Title: Targeting Obesity to Optimize Health in Cardiac Rehab (TOPCARE)
Date Approved: 11/18/2019
NCT03423238

Wake Forest®
School of Medicine

Section of Gerontology and Geriatric Medicine

TARGETING OBESITY TO OPTIMIZE HEALTH IN CARDIAC REHAB (TOPCARE)

Informed Consent Form to Participate in Research
Tina E. Brinkley, PhD, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this study is to determine whether overweight and obese men and women with heart disease who participate in an exercise-based cardiac rehabilitation program along with a weight loss program have greater improvements in exercise tolerance and other cardiovascular risk factors compared to those who only participate in cardiac rehabilitation.

This research study involves a 6-month program consisting of 3 supervised exercise sessions and 1 health education class per week. If you are assigned to the weight loss program, you will also be asked to eat two meal replacements per day (provided by the study) and meet with a dietitian on a weekly or biweekly basis. You will be asked to complete a screening visit to see if you qualify for the study. If you qualify, you will then complete a baseline study visit and 2 follow-up study visits, each lasting three to four hours. Assessments include vital signs (weight, height, blood pressure); a blood draw; questionnaires about your medical history, physical and mental abilities, and eating habits; physical function tasks such as handgrip strength, balance and walking; and blood flow measurements. You will also be asked to have a DXA scan. Like all research studies, there are some risks involved including muscle strains or pulls and a risk of falling from the physical function testing and exercise program and exposure to radiation from the DXA scan. Risks will be minimized by having experienced/trained staff conduct all assessments and oversee the diet and exercise sessions. Please read the appropriate section below for more information about risks. If you agree to take part in this study, there may or may not be direct benefit to you. You will receive information about your health and all study-related costs, including the meal replacements, cardiac rehabilitation, and parking costs will be paid for by the study. You will also be compensated $50 for every study visit you complete.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. Classes and testing procedures similar to those offered in this study are available in the community and usually involve a charge to participants. You will not lose any service, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of the study. Please read this description carefully. If you have questions or concerns regarding this study or if you want to withdraw from the study please contact Tina Brinkley, PhD. She is the person in charge of this study and can be reached at [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have heart disease and have been referred to cardiac rehabilitation at Wake Forest Baptist Health. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to determine whether overweight and obese men and women with heart disease who participate in an exercise-based cardiac rehabilitation program along with a weight loss program have greater improvements in exercise tolerance and other cardiovascular risk factors compared to those who only participate in cardiac rehabilitation.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

A total of 40 men and women will take part in this study. In order to identify the 40 participants needed, we may need to screen as many as 80 because some people will not qualify for the study.

WHAT IS INVOLVED IN THE STUDY?

If you agree to participate in this study by signing this consent form, you will be asked to come to one of the participating study sites (Wake Forest Baptist Medical Center, Davie Medical Center, or Lexington Medical Center) to complete a screening visit to see if you qualify for the study. If you qualify, you will then complete a baseline study visit before beginning a 6-month intervention involving supervised exercise sessions and health education classes. Approximately half the study participants will also participate in a weight loss program. You will also be asked to complete one study visit after the first 3 months of the intervention and one study visit at the end of the 6-month intervention. The baseline and follow-up study visits will take place at Wake Forest Baptist Medical Center in Winston-Salem. The details about all study visits and procedures are provided below. We will make every effort to follow the visit procedures in the order they are outlined below; however, it may be necessary at times to make changes to accommodate different schedules.

Screening Visit (SV)

This visit may occur at the end of your cardiac rehab consultation or on a separate day. At this visit, you will learn more details about the study and you will be given time to ask questions and get satisfactory answers. Then, you will be asked to sign this informed consent form. After signing this form, we will:

- Review your medical history and medications
- Measure your height and weight to confirm your BMI
- Measure your vital signs (blood pressure and heart rate)
- Ask you to answer questions related to your memory
- Allow you to sample or taste the shakes and bars that will be used in the study

This visit will take up to 1 ½ hours to complete. If you qualify for the study, you will be scheduled for a baseline visit. If you do not qualify, we will call you and/or send you a letter

explaining why you did not qualify.

