Using Exercise to Relieve Arthralgia (Joint Pain) and Improve AI Adherence in Older Survivors (REJOIN): A Pilot Study

Informed Consent Form to Participate in Research

Shirley Bluethmann, PhD, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to test the effectiveness of a self-management approach, combining education and exercise-based strategies (treatment group) compared to education only (control group), for improving Aromatase Inhibitor (AI)-related joint pain in older breast cancer survivors (≥60 years). You are invited to be in this study because you have been diagnosed with breast cancer, are 60 years old or older, have finished radiation and/or chemotherapy, and are ready to start anti-hormonal therapy to block estrogens as prescribed by your physician. Your participation in this research will involve 4 in-person visits and last about 1 year.

Participation in this study will involve (1) completing a phone interview for eligibility screening providing permission to access certain information from your medical record for research purposes, (2) completing surveys during your four on site study visits at Atrium Health Wake Forest Baptist which are not a part of your clinical care, (3) providing 2 teaspoons of your blood, which will be drawn by a trained technician to measure inflammation in your body at the four on-site visits, and(4) being randomized to one of two study groups. All research studies involve some risks. Risks to this study that you should be aware of is muscle soreness from exercise (if instructed to do so), which should get better with time, loss of confidentiality, discomfort answering survey questions (any questions you feel uncomfortable answering may be skipped), pain, bleeding, or bruising from blood draws (trained staff may minimize this discomfort). You may or may not benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study please contact the Principal Investigator at 336-716-3324 or 888-716-9253.

If you have any questions, suggestions, or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at 336-716-4542 or the Wake Forest University Health Sciences Research Subject Advocate at 336-716-7600.

INTRODUCTION

You are invited to be in a research study. Research studies help scientist learn new information that may help other people in the future. You are being asked to be in this study because you have been diagnosed with breast cancer, are 60 years or older, have finished radiation and/or chemotherapy, and are ready to start anti-hormonal therapy to block estrogen as prescribed by your physician. Your participation is voluntary. You do not have to be a part of this study if you do not want to. Please take your time in making your decision if you would like to join. 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?

We seek to understand if counseling and a program of physical activity will help a person who has completed a course of clinical breast cancer treatment become more physically active in a safe way. The primary purpose of this research study is to find out if providing specific information plus other resources (like exercise) can improve the experience of women that take medications to reduce the risk of cancer returning. Sometimes, these medications can cause joint pain. We want to provide tools to help.

Additionally, we want to know if older patients are accepting of exercise advice, coaching or other educational materials. While avoiding physical inactivity is recommended, we seek to understand if our counseling will help you become more active. We also believe if you are more active you will have fewer side effects to cancer treatment than if you were inactive, therefore we will ask you questions about these side effects and conduct some basic physical function testing.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

12 people will take part in this study. In order to identify the 12 subjects needed, we may need to screen as many as 500 because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

If you are eligible and agree to participate in this study, you will be randomly assigned to one of two groups: the **treatment group** or the **enhanced standard care group**. Randomization is like flipping a coin to determine your group assignment. You will have an equal chance (50/50) of assignment to the treatment group or the enhanced standard care group. The treatment group will take part in a 16-week virtual, group exercise program with counseling, and the other group will receive enhanced standard care. Both groups will be provided information on hormone therapy for breast cancer. You will receive a tri-axial accelerometer to provide objective measures of physical activity. You will not know in advance which group you will be assigned to, but both groups are necessary to help us understand the best approach with breast cancer survivors, like you. To participate, you must agree to be randomly assigned. Your assignment to treatment or enhanced standard care will be completed via a computer program at the end of your first (baseline) study visit.

If you agree to be in this study, you will be asked to sign and date this consent form. Participation is voluntary, and refusal to participate will not result in any penalty or loss of

benefits. If you do not sign this consent form, you will have the same access to cancer care that all patients at Atrium Health Wake Forest Baptist Cancer Center have.

