Children's Hospital of Philadelphia

Informed Consent and HIPAA Authorization Form

Study Title: NAD^+ Precursor Supplementation with Exercise Training to Increase Aerobic Capacity in Freidreich's Ataxia

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You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Study Overview

You or your child are being asked to take part in this research study because you have a confirmed genetic diagnosis of Friedreich's Ataxia (FA).

The purpose of this study is to measure the effect of dietary supplement Nicotinamide Riboside (NR) combined with exercise, on the aerobic capacity of participants with FA. Aerobic capacity refers to the body's ability to take in, transport, and use oxygen during exercise. In this form, NR may also be referred to as the "study supplement."

If you agree to take part, your participation will last for about 24 weeks and will involve 2 in-person study visits, each lasting 2 days, at The Children's Hospital of Philadelphia (CHOP) and the Hospital of the University of Pennsylvania (HUP). You will need to take the supplement Nicotinamide Riboside (NR) or placebo for about 12 weeks. A placebo is an inactive substance that looks like the study supplement, but does not contain any active ingredients. The supplement NR is not approved by the FDA. Not all subjects will receive the NR supplement (some will receive the placebo) and not all subjects will receive exercise training. There are differences between this study and your usual care. As a participant in the research you will:

- Receive a supplement or a placebo; you will not know which.
- Receive exercise testing and training. Some subjects will not receive exercise training. Subjects who did not receive exercise training during the research study, will be offered exercise training after the initial 12 weeks.
- Other research tests such as MRIs, blood draws, tracer-enhanced Oral Glucose Tolerance Testing (using a non-FDA approved stable isotope product), Continuous Glucose Monitoring (CGM) placement, remote cardiac monitoring devices, and optional muscle biopsies.

The main risks of this study are from the dietary supplement Nicotinamide Riboside (NR). These include: flushing, rash/itching, indigestion, diarrhea, and constipation.

Risks of exercise training include rapid or irregular heartbeat, falling, muscle strains or soreness, dizziness, and nausea.

You will not benefit directly from participating in this study. Potential indirect benefits include helping to gain knowledge about exercise and NR in individuals with FA.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time. If you do not choose to take part in this study, you can discuss treatment options with your doctor.

Please see below for additional details about the study.

Approximately 80 participants will take part in this study.

What is the current standard of treatment for this disease?

Currently, there is no proven treatment for FA. Supportive clinical care is recommended for patients, including regular neurological examinations, physical therapy, and routine orthopedic care.

What is involved in the study?

This is a randomized, placebo-controlled trial with four different study groups. You will be randomly assigned to 1 of 4 groups:

- Study Supplement (NR), WITH Exercise
- Study Supplement (NR), NO Exercise
- Placebo, WITH Exercise
- Placebo, NO Exercise

Participants who are not randomized to receive exercise training can choose to receive training at the conclusion of the main study.

What are the study procedures?

Some of the procedures in this study will be repeated multiple times. Tests that are part of your regular, routine medical care will continue to be performed. Additional tests may be performed if any of your initial test results are not normal. The study involves the following tests and procedures.

Experimental Procedures:

Dietary Supplement NR or Placebo: You will be randomized to take one capsule of supplement or placebo every day for about 12 weeks. You must not crush, chew, or open the capsules.

Exercise Intervention: If you are assigned to the exercise intervention, you will complete 3 exercise sessions a week on your in-home bike trainer, and 2 exercise sessions a

week using resistance bands and strength training exercises. Each exercise session will last no more than 60 minutes.

Activity Monitoring: A wearable device for in-home heart rate and physical activity monitoring will be distributed to each participant. You will be asked to download a website app on your mobile device to track your exercise, heart rate, physical activity, and any side effects experienced throughout your participation in the study. You will have to agree to the devices terms and conditions in order to participate in the study.

