# POST VIRAL RECOVERY PROGRAM

A Workshop Series for Health Care Professionals Seeking a Root Cause Approach


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# Project Timeline

**November 2021**
Expert working group assembled

**January 2022**
Prototype root-cause framework & standards for evaluating and treating long COVID

**February 2022**
Social listening study completed mining > 1 million conversations

**April 2022**
Presented research to support 5 primary drivers of long COVID

**July 2022**
Selected outcomes measures and developed Timeline & Progression of symptoms

**August 2022**
Presented 90-day program and protocol (beta)

**September 2022**
Finalized specialty supplement recommendations to address 5 drivers of Long COVID.

**October 2022**
Contracted with NUNM to develop REDCap patient registry

**December 2022**
First patients enrolled in virtual group visit program at Hennepin

**January 2023**
First patients enrolled from Mayo Clinic

**February 2023**
Enrolled first AndHealth “VIP” patients.

**April 2023**
- 100+ patients enrolled in registry with first patients completing 90-day protocol.
- Outcomes data analyzed.
- Completed development of 3-part provider education series

**May 2023**
2100+ practitioners registered for the PVRP education workshop series.

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# Current Landscape: 3 Years Into PASC

- Confusing terminology: Chronic COVID, Post Viral Syndrome, Long-Haul COVID, Long COVID…and more.
- 200+ symptoms
- No agreed upon definitions: CDC 30-days; WHO 90-days post-acute infection
- No proven treatments, no standards of care = no guidelines and no trained workforce
- Providers and patients frustrated - where to turn for guidance and help?
- NIH RECOVER: research and clinical trials -  $1.2 billion
  - Largely observational studies: no findings published
  - 5 clinical trials planned (2600 total patients, 25-100 sites/study)
  - Drugs (Paxlovid), CBT, exercise, rehab
  - Not a single patient enrolled to-date

# MORE IS NEEDED

## A ROOT-CAUSE, SYSTEMS APPROACH

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# Workshop Outlines

- Workshop 1: Post Viral Recovery in the COVID Era
- Workshop 2: Post Viral Recovery - A 90-Day Program and Protocol
- Workshop 3: Post Viral Recovery - Lifestyle Interventions & Case Studies
- Further Education: A4M, AIHM, IFM, PLMI
- Resources: Workshop replays, reference papers, tools
- How to join our learning community and enroll your patients

# Expert Clinical Working Group

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Patrick Hanaway, MD

Laurie Hofmann, MPH

Kara Parker, MD

Michael Stone, MD, MS

Kristi Hughes, ND

Monique Class, ARNP

Tom Guilliams, PhD

Bob Sheeler, MD

Heather Tick, MD

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# POST VIRAL RECOVERY IN THE COVID ERA

## ASSESSING PROGRESSION AND PERSONALIZING TREATMENT USING A ROOT-CAUSE APPROACH

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# LONG COVID PREVALENCE[1]

- Most Long COVID cases are cases with mild acute illness
- 1/3 of people with Long COVID have **no identified pre-existing conditions**

- 104,538,730 - reported
  >200,000,000 - reported + unreported estimate
- 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 million people with Post-COVID @ 12 months

# LONG COVID Root Cause Approach

## Risk of Long COVID

- Terrain
- Context/ Exposure
- History of Illness (timeline)

## Mechanisms of Long COVID

- Tissue Damage
- Inflammation

# Multiple early factors anticipate post-acute COVID-19 sequelae

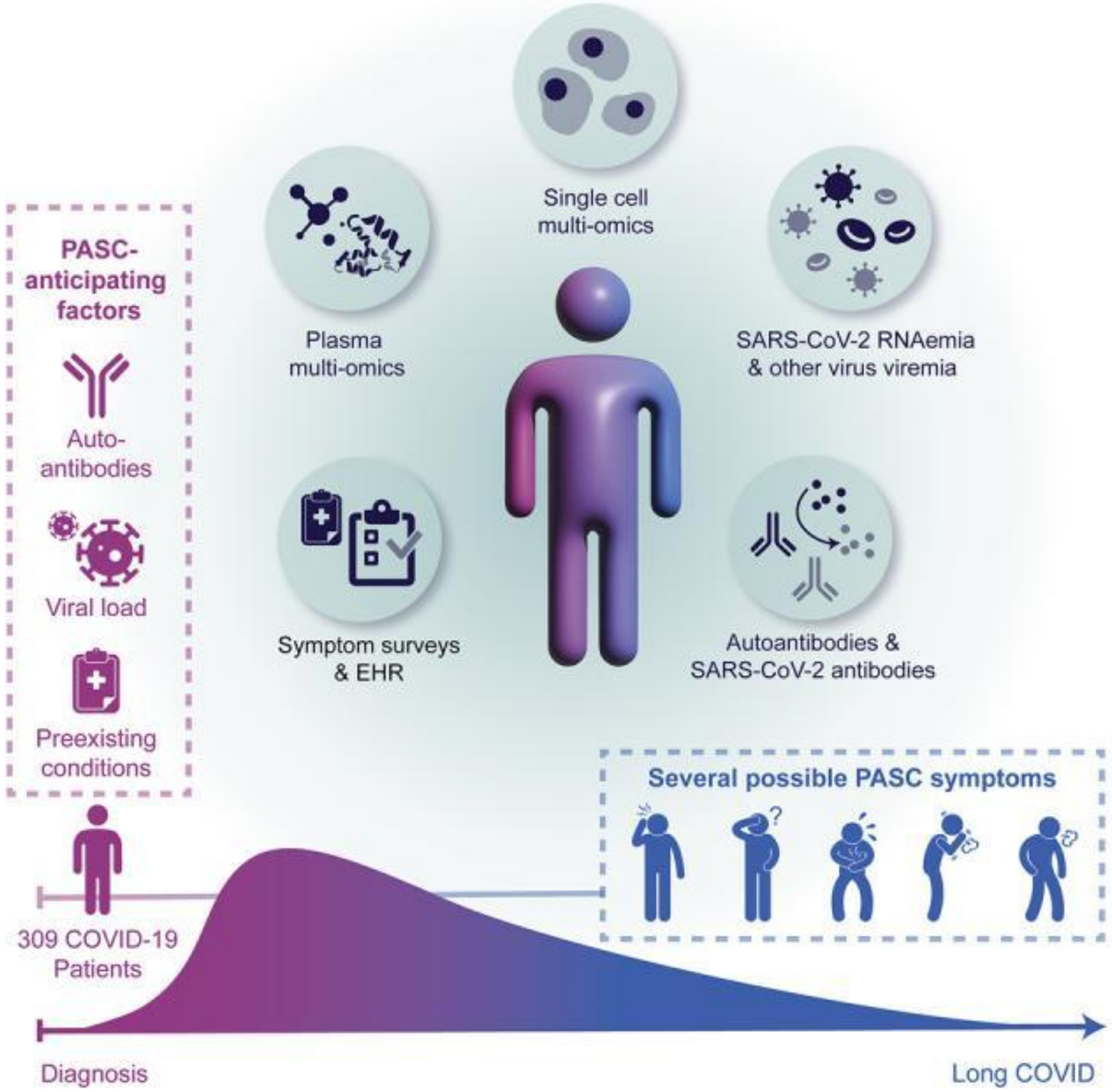
Su, Y, Yuan, D, et. al. (2022). Multiple early factors anticipate post-acute COVID-19 sequelae. Cell, 185(5). https://doi.org/10.1016/j.cell.2022.01.014

