UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study (this "Research Study")?

Sex differences in chronic and acute vascular responses to aerobic exercise in older adults

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

The principal investigator, Dr. Demetra Christou, may be reached by phone [redacted] (office) or [redacted] (cell phone) or by email [redacted]

4. Who is paying for this Research Study?

The sponsor of this study is the University of Florida and the National Institutes of Health (NIH).

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved?

We have developed a novel exercise intervention consisting of 8 weeks of supervised high-intensity interval training (HIIT) on a stationary cycle that exercises the arms and legs simultaneously (all-extremity cycle). We have successfully implemented this exercise intervention in middle-aged and older adults and have demonstrated improvements in heart health, maximal exercise capacity and glucose control. Our findings on the effect of HIIT on vascular (blood vessel) health suggest that men and women may respond differently to the exercise training. The current study will investigate sex differences in acute and chronic vascular responses to exercise in older adults and explore the factors that may contribute to these sex differences. Our goal is to build the foundation for developing sex-specific exercise prescription for maximizing vascular benefits similarly in men and women.

Your study participation will be completed over approximately 6-7 months depending on scheduling availability.

b) What is involved with your participation, and what are the procedures to be followed in the research?

All procedures will take place at the Integrative Cardiovascular Physiology Laboratory at the Center for Exercise Science on the University of Florida campus. The procedures will be completed over 15 visits ranging from 1 to 3 hours each and will total approximately 29 hours over 6-7 months.

The 8-week exercise training will be completed at home over 32 sessions (4/week) under remote live supervision using video conferencing (UF Zoom). A member of the Integrative Cardiovascular Physiology Laboratory will lead each virtual exercise session and will guide you through the setup, warm up, work out and cool down. You will be provided the following to use during the 8-week exercise training: an all-extremity cycle, a wearable device to monitor your exercise response and a tablet for video conferencing. You will perform 4 supervised exercise training sessions per week lasting approximately an hour each. A period of familiarization with all-extremity exercise will be provided. During this time, the exercise duration and pace will gradually increase with each session until you can complete the prescribed HIIT protocol. The total number of completed exercise sessions during your study participation will depend on your ability to perform all-extremity exercise, your initial fitness level and scheduling availability for the post-intervention procedures.

- To determine your eligibility to participate and to evaluate your overall health you will complete the following procedures: physical exam, general blood tests and assessments of your heart and vascular health, fitness level, physical activity, diet, quality of life and body composition (fat and fat free weight and bone density).

- To investigate the chronic effects of exercise, the procedures described above will be completed: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of supervised exercise training.
- To investigate the acute effects of exercise, your vascular health will be assessed: 1) at rest; 2) at the end of an exercise session; 3) after 1-hour recovery from exercise; and 4) after 24-hours recovery from exercise. These tests will be performed in the untrained state (at the beginning of the 8-week exercise training) and repeated in the trained state (after the 8-week exercise training) to examine how chronic exercise training influences the acute effects of exercise.

It is very important that you keep your dietary and physical activity habits the same throughout your study participation and to let us know if there is a change in the medications you are taking.

c) What are the likely risks or discomforts to you?

Our experienced research team will oversee all of the procedures and every effort will be made to keep the risks and discomforts involved in this study to a minimum. The main *likely* discomforts and risks include:

- fatigue or muscle soreness from maximal exercise testing and exercise training
- dry mouth from mouthpiece used for measuring oxygen use during maximal exercise testing
- mild to moderate intensity “pins and needles or numbing” sensation in forearm from cuff inflation that goes away as soon as cuff is deflated.
- discomfort from injection of local anesthetic (numbing medicine, lidocaine) to numb wrist prior to placing a catheter (thin hollow flexible plastic tube) in radial artery (blood vessel).
- discomfort from needle stick and placement of catheter (thin hollow flexible plastic tube) in radial artery (blood vessel) at wrist and vein (blood vessel) at elbow, forearm or hand; discomfort and bruising around the puncture site after catheter has been removed.
- small decrease in blood pressure and small increase in heart rate that goes away within 30 min of taking a nitroglycerin tablet. Nitroglycerin is an FDA approved medication that causes blood vessels to relax and will be used on three occasions to test your blood vessel function.