Baseline Visit (BV)
Within approximately one week, you will be asked to come to Wake Forest Baptist Medical Center in Winston-Salem in the morning after an overnight fast (nothing to eat or drink except water after midnight the night before). At this visit, we will:

- Review your medications and changes in your health
- Measure your weight
- Measure the size of your waist, hip, and thigh using a tape measure
- Measure your blood pressure and heart rate
- Measure the stiffness of your arteries
- Draw blood (about 3 tablespoons) from a vein in your arm to measure lipids (total, LDL, and HDL cholesterol, and triglycerides), insulin, glucose (blood sugar), hemoglobin A1c, blood cell counts, liver and kidney function, cardiac enzymes, and blood for storage
- Provide you with a light snack
- Ask you to complete a 6-minute walk test while wearing a heart rate monitor and an oxygen sensor on your finger
- Ask you to do a series of physical function tests including balance tests, a chair stand test, a narrow walk test, a short distance (4-meter) walk test, and a grip strength test
- Ask you to answer a series of questions about your mobile abilities on an iPAD
- Ask you to answer questions about your motivation to lose weight, eating habits, physical and mental energy levels, mood, and quality of life
- Perform a whole-body dual energy x-ray absorptiometry (DXA) scan
- Provide you with an activity monitor to wear continuously for 7 days. You will also be asked to record your activities in a daily log for all 7 days.

This visit will take approximately 3 – 4 hours. More details on the individual tests are provided in the Risks Section of this form.

Randomization to Study Groups
At the end of baseline testing, you will be randomly assigned to one of two study groups as described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in either group. You must agree to be in either of the two groups and you may not pick or change the group that you are assigned to. The two study groups are:

1) Cardiac rehabilitation only
2) Cardiac rehabilitation plus a weight loss program

All participants will be enrolled in a 6-month cardiac rehabilitation program at Wake Forest Baptist Medical Center, Davie Medical Center, or Lexington Medical Center. You will be provided with an individualized exercise plan and will be asked to attend three center-based exercise sessions per week under the supervision of trained exercise specialists. Each exercise session will last for 60 to 90 minutes and will include 5-10 minutes of warm-up and cool-down activities, up to 30 minutes of aerobic exercise (such as walking laps on a track or on a treadmill

or riding a stationary bike), and 15-20 minutes of upper and lower body resistance exercises using Thera-Bands. The exercise will progress to a longer time or a harder intensity each week for the first few weeks until you reach your target range. Blood pressure and heart rate will be measured and recorded before each exercise session. You will be asked to wear comfortable clothing and good walking shoes. You will also be asked to attend weekly group education classes that provide support and general information on healthy lifestyle behaviors and meet with a dietitian, usually within the first 2 weeks of the program, to discuss dietary concerns.

If you are assigned to the weight loss program, you will be provided with an individualized meal plan. You will be asked to attend individual sessions with the study dietitian to help you reduce your weight with a goal of achieving 5-10% weight loss over the 6-month intervention period. You will meet with the dietitian once a week during months 1-3 and then twice a month during months 4-6. You will be asked to prepare your own meals from the meal plans provided and consume meal replacements at breakfast and at lunch or dinner (2 per day). Meal replacements (shakes and bars) will be provided throughout the duration of the study. You will be asked to keep track of everything you eat and drink on a daily basis in a log book provided by the study. Your weight will be measured weekly.

Follow-up Visit 1 (FV1)

Approximately 3 months after you start the intervention you will be asked to come to Wake Forest Baptist Medical Center in Winston-Salem in the morning after an overnight fast (nothing to eat or drink except water after midnight the night before). At this visit we will:

- Review your medications and changes in your health
- Measure your weight
- Measure the size of your waist, hip, and thigh using a tape measure
- Measure your blood pressure and heart rate
- Measure the stiffness of your arteries
- Draw blood (about 3 tablespoons) from a vein in your arm to measure lipids (total, LDL, and HDL cholesterol, and triglycerides), insulin, glucose, hemoglobin A1c, blood cell counts, liver and kidney function, cardiac enzymes, and blood for storage
- Provide you with a light snack
- Ask you to complete a 6-minute walk test while wearing a heart rate monitor and an oxygen sensor on your finger
- Ask you to do a series of physical function tests including balance tests, a chair stand test, a narrow walk test, a short distance (4-meter) walk test, and a grip strength test
- Ask you to answer a series of questions about your mobile abilities on an iPAD
- Ask you to answer questions about your motivation to lose weight, eating habits, physical and mental energy levels, mood, and quality of life
- Perform a whole-body dual energy x-ray absorptiometry (DXA) scan
- Provide you with an activity monitor to wear continuously for 7 days. You will also be asked to record your activities in a daily log for all 7 days.

