Cover Page for ClinicalTrials.gov

Official Title of the Study:

Sex-specific Adaptation to Different Resistance Exercise Programs in Older Adults

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Consent Form for Participation in a Research Study
University of Massachusetts Amherst

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Study Title: **Sex-specific adaptation to different resistance exercise programs in older adults**

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1. WHAT IS THIS FORM?

This form is called a Consent Form. It will give you information about the study so you can make an informed decision about participation in this research.

This consent form will give you the information you need to understand why this study is being done and why you are being invited to participate. It will also describe what you will need to do to participate and any known risks, inconveniences or discomforts that you may have while participating. We encourage you to take some time to think this over and ask questions now and at any other time. If you decide to participate, you will be asked to sign this form and you will be given a copy for your records.

2. WHO IS ELIGIBLE TO PARTICIPATE?

To participate in this study, you must be healthy, relatively sedentary and 65-75 years of age. You may not have any of the following: neurological or neuromuscular disease; a history of stroke, peripheral vascular disease, cardiac or pulmonary disease; or have a history of any metabolic diseases/disorders such as diabetes. You may not have any metal implants or anything that would prevent you from undergoing a magnetic resonance imaging (MRI) exam. You may not have a health condition or be using medication that would prevent you from having a muscle biopsy performed. You must be non-smoking and weight-stable (change in body weight < 2.5 kg during the past 3 months). Finally, you must not be currently participating in an exercise or weight loss program.

3. WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to better understand how different resistance exercise training programs impact skeletal muscle function in older men and women. Physical function declines with age, and a key predictor of this decrease is the reduction in leg muscle power (product of force and velocity), which can be improved with exercise training. However, at this point, it is not clear what the best type of resistance training exercises are for older men and women, and this is partly because men and women can respond differently to the same exercise program. Therefore, we will determine how distinct resistance training programs affect leg muscle composition and function, and see if men and women respond differently to these exercise programs.

4. WHERE WILL THE STUDY TAKE PLACE AND HOW LONG WILL IT LAST?

For this research study, you will be asked to complete 7 testing visits (4 at baseline and 3 following the exercise program) for approximately 10-12 hours at the Human Testing Center on the University of Massachusetts Amherst campus. In addition, you will be asked to complete 3 resistance exercise training sessions per week for 16 weeks (3 per week x 16 weeks = 48 total training sessions) at the Totman Building. We expect the duration of each exercise session to be less than 1 hour. Therefore, we expect

the total time commitment for this study to be approximately 60 hours (12 hours of testing + 48 hours of training sessions).

5. WHAT WILL I BE ASKED TO DO?

Visit 1 (1 hour): Paperwork and Anthropometrics

Upon arriving at the Human Testing Center at the University of Massachusetts-Amherst, you will be asked to read this Informed Consent document. During the first visit, laboratory personnel will review the informed consent document with you and answer questions. Once consenting is complete, you will be asked to fill out the study questionnaires (PAR-Q+, Health History Questionnaire and MR Safety Screening Questionnaire) and sign a release form allowing us to send a letter to your personal physician clearing you to participate in the study. These procedures have been standard practice in Dr. Kent's lab for the past 15 years. After you complete these questionnaires, we will measure your height, body mass, blood pressure and heart rate. Lastly, you will be issued an activity monitor and provided with instructions on how to wear it and fill out activity logs for a period of 7 days.

Visit 2 (3-4 hours): Body Composition, Blood Draw and Muscle Biopsy

During your second visit, we will measure your body composition using MRI and dual-energy X-ray absorptiometry (DEXA). Both of these tests will determine the quantity of muscle and fat in your body. We will measure the composition of your thigh with MRI. Before entering the magnet room, we will review your MR Safety Screening Questionnaire, have you remove all jewelry, and change into paper scrub pants. We will then scan you for metal using a hand-held metal detector. Next, you will be escorted into the Magnet Room, where you will be positioned in the scanner on your back, with your head on a pillow and your arms resting comfortably at your side. We will lay a mat or circular coil on one of your thighs and slide you into the center of the magnet. This mat/coil will be used to obtain images of your thigh muscles. This will take about 20 minutes. We will then remove you from the magnet and place the mat/coil on your other leg. We'll then move you back into the magnet and repeat the MRI scans; this process will also take approximately 20 minutes. It will be important that you not move during the scanning. For the measures of both thighs, we will use Velcro straps to secure your feet so that you do not move in the event that you fall asleep during the study. Headphones will be provided to you to limit the amount of noise from the scanner, and to enable clear and constant communication between you and the investigators. We will talk with you and let you know when each set of measures will begin, and how long they will take. We will also measure your overall body composition using a DEXA scan. For this test, you will lie on an examination table, wearing a hospital gown, while the machine scans your entire body with a low-level X-ray. The measurement takes approximately 10 to 15 minutes depending on your height and weight.

