UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title:

The effect of high intensity interval training and surgical weight loss on distal symmetric polyneuropathy outcomes.

Company or agency sponsoring the study:

National Institutes of Health

Names, degrees, and affiliations of the principal investigator and study coordinator:

Principal Investigator:
Dr. Brian Callaghan, M.D., Department of Neurology

Study Coordinator:
Ericka Chant, MPH Department of Neurology

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains information that will help you decide whether to join the study. All information in this form is important. Take time to carefully review this information. After you finish, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your friends, family, or other doctors about your possible participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you do, be sure you understand what the study is about.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The purpose of our study is to evaluate how exercise and surgical weight loss affect how likely an individual is to develop peripheral neuropathy and other neurologic complications. Neuropathy is nerve damage which often causes numbness, pain, and tingling, usually beginning in the feet. This study is interested in patients who are bariatric surgery candidates whether or not they chose to undergo surgery. Patients do not need to have peripheral neuropathy to participate.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

You may be included in the study if:

- You are at least 40 years old and able and willing to provide written informed consent for the study.
- You are a patient attending a bariatric surgery clinic.
- You are willing to accept random treatment assignment to HIIT or routine exercise counseling;

You may not be included in the study if:

- You are taking any blood-thinning medications (anti-coagulants), other than aspirin.
- You have a medical condition, which could interfere with your ability to participate in the study or prevent you from completing the study.
- Require a walking assist device.
- History of distal symmetric polyneuropathy from causes other than diabetes and/or the metabolic syndrome as determined through medical history, family history, history of medications, occupational history, history of exposure to toxins, physical and neurological examinations.
- You have a contraindication to HIIT participation including a failed exercise stress test.
- You are participating in an experimental medication trial within 3 months of starting the study.
- You are currently undergoing treatment for cancer other than skin cancer.
- You are currently smoking.
- Your weight is over 450 pounds.

3.2 How many people are expected to take part in this study?
140 bariatric patients are needed to complete the study.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

Visit 1- Eligibility Screening Tests: Before participating in the study, you will be asked to take part in some tests to determine if you are eligible for the study. Based on the results of the tests, your participation in the study may end after the screening.

- **Medical History Review:** A member of the study team will review your medial history and ask you questions about your current medications. This should take approximately 10-15 minutes.
- **Covid-19 Screening:** Prior to completing the Exercise Stress Test a Covid-19 test may need to be completed (if required by the Universityof Michigan clinical care guidelines). COVID-19 testing generally involves a standard nasopharyngeal swab testing to determine if you have an active COVID-19 infection. A negative result will need to be documented and provided to the study team prior to the Exercise Stress Test.

- **Exercise Stress Test:** The exercise stress test will begin with a resting electrocardiogram (EKG or ECG). The EKG will take about 15 minutes to complete. An electrocardiogram is a test that checks for problems with the electrical activity of your heart. You will lie on a bed or table during this test. Certain areas of your arms, legs and chest will be cleaned and may be shaved to provide a clean, smooth surface to attach the electrodes. Several electrodes are attached to the skin (on each arm and leg and on your chest). These are hooked to a machine that traces your heart activity onto a paper. You will be asked to lie very still and breathe normally during the test. After your resting EKG is complete the technician will move on to the exercise stress test. Your blood pressure will be taken. You will begin to exercise by walking on a treadmill or pedaling a stationary bicycle. During this test you will breathe through a mouthpiece (in order for us to collect and measure the oxygen in the air you breathe out) and a nose clip will be used to prevent air escaping through your nose. You will also be connected to a heart monitor to evaluate your heart's activity during exercise. The rate of exercise or degree of difficulty will gradually increase. At regular intervals, the lab personnel will ask how you are feeling. T ell them if you feel

chest or arm discomfort, shortness of breath, dizziness, lightheadedness, or any other unusual symptoms. It is normal for your heart rate, blood pressure, breathing rate, and perspiration to increase during the test. The lab personnel will watch for anything on the EKG monitor that suggests the test should be stopped. After the test, you will walk or pedal slowly for a couple of minutes to cool down. Your heart rate, blood pressure, and EKG will continue to be monitored until the levels begin returning to normal. This test should take approximately 30-45 minutes.

OVERALL RESEARCH DESIGN (specific details provided below):

Visit 2- Pre-Baseline: This visit will last approximately 3 hours and 30 minutes. You must fast overnight prior to this visit (no food or liquids other than water).

