Wake Forest®
School of Medicine

Department of Neurology

A TELEHEALTH EXERCISE INTERVENTION FOR THE TREATMENT OF REFRACTORY EPILEPSY: A PILOT STUDY

Informed Consent Form to Participate in Research
Halley Alexander, MD Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to determine if exercise can improve seizure control and other aspects of epilepsy. You are invited to be in this study because you have uncontrolled epilepsy. Your participation in this research will involve 4 visits: 2 in-person visits and 2 telephone visits, and last about 28 weeks.

Participation in this study will involve being randomized to either a control group or the intervention group. Both groups will wear a Garmin activity tracker and keep a study diary which will include recording information on seizures, sleep, and activity. The intervention group will participate in a 12-week supervised aerobic exercise program that is individualized to each participant's fitness level and abilities. This group will meet weekly with a coach who will monitor progress and provide exercise goals. At the end of the intervention period, the control group will be offered the opportunity to participate in the exercise program as well. All research studies involve some risks. A risk to this study that you should be aware of is the risk of falls or injuries related to starting an exercise program. There is a possibility that you may 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. There may be other choices available to you. Some other choices may include do nothing and continue your current care. 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. The person in charge of this study is Halley Alexander, MD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is: [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 epilepsy. 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 a 12-week individualized aerobic exercise intervention is feasible in people with epilepsy. We will gather information on whether exercise has effects on markers of sleep and stress, and whether it can effect quality of life, mood, cognition, and seizure frequency.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Up to 30 people at Wake Forest Baptist Health System will take part in this study. In order to identify the 30 subjects needed, we may need to screen as many as 400 because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

At your first visit, study staff will review the inclusion and exclusion criteria to ensure that you still qualify for the study. After reviewing the informed consent document (this document), you will have your vital signs taken. You will perform a 10 meter walk, which the staff will use to calculate your gait speed, in order to ensure that you are physically able to participate in the study. You will then be asked to provide basic information related to your medical history and your epilepsy. You will be asked to perform some baseline assessments including a 6 minute walk, and a 10 minute resting heart rate measurement using a heart rate monitor. Guided exercise testing on a treadmill may be performed if deemed safe from a COVID transmission standpoint by the members of the study team. If exercise testing is not performed either due to staff or participant preference in the setting of COVID-19, then the exercise safety and heart rate reserve will be determined from the 6 minute walk test. You will be asked to complete some questionnaires that will assess or ask questions about your mood, stress level, sleep quality, quality of life, goal setting, and expectations. You will undergo cognitive testing by trained staff members. You will be given a Garmin Forerunner which will be setup with an application on your smartphone. You will be given a study diary, in which you will be asked to record your seizures, sleep, exercise, and any injuries, falls, or other issues that occur during the study period. This diary may be completed by paper or electronically through Redcap. You will then continue your normal habits for 4 weeks. It is important not to change your normal habits during this time. This visit will occur at either the Worrell Building, located on the Wake Forest University campus, or the Clinical Research Unit at Wake Forest Baptist Medical Center.

You will be randomized into one of the study groups 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. There are two groups you may be randomly assigned to in this

study, one is the exercise intervention group and the other is the waitlist control group. You will be called at the end of 4 weeks to let you know which group you are in.

If you are randomized into the study intervention group, this means you will participate in a 12 week exercise program that will take place in your own home, utilizing walking or other aerobic exercises provided to you by your coach. You will be paired with a coach, and will be required to meet with them weekly by way of video visit. At every weekly meeting with the coach, exercise goals will be tailored to your individual abilities and lifestyle and will include walking or performing other aerobic activities to achieve a certain heart rate for a certain period of time. You will use your Garmin to track your exercise and your progress will be reviewed each week with the coach. At the end of the 12 week intervention period, you will be encouraged to continue exercising on your own. We will evaluate your progress again at the end of another 12 weeks. During the second 12 week period, you will still fill out your diary and use your watch to track your exercise, but you will NOT meet with a coach every week.

On the other hand, you may be assigned to the control group. Participating in the control groups means that you will continue your usual habits for 12 weeks. You will continue to wear the Garmin activity tracker but will not be given an exercise program. You will continue to log your daily seizure, sleep, and injuries/falls information in the study diary. You will be contacted by a study coordinator every 2 weeks for health education. At the end of the 12 weeks, you will be offered free access to the exercise program if you want to participate.

