ISU IRB: 23-375-00
Approved Date: 04/16/2024
Expiration Date: 02/05/2025

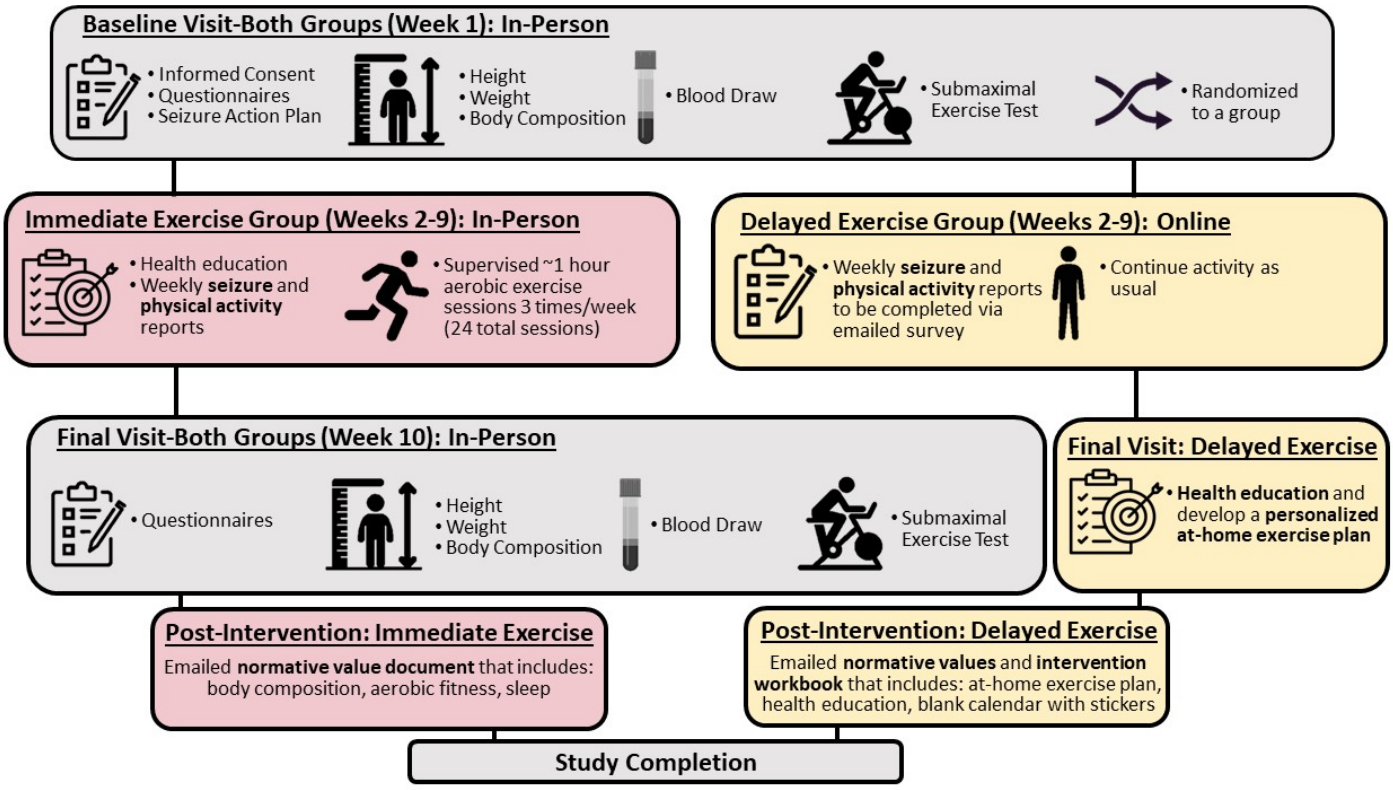
Iowa State University

Department of Kinesiology

Title of the Study: Feasibility, Acceptability, and Appropriateness of Aerobic Exercise for Epilepsy Management (EpiFIT Study)

Investigators: Sydney L. Churchill, MA (Principal Investigator), Jacob D. Meyer, Ph.D. (Supervisor)

This form describes a research project. It has information to help you decide whether or not you wish to participate. Research studies include only people who choose to take part—your participation is completely voluntary. Please discuss any questions you have about the study or about this form with the project staff before deciding to participate.