This visit will take approximately 3 – 4 hours. More details on the individual tests are provided in the Risks Section of this form.

Follow-up Visit 2 (FV2)

Approximately 3 months later, at the end of the 6-month intervention, you will be asked to come to Wake Forest Baptist Medical Center in Winston-Salem in the morning after an overnight fast (nothing to eat or drink except water after midnight the night before). At this visit we will:

- Review your medications and changes in your health
- Measure your weight
- Measure the size of your waist, hip, and thigh using a tape measure
- Measure your blood pressure and heart rate
- Measure the stiffness of your arteries
- Draw blood (about 3 tablespoons) from a vein in your arm to measure lipids (total, LDL, and HDL cholesterol, and triglycerides), insulin, glucose, hemoglobin A1c, blood cell counts, liver and kidney function, cardiac enzymes, and blood for storage
- Provide you with a light snack
- Ask you to complete a 6-minute walk test while wearing a heart rate monitor and an oxygen sensor on your finger
- Ask you to do a series of physical performance tests including balance tests, a chair stand test, a narrow walk test, a short distance (4-meter) walk test, and a grip strength test
- Ask you to answer a series of questions about your mobile abilities on an iPAD
- Ask you to answer questions about your motivation to lose weight, eating habits, physical and mental energy levels, mood, and quality of life
- Perform a whole-body dual energy x-ray absorptiometry (DXA) scan
- Provide you with an activity monitor to wear continuously for 7 days. You will also be asked to record your activities in a daily log for all 7 days.

This visit will take approximately 3 – 4 hours. More details on the individual tests are provided in the Risks Section of this form.

Additional testing

Neurovascular testing will be completed to determine how well your body is able to maintain blood flow to your brain while resting, during changes in posture, and during inhalation of a carbon dioxide gas mixture. Completion of these tests will coincide with the 3-month and/or 6-month follow-up visits. These tests can be scheduled on the same day as a regularly scheduled study visit, prior to a cardiac rehab session, or on a separate day. For these tests we will:

- Measure blood flow to your brain using Transcranial Doppler (TCD) ultrasound
- Continuously measure your blood pressure using an arm cuff and a double finger cuff
- Continuously measure your heart rate using 3-lead electrocardiography (ECG)
- Ask you to complete a series of sit-stand tests
- Ask you to inhale a carbon dioxide gas mixture through a face mask

This series of tests will take approximately 60 minutes to complete. More details on the individual tests are provided in the Risks Section of this form.

After completion of all study visits, a results packet that includes relevant health information collected over the course of the study will be mailed to you.

You will have approximately 3 tablespoons of blood drawn at each study visit. The total amount of blood drawn during the study will be approximately 9 tablespoons.

Storage of Biological Tissue

If you agree to participate in this study, we will draw about 5 tablespoons of blood from your vein to use for future research. This sample will be kept and may be used in future research to learn more about other diseases. Your sample will be obtained in the Department of Internal Medicine at Wake Forest University Baptist Medical Center. The sample will be stored in the Geriatrics Laboratory and it will be given only to researchers approved by Dr. Tina Brinkley. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample. In order to participate in this study, you must be willing to provide this sample for future research.

Your blood sample will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample. Identifiers (your name, address, date of birth, etc.) might be removed from the private information or biospecimens that are collected as part of this research. When the identifying information is removed your private information or biospecimen may be used for future research studies or given to other research investigators without getting additional informed consent from you or your legally authorized representative.

The research that may be performed with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood sample will not affect your care.

Your blood sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

How Long Will I Be in the Study?

