INFORMED CONSENT DOCUMENT

Project Title: **The effect of combined aerobic and muscle strengthening exercises on structural and functional cardiovascular adaptations in endometrial cancer survivors.**

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This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you have been diagnosed with endometrial cancer and are eligible to participate.

The purpose of this research study is to measure changes in vessel structure and function following a home-based exercise program. We want to measure how your vessels expand and contract, and the speed of the blood moving in your body from the beginning to the end of the study. We will also measure your blood to see how the exercise program improves measures in your blood such as cholesterol, blood sugar and blood pressure. In this study, we will ask you to exercise for 12 weeks. As a part of the study, we will ask you to exercise consistent with exercise guidelines for cancer survivors, including conducting muscle strengthening exercises on two days per week and doing 150 minutes per week of aerobic exercise.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 33 people will take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for 12 weeks of exercise over a total of approximately 14 weeks (to allow for device wear and scheduling visits). We will ask you to come in person to the Physical Activity and Cancer Survivorship (PACS) laboratory in the Iowa Bioscience Innovation Facility, twice over the course of the study, once at the beginning and once at the end of the approximately 14 week period. During these visits, we will also walk you to the Clinical Research Unit in the hospital for collecting study measures. These visits will last 4 hours in length, we recommend you bring a snack or something to eat to these visits after we complete blood collection.

WHAT WILL HAPPEN DURING THIS STUDY?

If you choose to participate in this research, you will be asked to:

1.) Attend two in-person study visits

Visits will be conducted at the PACS Lab within the Iowa Bioscience Innovation Facility (Room 127, 115 S Grand Ave) in Iowa city. The initial visit takes about 4 hours. During the first visit we will discuss the study goals and research activities as well as collect baseline measures described later in this section including those collected at the hospital. We will then ask you to wear a motion sensor for one week (described below) and let us know when you've finished wearing it. During this initial visit, we will provide you with materials and instructions on how to complete the exercises as a part of this study. Finally, all subjects will be asked to return for a final visit after approximately 14 weeks in the study where we will repeat the measurements collected at the first visit.

When you arrive:

The researchers will meet you at the entrance of the Iowa Bioscience Innovation Facility (115 S Grand Ave) and walk with you to the lab space. After completing measures in the lab space, we will walk with you to the Clinical Research Unit (CRU).

2.) Complete questionnaires

There is a questionnaire we will administer to collect information about you including your age, address, health history, and other demographic information. You are free to skip any questions that you would prefer not to answer. This questionnaire takes less than 5 minutes to complete.

At two time points (baseline and final visit) during the study, you will be asked to complete six questionnaires about your behavior, perception, social support, diet, and confidence for exercise. You are free to skip any questions that you would prefer not to answer. These questionnaires will take 30-45 minutes to complete and will be sent electronically for you to complete at your comfort.

3.) Complete study measures: Vascular measures, anthropometrics, FFT

At two timepoints (baseline and final visit) during the study, you will be asked to complete study measures. These include assessments of your blood vessel stiffness, endothelial function test, blood draw, height, weight, waist and hip circumference and an assessment of functional fitness through a battery of tests that reflect daily living.

Blood vessel stiffness test: To test the "stiffness" of the walls of your arteries we will do two sets of measures. First, we will take your blood pressure three times while you are laying down. Second, a small probe will be placed flat on the surface of your skin at four sites and will record each time your heart beats. The four sites are your carotid artery (side of neck), brachial artery (arm near elbow), femoral artery (upper leg/hip), and radial artery (wrist). The faster your pulse moves between the sites, the stiffer your arteries are.

Endothelial function test: We will place an ultrasound probe on your skin over the major artery in your upper arm. A small blood pressure cuff will be inflated tightly below your elbow cutting off the blood flow for 5 minutes. The blood flow and size of your vessel will be measured before and after inflating the cuff. This will allow us to measure your endothelial function (ability of blood vessels to dilate or get bigger). You will also have electrodes on your chest to trace the electrical activity of your heart (ECG).

Blood draw tests: The blood draw involves a research nurse or CRU staff drawing 50 ml (< 4 Tbsp) of blood from a vein in your arm. We send some of the blood to a lab to see if the proteins, blood sugar, lipids, etc. are within normal levels.