Remote Cardiac Monitoring Devices: Participants will wear a remote cardiac monitoring device to track cardiac data for up to 7 days at the beginning and end of the study. Some monitors are tracked 24 hours a day/7 days a week by trained technicians (Biotelemetry, Inc.) who will alert your physicians to any clinicially significant arrhythmias. Cardiac data will analyzed once the monitoring period ends, and you will be notified of any incidental findings Some monitors are dependent on cell phone and/or wireless connections and may not transmit data in real time if service is lost. You will place the patch on yourself and at the end of the 7 days you will remove the patch and return it via a pre-paid package. You will have to agree to the devices terms and conditions in order to participate in the study. You may be asked to give your permission for the maker of the monitoring device to use your monitoring data for future research puproses; you do not need agree to this use to participate in the study.

Routine Clinical Trial Procedures:

Medical Record Review: We will review your medical records throughout the study to collect information about your medical history, current health, diagnosis, treatments, medications, and results of clinical tests.

Research Record Review: Research-only data obtained as part of previous CHOP and HUP studies you participated in will be recorded by the study staff. We will incorporate results from any previous studies in conjunction with this current study's results.

Medical Interviews: A team member will take your medical history, along with a listing of any medications you are taking. Throughout the study you will be asked to report if you think that anything bad has happened as a result of the study.

Pregnancy Test: *For female participants:* If you are pregnant or nursing, you will not be allowed to participate in this study. All female participants will be asked to take a urine pregnancy test before starting this study. The results will only be shared with you. If you are found to be pregnant, then you will not be able to participate/continue participation in the study. If you are under 18 years old, we encourage you to share the results of a positive pregnancy test with your parents but we cannot make you do that.

Blood Tests: All blood tests will be performed after overnight fasting. Blood samples will be collected to monitor your safety and check levels of NR in your blood. We will draw approximately 57mL (12 tsps.) at each study visit. By agreeing to participle

in the study, you agree to provide these blood samples to CHOP for research purposes.

You will have the option to complete the HbA1c blood test in-person or by using a finger stick kit at home.

COVID-19 Testing: If required, the study team will facilitate COVID-19 testing 24-72 hours before study procedures. This test may be required as part of clinical care before the cardiopulmonary exercise test and is not being performed for research purposes. If you are required to have a COVID-19 test, we will help to arrange the test for you.

OGTT: The Oral Glucose Tolerance Test (OGTT) measures the amount of sugar (glucose) and insulin (the hormone that controls sugar) in the blood after a sugar drink. An IV will be inserted into a vein. After the IV is in place, you will drink the sugar drink. You will receive up to 2 grams of a glucose with stable-isotope tracer product. Blood samples will be taken from the IV at certain time points over a 3 hours. In total, we will collect approximately 6 tablespoons of blood during the OGTT. When the test is finished, the IV will be removed. You will then be invited to eat a small meal.

Continuous Glucose Monitor (CGM) Placement: A continuous glucose monitor (CGM) will be placed on your upper arm at the end of Day 1, Visit 1. The monitor sits on the skin with a tiny sensor that is under the skin. We will apply the CGM sensor on your skin using an applicator with a very small needle. The needle is then removed and the sensor remains on your skin. We will also provide instructions on how to care for the CGM when you are at home. This sensor will remain in place for up to 14 days. It will monitor blood sugar while it is worn. At the end of 14 days, or sooner, it can be removed at home and returned in a pre-paid envelope which will be provided by the study team. You will place your own second CGM monitor on your upper arm 1 week prior to Visit 2. It will be removed when you arrive. The study team will help you place the sensor via remote check-in and review. If the CGM sensor falls off early (3 days or fewer), is unable to be returned, or for another reason cannot be used, we will offer you the option to place an additional, new CGM sensor.

Fasting: You will need to not eat for at least 10 hours before coming for the blood testing and the OGTT. You will be reminded prior to those visits. You may have water and usual medications during the fasting period.

Physical Examination: A routine physical exam will be conducted at the baseline and follow up visits (i.e., listening to your heart and lungs, evaluating brain and nerve functions, etc.) We will also measure weight, height, arm length, leg length, and vital signs, including measurements of blood pressure, heart rate and respiratory rate. Finally, for pediatric participants, a study doctor will perform Tanner staging and the pubertal development scale, which are methods to measure sexual development. Tanner staging will not be performed on adult participants.

Disease Activity Assessments: You will complete study assessments which will ask you questions about your physical health, activity levels, and disease progression.

Questionnaires: You will complete study questionnaires related to your overall health and level of physical activity.

