Official Title: **RECOVER-ENERGIZE: A Platform Protocol for Evaluation of Interventions for Exercise Intolerance in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)**

NCT: NCT06404073

IRB Document Date: 15 Apr 2025

INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**Duke Clinical Research Institute (DCRI) / "RECOVER-ENERGIZE: A Platform Protocol for Evaluation of Interventions for Exercise Intolerance in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)"**
Protocol Number:	**RECOVER-ENERGIZE**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

KEY INFORMATION

CONCISE SUMMARY

Exercise intolerance and post-exertional malaise related to Post-Acute Sequelae of COVID-19 (PASC), or Long COVID, have significant detrimental effects for patients who are no longer able to be as active as they were before having COVID-19.

- 'Exercise intolerance' is the need to stop physical activity because of symptoms like shortness of breath and fatigue.

- 'Post-exertional malaise' (PEM) is the worsening of symptoms after minimal physical, mental, or emotional activity. PEM symptoms include difficulty with physical activity (exercise intolerance), difficulty thinking, trouble sleeping, sore throat, headaches, muscle aches, dizziness, or severe tiredness. These symptoms may worsen 12 to 48 hours after the activity and may last for days or even weeks.

RECOVER-ENERGIZE is a research study to find out if certain study treatments (study interventions) can help treat exercise intolerance and post-exertional malaise that started or got worse after a COVID-19 infection and have lasted for at least 3 months.

This research study will have 2 "study arms":

1. **Study Arm A - Personalized Cardiopulmonary Rehabilitation (Cardiopulmonary Rehab):** A program that combines exercise training with education to help participants with exercise intolerance improve their quality of life and ability to exercise.
2. **Study Arm B - Structured Pacing:** A training intervention designed to help participants with PEM get to know, control, and minimize PEM symptoms. The goal is more stable function in everyday life with less frequent and less severe PEM symptoms (fewer setbacks in function).

Based on your symptoms, you will be assigned to one study arm. Within each study arm, participants will be randomly assigned by chance (like the flip of a coin) to either the active study intervention group or the control group. The study intervention group will receive the intervention for their assigned study arm. The control group will be provided education about exercise and/or PEM and weekly phone calls.

Your participation in the study will last approximately 6 months.

You will be asked to wear an activity tracker/Fitbit connected to a smartphone as part of the study. If you do not have a smartphone or data plan that works with the activity tracker/Fitbit being used, then one will be provided to you.

There are potential risks and benefits from participating in this study. Participation may induce post-exertional malaise (PEM) in those prone to PEM. PEM may be triggered or worsened by travel to appointments, physical and/or cognitive exertion, or completing the study interventions. Possible risks related to cardiopulmonary rehab and physical ability tests include chest pain, increased blood pressure, increased heart rate, dizziness, and shortness of breath. Other risks related to blood draws, nasal swabs, and loss of confidentiality are also possible. However, every effort will be made to minimize these risks.

If you are involved in the RECOVER longitudinal cohort study, your study data (including a limited number of identifiers such as date of birth, dates of study, and health events) may be linked between RECOVER studies and analyzed together across studies.

You do not have to participate in this research to be treated for your condition. You can continue with your usual healthcare.

STUDY CONSENT

You are being asked to participate in the RECOVER-ENERGIZE study, part of the National Institutes of Health's Researching COVID to Enhance Recovery (RECOVER) Initiative. The RECOVER Initiative was created to research possible treatments for Long COVID. This study is part of that effort and is called "RECOVER-ENERGIZE: A Platform Protocol for Evaluation of Interventions for Exercise Intolerance in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)."

"Sequelae" means conditions and symptoms that are caused by a past disease, like COVID-19. A "protocol" is a detailed plan that researchers follow to do their research and collect information. Platform protocols are designed so other possible treatments can be added without the need to develop separate research studies. Studies using the RECOVER platform protocol design have similar goals and activities, but they are researching different study interventions.

This study will include about 660 adult participants across both study arms from many sites across the United States. Your participation is voluntary. Please review the important information below to help you decide if you want to take part in this study.

INTRODUCTION

Why am I being asked to take part in this study?

You are being asked to take part in this study because:

- You are at least 18 years old.
- You have previously had a COVID-19 infection.
- You have had new or worsened exercise intolerance and/or post-exertional malaise (PEM) for at least 12 weeks since your COVID-19 infection.
- You cannot do the level or amount of physical activity and/or daily activities that you did before getting COVID-19.

If you have exercise intolerance, as you try to exercise or physically push yourself, you may have to stop your efforts because of symptoms like shortness of breath, muscle weakness, or extreme tiredness.

If you are experiencing PEM, your symptoms may worsen following exercise or even minor physical, mental, or emotional exertion, with symptoms typically worsening 12 to 48 hours after activity and lasting for days or even weeks.

Why is this study being done?
Exercise intolerance and PEM are the most frequently reported symptoms in Long COVID. To decrease long-term COVID-19 symptoms, including effects on quality of life, study interventions attempting to reduce specific symptoms are being studied. If successful, this study may help people with Long COVID improve their ability to do physical activity and/or manage their PEM with fewer symptoms and may help researchers better understand these conditions and how to treat them.

