Researching COVID to Enhance Recovery (RECOVER)

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RECOVER
Researching COVID to Enhance Recovery

NIH National Institutes of Health
Researching COVID to Enhance Recovery

Long COVID Funding Update

$662 million in <u>new</u> funding, includes:

- $147 million recently reallocated
- $515 million invested by NIH earlier this year

$ to be allocated over FY 2025-2029 to support:

- RECOVER-TLC clinical trials (~$300 million)
- Compete adult and pediatric cohort studies
- Additional pathobiology studies
- Preserve & broaden access to data and biospecimens & maintain infrastructure

RECOVER Research Components

Observational
- EHR Data
- Adult, Pregnancy, and Pediatric Cohorts enrolled in pandemic
- Collaborative of pre-existing Community-based Cohorts

Pathobiology
- Biomarker Discovery
- Viral Persistence/Reactivation
- Immune Dysregulation
- Organ Damage/Dysfunction
- Tissue Pathology

Clinical Trials
- 5 Adaptive Platform Protocols
- 8 Clinical Trials
- 13 Active Interventions Tested

RECOVER Cores

Clinical Trial Data Coordinating Center

Clinical Science

Data Resource

Biorepository

RECOVER by the Numbers

Observational

60 Million
Electronic Health Records

30,000
Participants Enrolled in new Clinical Cohorts

60,000
Participants in pre-existing Community-based Cohorts

Pathobiology

>60
Studies of Pathogenesis

209
Autopsies Performed

Clinical Trials

>200
Candidate Interventions Evaluated for Inclusion

8 trials

13 Interventions

5
Adaptive Platform Master Protocols Across Multi-therapeutic Domains

Patient and Community Engagement

>1,000
Patients included in Protocol Design, Trial Application Review, and/or Symptom Survey Development

41
Public Seminars on Long COVID/RECOVER

>500
Diverse and Multi-disciplinary Investigators and Patients in RECOVER Consortium

Findings

- **55** Scientific Reports Published/Accepted
- **22** Scientific Reports Under Journal Review
- **86** Scientific Reports In Preparation

RECOVER Enrolling Cohorts

Adult (Including Pregnancy)

- Enrollment closed in October 2023 (100% enrolled)
- Participants Enrolled (Acute, uninfected, post-acute): 14,750

Pediatric (Including MUSIC and ABCD)

- Enrollment in progress (99.0% enrolled)
- Participants Enrolled (Acute, uninfected, post-acute): 14,942

Tissue Pathology/Autopsy

- Enrollment in progress (59.7% enrolled)
- Decedents Enrolled (Acute, uninfected, post-acute): 209

Data is from the Observational Portal as of 12/09/2024.

Deidentified Data Available to Researchers

>15,000 adults (+ sub-cohort of over 2,000 pregnant women):

- Study visits: >122,000
- Enrolling sites: 79
- Biospecimens: 822,000

>24,000 young adults, children, infants, and their caregivers:

- Study visits: 62,000
- Enrolling sites: 115
- Biospecimens: 85,000

Observational Cohorts Clinical Characterization Findings

RECOVER Findings (Examples from 50+ publications)

- Symptom-based definition of Long COVID in adults and children
  - Major step toward working case definition for diagnosis and patient monitoring
- Symptoms and conditions specifically associated with Long COVID in children (e.g. circulatory and respiratory)
- Vaccination significantly decreases risk of Long COVID
- Higher risk of new cardiovascular, neurologic, endocrine, GI symptoms in Black and Hispanic patients
- Distinguishing immune features of Long COVID identified

Patient Relevance

- Improved Diagnosis, Monitoring, and Care
- Better Preventative Care
- Better Diagnosis, Monitoring, Care, and Targeted Treatments

Observational Cohort Discoveries

1. The first structured framework for identifying Long COVID in Adults based on symptoms; characterization of the risk of Long COVID for different strains of SARS-CoV-2 (JAMA, 2023)

   -> Framework has been used by many other groups to define Long COVID; manuscript was the third most viewed, second most discussed, and highest Altmetric score of any published in JAMA in 2023.[1.]

2. The first framework for identifying Long COVID in children based on symptoms; characterization of the risk of Long COVID across age groups (JAMA, 2024)
3. 2024 Update of the RECOVER-Adult Long COVID Research Index (Augmentation) (JAMA, 2024)
4. Prevalence and risk factors for long COVID among individuals pregnant at the time of SARS-CoV-2 infection (Obstet Gynecol, 2024)
5. Refined the focus of long COVID pathobiological and biomarker research by revealing that 25 common blood lab tests do not serve as reliable biomarkers for Long COVID (Annals of Internal Medicine, 2024)
6. Identified circulating SARS-CoV-2 antigens in blood of individuals long after acute COVID-19, contributing to growing evidence that viral persistence may be a contributing mechanism to Long COVID (Clinical Microbiology and Infection, 2024)

[1] jamanetwork.com/journals/jama/fullarticle/2816228

RECOVER Pathobiology Studies

Key Findings

Advances in mechanisms, biomarkers, and treatment targets:

- Large # of samples/data points in deeply phenotyped individuals to investigate mechanisms of Long COVID, including in subgroups and sub phenotypes and will support future studies.
- Insights: disrupted immune responses and their link to viral persistence in Long COVID.