## In Brief:

By correlating patient symptoms with in-depth profiling of blood cells and plasma components throughout COVID-19 infection, this study identifies factors that may predict sustained disease.

# Multiple early factors anticipate post-acute COVID-19 sequelae

Su, Y, Yuan, D, et. al. (2022). Multiple early factors anticipate post-acute COVID-19 sequelae. Cell, 185(5). https://doi.org/10.1016/j.cell.2022.01.014



# 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

In Brief:

Long COVID may be driven by long-term tissue damage (e.g. lung, brain, and heart) and pathological inflammation (e.g. from viral persistence, immune dysregulation, and autoimmunity). The associated risk factors may include female sex, more than five early symptoms, early dyspnoea, prior psychiatric disorders, and specific biomarkers (e.g. D-dimer, CRP, and lymphocyte count), although more research is required to substantiate such risk factors. While preliminary evidence suggests that personalized rehabilitation training may help certain long COVID cases, therapeutic drugs repurposed from other similar conditions, such as myalgic encephalomyelitis or chronic fatigue syndrome, postural orthostatic tachycardia syndrome, and mast cell activation syndrome, also hold potential.

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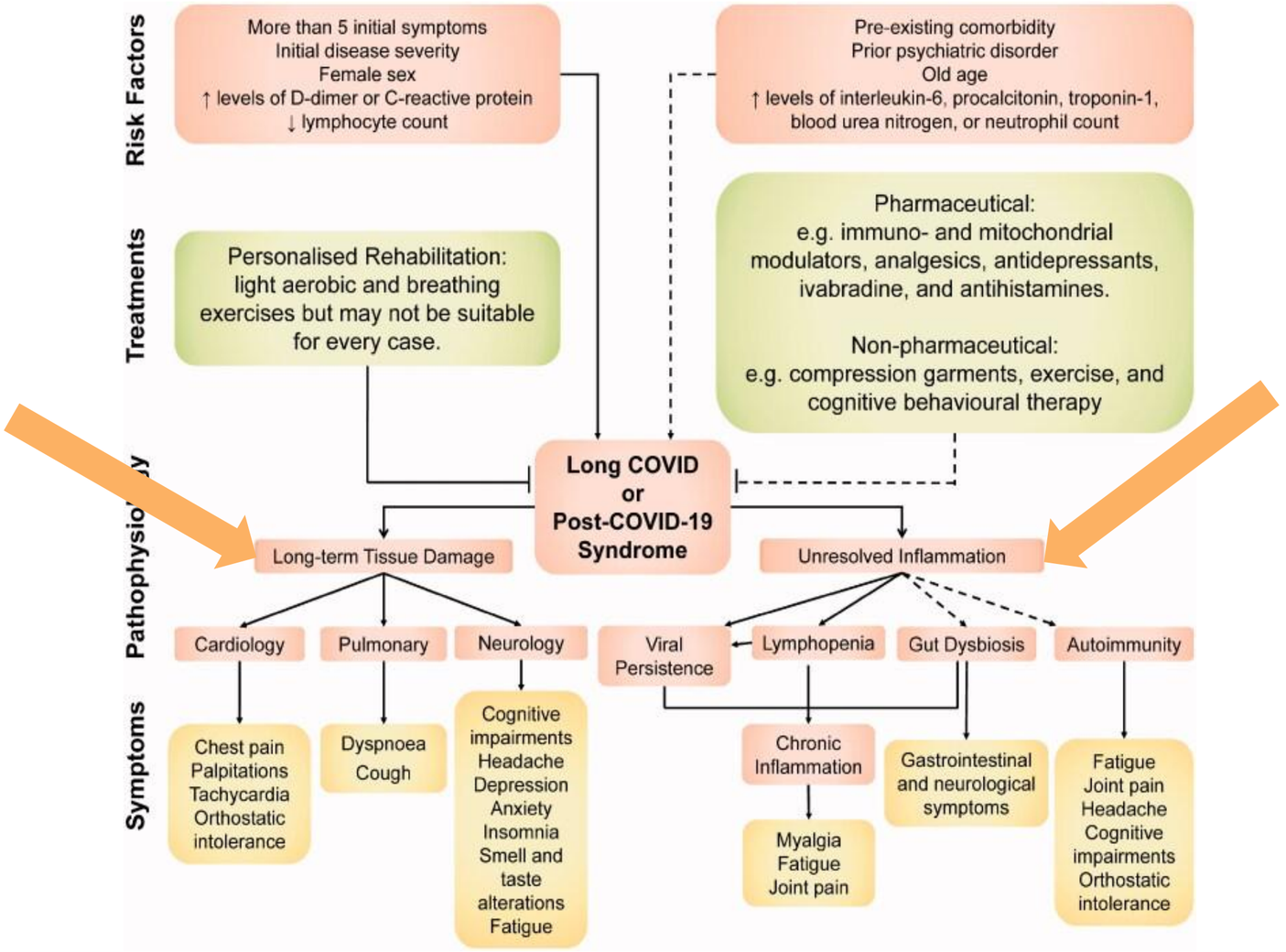
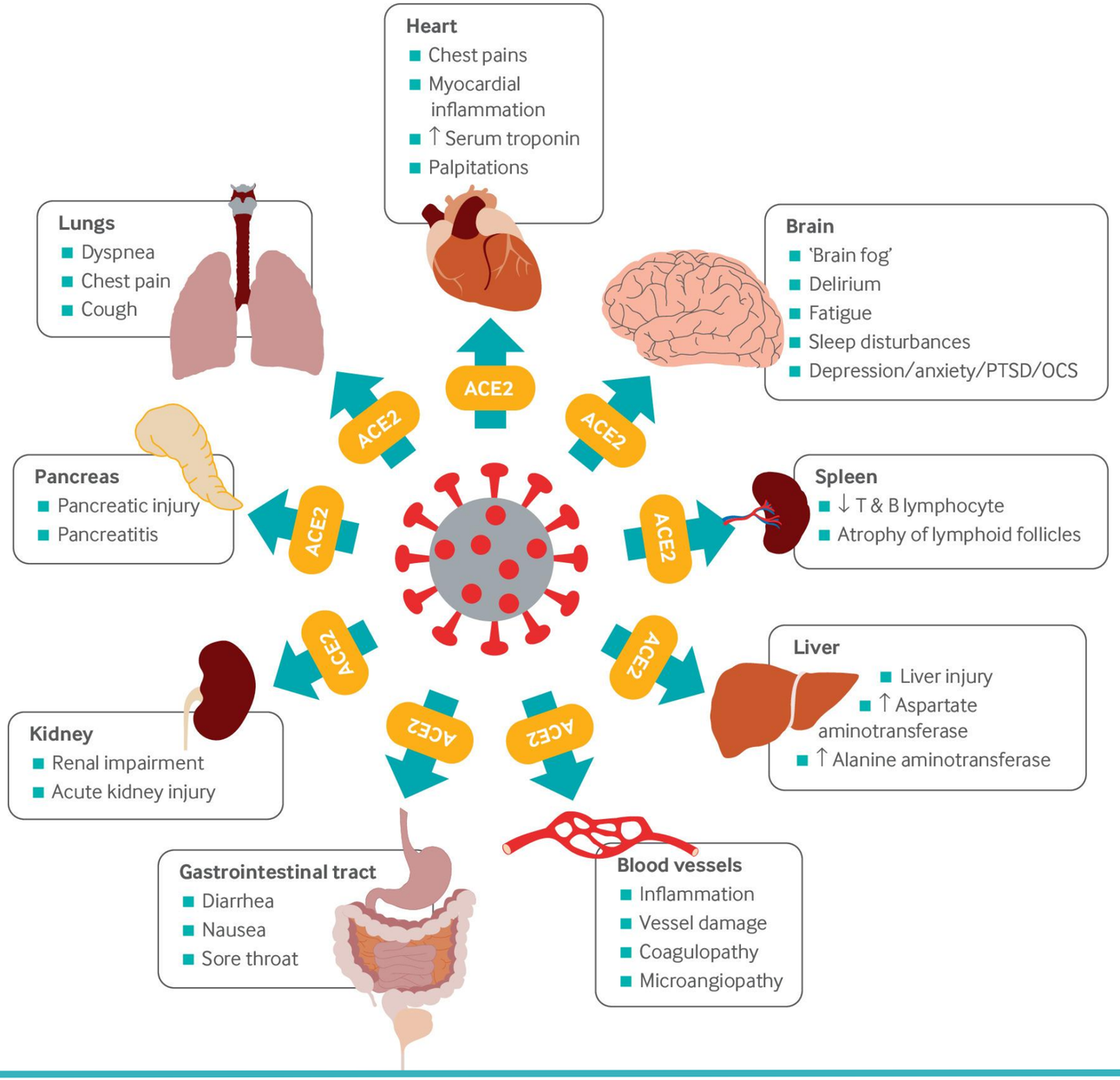