VOLUNTARY PARTICIPATION and POTENTIAL BENEFITS

Participation in this study is up to you. You can choose if you want to participate or not participate.

What if I don't want to participate?
You do not have to be in this study if you do not want to. If you decide to participate, you can decide to stop at any time. If you choose not to participate, your usual healthcare will not change. If you choose not to participate or if you stop participating after you join, you will not be punished or lose any benefits you already have.

Will there be any benefit to me or others?
We do not know if you will benefit from being in this study. The study intervention(s) may have a role in treating exercise intolerance and PEM in Long COVID. You may want to participate to help healthcare providers learn how to best care for adults with Long COVID. Even if you do not benefit from the study, the information learned from this study may benefit others like you in the future.

Will I be told about any new findings that may change my decision to participate?
Yes. We will let you know if any new or important information is discovered during the study that may affect your decision to continue being in the study.

WHAT to EXPECT IF YOU DECIDE TO join this study

How long will I be in this study?
Participation in the study may last about 6 months including:

- Screening and Baseline Visits (3 weeks)
- Intervention Period (12 weeks)
- Follow-up phone call (12 weeks after intervention)

SCREENING

The Screening Visit may take more than 1 visit to the study clinic to complete. During the Screening Visit, the following activities will be completed:

- Sign this informed consent form
- Complete a questionnaire about post-exertional malaise (PEM) symptoms
- Answer questions about your symptoms, general health, and well-being
- Give a blood sample
- Have your height and weight measured
- Receive an activity tracker/Fitbit to record your activity patterns
    - If you do not have a smartphone or a data plan that works with the activity tracker/Fitbit, then one may be provided to you. If the smartphone is provided to you, then you may keep the smartphone without the data plan at the end of the study.
    - The activity tracker/Fitbit must be used with a compatible mobile device.
    - The activity tracker/Fitbit will be used to measure your amount of rest, sleep, and activity. You are highly encouraged to wear the activity tracker/Fitbit while awake and asleep for the entire duration of your participation in the study.
- If you are eligible to be in the study, you will be offered to participate in **either Study Arm A or Study Arm B** based on your PEM questionnaire results.
    - **Study Arm A:** A program that combines exercise training with education to help participants with exercise intolerance improve their quality of life and ability to exercise. If you are assigned to this study arm, you will be asked to complete the following additional screening activities:
        - Electrocardiogram (ECG) to check the overall health of your heart. Electrodes (small, plastic patches that stick to the skin) are placed at certain spots on the chest, arms, and legs. The electrodes are connected to an ECG machine. The heart rate and electrical activity of the heart are then measured and printed out. No electricity is sent into the body.
        - Have your blood pressure, heart rate, oxygen level, and respiratory rate measured.
        - Walking test on a 10-meter (10.9-yard) track for as long as you can until you become too short of breath to keep up your speed or to maintain your pace.
        - Complete a questionnaire about PEM symptoms remotely (phone or online) 2 to 3 days after this visit.

- If after you complete these additional screening activities you seem to be a good fit for this study, and choose to continue participating, you will return to the study clinic for the Baseline Visit.

- **Study Arm B:** A training intervention designed to help participants with PEM get to know, control, and minimize PEM symptoms. If you are assigned to this study arm, you do not need to complete additional screening activities.
  - If after you complete the Screening Visit activities you seem to be a good fit for this study, and choose to continue participating, you will return to the study clinic for the Baseline Visit.

If you are assigned to STUDY ARM A, the following activities apply to you.

STUDY ARM A: BASELINE VISIT (DAY 0)

The purpose of the Baseline Visit is to collect more information about your physical health, and to better understand your Long COVID symptoms. Parts of this visit may be completed remotely or may take more than 1 visit to the study clinic to complete.

During this visit, you will be asked to:

- Answer questions about your symptoms, physical activity, general health, and well-being
- Complete questionnaires about post-exertional malaise (PEM) symptoms in-person during this visit and then remotely (phone or online) 2 to 3 days after this visit
- Give a list of your current medicines
- Give a blood sample
- Get an at-home stool (poop) collection kit with instructions to mail the stool sample
- Wear an activity tracker/Fitbit while awake and asleep for the entire duration of your study participation
- Complete 2 walking tests on a 10-meter (10.9-yard) track for as long as you can until you become too short of breath to keep up with your speed or your pace. You will rest for at least 30 minutes between tests.

ONLY at select sites: Complete Cardiopulmonary Exercise Testing (CPET). Two to 3 days after completing your in-clinic baseline visit, you will return to the study clinic to complete a

CPET. This is an exercise test that measures exercise abilities. The test will have a 2- to 3-minute warm-up, followed by 8 to 12 minutes of a more difficult exercise on a treadmill or stationary bike. You will be asked to avoid strenuous activities 12 hours before this test.

Participants are assigned to a group through randomization, which means your study assignment will be done by chance. After completing the above activities, if you are eligible, you will be assigned by chance to either the active study intervention group or the control group:

- **Active study intervention group: Personalized Cardiopulmonary Rehabilitation**
    - Cardiopulmonary rehabilitation is a comprehensive study intervention made up of exercise, education, and counseling to help participants' hearts and lungs work better. The study intervention will be tailored to your age and your ability to do physical activity.
- **Control Group**
    - This group will receive exercise education and information on PEM.

