Long COVID

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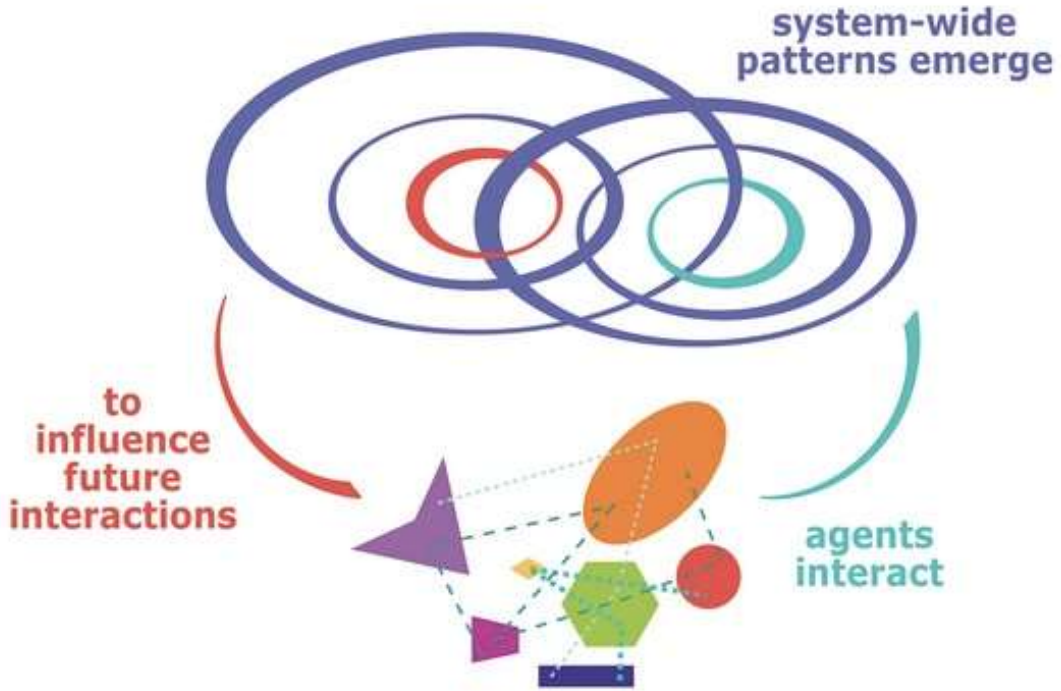
Site PI, NIH RECOVER trial at Cambridge Health Alliance

Site PI for NIH RECOVER

External Advisory Committee for NHS LOCOMOTION

Mass CPR Health Equity Committee

— Complex Adaptive System (CAS) —



Goal

Scaffolding, not a deep dive

How to think about the current and future state

PASC is still being defined

- How long ?
- How many people impacted ?
- What are the risk factors for PASC?
- What are the symptoms? Clusters?
- What are the best biomarkers ?

Defining PASC

- Standardizing questionnaires
- Large Cohort studies now in progress
- Many Smaller studies

Challenges to synthesizing many studies

- Different definitions of length of symptoms
- Lacking longitudinality
- Self reporting
- EHR studies
- Who is represented in the Data?

No standard for How / Where we care for PASC

Many patients with clear end organ damage treated primarily by specialists

Access to Long COVID clinics highly variable

PCPs seeing most patients

The evidence base is still being built


What do we know ?

Long Covid: New, Returning, or Ongoing problems as a result of COVID-19 infection after 4 weeks

New or Ongoing symptoms: A wide range of symptoms that can last weeks to months) or persistent post-Covid syndrome (PPCS)

