Together, we can explore options that may help improve Long COVID symptoms

RECOVER SLEEP

HYPERSOMNIA GROUP
(MODAFINIL OR PLACEBO)

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Welcome to RECOVER-SLEEP

About This Study

RECOVER-SLEEP is studying interventions, or possible treatments, for people who have sleep disturbances related to Long COVID. Sleep disturbances may include problems falling or staying asleep, feeling very tired during the day, or problems with the sleep-wake schedule.

Researchers want to better understand how the virus that causes COVID affects sleep and find possible treatments to improve sleep quality and daily functioning for people who have Long COVID. This study will enroll adults who have sleep problems or whose sleep problems have gotten worse as a result of Long COVID and who have not had another COVID infection in the past 4 weeks.

After completing a sleep evaluation, participants will be assigned to one of the following study groups that best matches the type of sleep disturbance they are experiencing:

Hypersomnia

- sleeping longer than usual or feeling very sleepy or tired during the day, even after uninterrupted sleep at night

Complex PASC-Related Sleep Disturbances (CPSD) including:

- problems falling or staying asleep
- poor-quality sleep
- an irregular sleep-wake schedule

The information in this brochure describes what participants in the Hypersomnia group (modafinil or placebo) can expect as part of the RECOVER-SLEEP trial.

Why Your Participation Matters

More than 500 million people around the world have had COVID, and it's possible that millions of them could have long-term symptoms. We need more information to support the safe use of potential treatments for people with Long COVID.

With your help, we can better understand why and how Long COVID affects people's sleep and explore ways to treat sleep disturbances associated with Long COVID. This research may help you, your loved ones, and other people with Long COVID.

What to Expect in the Hypersomnia Group (Modafinil or Placebo)

Length of Study	Study Visits	Study Drug	Follow-up
Participate in the study for 16 weeks (about 4 months)	Visit the study clinic 2 times	Take a study drug daily for 10 weeks, provided at no cost	Answer follow-up questions about your health and well-being

What You Will Receive

Study Drug

- You will be assigned by chance to receive an active or inactive study drug.
- You, your study doctor, and the study team will not know if you are receiving the active or inactive study drug, but they can quickly find out if needed for your safety or well-being.

Portable Blood Pressure Monitor

- You will use the portable blood pressure monitor to check your blood pressure multiple times for the first 3 weeks while taking the active or inactive study drug.
- If you develop moderate or more severe side effects or high blood pressure, the study team will lower your dose of the study drug.
- You may keep the portable blood pressure monitor for personal health monitoring after the study ends.

Activity Tracker

- During the study intervention period, you will be asked to wear an activity tracker on your wrist, similar to a watch, to record rest, sleep, and activity patterns.
- Please wear the activity tracker for 7 days before you start taking the study drug and for the last 7 days you are taking the study drug (14 days total).
- You are encouraged to wear the activity tracker during the entire study.
- The study team will help you set up the activity tracker and app. You will need to download an app to a mobile device and make sure your activity tracker is connected to WiFi once a day to send the data to the study team.
- You may keep the activity tracker for personal health monitoring after the study ends.

Sleep Diary (online or paper format)

- A sleep diary is a record of your rating of the quality of your sleep.
- You will be asked to complete the sleep diary for 7 days before you start taking the study drug and for the last 7 days you are taking the study drug (14 days total).
- This information will help researchers understand how the study interventions affect participants' day-to-day sleep patterns and sleep quality.

About the Study Drug: Modafinil

You have been assigned by chance to one of these groups:	
Modafinil (active study drug)	**Placebo (inactive study drug)**

In this study, modafinil and the placebo are both referred to as study drugs.

- **Modafinil** (pronounced mow-DAH-fuh-nil) is a pill taken by mouth that is used to help people stay awake during the day. This medicine is approved by the U.S. Food and Drug Administration (FDA) for treating adults with narcolepsy, sleep apnea, and shift-work disorder. It has not yet been studied widely for treating people with Long COVID.
- A **placebo** pill looks like the active study drug but has no active ingredients and should have no effect. If you receive a placebo as part of this study, your symptoms of sleep disturbances may not improve or may get worse.

Important Reminders about Pregnancy and Breastfeeding

- The effects of the study drug on a developing pregnancy or a breastfeeding infant are unknown. If you are pregnant or breastfeeding, you should not take part in this study.
- If you could become pregnant and you have a sexual partner who is able to have children, **you must use an effective method of birth control** to avoid becoming pregnant during the study and for at least 7 days after finishing the study drug due to potential side effects of the study drug.
- Some birth control pills may be less effective for people taking modafinil. If you have questions about what is considered effective birth control, please ask the study team.