Dynamometry: Muscle strength in the hands and ankles will be measured using dynamometer. For the hand-grip, you will squeeze the handle on the device with each hand and the strength of the "squeeze" will be measured. For the ankle, you will preform strengths tests of the ankle, and the strength of the movement will be recorded.

Cardiopulmonary Exercise Testing (CPET): You will be asked to undergo a heart-lung exercise test at the beginning and at the end of the study. A special bicycle will be used which allows you to pedal while sitting back. You will be tested while pedaling with your legs on the bike. All participants will be monitored carefully during this procedure. The following tests will be performed as a part of the CPET to monitor your safety.

- Electrocardiogram (ECG): ECG is an electrical tracing of the heartbeat or heart rhythm using small soft pads on your chest.
- Pulse oximeter: A small probe will be placed on your finger. This will measure the amount of oxygen in your blood.

MRI: An MRI scan takes pictures of your muscles. MRI uses a combination of a large magnet, radiowaves, and a computer to produce pictures. Over the entire study, we will ask you to complete 2 MRI scans to measure how your skeletal muscles are using energy, using investigational MRI sequences that are not FDA approved. There is no contrast and no sedation administered for the research MRI. Each MRI scanning session may up to last 2 hours. During the sessions, we will ask you to perform a brief light leg exercise once or twice. For the exercise, you will be asked to press down on a pedal, similar to a car accelerator or piano foot pedal repetitively over a 2-minute period.

If you may not safely have an MRI (e.g., implanted devices or hardware from previous procedures that may not be safe for MRI), this procedure will not be completed.

Muscle Biopsy (optional): A muscle biopsy involves inserting a special needle into the thigh muscle in your leg. The area will be numbed up with local anesthetic first. A small piece of muscle tissue is then removed. This procedure provides additional information about the effects of treatment on muscle tissue. Muscle biopsy is optional.

DXA: A special x-ray of the body called a "DXA scan" will be completed to measure body composition (i.e., the amount of muscle, fat, and bone) and bone mineral density. During the DXA scan, you will be asked to lie flat on your back on a table as the machine scans your body. The scan occurs for less than 15 minutes.

Echocardiogram (Echo) (If Needed): An Echo uses sound waves to create a moving picture of your heart. It can find problems with heart function. You will lie on a

padded table or a bed. A technician will glide a special device called a transducer across your chest to take pictures of your heart. A small amount of clear gel will be applied to your chest to help the transducer work better. An Echo will only be performed if you have not completed one within the last year.

Adverse Event Assessment: Our study team will contact you by telephone weekly and see you at in-person visits throughout the study to discuss how you are feeling. This is to help make sure you stay safe during your participation.

Visit Schedule

The table below provides a brief description of the purpose and duration of each study visit. In addition to the study visits below, you will be contacted by a member of the study team for weekly telephone calls.

Visit	Study Weeks	Main Procedures	Duration
Screening Visit	Up to 12 weeks before Visit 1	Review Inclusion/Exclusion Criteria, Echo (If Needed),	30 minutes
Visit 1, Day 1	Week 0	Informed Consent/Assent, Review Inclusion/Exclusion Criteria, Medical History, Physical Exam, Pregnancy Test, Blood Draw, Cardio Pulmonary Exercise Testing, Randomization, Exercise Training (if applicable), MRI, CGM & MCOT placement (if applicable)	8 hours
Visit 1, Day 2	Week 0	Muscle Biopsy (Optional), OGTT, DXA, AE Assessment, Dispense Study Supplement/Placebo	8 hours
Interim Labs	Week 6 ± 1	Blood Draw, AE Assessment	1 hour
Visit 2, Day 1	Week 12 ± 1	CGM & MCOT removal, Physical Exam, Pregnancy Test, Blood Draw, Cardio Pulmonary Exercise Testing, MRI, Supplement Compliance, AE Assessment	8 hours
Visit 2, Day 2	Week 12 ± 1	Muscle Biopsy, OGTT, DXA, AE Assessment	8 hours

What will be done with my data and specimens during this study?

During the study, we will collect blood and urine samples from you. By agreeing to participate in the study, you agree to give these samples to CHOP and HUP for research purposes.