STUDY ARM A: STUDY INTERVENTION PERIOD (WEEKS 1 TO 12)

The study intervention period will last about 12 weeks.

If you are assigned to the **Active study intervention group: Personalized Cardiopulmonary Rehabilitation**, you will be asked to:

- Complete an initial visit with a physical therapist to determine the type and level of aerobic, strength, flexibility, and balance exercises that are best for you. You will be asked to do tasks like walking, biking, and standing. This may be completed on the same day as the Baseline Visit (Day 0) and must happen before your first rehabilitation visit.
- Complete 2 to 3 supervised cardiopulmonary rehabilitation (rehab) sessions per week, as you can. This is a total of 24 to 36 rehab sessions over 12 weeks.
    - Rehab sessions will last about 1 hour, as tolerated.
    - The <u>first</u> week and <u>last</u> week of rehab must occur **in-person** at the study clinic.
    - You may complete remaining rehab sessions at the study clinic or remotely at your home. Your study team will work with you to decide on what is convenient and practical for you and the rehab staff.
    - Before you can complete the rehab sessions remotely, the study team will make sure you can do exercises by yourself.

  - Rehab sessions will include strength, flexibility, and exercises such as walking or cycling. A study team member will also provide education about nutrition, weight control, regular exercise, and how to manage stress, anxiety, and depression.
  - Exercises will be changed based on your symptoms and ability to do physical activity.
- Complete exercises at home on your own between rehab sessions for a total of 3 to 4 exercise sessions per week, as tolerated.
- You are encouraged to wear your activity tracker/Fitbit throughout the study.

If you are assigned to the **control group,** then you will be asked to:

- Complete 2 general education sessions.
  - The first session may be completed on the same day as the Baseline Visit. The second session will occur 2 to 3 weeks after the first education session.
  - Education sessions includes topics of interest like nutrition, weight control, and how to manage stress, anxiety, and depression.
- Complete a weekly follow-up phone call to check on your well-being.
- You are encouraged to wear your activity tracker/Fitbit throughout the study.

STUDY ARM A: MIDPOINT VISIT (WEEK 6)

You will be asked to visit your study clinic 6 weeks after starting the intervention. The following activities will be completed:

- Answer questions about your symptoms, physical activity, general health, and well-being
- Complete questionnaires about post-exertional malaise (PEM) symptoms in-person during this visit and then remotely (phone or online) 2 to 3 days after this visit
- Be weighed on a scale
- Give a list of your current medicines
- Ensure that you continue to wear your activity tracker/Fitbit
- Complete 2 walking tests on a 10-meter (10.9-yard) track for as long as you can until you become too short of breath to keep up with your speed or to maintain your pace. You will rest for at least 30 minutes between tests.

STUDY ARM A: END OF INTERVENTION VISIT (WEEK 12)

You will be asked to visit your study clinic 12 weeks after starting the intervention. During this End of Intervention Visit, you will be asked to:

- Answer questions about your symptoms, physical activity, health, and well-being

- Complete questionnaires about post-exertional malaise (PEM) symptoms in-person during this visit and then remotely (phone or online) 2 to 3 days after this visit
- Be weighed on a scale
- Give a list of your current medicines
- Give a blood sample
- Get an at-home stool (poop) collection kit with instructions to mail stool sample
- Ensure that you continue to wear your activity tracker/Fitbit
- Complete 2 walking tests on a 10-meter (10.9-yard) track for as long as you can until you become too short of breath to keep up with your speed or to maintain your pace. You will rest for at least 30 minutes between tests.
- Complete a questionnaire about post-exertional malaise (PEM) symptoms remotely (phone or online) 2 to 3 days after this visit

ONLY at select sites: Complete Cardiopulmonary Exercise Testing (CPET). Two to 3 days after completing your in-clinic end of intervention visit, you will return to the study clinic to complete a CPET. CPET is an exercise test that measures exercise abilities. The test will have a 2- to 3-minute warm-up, followed by 8 to 12 minutes of a more difficult exercise on a treadmill or stationary bike. You will be asked to avoid strenuous activities 12 hours before this test.

STUDY ARM A: END OF STUDY VISIT (6-MONTH FOLLOW-UP)

At about 6 months after the Baseline Visit, all participants will be asked to:

- Answer questions about your symptoms, physical activity, general health, and well-being
- Complete a questionnaire about your PEM symptoms
- Give a list of your current medicines
- Ensure that you continue to wear your activity tracker/Fitbit

If you are assigned to STUDY ARM B, the following activities apply to you.

STUDY ARM B: BASELINE VISIT (DAY 0)

The purpose of the Baseline Visit is to collect more information about your physical health and to better understand your Long COVID symptoms. Parts of this visit may be completed remotely or may take more than 1 visit to the study clinic to complete.

During this visit, you will be asked to:

- Answer questions about your symptoms, physical activity, general health, and well-being
- Complete questionnaires about your PEM symptoms
- Give a list of your current medicines
- Give a blood sample
- Get an at-home stool (poop) collection kit with instructions to mail the stool sample
- Wear an activity tracker/Fitbit while awake and asleep for the entire duration of your participation in the study

Participants are assigned to a group through randomization, which means your study assignment will be done by chance. After completing the above activities, if you are eligible, you will be assigned by chance to either the active study intervention group or the control group.