- Height and weight to calculate BMI.
- Blood pressure.
- Documentation of medications.
- A blood draw which will be used to order a lipid panel to check your HDL and LDL cholesterol, triglycerides levels (fat in the blood), creatinine levels in your blood (which is used to evaluate the function of your kidneys), and hemoglobin A1C. Approximately 6.5 milliliters (just over 1 teaspoon) will be collected for this purpose.
- Dual Energy X-ray Absorptiometry: This instrument is used to measure body fat, muscle mass, and bone density using low-dose x-ray. You will lie on your back for approximately 10 minutes while the x-ray machine is positioned over areas of your body. Depending on your size, we may need to scan half of your body at a time. *This measure will only be completed at the pre-baseline and 24-month time points.*
    - Subjects over the weight limit of the DEXA may complete the body composition with the BodPod as an alternative. Subjects are asked to wear form fitting clothing or a swimsuit during testing. Single layer compression shorts and/or lightweight bras without padding or wires may also be worn. A swim cap must also be worn to compress any air pockets within the hair. You will be asked to sit comfortably and quietly inside the BodPod for the brief measurement period. The Bodpod measurement takes less than 5 minutes.
- 75 g Glucose tolerance test: For this test, you will be asked to drink a sugary liquid, also known as glucola. Approximately 4.5 milliliters (just under a teaspoon) of blood will be taken before you do this and at 30, 60, 90 and 120 minutes after you drink the liquid. The amount of sugar (glucose) and insulin, in your blood will be measured at these time points to check for diabetes, pre-diabetes, impaired fasting glucose, or impaired glucose tolerance. A catheter may be inserted into your vein before the test begins and will remain there for the duration of the test so that you do not have to have multiple needle insertions into the vein. If the preliminary reading of your fasting glucose is greater than 126 mg/dL, you will not be asked to drink the glucola; the glucose tolerance test will be stopped. *Participants with a known diagnosis of diabetes will not receive this test.* Participants with a known diagnosis of diabetes will have their A1C and fasting glucose documented if it has not been documented in their medical record in the past three months. *This measure will only be completed at the pre-baseline time point. A fasting glucose and insulin will be drawn at 3 months, 1 year and 24-month time points.*
- Biorepository: Besides the information about the main study, the following information is specific to unspecified future use of identifiable data and/or biospecimens.
    - We would also like your permission to keep some of your medical information, blood, DNA, urine, skin, and subcutaneous adipose tissue to be collected and studied for future research. The future

research may be similar to this study or may be completely different. You can participate in this study and choose not to donate your medical information, blood, DNA, skin, subcutaneous adipose tissue, and urine for future research, or you can decide to participate in both studies.

- If you give us your permission, we will use your medical information, blood, DNA, urine, skin, and subcutaneous adipose tissue and medical information for future research. Even if you give us permission now to keep some of your blood, DNA, urine, skin, and subcutaneous adipose tissue and medical information, you can change your mind later and ask us to destroy it. Keep in mind, however, that once we have analyzed your blood, DNA, urine, skin, and subcutaneous adipose tissue, we may not be able to take the information out of our research.
- On a separate form, you will be asked to choose whether or not you wish to donate your samples for future research. As part of this biorepository, blood, DNA, urine, skin, and subcutaneous adipose tissue will be collected for storage. There are three different parts of the blood, called plasma, serum, and DNA. DNA is the genetic material (including the genes which are the blueprint for yourself) that you have inherited from your parents and passed on to any of your children. Materials will be stored indefinitely in our biorepository for future research which helps us better understand the genetic basis and metabolic basis for components of the metabolic syndrome and neuropathy.
- With appropriate permissions, your samples and collected information may also be shared with other researchers here, around the world, and with companies. Their research may be similar to this study or may be completely different. Once we have shared your samples and medical information with other researchers, we will not be able to get it back. Future use of your identifiable data and/or specimens will be conducted in compliance with applicable regulatory requirements. You will not find out the results of future research on your samples. Allowing us to do future research on your samples and medical information will not benefit you directly. Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.
- Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.
- Approximately 10 milliliters (2 teaspoons) of blood will be collected for this purpose. *This measure will be completed at pre-baseline, 3-month, 12-month and 24-month. DNA will only be collected at the pre-baseline visit.*
- Subcutaneous adipose tissue: We will also obtain a small sample of fat tissue from the area just underneath the skin near your belly button. This procedure also involves numbing a small region of skin near your belly button and using a needle, a small amount of fat tissue is removed from underneath your skin. During the procedure you will feel some pinching and pulling, but it should not be very painful. The injury resulting from the fat tissue biopsy is very minor. You will likely have some bruising, but it should not prevent you from performing your general daily activities. This procedure takes approximately 30-40 minutes. *This measure will only be completed at the pre-baseline and 24-month time points.*
- Urine: You will be asked to provide a first morning urine sample. *This measure will only be completed at the baseline and 24-month time points.*

Outcomes Visits (Visit 3 (baseline), 4 (3 Months), 5 (12 Months) and 6(24 Months)):

Visit 3 through 6 will be scheduled after your pre-baseline visit. The outcome appointments will take approximately 2.5-4 hours and the following will occur:

