Title of Study: Exercise Training and Increasing Non-Exercise Physical Activity (I-CAN study)
Clinical Trials ID: NCT02010060
Document date: 11/25/2013

East Carolina University

Consent to Participate in Research that is Greater than Minimal Risk

Information to Consider Before Taking Part in This Research

Title of Research Study: Exercise Training and Increasing Non-Exercise Physical Activity (I-CAN study)

Principal Investigator: Damon L. Swift
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Study Sponsor/Funding Source: American Heart Association

Researchers at East Carolina University (ECU) study diseases, health problems, environmental problems, behavior problems and the human condition. Our goal is to try to find better ways to improve the lives of you and others. To do this, we need the help of people who are willing to take part in research.

The person who is in charge of this research is called the Principal Investigator. There may be other research staff members who will perform some of the procedures.

The person explaining the research to you may be someone other than the Principal Investigator. Thus, a research coordinator or other research staff may be asking you to take part in this study.

You may have questions that this form does not answer. If you do have questions, feel free to ask the person explaining the study, as you go along. You may have questions later. Feel free to ask those questions, as you think of them. There is no time limit for asking about this research.

You are not under any obligation to take part in this research. Take your time and think about the information that is provided. If you want, have a friend or family member go over this form with you before you decide. It is up to you. If you choose to be in the study, then you should sign the form when you are comfortable that you understand the information provided below. If you do not want to take part in the study, you should not sign this form. That decision is yours and it is okay to decide not to volunteer.

This form explains why this research is being done, what will happen during the research, and what you will need to do if you decide to volunteer to take part in this research.

Why is this research being done?

The purpose of this research study is to determine the effects of exercise on your health. We are asking you to take part in this research. However, the decision is yours to make. By doing this research, we hope to learn the effect of exercise training and high physical activity levels (outside of training session) on risk factors for heart disease. Exercise training has been shown to have many beneficial effects on risk factors for heart disease. Current public health recommendations state that adults should obtain at least 150 minutes of moderate physical activity per week to maintain and improve health. Based on these guidelines, an individual may adopt a structured exercise program (e.g. 30 minutes of treadmill exercise 5 days per week) to meet these recommendations. While this approach is certainly beneficial, the health benefits of exercise could potentially be optimized by also increasing the amount of physical activity outside of these structured exercise training sessions (Non-Ex PA). While it seems logical that this approach

would lead to greater overall improvements in risk factors associated with heart disease, this has never been tested in a scientific study. This physical activity program may represent a simple and more effective physical activity program for sedentary adults with cardiovascular risk factors compared to simply exercise training alone.

We will study 45 obese adults with one other risk factor for heart disease. Participants will be randomly assigned to one of three groups for 6 months: (1) exercise training only, (2) exercise training with the additional goal of increasing the amount of physical activity outside of training sessions, or (3) a non-exercise control group.

Why am I being invited to take part in this research?

You are being invited to take part in this research because you are at least 40 years old and are not currently participating in an exercise program. If you volunteer to take part in this study, you will be one of about 45 people to do so.

Are there reasons I should not take part in this research?

Several factors may make you ineligible for the present study. You should not volunteer for this study if you have been diagnosed with type 1 or 2 diabetes, have had a previous heart attack or stroke. Due to the fact that this study will involve supervised exercise testing in our facility, you will not be eligible for this study if you plan to be away from the Pitt County area for more than 4 weeks in the next 6 months. This study also involves accessing a study website, so you should not volunteer for this study if you do not have regular home access to the internet. Lastly, you should not volunteer for this study if you are pregnant or are trying to become pregnant.

What other choices do I have if I do not take part in this research?

You have the choice of not taking part in this research study.

Where is the research going to take place and how long will it last?

The research procedures will be conducted at East Carolina Heart Institute (ECHI) and the Fitness Instruction Testing and Training(FITT) building at East Carolina University. A summary of the time demands of the I-CAN study by study visit are shown below. This study will take approximately 147 total hours.

Visit	Location	Time (hrs)
Screening	ECHI or FITT	1.5
Run-in 1	ECHI or FITT	0.5
Run-in 2	ECHI or FITT	0.5
Oral Glucose Tolerance Test	ECHI	2.5
Baseline assessment	FITT Building	2
Mid-study assessment	FITT Building or East Carolina Heart Institute	0.5
Follow-up assessment	FITT Building	2
Oral Glucose Tolerance Test	ECHI	2.5
Exercise sessions (exercise groups only)	ECHI or FITT Building	135
Total		147

What will I be asked to do?