Funding: This study is funded through Dr. Meyer's internal funds.

KEY INFORMATION

This research examines how regular aerobic exercise influences seizure frequency and psychological health among people with epilepsy. You are being invited to voluntarily participate in this research.

If you choose to enroll, you will complete a Baseline Assessment Visit and then be randomized to either the immediate exercise group or the delayed exercise group. Randomization means that you are put into a group by chance (like flipping a coin). If you are assigned to the delayed exercise group, after the Baseline Assessment Visit, you will complete weekly seizure and physical activity reports for 8-weeks and the Final Assessment Visit. At the Final Assessment Visit, you will be offered health education and develop a personalized, at-home exercise plan with a research member. After, you will receive an intervention workbook that includes your at-home exercise plan along with a normative values health report that include body composition and aerobic fitness. If you are in the immediate exercise group, after the Baseline Visit you will complete 8-weeks of aerobic exercise that last approximately 1-1.5 hours, 3 times a week (24 sessions total) followed by the Final Assessment Visit. After the Final Assessment, you will receive a normative values health report that includes body composition and aerobic fitness.

Risks include physical discomfort from exercise, potential risk of a seizure, and breach of confidentiality. Benefits include personalized results from the submaximal exercise test as well as personalized health education.

Detailed information about study procedures, risks, benefits, and how we protect your confidentiality contained in this document. Please review it carefully and ask the study team any questions.

Introduction:

The purpose of this study is to understand how regular aerobic exercise influences seizure frequency and psychological health in people with epilepsy. You are being invited to participate in this study because you:

- Age 18-65 years old
- Are clinically diagnosed with epilepsy
- Self-report having at least one seizure or event within the past year
- Can provide physicians consent to participate
- Are currently not meeting the US Physical Activity Aerobic Guidelines (engaging in less than 150 minutes of aerobic activity per week)
- Are currently not participating in a structured exercise program

Due to the potential impact of certain conditions on study outcomes, you may be excluded from participation in this particular study if you:

- Have had a change in antiepileptic drug regimen in the last 28 days

- Currently taking >3 antiepileptic drugs at the same time
- Have had status epilepticus within the past 2 years
- Have had a neurostimulation device implanted or activated for < 1 year prior to enrollment or a battery life unit that does not extend for the duration of the intervention
- Have had epilepsy surgery < 1 year prior to enrollment
- Have seizures that are triggered by exercise
- Binge drink alcohol (14 per week for men and 7 per week for women)
- Smoke cigarettes or vape
- Use cannabis or consume CBD-related products
- Are pregnant or planning to become pregnant during the intervention period

Research staff will make inclusion/exclusion decisions regarding your participation based on your responses to questions during the online pre-screener, phone screener, and the baseline visit. You will be excluded from participation if you are deemed ineligible to participate based on your responses.

*If you have any questions **about the inclusion and exclusion criteria for this study** and if this study might fit for you, please ask the study staff now.*

DESCRIPTION OF PROCEDURES

If you agree to participate, you will complete a Baseline Assessment Visit and then be randomized to either the immediate exercise group or delayed exercise group. If you are assigned to the delayed exercise group, after the Baseline Assessment Visit, you will complete weekly seizure and physical activity reports and the Final Assessment Visit. After the Final Assessment Visit, you will receive an intervention workbook that includes a personalized, at-home exercise plan. If you are in the immediate exercise group, after the Baseline Assessment Visit you will complete 8-weeks of supervised aerobic exercise followed by the Final Assessment Visit. Further descriptions of each visit are listed below.

Visit Preparation

Before your Baseline Visit and your Final Assessment Visit, you will be asked to refrain from consuming caffeine ~4 hours prior to your visit as caffeine can influence the submaximal exercise test. Further, you will be asked to wear loose-fitting, comfortable clothing and tennis shoes for the submaximal exercise test.