If you agree to take part in this study, we will:

- Ask you to come to Atrium Health Wake Forest Baptist for a baseline visit and allow us to collect information from your electronic medical related to your cancer diagnosis.
- Ask you to read a brochure about hormonal therapy for breast cancer.
- Collect about 2 teaspoons of your blood, which will be drawn by a trained technician to measure inflammation in your body. You will be required to fast for 8 hours prior to the blood draw. Future testing will be done on these blood samples to understand inflammation in your body. These samples will be stored in a secure lab at Atrium Health Wake Forest Baptist. Only authorized study personnel will have access to these samples.
- Assess your physical function as outlined in the Schedule of Formal Assessments below.
- Ask you to complete a variety of surveys as outlined in the Schedule of Formal Assessments below.

Schedule of Formal Assessments (Summary)

- Strength is measured by gripping and squeezing a small device with your hand that measures how hard you squeeze.
- Endurance is measured by 1) seeing how many times you can stand up/sit down in a chair over 30 seconds, and 2) seeing how quickly you can stand up from a chair, walk a few feet away, and return to sitting in the chair.
- Surveys will ask questions about your mood, memory, pain levels, AI's in survivorship, medications, daily living, support system, physical activity and confidence to do exercise.

Schedule of Formal Assessments				
	Baseline Week 0 Assessment V1	**Post Intervention Assessment V2**	**Six-month follow up V3**	**12-month follow up V4**
Geriatric Assessment				
Height, Weight, BMI	X	X	X	X
Fasting Blood Draw (2 tsp)	X	X	X	X
Geriatric Depression Scale	X	X	X	X
CARG Questionnaire	X	X	X	X
Timed up and Go Test	X	X	X	X
Orientation Memory-Concentration Test	X	X	X	X
Physical Activity Measures				
CHAMPS Questionnaire	X	X	X	X
Accelerometer (GT3X)	X	X	X	X
Exercise Logs		X		
AI-related Arthralgia				
Brief Pain Inventory	X	X	X	X
WOMAC	X	X	X	X
Quick Dash	X	X	X	X
Grip Strength	X	X	X	X
Behavioral Predictors				
Exercise Self-Efficacy	X	X	X	X
Social Support for Exercise	X	X	X	X
Knowledge assessment about AIs (TINQ)	X	X	X	X
Medication Adherence				
Self-report (Morisky Scale)	X	X	X	X
Adverse Events Tracking		X	X	X
Q-PRO Exit Interview				X

Intervention Procedures		
	Treatment Group	**Enhanced Standard Care Group**
Activity	X	
Baseline Assessment (V1)		
One-on-one exercise consultation	X	
Complete assessment measures (See Schedule of Formal Assessments)	X	X
Receive brochure on Hormonal Therapy for Breast Cancer	X	X
Group Intervention (8 weeks)		
Meet ≥ 2 times per week for 8 weeks for group exercise and education/discussion (16 total sessions)	X	
Submit weekly exercise log (8 reports)	X	
Home-based Intervention (8 weeks)		
Execute home-based exercise plan (i.e., exercise 2-3 times per week at home)	X	
Bi-weekly coaching phone calls to assess progress	X	
Complete weekly exercise log (8 reports)	X	
Post-Intervention Assessment at 4 months(V2)		
Complete satisfaction questionnaire	X	X
Complete formal assessments	X	X
Follow up Assessment at 6 months (V3)		
Complete formal assessment	X	X
Follow up Assessment at 12 months (V4)		
Complete final formal assessments	X	X
Participate in QPRO Exit Interview	X	X

Snapshot of Intervention Activities for Participants in Group Exercise Arm	
Start *with 8 Weeks* of Virtual Sessions	**Followed by *8 Weeks of At-home Sessions***
Meet ≥2x per week, 16 sessions of Fit & Strong program	Execute plan for at-home physical activity
Each scheduled session is 90 min total, including:	Aim for 120-150 min physical activity per week, 2-3x per week
- 60 min supervised exercise (e.g., 40 min cardio, 20 min light weights and stretching)	Receive coaching phone calls bi-weekly to assess progress
-30 min education and discussion	Resistance bands and ankle weights
Create a plan for at-home physical activity	Workout buddy encouraged

As part of this research study, you may be video recorded during your exercise virtual platform sessions for quality assurance and educational purposes. This may include capturing an occasional still-shot photograph. Only authorized REJOIN personnel will have access to these files. These videos will be considered Protected Health Information if they contain information that identifies you. You may request the taping be stopped at any time during the course of the research study. You may also withdraw your consent to use and disclose the tape or still shot photographs before they are used, but doing so may affect your eligibility to remain in the research study. You should also understand that you will not be able to inspect, review, or approve the video, photographs, or other media (including articles containing such) before they are used in this study.