- A blood draw which will be used to order a lipid panel to check your HDL and LDL cholesterol, triglycerides levels (fat in the blood), creatinine levels in your blood (which is used to evaluate the function of your kidneys), fasting glucose, fasting insulin, and hemoglobin A1C. Approximately 11 milliliters (2 teaspoons) will be collected for this purpose. *This will be completed at the 3-month, 12-month, and 24-month visit.*
- We will test for any changes in the nerves that surround your heart by recording your heart rate, blood pressure, and breathing at rest compared to during a deep breathing exercise, when you stand up, and when you perform a maneuver called a valsalva, which is performed by forcible exhalation against a closed airway, usually done by closing one's mouth and pinching one's nose shut. This is called Heart Rate Variability testing. This takes about 15 minutes to complete. *This measure will only be completed at the baseline and 24-month time points.*
- We will apply a small electric current to the skin at the ankle and knee in a test called Nerve Conduction Studies. This feels similar to a shock and is used to measure the health of the nerve being tested. This will take 30 minutes to complete. We will also measure the site circumference where the electrode is placed. *This will be completed at the baseline and 24-month visit.*
- You will be examined by a neurologist who specializes in nerve and muscle problems, including neuropathy (called a neuromuscular specialist). He/she will ask you some questions about yourself, any medical problems that you may have, any symptoms that are consistent with neuropathy, and do a brief physical exam. *This will be completed at the baseline and 24-month time point.* At each visit you will have your reflexes assessed; asked how well you can feel vibration, cold, and pinprick sensations; asked to walk; and have your feet examined for any signs of neuropathy.
- You will be asked to complete some questionnaires as part of participation in the study. This will be completed at home before your study visit:
    - A neuropathy-specific quality of life questionnaire named NeuroQoL. This questionnaire will assess if and how symptoms of neuropathy have affected your quality of life. This will take about 10 minutes to complete.
    - The McGill Pain Questionnaire. This questionnaire assesses the level of pain that you experience in your feet. This should take less than 5 minutes to complete. You will also be asked to rate your pain on a numeric rating scale.
    - The Michigan Neuropathy Screening Instrument. This short 15 question questionnaire will assess if and how many symptoms of neuropathy you may be experiencing. This will take less than 5 minutes to complete.
    - The Survey of Autonomic Symptoms questionnaire. This questionnaire will assess symptoms that appear if you have problems with the nerves which control the autonomic system. The autonomic system is the body system which controls muscle function which you do not have direct control over, such as your heart and digestion n. This may take you up to 5 minutes to complete.
    - The DNS- score and guidelines. This brief questionnaire will assess for symptoms of neuropathy. This will take less than 5 minutes.
    - The DN4 is a short questionnaire that estimates your probability of neuropathic pain, this will take less than 5 minutes to complete.

- Modified Falls Efficacy Test. This short 14 question questionnaire assess how confident you are at performing daily activities of living without falling. This survey takes less than 5 minutes.
- Demographics questionnaire that asks basic demographic information, this should take less than 5 minutes to complete. *This will be completed at the baseline visit.*
- Questionnaires that ask about your mood and how your weight has impacted your physical and emotional health. These should not take more than 20 minutes to complete.

- Berg Balance. You will also be asked to perform 14 simple balance related tasks, ranging from standing up from a sitting position, to standing on one foot. You will also be asked if you have fallen in the past year and the number of falls. This will take approximately 10 minutes. *This may be performed virtually to reduce time spent at the in-person visit.*
- 8-foot Get Up and Go Test. This test measures your measures power, speed, agility and dynamic balance. The test involves getting out of a chair, walking 8 feet to and around a cone, and returning to the chair in the shortest time possible. This will take approximately 2 minutes to complete. *This may be performed virtually to reduce time spent at the in-person visit.*
- Orthostatic Hypotension Assessment. We will measure your heart rate and blood pressure while lying down, standing for 1 minute and at 3 minutes of standing. *This may be performed virtually to reduce time spent at the in-person visit.*
- Anthropometric measurements. We will measure different circumferences on your body including abdomen, arm, buttocks/hips, calf, forearm, hips/thigh, mid-thigh and waist. This takes less than 5 minutes to complete. *This may be performed virtually to reduce time spent at the in-person visit.*
- We will measure how well you can feel vibration sensations in your feet because these sensations are often reduced in individuals with neuropathy. A neurothesiometer will be used to assess vibration sensitivity at your toe. For this test, a vibration stimulus will be placed on your toe. The intensity of the vibration will be increased until you can feel it and then decreased until you can no longer feel it. This takes approximately 2 minutes.
- We will assess your vision and the health of the nerves in your eyes.
  - We will look for vision problems by having you look into an instrument which will display multiple visual targets. You will indicate that you have seen the target by pressing a response button. This is called Frequency Doubling Technology (FDT) Perimetry. This exam is called the 24-2 FDT. This takes approximately 10 minutes to complete.
  - We will use a special camera called a “Fundus Camera” to take a color photograph of the fundus (back part) of your eye. This is a non-invasive procedure and we do not need to dilate your eye for this test. This takes approximately 5 minutes.
- Researchers will use a confocal microscope to take pictures of the central cornea of your eye. Topical anesthetic eye drops (numbing eye drops) and an eye moisturizing gel will be placed on the surface of your eye to protect the surface. This evaluation takes approximately 15-20 minutes.