Potential risks and discomforts, including those that are unlikely or rare, are described in detail in question 12.

d) What are the likely benefits to you or to others from the research?

You may or may not benefit directly from participating in this research study, but knowledge obtained from your participation will advance our understanding of how exercise responses differ between men and women which may improve sex-specific exercise prescription for cardiovascular disease prevention.

Possible benefits to you include receiving information regarding your health at no cost and health benefits from the supervised exercise training, although individual responses may vary. A detailed description of the type of health information and exercise-related health benefits you may receive is provided in question 13.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

If you do not want to take part in this study, then let the Principal Investigator listed in question 3 know and do not sign the Informed Consent Form

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.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

This study does not involve clinical care, and it should not interfere with any clinical care you are currently receiving. All medical tests will be completed for research purposes only and do not take the place of regular physician assessments.

7. What will be done only because you are in this Research Study?

Procedures:

- Coronavirus-19 (COVID-19) screening questionnaire. On every visit, we will ask questions regarding history and symptoms of COVID-19.
- Medical history. You will complete a medical history form.
- Physical exam. You will complete a physical examination similar to what you would experience in your doctor's office. This will consist of review of your medical history and check of your general physical condition including examination of your head and neck, heart, lungs, abdomen, nerves, muscles, joints and skin.
- 24-hour questionnaire. On every visit, we will ask questions regarding your sleep, food, drink, tobacco, alcohol, caffeine and medication intake and physical activity over the last 24 hours. We will also ask if you are experiencing any health problems (e.g., sore throat, head cold, upset stomach, etc.).
- Height. We will measure your height using a ruler attached to a wall.
- Weight. We will measure your body weight using an electronic scale.

- Heart rhythm. We will place small electrodes on your chest to record your heart rhythm.
- Blood pressure. We will measure your blood pressure with a cuff around your ankles. We will also measure your blood pressure with a cuff around your upper arms.
- Body composition scan and circumferences. We will measure your waist and hip circumferences using a tape measure. We will also measure your body composition including your body fat and fat free weight, as well as your bone density, using a non-invasive dual-energy x-ray absorptiometry (DXA) scan. This test requires that you lie very still on a padded table that gives off low-level X-ray radiation. The "arm" of the machine will slowly pass over your body to make the measures. This should take less than 10 min. Female participants who are younger than 62 years of age and who have not had a hysterectomy, will complete a urine pregnancy test prior to the scan.
    - To investigate the chronic effects of exercise on body composition and circumferences, these tests will be performed: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- Physical activity habits. We will ask questions regarding how hard, how often and for how long you perform a variety of physical activities. We will also ask you to wear an activity monitor for 4 days to track your activity.
    - These measures will be performed: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- Dietary habits. We will ask questions regarding what you ate and drank on the previous day.
    - This information will be collected: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- Quality of life questionnaire. We will ask questions about your perceptions of your health and your ability to perform daily activities.
    - This information will be collected: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- Maximal exercise test on treadmill. This test will measure how well your heart can cope with increasing levels of exercise. We will monitor your heart rhythm, blood pressure and your body's oxygen use (a measure of fitness) while you walk on a treadmill for as long as possible. To measure your body's oxygen use, you will breathe through a mouthpiece while wearing a nose clip to prevent air from going through your nose. The treadmill will begin slowly and the speed (pace) will gradually increase based on your walking ability and your heart rate. Upon completion of a 6-min warmup, the speed will remain the same while the treadmill will slightly tilt every 2 min to produce the effect of going up a small hill until you reach your maximal exercise capacity (usually 12 to 15 min excluding the warm-up period). At certain times during the test, we will ask you to point to

a scale which tells us how hard you feel you are working. If you have a problem walking on the treadmill you may perform the test on a stationary bicycle.

If any abnormalities occur during the test, you will be referred to your primary care physician for further testing. To get a high-quality recording of your heart rhythm we will ask for your permission to shave small areas of your chest, if needed, before placing the electrodes. Underwire bras may interfere with the recording and should not be worn during the test.

During the COVID-19 pandemic, our study clinician may prescribe a COVID-19 test to be completed prior to performing the maximal exercise test. The test will be performed at a UF Health location.

