**University of North Carolina at Chapel Hill**
**Consent to Participate in a Research Study**
**Adult Participants**

**Consent Form Version Date:** April 26, 2019
**IRB Study #** 16-3284
**Title of Study**: LCCC1630: Get REAL and HEEL Research Program
**Principal Investigator**: Claudio Battaglini, PhD
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**Funding Source and/or Sponsor:** Breast Cancer Research Foundation (BCRF)

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**What are some general things you should know about research studies?**
You are being asked to take part in a research study. To join the study is voluntary.
You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty. If you choose not consent to participate in this study (LCCC1630), you may still participate in the Get Real & Heel Program.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

**What is the purpose of this study?**
The purpose of this research study is to investigate in breast cancer survivors the potential benefits of a 16-week exercise program (Get REAL & HEEL) -- aerobic and resistance/strength training -- for cardiorespiratory function, physical function, cognition, balance, and symptom management (fatigue, depression, anxiety, quality of life). The safety and overall benefits of exercise in cancer survivors is well-established through decades of research in exercise oncology. However, there remain fundamental questions regarding the best exercise prescriptions for diverse cancer survivors – type, intensity, duration, and frequency of exercise training. Until these questions are answered using rigorous scientific evaluation, the ability to optimally use

exercise as a complementary therapy for the care of cancer survivors remains limited. This study aims to provide empirical evidence for the development of more specific exercise guidelines for cancer survivors.

You are being asked to be in the study because you meet the following eligibility criteria:

- histologically confirmed early stage (non-metastatic) breast cancer
- recently (within 1 year) completed your initial treatment (you may continue to be on endocrine treatment)
- able to read and speak English
- agree to adhere to the 16-week GR&H protocol and complete all baseline, immediate post-intervention, and 6 month post-intervention blood draws, assessments and questionnaires to the best of your ability
- agree to complete annual follow-up questionnaires for up to 5 years after you have completed the 16-week GR&H program to the best of your ability.

**Are there any reasons you should not be in this study?**

You should not be in this study if there is no evidence of a cancer diagnosis or completion of surgery, radiation and/or chemotherapy treatment or any other contra-indication to participate in regular exercise as determined by your physician.

**How many people will take part in this study?**

There will be approximately 120 people enrolled in this study; approximately 40 people will be consented to participate in the study per year.

**How long will your part in this study last?**

- Week 0: Pre-Intervention baseline assessments, questionnaires and blood draws -- 3 separate visits, each approximately 2 hours
- Weeks 1-16: Supervised exercise at GR&H facility -- 3 sessions per week, about 1 hour per session
- Week 17: Post-intervention assessments, questionnaires and blood draws -- 3 separate visits, each approximately 1 hour
- Follow-up at 6 months post-intervention: assessments, questionnaires and blood draws -- 3 separate visits, each approximately 2 hours
- Follow-up at 12 months post-intervention:, questionnaires, about 30 minutes
- Follow-up at 2 years post-intervention: Questionnaires, about 30 minutes
- Follow-up at 3 years post-intervention: Questionnaires, about 30 minutes
- Follow-up at 4 years post-intervention: Questionnaires, about 30 minutes
- Follow-up at 5 years post-intervention: Questionnaires, about 30 minutes

| Week 0 | Pre-test Week 1 | Pre-test Week 2 | GR&H Intervention | Post-test Week 1 | Post-test Week 2 | 6 mo Post-GR&H end (w/in 4 weeks) | 1-5 ys post-GR&H end (w/in 8wks) |
|---|---|---|---|---|---|---|---|
| Interest group Meeting | Participants will complete 2 days of pre-testing within 2 weeks of beginning GR&H. Immune subset will complete 1 extra day of pre-testing. (p16) | | 16 week Exercise Intervention | Participants will complete 2 days of post-testing within 2 weeks of completing GR&H. Immune subset will complete 1 extra day of post-testing. | | Participants will repeat the same post-tests over 2 days. Subset will have a standard blood draw (p16) on first day of post-testing and will not return for a third day of post-testing. | Take-home questionnaires only |

**What will happen if you take part in the study?**

All participants will have the same study procedures – there is no assignment or randomization.

