



NIHCM Webinar

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The 'Researching COVID to Enhance Recovery' (RECOVER) Initiative

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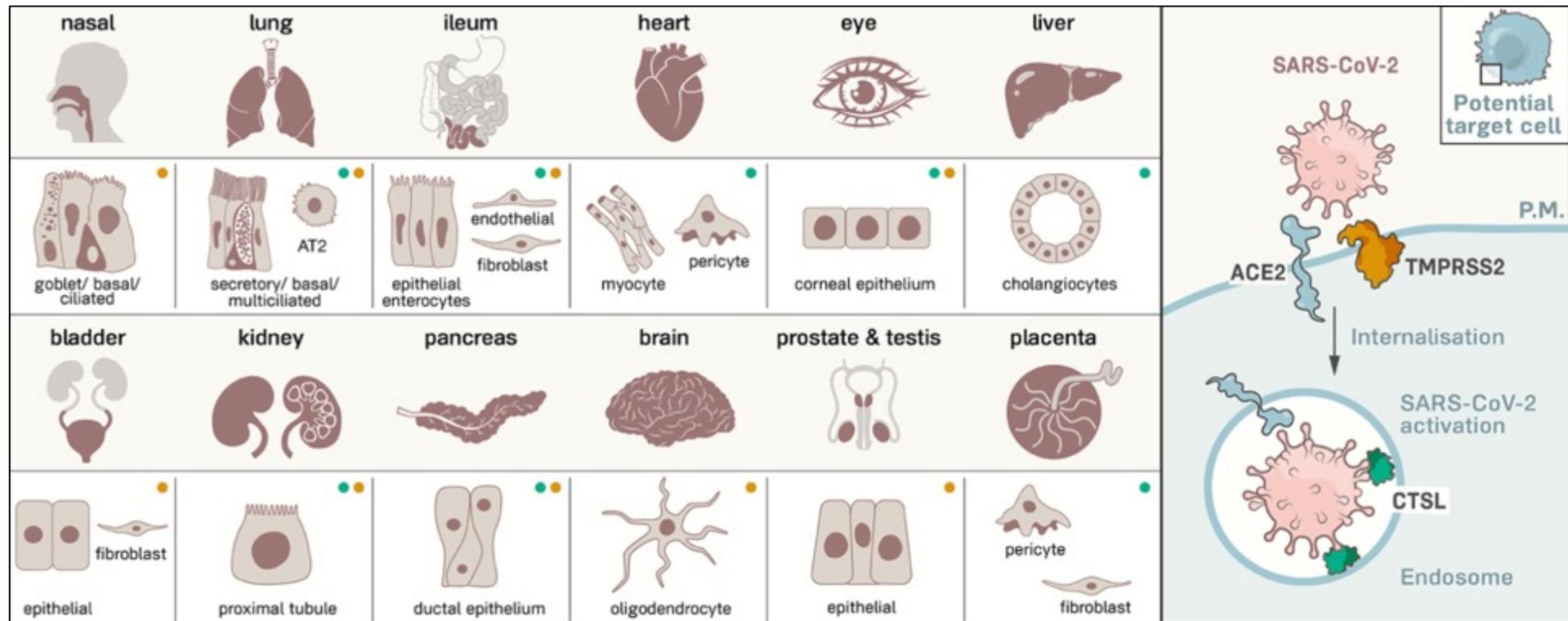
NIH Mission

*The mission of the National Institutes of Health are to seek **fundamental knowledge** about the nature and behavior of living systems and the application of that knowledge to **enhance** health, **lengthen** life, and **reduce** illness and disability.*

Goals:

- Foster fundamental creative discoveries, innovative research strategies, and their applications to protect and improve health
- Develop, maintain, and renew scientific human and physical resources that will ensure the Nation's capability to prevent disease
- Expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well-being and ensure a continued high return on the public investment in research
- Exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science.