An overview of the symptoms, putative pathophysiology, associated risk factors, and potential treatments involved in long COVID. Note: Dashed lines represent areas where evidence is relatively lacking compared to non-dashed lines. (Color online only).

# 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.

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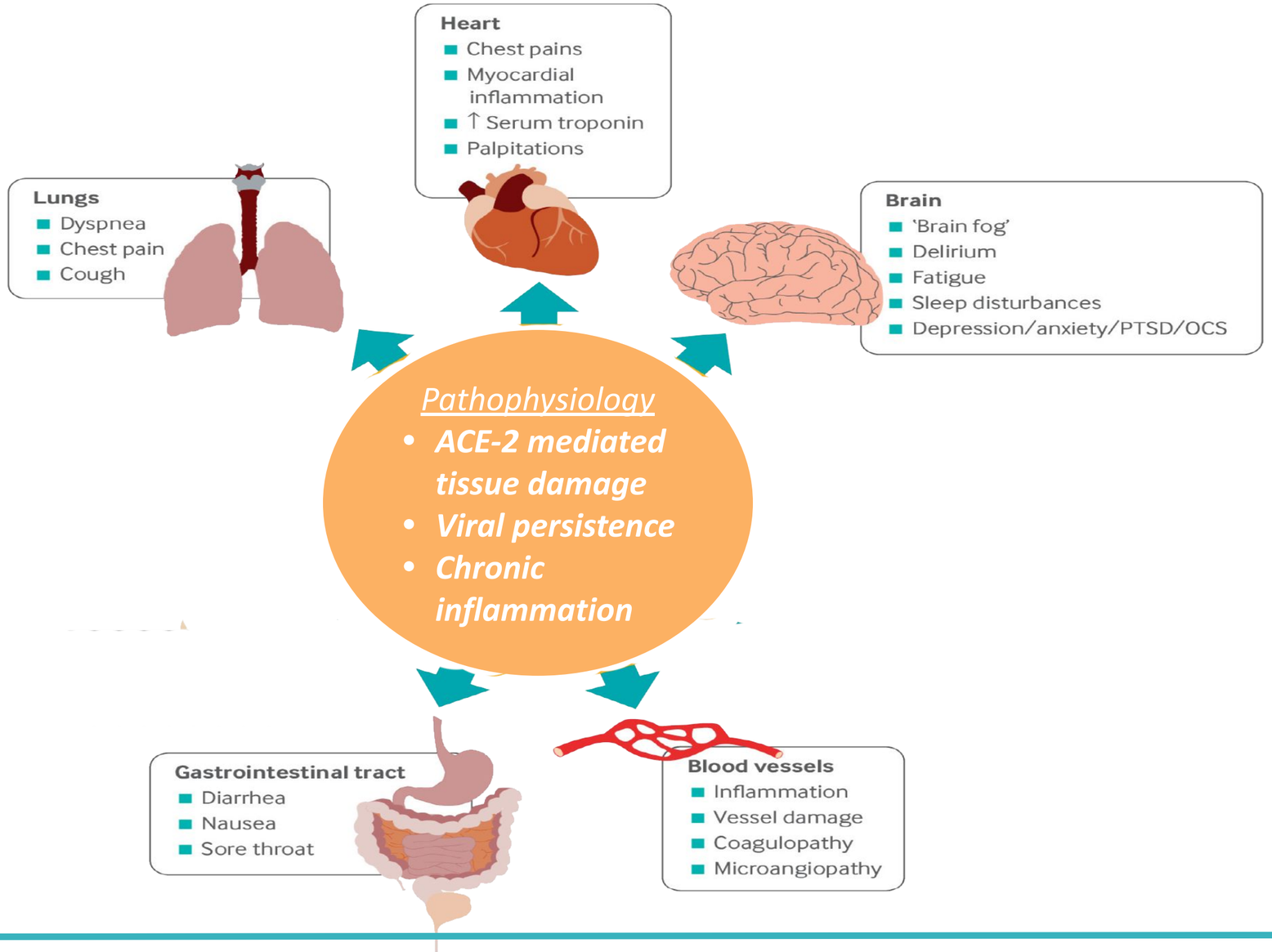
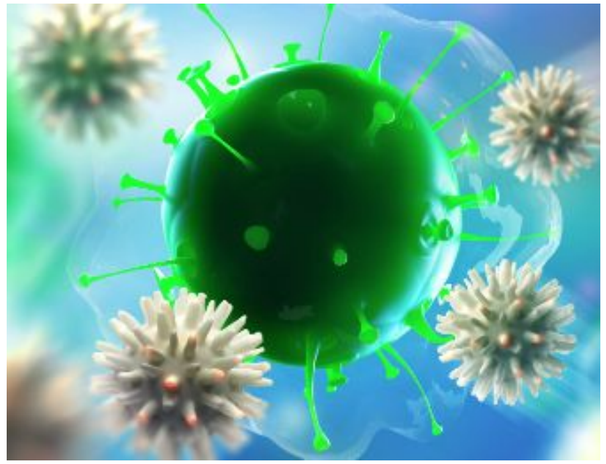
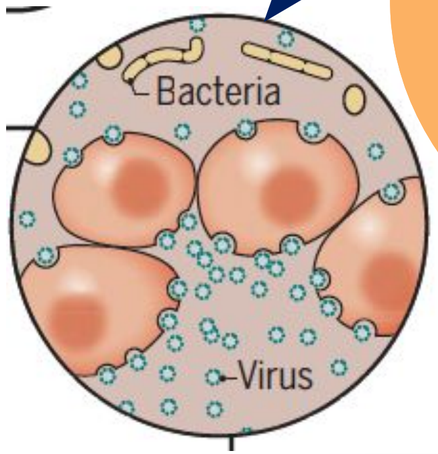
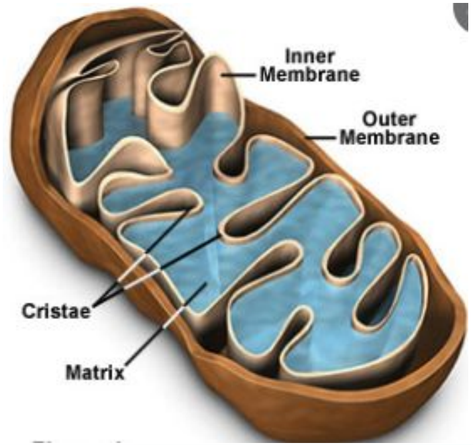

Heart
Chest pains
Myocardial inflammation
↑ Serum troponin
Palpitations
Lungs
Dyspnea
Chest pain
Cough
Brain
'Brain fog'
Delirium