Example findings:

- Severe COVID-19 may cause long-lasting alterations to the innate immune system, the first line of defense against pathogens, making some people susceptible to other infections.
- Symptoms for some Long COVID sufferers appear to be caused by persistent infection and may respond to antiviral medications.

Future RECOVER Pathobiology Studies

- ~$18 million (from initial $1.5 billion allocated to RECOVER) for 20 additional awards
- Adds to the more than 40 pathobiology research projects awarded in 2022 that are yielding results

Clinical Trials

VITAL

RECOVER-VITAL
Viral Persistence
PAXLOVID

NEURO

RECOVER-NEURO
Cognitive Dysfunction
BrainHQ, PASC-CoRE & tDCS

AUTONOMIC

RECOVER-AUTONOMIC
Severe POTS
IVIG

RECOVER-AUTONOMIC
Moderate POTS
Ivabradine

SLEEP

RECOVER-SLEEP
Hypersomnia
Modafinil/Solriamfetol

RECOVER-SLEEP
Complex Sleep Disturbances
Melatonin + Light Therapy

ENERGIZE

RECOVER-ENERGIZE
Exercise Intolerance
Personalized Cardiopulmonary Rehab

RECOVER-ENERGIZE
Post-Exertional Malaise
Structured Pacing

Status Update: RECOVER 1.0 Clinical Trials

as of 12/10/2024 **SITES:** Planned: **254** | Selected: 235

Platform	Percentage of Sites Activated	Enrollment Start Date	Patients Enrolled/ % Total to Enroll	Actual or Expected End of Enrollment	Follow-Up End Date
VITAL	**100%**	August 2023	964/ 100%	Sept 2024	March 2025
NEURO	**100%**	Sept 2023	328/100%	June 2024	Dec 2024
AUTONOMIC	100%	March 2024	103/28%	Sept-Nov 2025	Sept-Nov 2026
SLEEP	76%	August 2024	78/8%	Oct-Dec 2025	Jan-Mar 2026
ENERGIZE	52%	July 2024	71/11%	Aug-Oct 2025	Feb-Apr 2026

recoverCOVID.org

END OF PRESENTATION

Clinical Trials | 8 Trials Testing 13 Interventions

VITAL

RECOVER-VITAL Viral Persistence (PAXLOVID)

1. **PAXLOVID, an antiviral drug,** for either 15 or 25 days

NEURO

RECOVER-NEURO Cognitive Dysfunction (BrainHQ, PASC-CoRE & tDCS)

1. **BrainHQ**, an interactive online brain training program
2. **PASC-CoRE**, an online goals management training program
3. **tDCS (Transcranial direct current stimulation)** a safe, noninvasive form of brain stimulation

AUTONOMIC

RECOVER-AUTONOMIC Severe POTS (IVIG)

RECOVER-AUTONOMIC Moderate POTS (Ivabradine)

1. **Intravenous Immunoglobulin (IVIG),** a drug that modifies the body's immune response
2. **Ivabradine**, a drug used to decrease heart rate
3. **Coordinated non-drug care–** includes weekly phone calls with a coordinator and other interventions such as a high salt diet and wearing a compression belt

SLEEP

RECOVER-SLEEP Hypersomnia (Modafinil/Solriamfetol)

RECOVER SLEEP Complex Sleep Disturbances (Melatonin + Light Therapy)

1. **Solriamfetol,** a drug used to treat excessive daytime sleepiness
2. **Modafinil**, a drug used to treat excessive daytime sleepiness
3. **Melatonin**, a natural hormone in the brain that helps regulate the timing of sleep
4. **Light Therapy**, exposure to a high-intensity light that may help improve and regulate sleep-wake patterns

ENERGIZE

RECOVER-ENERGIZE Exercise Intolerance (Personalized Cardiopulmonary Rehab)

RECOVER-ENERGIZE Post-Exertional Malaise (Structured Pacing)

1. **Personalized Cardiopulmonary Rehab**, a program that combines supervised movement with education
2. **Structured Pacing**, a program designed to help people recognize, control, and minimize symptoms of exercise intolerance and post-exertional malaise (PEM)

Status Update: RECOVER 1.0 Clinical Trials

Pre-decisional

Below is a clinical trials update as of 12/10/2024.

CLINICAL TRIALS INFRASTRUCTURE

Administrative Coord. Center
Research Triangle Institute (RTI)

Clinical Trial Data Coord. Center (CT-DCC)
Duke Clinical Research Institute

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