Following the 12 week intervention period, there will be an in-person follow up visit (Visit 3). At this visit, you will return for post-intervention assessments and questionnaires similar to those that were given to you at the first visit. These include a 6 minute walk test and another 10 minute heart rate measurement using a heart rate monitor. You will be asked to complete the same questionnaires and will undergo similar brief cognitive testing. This visit may occur at the Worrell Building on Wake Forest University main campus or the Clinical Research Unit at the medical center.

At the end of 28 weeks, you will have a telephone visit (Visit 4) and will again answer a series of questionnaires and exit questions about being in the study. The study will conclude at this time.

The principal investigators and some of the study staff will not know which group you are in (intervention or control). This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

If you take part in this study, you will have the following tests and procedures:
All of the following procedures will be done for research purposes only:

- Vital signs: Your blood pressure, heart rate, and weight will be taken at all non-telephone study visits (Visits 1 and 3).

- 10 meter walk screen: At Visit 1, you will be asked to walk 10 meters. The staff will use to calculate your gait speed, in order to ensure that you are physically able to participate in the study. If you do not meet a certain speed, you will not be eligible to continue in the study.
- Collection of medical information: At Visit 1, your general information and medical information will be collected. This will include demographic information, and information about your epilepsy.
- Review medications: At all visits (Visits 1-4) your anti-seizure medications will be reviewed, to ensure that there have been no changes during the study.
- Garmin Activity Tracker: You will receive a Garmin watch and activity tracker to wear on your wrist. It will be set up with de-identified information and a research account. You will be asked to wear this continuously while awake and asleep, only removing it while showering and while charging. Because we want to collect information about your sleep and activity, we recommend charging the device during periods of relative inactivity, such as when you are watching television or eating dinner, etc. Your personal information will not be recorded.
- Study Diary: You will be asked to keep a study diary throughout the duration of the study period (28 weeks). You will record in this diary on a daily basis information regarding your seizures, sleep time, exercise, any fall/injuries, and hours wearing the Garmin device each day. You will be required to mail or email this study diary back to us every 2 weeks.
- Questionnaires: At Visits 1, 3, and 4, you will asked to complete a series of brief questionnaires regarding your mood, stress level, sleep quality, quality of life, and goal setting expectations. Some of these will be given in person and others will be sent to your through your email address.
- Heart-rate variability measurement: At Visits 1 and 3, we will measure an aspect of your heart rate called heart-rate variability. This simply requires you to sit quietly for 10 minutes while we record information with a heart monitor. It is not painful or invasive.
- 6 minute walk test: At Visits 1 and 3, you will be asked to complete a 6 minute walk test. The study staff will measure the distance that you are able to cover in 6 minutes. This is a measure of your physical fitness. You are allowed to rest during the test if you need to.
- Cognitive Testing: At Visits 1 and 3, you will undergo a few tests of your thinking and memory skills with a trained professional. These may involve simple puzzles, remembering lists, etc. This will take roughly 45 minutes and some of the questionnaires may be completed in between tests.
- Exit Questions: At your last visit, we will ask you to answer a few short questions about your experience being in the study and any positive or negative feedback you have to help improve future studies.

If you are in the INTERVENTION group, you will also have:

- Weekly in-person coaching: You will be required to have a 1:1 session with your coach each week. This will be performed using video visits over the internet. You will be educated on how to access these. During these visits, the coach will review your previous week's progress and help you set new goals for the coming week, based on your unique barriers and situation. You may also do a monitored exercise session during the visit. The entire visit will take roughly 1 hour.

- Exercise regimen: With your coach, you will develop an aerobic exercise plan to complete for the week, which you will accomplish on your own schedule. The easiest way to accomplish this is with walking, but if you prefer your coach can also provide you with other aerobic activities that you can perform in your home. Your coach will give you a prescribed target heart rate zone and a prescribed number of minutes to reach that zone each week. You will use the watch to monitor your heart rate during exercise.
- A post-intervention survey with questions asking how you liked, or didn't like, the exercise program.
- Follow-up assessments at Visit 4 (week 28) performed remotely including many of the same questionnaires that you completed at Visits 1 and 3.
- As part of this research study, you will be videotaped/audiotaped/recorded. This is being done only during the coaching sessions, so that our head coach can check in on the coaches to make sure that everything is being done correctly by your coach. These videotapes/audiotapes/recordings will be considered Protected Health Information if they contain information that identifies you. You understand that you may request the photographing, filming, taping or recording be stopped at any time during the course of the research study. You can also withdraw your consent to use and disclose the photograph/videotape/audiotape/recording before it is 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 photographs, videotapes, audiotapes, recordings 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 photograph/videotape/audiotape used in this research study:

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

If you are in the control group, you will also have:

- Telephone health education every 2 weeks. This phone call will last ~ 20 minutes.

