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INFORMED CONSENT DOCUMENT

Title of Study: Comparison of the Cardiovascular Benefits of Resistance, Aerobic, and Combined Exercise (CardioRACE)

Main Investigator: Duck-chul (DC) Lee, funded by The National Institutes of Health

Study Staff:

- Project Manager: Angie Brellenthin, abrellen@iastate.edu, 515-294-6351
- Primary study team contact address: cardioRACE@iastate.edu, 515-294-7223

This is a research study. This document contains information to help you decide whether or not you wish to participate. Please feel free to ask questions at any time.

Introduction: The purpose of this study is to examine the effects of aerobic exercise, resistance exercise, and a combination of both aerobic and resistance exercise compared to a delayed, preferred exercise group on cardiovascular disease risk factors.

You are being invited to participate in this study because you are 1) 35-70 years old, 2) at risk for high blood pressure (120-139/80-89 mmHg) and not on hypertension medication, 3) a non-smoker, 4) overweight or obese (BMI 25-40 kg/m^2; Asian 23-40 kg/m^2), 5) inactive (not meeting the current guidelines of ≥150 min/week of exercise over the past 3 months), 6) have a smart mobile device and/or regular, reliable internet connectivity, and 7) you are willing to be randomized to any of the 4 treatment groups

You should not participate if you are currently pregnant or planning to be pregnant, have a pacemaker or other implantable device, have a history of heart attack or stroke, are planning on being away for more than 4 weeks over the next year, have severe depression, have had unexplained or irregular weight loss/gain of more than 5% body weight change over the past 6 months, or have any life-threatening medical condition or a condition that can interfere with or be aggravated by exercise training (e.g., autoimmune disorders, such as rheumatoid arthritis; uncontrolled diabetes mellitus). You should not participate if you have uncontrolled diabetes (HbA1c > 7.0%), unstable coronary heart disease, decompensated heart failure, severe pulmonary hypertension, aortic stenosis, uncontrolled arrhythmias, acute myocarditis, endocarditis, pericarditis, or aortic dissection.

Description of Procedures: If you agree to participate, you will be asked to participate in an orientation, 5 education sessions, a randomization visit, and baseline, 6-month, and 1-year examinations in addition to exercise sessions 3 times per week (unless assigned to the delayed, preferred exercise group):

- Orientation (45 minutes): Complete a questionnaire about your medical history, lifestyle, and physical activity. We will also assess your blood pressure and body composition during the orientation. Peripheral blood pressure will be assessed in a seated position with a blood pressure cuff placed around your upper arm. Body composition will be assessed using bioelectrical impedance, which can assess the composition of various tissues in the body by determining their resistance to an electrical current. You will stand on a platform and hold onto handles. You will not feel the current flow through your body and the procedure is fast (< 2 minutes), completely safe, and painless.
- Two weeks of 5 education sessions (30-45 minutes in each session): healthy lifestyle education, dietary counseling, diet recall instructions, exercise education, and blood pressure measurement in each education session.

- Two days of baseline examinations (total 140-155 minutes):
  - First day (65-70 minutes):
    - Height, weight, and waist circumference measurements
    - Complete questionnaires related to past and current physical and mental health, medications, and lifestyle behaviors
    - Measure central blood pressure, peripheral blood pressure, and arterial stiffness: Central blood pressure and arterial stiffness will be assessed while lying down. A cuff will be placed around your upper thigh and a sensor will be applied to the side of your head. The procedure is painless. Peripheral blood pressure will be assessed in a seated position with a blood pressure cuff placed around your upper arm.
    - Bone mineral density and body composition: These will be assessed using dual-energy x-ray absorptiometry (DXA). You will lie down on a table while a scanner passes over your body. The procedure is painless; however, women will be asked to complete a Pregnancy Risk Acknowledgement questionnaire prior to the DXA scan. If you are a woman with child-bearing potential (i.e., having menstruated at least once in the past 12 months), you will be administered a urine pregnancy test as a safety measure to ensure that no pregnant woman is exposed to x-rays. A positive pregnancy test will exclude you from future participation. You will also be asked whether you have had unprotected sex in the 14 days prior to the scan, as pregnancy tests are not reliable in the first 14 days after conception.
    - Blood draw: 24 ml (approx. 5 teaspoons) of blood will be drawn from a superficial arm vein by a trained and experienced phlebotomist after a 12-hour fast for blood lipids, inflammatory markers, and glucose tests.
    - Optional: A 3D body scan. You have the option of having your body scanned for a segmental body composition and postural analysis. You will stand on a platform behind a privacy screen in your swimsuit or underwear and hold onto handles while the platform rotates 360 degrees. Your body scan results will be immediately available to you.
  - Second day (75-85 minutes):
    - Graded treadmill test: Cardiorespiratory fitness will be assessed with a graded treadmill test under a physician's supervision. You will wear a heart rate monitor and breathe through a facemask attached to a tube, which will measure your expired gases. You will begin walking on the treadmill at 3.3 mph with a 0% incline, 2% incline after 1 minute, then 1% increase per minute with the speed fixed at 3.3 mph until 25 min. If you are uncomfortable walking at an increased rate (i.e., up to 3.3 mph) we will use your highest comfortable walking speed to conduct the fitness test. After 25 min, the speed will be increased 0.2 mph each minute until you can no longer continue and request to stop.
    - Muscular strength tests: After being familiarized with the equipment, taught proper technique, and a warm-up, you will do several submaximal repetitions with a spotter using bench and leg press machines. Weight will be increased progressively by 5 pounds until you cannot complete a full repetition.
    - Diet log software training: You will register your study ID with the dietary tracking system (ASA24, provided by the National Cancer Institute). You will receive instructions to complete the diet log three days per week (1 week per month) as prompted by the software.
    - You will receive a pedometer and instructions on how to use it to log your steps. You will wear the pedometer on your body for the entirety of the intervention (i.e., all 12 months), and report your steps on a weekly basis to study staff.