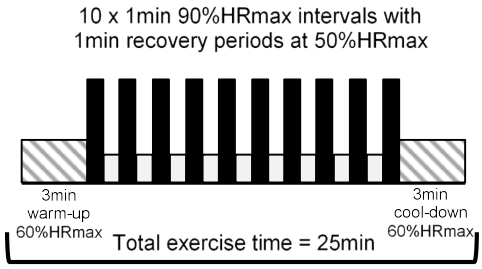
- You will have two pieces of the top layer of skin removed in a procedure called a skin biopsy. One biopsy will be taken from near your ankle and the other will be taken from your upper thigh. You will have 8 total biopsies performed throughout the study (four on the ankle and four on the upper thigh, i.e. one from each site during visits 3, 4, 5, and 6). The skin samples, or biopsies, will be 3-millimeters (approximately 1/10th of an inch or this O size) across. The skin will be numbed with a numbing medicine called lidocaine

(with or without epinephrine) before the biopsies are taken by a trained study team member who will give you instructions on how to care for the biopsies after you go home. We will be measuring how many nerves fibers you have in the skin because some individuals with neuropathy have less nerve fibers in their skin. We will also measure the site circumference at the location of the biopsy sites. This should take 30-60 minutes to complete. You may consent to have skin biopsy samples added to the biorepository.

- You will be asked to bring in a sample of your first morning urine to the appointment. Your urine sample will be used to check the level of creatinine and microalbumin. The ratio of creatinine and microalbumin in your urine is also used to evaluate the function of your kidneys. *This will be completed at the baseline and 24-month visit.*
- You will complete two additional tests that assess your thinking, reasoning, and remembering skills.
    - A 30 minute brief computer-based program will assess your language, attention, working memory, episodic memory, executive function, and processing speed. We are looking to see if the nerves in the brain are affected in a similar way to the nerves that go to the legs and arms. The computer program is called NIH Toolbox. *This will be completed at the baseline and 24-month visit. Part of this outcome may be performed virtually to reduce time spent at the in-person visit.*
    - A second short test called the Rey Auditory Verbal Learning Test will be given after the NIH Toolbox. This takes approximately 10 minutes to complete. *This will be completed at the baseline and 24-month visit. This may be performed virtually to reduce the time spent at the in-person visit.*

Exercise Training Programs: If you are eligible for the study, you will be randomized into one of two different exercise groups after the baseline visit is complete. Each subject has an equal chance of being assigned to any group, e.g. flip of a coin.

- Standard exercise counseling: Participants will receive counseling regarding exercise as a routine part of their participation in the bariatric surgery clinic. Specifically, they are counseled to participate in 60 min of aerobic exercise daily in addition to 2-3 non-consecutive days of strength training workouts every week. Participants are encouraged to contact the bariatric conditioning program, obtain a gym membership, purchase exercise equipment, join a walking group, and/or sign up for fitness classes (employer or city parks and recreation).
- High Intensity Interval Training(HIIT): If assigned to this group, you will start the HIIT regimen 6 weeks after surgery, once cleared by your surgeon. The exercise modality will be self-selected (e.g., walk/run (outdoors or treadmill), elliptical machine, stair climbing, cycling), and participants will be encouraged to regularly vary the exercise modality to reduce risk of overuse injury and to enhance the variety of the exercise program. You will first undergo a familiarization program for 1 week where you will perform conventional exercise. After this 1-week familiarization period, you will begin the HIIT regimen. The first session of the "ramp-up" period will combine conventional exercise and HIIT. After that first ramp up training session, 1 additional high intensity interval will be added to each training session, so by the beginning of week 3 of HIIT training, you will reach the full HIIT training protocol. You will continue this training protocol, 3 sessions/week (2 supervised and 1 unsupervised), for 24-months. Participants who may feel challenged by the rate of increase in the number of intervals during this ramp up period will be allowed to increase the number of intervals at a slower pace, but all participants must reach the full HIIT protocol during week 4 of HIIT training.



- Fitness activity monitor: Participants will be provided with a wearable physical activity monitor with a visible heart rate display. Participants will be asked to wear the fitness activity monitor during their supervised and unsupervised exercise sessions. Data from the fitness activity monitor will be downloaded wirelessly to a computer, and/or mobile device, which then automatically updates your physical activity profile on your personal fitness web-page. Our research study coordinator will receive permission to access your physical activity profile, enabling us to assess your exercise data.

- Exercise Fitness Test (VO2 max): The Exercise Fitness Test will take about 30 minutes to complete. An exercise fitness test will be done on a stationary bike, which will last approximately 7-10 min. During this test you will breathe through a mouthpiece (in order for us to collect and measure the oxygen in the air you breathe out) and a nose clip will be used to prevent air escaping through your nose. You will also be connected to a heart monitor to evaluate your hearts activity during exercise. After a four-minute warmup the workload will be increased approximately every minute until you voluntarily stop exercising because you can no longer continue cycling. The final few minutes of this short test feels like climbing a steep hill on a bicycle. *This test will be performed after 24 months of starting the HIIT regimen.*

- Your safety and well-being during the exercise interventions: You will be closely monitored throughout the exercise training period. Exercise training sessions during the 24-months will be supervised by exercise physiologists and trainers. After the first 2 weeks of the exercise training is complete, our research team will supervise at least 2 exercise training sessions per week. Non-supervised exercise training sessions will be monitored using the activity fitness monitor.