- **Active study intervention group: Structured Pacing**
    - This is a study intervention designed to help participants with PEM identify, control, and minimize PEM symptoms. The goal is more stable function in everyday life with less frequent and less severe PEM symptoms (fewer setbacks in function).
- **Control group**
    - This group will receive basic informational material on PEM.

Participants in both groups will continue receiving care from their regular healthcare providers.

STUDY ARM B: STUDY INTERVENTION PERIOD (WEEKS 1 TO 12)

The study intervention period will last about 12 weeks.

If you are assigned to the **Active study intervention group: Structured Pacing**, then you will complete the following activities:

- Meet your pacing coach for your initial pacing session. This may be done on the same day as the Baseline Visit.
- Complete 1 session of structured pacing per week over 12 weeks.
    - These sessions are designed to help you understand, control, and minimize PEM symptoms.
    - Attend pacing sessions at the study clinic, or remotely if the study clinic provides this option. Pacing sessions will last about 30 minutes, as tolerated.
    - Some sessions may be monitored and/or recorded for pacing coach training and quality control purposes. These recordings will not impact your participation in the trial.

If you are assigned to the **control group**, then you will complete the following activities:

- Receive basic education material about PEM
- Attend a weekly phone call with a study team member where they will provide support.

You are encouraged to wear your activity tracker/Fitbit throughout the study.

STUDY ARM B: MIDPOINT VISIT (WEEK 6)

You will be asked to visit your study clinic 6 weeks after the start of the intervention. The following activities will be completed:

- Answer questions about your symptoms, physical activity, general health, and well-being
- Complete a questionnaire about your PEM symptoms
- Be weighed on a scale
- Give a list of your current medicines
- Ensure that you continue to wear your activity tracker/Fitbit

STUDY ARM B: END OF INTERVENTION VISIT (WEEK 12)

You will be asked to visit your study clinic 12 weeks after the start of the intervention. During this End of Study Intervention Visit, all participants will be asked to:

- Answer questions about your symptoms, physical activity, health, and well-being

- Complete a questionnaire about your PEM symptoms
- Be weighed on a scale
- Give a list of your current medicines
- Give a blood sample – up to 5 ½ tablespoons (80 ml) of blood
- Get an at-home stool (poop) collection kit with instructions to mail stool sample
- Ensure that you continue to wear your activity tracker/Fitbit

STUDY ARM B: END OF STUDY VISIT- 6 MONTH FOLLOW-UP

At about 6 months after the Baseline Visit, all participants will be asked to:

- Answer questions about your symptoms, physical activity, general health, and well-being
- Complete a questionnaire about your PEM symptoms
- Give a list of your current medicines

The following activities apply to both Study Arms A and B:

EARLY DISCONTINUATION VISIT

Your health information is still very important to the study, even if you decide to stop participating before the end of the 6-month period. If this happens, we will ask that you return for an early discontinuation visit so we can ask you some questions and collect information. We will use this data to compare the active study intervention group and the control group.

The study team will ask all participants to:

- Answer questions about your symptoms, physical activity, general health, and well-being
- Complete a questionnaire about your PEM symptoms
- Give a list of your current medicines
- Get an at-home stool (poop) collection kit with instructions to mail the stool sample. (Note: This is not applicable if you have already collected 2 stool samples for the study.)

PERSONAL INFORMATION

If you decide to join the study, we will ask for your:

- Date of birth to confirm your age
- Social Security number so we can pay you for your time and complete the tax form
- Home address so we can contact you by mail and send your payment to you if not using electronic payment method
- Phone number and email address so we can contact you about upcoming study visits, study treatments, and if you have any questions or problems during the study
- Contact information for 2 people you trust, like a family member or a friend who does not live with you, so we can contact them if we cannot reach you. You may authorize your trusted contact to give us some information about your health if you are not able to.

We will ask for some additional information, including:

- Details about your COVID-19 infection(s) and COVID-19 vaccinations
- Your medical history, health, and well-being
- A list of medicines you are taking (prescription and non-prescription)
- Other therapies or treatments you are receiving
- Allergies

BLOOD SAMPLES

We will ask you to give blood samples at 3 specific visits. We will take up to 5½ tablespoons (80 milliliters) of blood from your arm at each visit to run study-specific tests and to store samples for future research, if possible. See the “Biorepository: Research Use of Data and Biospecimens” section for more information.

STOOL SAMPLES

At 2 different times during the study, you will be given an at-home stool (poop) sample collection kit and instructions to mail the sample. We will ask you to collect stool in the provided collection container during your next bowel movement. We will then ask you to mail the stool sample according to the instructions provided. The stool samples may be used for future research; see the "Biorepository: Research Use of Data and Biospecimens" section for more information.

WHAT IF I DECIDE TO STOP PARTICIPATING IN THE STUDY?

You can stop participating in this study at any time. Even if you stop the study intervention early, either the cardiopulmonary rehab intervention or the structured pacing sessions, we may ask that you continue to complete the study visits, if and when possible.

If you are thinking about stopping your participation, please let your study coordinator or study doctor know as soon as possible. Your study doctor can talk to you about options that might work for you to stay in the study, though you may still stop your participation if you so choose.

