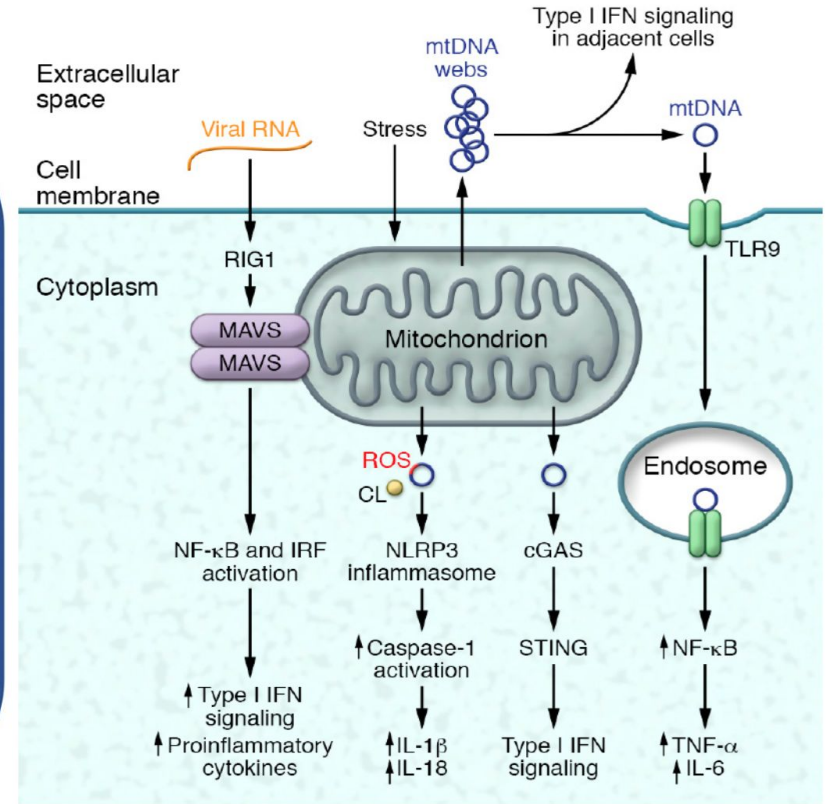
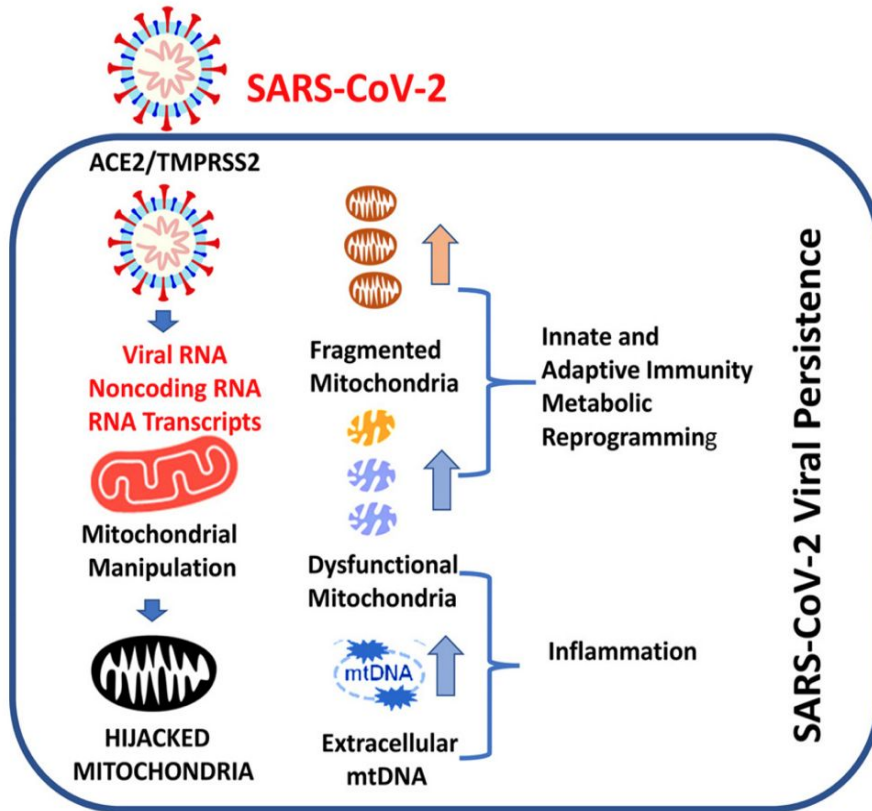


SARS-CoV-2



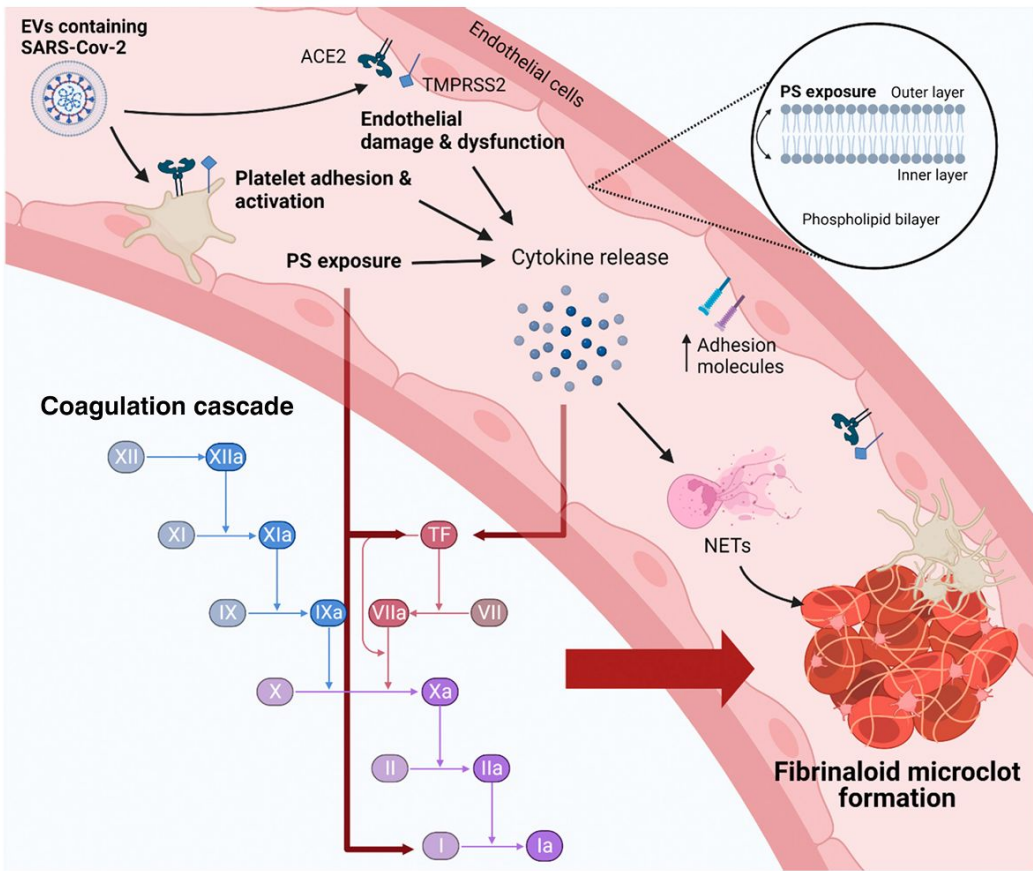
- **Viral binding to mitochondrial ETC** →
  - **Dysfunction & Fatigue**
  - **Chronic Inflammation**
  - **Immune Dysregulation**