We may send copies of your exercise test results to your personal physician, ONLY IF these results are concerning for an underlying medical problem. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study.

Do you request that we send important medical findings from your study tests/exams to your personal physician?

[ ] Yes [ ] No _____ Initials

How Long Will I Be in the Study?

You will be in the study for about 28 weeks.

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. There are no adverse risks to your health if you stop the study early.

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 participation include:

Risks and side effects related to wearing the Garmin:
• There is minimal risk to wearing the Garmin device, which in rare cases may cause skin discomfort or irritation.

Risks and side effects related to the fitness test and exercise program:
Likely
• Temporary shortness of breath and/or sweating from physical activity which is a normal physiological response but may be uncomfortable.
• Temporary muscle soreness or minor aches and pains after exercising.

Rare and Unexpected
• Severe shortness of breath or chest pain during the test, which may prompt further urgent or non-urgent work-up.
• Musculoskeletal injury causing more than temporary discomfort that requires further medical attention (such as ligament or tendon injury, muscle tear, muscle strain, etc.) Some injuries such as fractures or severe strains or tears could cause long-term physical discomfort.
• Worsening of seizures. For some people, exercise may trigger seizures. If you are in the intervention group and your seizure frequency worsens, we will not continue the intervention.

Risks from Completing Questionnaires:
• Some of the questions asked may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and go to the next question

Pregnant women are excluded from participation in this study. In the event you become pregnant while participating, you and your data will be removed completely from the study immediately.

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 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

During the study, we ask that your anti-seizure medications and devices <u>are not changed during the first 16 weeks of the study</u> because we are trying to see if exercise can improve your

epilepsy. You are probably used to your doctor making medication adjustments roughly every 3 months, so by participating in this study you may be prolonging this period of time by roughly 1 month. However, if medication changes are medically necessary, you can still continue in the study – please just let us know of any medication changes.

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 your mood and passive suicidal thoughts. 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.

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. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: improved sleep, lower stress, improved seizure control, improved mood, improved quality of life, and improved physical health.

Based on experience with exercise in animals with epilepsy and in people with other chronic diseases, researchers believe it may be of benefit to subjects with epilepsy. 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 do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:
-continue current medical care as you normally would.

The common standard of care is to continue increasing or adding anti-seizure medications, which have risks of side effects which vary according to the medication selected.

If your doctor wants you to consider epilepsy surgery, that work-up can still be pursued while you are in the study.

WHAT ARE THE COSTS?

All study costs, including any study medications and 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 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.

Participant 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?

You will be paid $100 in the form of a clincard if you complete all the scheduled study visits: $40 for each in-person visit and $10 for each telephone visit. If you withdraw for any reason from the study before completion you will only be paid for the visits that you completed.

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.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest University. 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 Halley Alexander, MD at [redacted] or after hours call at [redacted].

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 or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** medical history including medical diagnoses, medications, imaging and other test results, employment information, age, gender, height, weight, zip code, phone number, fitness assessments and results from questionnaires regarding mood, stress, sleep, quality of life, and goal setting.

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) or the Office of Human Research Protections (OHRP), 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.

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.

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 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 Halley Alexander, MD 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:

Halley Alexander, MD
[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.

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, Halley Alexander, MD at [redacted] or [redacted].

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] or the Research Subject Advocate 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

Legally Authorized Representative Name (Print):_____

The above named Legally Authorized Representative has legal authority to act for the research subject based upon (specify health care power of attorney, spouse, parent, etc.)

Relationship to the Subject:_____

Legal Representative Signature: _____ Date:_____ Time:_____ am pm

WFU School of Medicine
Institutional Review Board
IRB Number: IRB00068408
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