

NIH to Bolster RECOVER Long COVID Research Efforts Through Infusion of \$515 Million

RECOVER is taking a rigorous approach to improve our understanding of long COVID and increase the odds of identifying treatments that work.

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Four years after the COVID-19 pandemic began, long COVID remains an unsolved, complex and urgent healthcare crisis. According to the Centers for Disease Control and Prevention, 1 in 9 adults in the United States who have ever had COVID-19 continue to experience long COVID with a wide range of symptoms. Many symptoms are debilitating, affecting patients' ability to work and go to school.

To bolster long COVID research efforts, the National Institutes of Health (NIH) is investing an additional \$515 million over the next four years into the [Researching COVID to Enhance Recovery \(RECOVER\) Initiative](#), a nationwide research program to fully understand, diagnose and treat long COVID. Launched in 2021 with \$1.15 billion in Congressional appropriations, the RECOVER Initiative is taking a systematic, comprehensive and rigorous approach to improve our understanding of long COVID and increase the odds of identifying treatments that work.

Infection-associated chronic conditions, such as long COVID, have been notoriously difficult to solve. Despite years of research, the underlying biological mechanisms for conditions such as myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), post-treatment Lyme disease syndrome and a host of other infection-associated chronic conditions have not been identified, and many symptoms of these conditions remain difficult to treat. However, unlike some infection-associated chronic conditions for which the source of infection is unknown, we know that long COVID is caused by the SARS-CoV-2 virus, which may prove advantageous in research.

Nearly 90,000 adults and children are participating in RECOVER observational studies through more than 300 clinical research sites across the country. RECOVER sites have directly recruited more than 30,000 new people, including children and pregnant people, and simultaneously incorporated data from ongoing longitudinal studies to nearly triple RECOVER's number of participants. The amount of data being produced is unparalleled compared to any program in the world. Deidentified data and biospecimens from RECOVER are accessible and used by researchers and scientists to unravel this complex disease.

RECOVER findings, including the identification of major symptom clusters, are helping clinical researchers broaden the identification of long COVID in their patients and ultimately helping to inform diagnosis, treatment and care for all those suffering from long COVID. Findings from across RECOVER, including cohort, pathobiology and electronic health record studies and [valuable input from RECOVER patient representatives](#), have collectively informed the design of RECOVER clinical trials and the selection of at least 13 potential interventions and combination of interventions, four of which began last year. Additional clinical trials are expected to begin in the coming months.

[New publications](#) reporting on RECOVER-supported research are emerging at a swift pace, providing critical insights on the disease. Recent RECOVER studies have found that severe cases of COVID-19 [can change which genes are turned on or off](#) in certain stem cells; that [individuals with comorbid conditions, such as HIV, may have more severe long-lasting symptoms](#) following COVID-19 infection; that [virus can persist in tissues for many months, perhaps years](#), following initial infection; and there may be [changes in the immune system](#) in people with long COVID.

NIH expects this investment of time and resources in building a research program of this scale, scope and rigor will increase the odds in finding treatments that work. The \$515 million in additional funding will build on and continue this important work by:

- Testing additional interventions in clinical trials to find effective treatments to reduce the burden of long COVID.
- Deepening our understanding of how SARS-CoV-2 affects each part of the body as it triggers long COVID and identifying potential biological targets for diagnosis and treatment.
- Investigating longer-term effects of SARS-CoV-2 infection in adults and children to understand who fully recovers over the long term, how the virus affects risk for other diseases such as diabetes, cancer and neurological disorders, and factors and interventions that contribute to recovery.
- Maintaining support for data management and research infrastructure to continue the collection, integration, analysis and storage of many diverse types of clinical data and biospecimens necessary to further understand the effects of COVID-19 and inform interventions.

These studies, and others will provide important insights into long COVID and will improve our understanding of other infection-associated chronic conditions with similar symptoms to inform treatments.

Specific research plans are in development and specific allocations of the new funding may be adjusted to address changing scientific, clinical and public health questions. RECOVER clinical

trials use a flexible framework to rapidly identify treatments that work, remove those that don't and add new interventions for testing. NIH will continue to engage with the many communities that make up RECOVER, including patient and community representatives, advocates, researchers and clinicians, to gather input on potential research and clinical approaches.

NIH is committed to working with our partners to provide solutions for those with long COVID.

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