ACES - ACE Inhibitors Combined With Exercise for Seniors With Hypertension (ACES)

7/25/24

NCT03295734

UAB IRB
Approved
26-Jul-2023
until
25-Jul-2024

CONSENT FORM

Title of Research: ACES – Ace Inhibitors Combined with Exercise for Hypertensive Seniors

UAB IRB Protocol #: IRB-300000637

Principal Investigator: Thomas Buford, PhD.

Sponsor: National Institutes of Health

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of this study is to see if regular exercise when combined with one of three commonly used high blood pressure medications can improve the physical abilities of older adults to perform their daily life activities and lowers their risk for heart disease.
Duration & Visits	You will come to the Center for 7 assessment visits over a 32 week period. For the exercise intervention, you will come to the Center 2x/week for 20 weeks total (weeks 6 -26).

Overview of Procedures	If you decide to take part in this study, a computer will assign you by chance to one of three blood pressure medications. This is called randomization. You will either be assigned to perindopril, losartan or HCTZ. Participants are asked to track their physical activity habits, take their blood pressure medication daily, and test their blood pressure three times daily on a study provided home blood pressure monitor. During assessment visits, participants perform physical performance tests, questionnaires outlined in detail below. You will also be asked to check your blood pressure at home using the blood pressure monitor provided to you three times each day and report any abnormal values to study staff as soon as possible. The exercise intervention involves treadmill walking, stationary biking, and rowing followed by a balance and stretching routine. For home-based activity, you will be encouraged to perform walking at a moderate intensity throughout the duration of the study. You will also be asked to wear the hip worn physical activity monitor provided to you throughout the study period to monitor home-based activity.
Risks	The most common side effects of the study medications include excessive drops in blood pressure that can lead to dizziness, fainting, headache, drowsiness or falls. Other symptoms may include cough, weakness, sore throat, upset stomach, swollen ankles, hands or feet, flushing, confusion, breathing problems, weakness or heaviness of legs, or localized photo sensitivity rash could occur when exposed
	to UV light and rarely a systemic rash. With fasting, you may experience hunger, headache, and low energy. The risk of blood draw include discomfort from the needle stick and possible bruising. You may have some pain and soreness associated with the exercise training, and there is the risk of radiation exposure associated with the DXA scans.
Benefits	Potential benefits of this study to you include learning information about your health and overall physical function. Information gained from participation in this study may help to provide doctors with new information for prescribing medications to treat older adults for high blood pressure.
Alternatives	The alternatives is to not participate in the study.

Purpose of the Research

The purpose of this research study is to see if regular exercise when combined with one of three

commonly used high blood pressure medications can improve the physical abilities of older adults to perform their daily life activities and lowers their risk for heart disease.

You are being asked to be in this research study because you are over 60 years of age, have high blood pressure and also have some trouble performing your day to day activities.

The National Institute of Health has provided financial support to conduct this study.

There will be about 213 people enrolled in the full study. 107 people will be enrolled at the University of Colorado and Translational Research Institute for Metabolism and Diabetes, and 107 people will be enrolled here at the University of Alabama at Birmingham (UAB). However, should recruitment be slow at any site, recruitment targets will be adjusted to allow the other sites to perform additional recruitment.

How long will you be in the study?

You will be in this study for about 32-36 weeks. However you can withdraw at any time.

Explanation of Procedures

No procedures in this study will be part of your normal clinical care. Tests done only for research purposes will not be evaluated or used to diagnose or treat any of your medical problems. These tests may need to be repeated if required for your medical care in the future.

A telephone screening indicated that you may be eligible to participate in the study. The first study visit (Screening visit) will further determine if you are eligible to participate. Should you be eligible, you will be asked to participate in a structured physical activity (exercise) program for 20 weeks and take daily medication to control your blood pressure. There will also be 6 weeks before and after the exercise program to look at the effects of the medication alone. You will also be asked to return to the clinic for several additional assessment visits to monitor your safety and measure study results. Visits for the study and the physical activity program will take place at the Orthopedic Specialties Building, 133, University of Alabama at Birmingham. 1313 13th Street South, Birmingham, AL 35205 (UAB Center for Exercise Medicine). Due to COVID-19 some of the research procedures such as the written consent process, the assessment visits and its questionnaires, the exercise intervention and, the research procedures location may be adjusted and/or conducted remotely, if necessary.