Multiorgan effects of COVID-19

Effects of COVID-19 treatment/hospitalization

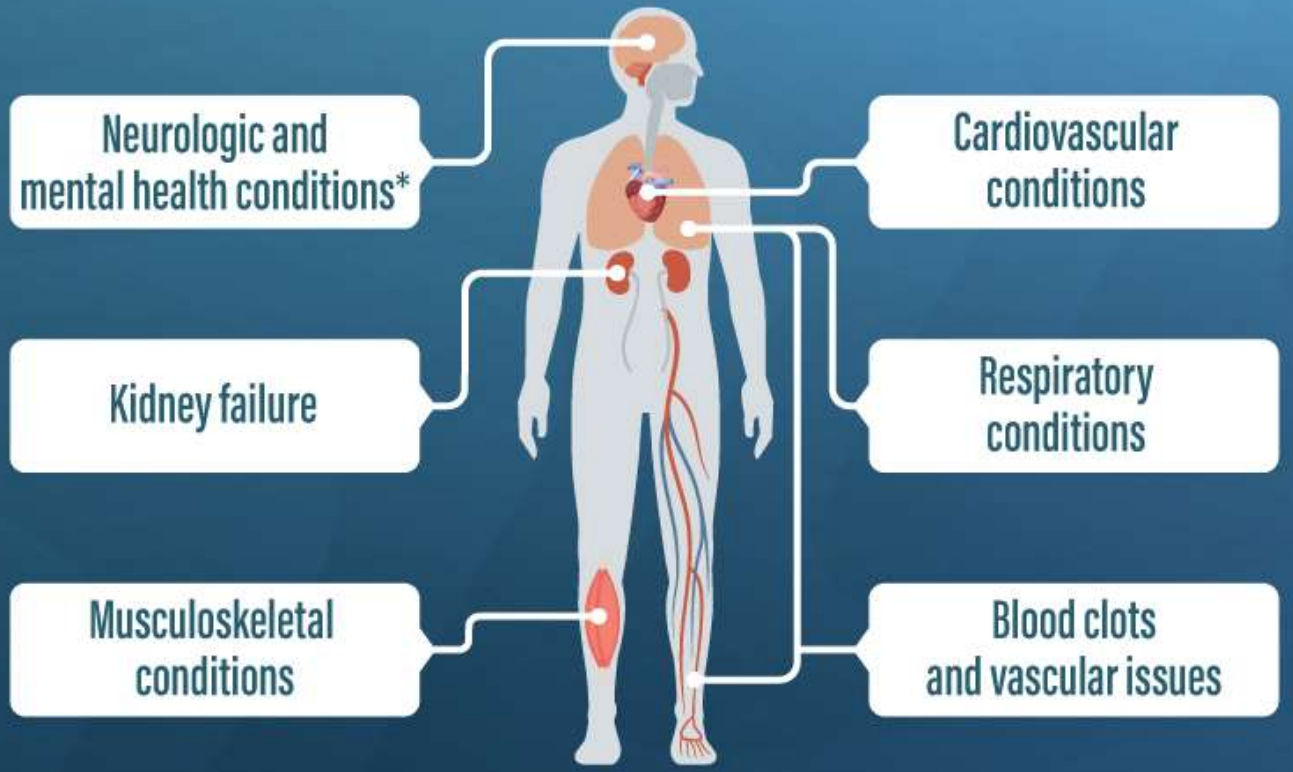
Takeaway #1

- Many people are impacted

Approximately

1 in 5 adults

ages 18+ have a health condition that might be related to their previous COVID-19 illness, such as:



Talk to your health care provider if you have symptoms after COVID-19

* Adults aged 65 and older at increased risk

bit.ly/MMWR7121

MAY 24, 2022

MMWR

Takeaway 2

- Higher risk of moderate, severe, and critical disease correlated with higher risk of PASC
- Some populations may have higher risk of multi-organ effects and long term disability

Broad Range of Reporting of PASC

Xie et al, Nature Communications 12, 6571 (2021)

- Self- reported symptoms range from 13.3% at ≥ 1 month to 2.5% at ≥ 3 months
- Based on electronic health data
  - Of non-hospitalized adults with COVID-19, 7.7% experienced one or more of 10 identified late-onset conditions 1 to 4 months post infection[2]
  - Burden of at least one symptom at 6 months differs by severity of acute COVID:[3]
    - Overall: 73.4/1,000 patients
    - Non-hospitalized: 44.5/1,000 patients
    - Hospitalized: 217.1/1,000 patients
      - ICU 360.5/1,000 patients

Risk factors for PASC

- Sex (female)
- Severity of initial disease
- presence of certain comorbidities (including obesity, diabetes, and chronic lung disease)
- socioeconomic status can affect the risk of an individual with COVID-19 developing PASC

Takeaway #3

- Patients with PASC symptoms have correlations with elevated biomarkers on average (at the population level)
- Still looking for and assessing other markers (ie peripheral nerve biopsy)

National COVID EHR findings (1.9 million patient records)