The following procedures will be done strictly for research purposes:

Following signing this consent form, you will participate in the initial screening visit and 2 run –in visits. The purposes of these visits are todetermine whether you are eligible to participate in this study Therefore, you will be asked to come to ECU 3 times over the course of two weeks to complete screening. These visits will take place at the (ECHI) or FITT

1. **Eligibility Criteria:**
    a. You may be eligible for the present study if you meet the following criteria:
        i. Age (40-65 yrs of age)
        ii. Body mass index between 30-40 kg/m^2
        iii. Not currently participating in exercise training program or have a high physical activity level
        iv. Have at least one risk factor for heart disease, which is based on your cholesterol levels, blood glucose levels, and blood pressure levels (if you are currently on medications to control these factors this will count as a risk factor).
        v. High waist circumference (a measurement of the distance around your waist)

    b. You will **NOT** be eligible for this study if you meet the following criteria:
        i. You have had a previous heart attack or a significant heart-related condition
        ii. Have been diagnosed with type 1,type 2 diabetes or taking diabetes medication
        iii. Blood pressure levels are excessively high at rest
        iv. Other medical conditions that are life threatening, aggravated by exercise training, or deemed by the research team to be above the safety limits of this study
        v. You plan to be away from Pitt County more than 4 weeks in the next 6 months
        vi. Do not have home assess to the internet
        vii. Currently participating in an exercise training program
        viii. Currently pregnant or plans to become pregnant
        ix. Not fulfilling study requirements during the screening process
        x. Currently participation or plans to engage in dieting or a weight loss program
        xi. Previous bariatric or gastric banding surgery
        xii. Currently using weight loss medications

The following information will be collected at screening:

a. Demographic information: We will ask and record your name, contact information, ethnic/racial identification information
b. Medical history: You will be asked questions about you medical history and current medication by a member of the study staff. We will ask that you bring in your medication bottles for confirmation of medication and dosage
c. Medical letter from physician: You will be given a medical clearance letter to be reviewed by your physician. The following letter will state that you have adequate health to participate in an exercise study, and ask questions regarding your medical history.
d. Height: Research staff will use a device (called a stadiometer) to measure your height
e. Weight: Your weight will be measured on a scale
f. Waist circumference: A simple measurement will be made around your waist using a flexible measuring tape
g. Blood pressure: Your blood pressure will be evaluated in the seated position
h. Food frequency questionnaire: This questionnaire collects information about your eating habits over a 12-month period.

i. Pedometer measurements: You will be given a device called a pedometer which measures the amount of steps that you walk. You will be asked to wear this over the course of one week, and log your steps on the study website during the run-in period
j. Accelerometry: You will be asked to wear a small device similar to a pedometer attached to a belt at your hip for 7 days. This device will measure your physical activity.
k. Blood Draw: A fasting blood sample (approximately 1.5 tablespoons) will be obtained for the analyses of glucose, blood lipids, and screening blood work. In addition, a portion of your blood sample will be saved and archived for future analysis.
l. Urinalysis: A urine sample will be obtained from female participants from whom a pregnancy test will be conducted.
m. Logging pedometer information in study website: During the run-in period, we will ask you to log into the online study website to confirm that you wore your pedometer, any long time-periods where you did not wear the device, and other questions related to monitoring your activity.

Intervention interview: We will have you meet with study staff to discuss any major barrier for study completion (adequate time for an exercise training study, time away from Pitt County area, and other major factors that could adversely affect adequate participation levels in the study).

ASSESSMENT VISITS: After we determine you are eligible to continue, you will take part in 5 assessment visits over the course of the study where study-related measurements will be taken.

Visit 1:An Oral Glucose Tolerance Test (OGTT) which is explained in detail below (2.5hrs)
Visit 2: Baseline visit (2 hr) will occur prior to your random assignment to a group.
Visit 3: The mid-intervention visit will occur at 3 months into the study (1/2hr)
Visit 4: At 6months you will have a follow-up OGTT(2.5hrs)
Visit 5: Follow-up assessment (2hr).. An Oral Glucose Tolerance Test (OGTT) which isexplained in detail below,(2.5 hrs,. And the
Oral Glucose Tolerance Test (OGTT) visits:

OGTT: an oral glucose tolerancethis test measures the changes in glucose and insulin after ingestion of a 75g a sugaryglucose solution. Blood samples will be drawn from an intravenous (IV) catheter(small fexible tube) placed in your arm at min 0, 30, 60, 90 120. Five blood draws will be taken in total, One before the sugary drink (min 0) and then four every 30 min after. The total amount of blood drawn for the OGTT will be approximately 2.5 tablespoons.At min 0 we will collect an additional 1.5 tablespoons to measure other health related factors such as cholesterol.