Baseline Visit (1.5-2 hours)

During the Baseline Assessment Visit, after reading and signing the informed consent document, you will complete questionnaires. After completion of the questionnaires, you will complete a Seizure Action Plan with a research member. A Seizure Action Plan contains

essential information that research staff may need to know in order to help you in the event of a seizure. It includes information on first-aid, caregiver and health-care provider contacts, known seizure triggers, and rescue medication*.

***NOTE:** **We as a research team are unable to administer rescue medication. If you anticipate that you will be needing rescue medication, please plan on bringing a caregiver with you to your baseline visit who is trained on rescue medication administration, since you will be engaging in a submaximal exercise test. If you end up in being in the immediate exercise group, you will need a caregiver with you at every session.**

After the Seizure Action Plan is filled out, a research member will make a copy of the plan and give it to you and will also keep one for exercise sessions (immediate exercise group) and the Final Assessment Visit (both groups). You will then complete anthropometric assessments. Anthropometric assessments will include height, weight, and body composition analysis (described below). Next, a trained phlebotomist will collect approximately 2 teaspoons of blood. These samples will be drawn via venipuncture. Blood samples will be collected to examine biomarkers associated with or potentially underlying treatment response.

Next, you will complete a submaximal exercise test to estimate your aerobic fitness level. This is a cycle test that will last approximately 10-minutes. You will complete a 2-minute warm-up and then bike at 50 revolutions per minute for 6-minutes at a workload that is aimed to obtain a steady heart rate between 125 and 170 bpm. Heart rate will be obtained at the 5^{th} and 6^{th} minute of the test and averaged to estimate maximal aerobic capacity (also termed VO_{2max}). After, you will complete a 2-minute cool-down. The test will take place in a private room with a minimum of two research staff present.

After the submaximal exercise test, you will be randomized to either the delayed exercise group or to the immediate exercise group. If you are in the delayed exercise group, you will be given instructions on how to complete weekly seizure and physical activity reports, which will be administered online. You will also schedule a visit for the Final Assessment Visit. At the Final Assessment Visit, you will be offered health education and develop a personalized, at-home exercise plan with a researcher. You will then be sent an intervention workbook that contains documents such as the finalized, at-home exercise plan, health education, and a blank calendar with stickers.

If you are in the immediate exercise group, you will schedule all study visits with a research member.

Immediate Exercise Group Procedures (~1 hour-1.5 hours, each)

If you are in the immediate exercise group, you will complete aerobic exercise training 3 times per week for a total of 8 weeks (24 sessions) at Research Park 6. All exercises will be performed using state-of-the-art aerobic exercise equipment, and all sessions will be fully supervised by a research staff member, available for questions and help at any time.

Each session will take place indoors and will last ~50 minutes, beginning and ending with a 5-minute warm-up and cool-down on your choice of a stationary bike, treadmill, or elliptical. At every exercise session, you will be asked to wear a heart rate monitor during exercise, as your rate of perceived exertion and your heart rate will be collected every 5 minutes of the session. The heart rate monitor can be your own personal monitor (e.g., a Fitbit. Garmin, Apple Watch, etc.). If you do not have a heart rate monitor, one will be provided for you. The progression of training will be based on your personal rate of perceived exertion, beginning with a light intensity at week one and ramping up the intensity each week until you can maintain a somewhat hard to hard perceived intensity for the last five weeks. You will be able to listen to music, play games on your device and/or watch television during your workout.

At the very first session, you will go through health education with a research member and develop a habit plan. This habit plan will include goal setting, preparation habits, and figuring out ways to cope with barriers. At subsequent sessions, you will review the habit plan each week. Additionally, at the first session of every week, you will fill out a seizure diary and report any physical activity done outside of the supervised aerobic exercise sessions.

Delayed Exercise Group Procedures

If you are in the delayed exercise group, you will continue activity as usual and complete weekly seizure frequency and physical activity questionnaires lasting approximately 5-10 minutes (8 total). These questionnaires will be sent via email and can be completed online. We will send you three reminders throughout the week to fill out the questionnaires.