COVID-19 Affects Multiple Organs



[The Scientist](#), April 2020

The Post-Acute Sequelae of COVID-19: Symptom clusters overlap with ME/CFS

Fatigue in almost 99% of those with PACS. Prevalence of post-exertional malaise maybe as high as 90%

Neurologic

- Memory/Word finding difficulties
- Concentration difficulties/"brain fog"
- Executive function difficulties
- Sleep disorders
- Pain syndromes- muscle, joint
- Abnormal sensations- tingling
- Headache
- Postural Orthostatic Tachycardia
- Abnormal smell/taste
- Visual abnormalities
- Dizziness/balance problems
- ? Confusional state/psychosis

CardioPulmonary

- Shortness of breath
- Dry cough
- Chest pain
- Exercise intolerance
- Postural Orthostatic Tachycardia
- Palpitations/ Fast heart rate
- Myocarditis
- Pulmonary fibrosis

Mental Health

- Post traumatic stress disorder
- Anxiety
- Depression

Gastrointestinal

- Diarrhea
- Decreased appetite
- Nausea
- Abdominal pain

Other

- Elevated temperature
- Chills, flushing sweats
- Sore throat
- Extreme thirst
- Skin changes
- Menstrual changes

Assessment of Long-COVID Symptoms



thebmj Visual summary 

“Long covid” in primary care

Assessment and initial management of patients with continuing symptoms

thebmj

Read the full article online

 <https://bit.ly/BMJlong>

Post-acute covid-19 appears to be a multi-system disease, sometimes occurring after a relatively mild acute illness. Clinical management requires a whole-patient perspective. This graphic summarises the assessment and initial management of patients with delayed recovery from an episode of covid-19 that was managed in the community or in a standard hospital ward.

An uncertain picture

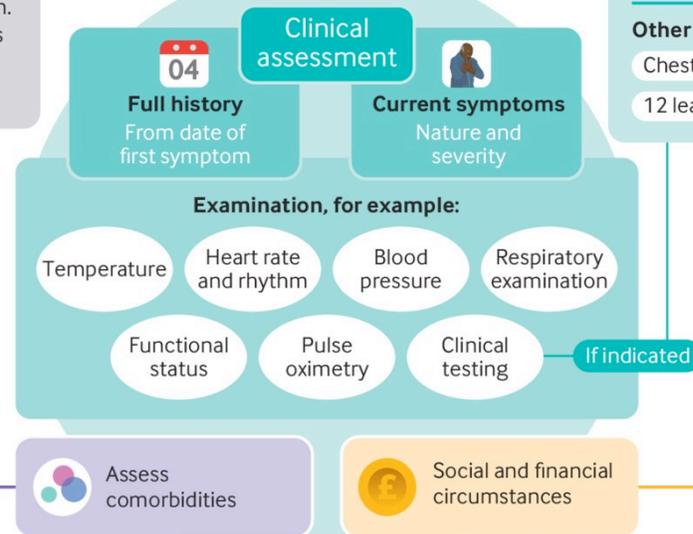
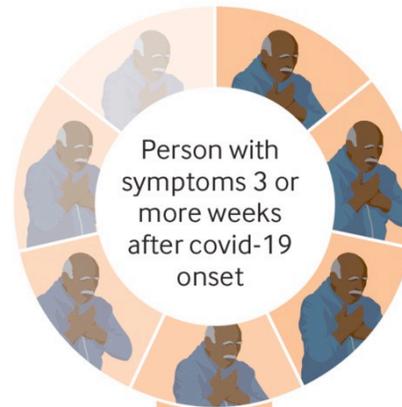


The long term course of covid-19 is unknown. This graphic presents an approach based on evidence available at the time of publication.

However, caution is advised, as patients may present atypically, and new treatments are likely to emerge

Managing comorbidities

Many patients have comorbidities including diabetes, hypertension, kidney disease or ischaemic heart disease. These need to be managed in conjunction with covid-19 treatment. Refer to condition specific guidance, available in the associated article by Greenhalgh and colleagues



Investigations

Clinical testing is not always needed, but can help to pinpoint causes of continuing symptoms, and to exclude conditions like pulmonary embolism or myocarditis. Examples are provided below:

Blood tests

- Full blood count
- Electrolytes
- Liver and renal function
- Troponin
- C reactive protein
- Creatine kinase
- D-dimer
- Brain natriuretic peptides
- Ferritin – to assess inflammatory and prothrombotic states