- Following the two baseline examinations, you will be randomized to one of four groups: 1) aerobic exercise only, 2) resistance exercise only, 3) combination of aerobic and resistance exercise, or 4) a delayed, preferred exercise group. Preferred exercise group participants will be offered the supervised exercise program of their choice for 1 year (in second year) following the 1-year intervention period. Individuals in all groups will complete their 3-day diet logs (1 week per month),and record their daily step counts (reported on a weekly basis via text message, email, or phone) for the whole year. All exercise programs will be prescribed based on individual fitness levels and monitored by a computer-controlled exercise training system (Technogym Wellness System).
    - Aerobic exercise only group: Train 3 days per week for 1 year. Each session will be 60 minutes in length during which you will ride a stationary exercise bike, exercise on the elliptical machine, or walk/jog on the treadmill at a moderate-to-vigorous intensity (gradual progression).
    - Resistance exercise only group: Train 3 days per week for 1 year. Each session will be 60 minutes in length in which you will perform 3 sets of 8-15 repetitions of 12 exercises for the major muscle groups using weight training machines.
    - Aerobic and resistance exercise group: Train 3 days per week for 1 year. Each session will be 60 minutes in which 30 minutes will be allocated to aerobic exercise, and 30 minutes allocated to resistance exercise. The protocol for the aerobic exercise will remain the same as above, but being half the time. For resistance training, you will perform 2 sets per exercise with 8-15 repetitions of only 9 exercises to account for the time difference.
    - Preferred exercise group: No exercise training in first year; however, you will submit copies of your daily reported steps on a weekly basis. You will be offered the supervised exercise program of your choice after 1 year.
- After 6 months (mid-intervention) and 1-year (post-intervention), you will complete the same two days of examinations (155-175 min total at each the 6-month and 1-year assessment point) that were conducted in the baseline sessions including height, weight, waist circumference, questionnaires, blood pressure, arterial stiffness, bone mineral density, body composition, fasting blood draw, graded treadmill test, and muscular strength tests. You will also receive a 15-20 minute in-person, individualized dietary counseling session and refresher course.
- You will be offered additional 15-20 minute in-person, individualized dietary counseling sessions at 3 and 9-months with a registered dietitian. These sessions will be available to all participants, no matter their treatment group, and will offer the opportunity to check-in with the dietitian and create a DASH diet goal. If you choose to attend these additional sessions, your height and weight will be assessed and recorded at the beginning of the session.

Risks or Discomforts: While participating in this study, you may experience the following:

- There is a risk of fetal radiation exposure as a result of DEXA scans performed on pregnant women.
- Discomfort from the blood draw procedure. The needle stick may hurt. There is a small risk of bruising and fainting and a rare risk of infection.
- Adverse changes including, but not limited to: abnormal blood pressure, dizziness, disorders of heart rhythm, and in very rare instances heart attack, stroke, or death
- Bodily injuries to the muscles, ligaments, tendons, and joints

Every effort will be made to minimize these occurrences by having a physician supervise cardiorespiratory fitness tests, supervision during exercise, and proper warm-up prior to exercise sessions, as well as your own careful control of exercise efforts.

Benefits: You may receive training benefits such as improved cardiorespiratory fitness and/or muscular strength. Other benefits may include a reduction in risk for hypertension, diabetes, hypercholesterolemia, and other chronic diseases for which the risks are known to be reduced by exercise. If you are randomized to the preferred exercise group, you will receive healthy lifestyle and diet counseling and be offered the same 1-year exercise program of your choice after 1 year. It is intended that the information gained from this study will benefit society by providing knowledge about the effects of different types of exercise on cardiovascular disease risk factors.