Fatigue
Sleep disturbances
Depression/anxiety/PTSD/OCS
Pathophysiology
ACE-2 mediated tissue damage
Viral persistence
Chronic inflammation
Gastrointestinal tract
Diarrhea
Nausea
Sore throat
Blood vessels
Inflammation
Vessel damage
Coagulopathy
Microangiopathy



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



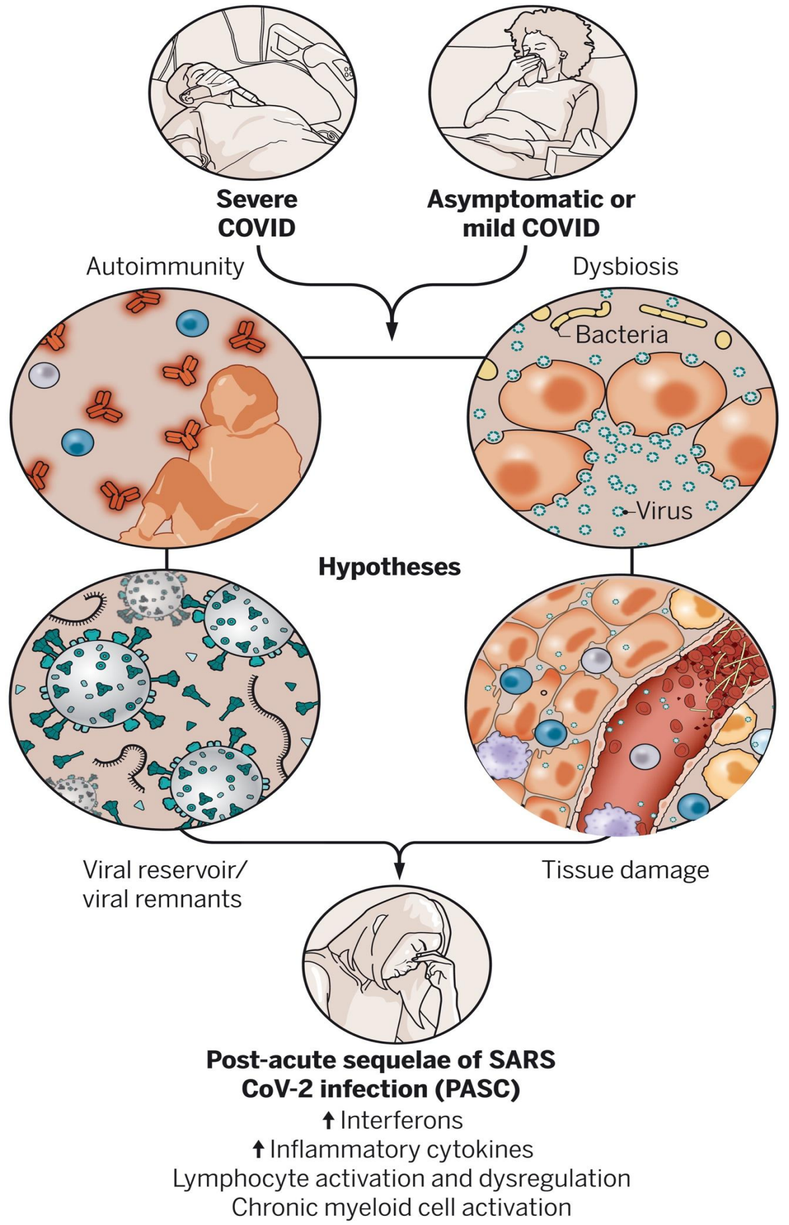



# Distinguishing features of Long COVID identified through immune profiling

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

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# 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, 2º 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]