- Elevation of ALT AST (liver enzymes), ferritin, c-reactive protein (CRP), white blood cell count (WBC), and absolute neutrophil count persisted longer in PASC patients compared to non-PASC patients
  - Elevation of these biomarkers returned to baseline 6 months post index date on average
- Albumin, fibrinogen, and absolute lymphocyte count persistently lower levels in PASC patients
- Serum creatinine levels in PASC patients diverged from non-PASC patients with increasing higher median levels approximately 3 months after acute infection; this divergence maintains after 100 days
- Pre-infection lymphocyte counts were lower in PASC patients
- These findings reveal differences in biomarkers among PASC and non-PASC patients

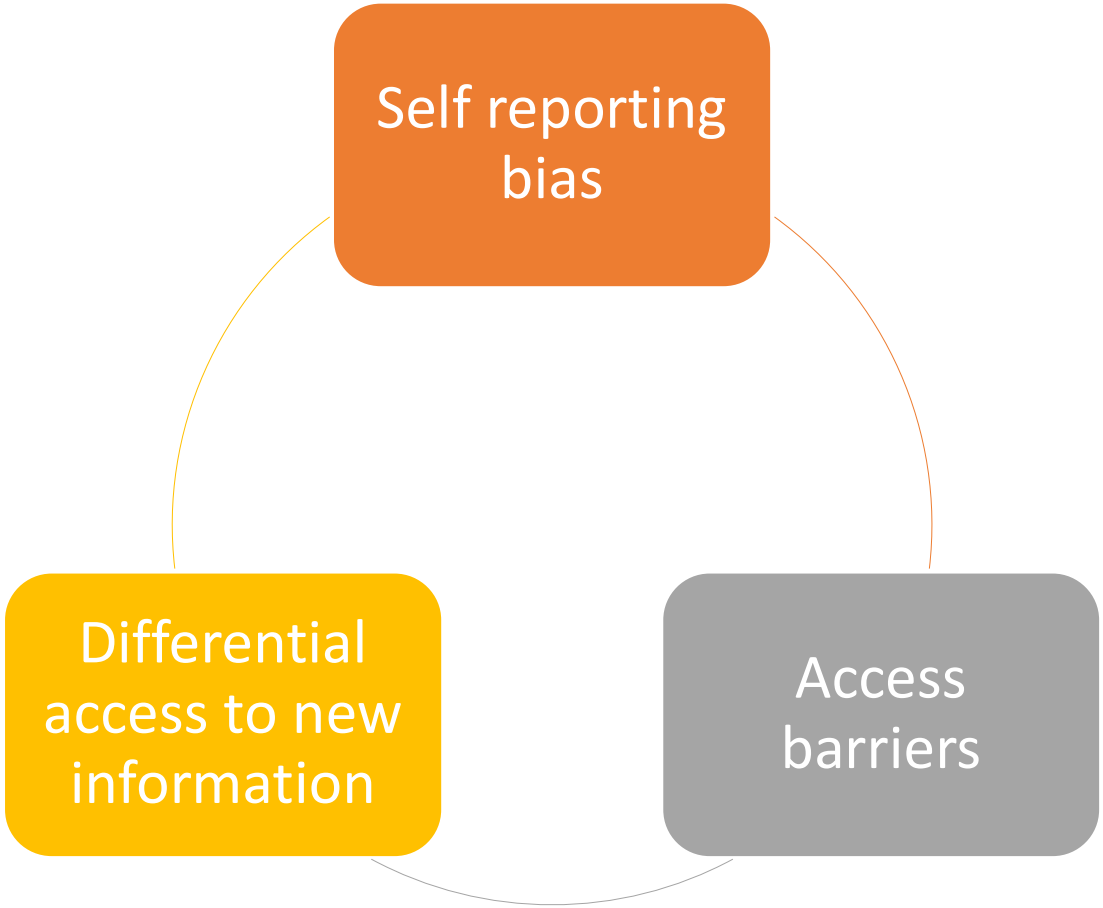
PASC Symptom Clusters

- olfactory dysfunction
- cardiopulmonary sequelae
- neurocognitive impairment
- Myalgic encephalomyelitis/chronic fatigue syndrome
- dysautonomia