- Maximal exercise test on all-extremity cycle. This test will measure your ability to perform all-extremity cycling for as long as possible. Your heart rhythm, blood pressure and body's oxygen use will be measured throughout the test as described above. You will complete a 6-min warmup by performing all-extremity cycling at a moderate pace. Upon completion of the warmup, the pace will gradually increase every 2 min until you reach your maximal exercise capacity (usually about 12 to 15 min excluding the warmup). Prior to this visit you will be given an opportunity to practice all-extremity cycling and breathing through a mouthpiece.
    - To investigate the chronic effects of exercise on maximal exercise capacity, this test will be performed: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.

  During the COVID-19 pandemic, our study clinician may prescribe a COVID-19 test to be completed prior to performing the maximal exercise test. The test will be performed at a UF Health location.

- 6-min walk test. The purpose of this test is to assess your ability to walk for 6 min. The test will be completed at your pace, walking back and forth between 2 cones. The objective is to walk as far as possible in 6 min. You are permitted to slow down, to stop, and to rest, as necessary.
    - To investigate the chronic effects of exercise on your walking ability, this test will be performed: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.

- Blood vessel tests. To measure the stiffness of your blood vessels, we will place a pencil-like device on your skin at your neck to record pressure waves while you lie still on your back and a pressure cuff is partially inflated on your thigh. To measure the ability of your blood vessels to widen in response to an increase in blood flow, we will place an ultrasound transducer (hand-held device that uses sound waves to create pictures) on your skin, a few inches higher than your elbow to record pictures of your brachial artery (blood vessel) while you lie still on your back. A small pressure cuff will be inflated on your forearm for 5 min and deflated to cause an increase in blood flow. The width of your artery and blood flow to your forearm will be measured before inflating and after deflating the cuff.

- To investigate the chronic effects of exercise on blood vessel function, these tests will be performed: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- To investigate the acute effects of HIIT on blood vessel function, these tests will be performed: 1) at rest; 2) at the end of a HIIT session; 3) after 1-hour recovery; and 4) after 24-hours recovery. **It is important to return to our lab 23 hours after the exercise finished. We will schedule this in advance and will communicate with you, on the day of exercise, the exact time to return the following day.** To examine how chronic exercise training affects the acute responses of exercise, these tests will be performed at the beginning and end of the 8 weeks of exercise training.
- To investigate the acute effects of maximal exercise on blood vessel function, these tests will be performed: 1) at rest; 2) at the end of the maximal exercise test on treadmill (described above); 3) at the end of the maximal exercise test on all-extremity cycle (described above); and after 1-hour recovery. To examine how chronic all-extremity exercise training affects the acute responses to maximal exercise test on all extremity cycle, these tests will be performed at the beginning and end of the 8 weeks of exercise training.

It is important to place the ultrasound device over the same location on your arm each time we perform a blood vessel test. For this reason, we will ask your permission to take a photograph of the position of the device on your arm. The photograph will be kept in a locked cabinet and on a password protected computer. The photograph will not be shown to any individual outside our research team and will be destroyed at the end of your participation. You have the right to refuse to have your photograph taken.

- Nitroglycerin test. This test evaluates the ability of your blood vessels to relax in response to a nitroglycerin tablet (an FDA approved drug which causes blood vessels to relax). Once the nitroglycerin tablet dissolves under your tongue, pictures of your brachial artery (blood vessel) will be recorded using an ultrasound transducer (hand-held device that uses sound waves to create a picture) for up to 10 min while you lie still on your back. Prior to administering nitroglycerin, a thin hollow flexible plastic tube (intravenous catheter) will be inserted in a blood vessel in your arm using a needle and will remain there for up to 30 min after taking the nitroglycerin tablet.
    - To investigate the chronic effects of exercise on blood vessel function, the nitroglycerin test will be performed: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- Blood draw. The amount of blood drawn over your study participation (6-7 months) will total 25 TBSP, which is less than a whole blood donation which is typically a pint. You should not donate blood during your study participation or within 2 months of completion.