Will I receive any results from the tests done as part of this study?

Results that could be important for your clinical care will be shared with you. We will not

share other research results with you.

What are the risks of this study?

Taking part in a research study involves inconveniences and risks. If you have any questions about the possible risks listed below, you should talk to your study doctor or your primary care provider/family physician. The main risks of taking part in this study are discussed below.

Risks associated with study supplement and exercise intervention:

The active supplement NR may cause side effects in some people. NR is a form of vitamin B3, and is available as a dietary supplement that is generally recognized as safe by the FDA.

The main risks of NR are listed in the table below. The described potential risks also include information about supplements that are similar to NR.

Common: (between 1 out of 10 and 1 in 100 participants affected)	• GI Upset: Nausea, Heartburn, Diarrhea, Constipation, Bloating • Rash, Itching
Less Common: (between 1 in 100 and 1 in 1,000 people are affected)	• Flushing • Changes in blood pressure • Muscle Pain/Soreness • Excessive Sweating
Rare: (between 1 in 1,000 and 1 in 10,000 participant affected)	• Liver Function Abnormalities or Toxicity • Blurred Vision • Swelling or fluid in the eye • Breakdown of muscle tissue that could lead to kidney damage

While very rare, serious or life threatening reactions known as anaphylaxis can occur while taking the study supplement. These reactions may include swelling of the throat or other body parts, blood pressure drops, difficulty breathing or swallowing, loss of consciousness, or death. A study physician will be available to treat any reactions, if one should occur during your study visit, and is available for contact any time during the study.

Some side effects, including the risk of an allergic reaction/anaphylaxis, may be life-threatening.

There may be other side effects that we do not know about yet. If you experience any other side effects, inform your physician or our study team. All clinically significant side effects will be immediately treated. **At any time during your participation, if you feel that you are experiencing ANY side effects from the study supplement contact a member of the study team immediately.**

If you are prescribed any new drugs during the study, you must notify the study doctor. Also notify the study doctor of any new over-the-counter drugs, supplements, herbal products, and vitamins.

If you require a clinical blood test, inform the doctor or nurse that you are actively on a study regimen, as it may affect clinical test results.

Reproductive Risks: You and your partner will need to practice safe methods (such as abstaining from sexual intercourse or using a medically accepted form of contraception) to prevent pregnancy through the duration of the study. If you have questions about preventing pregnancy, the study doctor, Dr. Shana McCormack, will be able to discuss your choices and methods. In addition, if you become pregnant during the study, you must immediately contact Dr. McCormack.

Exercise Intervention: There may be a risk of minor injury with exercise training, including but not limited to muscle strain and soreness. You may feel tired during or after exercise. There is a risk of falling during or after the exercises are completed. You will complete exercise orientation to make sure you stay safe, which includes instructing you in the correct lifting technique, and in the correct stretching and breathing techniques.

Risks associated with other study procedures:

Medical Interviews: There are no physical risks, but in-person and telephone interviews may cause temporary discomfort or embarrassment. You do not have to answer any questions that cause you to feel uncomfortable. These will be performed in private.

Urine Pregnancy Test (Females): You may feel embarrassment or discomfort.

Blood Test: Arm pain, bruising, bleeding, blood clot formation, and in rare instances, an infection might occur at the site where blood is drawn. There is also the possibility of dizziness or fainting while your blood is drawn.

Physical Examination: Potential risks include fatigue, feelings of anxiety and frustration, and discomfort.

Disease Activity Assessments: You might experience momentary embarrassment or discomfort.

Questionnaires: There are no physical risks but you might experience momentary embarrassment or discomfort. You do not have to answer any questions that make you too uncomfortable

Dynamometry: The dynamometer tests may result in mild, temporary hand and forearm or ankle and foot discomfort.

Activity Monitoring: Potential risks include discomfort associated with physically wearing the accelerometer device You will collect data for routine activities of daily living and should not anticipate any discomfort associated with activity that you routinely complete.

This study uses a mobile application to gather information for the researchers to use as part of this study. This application can collect information from your mobile phone that

would identify your geographic location when data is collected. To help protect your privacy, the research team can help to deactivate the location services.

There is a potential risk of confidentiality of your data. Every effort will be made to keep your information confidential.

