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CONSENT FOR RESEARCH

Penn State College of Medicine
The Milton S. Hershey Medical Center

NCT03280836 "Exercise Program in Breast Cancer Patients Receiving Neoadjuvant Chemotherapy"

Title of Project:
Women In Steady Exercise Research – Neoadjuvant Exercise Trial (WISER–NET)

Principal Investigator:
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Address:
Penn State Cancer Institute
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Telephone Numbers: Weekdays: 8:00 a.m. to 5:00 p.m. (717) 531-4387.
After hours call (717) 531-8521. Ask for the Oncology doctor on 24-hour call.

Subject's Printed Name: _____

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

1. Why is this research study being done?

You are being asked to participate in this research study because you are patient of the Penn State Hershey Medical Center and have decided to undergo neoadjuvant chemotherapy for breast cancer. The primary purpose of this study is to determine whether breast cancer patients can be enrolled, randomly assigned (like a flip of a coin) to a control or exercise group, and comply with 6 months of aerobic (walking/jogging) exercise training. Additionally, we seek to compare changes in clinical blood tests, fitness level, heart function, quality of life, and tumor response (tumor size) in exercisers vs. control.

You will be one of 20 patients in this study.

2. What will happen in this research study?

- Allowing us to utilize your breast tissue taken during your clinical biopsy and also your clinical surgical resection. No extra tissue will be taken for research purposes.

- Allowing us to utilize the images taken during your clinical breast MRI procedures.

- Allowing us to utilize the images taken during your clinical echocardiogram(s).

- Allow us to collect information from your electronic medical record related to your breast cancer diagnosis.

- Allowing us to take 2 extra tubes of blood (about 1 tablespoon) during a routine clinical blood draw before, at the midpoint, and following neoadjuvant chemotherapy. The blood samples will be used to look at various proteins and markers of inflammation.

- Completing surveys during your first, midpoint, and final neoadjuvant chemotherapy infusion which are not part of your clinical care. These surveys include:

    - Leisure time exercise activity-to assess how often you are exercising during your free time
    - Fatigue-to gain a better understanding of impact of fatigue on your daily life
    - Health-to gain a better understanding of overall health and how well you feel
    - Work productivity and activity impairment-to assess effect of your health problems on your ability to work and perform regular activities

- Completing an exercise test before and after neoadjuvant chemotherapy, this is not part of your clinical care.

- Completing an educational session with regard to exercise and safety, which is not part of your clinical care.

- For women with HER2(-) tumors (i.e. not receiving Herceptin therapy): completing an echocardiogram after chemotherapy that is not part of standard of care.

- If randomly assigned to the exercise intervention (there is a 50% chance you could be assigned to the exercise group):
    - You will be asked to complete the exercise intervention with 80% or greater adherence.

- If randomly assigned to the control group (there is a 50% chance you could be assigned to the control group):
    - We ask that you do not start an exercise program.

What is **exercise testing**:

-You will be asked to walk or jog on a treadmill with increasing speed and incline. We will ask that you push yourself until you feel as though you cannot continue and need to stop. This tells us the maximal amount of work you can do.

-As a study participant we will also monitor your blood pressure throughout the test and during recovery. The electrical activity of your heart will also be monitored with an EKG.

-In order to measure your fitness capacity we will ask that you breathe in and out of an apparatus that measures how much oxygen your body is using. This apparatus is similar to a scuba diving or snorkeling mouthpiece that is attached to a tube and a special analyzer. We will also place a nose clip on your nose to ensure we are measuring all the air you are breathing in and out.

-We will ask that you dress appropriately for exercise, perform no unusual physical efforts for at least 12 hrs before the test, continue taking any medications you normally would, not eat or smoke for ~3 hours before the test, refrain from caffeine intake that day if possible.

What is an **exercise education session**:

-We will instruct you regarding: the proper use of heart rate monitors, warm-ups, cool-downs, stretches, proper footwear for injury prevention, aerobic exercise safety, and completing exercise logs.

What is the **exercise intervention**:

-*If you are randomized* to the exercise intervention group, you will receive a three DVDs and an exercise binder prior to your chemotherapy.

-You will also receive a Polar Heart Rate monitor; the monitor will guide you in attaining the appropriate exercise intensity for you personally.

-You will be asked to keep an exercise log with the date, time, average heart rate obtained from a heart rate monitor, duration of workout and stretching, and any comments regarding the workout.