Singh, KK, Chaubey, G, Chen, JY, & Suravajhala, P. (2020). Decoding SARS-CoV-2 hijacking of host mitochondria in COVID-19 pathogenesis. *American Journal of Physiology-cell Physiology*, 319(2), C258–C267. <https://doi.org/10.1152/ajpcell.00224.2020>



Sack, MN (2018). Mitochondrial fidelity and metabolic agility control immune cell fate and function. *Journal of Clinical Investigation*, 128(9), 3651–3661. <https://doi.org/10.1172/jci120845>





These mechanisms culminate in the long term persistence of the disorder characterized by a thrombotic endothelitis, endothelial inflammation, hyperactivated platelets, and fibrinolytic microclots. –representing a unifying pathway for the various symptoms of LongCOVID.

Turner, S, Khan, MA, Putrino, D, Woodcock, A, Kell, DB, & Pretorius, E. (2023). Long COVID: pathophysiological factors and abnormalities of coagulation. *Trends in Endocrinology and Metabolism*, 34(6), 321–344. <https://doi.org/10.1016/j.tem.2023.03.002>

Figure 7. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may bind to endothelial cells via the angiotensin converting enzyme 2 (ACE2)/transmembrane protease serine 2 (TMPRSS2) receptors to promote endothelial damage and dysfunction, thereby promoting the activation of the coagulation cascade and formation of fibrinolytic microclots. In Long COVID, SARS-CoV-2 may hide in extracellular vesicles



# PROGRAM AND PROTOCOL OVERVIEW



# Long COVID Protocol

## ENROLLMENT

- Health History
- Timeline & Progression of Symptoms
- Previous Testing (if available)
- Evaluation of Function (PROMIS-29\*)
- Recovery Goals

## PHASE 1: 90-Day Program

- Lifestyle Components
- Specialty & Foundational Supplements

## LIFESTYLE:

- ❖ Food & Nutrition
- ❖ Sleep
- ❖ Movement & Exercise
- ❖ Stress Modification
- ❖ Social Connection
- ❖ Nutritional  
Supplementation

# PATIENT JOURNEY

1. Patient Enrollment and Completion of Intake Forms
2. Initial Visit and Review of History and Intake Forms
3. 2-week check-in with health coach
4. Visit 2: After completing 30-day surveys
5. Visit 3: After completing 90-day surveys followed by formulation of next steps and referrals

# TIMELINE & PROGRESSION OF SYMPTOMS

Please check your current symptoms and the time course of their expression:	Timeline and Progression of Symptoms						
	CURRENT Symptoms (What's Going on Now?)	Did you have these symptoms before COVID?	Symptoms developed during COVID, but are not worsening	Symptoms developed during COVID, and are worsening	Any symptoms developed after COVID, but are not worsening	Any symptoms developed after COVID, and are worsening	Any symptoms coming & going after COVID (e.g., highly variable)
- Tiredness or fatigue interferes with daily life	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Symptoms worse after physical or mental effort (post-exertional malaise)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Fever	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Difficulty breathing or shortness of breath	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Difficulty breathing or shortness of breath	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Cough (persistent)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Chest pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Fast or pounding heartbeat or palpitations	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Sore Throat	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Sinus/Nasal congestion	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Diarrhea OR Constipation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Stomach pain or bloating	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Nausea/ Vomiting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Joint swelling/ pain or muscle pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Rash	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Change in menstrual cycles	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- Erectile dysfunction	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other Significant Symptoms	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>Total</b>							
<b>For Practitioner Reference Only</b>							
		Other ... NonCOVID conditions	Injury	Acute Inflammation	Chronic Inflammation immune dysregulation	Chronic Inflammation Oxidative stress Mitochondrial Dysfunction	Re-infection or Re-activation

# PROMIS-29

Please respond to each question or statement by marking one box per row.

Physical Function	Without any difficulty (5)	With a little difficulty (4)	With some difficulty (3)	With much difficulty (2)	Unable to do (1)
Are you able to do chores such as vacuuming or yard work?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Are you able to go up and down stairs at a normal pace?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Are you able to go for a walk of at least 15 minutes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Are you able to run errands and shop?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Anxiety In the past 7 days	Never (1)	Rarely (2)	Sometimes (3)	Often (4)	Always (5)
I felt fearful	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I found it hard to focus on anything other than my anxiety	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
My worries overwhelmed me	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I felt uneasy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Sleep Disturbance In the past 7 days	Very Poor (5)	Poor (4)	Fair (3)	Good (2)	Very good (1)
My sleep quality was	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Sleep Disturbance In the past 7 days	Not at all	A little bit	Somewhat	Quite a bit	Very much
My sleep was refreshing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I had problems with my sleep	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I had difficulty falling asleep	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Ability to Participate in Social Roles and Activities	Never (5)	Rarely (4)	Sometimes (3)	Often (2)	Always (1)
I have trouble doing all of my regular leisure activities with others	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I have trouble doing all of the family activities that I want to do	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I have trouble doing all of my usual work (include work at home)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I have trouble doing all of the activities	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Fatigue During the past 7 days	Not at all (1)	A little bit (2)	Somewhat (3)	Quite a bit (4)	Very much (5)
I feel fatigued	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
I have trouble starting things because I am tired	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
How run-down did you feel on average?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
How fatigued were you on average?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

# POST COVID FUNCTION SCALE (PCFS)

**Can you live alone without any assistance from another person? (e.g. independently being able to eat, walk, use the toilet and manage routine daily hygiene)**

Yes                       No → If No, stop the questionnaire.