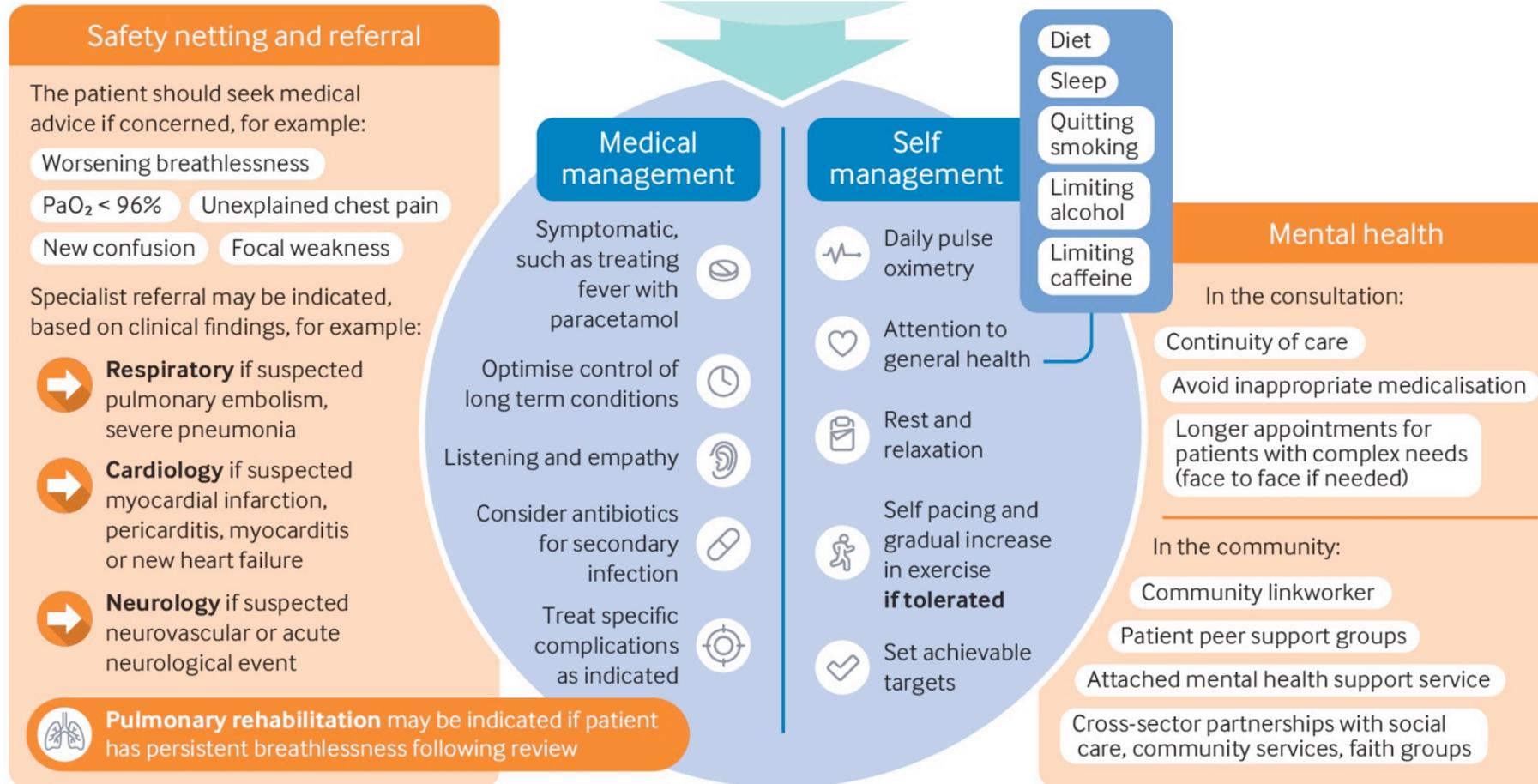
Other investigations

- Chest x ray
- Urine tests
- 12 lead electrocardiogram

Social, financial, and cultural support

Prolonged covid-19 may limit the ability to engage in work and family activities. Patients may have experienced family bereavements as well as job losses and consequent financial stress and food poverty. See the associated

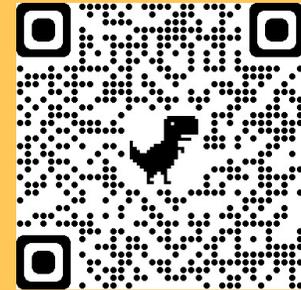
Proposed Treatment of Long-COVID Symptoms