I. **Assessments**:

**All participants will undergo assessments that include**: questionnaires used as a health screening for participation and assessment of quality of life (fatigue, depression, anxiety, and overall quality of life), physical fitness measures including cardiorespiratory function ($VO_{2peak}$, vascular health), muscular strength, body composition, cognition, balance, functionality tests (6 min walk test and Time Up and Go), and blood draw for the assessment of immune function and aging.

a. Baseline: In Week 0, over 3 days at the UNC Exercise Science Lab (each day approximately 120 minutes). Participants on the Wait List for more than 8 weeks will have the Baseline Assessment twice; once at consenting and the second time right before the GR&H exercise session starts.
b. Post-Exercise Program: In Week 17, over 3 days at the UNC Exercise Science Lab (each day approximately 120 minutes).
c. 6-Month Follow-Up after end of exercise program: Over 3 days at the UNC Exercise Science Lab (each day approximately 120 minutes).

Blood samples:

d. Baseline: at the start of the GR&H exercise program (with p16)
e. Post-Exercise Program: at end (no p16) of the GR&H exercise program
f. 6mo after end of exercise program (with p16)

Questionnaires:

g. Baseline: In Week 0, at the UNC Exercise Science Lab (each day approximately 30 minutes).
h. Post-Exercise Program: In Week 17.
i. 6-Month Follow-Up after end of exercise program: at the UNC Exercise Science Lab.
j. 1 year after the exercise program
k. 2 years after the exercise program
l. 3 years after the exercise program
m. 4 years after the exercise program
n. 5 years after the exercise program

Cardiorespiratory fitness ($VO_{2peak}$, Vascular Health): will be performed on an electronically braked cycle ergometer using a continuous incremental ramp protocol following standardized testing procedures. Participants will start pedaling will no load and every three minutes the load will be increased until they no longer are able to continue to pedal or the research team terminates the test. Non-invasive vascular health measures will be taken prior to, and immediately following the $VO_{2peak}$ test. Vascular health will be assessed non-invasively during rest (day 1), during submaximal exercise (day 1), and immediately following your cardiorespiratory fitness test (day 2).

Muscular strength: will be performed on an isokinetic dynamometer for assessments during isokinetic leg extension (lower extremity) and isometric low row (upper extremity) exercises. Participants will be instructed to complete three warm-up isokinetic leg extensions at 50% of perceived maximal effort at 60°/second. Participants will then proceed to complete a total of three isokinetic leg extensions as fast as possible at a velocity of 60°/second with three minutes of rest between each extension. For the isometric low row, participants will be asked to, in a sitting upright position secured to the chair of the dynamometer, to pull straight back as hard as possible on the lever arm for 3-4 seconds. Participants will complete 3 trials and the highest force generated will be used for analysis.

Body composition: will be performed using Dual X-ray Absorptiometry (DEXA). Participants will be asked to lie on their back on the DEXA scanner for 6 minutes (duration of the scan).

Cognition/cognitive function: participants will be asked to complete the following questionnaires: HVLT-R: Hopkins Verbal Learning Test-Revised, KEFS Verbal Fluency Test, TMT/Trial Making Task, and Digit Span Task.

Balance: will be assessed using the Sensory Organization Test (SOT) via the NeuroCom Balance Master. The SOT assesses postural stability by having participants step on a platform that assesses integrity of visual, somatosensory, and vestibular domains through 6 conditions while they balance themselves with eyes open or closed.

Functionality test/6 min walk test: participants will be asked to walk as quickly as possible around a 50-yd level ground course marked in 5-yd segments, for a total of 6 minutes. This test measures the distance one can walk on a flat surface in six minutes at a pace that they can maintain. Participants are allowed to stop and rest during the test if they need to do so.

Time Up and Go test: This test will be used to assess agility and dynamic balance. A chair will be placed securely against a wall and 8 feet away from a cone/marker that participants will walk around. Participants will begin seated in the chair with hands on their thighs. On a "go" signal, they will be asked to rise, walk around the cone, and return to a seated position in the chair as quickly as possible without running.

Blood draw for the assessment of immune function and aging: blood samples will be obtained to examine immune and markers of inflammation and a biomarker of aging that may influence the response to the exercise intervention. A trained research team member will perform the blood draws using standardized phlebotomy procedures.

II. **Get REAL & HEEL Exercise program**: This is a 16-week program conducted at the Get REAL & HEEL facilities adjacent to the UNC campus. Participants are asked to commit to attending supervised exercise sessions 3 times a week. The exercise sessions include cardiovascular exercises to be performed on a treadmill, cycle ergometer or elliptical machines, and resistance exercises performed with dumbbells, rubber bands, and exercise machines progressing from low to moderate intensity by the end of the 16 week intervention. Each exercise session lasts approximately 1 hour.