- Exercise compliance*:* In addition to the 2 supervised sessions per week, participants will be asked to complete 1 unsupervised session. During the unsupervised sessions, participants will wear their fitness activity monitor so that the exercise can be tracked. Participants will have access to the exercise trainers on the research team to discuss potential solutions to barriers, questions about exercises and to receive encouragement and feedback.

As a subject participating in this research study, you have certain responsibilities that may apply to this study, such as ensuring that you arrive at all of your scheduled appointments, and reporting any adverse reactions you may have during the study.

The table below shows the schedule for all of the testing that will occur in the study. An "X" indicates that the test will be done on that visit.

Table 6: Study Events Schedule						
Visit Number	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
Visit Description	Screening	Pre-Baseline	Baseline	3 Months	12 Months	24 Months
Time point	Before baseline	Day -70 to 0	Day -70 to 0	Month 3	Month 12	Month 24
Visit window	NA	70 days	70 days	± 14 d	± 14 d	± 14 d
Informed Consent/study criteria^						
Medical History Review	X					
Stress Test	X					
Randomized to Exercise Protocol			X*			
Laboratory Measures		X		X	X	X
Biorepository Measures						
Plasma		X		X	X	X
Urine			X			X
Subcutaneous Adipose Tissue		X				X
DNA		X				
Skin Biopsies (IENFD)[T]			X	X	X	X
Corneal confocal microscopy			X	X	X	X
FDT-24-2			X	X	X	X
Retinal Imaging			X	X	X	X
Electrophysiologic measures						
NCS			X			X
Heart Rate Variability			X			X
Clinical measures						
Neurologic examination			X			X
MNSI, UENS, mTNS, SAS, DNS, DN4			X	X	X	X
McGill pain questionnaire, NRS			X	X	X	X
Qualitative sensory testing						
Neurotheisiometer			X	X	X	X
Cognitive impairment						
NIH Toolbox^			X			X
Rey^			X			X
Anthropometric measures^			X	X	X	X
Orthostatic Hypotension Assessment^			X	X	X	X
Quality of Life measures:						
NeuroQol			X	X	X	X
Questionnaires			X	X	X	X
Demographics			X			
Functional Assessments						
Berg Balance Scale^			X	X	X	X
8-foot Get Up and Go Test^			X	X	X	X
Modified Falls Efficacy Scale			X	X	X	X
Aerobic Assessment						
VO2 max	X					X[+]
Dual Energy X-ray Absorptiometry (or BodPod)		X				X

*Participants will be randomized after completion of the baseline visit

[+]Only participants randomized to the HIIT will complete the second VO2 max

[T]Participants can consent to have skin biopsy added to the biorepository

^Participants may complete the consent and outcomes virtually prior to the upcoming visit to decrease in-person interaction due to Covid-19. If the outcome cannot be completed successfully it with be completed during the visit.

Data collected for clinical purposes as part of Bariatric Surgery Programs will be reviewed as part of this study and included in your study records.

4.2 How much of my time will be needed to take part in this study?

Visit 1 will take approximately 1 hour (Screening visit).
Visit 2 (pre-baseline) will take approximately 3.5 hours.
Visit 3 (baseline) will take approximately 4 hours.
Visit 4 (3-months) will take approximately 2.5 hours.
Visit 5 (12-months) will take approximately 2.5 hours.
Visit 6 (24-month) will take approximately 4 hours.

The optional subcutaneous adipose tissue biopsy for the study will take an additional 30 minutes at visit 2 and visit 6.

Participants who are randomized to the HIIT will have 2 supervised training sessions a week which will be approximately 1 hour in length, only 25 minutes of which will be exercise. Participants will be expected to have an additional unsupervised session during the week which matches the HIIT and should consist of 25 minutes of exercise. Exercise Fitness Testing (VO2 max) will take approximately 30 minutes and will occur at the beginning and after 24-months of the HIIT program. A COVID-19 test may be performed prior as outlined by the University of Michigan clinical care guidelines.

4.3 When will my participation in the study be over?
Your participation in the study will be over after completion of all study visits which includes all measures mentioned in section 4.1.

4.4 What will happen with my information and/or biospecimens used in this study?
Your biospecimens and collected information may be shared with National Institutes of Health.

With appropriate permissions, your biospecimens and collected information may also be shared with other researchers, here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks are:

- Covid-19 Screening: A nasopharyngeal swab test involves the patient leaning their head back so that a health care provider can gently put a long cotton swab in the back of the nose to get a sample from a specific place in the back of your nose. You may feel slight temporary discomfort and experience tears in

your eyes momentarily during the swab test. Most patients do not describe the test as painful, but many do describe some temporary discomfort.

- Stress Test: Stress tests are generally considered safe, especially since they are done in a controlled environment under the supervision of a trained medical professionals. However, there are some rare risks, such as chest pain, collapsing, fainting, heart attack, irregular heartbeat. Prior to completing the stress test, you will be asked about your medical history and will complete a resting EKG to screen for abnormal EKG patterns.