-You will be instructed to bring the workout logs to your infusion session for review with the staff exercise physiologist. The exercise physiologist will then provide ongoing support and monitoring of adherence in person at infusion sessions and via phone approximately once per week.

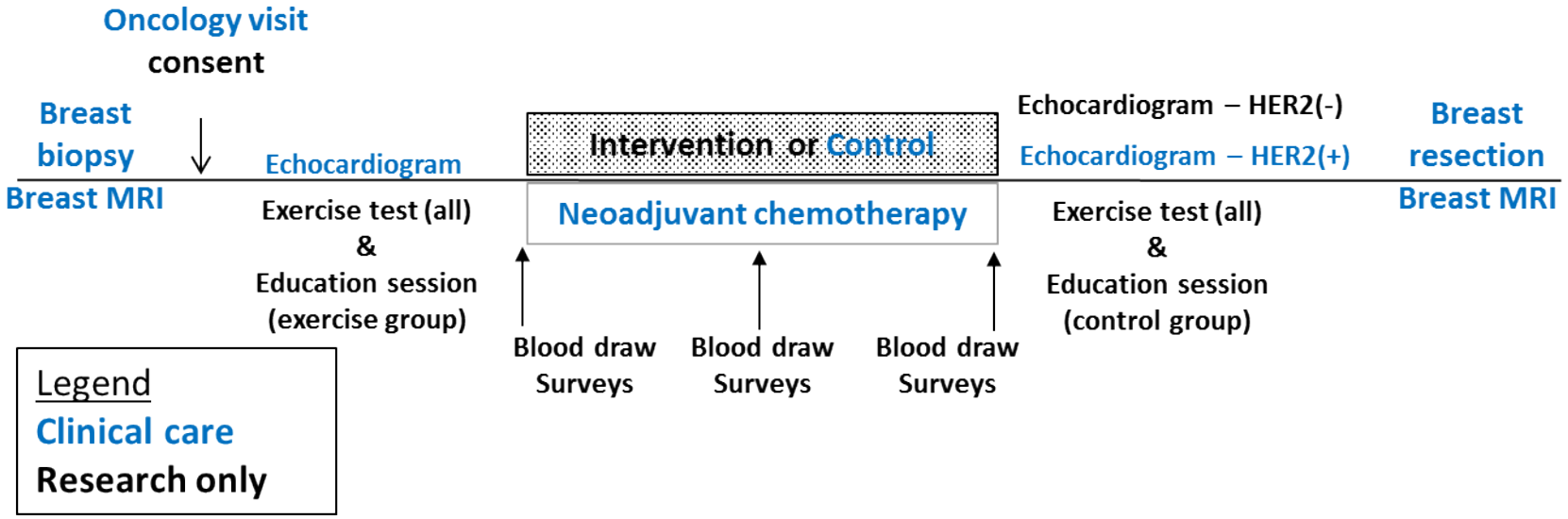
-*You will work towards the goal of 75+ minutes per week of moderate to vigorous exercise.*

-Weeks 1-2:
    20 minute sessions 3 days per week, at mild intensity
-Weeks 3-4:
    25 minute sessions 3 days per week, at mild intensity
-Weeks 5-11:
    25 minute sessions 2 days per week, at mild intensity
    25 minute session 1 day per week, at moderate intensity
-Weeks 12-24:
    25+ minute sessions 2 days per week, at mild to moderate intensity
    25+ minute session 1 day per week, at vigorous intensity

What does the **control group** do:

-You will be asked to maintain your usual level of physical activity and not to engage in any new exercise program during the study. We will contact you at infusion sessions or via phone to inquire about your experience and well-being during treatment.

-You will receive the DVDs and exercise binder after completing all study activities AND your surgical oncologist has cleared you for exercise following your surgical resection.



What are my responsibilities if I take part in this research?
If you take part in this research, your major responsibilities will include:

- coming to the scheduled appointments
- having the required testing & procedures
- completing the exercise prescribed to you (if randomized to the exercise group)

3. What are the risks and possible discomforts from being in this research study?

There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

The known foreseeable risks and/or discomforts to the study participant

Risks of exercise testing The risk of maximal cardiopulmonary exercise testing is approximately 1 nonfatal event in 10,000 maximal treadmill tests and only 1 fatal cardiac complication in over 70,000 maximal exercise tests. Major complications of exercise testing include death, myocardial infarction (heart attack), arrhythmia (irregular heart beat), fatigue, hemodynamic instability (fluctuations in heart rate, blood pressure, breathing) and orthopedic injury (injury to muscle, tendons, bone, etc). Skin irritation may occur at the sites where electrodes were placed.