III. **Patient Medical Records**: In the intervening periods between the end of the GR&H exercise program and pre-planned follow-ups with study participants, research personnel may review participant medical records to see if there are any medical developments that may affect the participant's continued participation in the GR&H study.

All questionnaires and assessments are voluntary. If at any time, you do not want to do a particular assessment or answer a particular question, you may do so. In the interest of research, we hope you are willing to complete all assessments and questionnaires, but we wish to assure you that all study aspects are voluntary. At at any point you no longer wish to participate in the study, you are welcome to continue the Real and Heel supportive care program without the assessments and questionnaires.

**What are the possible benefits from being in this study?**

Research is designed to benefit society by gaining new knowledge. The benefits to you from being in this study may be improvements in cardiorespiratory function, physical function, cognition, balance, fatigue, depression, anxiety, and quality of life.

**What are the possible risks or discomforts involved from being in this study?**

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

**Exercise testing and training -** In the unlikely event of injury during the fitness and physical function assessments or exercise training, such as muscle distensions and joint trauma, medical professionals on the research team will provide the appropriate care. Also, you will only be enrolled if your physician feels you are healthy enough to participate in all study fitness and functional testing and exercise training.

The risks associated with the cardiorespiratory exercise test ($VO_{2peak}$) are minimum, but there is a possibility of certain events to occur during testing. Some of these events include, but are not limited to, abnormal blood pressure and heart rate, chest pain, shortness of breath, fainting, and in rare instances, heart attack. Every effort will be made to avoid or minimize such occurrences through the physician's clearance and by careful observations during testing. Emergency equipment and trained personnel in the lab are available to deal with unusual situations, which may arise. To minimize these risks, you will have a trained exercise physiologist performing this procedure as well as a trained athletic trainer on site during testing. In addition, you will have an ECG, your heart rate, blood pressure, and rate of perceived exertion monitored throughout the test. The test will be discontinued if any abnormal heart rate or rhythm, blood pressure are detected or you desire to stop.

There is minimal risk during the 6-minute walk test; however, participants may experience leg cramps, shortness of breath, chest pain or fatigue. Participants will be monitored continuously during testing and if any abnormalities are observed, the testing will be stopped by a research team member who will provide the participant with appropriate care.

The risk associated with the muscular strength test is minimal. Despite this, there is always the chance that the strength test may result in soreness or injuries to the muscles, joints, and bones. Possible injuries from strength testing include muscle or joint aches, torn muscles, or sprained joints. If an unlikely injury does occur while participating in the study, members of the research team will assess the injured area and take appropriate actions for medical care if necessary. In the event any uncommon or previously unknown risks arise, participants will be asked to inform a member of the research team.

**Blood draws -** There is a minimal risk of bruising or infection from the blood draw procedure. To lessen this risk, only trained phlebotomists will be performing the procedure.

**Dexa scans -** You will be exposed to radiation at the time of the DEXA scan. The total effective radiation dose from one DEXA scan is 0.8 mrem. This amount of radiation exposure is about the amount of radiation exposure an individual receives from natural background sources in one day. The radiation risk from this research procedure is below the risk you may be subject to from clinically indicated radiation procedures, such as a chest X-ray or CT scan.

**What if we learn about new findings or information during the study?**

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

**How will information about you be protected?**

Participants will not be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for

example, the FDA) for purposes such as quality control or safety.

**What will happen if you are injured by this research?**

All research involves a chance that something bad might happen to you. This may include the risk of injury incurred while exercising. If such a problem occurs, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

**What if you want to stop before your part in the study is complete?**
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

**Will you receive anything for being in this study?**
You will be receiving no payment or gift for taking part in this study, other than parking passes for visits to the UNC Exercise Science Lab and free parking at the Get REAL & HEEL facility.

**Will it cost you anything to be in this study?**
It will not cost you anything to be in this study.

**Who is sponsoring this study?**
This research is funded by the Breast cancer Research Foundation (New York, NY). This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

**What if you have questions about this study?**
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on 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.

**What if you have questions about your rights as a research participant?**
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

If you chose not consent to participating in this study, you are welcome to join the Get Real and Heel supportive care program without the assessments and questionnaires.

**Consent Form Version Date:** November 21, 2017
**IRB Study #** 16-3284
**Title of Study**: LCCC1630: Get REAL and HEEL Research Program
**Principal Investigator**: Claudio Battaglini, PhD

**Participant's Agreement**:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____ _____
Signature of Research Participant Date

_____
Printed Name of Research Participant

_____ _____
Signature of Research Team Member Obtaining Consent Date

_____
Printed Name of Research Team Member Obtaining Consent