Final Assessment Visit

Both the immediate exercise and delayed exercise groups will attend the Final Assessment Visit. The Final Assessment Visit will be similar to the Baseline Assessment Visit. You will fill out questionnaires, have 2 teaspoons of blood drawn via venipuncture by a trained phlebotomist, will complete anthropometric assessments, and will end your visit with the submaximal exercise test. After the submaximal exercise test, both groups will be given information on the normative values document that they will expect to receive.

Additionally, if you were in the delayed exercise group, you will go through health education and develop a personalized, at-home exercise plan with a research member. This personalized exercise plan will be included within an intervention workbook that you can do on your own time and at your own pace.

Shortly after the Final Assessment Visit, both groups will receive their normative values health report and the delayed exercise group will also receive a finalized intervention workbook, which will mark completion of the study.

DESCRIPTION OF ASSESSMENTS:

Questionnaires: You will be asked to complete several questionnaires about your health (including medical history information), physical activity, and other psychological factors. Questionnaires will be completed electronically and all questionnaires will only be associated with your study ID number. You will be able to skip any questions that you do not feel comfortable responding to.

Body composition assessment: A handheld body fat loss monitor will be used at baseline and post-intervention for BMI and body-fat percentage. After inputting personal data such as your age, height, weight, and sex, you will stand with both feet slightly apart and hold the grip electrodes with your arms straight out at a 90-degree angle to your body for ~30 seconds. The device will send small electrical current through your body via two conductors. You will not be able to feel this happening.

Submaximal exercise test: The submaximal exercise test is used to determine estimated maximal oxygen uptake and assess fitness level. This will be estimated using the Astrand-Rhyming test on a stationary bike. The Astrand-Rhyming cycle test is a single-stage test lasting about 10-minutes. For the actual test, you will bike at 50 revolutions per minute (rpm) for 6-minutes at a workload aimed at obtaining a steady state heart rate between 125 and 170 bpm. Heart rate is obtained at the 5^{th} and 6^{th} minute and is averaged to estimate VO_{2max} from a nomogram. VO_{2max} refers to the maximum amount of oxygen your body can utilize during intense or maximal exercise. This measurement is used to assess aerobic fitness levels. During this test, there will be a minimum of two research staff members present. Further, the submaximal test will be held in a private room separate from the exercise area to maintain confidentiality.

Risks or Discomforts

There are some risks and/or discomforts you may experience during participation of this research study. Each risk is detailed below, along with a description of how the research team will attempt to minimize their occurrence.

Discomfort During or After Aerobic Exercise

Aerobic exercise, especially at a light to moderate intensity, is generally very safe and tolerable, even for inactive adults. Risks that are associated with general exercise include shortness of breath, feeling dizzy or fatigue. Extremely rarely a heart rhythm abnormality or heart attack may occur during exercise, requiring resuscitation and hospitalization. However, this is extremely uncommon during exercise session of individuals who pass study inclusion criteria. To minimize this risk, the research team will closely supervise all exercise sessions (immediate exercise group) and assessments (both groups) with at least 1 senior research personnel (e.g., Research Assistant, GRA) and 1 undergraduate research assistant, who will monitor for safety.

In addition, each exercise session (immediate exercise group) will begin and end with a 5-minute aerobic warm-up/cool down to reduce injury.

For participants assigned to the delayed exercise group, there is no anticipated risk or discomfort during the at-home exercise program. Participants will be doing practical aerobic exercise, using their own equipment, in their own homes. Participants will be familiar with their surroundings and will be able to decide when and how to exercise.

Discomfort from Blood Draws

There is a small risk of fainting or dizziness during blood draws. There is also a small risk of bruising or bleeding at the site of the needle (about 1 in 10 cases) and an extremely small risk (about 1 in 1000 cases) of infection. The total quantity of blood collected across all visits is much less than that taken during a single donation at the Red Cross Center or blood drive. On rare occasions, the needle may damage a nerve or the vein, causing the vein to become blocked. Additionally, there is a small risk of fainting or dizziness during and after sterile equipment in an area designed for the collection of blood samples. Two research staff members will be present in case you begin to feel faint or dizzy.