Blood and urine samples will be collected during the study in order to help us to determine your eligibility and safety to participate and continue in the study and also to determine the effects of the

study medication. You will be asked to fast (not eat anything for at least 8-12 hours) before blood and urine sample collection. After we collect your blood and urine samples we will provide you a snack to eat before you continue with your other visit procedures.

SCREENING VISIT (STUDY VISIT # 1):

The screening visit will take 2 to 3 hours of your time. Details of study procedures that will be done during this visit are listed below. The order of these procedures may vary based on the schedules of study staff.

Written Consent: Before any tests or procedures are done, you will be asked to give written consent to participate in this research study. The study team member will explain in detail what is involved in the study and answers any questions that you may have. If you decide to participate we will ask you to sign this consent form. If necessary, the study team member will email/mail the written consent form and schedule a meeting with you via telephone/ video to explain the details of the study and answer any questions you may have. If you decide to participate we will ask you to sign this consent form and bring it with you in the screening visit. After your consent, the following would be done:

Questionnaires: You will be asked to answer questionnaire for personal information, medical history and medication use.

Office blood pressure (sitting + standing): You will be asked to stand and sit while having your blood pressure tested.

Other vital signs: We will record your pulse.
Collection of fasting blood and urine samples: We will collect approximately 2 tablespoons of blood from a small vein in your arm and your urine sample.

Anthropometry: We will measure your height, weight, body mass index (BMI).
Electrocardiogram (ECG): An ECG will be performed for safety purposes and will be read by the study clinician after completion of the screening visit. ECG procedure involves having sticky pads placed on your chest to measure your electrical heart rhythm. If for some reason you are ineligible based on this test, you will be called to inform prior to scheduling a baseline visit and advise you if any follow up evaluation is recommended.

Physical exam: Our study clinician will also give you a short physical exam to determine if it is safe for you to participant in the study.

Tests of physical performance: You will be asked to complete tests of your physical ability that include: Walking at your fastest pace a distance of about ¼ of a mile (400 meters) which is roughly equal to the length of around 4 and half football fields

The study clinician team will look at the tests performed during the screening visit and determine if you are eligible and it is safe for you to participate in the study. The study team member will call you to let you know if you are eligible or not to participate in this research and to schedule your next visit if you are eligible.

BASELINE VISIT AND RANDOMIZATION (STUDY VISIT # 2):

This visit is expected to take 2 to 3 hours of your time and will include:

- Measurement of pulse and blood pressure
- Collection of fasting blood sample
- Tests of physical performance, including:
  - Walking as fast and far as you can for 6 minutes
  - Walking at your usual pace for a distance of 13 feet two (2) separate times
  - Standing from a seated position without using your arms five (5) times as fast as you can.
  - Holding your balance while standing in three (3) different positions.
  - Complete the Quick Food Scan and health-related quality of life questionnaires
  - WOMAC pain sub-scale
  - Waist circumference
- Measurement of body composition (DXA Scan): Body composition will be measured with a test known as a DXA scan. DXA scans, like x-rays, are painless, and involve exposure to very small amounts of radiation. The scan takes less than 10 min, you will be asked to lie on your back while the special x-ray machine is scanning your body. You will be given a report of your scan (not to be used for diagnostic purposes), if you wish. Women who have had hysterectomy (uterus removal surgery), removal of both ovaries, who are postmenopausal, or no possibility of pregnancy, will not need a pregnancy test.
- Additionally, you will also be given the following to take home a blood pressure (BP) monitor with instructions for its use, a hip worn Fitbit physical activity monitor, to wear and instructions for its use.

After the completion of baseline assessments, you will be randomly assigned (like flipping a coin) to receive either one of three study medications to continue treating your blood pressure

Perindopril
Losartan
Hydrochlorothiazide (HCTZ)

You will be given the study medications to take home until your next study assessment visit.

These medications are all standard, FDA-approved medications for the treatment of blood pressure. During the time of your participation in the study, you will be told how to stop the use of your current blood pressure medication(s) and instead take the medication given to you for the study. You must carefully follow all instructions of taking your blood pressure medication given to you by the study team.

These study medications will be put into similar looking capsules by the study pharmacy so that neither you nor the investigators will know which medication you are taking. However, if any medical or other reason arises during the study to know exactly what medication you are taking, this information can be obtained from the study pharmacy by the study investigators or other physicians treating you.

