RECOVER Research Program Announces New Long COVID Clinical Trials

The new “RECOVER—Treating Long COVID” trials will test three drugs and one surgical procedure.

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Key points you should know:

- RECOVER-Treating Long COVID (TLC) announced new clinical trials at the initiative’s second annual workshop. TLC is an offshoot of the broader $1.8 billion RECOVER program, run by the National Institutes of Health (NIH).
- The clinical trials include three new studies, testing low-dose naltrexone in children, a glucagon-like peptide-1 receptor agonist (GLP-1), and the stellate ganglion block procedure. RECOVER-TLC is also supporting an existing trial of the immune-modulating drug baricitinib.
- These new trials represent an improvement on RECOVER’s first round of trials (which predate TLC), but some people with long COVID say the initiative is still not moving quickly enough on finding treatments.
- Some long COVID researchers and advocates who have advised or closely followed RECOVER-TLC also expressed concerns about its patient engagement process for deciding treatments to trial and designing studies.
- RECOVER-TLC has space in its $300 million allocation for additional trials, but the exact budget has not yet been determined, said NIAID officer Joseph Breen.

After a yearlong deliberation process, the U.S.’s flagship long COVID research program has announced its second round of clinical trials.

To people with long COVID who have closely followed the initiative, the new studies represent an important research milestone and improvement on earlier trials. But some remain disappointed with slow progress toward finding treatments for a disease that has disabled millions.

The National Institutes of Health (NIH) announced the trials during a workshop for its RECOVER-Treating Long COVID (TLC) initiative. TLC is an offshoot of the broader $1.8 billion RECOVER program; upon its launch last year, its leaders promised to move faster and focus more on trials following criticism of the larger program.

On Tuesday, NIH staff announced that RECOVER-TLC's initial round of trials will test low doses of the addiction medication naltrexone in children and young adults; the immune system modulator baricitinib; one of the glucagon-like peptide-1 receptor agonist (GLP-1) drugs commonly used for weight loss; and stellate ganglion blocks, injections of numbing medicine into patients' necks.

This phase of RECOVER-TLC trials includes three new studies and support for one trial that is already underway. Rather than starting a new trial of baricitinib, RECOVER-TLC is providing additional funding for the existing trial REVERSE-LC, enabling it to add more study sites as the trial recruits participants.

Among people with long COVID, the trials have received mixed reactions. While officially announced this week, community members first learned of the planned treatments under study in early August when the NIH and Foundation for the National Institutes of Health (FNIH) posted a draft agenda for the RECOVER-TLC workshop.

In an unofficial poll posted on Twitter/X by advocate Billy Hanlon, the majority of respondents voted that they were not pleased with the treatments. Of 328 users who voted, 38.4% selected "strongly dissatisfied" and 30.2% selected "somewhat dissatisfied"; only 5.2% selected "strongly satisfied."

Some commenters expressed disappointment that the list didn't include more novel drugs, writing that RECOVER-TLC's selected treatments are already being tested in existing clinical trials and experimentation by people with long COVID. Others who were more optimistic about the trials shared questions about the study designs, writing that the studies would be most informative if they identified which patient subgroups may be helped by different treatments.

"In my opinion, there are a lot of promising targets that have not been explored yet and we need to be casting a wide net with available resources and gathering as much data as possible, not duplicating efforts," wrote David Putrino, director of the Cohen Center for Recovery from Complex Chronic Illnesses at Mount Sinai (CoRE) — which runs several long COVID clinical trials outside of the RECOVER ecosystem — in an email, explaining that he thought the critique from long COVID community members "has merit."

"Overall if [the first] round of trials was D grade, I'd put this in B- territory," wrote long COVID advocate Charlie McCone, a member of the Patient-Led Research Collaborative,* in a social media post.

RECOVER-TLC sought community input when considering which treatments to trial through a submissions form, then patient participation in working groups that discussed those submissions. But some people who participated in the yearlong process told The Sick Times that it hadn't succeeded at truly meeting the long COVID community's needs.

"If the process were truly incorporating patient perspectives, they would have sought to accelerate this process, because patients and providers have already waited so long for scientific evidence to support the health of people with long COVID," wrote one researcher to The Sick Times who has been a patient and community representative for RECOVER, and who asked to remain anonymous due to concerns about funding implications.