- To perform general blood tests including measures of your liver and kidney function and red and white blood cell counts and lipid (fat), sugar and insulin levels, a TBSP of blood will be collected: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- To investigate the chronic effects of HIIT, 2 TBSP of blood will be collected to measure circulating factors and factors in blood cells which are related to blood vessel health: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- To investigate the acute effects of HIIT, 2 TBSP of blood will be collected to measure circulating factors and factors in blood cells which are related to blood vessel health: 1) at rest; 2) at the end of a HIIT session; 3) after 1-hour recovery from HIIT; and 4) after 24-hours recovery from HIIT. To examine how chronic exercise training affects the acute responses of exercise, these tests will be performed at the beginning and end of 8 weeks of exercise training.

- Intra-arterial catheter and cell collection. After numbing the area by local injection of a numbing medicine (lidocaine), an experienced clinician will insert a thin hollow flexible plastic tube (catheter) into a blood vessel at your wrist (radial artery) using a small needle. Four very small-diameter (0.018 or 0.021 inch) sterile J-shaped flexible soft guidewires will be inserted one at a time through the catheter and will be advanced ~4 inches and immediately removed. A small amount of blood will coat the guidewires which will be used to obtain a small sample of cells that line the inside of your blood vessel. Blood will also be drawn through this catheter to perform the blood tests described under the Blood draw section above. The intra-arterial catheter will be removed as soon as the cells and blood are collected.
    - To investigate the chronic effects of HIIT, cells will be collected to measure factors related to blood vessel function: 1) at baseline; 2) after 8 weeks of normal lifestyle; and 3) after 8 weeks of exercise training.
- Intravenous catheter to investigate acute effects of HIIT. Using a small needle, a thin hollow flexible plastic tube (catheter), will be placed in a vein (blood vessel) in your arm where it will remain for up to 3 hours to collect blood to examine the acute effects of HIIT.
    - This procedure will be performed at the beginning and end of 8 weeks of exercise training.

Please note that some of the procedures you complete in this Research Study require that you fast for 4 or 12 hours or abstain from caffeine and alcohol for 12 hours or wear short sleeves/shorts and athletic shoes suitable for exercise. This information will be described in the study materials you receive, and reminders will be provided prior to each appointment.

Exercise Intervention:
During the 8 weeks of exercise training, you will perform 4 supervised exercise training sessions per week lasting approximately an hour each, which will include stretching and 40-min HIIT (see **Diagram** below).

Warm up: moderate pace 10 min	Interval: fast pace 4 min	Active Recovery: moderate pace 3 min	Interval: fast pace 4 min	Active Recovery: moderate pace 3 min	Interval: fast pace 4 min	Active Recovery: moderate pace 3 min	Interval: fast pace 4 min	Cool down: moderate pace 5 min

Diagram. High-intensity interval training (HIIT) will consist of 10-min warmup at a moderate pace, 4x4-min intervals at a fast pace interspersed by 3-min bouts at a moderate pace and a 5 min cool down at a moderate pace.

The exercise sessions will be performed at your home and will be supervised by study staff live using video conferencing. You will be provided the following to be used during the 8-week exercise training: an all-extremity cycle, a wearable device to monitor your exercise response (heart rate, breathing rate, body temperature, calories burned, physical activity) and a tablet for video conferencing and monitoring your exercise response. Using video will allow our team to safely supervise each participant during the exercise sessions and provide an opportunity for participants to interact which may encourage participation. The exercise sessions will not be recorded and requests for private sessions will be accommodated. A member of the Integrative Cardiovascular Physiology Laboratory will lead each virtual exercise session and will guide you through the setup, warm up, work out and cool down. We will have a practice session to teach you how to use the wearable device, and video conference via password-protected UF ZOOM sessions.

Prior to initiating the 8-week training program, a period of familiarization with all-extremity HIIT exercise will be provided. During this time, the exercise duration and pace will gradually increase with each session until you are able to complete the prescribed HIIT protocol. From our experience, most participants need approximately 5 sessions to achieve this goal. The total number of completed exercise sessions over your study participation will depend on your ability to perform all-extremity exercise, your initial fitness level and scheduling availability for the post-intervention procedures.

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact the Principal Investigator listed in question 3 of this form.