You will also be asked to check your blood pressure at home using the blood pressure monitor provided to you three times each day and report any abnormal values to study staff as soon as possible. This monitor automatically records each blood pressure reading. You will be given instructions on how to use the monitor and you will also be asked to bring this monitor to each assessment visit so that study staff can download the stored blood pressure readings. We will ask you to return this monitor at the end of your study participation.

Please report immediately to the study team if you blood pressure reading is lower than 90/60 mm Hg or higher than 180/100 mm Hg. If you have such readings twice, you will be asked to come for an additional study visit and will be seen by the study provider.
It may be possible that the study physician indicates that you need nutritional supplement or another medication prescribed along with your assigned blood pressure medication to safely control your blood pressure. If this is this case, this supplement (Potassium Chloride 20 – 40 mg) or medication (Amlodipine 2.5, 5, or 10mg) will be provided to you by the study team.
It is also possible, that based on the study provider's advice, you will be taken out from the study for your safety. Your treatment will be changed back to the medications that you were taking before joining the study and you will be referred to your Primary Care Physician (PCP) to manage your high blood pressure. You must carefully follow all instructions given to you by the study team when returning back to your previous treatment of high blood pressure.

STUDY INTERVENTION:

Study interventions will be divided into 3 phases:

A. 6 week pre-exercise observational phase

B. 20 week structured exercise phase

C. 6 week post-exercise observational phase or close-out visit

[A] 6 WEEK PRE-EXERCISE OBSERVATIONAL PHASE:

In this phase, you will be started with a low dose of the medication for two weeks after which, if your study provider agrees, the dose will be increased. If the higher dose is not tolerated then you will be given the lower tolerated dose. For example if you are assigned to receive perindopril, you will be given an initial dose of 4 mg/day for two weeks after which, following approval of the study provider the dose will be increased to 8 mg/day. Similarly the dose increase for Losartan would be from 50mg/day to a maximum of 100 mg/day and for HCTZ would be from 12.5mg/day to a maximum of 25 mg/day.

Study staff will check your blood pressure during the study and any necessary adjustments to the medication will be made by the study clinician. Your PCP will be told about your enrollment in the study as well as of any medication changes by phone or fax.

Two study assessment visits will be done during this phase:

TWO WEEKS AFTER STARTING THE DRUGS (STUDY VISIT # 3):

This visit will take 45 minutes to 1 hour of your time and will include:

- Fasting blood draw and urine collection
- Measurement of vitals (body weight, pulse, blood pressure (sitting + standing)
- Collection of home BP monitor data and Fitbit data
- Questions about any bad experiences since starting the drug
- Providing you with study medications

COMPLETION OF 6 WEEK PRE-EXERCISE OBSERVATIONAL PHASE (STUDY VISIT # 4):

This visit will take 1 to 2 hours of your time and will include:

- Measurement of vitals (body weight, pulse, blood pressure (sitting + standing)
- Collection of fasting blood and urine sample

- Completion of physical performance tests which includes 4 meter walk test and a 6-minute walk test,
- Collection of home BP monitor data and Fitbit data
- Quick Food Scan questionnaire
- Positive and Negative Affect Scale (PANAS) and the Brief Pain Inventory (BPI)
- Questions about any bad experiences since starting the drug

[B] STRUCTURED EXERCISE PHASE:

During this phase in addition to taking the study drug, you will also take part in a 20 week structured exercise intervention. The intervention will include twice weekly, center-based, aerobic exercise as well as home-based walking. This intervention is designed to achieve a total of 150 minutes of aerobic activity per week.

Each center-based session will begin with a brief warm-up followed by moderate-intensity aerobic exercise including treadmill, stationary bicycle, and rowing machine exercises. . You will be introduced to the intervention exercises in a structured way such that you begin with lighter intensity and gradually increase during the first weeks of the intervention. You will also be asked to perform light stretching and/or balance exercises as a part of warm-up and cool-down for the session. The center-based exercise intervention may be re-adjusted due to extended interruptions due to COVID-19, if necessary.

During each exercise session, you will also be asked to wear a heart rate monitor to measure mean pulse during your exercise sessions. This will help to maintain moderate-intensity exercise and help to guide in advancing you through the protocol. Walking/cycling distance and grade will also be monitored during each session and you will be encouraged to increase the distance and grade each exercised session.