Blood Pressure, Heart Rate: We measure blood pressure and heart rate during the blood vessel stiffness and endothelial function test. We apply three sticky tabs to the skin of your chest. The tabs connect to an electrocardiogram (ECG) machine that records heart rate. During these tests, we can measure blood pressure in any of two ways. a) We inflate a cuff on your upper arm while we listen at the inside of your elbow with a stethoscope. b) Likewise, an automated machine inflates a cuff on the upper arm and uses a sensor in the cuff to measure blood pressure.

Functional Fitness Test (FFT): The functional fitness test (FFT) is a battery of six tests measuring strength, flexibility, aerobic capacity, and agility. The functional fitness test battery includes the following seven assessments:

a) Handgrip dynamometer, which assesses the strength of your grip. You will have three repetitions for each hand to generate maximum force from your grip using a dynamometer.
b) The 30 second chair sit to stand, which assesses the strength of the lower body. You will have 30 seconds to stand up and sit down from a chair as many times as possible within the time frame.
c) The 30 second arm curl assesses the strength of the upper body, where you will hold a 5-pound dumbbell in a seated position, and you will have 30 seconds to curl your arm and extend it as many times as possible within the time frame.
d) The 6-minute walk test measures the total distance that you can quickly walk on a flat, hard surface within a period of 6 minutes.
e) The chair sit and reach assesses the lower body flexibility where you will sit in a chair, extend one leg in front of you and flex at the waist, reaching towards your toes, and we will measure the distance between your toes and fingers.
f) The timed 8-foot up and go is an assessment of speed, agility and balance. With this assessment, you begin in a seated position, and will be timed for the duration it takes to rise from the chair, walk as quickly as possible around a cone 8 feet away from the chair, and return to a seated position.
g) The back scratch test is an assessment of the flexibility of the upper body, where you will be seated and one arm will be flexed behind your head, and the other arm will be extended behind your shoulder. The assessment measures the distance between the fingertips of both hands.

Short Performance Physical Battery (SPPB): The short performance physical battery (SPPB) is a series of tests that measure balance, strength in the lower body, and walking speed. The short performance physical battery includes the following assessments:

a) To assess balance, you will stand once with your feet together, once with your feet slightly separated, and once with one foot directly in front of the other, for 10 seconds each time.
b) The repeated chair stand is an additional assessment of lower body strength. You will stand up and sit down from a chair as quickly as you can for a total of five times.
c) The 3-meter walk measures your walking speed. You will walk a distance of three meters at your typical everyday pace on a flat, hard surface.

4.) Wear Motion Sensors

At two time points (baseline and final visit) during the study, you will be asked to wear a waist-worn motion sensor for all your waking hours for 7 days. This sensor is used to objectively tell us about your overall physical activity, and the monitors are worn on a belt and are relatively unobtrusive.

5.) Participate in Video Calls

You will be asked to participate in scheduled video-based coaching calls over the course of the intervention. These calls will take 15-30 minutes and are intended to help you reach the study goals. All participants will complete weekly calls for the first five weeks, and then at week 6 you will have the choice of keeping the weekly calls (for a total of 12 calls) or switch to a taper call schedule where you will only meet every other week or less frequent (for a total of 8 calls). Participation in these calls is an important aspect to this study. The calls can be scheduled for a time that is convenient to you.

6.) Participate in the Exercise Program

You will be asked to participate in two sessions of home-based strength training per week, each session having 8 exercises with 2-3 sets of 8-12 repetitions at an appropriate intensity. These are exercises that strengthen the muscles of the body, including exercises like a biceps curl, a squat, a chest press, or a calf raise, all of which you can do at home with the exercise equipment that we will provide. You will be asked to log, track, and report all exercises you complete over the course of the study. You will be able to keep your exercise equipment after the study is over.

We will also ask that you increase your aerobic exercise over the course of the study using the study-provided Fitbit device. You can track your steps and active minutes, with the goal of achieving 150 minutes per week of activity. This amount is recommended by many research and health organizations including the American Cancer Society. You will be asked to log, track, and report all aerobic exercise via logs that you will complete over the course of the study. This log tracking is in addition to wearing the Fitbit device.

