

NIH Research Initiative on Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)

Overview of RECOVER

Advisory Committee to the NIH Director Meeting
June 10, 2021



Why Study PASC?

Patients vary in the timing and extent of their recovery from SARS-CoV-2 infection:

- Many recover quickly while others may experience important **post-acute sequelae** of SARS-CoV-2 Infection (PASC)
 - Reported symptoms range from mild to incapacitating, may involve multiple organs and systems, and can adversely affect overall quality of life
 - In some cases, timing of infection is linked to new symptoms and findings but emerge subsequently and evolve over time

The public health impact is currently unknown, but potentially large given the numbers of individuals across the age spectrum who have been/will be infected



NIH PASC Research: Toward Recovery from SARS-CoV-2 Infection

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?

Recovery Cohort

Acute
SARS-CoV-2
Infection Cohorts



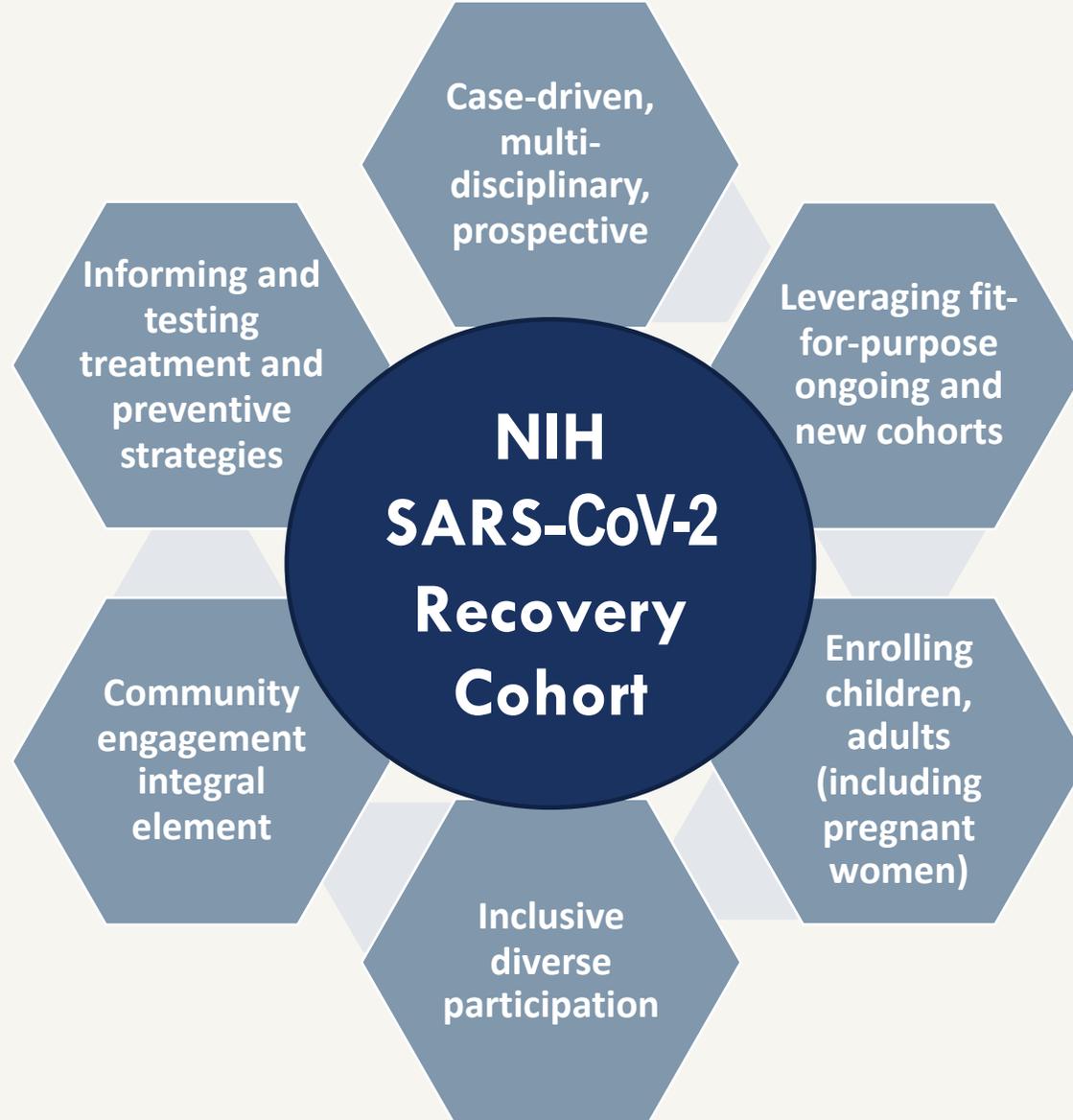
Post-Acute
SARS-CoV-2
Infection Cohorts

Goal: To understand and be able to treat and prevent PASC

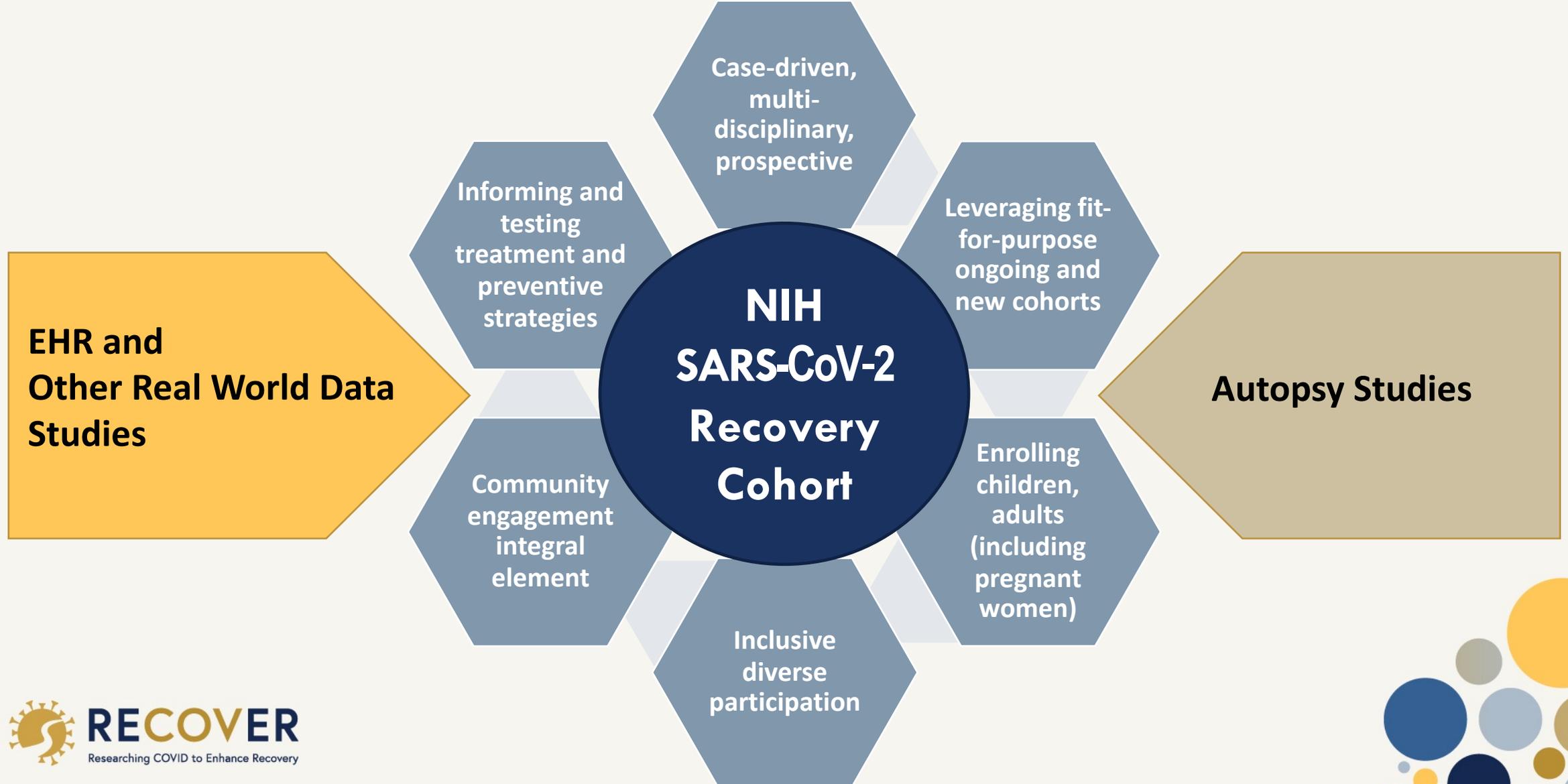
Aiming for a national, inclusive, diverse patient population that spans the life cycle.