Please choose one of the following regarding the use and disclosure of the recording and photograph used in this research study:

_____ I would like the recording and photographs of me to be destroyed once their use in this study is finished. I understand that destroying the photographs at the end of this study will not affect any prior use of the photographs/videotapes/audiotapes/recordings.

____ The recording and photographs of me can be kept for use in future studies provided they are kept secure, and any future study will be reviewed by an IRB. I understand that I will not be able to inspect, review or approve their future use.

STORAGE OF BIOLOGICAL SPECIMENS

If you agree to participate in this study, some of the samples will be kept and may be used in future research to learn more about other diseases. The sample will be stored, and it will be given only to researchers approved by Dr. Shirley Bluethmann. An Institutional Review Board (IRB) must also approve any future research study using your blood sample. In the future, research on your specimen may involve whole genome sequencing.

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. 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.

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, or social security number. 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.

How Long Will I Be in the Study?

If you agree to participate, there will be four on-site clinic visits for study assessments that last approximately 60 minutes each. These assessments will be completed at approximately 4 months, 6 months, and 12 months, after the date of study enrollment.

If you consent to participate and are randomly selected for the **treatment group**, you will be asked to attend two virtual 1 hour exercise and orientation consultations, in addition to virtual educational and exercise classes about twice a week for 8 weeks (16 total classes), with each class taking approximately 1 hour and 30 minutes. After the 8 weeks of educational and exercise-oriented classes, participants will be asked to carry out 8 weeks of at home unsupervised exercise sessions, with the goal of 120-150 minutes per week. During the 8 week at-home exercise portion of the intervention, participants will receive exercise counseling via phone calls from one of the exercise trainers every other week, which will last approximately 30 minutes each.

If you consent to participate and are enrolled in the **enhanced standard care group**, you will be provided with education materials on AIs. No further activities will be required except for the 4-, 6-, and 12-month study visits at Atrium Health Wake Forest Baptist.

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 exercise training, surveys, physical functions testing, bloodwork and randomization are outlined below.

Risks of exercise training: The risk of an exercise training induced heart event is low. Previous evidence shows that there is a greater risk of a heart event from being inactive than participating in aerobic activity. Engaging in an exercise program when one has been inactive for a considerable period of time includes some foreseeable risk of injury such as mild strains, sprains, and muscle soreness that are expected to pass within one week. This may be particularly so for older individuals. To minimize risk of injury, participants will start at a lower intensity and will be increased gradually to ensure safety and effectiveness of the program. However, serious physical injury is considered unlikely. Moreover, a nurse or similarly qualified clinician will be onsite during physical function testing. Exercising while supervised in a virtual format comes with a mild risk increase as opposed to in-person supervision. This has been taken into

consideration when choosing physiological testing to select the safest options. To complement this, all participants will be asked to have someone present in the household with them, while they exercise, in the event of an emergency. If they forgo this, they will be required to provide emergency contact information such as address, so that the study team may contact emergency services on their behalf. The injury rate observed in the general population in those who report involvement in strength training is 3-4% over a 30-day period.

Risks for surveys: There are no medical risks associated with filling out surveys, however one may become uncomfortable providing personal information. Any questions that make you uncomfortable can be skipped.

Risks for physical functioning testing: Performance of the chair stands, timed up and go, and balance tests can result in muscle injury or falls. This risk will be minimized by having trained staff perform the tests and monitor participants closely. If it becomes apparent that the activity cannot be continued without injury, the staff will stop the evaluation activity.

Risk of bloodwork: Blood draws may cause pain, bleeding, and/or bruising and discomfort. However, an experienced technician will try to minimize this discomfort. Fasting prior to the blood draw may cause dizziness, headaches, low-blood sugar, or fatigue. However, we will work to minimize this discomfort by scheduling early morning visits when possible, and providing snacks as soon as blood has been drawn.