List of Procedures and Duration by Visit

Consent (1.5 hrs) Informed consent Medical history and activity questionnaire
Visit 1 (1.5 hrs) 24hr questionnaire and activity monitor pick up Height/weight Blood pressure
Visit 2 (1.5 hrs) 24hr questionnaire Weight Physical exam Blood pressure and heart rhythm Maximal exercise test on treadmill Pre-exercise and end of exercise: Blood vessel tests
Visit 3 (1 hr) Questionnaires Pregnancy test Weight, waist/hip circumferences, body composition scan 6-min walk test All-extremity cycling practice
Visit 4 (1 hr) 24-hr questionnaire Weight Blood pressure and heart rhythm Maximal exercise test on all-extremity cycle
Visit 5 (2.5 hrs) 24-hr questionnaire Weight Blood pressure and heart rhythm Blood vessel tests Nitroglycerin test and intravenous catheter Intra-arterial catheter, cell collection and blood draw
8-week control period: normal lifestyle
Visit 6 (1 hr) Questionnaires and activity monitor pick up Pregnancy test Weight, waist/hip circumferences, body composition scan 6-min walk test All-extremity cycling practice

Visit 7 (2.5 hrs) 24-hr questionnaire Weight Blood pressure and heart rhythm Blood vessel tests Nitroglycerin test and intravenous catheter Intra-arterial catheter, cell collection and blood draw
Visit 8 (3 hrs) 24-hr questionnaire Weight Maximal exercise test on all-extremity cycle Pre-exercise, end and 1-hour post-exercise: Blood pressure and heart rhythm Blood vessel tests
All-extremity HIIT Practice Prior to initiating the 8-week training program, a period of familiarization with all-extremity HIIT exercise will be provided. During this time, the exercise duration and pace will gradually increase with each session until you are able to complete the HIIT protocol.
Visit 9a (3 hrs) 24-hr questionnaire Weight Exercise session on all-extremity cycle Pre-exercise, end and 1-hour post-exercise: Blood pressure and heart rhythm Blood vessel tests, intravenous catheter and blood draw
Visit 9b (1 hr) 24-hr questionnaire Weight Blood pressure and heart rhythm Blood vessel tests and blood draw
8-week training period: 40 min/session scheduled every week on M, T, Th, F
Visit 10 (2.5 hrs) 24-hr questionnaire and activity monitor pick up Weight Blood pressure and heart rhythm Nitroglycerin test and intravenous catheter Intra-arterial catheter, cell collection and blood draw
Visit 11 (1 hr) Questionnaires Pregnancy test Weight, waist/hip circumferences and body composition scan 6-min walk test
Visit 12a (3 hrs) 24-hr questionnaire Weight Exercise session on all-extremity cycle

Pre-exercise, end and 1-hour post-exercise: Blood pressure and heart rhythm Blood vessel tests, intravenous catheter and blood draw
Visit 12b (1 hr) 24-hr questionnaire Weight Blood pressure and heart rhythm Blood vessel tests and blood draw
Visit 13 (3 hrs) 24-hr questionnaire Weight Maximal exercise test on all-extremity cycle Pre-exercise, end and 1-hour post-exercise: Blood pressure and heart rhythm Blood vessel tests

These visits will be scheduled over 6-7 months which should alleviate some of the burden:

a) visits 1-5 will be scheduled over 2-3 weeks and will total 7.5 hours;
b) during the 8-week control period of normal lifestyle there will be no scheduled visits;
c) visits 6, 7, 8, 9a and 9b will be scheduled over 2-3 weeks and will total 10.5 hours;
d) during the 8-week exercise training period there will be 4 scheduled exercise sessions/week;
e) visits 10, 11, 12a, 12b and 13 will be scheduled over 2-3 weeks (10.5 hours total).

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect the following information:

- Medical history
- Records of physical exam
- Height, weight, circumferences, and body composition results
- Blood pressure at rest and during exercise
- Heart rhythm at rest and during exercise
- Heart rate, breathing rate, body temperature, physical activity and calories burned during the exercise sessions.
- Maximal exercise test on treadmill results
- Maximal exercise test on all-extremity cycle results
- 6-min walk test results
- Physical activity, quality of life and dietary information
- Blood test and cell analysis results
- Blood vessel test and Nitroglycerin test results

- Pregnancy test results
- Demographic information
- Social Security Number for research payment purposes
- COVID-19 screening questions and test results

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals, or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team and the Principal Investigator listed in question 3 above will use or share your health information as described below to carry out this research study.