You will be in the study for approximately 7 months (which includes the 6-month intervention and the screening, baseline, and follow-up study visits). You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the intervention and procedures include:

6-Minute Walk Test

You will be asked to walk as quickly as possible on an established course, covering as much ground as you can during the allotted time, without running. There is a slight risk of falling during this test, and occasionally participants become short of breath or fatigued and must rest and/or stop the test. To minimize risk, American Thoracic Society (ATS) guidelines will be followed for performing and stopping the test. Participants will be closely monitored during the test, including measurement of blood pressure, heart rate and oxygen saturation. We will also make sure that the walking path is clear and that trained staff is always nearby. We have had no serious adverse events during or after 6-minute walk tests in over 500 middle-aged and older study participants.

Physical Function Tests

There is a small risk of injury during the physical function tests, such as muscle strains or pulls, falls, or joint injury. Risks will be minimized by having experienced/trained staff conducting these assessments. A warm-up and range of motion practice will be conducted before testing. If you experience pain, dizziness, or other medical problem, the test will be terminated.

Radiation Exposure from DXA scans

You will undergo a DXA scan so that we can determine the amount of bone, fat and muscle you have in your body. During the DXA scan, you will lie flat on a padded table. The table and the arm of the machine will move around for about 3.5 minutes. You will be asked to lie as still as possible, and you will not be able to get up until the scan is complete. The DXA scan is painless, and other than minimal exposure to radiation, there are no risks associated with the DXA scan.

If you participate in this study, you will be exposed to small amounts of radiation from the whole-body DXA scan. The amount of radiation exposure that you will receive is equivalent to a uniform whole body exposure of 3 millirems. This is equal to 0.01 times the amount of natural background radiation that the average person in the United States receives each year (300 mrem). The risk of this procedure is small and is similar to that received from clinical x-ray and nuclear medicine studies. To be sure that you do not receive an unhealthy amount of radiation from your participation in this study, you should let your study doctor know if you have had, or are going to have, any other scans or x-rays as part of your medical or dental care. It is very important that you let your study doctor know if you already are participating in, or plan to participate in, any other research study that involves radiation exposure.

Please be aware that this radiation exposure is necessary for this research study only and is not essential for your medical care. The Wake Forest University/Baptist Medical Center's Radiation Safety Committee, a group of experts on radiation matters, has reviewed the use of radiation in this research study and has approved this use as being necessary to obtain the research information desired. The potential long-term risk from these radiation doses is uncertain, but these doses have never been associated with any definite adverse effects. Thus, the risk to you, if any, is estimated to be slight.

Blood Draws

Blood samples will be drawn from a vein in your arm at 3 separate visits after an overnight fast. You may experience discomfort, bruising and/or bleeding where the needle is inserted.

Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. To minimize these risks, blood will be drawn only by trained and experienced phlebotomists.

Exercise-Based Cardiac Rehabilitation

The risks of the exercise program are minimal, but may include musculoskeletal problems and muscle soreness in the early phases of the training. This will be minimized since all exercise sessions will be supervised by trained exercise specialists, who will instruct participants in the proper exercise techniques and proper footwear. Procedures to minimize injury include warm-up and cool-down activities that involve large muscle movements and stretching. Participants will begin with an easier exercise stimulus and will gradually increase in intensity over several weeks. Other potential risks from exercise, such as an abnormal heart rhythm, a heart attack, a stroke, or even death, are rare (less than 1 in 50,000 patient hours of exercise). Exercise physiologists or trained study staff, trained in cardiac life support, will supervise all exercise sessions and practice codes are conducted quarterly. Additionally, a fully stocked crash cart will be available with all necessary emergency equipment (drugs, defibrillator, airway management) to deal with medical emergencies. Institutional and community EMS services will also be activated if needed.