**Are there any duties/activities at home or at work which you are no longer able to perform yourself?**

Yes → If Yes, stop the questionnaire.                       No

**Do you suffer from symptoms, pain, depression or anxiety?**

Yes                       No → If No, stop the questionnaire.

**Do you need to avoid or reduce duties/activities or spread these over time?**

Yes                       No

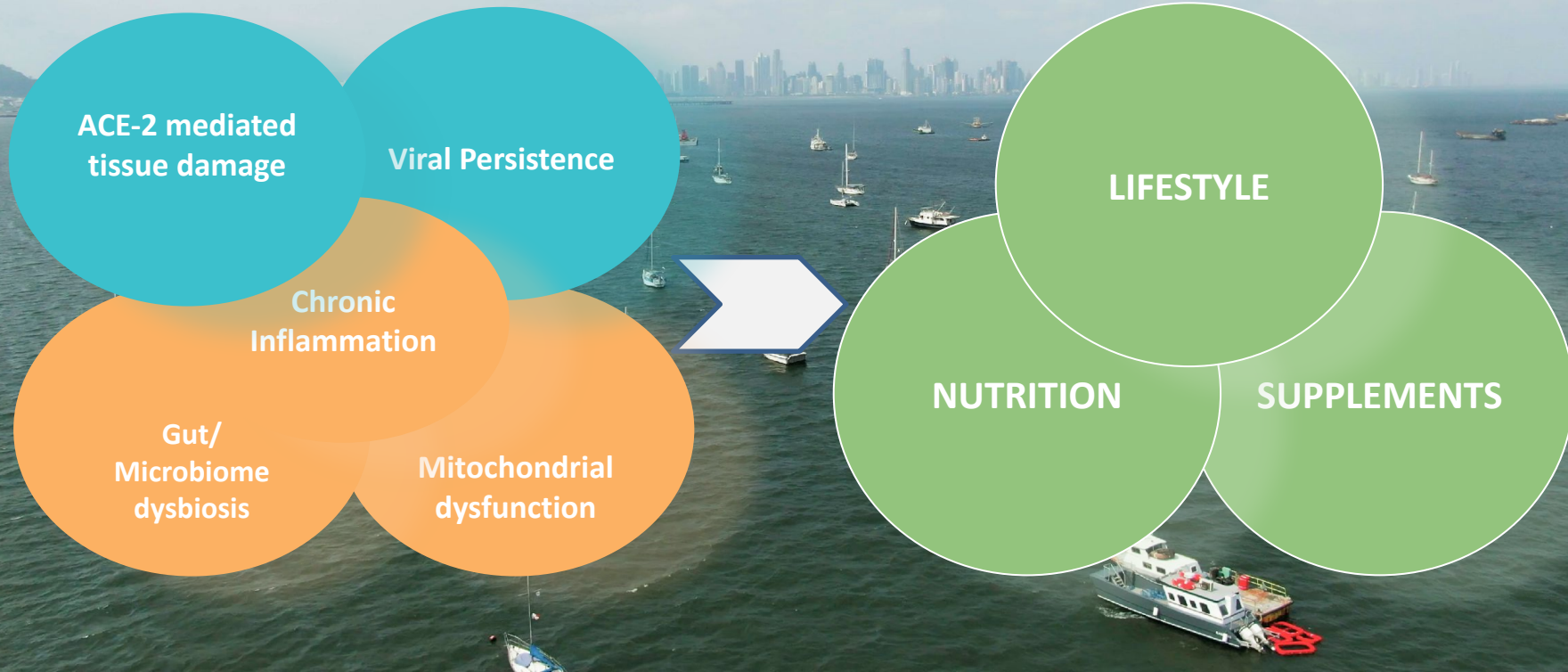
# Long COVID Patient Journey

## Follow-Up: 30, 60, 90-day patient registry surveys

- ❖ Updated timeline and progression of symptoms at 30-day intervals
- ❖ Adherence to food plan, nutritional supplements, and lifestyle recommendations
- ❖ PROMIS-29\*
- ❖ Post COVID Function Scale (PCFS)



# A Rising Tide Lifts all Boats





# KEY LIFESTYLE INTERVENTIONS OVERVIEW



# KEY LIFESTYLE INTERVENTIONS OVERVIEW

- Food, Nutrition + Supplements
- Restorative Sleep
- Movement & Exercise
- Stress Modification
- Social Connection



# WHY LIFESTYLE?

- In a prospective cohort study of 2000 women. Adherence to a healthy lifestyle prior to COVID-19 infection was inversely associated with risk of Post-COVID Conditions (PCC).
- Compared with those who did not have any healthy lifestyle factors, those with 5 or 6 had half the risk of PCC.
- Adequate sleep and healthy weight had the greatest impact on symptoms.



Wang S, Li Y, Wang S, Li Y, Yue Y, et al. Adherence to Healthy Lifestyle Prior to Infection and S, Li Y, Yue Y, et al. Adherence to Healthy Lifestyle Prior to Infection and Risk of Post-COVID-19 Condition. JAMA Intern Med. 2023;183(3):232–241.

# FOOD & NUTRITION

- Including plant-based foods, colorful and nutrient dense, with high quality protein and fats.
- Eliminating processed foods and drinks.