You will also be asked to undergo a blood draw (to examine testosterone and dihydrotestosterone levels in men and estradiol levels in women) of 30 ml (~2 tablespoons) and biopsies of the thigh muscle from your right and left legs. You need to be fasted (no food, but you can drink as much water as you like) for at least 8 hours before both of these procedures. The biopsy procedure allows us to obtain muscle tissue to test the function of the individual fibers that make up your muscles (muscle fibers are 'cells' that make up your muscles). Because we expect the function of your muscle fibers to change as a result of the exercise training, it is necessary to perform a biopsy at baseline and then after you complete the exercise program. However, because you will be performing different types of resistance training exercise with your left and right legs, it is necessary for us to test the function of muscle fibers from each leg to determine if they are different. For example, if your left leg is assigned to traditional resistance training and your right leg is assigned to power training, we want to determine how the

function of muscle fibers in each leg changes following the programs. The details of the muscle biopsy are described below.

You will be instructed not to consume any anti-inflammatory drugs (i.e. Ibuprofen or aspirin) or any aspirin-containing drugs such as Alka-Seltzer, Pepto-Bismol, or certain decongestants that contain anti-inflammatory drugs (i.e. Dristan) within 4 days of the muscle biopsy to reduce risk of bleeding. You will be given a telephone number that may be used to reach the Muscle Biology Laboratory. If you are unsure as to whether a medication you intend to take contains aspirin, it is strongly advised that you call one of the study investigators before taking the medication.

A trained physician will perform the needle biopsy procedure, which involves the removal and examination of a piece of muscle tissue. The muscle biopsy will be obtained under local anesthesia. A small incision (about 1 cm) is made into the skin and fascia. To take a biopsy, a needle is then inserted into the muscle. A small "plug" of tissue remains in the needle when it is removed from the muscle. This is about the size of 2-3 grains of rice. More than one needle insertion may be needed to obtain a large enough specimen for testing and examination.

The muscle that we will biopsy is the outer thigh muscle at a location of about mid-way between the knee and hip. You will feel some pressure or "tugging" sensations. Many people experience mild discomfort, but some subjects find the biopsy procedure painful. If there is pain, the physician will provide more anesthetic to the area to reduce the pain. The anesthetic is called Lidocaine (like Novocaine) and may burn or sting when injected (before the area becomes numb). After the anesthetic wears off, the area may be sore for about a week and may limit your activity. The risks are small and may include the following: infection (a slight risk any time the skin is broken), bleeding of the site, hematoma (blood collected beneath the skin that under very rare conditions could require surgery), bruising of the area, and damage to the muscle tissue or other tissues in the area (very rare). These risks are very low because there are no big blood vessels near the biopsy site and because the muscle tissue usually stops any bleeding by pressing against itself. Also, studies have shown that the muscle rapidly repairs itself after the biopsy. It is possible that you may have temporary numbness around the biopsy site for several days to weeks. At the biopsy site, a small scar about 1 cm long or less could result, but usually this will fade in time. Risks are minimized by having a trained and qualified medical physician perform the biopsy.

Visit 3 (45 minutes): Biopsy Sites Check and Dynamometer Familiarization

Three to four days after your biopsies, you will come to the Human Testing Center so we can check your biopsy sites. These checks will be performed by Dr. Miller and/or trained members of his laboratory. At this time, you will also become familiar with the dynamometer that will be used during Visits 4 and 5 to measure your leg muscle strength and power. This will involve extending and flexing your legs at different speeds while in a seated position until you are comfortable performing this task.