This work is "never fast enough" for the patient community, said Joseph Breen, who co-chaired this week's meeting and helps lead RECOVER-TLC, among other duties at NIAID, in an interview with The Sick Times. He acknowledged that it took time for the TLC team to "figure out how we were going to do this," and said the initiative "had a few hiccups" when Trump's second term started. But the initiative will continue to take patient feedback, particularly as it considers further trials, he said.

Improving on the prior RECOVER trials

RECOVER started in 2021 with $1.15 billion in funding, provided by Congress in late 2020. The program — magnitudes larger than other long COVID research efforts and those that studied related infection-associated chronic diseases pre-pandemic — initially focused on observational research. The NIH dedicated more than half of its initial funding to studies tracking people's symptoms and collecting biological specimens.

In summer 2023, RECOVER finally announced clinical trials. But many people with long COVID and researchers outside the program considered them "underwhelming": the studies largely tested behavioral interventions and treatments that many with the disease had already tried on their own. One study tested exercise, which advocates and researchers warned could harm participants with post-exertional malaise.

Patient advocates and outside researchers also criticized the NIH for selecting researchers without prior experience in infection-associated chronic diseases to lead large parts of RECOVER, as The Sick Times reported last year, and for failing to meaningfully incorporate patient perspectives.

Last summer, in response to these critiques, the NIH announced RECOVER-TLC — an offshoot of the larger program focused explicitly on clinical trials and led directly by NIAID and FNIH. TLC launched with a workshop in September 2024 to discuss trial considerations and collect feedback, then solicited treatment suggestions from the community. The NIH also allocated further funding to RECOVER in 2024, bringing the program's total support to $1.8 billion, with $300 million dedicated to trials through TLC.

Long COVID community members have submitted over 500 potential treatments to RECOVER-TLC through August 2025. Since last fall, researchers, clinicians, and community representatives have

discussed these suggestions in working groups, eventually agreeing on several treatments that are top priorities to trial. TLC announced four of those this week; more will start in the coming months. When asked how much of the $300 million will be spent on these four trials, Breen said that the exact budget hasn't yet been determined as the studies are still being designed.

RECOVER-TLC originally planned for "at least two large pivotal trials and then at least four [smaller] mechanistic studies," he said. The LDN study will fit into the pivotal category; the GLP-1 and stellate ganglion block studies will be mechanistic; and the baricitinib trial falls in between, as the initiative is supporting an existing trial. There may be space in RECOVER-TLC's budget for more mechanistic studies, possibly also a second larger trial, Breen said.

Unlike the first round of RECOVER trials, the new TLC trials are testing only biological interventions: three drugs and one surgical procedure. RECOVER-TLC offers "an opportunity to study higher-risk potential treatments that providers might only be willing to prescribe given evidence from a clinical trial," said the researcher who had served as a RECOVER representative. "More of the planned RECOVER-TLC trials fit into that category than the initial round of RECOVER trials, so that is promising."

Of the four interventions, low-dose naltrexone (LDN) has the most prior evidence. Physicians have used it for decades to treat myalgic encephalomyelitis (ME) as well as chronic pain and other diseases with inflammation. Some people with long COVID have tried it off-label and reported that it helped alleviate symptoms, while others haven't found the drug effective.

Multiple LDN clinical trials for long COVID and ME are currently underway, but these trials focus on adults — RECOVER-TLC's will be the first studying this drug in children. "Pediatricians we talked to, they want safe drugs to give to kids," Breen said, and it's difficult to translate anecdotal reports from adults to children.

Speaking ahead of the meeting, Tess Falor, founder of the patient-led research organization Renegade Research, said she "understands the frustration" that community members have shared about RECOVER-TLC replicating existing trials and patient experiences. With LDN, for example: "so many people have tried this already, we already know that it works for a certain amount of people."

Falor noted that RECOVER-TLC's trials might be valuable in determining which potential treatments may be best suited to help different groups of patients and moving drugs toward Food and Drug Administration (FDA) approval. "If it helps to get [LDN] approved by the FDA for long COVID, then that's a good thing," she said. Indeed, RECOVER-TLC will seek to develop a "regulatory-grade LDN study product" that may be a candidate for approval alongside the trial, said NIAID medical officer Kay Tomashek during the meeting.