Takeaway #4

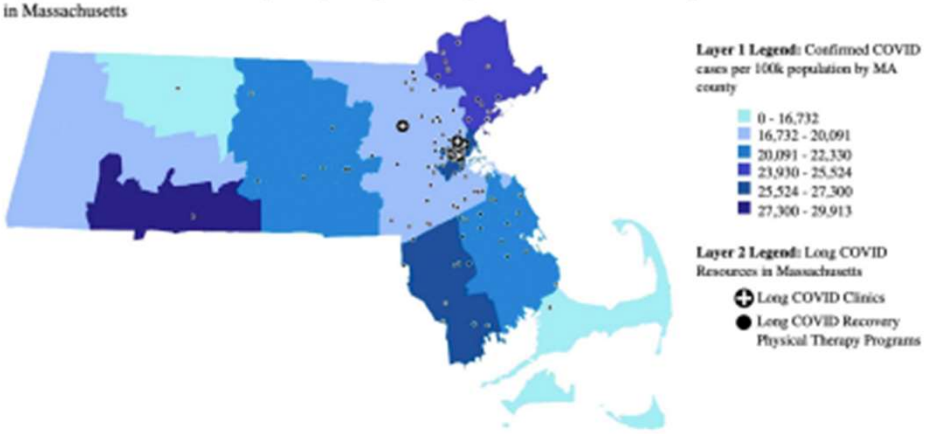
- Not all patients are accessing care in the same way or at all

Missing Not at Random



Long COVID Care Site Assessments

Figure. Per Capita COVID Cases by County through March 25, 2022 and Distribution of Long Covid Clinical Resources in Massachusetts



Note. Data source: Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University; the Census American Community Survey; the Department of Health and Human Services; and the Bureau of Labor and Statistics. Retrieved from https://coronavirus.jhu.edu/us-map on March 25, 2022

- **Conducted Zoom interviews** with clinic directors, 30-45 minutes via Zoom with a prepared set of questions
- Spoke with **all currently operating clinics** in the state (excluding physical therapy-only sites) focused on **adult care**

Site Assessment Findings: Patient Demographics

Themes from clinics where data was captured (many don't have the administrative capacity to track this information)

- 70-90% of patients at academic medical center clinics are white
- 80-90+% speak English as their primary language
  - Only small percentage list Spanish as their primary language; huge shift from the population that was seen in the ICU during the first surge
- Majority of patients at academic medical center clinics have private insurance
- Median age ranges from 40-60

Mass CPR study

In marginalized patient populations:

Less familiarity with diagnosis of Long COVID despite symptoms

Impacting health and well being

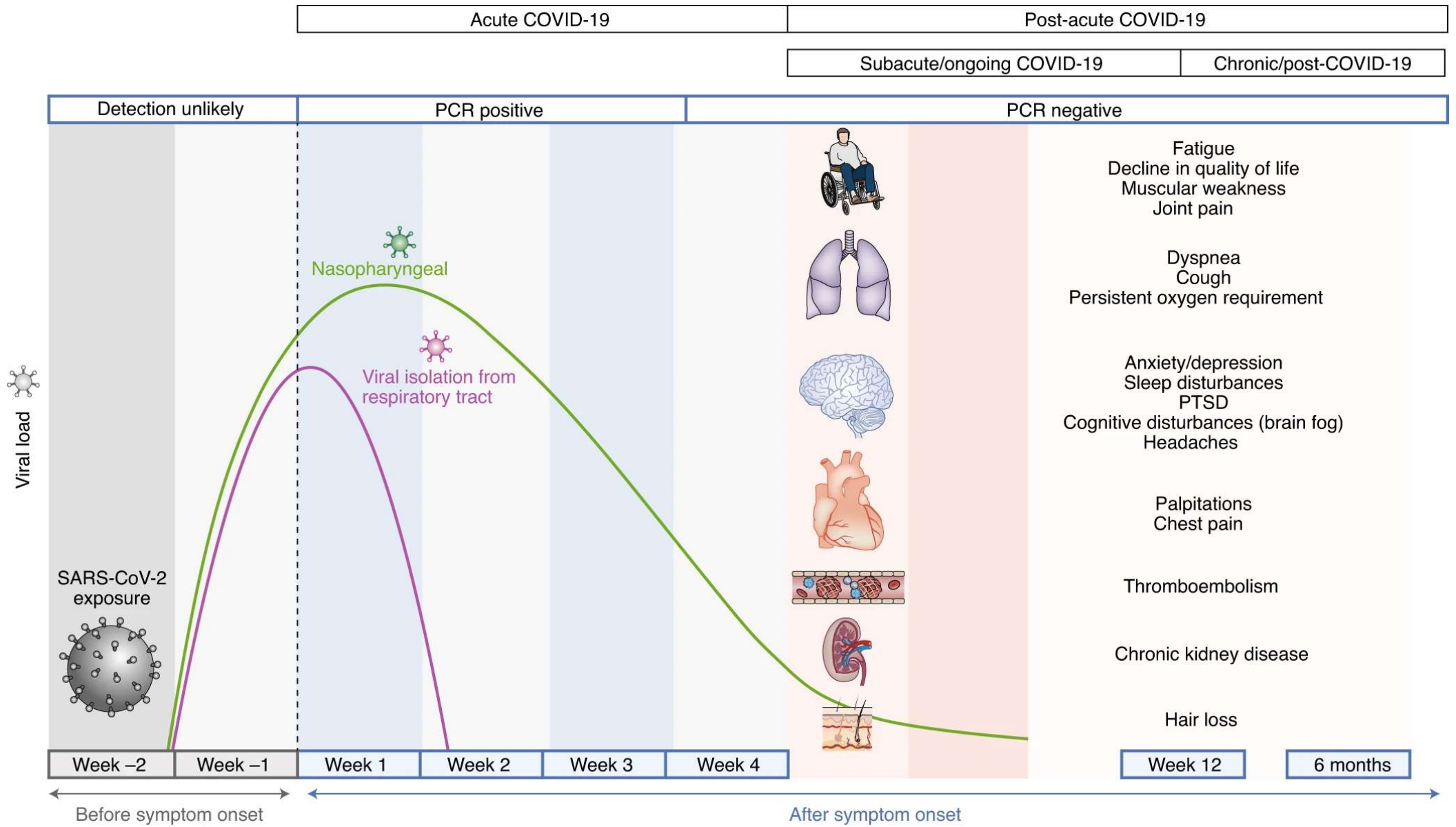
- Social, economic, mental health, physical health