Remote Cardiac Monitoring Devices: Minor discomfort may occur when the patch is attached to the skin. Some people with sensitive skin may have difficulty when applying. Mild itching or irritation underneath the patch area may occur, and is usually temporary. The monitoring devices are not an emergency response system. The monitor cannot be used to make outgoing calls even during an emergency. Please dial 911 in the event of an emergency and follow-up with the study doctor.

Cardio Pulmonary Exercise Testing:

- Cardiac arrhythmia- irregular heartbeat. You will be monitored by ECG, pulse oximetry and blood pressure monitoring along with direct visualization by medically trained staff. If you experience a clinically concerning irregular heart beat the test will be stopped.
- Redness or swelling- There is a small risk that this could develop from the ECG electrodes (pads) that will be placed on the chest. You may feel slight pressure when the probes are attached to your chest.
- Injury due to falls- All appropriate steps necessary will be taken to ensure your safety.
- Dizziness and nausea- Some people may experience this, supportive care will be given if needed.

DXA Scan: You will be exposed to radiation during the DXA scan. However, this is a very minimal dose of radiation. The radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.

Muscle Biopsy: There will be pain at the muscle biopsy site. There is also a small risk of bleeding and infection.

Oral Glucose Tolerance Test (OGTT): The risks associated with the OGTT are the same as those for having blood drawn. The OGTT may also cause high or low blood sugar, as with any sugary drink. You may also feel a little sick to your stomach for a few minutes after drinking the sugary drink, as with any sugary drink.

Continuous Glucose Monitor (CGM) Placement: There is a small risk of symptoms associated with the sensor application including infection, inflammation, bleeding, swelling, rash, itching, pain, bruising, and hardening of the skin. Also, real or false data may result from interfering medications. If we find that there are any concerning results, we will discuss this with you, and invite you to review in more detail with your usual care team.

Fasting: Fasting may cause discomfort and hunger. We will schedule the study procedures so as to reduce the amount of fasting time. If you feel unwell fasting before the study, you can stop fasting at any time.

MRI: There are no known physical risks associated with MRI scanning in properly screened individuals. However, MRI machines produce loud noises, which may cause discomfort and irritation. We will provide you with earplugs or earphones to quiet the noise. You may also feel uncomfortable lying inside the magnet due to claustrophobia or inability to lie still. If you become anxious, you can tell us and we will remove you from the machine.

The MRI magnet is always activated and attracts certain metal objects. Any metal object on or inside of your body may heat up, move, and/or improperly function within the scanning room. Metal objects in the room can fly through the air toward the machine (magnet) and hit those in the area. However, there are many safety measures to prevent or reduce these risks.

Echo: Echos are very safe. The gel may feel cold when it is first placed. Some people with sensitive skin can develop a rash from the gel.

Incidental Findings: It is possible that during the course of the study we will find new health problems. If this happens, we will discuss them with you and help to review your best options with your usual physicians.

Are there any benefits to taking part in this study?

There is no direct benefit to taking part in this study. The knowledge gained from this research may help doctors gain additional knowledge for participants with FA in the future.

Do you need to give your consent in order to participate?

If you decide to participate in this study, you must sign this form. A copy will be given to you to keep as a record.

What are your responsibilities?

Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study. You will need to follow the study doctor's instructions, keep all study appointments, and take the study supplement/placebo and follow the exercise regimen as directed.

What happens if you decide not to take part in this study?

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP and/or HUP.

If you decide not to take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason.

Can the study doctor take you out of the study early?

The study doctor may take you off of the study if:

- Your condition worsens.
- The study is stopped.
- The study supplement is no longer available.
- You cannot meet all the requirements of the study.
- New information suggests taking part in the study may not be in your best interests.

What choices do you have other than this study?

There are options for you other than this study including:

- Continuing to receive your usual clinical care
- Not participating in this study.
- You may discuss other options available to you with your doctor.