9. With whom will this health information be shared?

This health information may be shared with:

- the study sponsor (listed in Question 4 of this form);
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- Government agencies which are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.
- The IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

Your total participation will be completed over approximately 6-7 months depending on scheduling availability.

This Authorization to use and share your health information expires at the end of the study unless you revoke it (take it back) sooner.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You have been informed that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. That is, if you give written consent for the release of information, we cannot withhold that information and we cannot hold responsibility for how that person may use your information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances. If we learn about child abuse, elder abuse, or intent to harm yourself or others, we will report that information to appropriate authorities.

11. How many people are expected to take part in this Research Study?

A total of 165 individuals are expected to take part in this study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

Every effort will be made to keep the risks and discomforts involved in this study to a **minimum. Possible discomforts and risks are described for each procedure below:**

- Blood vessel tests: Expected mild to moderate intensity “pins and needles or numbing” sensation in the forearm and hand from cuff inflation which goes away as soon as the cuff is deflated. This is similar to having your blood pressure measured.
- Body composition scan: This research study involves exposure to radiation from x-rays. You will receive three DEXA scans during this study. The radiation exposure from each DEXA scan is equal to about 3 millirem, which is comparable to about 4 extra days of natural background radiation to which people in the United States are exposed to during their lives. The risk from this radiation exposure is considered to be extremely low when compared to other every day risks.

  Because radiation exposure might affect an unborn baby, a body composition scan will not be given to any individuals who are pregnant. All women of childbearing potential (younger than 62 years of age who have not had a hysterectomy) must take a pregnancy test prior to completing a scan. The results of the pregnancy test will be made available to you.

- Maximal exercise test: Possible fatigue, muscle soreness, or dry mouth from mouthpiece or irregular heart rhythm and very rarely chest pain or a heart attack in those with heart problems which could potentially lead to death. Risks will be minimized by health screening (medical history and physical exam), providing clinical supervision and having emergency medications and equipment available.
- Exercise training: When one begins a new exercise program there is a risk that it may lead to fatigue or muscle or joint soreness, or injury. There is a small risk of irregular heart rhythm; very rarely heart attack or stroke which could potentially lead to death. In general, exercise does not lead to heart problems or stroke in individuals who have completed health screening and are free of heart disease. Overall, the widely accepted benefits of exercising should outweigh the risks. Risks will be minimized by health screening (medical history, physical exam, maximal exercise testing, general blood tests). To minimize the risk of injury, your activity level will be gradually increased as tolerated. As your fitness level increases and you become accustomed to the exercise, your energy levels should increase, and you should not experience muscle soreness. The home exercise sessions will be supervised by study staff live using video conferencing and emergency procedures are in place. To allow monitoring of your exercise response using the wearable device, the location option on the tablet must be turned on. Neither the study team nor the company that manufactures the wearable device will have access to your location information. But there is a small risk that an unauthorized person may get access to this information, while you use the tablet.
- Intravenous catheter and blood draw: Discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection or blood clot; and, uncommonly, faintness from the procedure. Risks will be minimized by health screening and having experienced research staff perform the procedure.
- Intra-arterial catheter, cell collection and blood draw: Discomfort from injection of local numbing medicine (lidocaine) to numb wrist prior to placement of catheter (thin hollow flexible plastic tube) in radial artery (blood vessel). Discomfort from needle stick and placement of catheter at the time it is inserted or after it has been removed. Possible bleeding, bruising, and swelling around the puncture site. Rarely a local blood clot, infection, significant blood loss, nerve or artery damage, tissue injury and damage of surrounding tissue and extremity. *Aspirin and other blood thinning medications can cause complications such as excessive bleeding; if you are currently taking these medications, you cannot participate in the study.* The risks related to the cell collection are similar to those associated with an intra-arterial catheter, although the risk of blood clot, infection or blood vessel damage may be slightly greater compared to having intra-arterial catheter placement without cell collection. Risks will be minimized by health screening and having an experienced clinician perform the procedure using ultrasound imaging (sound waves to create a picture) to help guide the insertion of the catheter to avoid injury to nerves and surrounding structures.
- Lidocaine (numbing medicine): Expected sensation of coolness or numbness at injection site; likely mild temporary skin irritation including burning, redness or

swelling at injection site; unlikely but possible reactions include nausea, vomiting, dizziness, ringing in ears, nervousness and blurred or double vision; extremely rare allergic reaction. Risks will be minimized by health screening and having an experienced clinician perform the procedures.