Difficulty accessing health care related to these issues

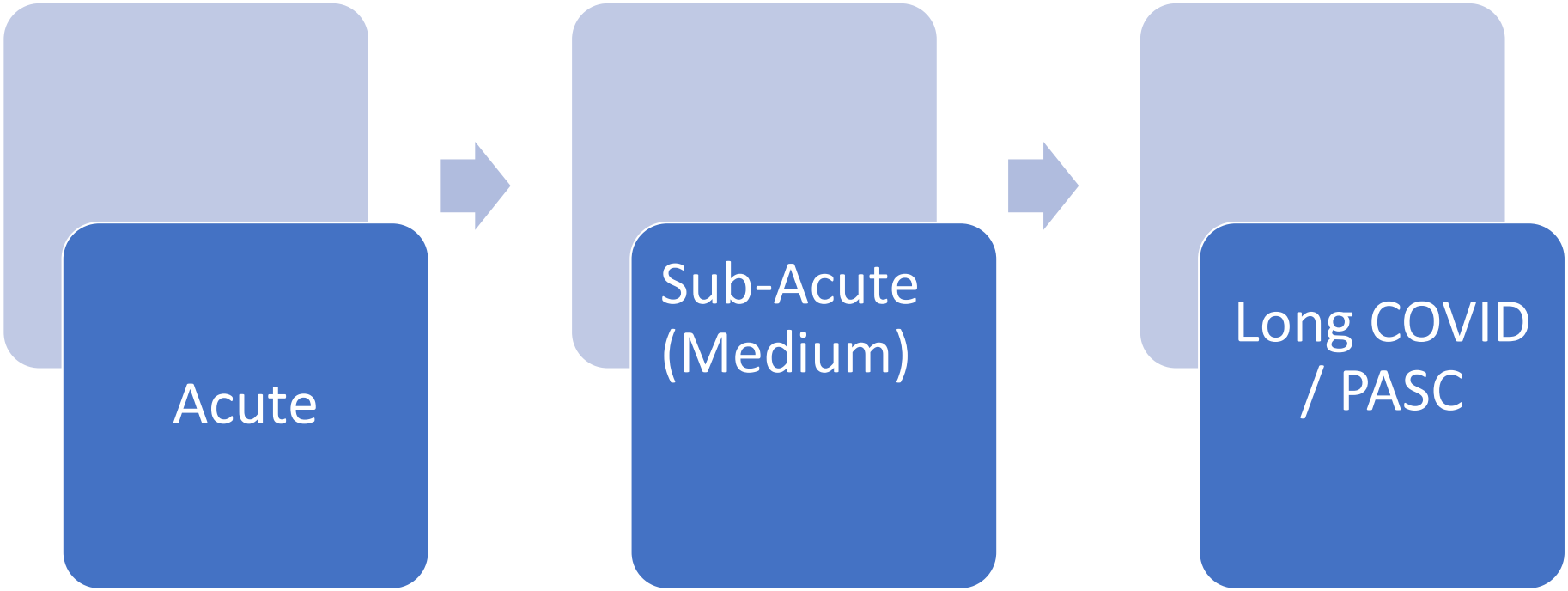
- Providers with variable knowledge
- Few solutions
- Cost of Care, Time lost in ongoing way from work
- Social pressure to ‘move on’
- “Its just in your head”