Visit 4 (1.5-2 hours): Leg Strength, Physical Function and Start of Exercise Training Program

During your fourth visit, we will measure your leg muscle strength and power using a dynamometer. We will test the strength of your right and your left legs. For these tests, you will be asked to extend and flex your leg several times while in a seated position. For each leg, you will be asked to perform this movement at 7 different testing speeds, and each speed will require 3 repetitions (7 speeds x 3 repetitions = 21 repetitions). In addition to the voluntary contractions, electrical stimulation will be used to examine muscle activation. For this test, two self-adhesive electrode pads will be attached to your thigh, one near your knee and one at the top of your thigh. These pads will briefly (0.5 s) stimulate your thigh muscle and make it contract. This procedure will be performed several times until the current produces a muscle contraction that is about half the strength of your maximal voluntary contractions. Collectively, the leg muscle strength tests take approximately 30 minutes to complete. You will also be

asked to complete the Advanced Short Performance Physical Battery (SPPB-A) to assess mobility function. The SPPB-A includes a short walk, static and dynamic balance assessments, and repeated chair stands. You will also be asked to complete the single-step test (SST) to measure limb performance unilaterally. To perform the SST, you will be asked to stand on one leg (test leg) on a 15 cm high, single step and must touch the ground with your other leg by performing a squat with the test leg and then return to the standing position. During this visit, we will also familiarize you with the muscle strength testing procedures on the dynamometer. Following the completion of the physical function tests, you will begin the exercise training program.

Exercise Training Program
After you complete the 3 baseline testing visits, you will begin the resistance training exercise program at the Totman Building. The exercise program will last 16 weeks and you will be asked to complete 3 training sessions per week. Thus, you will be asked to come to the Totman Building for 48 exercise training sessions (16 weeks x 3 sessions/week). We expect each training session to be < 1 hour in duration. During the first training session, you will have your dominant or non-dominant leg randomly assigned to traditional resistance training (TRT) and the other leg assigned to power training (PT). For the TRT program, you will train at 80% of your one-repetition maximum (1-RM) for 3 sets of 8 repetitions. For the PT program, you will train at 40% of your 1-RM for 3 sets of 16 repetitions. Both of the training programs will include 3 lower-body exercises: 1) leg press; 2) knee extension; and 3) knee flexion. Each exercise will be performed for TRT for one leg and then for PT in the other leg before moving on to the next exercise. Prior to and at the end of each exercise session, you will warm-up/cool-down on an exercise bike for 5 min.

Visit 5 (1.5-2 hours): Physical Function and Leg Strength Tests
Approximately one-week before completing the 16-week exercise training program, you will be asked to complete the same tests that you did during Visit 4.

Visit 6 (3-4 hours): Body Composition, Blood Draw and Muscle Biopsy
After completing the 16-week exercise training program, you will be asked to undergo body composition tests (MRI and DEXA), a blood draw, and biopsies of the thigh muscle from your left and right legs, similar to Visit 2.

Visit 7 (5 minutes): Biopsy Site Check
Two to four days after your biopsies, you will stop by the Human Testing Center so we can check your biopsy sites. These checks will be performed by Dr. Miller and/or trained members of his laboratory.

Total compensation for this study can be $500.

Visit	Description	Time Commitment	Compensation
1	Complete Paperwork and Anthropometrics	1 hour	$20
2-4	Complete Baseline Testing	4.5-6 hours	$160
	Complete Exercise Training Program	48 hours	$160
5-7	Complete Post-training Testing	4.5-6 hours	$160

6. WHAT ARE MY BENEFITS OF BEING IN THIS STUDY?
You may not directly benefit from this research. However, participation in the exercise training program may increase the strength and power of your leg muscles, which could improve activities of daily living.

Ultimately, we hope that your participation in this study will help us better understand how different exercise programs impact skeletal muscle health in older men and women.

7. WHAT ARE MY RISKS OF BEING IN THIS STUDY?
All the research procedures outlined above will be supervised by trained personnel who will monitor you on a regular basis.

Blood pressure measurement, questionnaires and activity monitoring have no associated risks.

MRI
The United States Food and Drug Administration (FDA) has established guidelines for magnet strength and exposure to radio waves, and we carefully observe those guidelines. No ill effects have been reported for the radio wave exposure associated with this protocol. Some people may feel uncomfortable or anxious while in the MR scanner, which is a large magnet. If this happens to you, you may ask to stop the study at any time and we will take you out of the scanner. On rare occasions, some people might feel dizzy, get an upset stomach, have a metallic taste, feel tingling sensations, or experience muscle twitches. These sensations usually go away quickly but please tell the research staff if you have them.