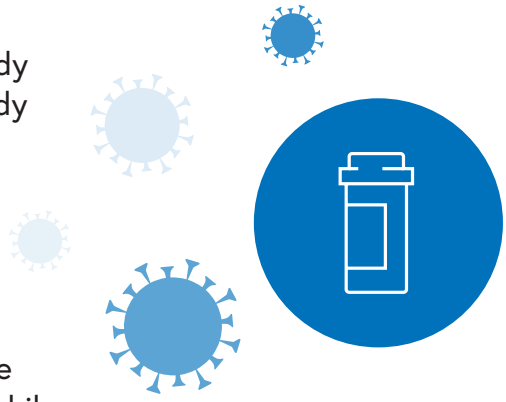
Other Important Reminders

- The study drug should be stored at room temperature (68°F to 77°F). Do not freeze the study drug.
- You will need to return any extra study drug pills at your End of Intervention clinic visit.

How to Take the Study Drug

You will receive a pill bottle with enough of the study drug to last 10 weeks. The placebo pill looks like modafinil, but has no active ingredients and should have no effect.

Weeks 1 to 3: Titration Period



During the first 3 weeks of the study, you will work with the study team to safely introduce your body to the active or inactive study drug and find the right dose for you. Your dose will be gradually increased every few days until you are taking the best dose for you, **a process called titration**.

During this process, the study team will call you about every 5 days to ask how you are feeling and to record any symptoms. They will monitor and adjust your dose as needed. Please let the study team know if you have any new or worsening symptoms while taking the study drug.

You will be asked to use the **portable blood pressure monitor** multiple times to check your blood pressure during the titration period. If you develop moderate or more severe symptoms or high blood pressure, the study team will lower your dose of the study drug.

Please follow your study team's instructions on how many study drug pills you should take each day and when the pills should be taken. Over the first few weeks, the number of pills may be increased to a maximum of 4 pills. The titration schedule for Modafinil is:

1. 100 mg daily in the morning (1 pill) ⬭
2. 200 mg daily in the morning (2 pills) ⬭⬭
3. 200 mg daily in the morning and 100 mg in the early afternoon (3 pills) ⬭⬭●
4. 200 mg daily in the morning and 200 mg in the early afternoon (4 pills) ⬭⬭●●

⬭ **Morning** is 11:59 a.m. or earlier.
● **Early afternoon** is at least 4 hours after morning dose and at least 8 hours before desired bedtime.

For example, if your bedtime is 11:30 p.m., you would take the early afternoon dose no later than 3:30 p.m., and you would need to take the morning dose no later than 11:30 a.m.

Weeks 4 to 10: Maintenance Period

After finding the right dose for you during the titration period, you will then take that dose for the next 7 weeks. **Please follow your study team's instructions on how many study drug pills you should take each day and when the pills should be taken.**

Notes

RECOVER-SLEEP: Modafinil Participant Schedule

This schedule summarizes the study activities for participants assigned to the Hypersomnia group (modafinil or placebo). You will take the study drug and complete the activities listed here.

Keep this schedule in a safe place so you can refer to it throughout the study.

STUDY ACTIVITIES: 16 Weeks (4 Months Total)

Screening and Baseline Period: 1 Week

Screening visits will take about 5 hours

	Information	Assessments	Receive
Randomization Visit (about 2 to 4 hours) **Date: _____**	• Review current medicines • Review study requirements • After this visit, complete a survey about how you are feeling	• Surveys • Sleep symptoms and habits • Attention and thinking speed test • Blood sample • Nasal swab sample • Check-in • Pregnancy test, if applicable	• Study drug • Portable blood pressure monitor • Activity tracker • Information on healthy sleep habits • At-home stool (poop) sample kit • Sleep diary (if using paper format)

Pre-Study Intervention Period: 1 Week

From _____ to _____	**For 7 days before you start taking the study drug at home** • Wear the activity tracker to record your rest and activity • Fill out Sleep Diary 1 (online or on paper) to record the time you spent sleeping and napping and the quality of your sleep

Study Intervention Period: 10 Weeks (2.5 Months)

Take the Study Drug **From _____ to _____**	• Take the study drug by mouth daily (the dose will be gradually increased over the first 3 weeks to find the best dose for you) • Receive check-in phone calls that will last about 30 minutes from the study team every 5 days during the first 3 weeks • Use the portable blood pressure monitor for the first 3 weeks while taking the study drug • Wear the activity tracker on your wrist daily (recommended, but not required)