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about you will be collected. This will include information from past and present medical records, study procedures and tests, and interviews that are part of this research. Information related to your medical care at CHOP and/ or HUP will go in your medical record. This includes laboratory test results (including results of COVID-19 testing, if required) and imaging studies, except for tests that are performed for this research only. Medical records are available to CHOP and/or HUP staff. Staff will view your records only when required as part of their job. Staff are required to keep your information private. Information that could identify you will not be shared with anyone - unless you provide your written consent, or it is required or allowed by law. Laboratory test results will appear in your medical record with the exception of non-CLIA approved test results, which are research labs performed only for this study. We will do our best to keep your personal information private and confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at CHOP and HUP

- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services, Office for Human Research Protections.
- Groups monitoring the safety of this study (DSMB)
- The National Institutes of Health who is sponsoring this research
- MCOT trained technicians from BioTelemetry, Inc.;
- BioTelemetry Health, Inc
- The Food and Drug Administration (FDA)

By law, CHOP and HUP required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP and HUP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.
There is no set time for destroying the information that will be collected for this study.

Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

Certificate of Confidentiality (CoC)

A Certificate of Confidentiality (CoC) covers this research. A CoC helps protect your identifiable information and biological samples.

A CoC protects your private information from all legal proceedings. Unless you consent, information from this research study that identifies you will not be shared outside this research.

- No one can be forced to share your identifiable information or biological samples for a lawsuit.
- Your information can't be used as evidence even if there is a court subpoena.

If you consent, your data or biological samples could be shared for:

- other scientific research

The CoC does not prevent some disclosures.

- The researchers can't refuse requests for information from those funding this research. The NIH may need information to assess this project.
- You can still share information about yourself. You can also freely discuss your involvement in this research.
- The researchers must disclose things required by law. This includes suspected child abuse and neglect, harm to self or others, or communicable diseases.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you inform the investigator in writing.

Shana E. McCormack, M.D.
The Children's Hospital of Philadelphia
Buerger Center for Advanced Pediatric Care
Division of Endocrinology and Diabetes, 12th Floor
Philadelphia, PA 19104

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. If you withdraw your permission to use your personal health information, you will be withdrawn from the study.

Additional Information

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study.

You will be informed if changes to the study are needed to protect your health. You will be told about any new information that could affect your willingness to stay in the study, such as new risks, benefits or alternative treatments.

Financial Information

While you are in this study, the cost of your usual medical care – procedures, medications and doctor visits – will continue to be billed to you or your insurance.

Will there be any additional costs?

Additional mobile charges may be incurred as a result of the mobile application study procedures.

CHOP is providing financial support and material for all experimental procedures, as listed above, for this study. The following research procedures, study supplement, and study visits will be paid by study sponsor or CHOP

- Cost of travel (up to $3,000), parking, and meals;
- Cost of study supplement, stable isotope tracer for OGTT, MCOT monitor, CGM sensor, and exercise intervention equipment
- Study procedures performed at each visit

Will you be paid for taking part in this study?

The compensation provided at each visit is designed to cover the cost of travel, parking, and meals, as well as your time and efforts. If you are under 18, your compensation will be provided to your parents. Additional compensation will be provided, if there is an Unscheduled Visit(s) or additional safety check assessment (s). Compensation will be prorated according to the completion of scheduled procedures. This will allow

compensation for participants who are only able to complete certain procedures due to unforeseen circumstances. Participants/Families will be compensated as outlined below:

Study Visit	Participant/Family Dollar Amount
Visit 1: Day 1	$200.00
Visit 1: Day 2	$200.00
Muscle Biopsy (Optional)	$50.00
Interim Lab Visit	$50.00
Visit 2: Day 1	$200.00
Visit 2: Day 2	$200.00
Muscle Biopsy (Optional)	$50.00
Study Completion	$200.00
TOTAL:	$1,150.00

Non-local participants/families traveling to CHOP and HUP for study participation from outside a 100 mile radius will be eligible for at least partial reimbursement of travel expenses (up to $3,000 per participant) over the duration of participation in the study. While COVID-19 restrictions last, all participants will be eligible for travel reimbursement to support additional travel. Eligible expenses for reimbursement include mileage, tolls with receipts, and hotel/lodging with receipts according to reimbursement guidelines.

Participants/families will be eligible for study related reimbursements, for exercise equipment expenses. Participants may be traveling from a distance for a study visit and will be permitted to purchase and ship necessary equipment (super-poles, bike trainers, pedals, etc.) directly to their homes. Eligible expenses with receipts will be reimbursed according to reimbursement guidelines.