For home-based activity, you will be encouraged to perform walking at a moderate intensity throughout the duration of the study. You will also be asked to wear the hip worn physical activity monitor provided to you throughout the study period to monitor home-based activity. You will also be asked to return this monitor by the conclusion of this study.

Two study assessment visits will be done during this phase:

TEN WEEKS AFTER STARTING EXERCISE (STUDY VISIT # 5):

This visit is expected to take 1 hour of your time and will include:

- Measurement of vitals (body weight, pulse, blood pressure (sitting + standing)
- Collection of fasting blood and urine samples.
- Collection of home BP monitor data and Fitbit data
- Questions about any bad experiences since starting the drug
- Providing you with study medications, collect leftover medication

COMPLETION OF EXERCISE PHASE AT 20 WEEKS (STUDY VISIT # 6):

This visit is expected to take 1 to 2 hours of your time and will include:

- Measurement of vitals (body weight, pulse, blood pressure (sitting + standing)
- Collection of fasting blood and urine samples.
- Completion of physical performance tests completed at baseline.
- DXA scan for body composition, waist circumference measurement
- Collection of home BP monitor data
- Collection of physical activity monitor data
- Quick Food Scan questionnaire
- Positive and Negative Affect Scale (PANAS) and the Brief Pain Inventory (BPI)
- Questions about any bad experiences since starting the drug

[C] 6-WEEK POST-EXERCISE OBSERVATIONAL PHASE/CLOSE-OUT VISIT (STUDY VISIT #7):

This visit is expected to take 2 to 3 hours of your time and will include:

- Measurement of vitals (body weight, pulse, blood pressure (sitting + standing)
- Collection of fasting blood samples.
- Completion of physical performance tests which includes a 4 meter walk test and a 6-minute walk test.
- Collection of home BP monitor data
- Collection of physical activity monitor data
- Quick Food Scan and health- related quality of life questionnaires
- Collection of leftover study medication
- Questions about any adverse experiences since staring the drug and exercise

Risks and Discomforts

Risk of Randomization:
You will be assigned to a group by chance, which may prove to be less effective or to have more side effects than the other study group or alternatives.

Risk from study medications:
Risks include excessive drops in blood pressure that can lead to dizziness, fainting, headache, drowsiness or falls. Other symptoms may include cough, weakness, sore throat, upset stomach, swollen ankles, hands or feet, flushing, confusion, breathing problems, weakness or heaviness of legs, or localized photo sensitivity rash could occur when exposed to UV light and rarely a systemic rash.

These risks are similar to that which you would be exposed to during your normal use of blood pressure medications. Changing your blood pressure medication could also result in an increase or excessive drops in your blood pressure. Increases or excessive drops in your blood pressure may increase your risk of cardiovascular events such as stroke or heart attack.
The study team will closely monitor your blood pressure and laboratory blood tests to minimize the risks associated with the switching of your blood pressure medication and use of study medications that are possibly different from what you were taking before.

Risk of fasting:
The risks of short-term fasting include hunger, headaches, low energy, heartburn, bloating and constipation.

Risk of blood draw:
The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure.

Risk from Physical activity:
There may be some pain or soreness at the start of the study from increasing your physical activity. The possibilities include, but are not limited to, some muscle and joint stiffness. This stiffness generally subsides in 1 or 2 days, and is not considered to be serious. You might suffer an exercise-related injury such as a strain, sprain, or other injury to your muscles or joints. Other possible harmful physical responses include abnormal blood pressure, fainting, abnormal heart beats, and, in rare instances, heart attack, stroke, and death. Every effort is made to minimize these risks by reviewing information about your health before the activities begin. We will minimize the risks by showing you how to properly do the exercises in a safe manner and performing warm-up and cool-down exercises.

We will also monitor heart rate and blood pressure before and after your exercise sessions. You will also be encouraged to report and discuss any discomforts with members of the study staff.

There is also a risk of losing your balance and falling associated with the physical performance-based testing (e.g., walking and rising from a chair). A fall places you at risk of a bone fracture. We will minimize this risk by: (1) safely escorting you to chairs located along the walking course should you become unsteady; (2) following you at a close distance; and, (3) being at your side should you need assistance.