We will tell you if we learn anything new that might affect your decision about whether to continue participating in the study. If we lose contact with you, you will be automatically withdrawn from the study, and no further information will be collected.

Your participation in the study may be stopped permanently or temporarily by your study doctor at any time without your consent. The study doctor may stop the study and end your participation at any time for any reason in order to ensure your safety. Some of the possible reasons include:

- Failure to follow study instructions
- Continuing could be harmful to your health
- The study ends unexpectedly
- Other unanticipated circumstances

If your participation is stopped by your study doctor without your consent, you will be notified of the decision and the reason why you are no longer a participant.

CAN I PARTICIPATE IN THIS STUDY IF I AM ALREADY ENROLLED IN OTHER STUDIES?

If you are in another study that involves an intervention or is treating exercise intolerance and/or post-exertional malaise, you will not be eligible for this study. You should notify your study doctor if you are participating in any other studies.

WILL OTHER TYPES OF INTERVENTIONS BE STUDIED LATER ON?

Over time, this study may expand to test additional study interventions. After the study is complete, researchers will analyze data from the studies to learn if the studied interventions had an effect on participants' exercise intolerance and/or post-exertional malaise symptoms.

HOW WILL YOU PROTECT MY PRIVACY?

In any research, there is a risk that your personal information may not stay private. We will make every effort to keep your personal and health information safe, but we cannot guarantee complete confidentiality.

To protect your privacy, this study is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH) and the U.S. Department of Health and Human Services. This means that the study team cannot share any information that could identify you with anyone who is not a part of the research. However, there are a few situations where study team might need to share information, like when it is required by law to report child or elder abuse, certain diseases, and threats to harm yourself or others. Your information will not be used as evidence in court unless you give your permission.

Your information that is protected by the Certificate of Confidentiality may still be shared or used when the information:

1. Is shared with people connected with the research. For example, the information may be used within the NIH to check on the progress of the study.
2. Is required to be shared by federal, state, or local laws. For example, when information must be shared to meet the legal requirements of the federal U.S. Food and Drug Administration.
3. Is necessary for your medical treatment and you have given your permission to share this information.
4. Is used for other research that is allowed by federal regulations.
5. Is shared with your permission. For example, if your healthcare provider gets your written consent for us to share the research information.

By signing and dating this consent form, you are agreeing to your information being used as described above.

The Certificate of Confidentiality does not stop you or a loved one from sharing information about yourself or your participation in this research. If you want your research information to be shared with an insurer, healthcare provider, or any other person not connected to the research, you must give your permission. This means that you and your loved ones must also actively protect your own privacy.

You should understand that the study doctor can take action to prevent serious harm to yourself or others, including informing the authorities.

Receiving Information from Your Medical Record

While you are in the study, we may look at your medical record. Your medical record may include information about visits to your study doctor's, the hospital, or emergency room during the study. We may also collect information about medicines, lab results from blood or urine tests, and other information that may be useful to the study. All of this helps us understand your health while you are in the study. If the study clinic is not the same institution as your primary care doctor, we will ask you to sign a medical release form in order for us to obtain your medical record.

ALTERNATIVES

What other choices are there?

Your other choice is not to participate. You can continue to get your usual healthcare whether or not you participate in the study.

Currently, there are no FDA-approved medicines or interventions to treat Long COVID. However, other options may be available to you if you choose not to participate in this study. Talk to the study doctor or your primary care doctor about these other options. The study doctor will discuss with you the major risks and benefits of usual care and alternative treatment options.

RESULTS AND STUDY PROGRESS

Will I be told the results of the research?

We will summarize what we have learned when the final study results become available. We will share the summary of results on the study website: trials.recovercovid.org/energize. Research summaries or articles published about the study will not include any information that could identify you. Before the final study results, we may contact you with notes, newsletters, or other updates related to the study.

A description of this clinical trial is available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a general summary of all participant results. You can search this website at any time.

POSSIBLE RISKS and DISCOMFORTS

A team of health experts called the Data and Safety Monitoring Board, chosen by the National Institutes of Health, will regularly check on the safety of study participants and how well the study is going.

What risks can I expect from taking part in this study?
Below are possible risks associated with electrocardiogram (ECG), blood draws, nasal swabs, and walking tests. Loss of privacy is also a risk. Every effort will be made to protect your information, as described throughout this consent form. There may also be risks from participation that we do not know about yet.

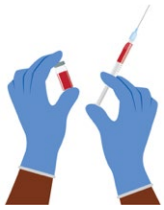
Risks Associated with Walking Test

The walking test may cause some people to feel frustrated, tired, lightheaded, weak, and/or experience shortness of breath. There is a risk of falling during the walking test. The study team will stay by your side during the test to minimize this risk.

Risks Associated with ECG

Possible side effects of the ECG are skin irritation, itching and redness from the ECG electrode pads.

Risks Associated with Blood Draws



Getting your blood drawn might cause bleeding at the puncture site, bruising, and pain. Bleeding and bruising occur in a very small number of people who have their blood drawn. Most people only feel a short period of pain when the needle is inserted. Some people may become dizzy, lightheaded, or feel faint. On rare occasions, infection of the area where the blood was drawn may occur. Experienced study team will perform the blood draws and will monitor you.