Another potentially duplicative RECOVER-TLC trial will test a GLP-1 drug. These drugs have become ubiquitous as weight-loss drugs in recent years, but some people with long COVID have

also tried them off-label. Scientists at Scripps Research are planning a clinical trial of a GLP-1 for long COVID; it's not yet clear how the two studies may overlap.

Stellate ganglion blocks have a similar reputation in the long COVID community as a treatment that can help some people. In the procedure, a surgeon injects anesthesia into an area of nerves called the stellate ganglion. Some small observational studies and case series have suggested that the procedure can help with symptoms such as cognitive issues, changes to smell and taste, and PEM.

In a more novel move for RECOVER-TLC, additional support is going to an existing trial of the JAK inhibitor baricitinib. This drug rose to the top of the treatment list as the initiative was considering community member suggestions, said Wes Ely, one of the principal investigators of the baricitinib trial, called REVERSE-LC. NIAID contacted him and invited him to collaborate, adding further funding to the trial's prior support from the NIH's National Institute on Aging.

"We're going to get across the finish line faster," Ely said. RECOVER-TLC's support will allow the trial to add 11 additional trial sites to its existing four, enabling people with long COVID to participate from more places around the country without the need to travel long distances. Speaking in late August, Ely said he was currently interviewing researchers at potential new site locations and aimed to determine them in the next month.

Ely added that he and his colleagues chose to expand the sites rather than increase the trial's sample size, which had been another option for using NIAID's support. "We said … let's get this thing done faster, get the answer out, and then we'll go to the next study after," he said, noting that leaders at NIAID have a similar attitude in getting answers as quickly as possible.

Engagement and access concerns

What NIH staff consider fast movement on clinical trials can feel very slow for people with long COVID — some of whom have been debilitated by the disease for over five years.

This week's trials announcement comes nearly one year after the first RECOVER-TLC workshop in September 2024, at which program staff committed to continued transparency and engagement with the long COVID community. Community members who participated in or closely followed the process of deciding on trials told The Sick Times that there have been some improvements from earlier phases of RECOVER, but concerns remain about moving quickly, incorporating patient feedback, and making both the program's infrastructure and trials themselves accessible.

Working groups within RECOVER-TLC have spent months discussing treatment suggestions. During a webinar sharing updates in early January, Breen said that he and his colleagues "hope to have some idea of the interventions that have been prioritized from the working groups" sometime in February, as the deadline for the initiative's initial request for public feedback was February 1. In fact, the first announcement of trials has come more than six months after that deadline — a timeline that has frustrated some working group participants who spoke to The Sick Times.

Meighan Stone, executive director of the advocacy group Long COVID Campaign, said she noticed at last year's RECOVER-TLC meeting that "the list of leading drug candidates for long COVID trials had barely changed in years." She added, "There was no need for FNIH to fund a new web page or for NIAID to add layers of review — researchers were ready to move." Stone also called for more transparency from the NIH about how they have spent RECOVER-TLC's funding so far.

Some people with long COVID who submitted treatment suggestions are disappointed not only with the agents chosen for trials so far but also with RECOVER-TLC's process and rationale for those suggestions. Jon Douglas, a patient advocate involved in TLC's working groups, said that he observed some group members seemed new to the complexities of Long COVID. A lot of meetings he'd attended spent a lot of time circling the question, "What is long COVID?" which he said shouldn't be acceptable.

Amy Mitchell, an advocate with the group Long COVID Action Project (LCAP), submitted all 49 treatments on a list that she and other LCAP members compiled in a campaign for accelerated trials, called ACT NOW, which focuses on addressing viral persistence.

Of the 49 treatments, only one, baricitinib, is part of RECOVER-TLC's first round of trials. Mitchell received updates from the initiative's staff in response to eight of her submissions and shared several of them on Twitter/X and with The Sick Times. In all of those responses, staff wrote that "other therapeutic or biologic agents were determined to better align" with RECOVER-TLC's criteria, with those criteria described in an attached document.

One proposal, the monoclonal antibody AER002, was deferred due to a prior clinical trial "generating negative data" — though researchers from that trial have not yet published a paper sharing their full results. In response to another proposal, for the HIV/AIDS antiviral tenofovir, staff wrote that reviewers wished "to see greater scientific rationale for targeting long COVID." The same drug is currently part of a trial at Mount Sinai's CoRE, tested along with other HIV/AIDS drugs in the combination called Truvada [tenofovir disoproxil fumarate/emtricitabine]. Mitchell raised questions about those responses, such as what definition of long COVID the reviewers used.