7.) Complete the Post Study Satisfaction Survey

Once you have completed all study components after the final visit, we will email you a brief survey to assess your experience and satisfaction with our intervention. We would like to know what parts of the study you liked, how did you find your interactions with our research staff, and what would you improve for the future. This survey allows us to improve our approach for future studies, and your opinions shared will be held anonymously.

HIPAA Information

From your medical records and health records kept by the University of Iowa, we will collect/access the following data:

-Details of your endometrial cancer diagnosis including date of diagnosis, tumor stage, recurrence, tumor type, treatment(s) received and dates of treatment.

This information will be used to describe the types of participants in our study, and they will only be reported as a group meaning no individual level data will be reported.

Your information collected as part of the research, even if identifiers are removed, will not be used or

distributed for future research studies.

WILL I BE NOTIFIED IF MY BIOSPECIMENS RESULT(S) IN AN UNEXPECTED FINDING?

The results from the biospecimens we collect in this research study are not the same quality as what you would receive as part of your routine health care. The biospecimens results will not be reviewed by a physician who normally reads such results. Due to this, you will not be informed of any unexpected findings. The results of your biospecimens will not be placed in your medical record with your primary care physician or otherwise. If you believe you are having symptoms that may require care, you should contact your primary care physician.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Endothelial function Test: Inflating the blood pressure cuff just below your elbow during this test may cause a moderate intensity pain "pins and needles" or numbing sensation that goes away as soon as the cuff is deflated.

Blood Pressure: The researchers measure blood pressure with the method used in a doctor's office and they can use a machine. A cuff inflates on the upper arm. As the cuff slowly deflates, the researchers listen with a stethoscope at the bend in the elbow or the machine takes a reading. During the short time the researchers inflate the cuff, your arm may feel numb or tingly. The cuff could cause mild bruising.

Blood Draw: Blood draws often cause mild pain, bruising, swelling, or bleeding. There is also a slight chance of infection or a small clot. If you are nervous about needles, your blood pressure and heart rate may increase for a little while. You may also feel lightheaded, sick to your stomach, or may faint. Using the same techniques used in hospitals keeps the chance of infection minimal.

Exercise and fitness testing: Exercise and physical activity have a risk of acute injury or musculoskeletal soreness. We have minimized our risks as much as possible, and will provide you with a guided, graded exercise program to ease into exercise.

Potential long-term risks: There are currently no known rare, serious risks related to exercise that are not listed above. Participants could suffer an acute musculoskeletal injury because of exercise, but individuals can recover from those events, although they are not good events.

There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

WHAT ARE THE BENEFITS OF THIS STUDY?

You will not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because the knowledge gained will contribute to the scientific knowledge aimed at understanding the potential benefits of exercise for improving vessel health in endometrial cancer survivors.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You may also need to provide your address if a check will be mailed to you.

You will receive $100 for participating in this study. A $50 check will be sent after the baseline visit, and an additional $50 will be sent after the final visit.

Parking will be provided for all visits.

You are allowed to keep all exercise materials (dumbbells, bands, Fitbit) regardless of your choice.

WHO IS FUNDING THIS STUDY?

The University and the research team are receiving no payments from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will take extensive measures to ensure the safety and security of your data. All study staff will complete IRB/HIPAA training prior to having contact with participants or with study data. Paper files will be kept in a locked file cabinet in the PI's lab in the Iowa Bioscience Innovation Facility (115 S Grand Ave, Iowa City, IA 52240). The office door is always locked. Any electronic data, including the data we receive from the devices we will ask you to wear for monitoring your activity, are kept on a sever maintained by the University of Iowa Technology Services. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires your health care provider to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study. Once your health care provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research related. Your signature on this Consent Document authorizes your health care provider to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to Dr. Jess Gorzelitz via email (Jessica-gorzelitz@uiowa.edu) or via postal mail at Room 110 IBIF, 115 S Grand Ave, Iowa City IA 52240. However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

If you decide to leave the study early, we will ask you to notify the research staff. If possible, we would like to know the reason for withdrawing, although this is not required. If you do not complete the final study measures, you will not be paid the $50 final visit compensation.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: **Jessica Gorzelitz (319) 467-0849.** If you experience a research-related injury, please contact: **Jessica Gorzelitz (319) 467-0849.** You may also email her at Jessica-gorzelitz@uiowa.edu at any time with any questions or concerns.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

_____	_____
(Signature of Subject)	(Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)