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8. **Clotting/ Coagulation Vascular Issues [ACE2]**

ACE-2 mediated tissue damage

Viral Persistence

Chronic Inflammation

Gut/Microbiome dysbiosis

Mitochondrial dysfunction

# Long COVID: Risk Factors & Mechanisms

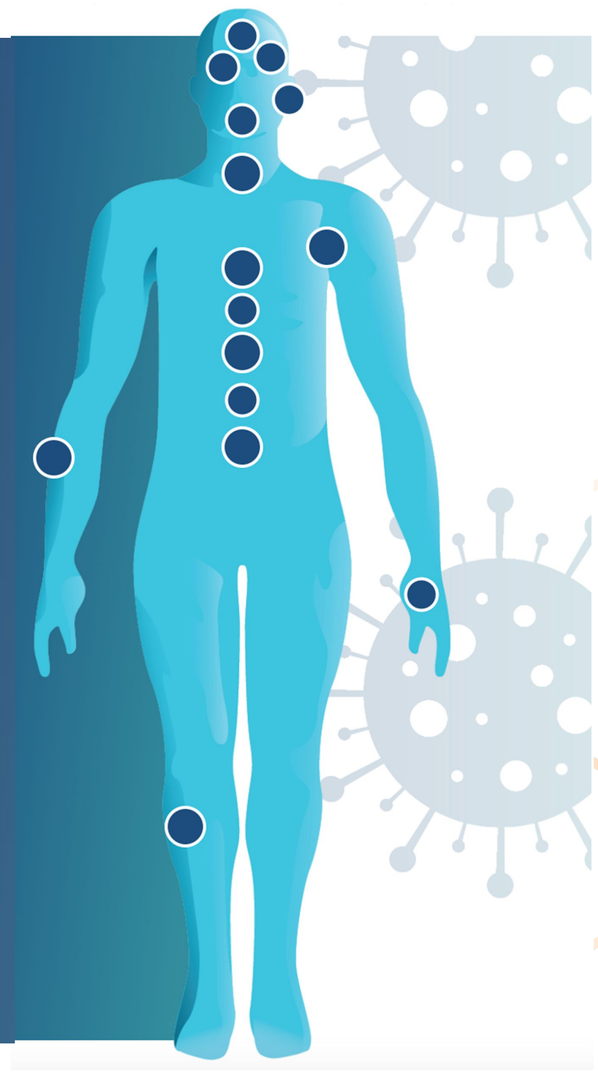
## Risk of Long COVID

- Terrain
  - Family History
  - Past Medical History
    - Co-morbidities
    - Gut microbiome
- Context/ Exposure
  - Infectious Dose
  - SARS-CoV-2 Variant

- History of Illness (timeline)
  - Varied Symptoms
    - → Damage
  - Acute Illness
    - → Long COVID
  - Multiple infections?

# Long COVID: Symptoms

- Whole Body
- Brain and Nerves
- Eyes
- Ears
- Smell and Taste
- Neck
- Lungs
- Heart and Blood
- Kidneys
- Hands
- Legs and Feet
- Reproductive Systems
- Digestive Systems
- Skin and Hair
- Muscles and Bones



*Long COVID | NIH COVID-19 Research*. (n.d.). NIH COVID-19 Research. https://covid19.nih.gov/covid-19-topics/long-covid

# Long COVID: Risk Factors & Mechanisms

## Mechanisms of Long COVID

- Tissue Damage
  - Heart
  - Lungs
  - Blood Vessels
  - Brain/ Neuro
  - GI Tract
- Chronic Inflammation
  - Viral Persistence
  - Reactivation of Pathogens
- Gut/Microbiome Dysbiosis
- Mitochondrial Dysfunction