Mitchell, along with other advocates, would like to see RECOVER-TLC test antivirals and monoclonal antibodies that "would directly address viral persistence in long COVID." She said: "NIH has access to every kind of medication and test, even those not yet FDA-approved. Patients needed NIH to trial the tests and treatments their doctors can't prescribe, or at minimum to test the effectiveness of off-label antivirals."

Responding to the criticism about a lack of antiviral trials in RECOVER-TLC's selections, Breen said that the initiative recognizes the science in viral persistence, but that "the ability to measure it consistently has been a struggle." He wants to hear from workshop attendees about different potential next steps, he said, which might include supporting biomarker research or testing multiple drugs in combination.

While not part of the initial list of trials, the RECOVER-TLC workshop will also feature a monoclonal antibody research effort: the SPEAR Study Group, run by biotech company Invivyd and leading

long COVID scientists, including Putrino. He will present about the group's work on Wednesday. "I will be strongly advocating for a collaboration between Invyvid and RECOVER-TLC," he wrote ahead of the talk, adding, "this is a trial that MUST happen urgently."

Community members have also shared questions about how RECOVER-TLC's trials will be designed. One major concern is incorporating PEM into trial design — which was a common point of feedback in last year's workshop, too. Patient-researchers and those who study ME emphasize that clinical trials must seek to minimize exertion among participants and measure PEM both when evaluating a treatment's success and considering potential safety issues.

Victoria C., a social worker with long COVID who has served as a RECOVER representative, will speak about PEM during the workshop, emphasizing that accessibility considerations must be "baked into the design" of studies. (She asked that her last name not be used due to privacy concerns.)

Past RECOVER trials have also been inaccessible for people with more severe long COVID symptoms, who are unable to leave their homes or beds and cannot travel to medical centers for testing. "As someone who is bedbound I have given up on participating in any RECOVER trial," Victoria said. Leaving out this patient group could mean that trials don't fully capture "the full picture" of long COVID, she added.

Victoria also noted accessibility concerns for the RECOVER-TLC workshop itself. Long COVID community members criticized last year's workshop for not requiring masks or other COVID-19 safety measures for in-person attendees, as well as challenges with accessing the livestream for people watching virtually. This year's meeting does not require masks, either, though staff are providing KN95s and conference rooms "are equipped with HEPA-grade air filters," according to an email sent to attendees.

The long COVID community watches RECOVER so closely in part because it is the largest federally funded program for the disease and is one of the few programs to continue amid research cuts by the Trump administration. In a Senate hearing last week, Health Secretary Robert F. Kennedy Jr. claimed he would support further long COVID research, in response to questions from Senator Todd Young (R-Ind.).

But to some researchers and advocates, additional funding seems uncertain, increasing the pressure for RECOVER-TLC to spend its current resources wisely. To Mitchell, the vast majority of RECOVER's $1.8 billion has been wasted on symptom surveys and trials that don't target the underlying causes of infection, she said. "As much as I wanted them to succeed, RECOVER has squandered their funding and risked the lives of everyone with long COVID."

Reflecting on last year's RECOVER-TLC meeting, Douglas said that the patient community was expecting "ambitious" clinical trials. But, he added, the treatments selected for trials haven't quite met those expectations. Still, Douglas remains optimistic that RECOVER-TLC will consider feedback. The open question is, he said, how quickly can the program adapt, and can it collaborate with other researchers already doing cutting-edge work?

“American patients need a diversified federal long COVID research portfolio that delivers solutions — across not just the NIH, but at [the Advanced Research Projects Agency for Health], [Department of Defense], and beyond,” said Stone from the Long COVID Campaign, citing Sen. Young’s questions to Secretary Kennedy last week.

“What’s needed now is more high-risk, high-reward research with a bias toward action,” she said. “We also need cooperation from pharma and global governments for a truly multi-year, multilateral effort.”

RECOVER-TLC’s treatment submission form remains open for new entries. Community members can also re-submit the form with new evidence for a previously-submitted treatment or can email new evidence to FNIH staff.

Betsy Ladyzhets, co-founder and managing editor at The Sick Times, will continue covering NIH RECOVER. Send her tips at betsy@thesicktimes.org or reach out on Signal.

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