# FOOD & NUTRITION

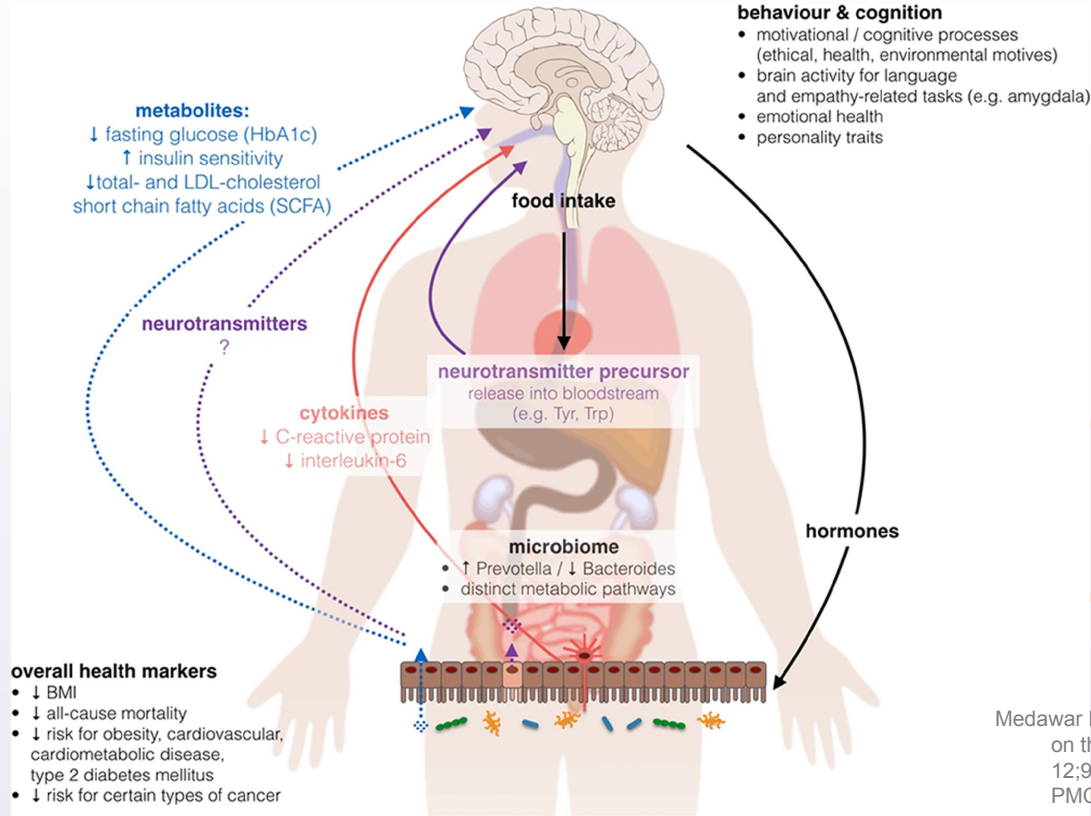


- Plant-based nutrition is associated with less hospitalization and death from acute covid.
- And greater recovery from acute and post covid.

Kim H, Rebolz CM, Hegde S, LaFiura C, Raghavan M, Lloyd JF, et al. Plant-based diets, pescatarian diets and COVID-19 severity: a population-based case-control study in six countries. *BMJ Nutrition, Prevention & Health*. 2021 May 18;

Storz MA. Lifestyle Adjustments in Long-COVID Management: Potential Benefits of Plant-Based Diets. *Curr Nutr Rep*. 2021 Dec;10(4):352-363. doi: 10.1007/s13668-021-00369-x. Epub 2021 Sep 10

# FOOD & NUTRITION



Medawar E, Huhn S, Villringer A, Veronica Witte A. The effects of plant-based diets on the body and the brain: a systematic review. *Transl Psychiatry*. 2019 Sep 12;9(1):226. doi: 10.1038/s41398-019-0552-0. PMID: 31515473; PMCID: PMC6742661.

# FOOD & NUTRITION

## TIPS for Coaching on Eating for Post Viral Recovery

- Personalize to individual GI symptoms, intolerances, energy and budget
- Use a health coach or nutritionist
- Advise on time restricted eating
- Rx low glycemic diet
- Optimize fermented foods and prebiotics
- Reduce histamines if symptoms correlate
- Suggest spices for added benefit & taste



# SLEEP

“COVID-19 and sleep disorders can induce BBB leakage via neuroinflammation, which might contribute to the ‘coronasomnia’ phenomenon. The new studies suggest that the control of sleep hygiene and quality should be incorporated into the rehabilitation of COVID-19 patients.”

Coiro MJ, Asraf K, Tzischinsky O, Hadar-Shoval D, Tannous-Haddad L, Wolfson AR. Sleep quality and COVID-19-related stress in relation to mental health symptoms among Israeli and US adults. *Sleep Health*. 2021;7(2):127–33

Gupta R, Grover S, Basu A, Krishnan V, Tripathi A, Subramanyam A, et al. Changes in sleep pattern and sleep quality during COVID-19 lockdown. *Indian J Psychiatr*. 2020;62(4):370–378

Jahrami HA, Alhaj OA, Humood AM, et al. Sleep disturbances during the COVID-19 pandemic: A systematic review, meta-analysis, and meta-regression. *Sleep Med Rev*. 2022;62:101591. doi:10.1016/j.smrv.2022.101591

Alzueta E, et al. An international study of post-COVID sleep health. *Sleep Health*. 2022 Dec;8(6):684-690. doi: 10.1016/j.sleh.2022.06.011. Epub 2022 Sep 23. PMID: 36163137; PMCID: PMC9501615.





# SLEEP: Improving Sleep Hygiene



Up to 40% of people with LC have sleep disruption which can cause a feed forward cycle in brain fog, inflammation, pain and mental health disturbances.

Find personalized experiments to achieve restorative sleep

Alzueta E, et al. An international study of post-COVID sleep health. *Sleep Health*. 2022 Dec;8(6):684-690. doi: 10.1016/j.sleh.2022.06.011. Epub 2022 Sep 23

Semyachkina-Glushkovskaya O, Mamedova A, Vinnik V, Klimova M, Saranceva E, Ageev V, Yu T, Zhu D, Penzel T, Kurths J. Brain Mechanisms of COVID-19-Sleep Disorders. *Int J Mol Sci*. 2021 Jun 28;22(13):6917. doi: 10.3390/ijms22136917. PMID: 34203143;

Pena-Orbea, C, et al. (2023) Sleep Disturbance severity and correlation in post-acute dequelae of COVID-19 (PASC) *Journal of Gneral Internal Medicine*

# SLEEP

- Both quality and quantity matter
- Improving sleep hygiene >
- Supplements that support sleep
- Practicing ultradian rhythm break or URB >