Takeaway #5

- COVID-19 with time variable impacts


Acute COVID-19
Post-acute COVID-19
Subacute/ongoing COVID-19
Chronic/post-COVID-19
Detection unlikely
PCR positive
PCR negative
Viral load
Nasopharyngeal
Viral isolation from respiratory tract
SARS-CoV-2 exposure
Fatigue
Decline in quality of life
Muscular weakness
Joint pain
Dyspnea
Cough
Persistent oxygen requirement
Anxiety/depression
Sleep disturbances
PTSD
Cognitive disturbances (brain fog)
Headaches
Palpitations
Chest pain
Thromboembolism
Chronic kidney disease
Hair loss
Week –2
Week –1
Week 1
Week 2
Week 3
Week 4
Week 12
6 months
Before symptom onset
After symptom onset

COVID complications / Timing



Managing COVID sequelae

Goals of Evaluation

Assess for end organ damage

Support patients in understanding of possible trajectory

Framing Current State of understanding with the Patients

Functional Goals and prioritization

Avoid Medical Gaslighting

CARE COORDINATION among multiple specialists

Assess for end organ damage

Organ Damage in COVID

- Subacute
  - Blood Clots / PE
  - Hepatitis
  - Pericarditis / myocarditis
  - Renal failure
  - Stroke
- “Long”
  - Heart Failure
  - Pulmonary Fibrosis
  - Rheum
  - Autoimmune conditions
  - Endocrine (ie new onset Diabetes, thryoid)

Assess for End Organ Damage

- Some who are symptomatic will have findings that are clinically relevant and/or urgent
- Red Flag Symptoms such as chest pain, stroke like symptoms
- New onset Symptoms During Subacute phase
- Sudden Worsening of Symptoms during Subacute phase
- Ongoing Hypoxia or exertional hypoxia

Manifestations with difficult Dx / Tx

Urticaria	GI issues	Sleep Dysfunction	Dysautonomia / POTs
Tachycardia	Breathlessness	Visuospatial, executive function, short term memory issues	Anxiety / Depression
Psychosis	New onset thyroid, DM	Body pain (fibromyalgia picture)	PTSD

Trajectory

- *Many* patients without clear end organ damage will get better over time
- Patients with ARDS may find improvement up to 2 years
- Some Patients have relapsing / remitting Symptoms
- Different symptom clusters resolve at different rates