Risks of exercise training The risk of an exercise training induced cardiac event (heart attack, irregular heart beat) is 2 nonfatal cardiac events in 375,000 subject hrs of exercise, or about 1 event per 1.7 million walk/jogging miles, based on a large Dallas, TX physical activity center study. Further risks of the exercise intervention include: muscle pain, muscle strains/sprains, joint pains (such as hip, knee, ankle or foot pain), fatigue, and risk of fall resulting in trauma/fracture.

Risks of echocardiography There are no serious risks associated with transthoracic echocardiography. It is possible that subjects may experience mild, temporary discomfort from the ultrasound probe being pressed against the chest or from lying down during the additional imaging.

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

Risks of standard venipuncture The discomfort associated with removing blood by venipuncture (by needle from a vein) is a slight pinch or pin prick when the sterile needle enters the skin. The risks include mild discomfort and/or a black and blue mark at the site of puncture. Less common risks include a small blood clot, infection or bleeding at the puncture site, and on rare occasions fainting during the procedure. No additional blood draws will be done outside of standard clinical care.

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.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?

There is no guarantee that you will benefit from this research. The possible benefits you may experience from this research study include decreasing your risk for cardiovascular disease and increasing your physical fitness.

4b. What are the possible benefits to others?

The information obtained from this research study may benefit future breast cancer patients by demonstrating safety and efficacy of an at home aerobic exercise intervention.

5. What other options are available instead of being in this research study?

You may choose not to be in this research study.
Another option is self-directed exercise.

6. How long will I take part in this research study?

If you agree to take part, it will take you about 8 months to complete this research study. You will be asked to return to the research site 0-2 times depending on your schedule.

We will make every effort to link research activities to clinical visits to limit the requirement to come to the Medical Center specifically for study activities.

- Baseline testing: Exercising testing and the exercise education session (if randomized to exercise group).
  ~ 1hr addition for exercise testing (all participants)
  ~ 1hr addition for exercise education session (*if randomized to exercise group*)

- Final testing: Exercise testing and the exercise education session (if randomized to control group), echocardiogram (which is only for research and not part of clinical care, if HER2(-)).
  ~2 hrs for echocardiogram and exercise testing (all participants)
  ~1 addition for exercise education session (*if randomized to control group*)

Surveys will be administered while you are at your infusion session.

Blood draws will be obtained when you go for clinical laboratory testing.

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

Your blood tubes will be labeled with your subject ID number, and surveys will be coded with your subject ID number. Your clinical data we obtain will have your name and date of birth on it.

7a. What happens to the information collected for the research?

Efforts will be made to limit the use and sharing of your personal research information. In our research files at The Milton S. Hershey Medical Center (HMC) and Penn State College of Medicine (PSU) we will

include these identifiers your name, address, phone number, email address, date of birth, medical record number, a code number

- A list that matches your name with your subject ID number will be kept in a locked file in Dr. Schmitz's office.
- Your research records will be labeled with subject ID number and will be kept in a safe area in Dr. Schmitz's research office.
- Your research samples will be labeled with your subject ID number and will be stored in our freezers in a passcode protected laboratory.
- Results of some of the research-related tests (including but not limited to your echocardiogram following chemotherapy, will be kept in your HMC medical record.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

7b. How will my identifiable health information be used?

If you give your consent, health information that can be traced to you will be collected for this research study. In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so. We will use and disclose your information only as described in this form and in the HMC Privacy Notice.

The research team may use the following health information:

- Past, present, and future medical records
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

The following people/groups may see, use, and share your identifiable health information:

- HMC/PSU research staff involved in this study
- The HMC/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare
- The HMC/PSU Human Subjects Protection Office
- The HMC/PSU Research Quality Assurance Office
- Non-research staff within HMC/PSU who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- Federal and state agencies (such as the U.S. Food and Drug Administration, the Office for Human Research Protections, the Department of Health and Human Services, the National Institutes of Health (NIH), and other U.S. or foreign government bodies that oversee or review research)
- The NRG Oncology Foundation and the National Cancer Institute (NIH) that oversees the data and safety of this research

These groups may also review and/or copy your original PSU/HMC records while looking at the results of the research study. It is possible that some of the other people/groups who receive your health

information may not be required by Federal privacy laws to protect your information. We share your information only when we must, and we ask anyone who receives it from us to protect your privacy.

Because research is an ongoing process, your permission for the use, storage and sharing of your health information will continue indefinitely.