At baseline and follow-up (6 months) visits, you will complete the following assessments:

1. DEXA scan: A DEXA scan will be conducted to determine your body composition (the amount of muscle and fat in your body). The scanning method will require you to lie quietly on the scanning table for approximately 10 minutes. The scan will subject you to a very low dose of radiation, approximately 5-10% of the exposure of a typical chest x-ray.
2. Exercise stress test: An exercise stress test will be conducted to determine your fitness level. During this test, you will wear a mouthpiece so the gases you breathe out can be collected for analysis of oxygen consumption. You will begin by walking on the treadmill at a slow speed for 2 minutes. Thereafter, the inclination will be increased every two minutes until you feel exhausted to the point that you can no longer continue. The starting speed and incline will be adjusted with the goal of reaching exhaustion within 8-12 minutes.
3. Blood pressure (described above)
4. Weight (described above)
5. Waist circumference (described above)
6. Food frequency questionnaire

At mid-intervention (3 months): you will complete the following assessments.

1. Food Frequency questionnaire (described above)
2. Waist Circumference (described above)
3. Accelerometery (described above)

RANDOMIZATION:
After completion of the baseline visit, you will be randomized to a study group for the next 6 months. Randomization means that the study group you will participate in will be randomly determined (i.e like flipping a coin). Neither you or the research staff will be able to change the group you are assigned.

STUDY INTERVENTION:

1. **Control group**: The control group will be asked to not alter physical activity or dietary habits over the next 6 months. You will be asked to wear a pedometer in blind-mode (the pedometer will count the amount of steps you have walked without showing that number on the display). During the intervention, you will log on to the study website on a daily basis to report if you wore your pedometer each day. You will be asked to come to ECU once a month to allow the study staff to download data from your pedometer.
2. **Exercise Training group**: You will perform aerobic exercise training on a treadmill 3-5 times per week for 6 consecutive months. To ensure that the walking/running is within the appropriate intensity, study staff will monitor your heart rate. These visits will last approximately 30-60 minutes per sessions depending on the amount of exercise you need to complete (determined by study staff). You will also be asked to wear pedometers in blind mode during the 6 month intervention, but will be asked not to alter the amount of physical activity outside of your exercise sessions. During the intervention, you will log on to the study website on a daily basis to report if you wore your pedometer each day.
3. **Exercise training and Increasing physical activity group**: This group will participate in exercise training in the same manner as the Exercise Training only group. In addition to exercise training at our facility, you will be asked to also increase the amount of physical activity in your daily life (e.g the amount of steps that you walk). Study staff will instruct you on the amount of steps you should aim for outside of your training sessions. You will meet periodically with study staff before or after your training sessions to discuss your goals for increasing your physical activity outside of training sessions and determine the best strategies to reach these goals (approximately 10-15 mins per session). On a daily basis, you will record the amount of steps that you have recorded on your device and report other aspects of pedometer monitoring on the study website.

The study procedures are strictly for research purposes only. You should continue to see your primary care physician for ongoing care.

What possible harms or discomforts might I experience if I take part in the research?

There are always risks (the chance of harm) when taking part in research. We know about the following risks or discomforts you may experience if you choose to volunteer for this study. These are called side effects. The following side effects are known to occur in some people:

Exercise: Risks associated with the exercise testing and training protocols are as follows:

- Light-headiness or dizziness during or following exercise (rare, 1 to 4 out of 100 people)
- Ventricular arrhythmia which is an abnormal heartbeat (rare, 1 to 4 out of 100 people)
- Falls associated with exercising on equipment: There is also a slight risk that a person could fall off the treadmill while exercising. To reduce this risk, qualified personnel will supervise all volunteers while they are exercising at the fitness center (rare, 1 to 4 out of 100 people)

- Musculoskeletal injury (occasional, 5 out of 100 people): Joint and muscle-related injuries can occur with exercise training. Many, but not all musculoskeletal injuries get better with rest.
- Muscle soreness (common, 90 out of 100 people) is to be expected during at the first few weeks of the exercise training program. This soreness is a normal response to the increase in physical activity, and should lessen over the course of the exercise training program.
- Death (very rare, fewer than 1 in 10,000 deaths in patients who are known to, or suspected of, having heart disease). The risk is expectedly much smaller in a group of people without known heart disease or diabetes. To minimize this risk, we will have a physician present and heart (ECG) monitoring during exercise stress tests where appropriate.
- Blood Draw: The total amount of blood drawn (3 tablespoons) is negligible. There is an extremely small risk of local hematoma or infection associated with insertion of intravenous catheters. Bruising at the site of the blood draw can occur.
- DEXA Scan: There is a negligible risk associated with the DEXA scan method of determining body composition. You will be exposed to a very low dose of radiation that is equivalent to approximately 5-10% of what you would be exposed to during a typical chest x-ray.
- Oral Glucose Tolerance Test - You may feel some pain during the insertion of the plastic catheter into your arm. Possible risks associated with the test are nausea, bruising, and a small chance of infection. To minimize risk, the procedure will be performed using sterile techniques by qualified personnel in ECHI.