Risk from DXA Scan:

There is a low risk of radiation exposure from the two DXA scans. The radiation exposure from the two scans is equal to about 8 days of natural background radiation. A DXA scan is an x-ray scan that uses a very low level of radiation to measure your [bone density | fat content]. You will be asked to lie still on a table for about a minute while the scanner takes data. In this study you will be exposed to a very low level of radiation during the 2 DXA scans. Each DXA scan is equivalent to about 4 days of natural background radiation. Background radiation is radiation normally received from sources such as cosmic rays and natural radioactivity in building materials and the ground.

Loss of privacy:

There is a risk of loss of your confidentiality in research. We will, however, make every effort to protect your confidential information to minimize this risk.

Benefits

Potential benefits of this study to you include learning information about your health and overall physical function. Also, you will have the chance to have supervised exercise training and instruction about how to maintain physical activity habits at home. Participation in these activities has the potential to improve your health and quality of life.

Information gained from participation in this study may help to provide doctors with new information for prescribing medications to treat older adults for high blood pressure. The study may also provide scientists and physicians with new knowledge about how to prevent physical disability among older adults with high blood pressure.

Alternatives

The alternative is to not participate in this study. If you do not join, your care at UAB will not be affected.

Confidentiality

Information obtained about you for this study will be kept confidential to the extent allowed by law. However, research information that identifies you may be shared with people or organizations for quality assurance or data analysis, or with those responsible for ensuring compliance with laws and regulations related to research. They include:

- The UAB Institutional Review Board (IRB). An IRB is a group that reviews the study to protect the rights and welfare of research you.
- National Institutes of Health (NIH)
- The Office for Human Research Protections (OHRP)

The information from the research may be published for scientific purposes; however, your identity will not be given out.

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

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study clinician must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?

All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms

from past studies that might be in your medical record.

Who may use and give out information about you?
Information about your health may be used and given to others by the study clinician and staff. They might see the research information during and after the study.

Who might get this information?
All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections(OHRP)
- the U.S. Food and Drug Administration(FDA)
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there

is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the 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.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

What if I decide not to give permission to use and give out my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others, outside of UAB, without your permission.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed by UAB.

You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution. However, you should return to see the study provider for safety reasons so you can be taken off the study drug and referred for follow-up care. Contact the study staff at 205-996-3005 if you want to withdraw from the study.

You may be removed from the study without your consent if the sponsor ends the study, if the study provider decides it is not in the best interest of your health, if new information suggests that taking part in the research study may not be in your best interests or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study. All supplements, exams, and physical activity sessions related to this study will be given to you at no cost during the 8-month study period.

All other medical services provided to you that are not directly related to the study will be billed to you or your insurance company. You will be responsible for paying any deductible, co-insurance, and/or co-payments for these services, and any non-covered or out-of-network services. Some insurance companies may not cover costs associated with research studies. Please contact your insurance company for additional information.

Payment for Participation in Research

You can be compensated up to $450 total if all study visits are completed.
A gift card in the amount of $10 will be given at the completion of the screening visit.

If you are eligible and choose to participate, the gift card will be reloaded with a total of $40 upon completion of each additional study assessment visit. If you complete all 6 study assessment visits you can receive up to a total of $240.

After completing the exercise training period, you can receive up to a total of $200. In order to receive the full $200 you must complete all exercise training visits. This would make each exercise training visit $5 each and is paid in one lump sum upon completion.

Payment for Research-Related Injuries

UAB has not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

Significant New Findings

You will be told by the study provider or the study staff if new information becomes available that might affect your choice to stay in the study.

Optional Research

Please note: This section of the consent form is about optional research that is being done with people who are taking part in this study. These procedures will be used to provide more information on how your body adapted to the exercise + study medication. Please take as much time as you need to decide. You may ask any questions that you may have and discuss this with the study team (your study provider and his/her staff). You may take part in this optional research if you want to. You can still be a part of this study even if you say no to take part in any of the optional research.

Optional Research #1

These are additional procedures that ask you to complete two additional visits. During each of these two visits, you will be asked to complete a strenuous exercise test on a treadmill and provide a sample of muscle tissue collected via a procedure known as a biopsy and perform

the skeletal muscle function test. These additional visits for the exercise test, muscle biopsy, and skeletal muscle function test will occur after visit #2 at week 0 and visit #6 at week 26.