Middle of Study Intervention Phone Call (about 30 to 60 minutes) **Date: _____**	Between week 5 and week 7, the study team will call you for another check-in.		
Pre-End of Study Intervention Period **From _____ to _____**	**For the last 7 days you are taking the study drug** • Wear the activity tracker to record your rest and activity • Fill out Sleep Diary 2 (online or on paper) to record the time you spent sleeping and napping and the quality of your sleep		
End of Study Intervention Clinic Visit (about 2 to 4 hours) **Date: _____**	**Information**	**Assessments**	**Receive / Return**
	• Review current medicines • After this visit, complete a survey about how you are feeling	• Study drug pill count • Surveys • Sleep symptoms and habits • Attention and thinking speed test • Blood sample • Check-in	Receive • At-home stool (poop) sample kit Return • Remaining study drug, if applicable • Completed Sleep Diary (if using paper format)
End of Study: 4 Weeks (1 Month) Later			
End of Study Follow-up Phone Call (about 30 to 60 minutes) **Date: _____**	A study team member will call you for a check-in about 4 weeks after you finish taking the study drug. During this call, we will ask if you have any new or worsening symptoms.		

Notes

About the RECOVER Research Biorepository

The RECOVER Research Biorepository is designed to collect and store biospecimens for future research related to the RECOVER Initiative. Biospecimens may include samples of blood, stool (poop), and nasal swabs. These samples will be stored securely until they are used up.

Participating in this study means you agree to share your data and biospecimens with the RECOVER Research Biorepository. **If you choose to participate in this study, your data and samples may also be shared with other researchers for future research, such as developing new tests and treatments for Long COVID or other health problems**. You can change your mind later, but researchers might still use your data and biospecimens if they have already been shared and we are not able to link your samples back to you because they have already been de-identified.

Why is a biorepository needed?

Biospecimens from a blood sample can provide valuable information to researchers. This information is called a "biomarker." For example, a person's blood sugar level is one of the biomarkers for diabetes. Biomarkers can be measured and may provide important information about Long COVID. They may also predict how a patient will respond to a treatment.

How could a biorepository help with Long COVID research?

Sharing your data and biospecimens with the RECOVER Research Biorepository may:

- Increase the possibility of developing new interventions and possible treatments related to Long COVID
- Improve our understanding of how antiviral drugs and other interventions may work to reduce Long COVID symptoms
- Enhance our understanding of how and why Long COVID affects people differently
- Help researchers make important discoveries and uncover possible therapies that could help your family and others in the future

How will my privacy be protected?

Your data and samples will be de-identified, which means they will not include any information that can personally identify you, and researchers cannot easily link your identifying information to the data and samples.

What will the samples be used for?

RECOVER research
The samples will be used for research on COVID and the long-term effects of the virus that causes COVID-19. They may also be used for research on other health problems.

Genetic testing (optional)
The use of your samples for genetic testing is optional, and you can let the study team know your decision in the Informed Consent Form. If you give your permission, researchers may study your genes to look for links to Long COVID. Genetic tests can determine if a person or groups of people are more likely to have certain genetic diseases or conditions. Choosing to say no to genetic testing will not limit your ability to participate in other parts of this study, including using the study intervention.

Will I get any results back from future research use of my data and biospecimens?

No. You should not expect to receive results from any future research that may use your data and biospecimens.

Blood Samples

When will I have blood drawn for the biorepository?
The study team will take about 5 tablespoons (80 ml) of blood from your arm during specified study visits.

Stool Samples

How will I provide stool samples?
After the Baseline and End of Study Intervention visits, you will be asked to provide a stool (poop) sample using an at-home kit. The at-home kit will include a confidential pre-paid box for you to mail your sample directly to the RECOVER Research Biorepository where it will be stored securely.

Why are stool samples important to this research?
People who have had COVID can have changes in their microbiome (microorganisms like fungi, bacteria, and viruses that live in the intestines) in their stool after their infection. Collecting stool samples helps researchers understand changes in the microbiome caused by the COVID-19 infection.

If You Become Ill or Injured
Get the medical care that you need right away. Visit your doctor, go to urgent care, or go to the emergency room if needed.

Contact Your Study Team if You
- Start taking any new medicines
- Change your phone number, email, or home address
- Have questions about the study or the study drug
- Experience new or worsening symptoms
- Receive emergency medical care or are hospitalized
- Become pregnant or think you could be pregnant

Site Contact Information

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For more information and study updates, visit trials.recovercovid.org/sleep

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