Researching COVID to Enhance Recovery



recoverCOVID.org



RECOVER Listening Session

30

Of 40 RSVPs attended

At peak,

~140

people watched the
NIH VideoCast live

Impressions and Observations

- Messaging needed on the **critical nature of research** and ability to inform treatments, clinical decisions, and health care policies around PASC.
- **Interest groups around Long COVID are engaged** and want to be involved.
- **Currently a lack of public knowledge on the roles Federal agencies serve** generally, especially as it relates to responding to COVID-19.
- **Strong desire to have patients – and patient interest leaders – integral to the planning and implementation** of the research.
- **The most powerful voice(s) are those of the people affected.**





Goal

- ▶ Rapidly improve our **understanding** of and **ability to treat** and prevent PASC

Key Scientific Questions

- 1 What are the clinical spectrum of and biology underlying recovery from acute SARS-CoV-2 infection over time?
- 2 For those patients who do not fully recover, what is the incidence/prevalence, natural history, clinical spectrum, and underlying biology of this condition? Are there distinct phenotypes of patients who have prolonged symptoms or other sequelae?
- 3 Does SARS-CoV-2 infection initiate or promote the pathogenesis of conditions or findings that evolve over time to cause organ dysfunction or increase the risk of developing other disorders?

PASC Initiative Components



SARS-CoV-2 Recovery Meta-Cohort

- Clinical Recovery Cohort
- Autopsy Cohort (Acute and PASC)
- EHR- and Other Real-World Data-Based Studies



Investigator Consortium

All study investigators will work together to:

- Conduct rapid systematic screening and follow-up evaluations of infected individuals, to provide a resource for in-depth multi-disciplinary phenotyping, and to pool data and share biospecimens and data from across studies
- Develop a streamlined set of common core protocol elements (specific hypotheses, design elements, screening evaluations, exams, lab tests, functional assessments, imaging, etc.) and to provide a collaborative for multi-disciplinary phenotyping

RECOVER Organization: Cores and Cohorts



ADMINISTRATIVE
COORDINATING
CENTER



CLINICAL SCIENCE
CORE



DATA RESOURCE
CORE



BIOREPOSITORY
CORE

 MAYO CLINIC

NIH
SARS-CoV-2
Recovery
Cohort

ACUTE &
POST-ACUTE
SARS-COV-2
INFECTION
COHORTS

EHR /
REAL-WORLD
DATA
COHORT

AUTOPSY
STUDIES



RECOVER Research Awardees (So Far)



Adult Population Awardees

Brigham and Women's Hospital
Case Western Reserve University School of Medicine
Howard University College of Medicine
Icahn School of Medicine at Mount Sinai
University of Alabama at Birmingham Heersink School of Medicine
University of Arizona College of Medicine- Tuscon
University of Illinois Hospital & Health Sciences System
University of Texas Health Science Center
University of Utah Health
West Virginia University of Health Sciences
Emory University

Pediatric Population Awardees

Arkansas Children's Research Institute
Children's Hospital Los Angeles
Rhode Island Hospital
Rutgers Robert Wood Johnson Medical School

Pregnant Population Awardees

University of Utah Health

Tissue Pathology Study Awardees

Brigham and Women's Hospital
CVPath Institute
Icahn School of Medicine at Mount Sinai