All participants will receive the exercise equipment at the end of their participation.

If you receive payment using a bankcard, the bank will have access to identifiable information. The bank will not have access to any medical information.

If your travel to CHOP/HUP (e.g. flight, hotel) is arranged and paid for by the study team, the agency making the reservations and their representatives will have access to identifiable information.

If your reimbursements exceed $600 in a calendar year, you will receive a W9 form.

Who is funding this research study?

The National Institutes of Health is providing funding for this study.

What if you have questions about the study?

If you have questions about this study or how your samples/data are going to be used, call the study doctor, Dr. McCormack at 215-590-3174. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

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

What happens if you are injured during the study?

If you are hurt or get sick from something that was done as part of this study, doctors at the clinic or hospital can arrange for emergency medical care. The Hospital does not offer financial compensation or payment for injuries due to participation in this research.

You and your insurance company will be billed for the costs of any care or injuries.

If you think you have been injured from taking part in this study, call Dr. McCormack at (215)-590-3174. She can go over things with you, let you know of resources that may be available and give you information on what you need to do.

In case of injury resulting from this study, you will not lose any legal rights by signing this form.

Optional Consent for Use of Identifiable Data and Specimens for Future Research

As part of the study, we will collect data, along with blood and tissue specimens. We may wish to use and share this information in future studies.

Research could occur at CHOP, HUP, or at outside institutions, which could include for profit companies. The data/samples will be given a unique code and may include information that can identify you. Coded samples will be stored in a secured laboratory freezer at CHOP or HUP. Information that can identify you, your data, or your blood and tissue specimens may be kept permanently on a secured share drive at CHOP or HUP.

We may not ask for your consent before using or sharing your identifiable data/specimens. You will not receive any results or financial benefit from the future research done on your data/specimens. We may share your identifiable data/specimens with outside researchers who will use them for future research.

If you leave the study, you can ask to have the samples destroyed. You can also ask us to remove information that identifies you from the samples. This may not be possible if your samples have already been shared.

Please indicate whether you will allow the identifiable samples to be used for future research by putting your initials next to one of the following choices:

_____ (initials) NO, my identifiable specimens may not be used for future research. They may be used for this study only.

_____ (initials) YES, my identifiable specimens may be used for other future research studies.

Consent to Inform Your Doctors of Your Study Participation (OPTIONAL)

Please indicate whether you would like us to inform your non-CHOP doctor(s) of your participation in this study. Please note that this only applies to non-CHOP doctors, as research results will be included in your medical record at CHOP and HUP.

_____ (initials) I request that my non-CHOP doctor(s) **not** be informed of my participation in this study.

_____ (initials) I request that my non-CHOP doctor(s) be informed of my participation in this study.

OPTIONAL Consent for Muscle Biopsy

Please indicate whether you wish to participate in the muscle biopsy for the study:
_____ (Initials) I agree to complete the muscle biopsy.

_____ (Initials) I **DO NOT** agree to complete the muscle biopsy.

OPTIONAL Consent to be Contacted for Future Research Studies

Please indicate whether you grant permission to be contacted for future research studies by signing next to one of the following choices:

_____ (Initials) I agree to be contacted for future research studies.

_____ (Initials) I **DO NOT** agree to be contacted for future research studies.

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

The research study and consent form have been explained to you by:

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to take part and to allow your child to take part in this research study, and you are legally authorized to consent to your child's participation. You are also agreeing to let CHOP use and share the health information that will be collected for this study, as explained above. If you don't agree to the collection, use, and sharing of health information, you and your child cannot participate in this study.
NOTE: *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Subject	
Signature of Subject (18 years or older)	Date

If children are research subjects, both parents must sign this consent form

Name of Authorized Representative 1	Relationship to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #1	Date
Name of Authorized Representative #2	Relationship to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #2	Date

If the second representative is unavailable, per §46.408(b) / §50.55(e)(2), explain the reason.

Child Assent to Take Part in this Research Study

For children capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date

This study has been explained to me and I agree to take part.

_____ _____
Signature of Subject (optional) Date