Costs and Compensation: You will not have any costs from participating in this study. You will be compensated up to a total of $300 for participating in this study. We will be providing $60 at each examination time point (baseline, 6-month, and 1-year, up to $180) and then we will be providing an additional $10/month that you complete at least 85% of your pedometer step count logs and your online 3-day diet logs. Completing these logs will result in up to an additional $120 over 12 months. These monthly allotments will be tracked and given in addition to the $60 at the 6-month and 1-year examination times (e.g., 6 months of complete pedometer and diary logs = $60, in addition to the $60 for the 6-month examination = $120 total, in two separate payments of $60, at the 6-month time point).

You will need to complete a form to receive payment. Please know that payments may be subject to tax withholding requirements, which vary depending upon whether you are a legal resident of the U.S. or another country. If required, taxes will be withheld from the payment you receive.

In addition, you will receive a t-shirt, water bottle, and gym towel at the start of your exercise program (after 1 year for preferred exercise group).

Optional Compensation: There will be occasional drawings for gift cards and prizes valued up to $50. Your name may be entered into the drawing one or multiple times based on how much of the project you complete each month beyond 80%-85% adherence, depending on your study group. Study adherence includes your exercise attendance, your pedometer steps, and/or submitting your dietary recalls. These drawings will be held as often as monthly, but may be less frequent depending on the availability of additional funds.

Participant Rights: Participating in this study is completely voluntary. You may choose not to take part in the study or to stop participating at any time, for any reason, without penalty or negative consequences. You can skip any questions that you do not wish to answer.

If you have any questions *about the rights of research subjects or research-related injury*, please contact the IRB Administrator, (515) 294-4566, IRB@iastate.edu, or Director, Office for Responsible Research, (515) 294-3115, 2420 Lincoln Way, Suite 202, Ames, IA 50014.

Research Injury: Please tell the researchers if you believe you have any injuries caused by your participation in the study. The researchers may be able to assist you with locating emergency treatment, if appropriate, but you or your insurance company will be responsible for the cost. By agreeing to participate in the study, you do not give up your right to seek payment if you are harmed as a result of

being in this study. However, claims for payment sought from the University will only be paid to the extent permitted by Iowa law, including the Iowa Tort Claims Act (Iowa Code Chapter 669)."

Confidentiality: Records identifying participants will be kept confidential to the extent permitted by applicable laws and regulations and will not be made publicly available. To ensure confidentiality, all data will be kept in a locked filing cabinet, password-protected computer files, and access will be limited to the researchers. Each participant's data will be assigned a number for identification. The key that links personal identifiers to study data will be destroyed upon completion of the 1-year examination. After the study, we will retain your email address in order to make you aware of future research opportunities in our lab. You can request to have your email address removed from this list at any time.

The information collected from you during this study will be used by the researchers and research staff at Iowa State University for the purposes of research only. A description of this trial and its outcomes will be available on the Physical Activity Epidemiology website http://www.kin.hs.iastate.edu/research/physical-activity-epidemiology/. Your study records may also be shared with others at Iowa State University including auditing departments of Iowa State University, and the Institutional Review Board (a committee that reviews and approves human subject research studies), which may inspect and/or copy study records that may contain private information for quality assurance and data analysis.

Your research data may also be shared with other entities outside of Iowa State University including federal agencies such as the National Institutes of Health and Clinical Trials.gov. 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. In addition, de-identified information (including biospecimens) collected about you during this study may be used for future research studies or shared with other researchers outside Iowa State University who submit a written request and receive official approval from the study team and, when applicable, an Institutional Review Board. In these instances, your study data will be de-identified (i.e., not include names or other identifying information such as date-of-birth, addresses, or other contact information). We will not obtain additional informed consent from you before sharing the de-identified data.

Certificate of Confidentiality

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 National Institutes of Health, which is funding this project, or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of such as child abuse and neglect, or imminent threat of harm to self or others.

Questions: Please ask questions at any time during this study. Contact the study team at 515-294-7223/cardioRACE@iastate.edu, Angie Brellenthin at 515-294-6351/abrellen@iastate.edu, or Duck-chul (DC) Lee at 515-294-8042/dclee@iastate.edu.

Consent and Authorization Provisions:
Your signature indicates that you voluntarily agree to participate in this study, that the study has been explained to you, that you have been given the time to read the document, and that your questions have been satisfactorily answered. You will receive a copy of the written informed consent prior to your participation in the study.

Participant's Name (printed) _____

_____ _____
Participant's Signature Date