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

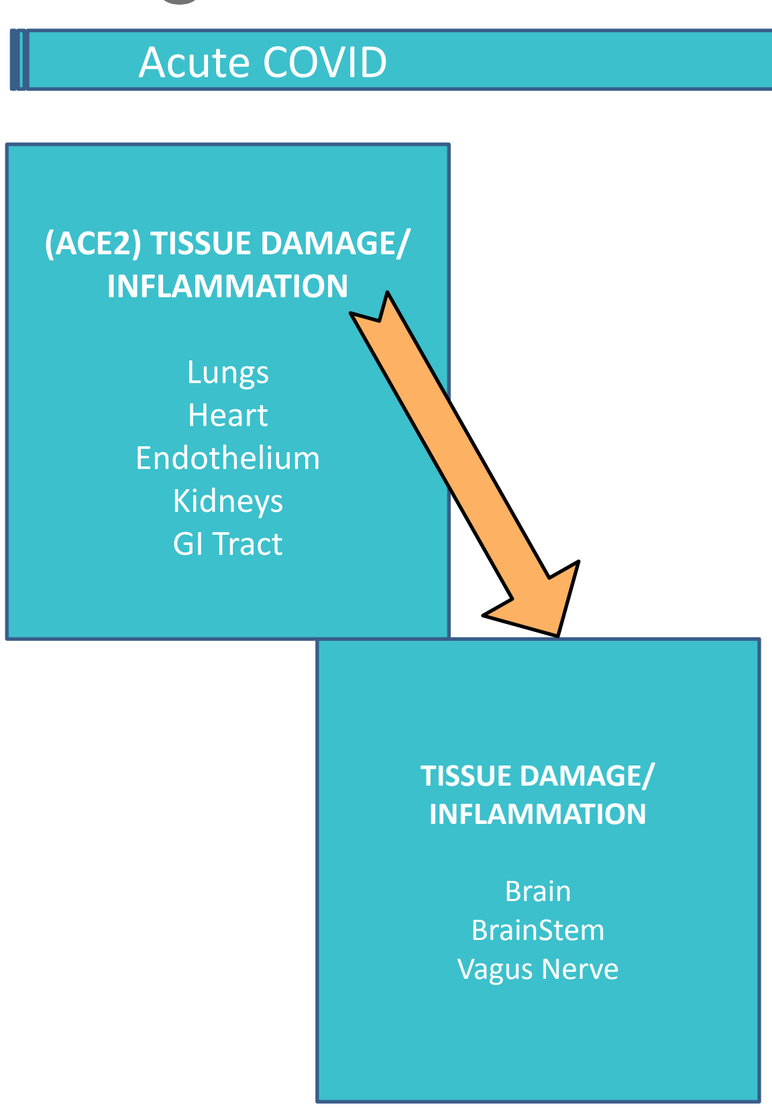
## ACE2 TISSUE DAMAGE

- 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

# Progression to Long COVID



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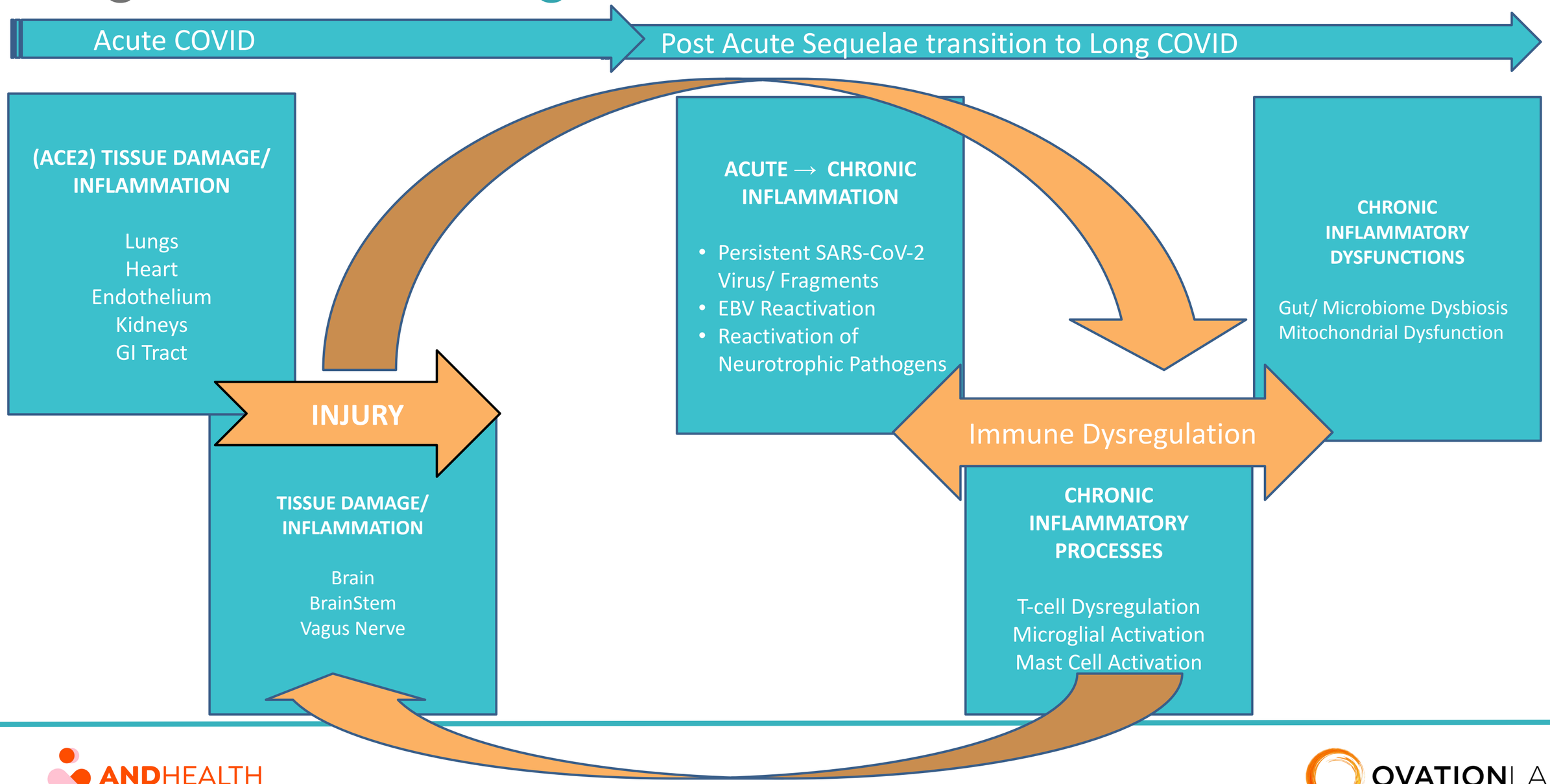