Explanation of Procedures

Muscle biopsy

A small piece about the size of a pencil eraser or "quarter of an inch" of muscle and/or fat tissue will be taken from your thigh. The muscle tissue will be taken from your vastus lateralis muscle which is located on the outside of your thigh and will be taken about one hand above your knee. A one inch by one inch area of hair may need to be shaved. We will inject an anesthetic (lidocaine) to numb the area. A small cut is made and a needle is inserted to pinch a piece of muscle for lab tests. The cut will be closed with a stitch and you will be told how to care for the area. This procedure will take about 30 minutes of your time.

Treadmill test

During this test you will be fitted with a mask that will collect inhaled and exhaled gases from your breath. The mask is placed over your nose and mouth and if you want we can show you the mask before you give informed consent. Then you will have sticky pads placed on your chest and asked to walk on a treadmill. You may hold onto the safety rails during the entire test.

First you will walk at a slow pace as a warm-up. After the warm-up phase, we will increase the elevation of the treadmill that may feel like walking up a hill which would make walking a little hard for you. We will ask you to walk as long as you can until you are too tired to continue.

The test will take around 10-20 minutes depending on how long you can walk on the treadmill. We will closely monitor your heart, breathing and blood pressure after the test so we make sure your values return to normal. If for any reason your heart rhythm becomes abnormal we will stop the test and ask you to take advice from your primary care physician.

Skeletal Muscle Function test

You will be asked to push your leg against a machine which pushes against you to measure the strength of your leg muscles.

Risks and Discomforts

Muscle Biopsy:

With the muscle biopsy procedure, there is a risk of bleeding, bruising, soreness, pain,

infection, and scarring of the skin. Bleeding could rarely result in development of a hematoma (deep tissue collection of blood). Pain and soreness usually resolves within 24-48 hours post-procedure. Numbness of the skin near the biopsy site may occur and is usually temporary, but this numbness may persist indefinitely.

Risk of anesthetic lidocaine:
You will be asked about any known lidocaine allergy to determine eligibility for the sub-study. Common side effects include numbness and tingling in the fingers and toes, swelling at the site of administration.

Treadmill Test:
There are risks associated with the exercise capacity testing on the treadmill. In general, treadmill testing is a relatively safe procedure. Anytime that you increase your heart rate there is a risk of heart complications. We will do screening tests to help protect you and we will monitor your heart during the test. However, there are no tests that can completely clear you from possible heart complications. If there is a complication, trained personnel monitoring the test will have the appropriate equipment and supplies to care for you.

During the test you may experience some sweating and breathing discomfort due the strenuous nature of the test. There is a risk of potentially tripping on the treadmill; however hand rails are in place to help to prevent falls. Plus, the glue that holds the pads to your chest may cause some mild irritation that will clear up in a day or two.

Skeletal Muscle Function test:
Risks from the skeletal muscle function test include muscle tightness, soreness or stiffness, fatigue, and possibly results in a strained muscle. This test will require physical exertion.

Voluntary Participation and Withdrawal

You can change your mind at any time about providing these muscle biopsy samples and allowing them to be used for this research.
You can request destruction of your samples by making a request to the study provider by calling study staff at 205-996-3005 and the sponsor will remove and destroy your samples. However, any data already generated from the samples will be kept to preserve the value of the research.

If you withdraw or are taken out of the main study at the discretion of the investigator or sponsor for safety, behavioral, or administrative reasons, any samples you have provided will

continue to be stored and used by the sponsor unless you tell the study provider you would like them to be destroyed.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no charge to you for collection of the optional biopsy samples used for this research.

Payment for Participation in Research

You will be paid a total of $300 in a gift card for completing all components at both visits (i.e. 2 treadmill tests, 2 biopsies, and 2 skeletal muscle function tests). You must complete all six of these procedures to receive compensation for this optional research. Initial your choice below:

___I agree to have my muscle biopsy samples collected and to take the treadmill test for this study.

__I do not agree to have my muscle biopsy samples collected and to not take the treadmill test for this study

Optional Research #2

These are additional procedures that ask you to complete at three study visits. At the end of these visits you will be provided a three-day diet record, a plastic container to supply a 24-hour urine collection and plastic container to supply a fecal sample. You will be asked to record everything you eat for the three days leading up to sample collection. Additionally, you will be asked to drink a sugar solution and to take the containers home and provide the 24-hour urine collection and a fecal sample. At the end of your 24-hour urine collection, we ask that you bring the containers with your collection to us as soon as possible. Once the fecal sample is collected, we ask that you bring your sample and diet record to us within one hour. We also ask that for the 2nd and 3rd collections you eat the same as you did for the first. The three-day diet recall,

24-hour urine collection, and fecal sample collection will occur after visit #4 at week 6, visit #6 at week 26, and visit #7 at week 32.