Risks Associated with Nasal Swabs

Nasal swabs might cause some discomfort, mild irritation, mild pain in your nose, and minor bleeding from your nose.

Risks Associated with Cardiopulmonary Rehabilitation

A specific risk for persons with PASC is that exercise may lead to a decrease in energy in the hours or days after exertion, a condition known as post-exertional malaise. A related risk may be the worsening of post-exertional symptoms. Because of this, it is important to notify the study team of any new or worsening conditions you may experience during or after your exercise training, or if any current problems get worse while you are taking part in this study.

It is also important to tell the study team about any new or current medications you are taking. Some medications can affect the way you respond to exercise and cause serious or life-threatening side effects. Below are some possible, known risks. There may also be risks from participation that we do not know about yet.

Possible side effects of exercise training are:

- Shortness of breath
- Muscle aches
- Post-exertional malaise (PEM)

These side effects are uncommon:

- Chest pain
- High blood pressure
- Fainting or passing out

Risks Associated with Structured Pacing Intervention

The primary risk of this intervention is worsening of PEM symptoms or feeling too ill to actively participate in the study. Pacing coaches will work with participants closely to make quick determinations of when PEM symptoms may be getting worse.

Future Contact

We may contact you to ask if you are interested in participating in additional visits related to the RECOVER Initiative. These follow-up calls and visits are optional and are a part of this consent form. If you agree to join further research, you will be told about additional follow-up calls or visits to expect and you will be asked to sign a separate consent form.

PAYMENT AND COSTS

«Compensation»

Will I be paid for being in this study?

<u>Study Arm A</u>

Participants in Study Arm A may receive up to $1350 for completing:

- $150 - Screening Visit
- $250 - Baseline Visit
- $250 - Middle of Intervention Visit

- $250 - End of Intervention Visit
- $150 - End of Study Visit
- $300 - Stool (poop) samples at Baseline and End of Intervention Visits ($0 for first sample, $300 for the second sample). There is no payment if you only submit one sample.

If you are assigned to the **Study Arm A Active study intervention group: Personalized Cardiopulmonary Rehabilitation**, you may also receive up to $2775 for completing the study intervention period:

- $75 for the initial physical therapy assessment
- $75 for each cardiopulmonary rehabilitation session completed (2-3 sessions per week for 12 weeks)

If you are assigned to the **Study Arm A control group,** you may also receive up to $700 for completing the study intervention period:

- $100 for education sessions at the beginning of the study intervention ($50 for education session #1 and $50 for education session #2)
- $50 for each weekly phone call completed (one phone call per week for 12 weeks)

<CPET compensation – text below applicable ONLY at select sites>
If you are offered to complete Cardiopulmonary Exercise Testing (CPET), you may also receive additional compensation of $250. CPETs are available to a limited number of participants in the study. The study team will let you know if this test is available to you.

- $125 – CPET at Baseline Visit
- $125 – CPET at End of Intervention Visit

Study Arm B

All participants in Study Arm B may receive up to $1200 for completing:

- $150 - Screening Visit
- $200 - Baseline visit
- $200 - Middle of Intervention Visit
- $200 - End of Intervention Visit
- $150 - End of Study Visit

- $300 - Stool (poop) samples at Baseline and End of Intervention Visits ($0 for first sample, $300 for the second sample). There is no payment if you only submit one sample.

If you are assigned to the **Study Arm B Active study intervention group: Structured Pacing**, you may also receive up to $2475 for completing the study intervention period:

- $75 for the initial pacing coach assessment
- $200 for each structured pacing coaching session completed (one session per week for 12 weeks)

If you are assigned to the **Study Arm B control group,** you may also receive up to $600 for completing the study intervention period:

- $50 for each weekly phone call completed (one phone call per week for 12 weeks)

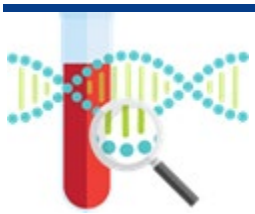
Do I have to pay anything to be in this study?
No. There will be no charge to you or your health insurance provider for taking part in this study. Any tests and interventions that are needed for this study that are not part of your usual healthcare will be paid by the study. “Usual healthcare” is the care you would receive whether or not you are part of this study. If you receive your usual healthcare during the study, your health insurance provider will be billed for that care, as it is unrelated to the study.

COMPENSATION FOR INJURY

What should I do if I become ill or injured during the study?
If you become ill or are injured while you are in the study, get the healthcare that you need right away. You should tell the healthcare provider treating you that you are participating in this study. If you tell the study team that you think you have been injured, they will help you get the care you need. However, there is no commitment by the study site, your healthcare providers or study doctors, any device provider, Duke University (Duke Clinical Research Institute), or the NIH to cover the cost of healthcare or provide monetary compensation in the event of a study-related injury. The study sponsor has no plans to pay for the cost of any extra care beyond what is provided as part of the study.

By signing this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility.

BIOREPOSITORY: RESEARCH USE OF DATA AND BIOSPECIMENS



A biospecimen is a sample such as urine or blood taken from your body for tests. With your permission, these samples—blood, stool, and nasal swabs—will be sent to a storage place called the RECOVER Research Biorepository at Mayo Clinic in Rochester, Minnesota. They will use these samples for research on COVID and the long-term effects of COVID. These samples may also be used for research on other health problems.