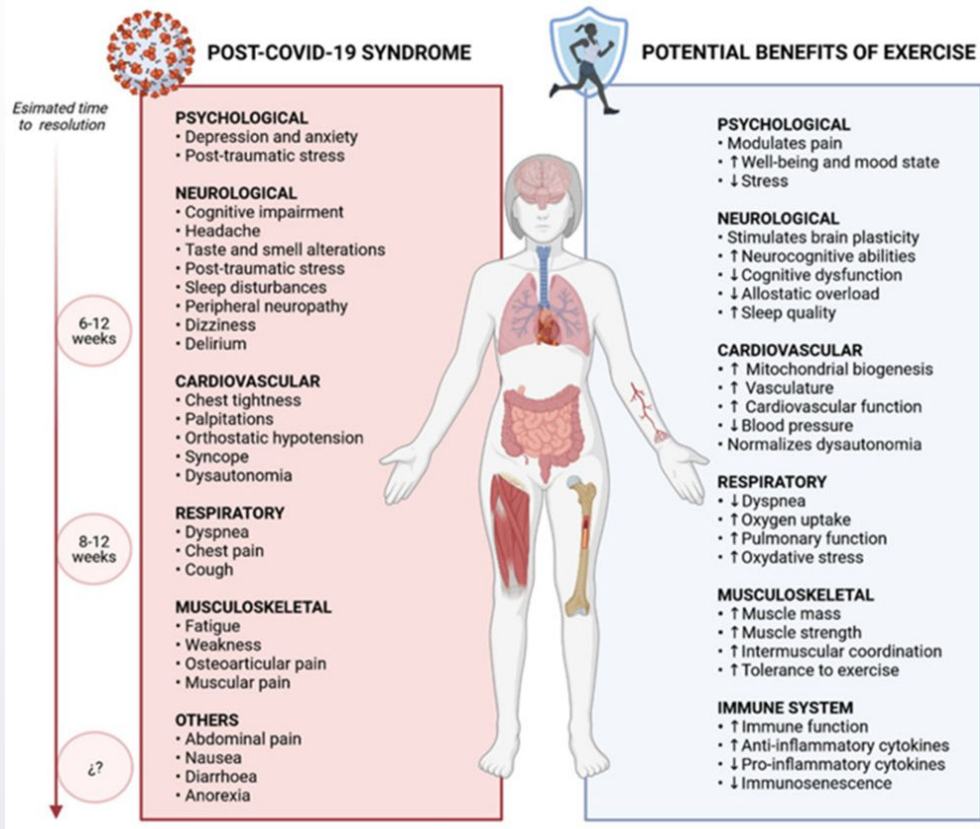
# MOVEMENT & EXERCISE >>

- Moderate, regular activity is essential to functioning of immune system, circulation, and tissue oxygenation
- In the multivariate analysis, physical activity during the pandemic was associated with a reduced likelihood of long COVID (prevalence ratio [PR]: 0.83; 95% confidence interval [CI]: 0.69–0.99) and a reduced duration of long COVID symptom



Feter N, et al. Physical activity and long COVID: findings from the Prospective Study About Mental and Physical Health in Adults cohort. Public Health. 2023 Jul;220:148-154. doi: 10.1016/j.puhe.2023.05.011. Epub 2023 Jun 13. PMID: 37320945; PMCID: PMC10263464.

# MOVEMENT as Post COVID Treatment



Jimeno-Almazán A, Pallarés JG, Buendía-Romero Á, Martínez-Cava A, Franco-López F, Sánchez-Alcaraz Martínez BJ, Bernal-Morel E, Courel-Ibáñez J. Post-COVID-19 Syndrome and the Potential Benefits of Exercise. *Int J Environ Res Public Health*. 2021 May 17;18(10):5329. doi: 10.3390/ijerph18105329. PMID: 34067776; PMCID: PMC8156194.

# TIPS TO GET MOVING

These experiments may help keep your body's stress response in check and help bring more physical activity into your day:

- Personalize it
- PACE it!.
- Start small
- Plan it out.
- Step outside.
- Utilize daily activities.
- Take it slow.
- HIIT It.
- Find support.



# STRESS MODIFICATION >>

Techniques to modify the impact of stress on augmenting inflammation and decreasing immune function



# STRESS MODIFICATION



- Acute COVID is associated with elevated evening cortisol levels.
- Long COVID is associated with low cortisol levels and low activation of the HPA axis.
- Stress modification and adrenal restoration are treatment for post -viral conditions

Lamontagne S.J., Pizzagalli D.A., Olmstead M.C. Does inflammation link stress to poor COVID-19 outcome? *Stress Health*. 2021;37(3):401–414.

Sandrini L., Ieraci A., Amadio P., Zara M., Barbieri S.S. Impact of acute and chronic stress on thrombosis in healthy individuals and cardiovascular disease patients. *Int. J. Mol. Sci.* 2020;2

Yavropoulou MP, Tsokos GC, Chrousos GP, Sfikakis PP. Protracted stress-induced hypocortisolemia may account for the clinical and immune manifestations of Long COVID. *Clin Immunol.* 2022 Dec;245:109133.

# STRESS MASTERY TECHNIQUES >>

Like stress triggers, what helps someone navigate stressful situations varies. Some common experiments include:



- Relaxation techniques
- Meditation
- Finding support from others
- Being physically active (this can add stress to the body but may help mental and emotional stress).
- Spending time in nature
- Diversion tactics
- Gratitude practices
- Laughter, joy, and play
- Engaging in arts, music, and crafts



# STRESS: MIND and MENTAL HEALTH

Worsened by stress, mental health and performance impacts post-viral recovery:



- Brain fog is a common symptom this program addresses .
- Mental health conditions are often new or worse post COVID and appropriate referrals and support are imperative to recovery.
- Mindset matters in recovery

Taquet M, et al. Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients. *Lancet Psychiatry*. 2022;9:815–827. doi: 10.1016/S2215-0366(22)00260-7.

Schou TM, Joca S, Wegener G, Bay-Richter C. Psychiatric and neuropsychiatric sequelae of COVID-19 - A systematic review. *Brain Behav Immun*. 2021 Oct;97:328-348. doi: 10.1016/j.bbi.2021.07.018. Epub 2021 Jul 30.

R. Zion a, Kengthsagn Louis a, Rina Horii a b, Kari Leibowitz a, Lauren C. Heathcote c d, Alia J. Crum. Making sense of a pandemic: Mindsets influence emotions, behaviors, health, and wellbeing during the COVID-19 pandemic. *Social Science & Medicine*. Volume 301, May 2022, 114889

# STRESS: MIND and MENTAL HEALTH TIPS



- Refer people to mental health providers as appropriate
- Listen deeply, and offer support
- Acknowledge grief over losses
- Set expectations for a variable course of improvement
- Ask specifically what is working/ improving
- Support strengths
- Work with mindset to envision health
- Assist people to find community and reduce isolation

<https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/care-post-covid.html>

Burton A, Aughterson H, Fancourt D, Philip KEJ. Factors shaping the mental health and well-being of people experiencing persistent COVID-19 symptoms or 'long COVID': qualitative study. BJPsych Open. 2022 Mar 21;8(2):e72.

# SOCIAL CONNECTION >>

People impacted by long COVID reflect how isolated they continue to feel isolated as others move on.

Connecting participants to community, and especially to support of people experiencing similar losses is essential to recovery.



# POST VIRAL RECOVERY:

Applying the protocol in clinical practice

# SUPPLEMENT TARGETING

- ❖ ACE-2 mediated damage (tissue damage)
- ❖ Viral persistence
- ❖ Chronic inflammation
- ❖ Mitochondrial dysfunction
- ❖ Gut / Microbiome dysbiosis

After simplifying the Post COVID Recovery Framework, we found ourselves needing a curated suite of nutritional product solutions to target the five main drivers of Long COVID.