Additionally, there may be unforeseen risks involved with this and all research studies.

Are there any reasons I might want to withdraw from the research or you might take me out of the research?

During the study, information about this research may become available that would be important to you. This includes information that, once learned, might cause you to change your mind about wanting to be in the study. We will tell you as soon as we can. This might include information about the side effects that are caused by taking part in this study. If that happens, we can tell you about these new side effects and let you decide whether you want to continue to take part in the research.

There may be reasons we would need to take you out of the study, even if you want to stay in. We may find out that it is not safe for you to stay in the study. It may be that the side effects are so severe that we need to stop the study or take you out of the study to reduce your risk of harm. If we find that the research might harm you or that it is not providing enough of a benefit to justify the risks you are taking, we will inform you of the reason you are being taken out of the study, and you will be compensated based on how far along you are in the study. We may also find that you are not or cannot take your medicine properly or you are not or cannot come for your study visits as scheduled. If those things are found to be true, we will need to take you out of the study.

What are the possible benefits I may experience from taking part in this research?

We do not know if you will get any benefits by taking part in this study. There may be no personal benefit from your participation but the information gained by doing this research may help others in the future. You may benefit from the valuable information obtained from this research such as health-related information (e.g. weight, waist circumference, exercise testing) and the opportunity to participate in supervised exercise training. The results of this study may provide insight regarding whether exercise training and increasing physical activity provides more health benefits compared to exercise training alone. The risks are considered minimal compared to the benefits.

Will I be paid for taking part in this research?

We will pay you for the time you volunteer while being in this study. If you complete all study visits for the study, we will pay you up to $300 for your time. You will receive $50 for completing the OGTT, $30 for completing the

baseline visit, $20 dollars for the mid-intervention visit, $50 for the follow up IVGTT and $50 dollars for the follow-up visit. If you complete the exercise training program with adequate attendance to exercise sessions (≥75%), you will receive $100 dollars. Compliance rates for training between 65-75% will receive $75. If your compliance rates are below 65%, you will receive $50. If you decide to withdraw from the study at any point, you will receive payment that is pro-rated based on the visits (shown above) you have completed. Participants who start the intervention (meaning are in the control group or one of the exercise training groups), but withdraw prior to completion of the study will receive $25 for exercise training portion of the study. You will receive payment for the study procedures following the completion of the study. During the research study, we may also raffle for incentive items (e.g. mug, tee shirt) to help encourage adherence during the intervention.

Individuals in the control group will be offered the use of our exercise training facility for 3 months at no charge, following the completion of the study.

What will it cost me to take part in this research?

It will not cost you any money to be part of the research. The sponsor of this research will pay the costs of will pay the costs of all research related testing performed in this study.

However, you will be expected to pay for the cost of transportation to and from the testing facility. In addition, you may need to purchase appropriate exercise attire (e.g. work-out clothes, sneakers, etc.)

Who will know that I took part in this research and learn personal information about me?

To do this research, ECU and the people and organizations listed below may know that you took part in this research and may see information about you that is normally kept private. With your permission, these people may use your private information to do this research:

- The research team, including the Principal Investigator, study coordinator, research nurses, and all other research staff.
- Any agency of the federal, state, or local government that regulates this research. This includes the Department of Health and Human Services (DHHS), the North Carolina Department of Health, and the Office for Human Research Protections
- The ECU University & Medical Center Institutional Review Board (UMCIRB) and the staff who have responsibility for overseeing your welfare during this research, and other ECU office staff who oversee this research.

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

How will you keep the information you collect about me secure and how long will you keep it?

Any paper data collection will be stored in a locked file cabinet in locked room (office, or training facility) within the FITT building. The key to that cabinet will be kept in a different room .All electronic data will be kept in secure databases (stored on the departmental drive space), with access restricted to study staff. The codes to the de-identified

data will be kept separately. Access to the data files within the database will require user name and password information. All data sources will be stored for at least 6 years following study completion.

Data from the present study may be utilized by researchers at ECU or other institutions for future research to write research papers, support grant applications or other research-related activities. In this case, a dataset will be provided which will not include information that will identify you (i.e. information such as name, address, etc. will not be included in the dataset).