RECOVER Research Approach



RECOVER Research Approach



PASC Characterization Strategy

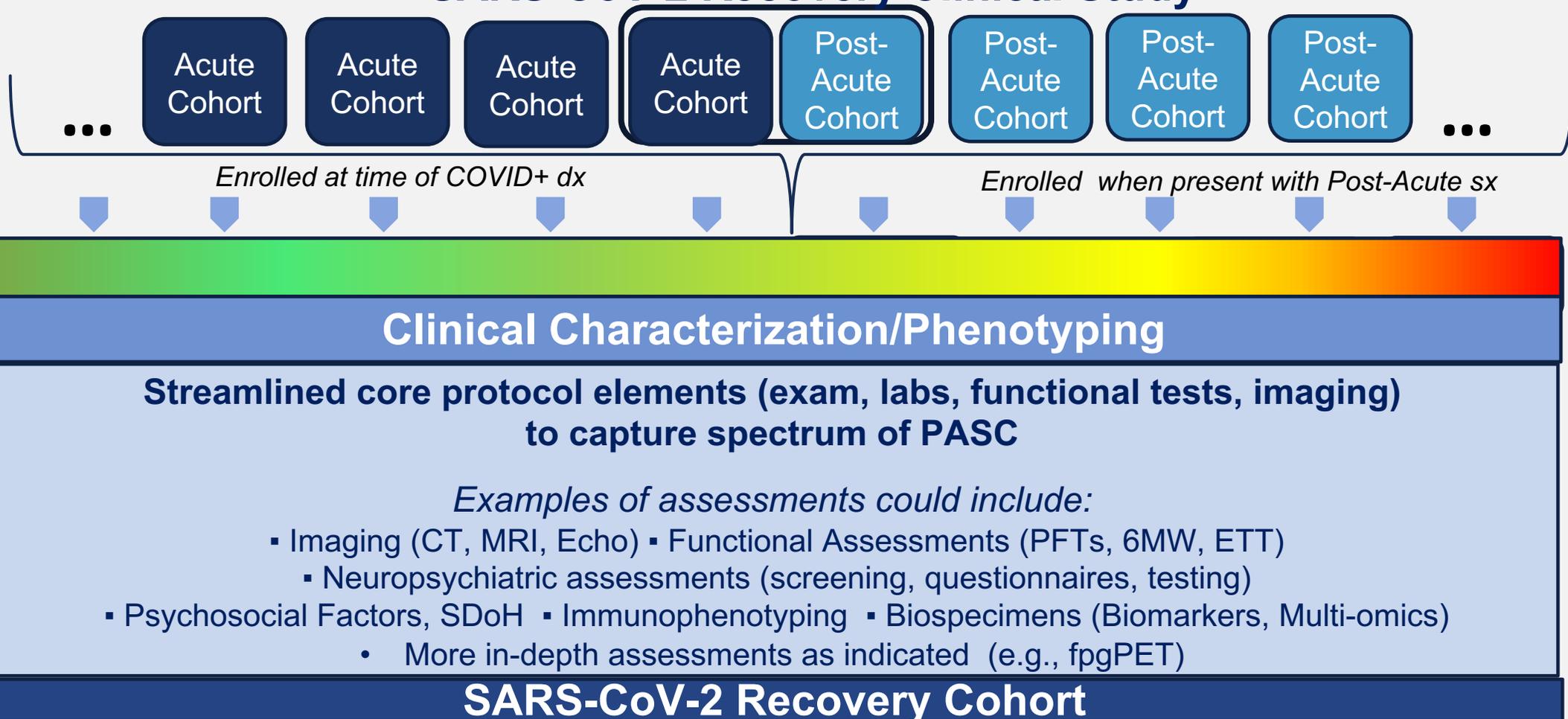
Notes:

Includes Peds & Pregnancy Cohorts Studies

Includes new and leveraged ongoing studies

Broad Spectrum of Recovery Phenotypes

SARS-CoV-2 Recovery Clinical Study



RECOVER Initiative Components

SARS-CoV-2 Recovery Meta-Cohort

- Clinical Recovery Cohort (Adult, Peds, and Pregnancy)
- Autopsy Cohort (Acute and PASC)
- EHR-/ Other Real-World Data-



Investigator Consortium

- **Cross-disciplinary investigator teams** will work together to:
 - Achieve **speed and scale/breadth**
 - Set of common core protocol elements
 - Conduct systematic screening and **in-depth follow-up evaluations**

Clinical Science Core

Data Resource Core

Biorepository Core

Admin Coord. Ctr



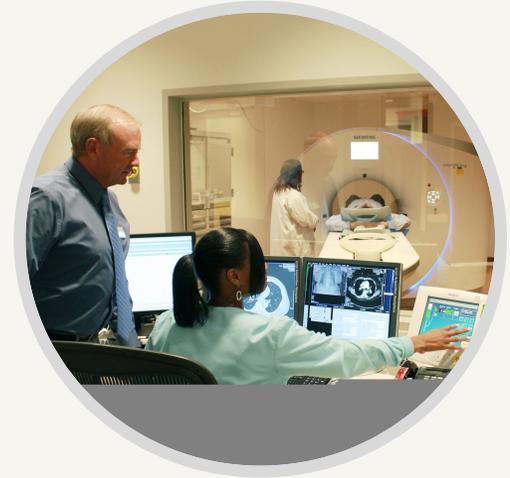
Additional Key Features

- **Collaborative community/patient/stakeholder involvement at multiple levels**
 - Listening Sessions
 - Community Advisory Board (CAB)/Community Based Organization: Study level
 - RECOVER CAB
 - Participation in Consortium activities
- **Mobile Health/Digital technology to enable broader outreach to patients and facilitating participation**
 - Reporting symptoms
 - Receiving updates/notices
 - Personal sensor technology



Additional Key Features (continued)

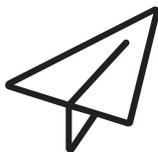
- **Longitudinal follow-up**
 - Vary in depth/intensity as well as duration
 - Will need to adjust plans as results become available
- **Adapt and innovate** as science evolves
- **Clinical Trials** are an important component



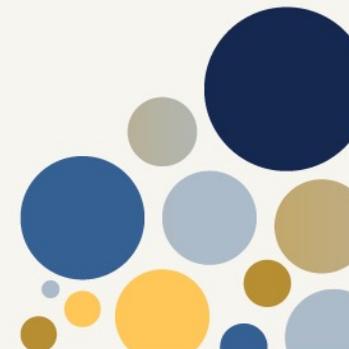
Staying connected with the RECOVER Initiative



Visit the [Research Initiative website](#)



Email the team at RECOVER@nih.gov





FACT SHEET

Post-acute Sequelae of SARS-CoV-2 Infection (PASC)

Recovery from infection with SARS-CoV-2, the virus that causes COVID-19, can vary from person to person. Most patients seem to recover quickly and completely, while others report symptoms that persist for weeks or months after the acute phase of illness has passed (a condition often referred to as PASC). New symptoms and findings emerge after the acute phase was asymptomatic. Collectively, these long-term post-acute sequelae of SARS-CoV-2 infection (PASC) are a complex and emerging area of research.