- Heart rate variability testing: You may find the testing procedures to be unusual and/or confusing and repeated blood pressure measurements may be uncomfortable for you. The research member administering the tests will give you instructions which will help prevent confusion and check to make sure that the blood pressure measurements are not too uncomfortable for you. Part of this test requires a Valsalva maneuver, which can include a risk for fainting. The Valsalva maneuver is performed while laying down, and study staff will monitor you closely during this part of the test to ensure that you feel well enough to perform it.

- Dual Energy X-ray Absorptiometry: This scan gives you a small amount of radiation that is less than in a chest x-ray and less than the average annual background radiation exposure. During the course of this study, the average size adult subject will be exposed to radiation for research purposes in the form of a DEXA. The biological effect of this radiation is termed the 'effective dose' (ED) and is expressed in milliSieverts (mSv). The radiation for research the average size adult is exposed to in this study will amount to 0.002 mSv. The effects on the person's body of this radiation exposure will be added to the overall lifetime exposure. The lifetime risk of developing cancer also includes any radiation that may have been received in the past, and any such radiation that may be exposed to in the future. The average size adult's lifetime radiation risk includes the background radiation they are exposed to naturally like everyone else in Michigan, which averages about 3 mSv per year. The radiation a person will be exposed to in this study is 1500% times less the yearly background radiation. The amount that will be received in this study will be 100 times less than the amount of radiation received in routine chest x-rays, which is approximately 0.2 mSv. On average, it is predicted that approximately one individual in 1000 will develop cancer in their lifetime from an exposure to 10 mSv. The risk estimate is considered to be very small.

- BodPod: Even with its ample size, you may still feel claustrophobic. Although measurements take only a few minutes, if you are unable to tolerate being in the BodPod, we will simply stop the test and have you step out.

- The nerve conduction studies described above have the risk of discomfort due to the static current of electricity applied to the skin. These feel like a static shock and are discomforting to some people but do not have any other risks involved. The researchers will try to minimize these risks by having the procedure performed by licensed and trained members of the research team and taking the time to explain the procedure to you and making you as comfortable as possible during the testing.

- Questionnaires and doctor's exam: Any questions asked about a person's health and well-being or doctor's exam may cause you some discomfort in answering but is no more so than any standard health questionnaire or doctor's visit. The researchers have tried to minimalize this risk by using standard questionnaires that have been used in the health practice for many years.

- Measurement of vibration sensitivity: There are no known risks of using the neurothesiometer. The research member conducting the test will read you instructions prior to the testing procedure and you will be given the opportunity to ask any questions before testing begins.

- Balance and strength measures: Some people may find performing the balance and strength measures to be difficult, strenuous, or uncomfortable. If you have any health conditions which prevent you from being able to perform these measures, please notify the study team so that they can be modified to prevent discomfort or pain.

- Orthostatic Hypotension Assessment: There is a small risk of dizziness, weakness or visual changes. If you experience any of these symptoms you will be asked to sit and the assessment will be stopped.

- Cognitive testing: Some participants could find the information sensitive; however, it is not anticipated to be disturbing or traumatic. The risk of discomfort is minimized because you have the option of not answering any questions you prefer not to answer. The study team will review your score from the testing which may require the study team to refer you for further evaluation and to take additional steps according to our hospital's policies to prevent serious harm to yourself or others.

- Visual testing (24-2 FDT and retinal imaging): There are no known risks of this testing. The research member conducting the test will read you instructions prior to the testing procedure and you will be given the opportunity to ask any questions before testing begins. The retinal imaging does not require the eyes to be dilated.

- CCM: There is a small risk of discomfort from the confocal microscope since the instrument lens can be felt along the eyelid. It's usually described by patients as an unusual sensation, but not painful.

- Skin biopsies and Subcutaneous adipose tissue sampling: These procedures have the risk of discomfort or pain from the needle stick to numb the area to be biopsied. During the biopsies, you may experience some bleeding, bruising and clotting, the application of direct pressure at the needled/sensor insertion and biopsy sites will be used to help prevent these symptoms. There is a small risk of infection. There is a risk of scarring at the site of the biopsy. There is also the possibility of a reaction to the numbing medicine (lidocaine with epinephrine) used to perform the biopsy. Please notify study personnel if you have a history of allergic reactions to local anesthetics. These procedures may also result in dizziness or fainting. To reduce the chance of feeling faint or dizzy, these procedures will be performed while you are in bed, which will prevent possible injury due to falling. The researchers will try to minimalize these risks by having trained members of the research team perform this procedure and using sterile technique and equipment in the performance of this procedure. A bandage will be applied to the biopsy sites after the procedure and you will be given instructions on care of the wound. The instructions also have contact information for the study team if you have any questions or concerns after the procedure.

- Blood draw for the lipid panel, and glucose tolerance test: Blood drawing is mildly painful from the insertion of the needle and can cause bruising and very rarely fainting, blood clots, or an infection at the needle stick site.