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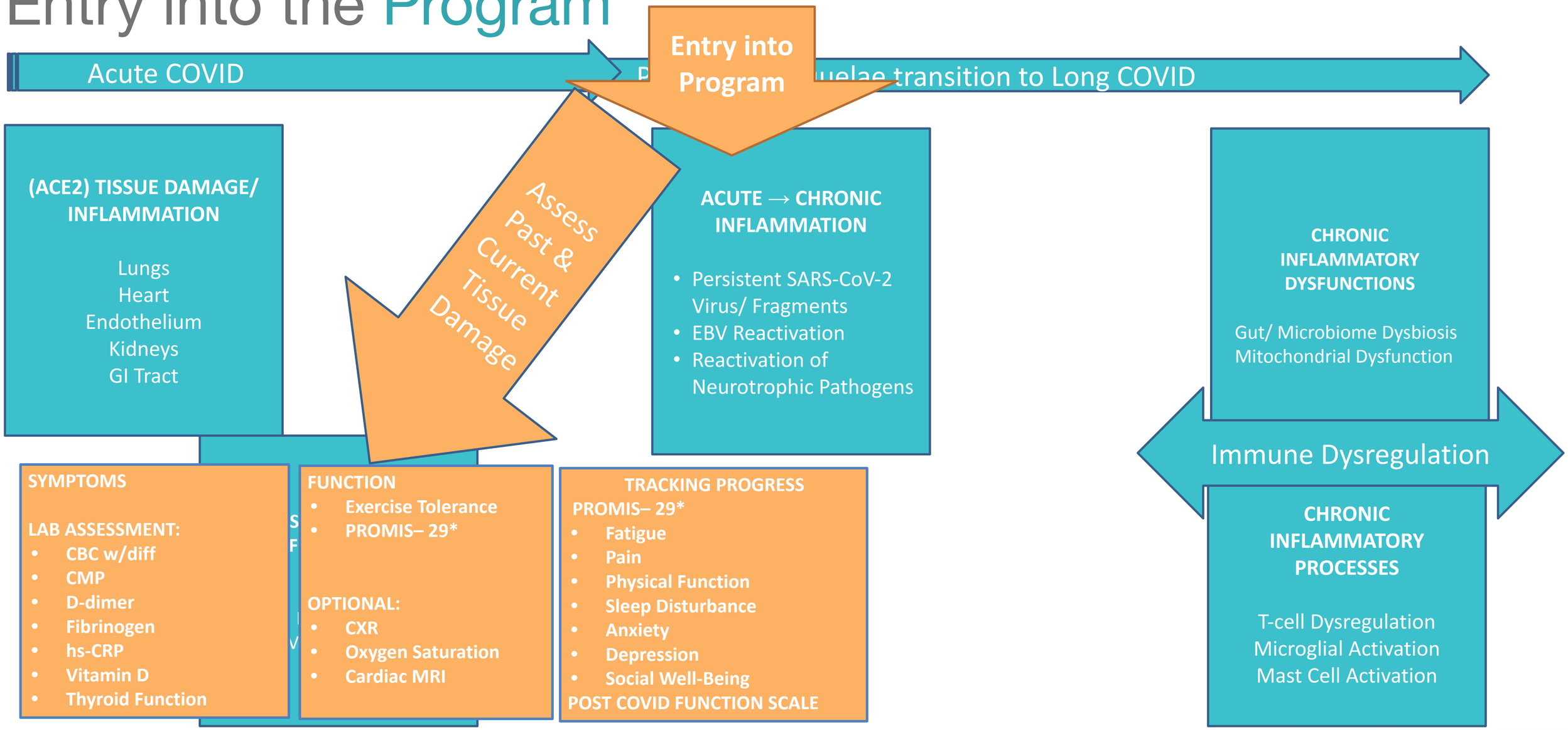
# Entry into the Program

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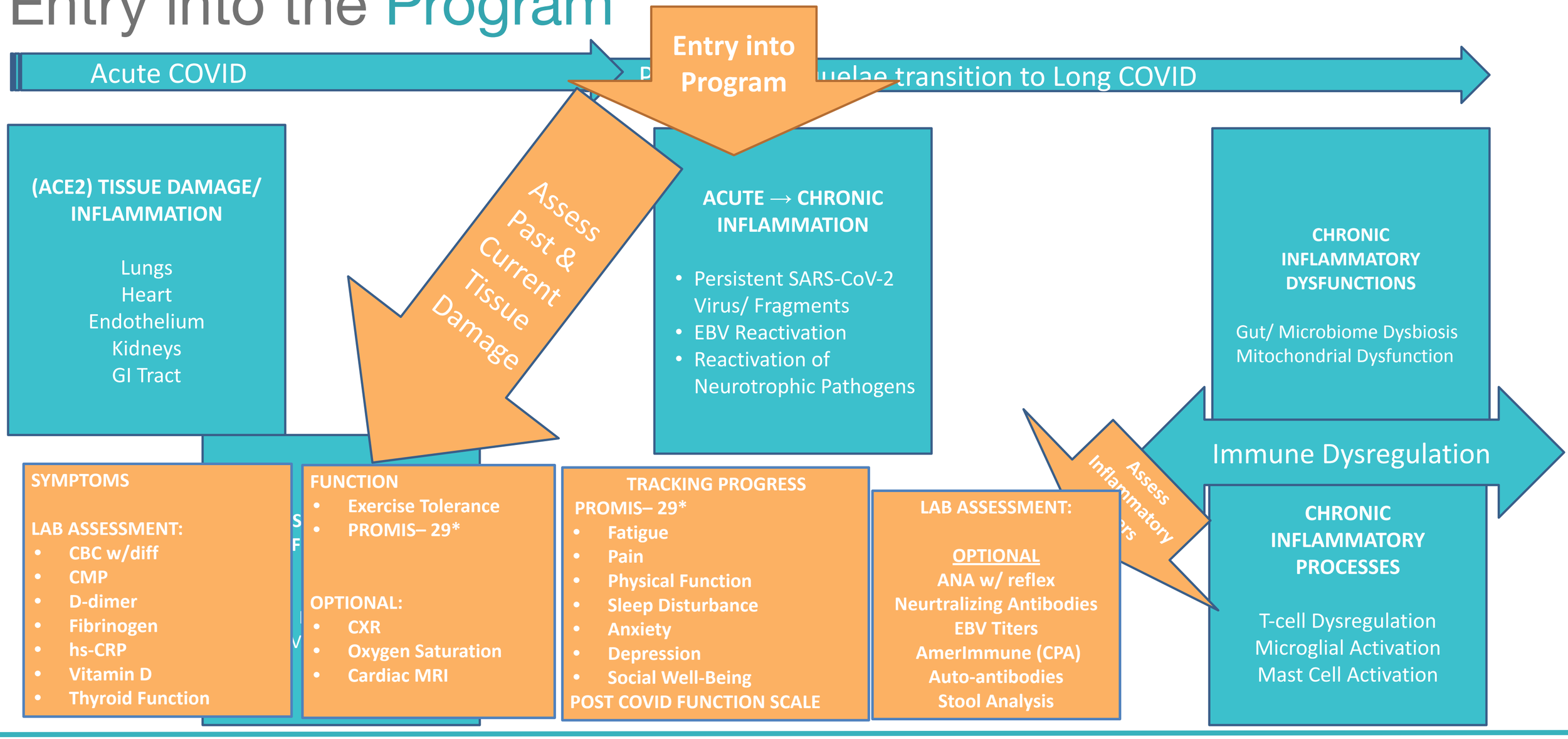