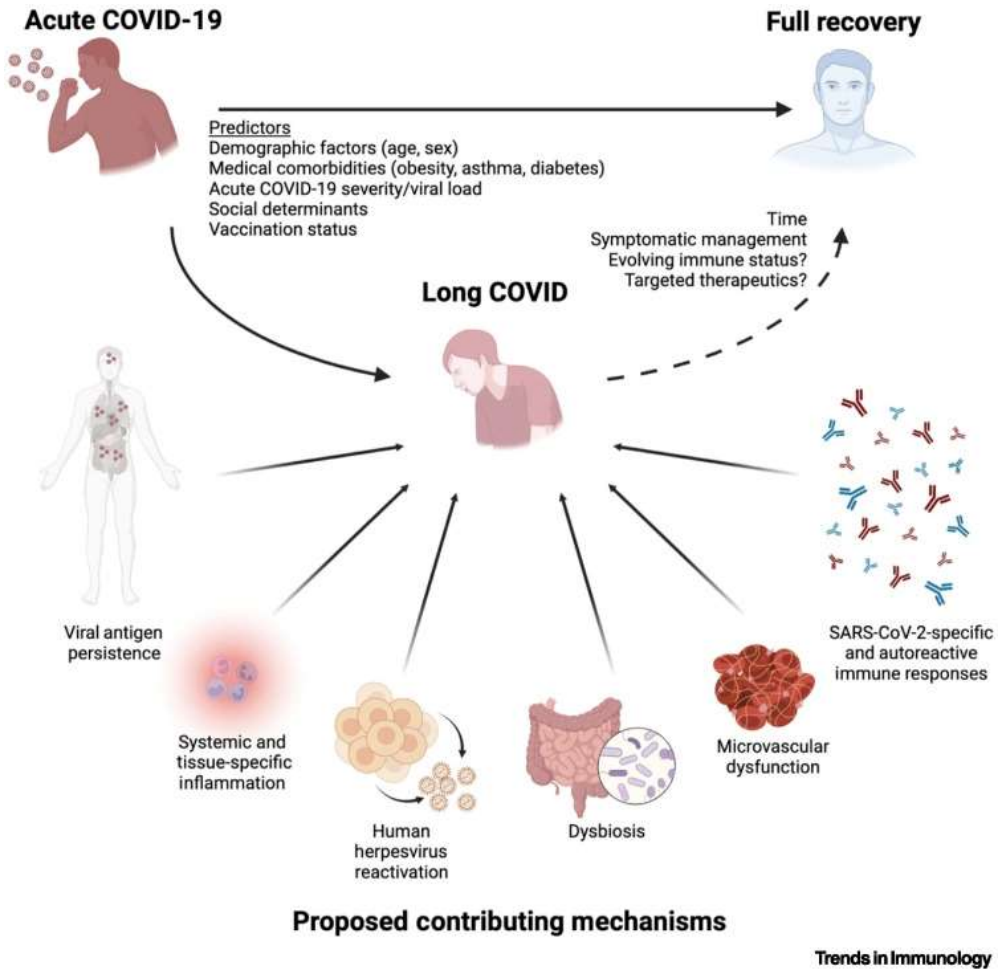
Current State of Science

- Still Defining the disease
- Simultaneously looking for causalities and themes
- Also searching for treatment targets
- Few clinical trials yet online (coming soon)

Early clues regarding the pathogenesis of long-COVID

Trends Immunol. 2022 Apr; 43(4): 268–270.

Peluso, Deeks.