Why are biospecimens needed?
Biospecimens can tell researchers a lot. For example, blood is made up of clear fluids called serum and plasma, which contain things like hormones, antibodies, and other substances that can be measured. Blood also has cells that float in the bloodstream. These cells include red blood cells (which give blood its red color and provide oxygen throughout our body), platelets (which help our blood to clot), and white blood cells (which fight infection).

Plasma and serum from a blood sample contain many substances. New substances are still being discovered, and methods for measuring these substances are being developed all the time. Tests to measure the amount or presence of a substance are used by doctors to assess health.

Some substances found in biospecimens are called “biomarkers.” Biomarkers are things that can be measured and may provide important information about Long COVID. An example of a biomarker is blood sugar level in diabetes. Biomarkers may help predict how a patient will respond to a treatment.

How will my biospecimens be used for research?
In this study, biospecimens will be used to see how the study intervention affects your immune system (body’s defense against infection). We will also look for evidence that the virus that causes COVID-19 or that other infectious germs can be found in the biospecimens. The collection of these biospecimens is required as part of this study.

Your data and biospecimens might also be used for future research. The research may be about similar health issues related to this study or about unrelated diseases, conditions, or other types of research. These studies may be done by researchers at this institution or other institutions, including companies.

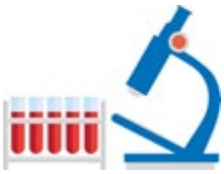
Although you will not receive any direct benefits, sharing your data and biospecimens with the RECOVER Research Biorepository may:

- Contribute to research that could help others in the future and improve medical care and public health
- Help researchers make important discoveries about medical conditions and possible therapies
- Improve our understanding of how antiviral drugs and other interventions may work to reduce Long COVID symptoms
- Increase the possibility of developing new interventions and treatments related to Long COVID
- Enhance our understanding of how and why Long COVID affects people differently

Will my biospecimens be used for genetic testing?

This is optional. Researchers can look closely at large amounts of your genetic information by sequencing, or "reading," every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research **will include** whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen). At the end of this consent form, you can decide if you want to allow researchers to use the samples we collect for genetic testing. Genetic testing looks at your DNA, the stuff that makes up your genes. Genes are like instructions that tell our bodies how to grow and function, and they are passed from parent to child. Researchers may also analyze all of the genes (whole genome analysis) in your DNA to study linked to Long COVID. Usually, researchers study just a few areas of your genes that are linked to a disease or condition. In whole genome studies, all or most of your genes are analyzed and used to study 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.

Will researchers be able to identify me based on my data and biospecimens?



We will do our best to protect your data and biospecimens during storage and when they are shared. However, there remains a possibility that someone could identify you. There is also the possibility that unauthorized people might access your data and biospecimens. In either case, we cannot reduce the risk to zero.

To protect your privacy, your name and identifying information will be removed from any data and biospecimens during this study before they are used for future research studies or shared with other researchers for future research studies without additional informed consent. Your de-identified data and biospecimens may be shared with researchers around the world.

However, the decision to share your data is controlled by the National Institutes of Health (NIH) and future researchers will need to get NIH approval to access data. The data and biospecimens submitted to a storage place or shared for research use will not include any information that can personally identify you, and researchers cannot easily link your identifying information to the data and biospecimens.

Genetic Information Nondiscrimination Act. Your data and biospecimens from this study are also protected by a federal law in the United States called the Genetic Information Nondiscrimination Act (GINA), that protects your genetic information from being used against you by health insurers and prevents certain genetic discrimination. GINA does not protect against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA does not protect you against discrimination based on a genetic disease or condition that is already diagnosed.

Will I need to give additional permission for researchers to use my data?
No. You do not need to give extra permission for future research to use your data. However, all future research studies will be approved by an independent scientific committee or ethics board.

Will I be paid for any future use of my data and biospecimens?
No. You will not be paid for any future use of your data or biospecimens. Your data and biospecimens will not be sold, but the use of your information or samples may lead to new tests, drugs, devices, or other products or services with commercial value. These products or services could be patented or licensed. There are no plans to provide any payment to you should this occur. Your biospecimens collected during this study may be used for commercial profit (even if identifiers are removed), and **you will not share in this profit**.

How long will my data and biospecimens be stored for future use?
Your data will be stored indefinitely. Your biospecimens from this study will be kept until they are used up.

Will I get any results back from future research use of my data and biospecimens?
No. You should not expect to get any results from any future research using your data and biospecimens. Research results that are clinically relevant, including individual research results, **will not be disclosed to you**.

What if I change my mind about future use of my data and biospecimens?
Participating in this study means you agree to share your data and biospecimens. You can change your mind later, but researchers might still use your data and biospecimens if they have already been shared. If you do not want your data and biospecimens used for other research projects, you should not participate in this study.

If you decide that you do not want us to use or share your data and biospecimens, you can contact your study clinic to request they destroy any remaining samples. Please see the contact information at the end of this consent form. You will be notified of compliance with such a request, and supporting materials will be maintained for tracking.