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# Long COVID Protocol

**ENROLLMENT**

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

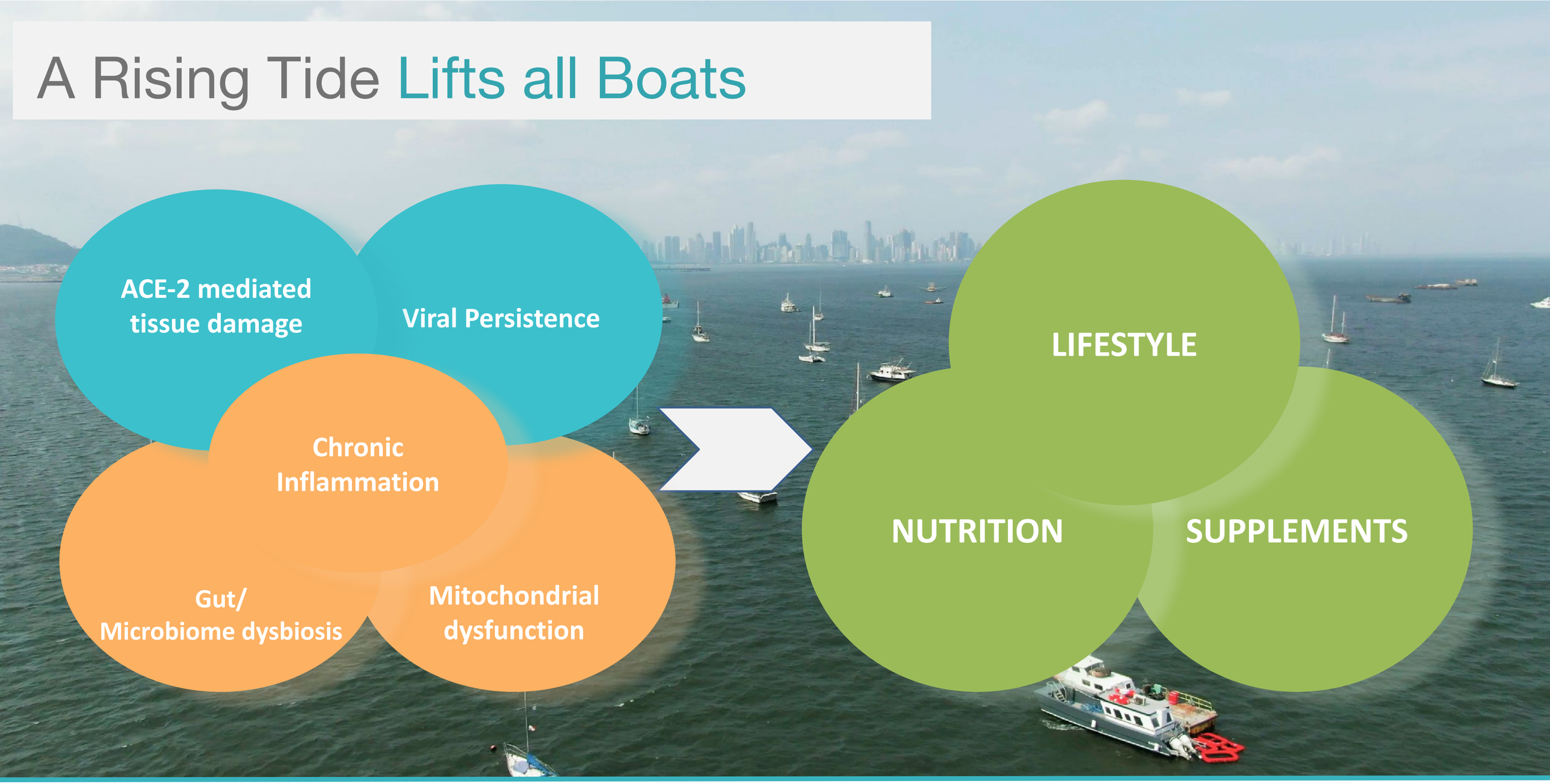
**PHASE 1: 90-Day Program**

- Lifestyle Support
- Baseline Supplements

## LIFESTYLE:

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

# A Rising Tide Lifts all Boats

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# Long COVID Protocol

## ENROLLMENT

**LABS (Baseline)**:

- CBC w/ diff
- CMP
- D-Dimer
- Fibrinogen
- hs-CRP
- Vitamin D
- Thyroid Function (if not done)

**Immune LABS (Optional)**:

- EBV Titers
- Neutralizing Antibodies
- Auto-antibodies
  - ANA w/ reflex
- AmerImmune (CPA)
- Microbiome Analysis

***ESOTERIC LABS* (Optional):**

- AM Cortisol

# Long COVID Protocol

## PHASE 1

**Specialty Nutritional Supplements**

Selected to address the primary drivers of long COVID

**Foundational Supplements**

Selected to support optimal health and wellbeing

# 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)

# Question and Answer Session

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# Recommended Education Programs and Online Courses

The American Academy of Anti-Aging Medicine (A4M)

*Use the code **VIRAL200** for $200 off your registration fee*

- The Fire Inside 2023 – May 18-20, 2023
- Longevity Fest 2023 – December 14-16, 2023

The Academy of Integrative Health & Medicine (AIHM)

*Use the code **OVATION100** for $100 off your registration fee to the October Conference*

- Annual Conference - October 5-8, 2023

The Institute of Functional Medicine (IFM)

*Use the code **OVATIONLAB10** for 10% off your registration fee*

- Applying Functional Medicine in Clinical Practice™ May 2023 (AFMCP) - online
- Advancements in Clinical Research and Innovative Practices in Functional Medicine – June 1-3, 2023
- Lifestyle: The Foundations of Functional Medicine – on-demand, online

Personalized Lifestyle Medicine Institute (PLMI)

- Is COVID Long-Haul a disease of the gut – May 30, 2023, online

# Post Viral Recovery: A 90-Day Program and Protocol

## Workshop No. 2, Wed May 17, 7 pm ET/4 pm PT

### What we'll cover

- 90-day Post Viral Recovery Program and Protocol
- Our current registry data and statistics
- Specialty and foundational supplement protocol
- Implementing the protocol in your practice

# THANK YOU


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# References


1. Su et al. [ISB]. Multiple early factors anticipate post-acute COVID-19 sequelae. Cell. 2022. Mar 3;185(5):881-895.e20. doi: 10.1016/j.cell.2022.01.014.
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3. Crook et al [UK]. LongCOVID – Mechanisms, risk factors, and management. BMJ. 2021 Jul 26;374:n1648. doi: 10.1136/bmj.n1648.
4. Peluso MJ, Deeks SP [UCSF]. Early clues regarding the pathogenesis of long-COVID. Trends in Immunology. 2022. Apr;43(4):268-270.doi: 10.1016/j.it.2022.02.008.
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6. Merad M, Blish CA, Sallusto F, Iwasaki A. [Yale]. The Immunology and ImmunoPathology of COVID-19. Science. 2022. 375:1122-1127. doi: 10.1126/science.abm8108

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