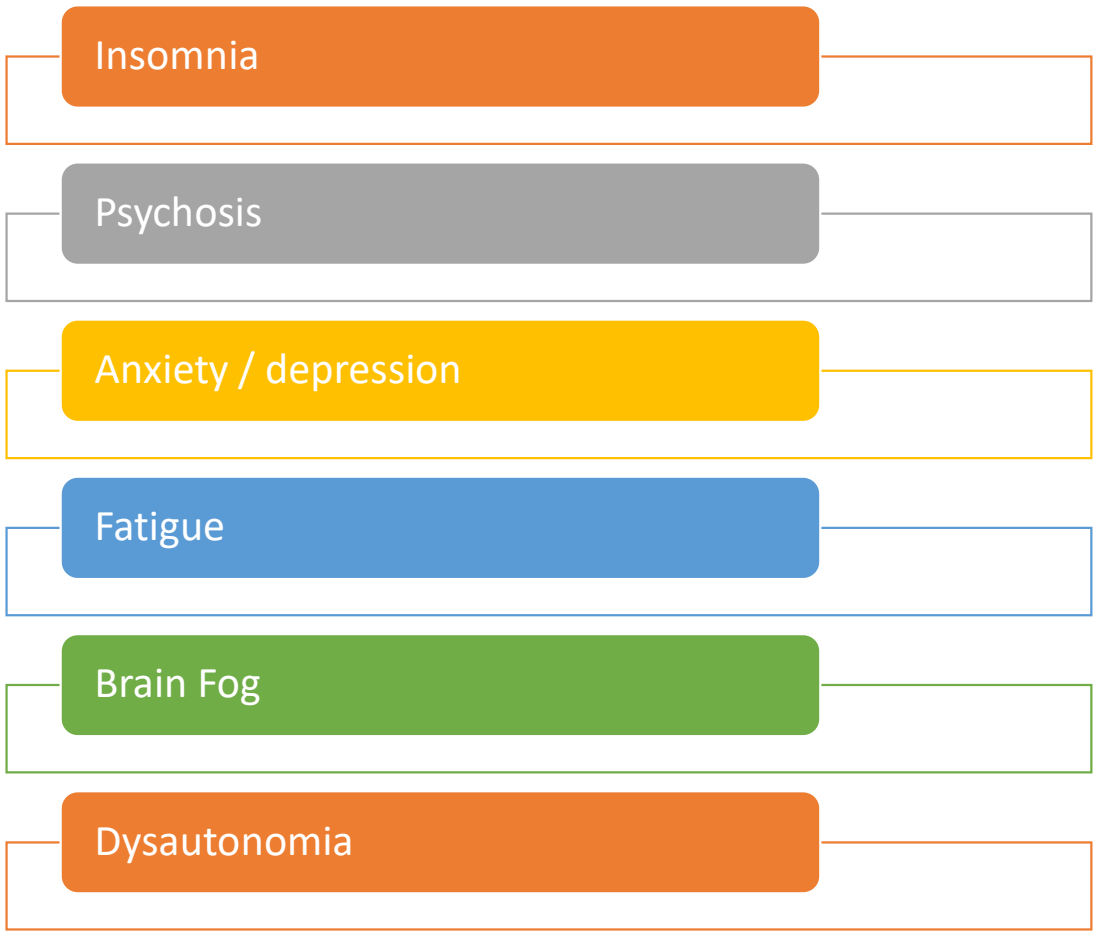
Possible Causalities - UK locomotion

- Endothelial Cell Dysfunction
- Amyloid Microclots
- Mast Cell Activation
- Neuroinflammation / Small fiber neuropathy

Functional Goals and Prioritization

- Prioritization and Representation in larger studies
- Hair Loss or Anosmia may be the most impactful manifestation
- Blue Collar / White Collar
- Value of trying a low harm intervention without a strong evidence base (ie supplements)

Symptom and Syndrome Treatment



Brain Fog

- Consider neuropsych, however long wait lists
- Graphic Organizers
- Calendars and check lists
- Accommodations
- Consider Clinical trial – may be focused on assessment or treatment

Sleep

- Often underlying sleep dysfunction
- Use a standard sleep tool kit
- Consider trauma related Sleep dysfunction (ie nightmares)
- Be careful not to make the fatigue worse

Dysautonomia

- Good assessment of orthostasis
- Normal orthostatic vitals do NOT rule out orthostatic hypotension
- Get a good history of symptoms such as posturally linked tachcardia
- Research focused on possible treatments
- Current state = focus on symptomatic treatments

Multisystem Involvement in Post-Acute Sequelae of Coronavirus Disease 19

Peter Novak MD, PhD,Shibani S. Mukerji MD, PhD,Haitham S. Alabsi DO,David Systrom MD,Sadie P. Marciano PA-C,Donna Felsenstein MD,William J. Mullally MD,David M. Pilgrim MD

Exertional Shortness of breath

- Check Ambulatory O2
- Assess for drop in O2 > 3 % points (Make sure you ambulate to the point of sx)
- Positional or exertional hypoxia is a red flag
- CXR if they haven't had one

Practical supports

- Breathing
- PT / Pulm Rehab
- Short / Long term disability / FMLA / intermittent FMLA
- Mindfulness or Survivorship Groups
- Connect with Patient Communities

Patient Resources

https://www.yourcovidrecovery.nhs.uk/

Stasis Breathing (not free)

ICU survivorship programs

Disability

- To qualify for federal programs, Social Security Disability Insurance (SSDI) and Supplemental Security Income (SSI), applicants must be unable to work and have health conditions that last for at least one year or result in death

Current State of Research

- Defining disease
- Finding treatment targets
- Most Clinical trials are small and local currently
- More coming, funding is mostly connected to RECOVER

Avoid Medical Gaslighting

Really listen on timing

‘I don’t know’ or ‘we are still learning a lot’

Tests being normal does not equal nothing physically wrong

Take great care not to dismiss as behavioral health

Something being common doesn’t mean we shouldn’t try to impact what we can (ie Exacerbated diabetes)

Shared Decision Making

01

Recognizing and acknowledging that a decision is required (Ie clinical trials vs not)

02

Knowing and understanding the best available evidence (this is being generated fairly quickly)

03

Incorporating patient's values and preferences into the decision

WHO Clinical Guidelines

- Strong Recommendations
  - Rule out Exertional desaturation and cardiac impairment prior to physical exercise training
- Conditional Recommendations
  - Early Delivery of Rehab
  - Pacing
  - Breathing strategies
  - Education / Skills / self management strategies for Cognitive impairment
  - Etc

  - https://www.who.int/publications/i/item/WHO-2019-nCoV-Clinical-2022.2

https://www.som.org.uk/sites/som.org.uk/files/Long_COVID_and_Return_to_Work_What_Works.pdf

UpToDate

- https://www.uptodate.com/contents/covid-19-evaluation-and-management-of-adults-with-persistent-symptoms-following-acute-illness-long-covid#H385307378

Thank you!