If any important new information about the study develops that may affect your health, welfare, or willingness to stay on the study, your study doctor will tell you. You may be asked to sign another consent form at that time.

Risk of Randomization: you will be assigned to a treatment program by chance. The treatment you receive may prove to be less effective or to have more side effects than the other research treatment or other available treatments.

There also may be other risks 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 to your health.

A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study to identify possible safety issues to participants and to provide advice and recommendations on possible changes to the research study for the protection of participants.

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 information obtained from this research study may benefit future cancer patients by demonstrating safety and utility of education and advice about lifestyle (including the importance of exercise) for older breast cancer survivors. The benefits of participating in this study are as follows: You may decrease your risk for chronic diseases and cancer related fatigue, improve quality of life, and recover with better function than if you do not receive advice about your medications or how to exercise. There is no guarantee that you will benefit from being in this

research. Because individuals respond differently to therapy, no one can know in advance if it will be helpful in your particular case.

What Other Choices Are There?

You can choose to start exercising on your own even if you do not take part in the study. You should talk to your doctor about what options would be best for you.

What Are the Costs?

All study costs, including any study products or procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own 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, or permitted by law, or necessary to protect the safety of yourself or others.

Your information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

Will You Be Paid for Participating?

Participants will receive stipends for completing surveys and for returning accelerometers after use. For completing each of four in-person study visits, each participant is eligible to receive $30 for up to $120 total per person. Additionally, participants may receive $10 for returning the accelerometer after each assessment (up to $40 additional per person). If you do not complete the study for any reason, you will be paid for the visits you have completed. Payment will be received by a reloadable MasterCard. Details of the MasterCard are explained on an additional sheet provided when you are first given the card.

When a visit is completed, funds will be approved and loaded onto your card. The funds will be available within 2-3 business days. In order to assign a MasterCard to you and load funds onto it we will use your Study/Subject ID, name, address, date of birth, and social security number.

To receive payment, 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.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by The American Cancer Society. The sponsor is providing money or other support to the researchers 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?

Wake Forest University Baptist Medical Center maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of injuries or illnesses to some participants in certain research studies. 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. To the extent research coverage is not available, you or your insurance company may be charged for the costs of medical care. You may receive care at Wake Forest University Baptist Medical Center and/or Atrium Health.

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 Shirley Bluethmann at 336-716-3324 or 888-716-9253.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes names, date of birth, gender, email and mailing address, diagnoses, past, present and future medical records, new health information from tests, procedures, in person and virtual visits, interviews, or forms filled out as part of this research study.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with the health care operations of Atrium Health, Wake Forest University Health Sciences, and their respective affiliated entities.

We will take steps 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 Atrium Health Facilities; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS), The American Cancer Society (ACS) 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, videotapes, audiotapes, or other recorded media which identify you unless we have your written authorization.

Monitors, auditors, IRB, or other regulatory agencies will be granted direct access to your medical record for verification of clinical trial procedures or data to the extent permitted by other applicable laws. These monitors, auditors, and other individuals are also required to maintain the confidentiality of your protected health information.

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.

You can tell Shirley Bluethmann 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:

Shirley Bluethmann
1 Medical Center Blvd.
Winston Salem, NC 27157

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 Atrium Health Wake Forest Baptist, or their respective affiliated entities 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. Authorization to access this part of the medical record will only be available to people who have a need to know this information in order to perform their job-related duties. If you are not a patient of these health care facilities, a medical record will be created for you to provide access to this important information to providers 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 website at any time.

Laboratory test results and other clinically relevant medical reports created as a result of your participation in the research study may be entered into the computer systems of Atrium Health Wake Forest Baptist, and/or their respective affiliated entities. These results and reports will be kept secure in compliance with applicable laws, with permission to access this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A medical record will be created for all study participants seen on-site if a medical record doesn't already exist. Information about your participation in the study will be placed in the medical record, along with any routine medical test results that were obtained 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 it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

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, **Shirley Bluethmann at 336-716-3324 or 888-716-9253.**

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 (336) 716-4542 or the Research Subject Advocate at (336) 716-8372.

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