Weight Loss

If you are assigned to the weight loss program, you will be asked to consume 2 meal replacements per day as part of a calorie-restricted diet. The risks of caloric restriction are small and include excessive weight loss, loss of lean mass (muscle and bone), and changes in usual bowel function (diarrhea and/or constipation) due to differences between the prescribed diet and your usual diet. These risks will be minimized by the direct involvement of a registered dietitian with extensive research experience and medical oversight by the study physician. To ensure safety of study participants, meal plans will be tailored to individual preferences and calorie goals will be closely monitored to encourage weight loss of 1-2 lbs/week. Procedures to minimize constipation and loss of muscle and bone during the weight loss intervention include prescription of a dietary program that does not result in excessively rapid weight loss (e.g., >2 lbs/week), inclusion of increased weight-bearing activity (exercise intervention), and incorporating dietary recommendations and meal plans that include the current Recommended Dietary Allowance (RDA) for protein, fiber, calcium, and vitamin D. Weight loss interventions also have the potential to increase risk of hypoglycemia (low blood sugar) and hypotension (low blood pressure). To minimize these risks, study staff will contact the primary care provider of any participant treated with diabetes or blood pressure-lowering medications who develops symptoms of hypoglycemia or hypotension (such as feeling light-headed, shaky, confused, or weak) to discuss adjustment or discontinuation of these medications. If a primary care provider cannot be contacted in a timely manner, the study physician may choose to adjust these medications on their own and the personal care provider will be notified by phone and in writing.

Arterial Stiffness Testing

To measure how stiff your blood vessels are, you will complete a series of tests while lying down quietly for up to 30 minutes. During these tests we will place blood pressure cuffs on your upper arm and upper thigh and press a pencil-like sensor on the side of your neck to obtain information about your pulse. As the cuffs inflate, the pressure might be uncomfortable but should only last a

few seconds. The pulse sensor may leave a small circular indentation from where it is pressed down on your neck. The pressure is minimal and the indentation will go away within an hour.

Questionnaires

We will ask you some questions about your background, medical history, medications, memory, mood, and your physical abilities. You may get tired or frustrated answering these questions. You can stop answering these questions at any time.

Neurovascular Testing

The neurovascular tests will involve TCD ultrasound, continuous blood pressure and heart rate monitoring, a series of sit-stand tests, and a carbon dioxide challenge. Collectively, these measurements will help us understand how blood flow to your brain adapts to changes in posture and changes in carbon dioxide levels. You should be aware that these tests are performed for research purposes, not medical treatment or diagnosis. However, it is possible that we may observe something that appears to be abnormal when using TCD. If so, we may refer you to your primary care physician for further diagnostic testing and evaluation.

Cerebral blood flow monitoring: TCD is a non-invasive test that uses sound waves to measure blood flow through arteries in the head. A TCD headband will be placed around your head with the ultrasound probes placed close to your temples so that we can measure blood flow in the middle cerebral artery (one of the three major arteries that supplies blood to the brain). A small amount of gel may be applied to allow easy conduction of sound waves through the skin. You will not hear or feel any waves. The gel is hypoallergenic, non-sensitizing (meaning it will not sting or burn), and will not stain your clothes. Risks and side effects related to TCD monitoring include reaction from the gel and risk of skin irritation from the TCD headband. However, these are very rare occurrences and no adverse events associated with TCD usage have been reported in the literature. Study staff will closely monitor you for any signs of pain or intolerance to the procedure while the TCD headband is on. If this is observed or if you report discomfort or irritation, the headband will be removed.

Continuous blood pressure and heart rate monitoring: Electrodes will be placed on your chest to obtain an ECG tracing and monitor you heart rate. Some people may develop a mild rash or skin irritation where the electrodes were attached. This irritation usually goes away once the electrodes are removed. An arm cuff and a double finger cuff will be used to monitor blood pressure throughout testing. You may feel a slight squeeze. If you experience discomfort, another finger will be used for the measurement. If the discomfort persists, testing will be stopped immediately.

Sit-stand tests: To measure changes in blood flow during normal activity, you will be asked to wear the TCD headband, ECG electrodes, and blood pressure cuffs at rest and during up to 3 different posture changes: 1) supine (lying down) to standing, 2) a single sit-stand, and 3) a repeated sit-stand. The single sit-stand test involves 2 minutes of sitting, followed by 1 minute of standing. You will repeat this sequence a total of 3 times. After a brief recovery period, you will be asked to complete a repeated sit-stand test which involves 15 cycles of sitting for 10 seconds, followed by standing for 10 seconds. The repeated sit-stand test takes a total of 5 minutes to complete. Some fatigue during the sit-stand tests is normal, but if you experience pain, dizziness, or other medical problem, the test will be terminated. Risks will be minimized by having experienced and trained staff conduct these tests.