- Optional study involving the storage and analysis of materials: Materials including plasma, DNA, urine, skin, and subcutaneous adipose tissue will be stored indefinitely. This research involves the possible identification of genetic information about you (and individuals genetically related to you). No information will be provided to you from the genetic testing. Learning about your genetic makeup can cause you to

worry about known and unknown consequences. Although research data will be maintained in a confidential manner, genetic information derived from your samples and provided to you could affect your access to insurance, employment or social relationship.

- Glucose tolerance test: Drinking the sugary liquid may be uncomfortable or unpleasant for some individuals and may cause your blood sugar to rise temporarily. In some individuals, sugar levels will then fall below a comfortable range by the end of the test. Blood drawing will be done by experienced personnel to minimize discomfort. Blood sugar levels will be checked and reviewed before you drink the sugary liquid to make sure your blood sugar levels are not too high to safely drink the sugary liquid and before you leave to make sure that they are in a safe range. A snack will also be provided at the end of the glucose tolerance test to prevent any discomfort related to low blood sugar.

- Exercise Fitness Test (VO2 max): The fitness test that you will be asked to perform will require you to exercise at a high level until you are too tired to continue. This test will likely last only 7-10 minutes. However, it can be very stressful to your cardiovascular system. Although unlikely, it is possible that this high level of exercise could result in a serious cardiovascular event (e.g.; heart attack, irregular heartbeat, and stroke). The facility where you will be tested will be equipped to handle these types of emergencies and the staff involved in the testing procedure will be well trained. However, you must understand that the stress of exercising at high levels can be dangerous and that you may stop the test at any time.

- High Intensity Interval Training(HIIT): The exercise you will be asked to perform during your training sessions will also require you to exercise vigorously (but not as vigorously as the fitness test and not to exhaustion). While this level of exercise is generally considered very safe to perform, it can also be stressful to your cardiovascular system. Although unlikely, it is possible that this high level of exercise could result in a serious cardiovascular event (e.g.; heart attack, irregular heartbeat, and stroke). Completing an exercise stress test prior to beginning the exercise program will may help to decrease the risk of a cardiac event occurring. The exercise intensity and duration will ramp up during the first few/several weeks of training to allow your body to get "used" to the exercise program. We have a planned protocol for this ramp up – but if you are uncomfortable with the rate of increase in intensity/duration this ramp up can be modified somewhat to accommodate your needs. You must understand that the stress of exercising at high levels can be dangerous and that you may stop exercise at any time.

- It is also possible that you may get injured as a result of the exercise training. The most common injuries during exercise training include soft-tissue injuries to your joints and limbs of your lower body (e.g., sprained/twisted knee or ankle, shin splints). Throughout the entire training program, the type of exercise you perform will be self-selected (e.g., walk/run (outdoors or treadmill), elliptical machine, stair climbing, cycling), and you will be encouraged to regularly vary the type of exercise used to reduce risk of overuse injury and to enhance the variety of the exercise program. Any injuries that occur during training will be managed on a case-by-case basis. For relatively minor injuries (e.g., strained muscle, shin splints, minor joint discomfort) the Exercise Physiologists on the research team will closely monitor your activity and revise (or suspend) the training program to aid in recovery. For more severe musculoskeletal injuries (e.g., sprained ankle/knee, etc.) your primary care physician may be consulted and your continued participation in their prescribed exercise protocol will be evaluated on a case by case basis. All injuries will be monitored closely, and we will assure that you receive appropriate medical attention.

- If assigned to the High Intensity Interval Training group, a University of Michigan gym will be available for use. Participants may choose to join an independent gym for supervised training sessions, however it is not

needed to participate in the study. If you would like to choose to independently join another gym any membership agreement, arrangements, and/or contacts will be between the participant and the gym. Outside gyms may have their own rules, requirements, and agreements for membership that will be agreed upon by the participant and are separate from the University of Michigan and the study.

- Additionally, there may be a risk of loss to confidentiality or privacy. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any personal benefits from being in this study. However, others may benefit from the knowledge gained from this study. During this study you may be randomized to participate in an exercise training program. General health benefits from exercising and exercise training are well established. The study is designed to collect information to determine if exercise and surgical weight loss have any relation to peripheral neuropathy and its development and treatment. You may, however, request records for yourself or your doctor(s) of your lipid panel, glucose tolerance test and a summary of your nerve conduction studies and/or neurologic exam.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?
There is no penalty to you if you choose not to participate in this study or to complete all study procedures. You still will be treated at the University of Michigan with your regularly covered care.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information”.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
There is no harm to you in leaving the study before it is finished. The researchers may contact you to ask you if you would be willing to complete any unfinished procedures prior to leaving the study, or to provide information as to why you no longer wish to be part of the study.

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researcher's telephone number listed in Section 10.1.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call Dr. Callaghan immediately, at 734-936-8778. The doctor will either treat you or send you to another doctor for treatment.

You will get free medical care at the UMHS for any hospitalization or ER visits directly caused by the study drug, device, or procedure. The UMHS and the study doctor are responsible for determining whether your condition was the result of your participation in the study.