What is NIH doing to address PASC?

In February 2021, NIH announced the establishment of the PASC Initiative⁴ to support research that will help us better understand PASC and identify effective treatments and potential ways for preventing it. To ensure our research efforts are informed by the patient experience, the PASC Initiative will engage patient voices throughout multiple stages and levels.

At the heart of the PASC Initiative is a SARS-CoV-2 Recovery Cohort that includes diverse populations of both adults and children. This meta-cohort will include patients from Long COVID clinics, from NIH-supported COVID-19 studies and networks, and from previously established NIH-supported longitudinal cohort studies such as those focused on age-related heart and lung disease. Investigators leading Recovery Cohort studies will collaborate in a multi-disciplinary consortium to determine a core set of information that will be collected and tests that will be done on all Recovery Cohort participants. A data science core will support analysis of data gleaned from clinical exams, health records, and mobile devices, and a biobank will collect tissue samples that can be used to analyze the tissue and organ injury caused by SARS-CoV-2 infection.

Some of the initial underlying questions that the PASC Initiative hopes to answer are:

- What does the spectrum of recovery from SARS-CoV-2 infection look like across populations?
- How many people experience PASC?
- What is the underlying biological cause of these long-term effects?
- What makes some people vulnerable to PASC but not others?
- Does SARS-CoV-2 infection trigger changes in the body that increase the risk of other conditions, such as chronic heart or brain disorders?

⁴<https://www.nih.gov/about-nih/who-we-are/nih-director/statements/nih-launches-new-initiative-study-long-covid>

What are the symptoms of PASC, and who is affected?

Symptoms range from mild to incapacitating and may involve multiple organs and systems. Some of the more common symptoms include fatigue, shortness of breath, cognitive difficulties or "brain fog," sleep problems, fever, anxiety, and depression. PASC includes multisystem inflammatory syndrome in children and adults (MIS-C and MIS-A), which are rare but severe immune responses to SARS-CoV-2 that often involve cardiovascular complications.

Some people, especially those who were severely ill, have lingering lung problems. In one study, about half of patients who needed ventilation for acute COVID-19 had lower than normal blood oxygenation capacity six months later¹. Another study found that a significant percentage of patients continued to have shortness of breath four months after being hospitalized with COVID-19². There is also potential for cardiac complications down the line among a portion of COVID-19 patients³.

The public health impact of PASC is unknown, but it could potentially be very large, given the number of adults and children who have been or will be infected with SARS-CoV-2.

¹<https://pubmed.ncbi.nlm.nih.gov/33428867/>
²<https://pubmed.ncbi.nlm.nih.gov/33729425/>
³<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7385669/>



How will the PASC initiative evolve?

Calls for other kinds of research are expected over the next few months, specifically opportunities focused on clinical trials to test strategies for treating long-term effects and promoting recovery. Data will also be shared with the broader research community to facilitate new analyses. In addition, a key feature of the Initiative will be long-term follow-up of patients and adaptive research strategies as our understanding of PASC evolves.

In addition to addressing the immediate public health impact of SARS-CoV-2 infection, the PASC Initiative also has the potential to enhance our basic knowledge of how humans recover from viral

To keep up to date on the PASC Initiative, visit:

<https://covid19.nih.gov/research-highlights/when-COVID-19-symptoms-linger>





RECOVER

Researching COVID to Enhance Recovery



National Institutes of Health

Turning Discovery Into Health