- ❖ **Tollovid** (3 capsules, 4x/day for 30 days, 2 capsules, 4x/day next 7 days, then 1 capsule, 2x/day for 30 days)
- ❖ **MegaSporeBiotic** (1 capsule/day for 7 days then 2 capsules/day until bottle completion)
- ❖ **MegaPreBiotic** (3 capsules/day, following completion of MegaSporeBiotic up to 90 days)
- ❖ **ITIS** (2 capsules, 3x/day for 90 days)
- ❖ **Arterosil** (2 capsules, 2x/day for 30 days then 1 capsule, 2x/day until 90 days)

### Tollovid: Blocks viral replication capacity

Coronaviruses use their signature “spikes” to fuse themselves to a cell’s outer membrane via the ACE2-receptor to gain entry inside.

### MegaSporeBiotic

- ❖ Probiotic blend of 5 Bacillus spores that have been shown to maintain healthy gut barrier and immune function
- ❖ Aims to RECONDITION the gut instead of reseeded with probiotic strains that cannot survive digestion or colonize the gut.

### MegaPreBiotic

- ❖ Contains non-digestible oligosaccharides that can increase microbial diversity and selectively feed beneficial bacteria like Akkermansia muciniphila, Faecalibacterium prausnitzii, and Bifidobacteria
- ❖ REINFORCES the beneficial microbial changes created by MegaSporeBiotic™ to promote a strong and diverse microbiome..

## Specialty Supplements

- ❖ **Tollovid** (3 capsules, 4x/day for 30 days, 2 capsules, 4x/day next 7 days, then 1 capsule, 2x/day for 30 days)
- ❖ **MegaSporeBiotic** (1 capsule/day for 7 days then 2 capsules/day until bottle completion)
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- ❖ **ITIS** (2 capsules, 3x/day for 90 days)
- ❖ **Arterosil** (2 capsules, 2x/day for 30 days then 1 capsule, 2x/day until 90 days)

### ITIS Formula:

- ❖ Reduces pain & inflammation
- ❖ Maintains comfortable joint & muscle function
- ❖ Soothes an irritated immune system

### Arterosil: Protects and repairs the Endothelial Glycocalyx (EGx)

- ❖ Selectively permeable barrier that prevents blood components from sticking to the vessel wall
- ❖ Harbors Super Oxide Dismutase (extracellular SOD)
- ❖ Regulates vascular permeability, inflammation, coagulation, and fluid balance

## Foundational Supplements

- ❖ MitoCore [MVit + AntiOx]  
(2x/day 90 days)
- ❖ Vitamin K2 with D3  
(up to 10,000IU)
- ❖ Ω-3 Oil (1000mg 2x/day 90 days)
- ❖ Magnesium Glycinate (200mg  
2x/day 90 days)
- ❖ Quercetin (500mg 2x/day 90 days)
- ❖ Coenzyme Q10 (100mg/day 90  
days)

### MitoCore key features:

#### Comprehensive MVI with Antioxidant and Mitochondrial Support

- ❖ NAC 500 mg
- ❖ Glucoraphanin 40 mg
- ❖ Alpha Lipoic Acid, Resveratrol and EGCG
- ❖ Acetyl L-carnitine 500 mg, Magnesium
- ❖ Manganese, Zinc

### Vitamin K2 with D3 dosing based on levels:

- ❖ serum level-<40 ng/mL, use 10000 IU;
- ❖ if 40-60 ng/mL, use 5000 IU daily
- ❖ if >60 ng/mL no additional needed

### Quercetin:

- ❖ Immunomodulatory and may improve T-Reg function
- ❖ Demonstrated anti-viral activity against both RNA and DNA viruses





# Group Medical Visits

**Dr. Kara Parker, MD, IFMCP**  
Faculty, Department of Family Medicine  
Director of Group Medical Visits  
Hennepin Healthcare Whittier Clinic

# PVRP Group Medical Visit Components



Scaled education on the benefits of and resources for specific Lifestyle factors for recovery after COVID



Group instruction and exploration on plant based or forward anti-inflammatory diet tailored to each person's needs



Group teaching on the specialty and foundational supplements for post Viral recovery



Time for support, connection, questions, and group practices for each part of the program

# PVRP Group Visit **Our Topics**

- ❖ Overview of program, Intros, Patient Post COVID story
- ❖ Food & Nutrition
- ❖ Sleep & Mood
- ❖ Movement & Exercise
- ❖ Stress Modification
- ❖ Brain and Microbiome
- ❖ Mitochondria



# PVRP Group Medical Visits Stats/ Insights:

7/2020 to current, 13 groups, average 12 pts

3 groups using the protocol supplements

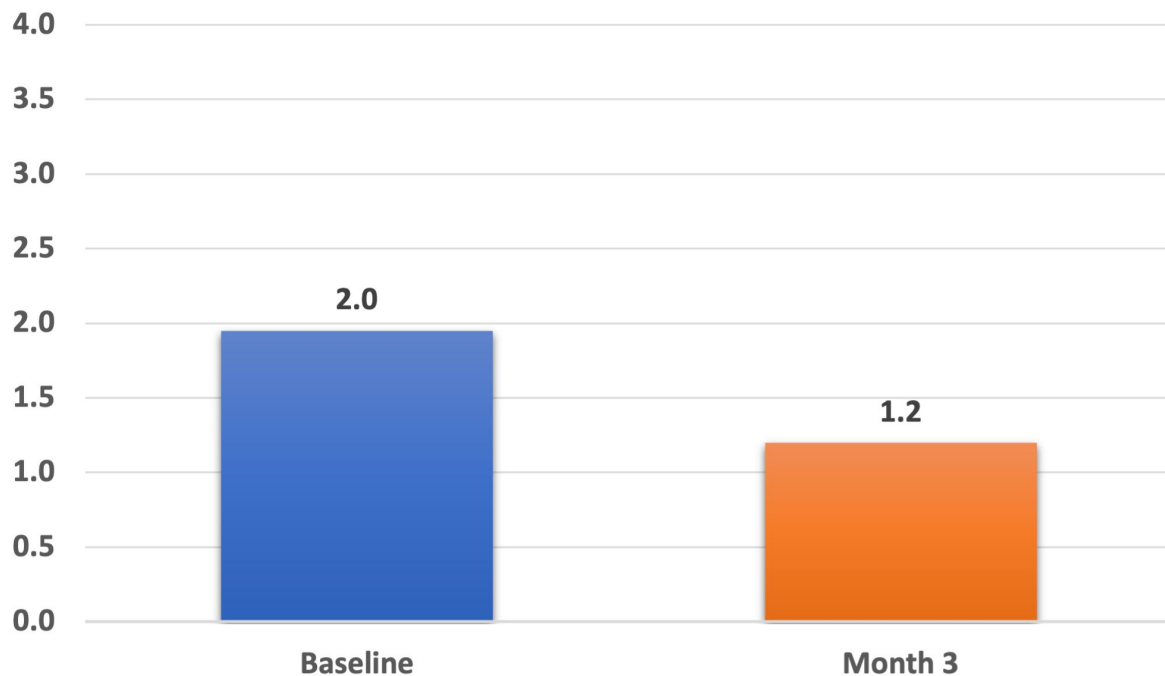
- ❖ Patients who feel alone, isolated, and misunderstood benefit from connection
- ❖ The lifestyle and supplements (protocol) fit well in a GV format
- ❖ I have learned on care of pts w LC by listening to pts w LC share needs & wins
- ❖ Benefits multiply for pts and practitioners in the care and presence of others