Your privacy rights:

- You have the right to refuse to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you will not be able to take part in this research study.
- You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing using the address on the front of this form. Once permission is withdrawn, you cannot continue to take part in the study.
- If you withdraw your permission, we will stop collecting health information about you for this study; we may continue to use and share your health information that we already have if it is necessary for safety and scientific soundness of the research study; and we will not be able to take back information that has already been used or shared with others.
- You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. However, you may not be allowed to see or copy certain health information that is a part of this research study. This is only for the period of the study. You will be allowed to see that information when the entire research study is complete.

8. What are the costs of taking part in this research study?

8a. What will I have to pay for if I take part in this research study?

For costs of tests and procedures that are only being done for the research study:

- The intervention materials (DVDs and exercise binder) will be provided by the research budget at no cost to you.
- You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition.
- The research-related tests and procedures that will be provided at no cost to you include: an echocardiogram following chemotherapy, and exercise testing.

For costs of medical services for care you would receive even if you were not in this research study:

- You and/or your insurance company will be responsible for the cost of routine medications, tests and procedures that you would receive even if you were not in this research.
- You and/or your insurance company will be billed for the costs of these routine tests and procedures in the usual manner.
- You will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage.
- You will be responsible for any charges not reimbursed by your insurance company.
- Some insurance companies may not pay for routine costs for people taking part in research studies. Before deciding to be in this research you should check with your insurance company to find out what they will pay for.

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?

It is possible that you could develop complications or injuries as a result of being in this research study. If you experience a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If you experience a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and the principal investigator will arrange for medical treatment.

HMC/PSU compensation for injury

- There are no plans for HMC/PSU to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your insurance carrier or to you.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility.

9. Will I be paid to take part in this research study?

You will not receive any payment or compensation for being in this research study. All participants will receive three DVDs and an exercise binder. The timing of when you receive these materials depends on which arm of the trial (intervention or control) you are randomized to.

10. Who is paying for this research study?

The NRG Oncology Foundation and the National Cancer Institute (NIH) is providing funding for the costs of the intervention and testing.

11. What are my rights if I take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect medical information from your routine medical care. If you agree, this data will be handled the same as research data. If you withdraw completely from the research study, no further information will be collected and your participation will end. You may discontinue taking part at any time without penalty or loss of benefits to which you are otherwise entitled.

Dr. Schmitz may take you out of the research study without your permission.

- Some possible reasons for this are: continuing the research would be harmful, you did not follow the instructions of the study doctor, you experience serious side effects.

- If your participation ends early, you may be asked to visit the research doctor for a final visit.

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?

Please call the head of the research study (principal investigator), Kathryn Schmitz at 717-531-4387, or the Oncology doctor on 24-hour call at 717-531-8521 if you:

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the research protection advocate in the HMC Human Subjects Protection Office (HSPO) at 717-531-5687 if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns or general questions about the research.
- Have questions about your privacy and the use of your personal health information.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the HSPO's web site at http://pennstatehershey.org/irb under research subject information for:

- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the HSPO at (717) 531-5687.

INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative and have answered any questions he/she has about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and agree to allow your information to be used and shared as described above.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name

Optional part(s) of the study
In addition to the main part of the research study, there is another part of the research. You can be in the main part of the research without agreeing to be in this optional part.

Optional Analysis of DNA (material in your genes)
In the main part of this study, we are collecting blood from you before, at the midpoint, and after neoadjuvant chemotherapy. If you agree, we would like to assess the level of tumor DNA in the blood sample. Also, we would like to assess specific changes to how your DNA is packaged in white blood cells in the blood sample. We will not conduct genetic testing (research about diseases that are passed on in families). These studies may be helpful in understanding how cancer cells and your immune system change during treatment.

- It is unlikely that these studies will have a direct benefit to you.
- The results of these tests will not have an effect on your care.
- Neither your doctor nor you will receive results of these future research tests, nor will the results be put in your health record.
- The blood samples will be labeled with a code number that links the information obtained in study to the samples.

You should initial below to indicate what you want regarding allowing researchers to analyze your blood for levels of tumor DNA and changes to how DNA is packaged.

Your sample*s* may be used for research on tumor DNA and DNA packaging.
_____ Yes _____ No

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the optional part(s) to the research to the subject or subject representative and have answered any questions he/she has about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

Signature of Person Giving Informed Consent
Signature of Subject

By signing below, you indicate that you have read the information written above and have indicated your choices for the optional part(s) of the research study.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name