If we are not able to link your samples back to you because they have already been de-identified, we will not be able to locate the samples to destroy them. In addition, if the data are needed to preserve the integrity of the study database for regulatory purposes, we will not be able to remove individual data until the regulatory processes are completed. We will also not be able to destroy any samples that have already been used or shared.

USE OF PROTECTED HEALTH INFORMATION FOR RESEARCH

What is Protected Health Information (PHI)?

The PHI collected for this research study includes your name, address, phone number, email address, date of birth, Social Security number, and health information.

Will my PHI remain private?
We will make every effort to keep your PHI safe. We will store records in a locked cabinet or clinic or on a password-protected computer. We will give your study information a code and keep it separate from your personal record. Your identity and PHI will not be shared unless it is required to protect your safety, the safety of others, or if you give us permission to share it.

Who will have access to or receive my PHI?
Your PHI may be shared with others only if needed for reasons like determining the results of the study, making sure the study is being done correctly, and providing required reports.

Your medical and research records may be seen by:

- Your study doctor and other study team members
- The Sponsor (DCRI) and its representatives (including its affiliated companies that help carry out the research)
- People or organizations providing services for, or collaborating with, the Sponsor
- Other researchers, including researchers involved in the study at study sites other than the one where you are participating in the study
- Any organization that obtains all or part of the Sponsor's business or rights to the product under study
- Government or regulatory authorities, such as the FDA, including those located in other countries
- Advarra Institutional Review Board, an independent committee established to oversee the study and help protect the rights of research participants
- A team of health experts called the Data and Safety Monitoring Board, chosen by the NIH, who will regularly monitor the safety of study participants and the progress of the study overall

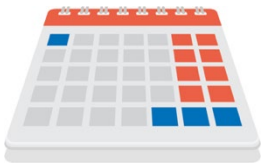
In addition:

- If we cannot reach you during the study period to confirm your health status, we may search for you or assign a study team member to search for you using publicly available data to check on your health and well-being.

Those who receive your information for the purpose of conducting the study may share it without your permission. Federal privacy rules may not apply to these groups. However, these groups have their own rules and codes to make sure that all efforts, within reason, will be made to keep your PHI private.

How long will you keep my Protected Health Information PHI?

We will keep your permission to use and share your PHI for 6 years, unless you take it back sooner.



You may take back your permission to use and share your PHI at any time by writing to the study doctor at the address listed on page 1 of this consent form. If you do this, you will not be able to stay in this study. We will not collect new information, but PHI that has already been collected may still be used and given to others as described in this authorization form.

What about my medical record?

Information about your participation in this research will be in your medical record. Other than you, only people who have access to your medical record (like your study doctor and the study team) will be able to see this part of your medical record. The study team may send copies of parts of your medical record to the Duke Clinical Research Institute (DCRI) to monitor the study. Monitoring means DCRI staff will review study records, including your signed consent, to make sure that your information was entered correctly in the study records.

Like all your other information, we will keep your data as safe and secure as possible. During the study, you will not be able to access your health data in the study records to make sure the study results are accurate. You will be able to access your study health information when the study is over.

What if I do not want to share my PHI with you?

If you decide not to sign this authorization form, you will not be able to take part in this study. If you take back your permission for us to use your PHI, you will not be able to continue in this study.

STATEMENT OF AUTHORIZATION

I have read this consent form, its contents were explained to me, and my questions have been answered. I voluntarily agree to allow the study team to collect, use, and share my personal and health information as specified in this

consent form. I will receive a signed and dated copy of this form for my records. I understand that I am not giving up any of my legal rights by signing this form.

Participant:

Print name: _____

Signature: _____

Date: _____ **Time:** _____

HOW CAN I LEARN MORE ABOUT MY LEGAL RIGHTS WHILE PARTICIPATING IN THIS STUDY?

The Public Readiness and Emergency Preparedness (PREP) Declaration was issued by the U.S. Department of Health and Human Services on March 10, 2020. This declaration may limit the legal rights of a participant in a COVID-19 clinical study that uses a drug, device, or vaccine designed to treat, diagnose, cure, or prevent COVID-19. This includes the study drug. Participants using the study drug may have limits on their right to sue the manufacturers, the study sponsor, healthcare providers, and others for significant injuries and adverse reactions. Under some circumstances, compensation may still be available under the PREP Declaration for certain participants who sustain injuries. To find out more, go to hrsa.gov/cicp/about/index.html or call 1-855-266-2427.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research participant;
- Eligibility to participate in the study;
- The study doctor's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

Please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00068561.

OPTIONAL: SAMPLE COLLECTION FOR GENETIC TESTING

Please **initial** the appropriate line below to let us know whether or not you want to allow your samples to be used for genetic testing. By writing your initials below, you confirm you have been told that you can still participate in the study without providing samples for genetic testing.

Initials _____	**Yes,** I give the study team permission to collect samples for future unspecified genetic testing.
Initials _____	**No,** I do not give the study team permission to collect samples for future unspecified genetic testing.

STATEMENT OF CONSENT

A copy of this consent form will be given to you. The purpose of this study, the procedures to be followed, and the risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told who to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to get information about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form.

Participant:

Print name: _____

Signature: _____

Date: _____ **Time:** _____

Person Who Obtained Consent:

Print name: _____

Signature: _____

Date: _____ **Time:** _____