MRI poses some risks for certain people. If you have a pacemaker or certain types of metal objects inside your body, you may not be in this study because the strong magnet might harm you. Due to the strong magnetic field, another risk is a metallic object flying through the air toward the magnet and hitting you. To reduce this risk, we require that all people involved with the study remove all metal from their person and all metal objects from their pockets. Nothing metal can be brought into the magnet room at any time. Also, once you are in the magnet, the door to the room will be closed so that no one accidentally brings a metal object near the magnet while you are in it.

DEXA
As outlined above, this study will require you to undertake a whole body DEXA scan for the measurement of body composition (% fat and % lean mass). During the scan you will be exposed to low amounts of ionizing radiation; these levels are approximately 2% of that you would be exposed to during a chest X-Ray or 5% of that you would receive from a cross-country airplane flight. In accordance with Massachusetts Department of Public Health guidelines, all DEXA scans are performed by a Certified Bone Densitiometry Technologist and under the prescription and review of Dr. Robert Licho of UMass University Health Services.

The investigators for this research project are not licensed or trained diagnosticians or clinicians. The testing performed in this project is not intended to find abnormalities, and the images or data collected do not comprise a diagnostic or clinical study. However, on occasion the investigators may perceive an abnormality. When this occurs, UMASS Amherst researchers will consult with Dr. Licho. If Dr. Licho determines that additional inquiry is warranted, the researcher will contact you. In such a case, you are advised to consult with a licensed physician to determine whether further examination or treatment would be prudent. Although the images or data collected for this research project do not comprise a diagnostic or clinical study, the images or data can be made available to you for clinical follow-up.

Blood Draw
Blood sampling has the possibility of causing infection at the site where the skin is broken, although this is extremely low. You may also experience some bruising and soreness at the site of the blood draw.

Muscle Biopsy
The muscle biopsy procedure may cause you some discomfort (burning feeling) from the local anesthetic. Additionally, although rare, it is possible that you may experience an allergic reaction to the lidocaine. During the incision and biopsy procedures, you should feel minimal or no pain. You may experience mild muscle cramping when the biopsy sample is taken. For a day or two after the procedure, your leg muscle may be sore at the biopsy site. Volunteers have described that this pain is similar to having a 'charlie horse' in your thigh muscle. The primary risk involved in this procedure is infection at the site where the biopsy was taken. The possibility of an infection occurring is very low. All equipment used will be sterile and every precaution will be taken to reduce the possibility of infection. Notably, chances of an untreated infection are remote, as there is one follow-up visit planned post-biopsy to examine the incision. There is a possibility of a scar tissue forming at the ~1 cm biopsy incision site. Finally, risk will be minimized by having a trained and qualified clinician perform the muscle biopsy.

Muscle Strength Testing and Exercise Training
Muscle strength testing and exercise training may cause muscle soreness or, in rare cases, muscle injury. The electrical stimulation portion of strength testing can be uncomfortable, but each stimulation is very quick (0.5 s). Appropriate warm-up exercises will be performed to prevent muscle injury prior to whole muscle functional testing and exercise training. During exercise training, the project coordinator will be present to ensure that the exercises are performed correctly so that the risk of pulls or strains is limited. In addition, there will be a slow acclimatization to the training programs for the first 3 weeks. However, during any type of exercise, there are potential health risks, along with the possibility of fatigue, cardiovascular events, and muscle soreness. The muscle strength testing and/or exercise training will be terminated if you show any contraindications (shortness of breath, chest pain, dizziness, etc.) or if you wish to stop at any time. If necessary, the 911 emergency response system will be activated.

8. HOW WILL MY PERSONAL INFORMATION BE PROTECTED?
The following procedures will be used to protect the confidentiality of your study records. The records and measurements obtained from this study are for research purposes only and will not be included in your medical records. Confidentiality will be maintained throughout the studies. All study data will carry an identifying code, not the actual participant's name to ensure confidentiality. A master key that links names and codes and any identifiable health information will be maintained in a separate and secure location. Identifiable data, including signed consent documents, and the master key will be kept separately from the study data, in a locked cabinet that can only be accessed by the investigators. All electronic data will be stored on a secure server and password-protected computers. The master key will be destroyed 6 years after the close of the study. Only Dr. Miller and/or Dr. Kent will have access to this data. At the conclusion of this study, the researchers will publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations.