The UMHS will pay for your treatment only if the need for treatment has been caused by the study drug, device or procedure. This means that you or your health plan must pay for any treatment that is part of your usual medical care or that is related to a medical condition you had before participating in the study. It is not the general policy of the federal funding agencies to compensate or provide medical treatment for human subjects in federally funded studies.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
Yes. You will be paid $45 for completion of Visit 1 (screening visit), $25 for completion of Visit 2 (pre-baseline visit), $100 after completion of Visit 3 (baseline), $100 for completion of Visit 4 (3-month), $100 for completion of Visit 5 (12-month), $100 after completion of Visit 6 (24-month). Total compensation for completing all outcome measures during the course of the study is $470. This is to help compensate for your time and travel expenses but will not necessarily cover all of these costs. The cost of parking will also be compensated at each visit at the main hospital. Payment will be in the form of check, payment coupon, or Visa card.

If you decide to take part in the optional procedures, you will be compensated for these as well. You will be paid $25 for each time you have a subcutaneous adipose tissue biopsy. Total compensation for completing all optional measures during the course of the study is $50.

Participants that are randomized to the HIIT exercise program will be compensated every 8 weeks, with the final payment at study completion. Participants who complete 80% (20/24 workouts based on 8 weeks) of their exercise workouts supervised and unsupervised will receive full compensation. Compensation will be pro-rated based on compliance. Compensation is as follows:

8 weeks: $50	56 weeks: $100
16 weeks: $60	64 weeks: $100
24 weeks: $60	72 weeks: $120
32 weeks: $80	80 weeks: $120
40 weeks: $80	88 weeks: $140
48 weeks: $100	104 weeks: $160

Participants in the HIIT group will also be compensated an additional $30 for completing VO2 max at the end of HIIT training.

Total potential compensation for exercise is an additional $1,200.

Participants that are randomized to the standard exercise program will be compensated every 8 weeks with a stipend to use towards a gym membership. Participants will receive 12 payments of $44 every 8 weeks. Total potential compensation for standard exercise program is an additional $528.

8.3 Who could profit or financially benefit from the study results?
No person or organization has a financial interest in the outcome of this study.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?

Your privacy will be covered and protected under the University of Michigan's policies and procedures for the protection of health and personal information (HIPAA) policy. The researchers will remove any identifiers (name, date of birth, etc.) from your paper records and will assign your information a research code. The key to this code and your personal identifiers will be kept in a secure database maintained by the University of Michigan. Only members of the research team will have access to this secure database. Consent forms will retain your identifying information and will be stored separately from the research records.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the SPONSOR which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of harm to self or others. The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

GINA does not apply to the following groups; however, these groups have policies in place that provide similar protections against discrimination:

- Members of the US Military receiving care through Tricare
- Veterans receiving care through the Veteran's Administration (VA)
- The Indian Health Service
- Federal employees receiving care through the Federal Employees Health Benefits Plans

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.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, Social Security number, payment amount, and related information for tax reporting purposes.

- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?
As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?
Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?
Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator:

Brian Callaghan, MD, MS
Mailing Address: 109 Zina Pitcher Place, 4021 AAT-BSRB, Ann Arbor, MI 48109
Telephone: 734-764-7205, pager 16266 (for urgent issues only)

Study Coordinator:

Ericka Chant, MPH
Mailing Address: 300 North Ingalls St. Room 3D02-SPC 5431 Ann Arbor, MI 48109
Telephone: 734-936-8778

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?
You will receive a copy of the signed and dated informed consent.

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Consent/Assent to Participate in the Research Study:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent/Assent to Collect for Unspecified Future Research:

This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to allow future use of my specimens. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to let the study team keep my specimens for future research.

_____ No, I do not agree to let the study team keep my specimens for future research.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent/Assent for Participating in an Optional Genetic Sub-Study:

This project involves optional participation in a genetic sub-study. I understand that it is my choice whether or not to take part in the sub-study. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to take part in the optional genetic sub-study.

_____ No, I do not agree to take part in the optional genetic sub-study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent/Assent for Participating in an Optional Subcutaneous Adipose Tissue Sub-Study:

This project involves optional participation in a subcutaneous adipose tissue sub-study. I understand that it is my choice whether or not to take part in the sub-study. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to take part in the optional subcutaneous adipose tissue sub-study.

_____ No, I do not agree to take part in the optional subcutaneous adipose tissue sub-study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Consent/ Assent for Participating in an Optional Skin Tissue Sub-Study:

This project involves optional participation in a skin tissue sub-study, allowing the skin biopsy tissue to enter the biorepository for use in future research studies. The skin biopsy tissue would be used for unspecified future research. I understand that it is my choice whether or not to take part in the sub-study. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to take part in the optional skin tissue sub-study.

_____ No, I do not agree to take part in the optional skin tissue sub-study.

Print Legal Name: _____

Signature: _____

Consent/ Interest in Participation in Future Research Studies:

_____ Yes, I am interested in future research studies. Please contact me about future research studies here at the University of Michigan.

_____ No, I am not interested in future research studies. Please do not contact me about future research studies here at the University of Michigan.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____