Real-World Data Awardees

University of Colorado

RECOVER Initiative Stats



39M+

People with a SARS-CoV-2 infection in the US ... and counting

10%-30%

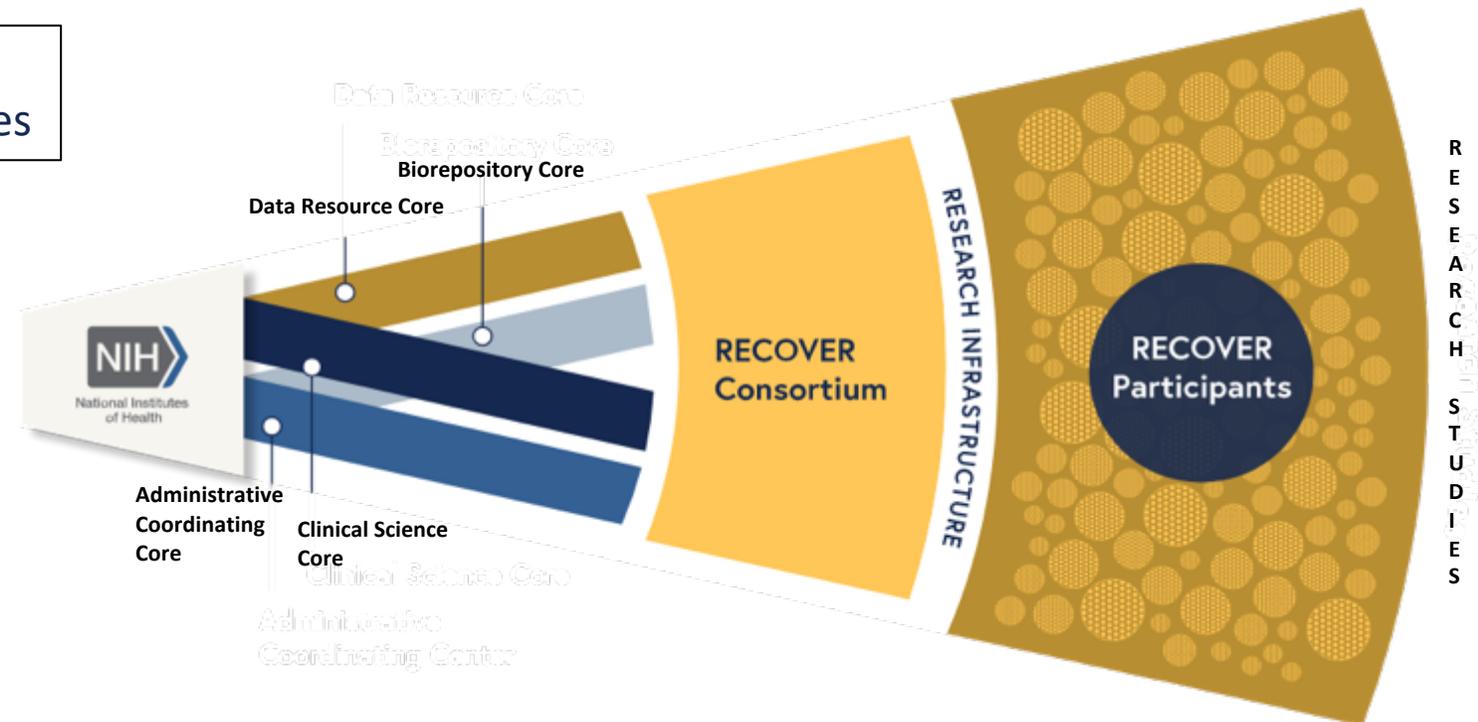
Preliminary estimate of the percentage of people infected with SARS-CoV-2 who will experience PASC

200+

Estimated number of RECOVER research clinical sites

Many 100s

Number of researchers involved in RECOVER





- Over 2 dozen studies in various stages of completion in adult patients:
 - Phase 2 trial in Long COVID Adults testing efficacy of RSLV-132
 - Remdesivir
 - Hyperbaric oxygen versus Placebo
 - Naltrexone
 - Serotonin enhances
 - Anti-fibrotic medication
 - Anti-inflammatory interventions
 - Sirolimus in Treating COVID019 Pneumonia for prevention of Post-COVID Fibrosis
- A pediatric trial studying efficacy of resistance exercise

Beyond the Symptom: The Biology of Fatigue Workshop



Main conclusions:

- Instruments and measures of fatigue vary significantly in studies of different diseases making it difficult to compare across studies
- Very little research on the transition of acute fatigue to chronic fatigue in the setting of disease
- Neuroimmune interactions important, but mechanisms not understood
- Gut-brain interactions also important, but does it impact fatigue?
- Risk factors for post-infectious and post-cancer chronic fatigue not known
- New studies on glymphatics, CSF flow and relationship to sleep may be critical in understanding fatigue
- Need to apply new technologies to the study the neurobiology of fatigue
- Model systems are needed and will be critical in studying the cellular mechanisms of fatigue



Beyond the Symptom: The Biology of Fatigue
A virtual workshop via Zoom webinar
September 27-28, 2021

 NIH **Blueprint**
for Neuroscience Research

 Sleep
Research
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Thank you!

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