Explanation of Procedures

24-hour urine collection

You will be provided with containers to store your 24-hour urine collection, a smaller urine cup, and a cooler with ice packs to take home. You will be asked to collect all urine produced over the 24-hour time span specified using the smaller urine cup for collection and transfer to the containers. You will be asked to store the containers on ice packs in the cooler provided, or in a refrigerator. Once the 24 hours is over, you will be asked to bring the collection containers into the laboratory as soon as possible.

Fecal sample

You will be provided a three-day diet record prior to each sample collection. You will be asked to record what you eat for the three days leading up to the first sample collection. For the two subsequent samples you will be asked to consume the same items you did for the first collection. For each collection you will be provided with a cooler, ice packs, a plastic container, and a holder that fits over a toilet seat, to take home. Once sample collection is complete, you will be asked to immediately store the sample on ice packs in the cooler provided and bring the sample and diet record into the laboratory within 1 hour to ensure minimal degradation.

Risks and Discomforts

24-hour urine collection

Risks from the 24-hour urine collection are contamination of skin, clothing, and food with urine. The urine collection supplies are designed so urine can be collected with minimal discomfort. To help prevent risk, please was your hands after collecting your sample.

Fecal sample

Risks from the fecal sample collection are contamination of skin, clothing, and food with feces. Contamination with food could lead to food borne illness. The stool collection kit is designed so that the samples can be collected without touching the stools, however, there is a small chance this may occur. To help prevent risk please wash your hands after collecting your sample.

Voluntary Participation and Withdrawal

You can change your mind at any time about providing the 24-hour urine collection and fecal

samples and allowing them to be used for this research.

You can request destruction of your samples by making a request to the study provider by calling study staff at 205-996-3005 and the sponsor will remove and destroy your samples. However, any data already generated from the samples will be kept to preserve the value of the research.

If you withdraw or are taken out of the main study at the discretion of the investigator or sponsor for safety, behavioral, or administrative reasons, any samples you have provided will continue to be stored and used by the sponsor unless you tell the study provider you would like them to be destroyed.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no charge to you for collection of the optional fecal and urine samples used for this research.

Payment for Participation in Research

You will be paid a total of $225 in a gift card for completing all components of the fecal and urine sample collection (i.e. 3 fecal samples and 3 24-hour urine collections). You must complete all sample collections to receive compensation for this optional research.
Initial your choice below:

___I agree to have my urine and fecal samples collected

____I do not agree to have my urine and fecal samples

collected

Storage of Specimens for Future Use

As part of this study, we would like to store some of the blood and optional muscle biopsy specimens, and fecal samples collected from you for future research related to exercise and/or aging.

The future research may be conducted by the study provider or by other researchers that obtain IRB approval for their research. The specimens will be labeled with a code that only the study provider can link back to you. Results of any future research will not be given to you or your doctor. The specimens obtained from you in this research may help in the development of a future commercial product. There are no plans to provide financial compensation to you should this occur. You do not have to agree to allow your specimens to be stored in order to be part of this study.

You may request at any time that your specimens be removed from storage and not be used for future research. If you decide you want your specimens removed, you may contact the study provider. Once the request is received, and if your specimens have not already been used for other research, they will be destroyed. If you do not make such a request, your specimens will be stored indefinitely or until used.

____I agree to allow my specimens to be kept and used for future research on exercise and /or aging.

____I do not agree to allow my specimens to be kept and used for future research on exercise and /or aging.

Questions

If you have any questions, concerns, or complaints about the research, you may contact study staff at 205-996-3005. If the concern is related to a research-related injury including available treatments, please contact the study clinician at 205-996-0832. The study clinician oversees medical safety.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855- 860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agrees to participate in this study. You will receive a copy of this signed consent form.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date