Research resources generated with funds from this grant will be freely distributed, as available, to qualified academic investigators for non-commercial research. Final data will be shared primarily through peer-reviewed publication. Raw data will be considered for sharing under the rules indicated below. Raw datasets to be released for sharing will not contain identifiers. Data and associated documentation will be made available to users only under a signed and properly executed data-sharing agreement that provides for specific criteria under which the data will be used, including but not limited to a commitment to: 1) using the data only for research purposes; 2) securing the data using appropriate computer technology; and 3) destroying or returning the data after analyses are completed.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). 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); 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 NIH which is funding this project. 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.

9. WILL I RECEIVE ANY PAYMENT FOR TAKING PART IN THE STUDY?
You will receive $500, in the form of cash, if you complete this study. However, if you decide to withdraw from the study before completion, compensation will be prorated according to the table in section 5.

10. WHAT IF I HAVE QUESTIONS?
You are encouraged to ask questions about the study. The investigators will attempt to answer all of your questions to the best of their knowledge. The investigators fully intend to conduct the study with your best interest, safety, and comfort in mind. Please address any questions regarding the study to the Muscle Biology Laboratory. Our phone number is (413) 545-6084 or by email at UMassCHAMP@gmail.com. You may also address questions to Prof. Miller by calling him at (413) 577-4701 or by emailing him at markmiller@kin.umass.edu. You may also address questions to Dr. Chipkin by calling him at (413) 545-3352 or by emailing him at schipkin@kin.umass.edu. If you would like to speak with someone not directly involved in the research study, you may contact the Human Research Protection Office at the University of Massachusetts via email at humansubjects@ora.umass.edu; telephone (413) 545-3428; or mail at the Human Research Protection Office (HRPO), Mass Venture Center, 100 Venture Way, Suite 116, Hadley, MA 01035.

11. CAN I STOP BEING IN THE STUDY?
You do not have to be in this study if you do not want to. If you agree to be in the study, but later change your mind, you may drop out at any time. There are no penalties or consequences of any kind if you decide that you do not want to participate. If you decide to withdraw prior to finishing the study, you will still be compensated for the visits you completed, but not those that you have not completed.

12. WHAT IF I AM INJURED?
In the unlikely event of an injury resulting directly from participation in this study, we will do everything we can to assist you in seeking medical treatment. The University of Massachusetts-Amherst does not have a program for compensating subjects for injury or complications related to human subject research.

13. SUBJECT STATEMENT OF VOLUNTARY CONSENT

By signing this form, I am agreeing to voluntarily enter this study. I understand that, by signing this document, I do not waive any of my legal rights. I have had a chance to read this consent form, and it was explained to me in a language that I use and understand. I have had the opportunity to ask questions and have received satisfactory answers. A copy of this signed Informed Consent Form will be provided to me.

May we contact you about future studies that may be of interest to you? Only your name and contact information (phone number/email) will be kept.

☐ Yes ☐ No

May we use the sample from your blood draw for future research? Your de-identified specimen will be stored for up to 10 years after completion of the study in a -80°C freezer to ensure its stability and handled by the researchers of this study or trained personnel in their laboratories.

☐ Yes ☐ No

May we use the tissue sample from your muscle biopsy for future research? Your de-identified specimen will be stored for up to 10 years after completion of the study in a -80°C freezer to ensure its stability and handled by the researchers of this study or trained personnel in their laboratories.

☐ Yes ☐ No

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Participant's name Address

_____

Signature Phone Number Date

STUDY REPRESENTATIVE STATEMENT:

The investigator has read and understands the federal regulations for the Protection of Human Research Subjects (45 CFR 46) and agrees to comply with all of its clauses to the best of her ability. The investigator also pledges to consider the best interests of the subject beyond the explicit statement contained in the aforementioned federal regulations and to exercise professional expertise to protect the rights and welfare of the subject.

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Name of Person Obtaining Consent

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Signature of Person Obtaining Consent Date