# Patient Registry Early Outcomes



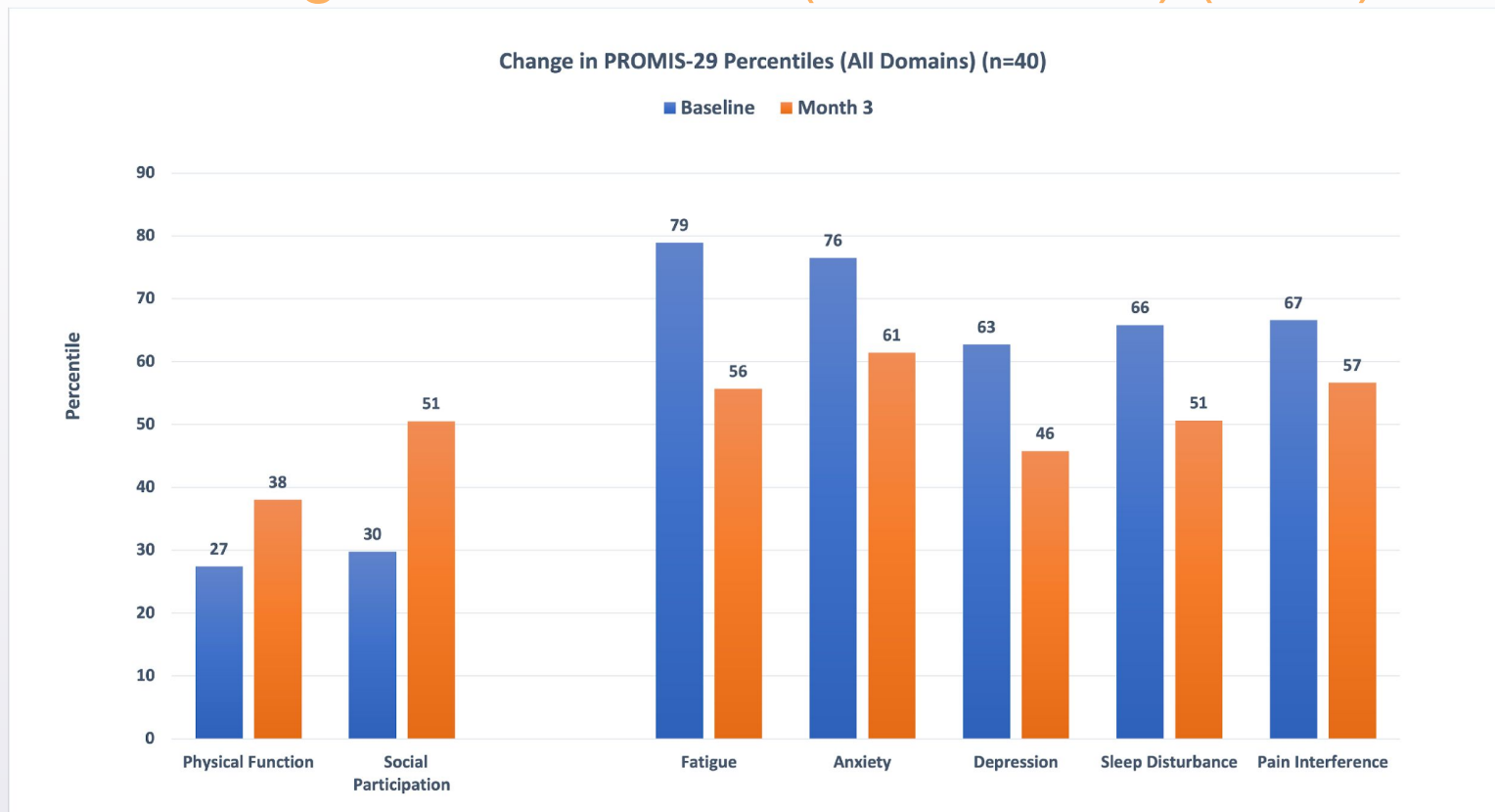
# Change in Post-COVID-19 Functional Status Scale (n=40)