Carbon dioxide challenge: This test is used to evaluate cerebral vasomotor reactivity,

which measures the ability of the major blood vessel in your brain to increase or decrease in size in response to changes in carbon dioxide levels. During this test you will breathe a special mixture of room air containing 5% carbon dioxide while wearing the TCD headband, ECG electrodes, and blood pressure cuffs. You will first be instructed to hyperventilate by breathing deeply and forcefully through your mouth at a normal breathing rate. Then a special face mask called a non-rebreathing mask will be placed over your nose and mouth to allow you to breathe in the gas mixture. Some participants may begin to feel claustrophobic when the mask is placed over the nose and mouth. If this occurs we will remove the mask and stop the test.

Confidentiality

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

As part of this study, you will be asked questions about depression. If we learn that you or someone else is in danger of harm, the study team is required to report that information to the proper authorities.

A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. The benefits of participating in this study include receiving information about your risk factors for heart disease including cholesterol, blood pressure, blood sugar, body fat amount and location, and functional status. A possible benefit is that by losing weight and/or increasing your physical activity you may reduce your risk of having another heart attack or needing additional heart surgery, and you may increase your functional ability. Because individuals respond differently to diet and exercise, no one can know in advance if it will be helpful in your particular case. Either way, we hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to participate in an exercise-based cardiac rehabilitation program. Classes, weight loss programs (such as Weight Watchers and Nutrisystem) and testing procedures similar to those offered in this study are available in the community and usually involve a charge to participants. You should talk to your doctor about all the choices you have.

WHAT ARE THE COSTS?

There are some costs to you for taking part in this study. The cost to buy food needed to follow

the individualized meal plan during the 6-month weight loss program and the calcium and/or vitamin D supplements recommended to ensure you are getting proper nutrition will be your responsibility. Costs for your regular medical care, which are not related to this study, will also be your own responsibility. All study costs, including the meal replacements and any procedures related directly to the study, will be paid for by the study. The study will also pay for you to attend cardiac rehabilitation for 6 months, including parking costs related to the intervention and study visits. Transportation to/from cardiac rehabilitation will be your responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

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.

Since this study involves a partnership with the Cardiac Rehabilitation Programs at Wake Forest Baptist Health we will have access to your personal and medical information collected as part of the standard medical evaluation, as well as information on your attendance and progression through the exercise-based program. Program staff will also have access to medical information collected by study staff as needed to ensure the safety of all study participants.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid $150 if you complete all the scheduled study visits. If you withdraw for any reason from the study before completion you will be paid $50 for each completed study visit. To receive payment (either checks or gift cards), you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study, but you will not be paid. You may also be eligible to receive transportation to/from Wake Forest Baptist Medical Center for the study visits.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the National Institutes of Health. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product

being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research-related injuries or to report a study-related illness, adverse event, or injury you should call Tina Brinkley, PhD at [redacted] during normal business hours or [redacted] after hours and identify yourself as a participant in the TOPCARE study.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes: your health history, how you respond to study interventions or procedures, laboratory and other test results, and information from study visits, phone calls, questionnaires, and physical examinations.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the

study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

1) Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

2) Representatives from government agencies such as the Office for Human Research Protections and other similar agencies.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Tina Brinkley that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Tina Brinkley, PhD
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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 Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital (NCBH). These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because:

- your study doctor feels it is in your best interest;
- you are not following the instructions properly;
- you do not later consent to any future changes that may be made in the study plan;
- or for any other reason.

You will be given any new information we become aware of that would affect your willingness

to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Tina Brinkley, PhD at [redacted] during normal business hours or [redacted] after hours and identify yourself as a participant in the TOPCARE study.

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed): _____

Subject Signature: _____ Date: _____Time: _____ am pm

Person Obtaining Consent (Printed): _____

Person Obtaining Consent: _____ Date: _____ Time: _____ am pm