- Nitroglycerin test: Expected small temporary decrease in blood pressure and increase in heart rate; possible lightheadedness, tingling on the tongue and in the arms and legs, light headache; rarely decrease in heart rate and fainting. Risks will be minimized by health screening, providing clinical supervision and having an intravenous catheter and emergency medication and equipment available.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform the Principal Investigator listed in question 3 or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or contact the Principal Investigator, Dr. Demetra Christou, by phone [redacted] (office) or [redacted] (cell phone) or by email [redacted]

13a. What are the potential benefits to you for taking part in this Research Study?

You may or may not benefit from participating in this research study. Possible benefits include receiving the following information regarding your health at no cost: general blood tests, blood pressure, body fat content, bone density, heart health, aerobic fitness, physical activity, and dietary analysis. Although individual responses may vary, exercise training has been shown to lead to many health benefits that may improve quality of life or lower the risk for heart disease including higher fitness level, improved heart function, healthier blood vessels, lower blood pressure, lower body fat and blood lipids, reduced stress, and depression.

13b. How could others possibly benefit from this Research Study?

Information collected from your participation will help expand medical knowledge regarding exercise prescription for cardiovascular disease prevention which may benefit others.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team and the Principal Investigator listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

13d. Will you be allowed to see the research information collected about you for this Research Study?

Information regarding your general blood tests, heart health, aerobic fitness, blood pressure, physical activity, diet and body composition including body fat and bone density will be provided to you at the end of your study participation. Additional research information collected about you for this Research Study can be provided to you after the completion of the entire study, by sending a written request to the Principal Investigator, Dr. Demetra Christou, [redacted].

14. What other choices do you have if you do not want to be in this study?

If you do not want to take part in this study, tell the person reviewing this consent and do not sign the Informed Consent Form.

You may also refuse to authorize the use of your health information, but if you refuse, you will not be allowed to be in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the person listed in question 3 of this form. She will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the person listed in question 3 of this form to let her know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with the Principal Investigator, Dr. Demetra Christou, by phone [redacted] (office) or [redacted](cell phone).

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- If you do not follow the instructions given to you by the Research Team
- If you do not keep your scheduled appointments to complete all procedures
- If you do not complete your scheduled supervised exercise sessions

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

No, there will be no extra cost to you for participating in this Research Study.

17. Will you be paid for taking part in this Research Study?

You will receive a total of $360 for completing visits 5-13 in the form of a gift card upon completion of your study participation. In addition, for every week that you complete all 4 supervised exercise sessions you will be compensated an additional $5 (e.g., if you complete 4 sessions/week for 8 weeks, then you will receive an additional $40, thus increasing your total compensation from $360 to $400). It may take a few weeks to receive payment following completion of your participation or withdrawal from the study. Please contact the Research Team if you have any questions regarding payment.

If you do not complete the entire study financial compensation will be prorated as described in the following table:

Visits 1-4	You will receive the health screening results at no cost. No financial compensation will be provided.
Visit 5	$45
Visit 6	$10
Visit 7	$45
Visit 8	$25
Visit 9a	$25
Visit 9b	$10
Visit 10	$75
Visit 11	$10
Visit 12a	$45

Visit 12b	$20
Visit 13	$50
Exercise sessions	You will receive supervised exercise training at no cost. An additional $5/week will be provided for each week that all 4 supervised sessions are completed.

If you are paid more than $75 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. Payments to nonresident aliens must be processed through the University of Florida Payroll and Tax Services department. If the payments total $600 or more in a calendar year, the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

If you have any problems regarding your payment, contact the study coordinator.

18. What if you are injured while in this Research Study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists, or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact the Principal Investigator listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing Date