## Potential interpretation:

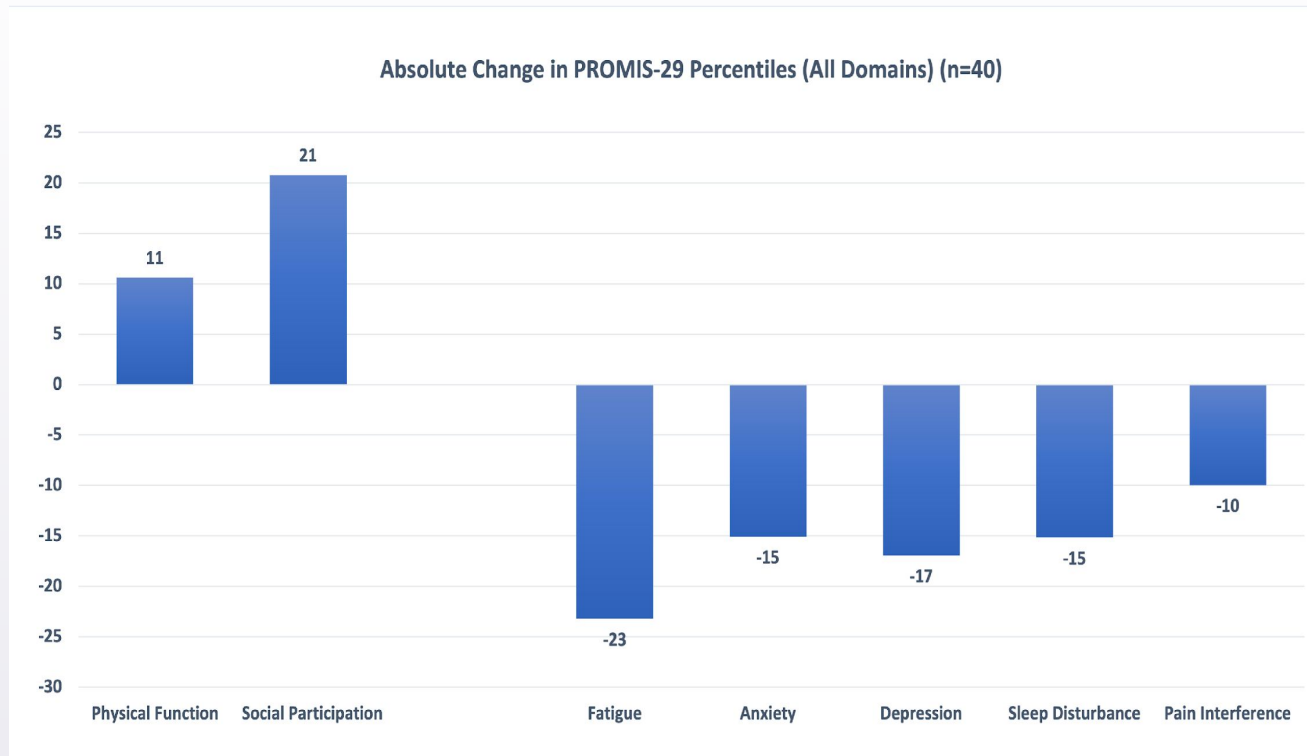
On a scale of 0 to 4, with 4 being the lowest function, patients' Post-COVID functional status improved from 2.0 to 1.2, on average. This represents a 38.5% improvement in function.

# PROMIS Change in Percentiles (All Domains) (n=40)





# PROMIS Absolute Change in Percentiles (All Domains) (n=40)



## Potential interpretation:

This figure shows the magnitude of the absolute change in percentile for each of the 8 domains of the PROMIS-29. You can see that the greatest improvements were seen in social participation, fatigue, anxiety and depression.

*“My blood oxygen used to go down to 82% while doing PT at the hospital little effort. Now I stay over 90% O2 sat with a lot more movement in 2 weeks on the supplements.”*

*“The group visits tools give me power – I have agency when I have scary and dangerous symptoms, they no longer overwhelm me.”*

*“My body shape is changing, and I’m convinced it (the protocol) is helping everything.”*

## Early Patient Quotes

- ❖ “My migraines are gone now, just small daily headaches remain, they are less.”
- ❖ “My chest pain was really bothering me, I almost went to the ER again but they never find anything. I took an Arterosil and my pain reduced enough to stay home. Now that I’m on it 2 weeks I don’t have those pains anymore.” (Patient cried with gratitude when sharing this).
- ❖ “My pain with exertion is less, and I can move more without being set back.”
- ❖ “I have much more mental clarity.”
- ❖ “I have much better energy and much better mood.”
- ❖ “My muscle fatigue is much less since starting the program.”
- ❖ “I am done with the Tollovid. It helped my energy. On the Arterosil now for a month I continue to have a lot less pooling and swelling in my legs, and my POTS symptoms are less.”
- ❖ “I know more than my regular doctors about my condition. I wish more knew about mitochondria, vagal tone, cortisol and adrenal health, Ace-2 receptors and how it all affects long COVID symptoms.”
- ❖ “I no longer feel alone in what I am dealing with. Hearing everyone else’s stories heals me. Hearing everyone’s tools and ways of coping gives me hope and options.” (6 people emphasize this).



# RESOURCES

[www.ovationlab.com/Resources](http://www.ovationlab.com/Resources)



# POST VIRAL RECOVERY PROGRAM

Resources for Providers and Patients



Presented by



Research and Program Development Sponsor



## UPCOMING EVENTS

A ROOT-CAUSE APPROACH TO LONG COVID IN THE POST-PANDEMIC ERA

ANDHEALTH OVATIONLAB

Wednesday, September 27th  
7 pm ET/4 pm PT

## WORKSHOP REPLAYS


POST VIRAL RECOVERY IN THE COVID ERA  
WORKSHOP NO. 1

POST VIRAL RECOVERY A 90-DAY PROGRAM AND PROTOCOL  
WORKSHOP NO. 2


POST VIRAL RECOVERY LIFESTYLE INTERVENTIONS, CASE STUDIES & LEARNINGS  
WORKSHOP NO. 3

## PRACTITIONER RESOURCES AND TOOLS

### FULLSCRIPT RESOURCES

- [Protocol Application with Fullscript](#) 
- If you do not have an active Fullscript account, please use [this link](#) to create your no-cost account.
- If you would like to prescribe the **specialty products only**, please use [this link](#).
- If you would like to prescribe the **full protocol** or make modifications to it, please use [this link](#).
- [Dispensary & individual patient discounts](#)

### NUTRITIONAL SUPPLEMENT SELECTIONS

- [Supplement Selection](#) 
- [Fullscript Patient Protocol](#)

### SAMPLE SURVEY INSTRUMENTS

- [LongCOVID Patient Intake Form](#)
  - [WHO Post COVID-19 CRF](#)
- [Timeline and Progression of Symptoms Table](#)
- [PROMIS29](#)
- [Post COVID Function Scale](#)
  - [The Post-COVID-19 Functional Status scale](#)

**PATIENT CASES** - Coming

## PATIENT RESOURCES AND TOOLS

### WHOLE30 PROGRAM RESOURCES

- [Program Rules](#)
- [Plant-Based Whole30 Prep Pack](#)
- [Grocery Guide](#)
- [Shopping List](#)
- [Meal Planning](#)
- [Plant-Based Recipes](#)

### LIFESTYLE INTERVENTION RESOURCES

- [How to Improve Sleep Hygiene](#)
- [Circadian Rhythms](#)
- [Stress Management](#)
- [Physical Activity and Stress](#)
- [Exercise Tolerance Assessment for Exercise Fitness & HR Recovery. Instructions \(from Share Care\).](#)

- [WHO Support for Rehabilitation](#)
- [The Levine Protocol For Exercising With POTS - Better By The Beat](#)
- [Instructions for POTS Exercise Program—Children's Hospital of Philadelphia the Structure of the Training. Calendars](#)
- [Coronavirus Recovery: Breathing Exercises | Johns Hopkins Medicine](#)
- [Bouncing Back From COVID-19](#)
- [5 At-Home Exercises for COVID-19 Recovery | Patient Care](#)



# Q&A Session

# THANK

# YOU





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