What if I decide I do not want to continue in this research?

Participating in this study is voluntary. If you decide not to be in this research after it has already started, you may stop at any time. You will not be penalized or criticized for stopping. You will not lose any benefits that you should normally receive.

What if I get sick or hurt while I am in this research?

If you need emergency care:
Call 911 for help. It is important that you tell the doctors, the hospital or emergency room staff that you are taking part in a research study and the name of the Principal Investigator. If possible, take a copy of this consent form with you when you go.

Call the principal investigator as soon as you can. He needs to know that you are hurt or ill. Call Dr. Damon Swift at 252-737-1338

If you do NOT need emergency care, but have been hurt or get sick:
Contact Dr. Damon Swift at 252-737-1338. Call the principal investigator as soon as you can. As necessary, go to your regular doctor. It is important that you tell your regular doctor that you are participating in a research study. If possible, take a copy of this consent form with you when you go.

If necessary, the Principal Investigator or your regular doctor can assist you in identifying the appropriate place to get care.

If you are harmed while taking part in this study:
If you believe you have been hurt or if you get sick because of something that is done during the study, you should call Dr. Damon Swift at (252) 737-1338 immediately. There are procedures in place to help attend to your injuries or provide care for you. Costs associated with this care will be billed in the ordinary manner, to you or your insurance company. However, some insurance companies will not pay bills that are related to research costs. You should check with your insurance about this. Medical costs that result from research-related harm may also not qualify for payments through Medicare, or Medicaid. You should talk to the Principal Investigator if you have concerns.

Who should I contact if I have questions?

The people conducting this study will be available to answer any questions concerning this research, now or in the future. You may contact the Principal Investigator, Dr. Damon Swift at 252-737-1338 (days) or 434-825-5762 (nights and weekends).

If you have questions about your rights as someone taking part in research, you may call the ECU Office for Human Research Integrity (OHRI) at phone number 252-744-2914 (days). If you would like to report a complaint or concern about this research study, you may call the Director of OHRI, at 252-744-1971

I have decided I want to take part in this research. What should I do now?

The person obtaining informed consent will ask you to read the following and if you agree, you should sign this form:

- I have read (or had read to me) all of the above information.
- I have had an opportunity to ask questions about things in this research I did not understand and have received satisfactory answers.
- I understand that I can stop taking part in this study at any time.
- By signing this informed consent form, I am not giving up any of my rights.
- I have been given a copy of this consent document, and it is mine to keep.

_____ _____

Participant's Name (PRINT) **Signature** **Date**

Person Obtaining Informed Consent: I have conducted the initial informed consent process. I have orally reviewed the contents of the consent document with the person who has signed above, and answered all of the person's questions about the research.

_____

Person Obtaining Consent (PRINT) **Signature** **Date**

FUTURE TESTING OF BLOOD SAMPLES

Upon termination of this study, the blood samples collected for this study will be stored for up to 10 years to research scientific questions. These research questions are yet to be identified, but will likely address risk factors for heart disease, type 2 diabetes, obesity, and aging. It is possible that other indicators of health may be measured in these samples. You will continue to be the owner of the samples and retain the right to have the sample material destroyed at any time during this study by contacting the study principal investigator. During this study the samples will be stored with number identifiers only; however, the number identifier will be linked to a specific name and will be kept on file in the possession of the principal investigator. The linked file will be encrypted with password protection and stored on a password protected computer. A backup file will be made and will be encrypted with password protection. No other individuals outside the research team will have access to these identifying materials unless the principal investigator is required by law to provide such identifying information. Data will not be publicly available and participants will not be identified or linked to the samples in publication. If a commercial product is developed from this research project, you will not profit financially from such a product.

Your consent to have future testing of your blood samples is a required for the present study. Therefore, if you do not consent to future testing of your blood samples, you will not be eligible for the present study.

CONSENT TO PARTICIPATE IN FUTURE TESTING OF BLOOD SAMPLES

I certify that I have read all of the above, asked questions and received answers concerning areas I did not understand, and have received satisfactory answers to these questions. I willingly give my consent for participation in this research study. (A copy of this consent form will be given to the person signing as the subject or as the subject's authorized representative.)

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Participant's Initials

Participant's Name (PRINT) **Signature** **Date**

Person Obtaining Informed Consent: I have conducted the initial informed consent process. I have orally reviewed the contents of the consent document with the person who has signed above, and answered all of the person's questions about the research.

Person Obtaining Consent (PRINT) **Signature** **Date**

Consent Version # or Date:_____

Participant's Initials