Risk of a Seizure

Exercise is generally considered safe and is often recommended by neurologists and physicians for people with epilepsy. However, it is essential to acknowledge that while the likelihood is low, there remains a possibility that you may experience a seizure during exercise. To mitigate this risk, we will have you choose your form of aerobic exercise based on your comfort level and you can stop exercising at any time. We will also be starting you off on light exercise based on your perceived effort. Additionally, for the immediate exercise group, there will be a minimum of two research staff members present at every visit.

If you are in the delayed exercise group, the intervention workbook that you will be given will include safety tips for exercising with epilepsy that are recommended by the Epilepsy Foundation, such as using a buddy system, to further enhance a safe exercise experience. Similar to the immediate exercise group, you can choose your form of aerobic exercise based on your comfort level, the intensity that you exercise at, and you can stop exercising at any time, as the intervention workbook will be designed to be done at your own pace.

Psychosocial Risks

There may be limited psychological stress related to completing the mental health questionnaires. If any severe responses are encountered during any of the questionnaires, study personnel will respond by contacting appropriate emergency services - either by contacting the director of the Wellbeing and Exercise Laboratory, Dr. Meyer, or calling 911, depending on the severity of the issue.

Social Risks

You may feel slight social discomfort from body composition assessment and VO_2 fitness testing result. This risk will be minimized by only allowing approved personnel to conduct the tests and access the data.

Benefits
As part of the study, you will receive personalized data via email on body composition and fitness assessments. These data will be collected using state-of-the-art equipment, providing detailed and accurate data. Such assessments are costly but will be provided free of charge for participation in this study. Further, you will receive exercise training along with a personalized, health education.

Additionally, you will receive incentives throughout the intervention for achieving intervention milestones (e.g., completing Baseline/Final Assessment Visits). These may include: a study t-shirt, water bottle, hat, and a bag.

Costs and Compensation
There are no cost and no compensation associated with this study.

Participant Rights
Participating in this study is completely voluntary. You may choose not to take part in the study or to stop participating at any time, for any reason, without penalty or negative consequences. You can also skip any questions that you do not wish to answer. Participating or choosing not to participate will not affect your relationship with any of the study personnel or with your health care provider. You can continue receiving care from your primary health care provider regardless of your participation in the research. Your choice of whether or not to participate will have no impact on you as a student/employee of Iowa State University in any way. If you become pregnant during this study or if the medications you routinely take change, please inform the staff, and you will be removed from the study. You have the right to ask the researchers to remove your data if you stop participating.

If you have any questions *about the rights of research subjects or research-related injury*, please contact the IRB Administrator (515) 294-4566, the IRB Director (515) 294-3115, or IRB@iastate.edu.

Research Injury
Please tell the researchers if you believe you have any injuries caused by your participation in the study. The researchers may be able to assist you with locating emergency treatment, if appropriate, but you or your insurance company will be responsible for the cost. Eligible Iowa State University students may obtain treatment from the Thielen Student Health Center. By agreeing to participate in the study, you do not give up your right to seek payment if you are harmed as a result of being in this study. However, claims for payment sought from the University will only be paid to the extent permitted by Iowa law, including the Iowa Tort Claims Act (Iowa Code Chapter 669).

Confidentiality

Records identifying participants will be kept confidential to the extent permitted by applicable laws and regulations and will not be made publicly available. However, federal government regulatory agencies, auditing departments of Iowa State University, and the Institutional Review Board (a committee that reviews and approves human subject research studies) may inspect and/or copy study records for quality assurance and data analysis. These records may contain private information.

To ensure confidentiality to the extent permitted by law, the following measures will be taken. Only subject ID codes will be used for data processing and analyses. Physical activity, self-report measures, blood samples, and all assessments (anthropometric, submaximal tests, and aerobic exercise) will be de-identified and marked with subject ID code to minimize any risks of confidentiality.

Additionally, we will use REDCap software which will eliminate the need for hard copies of each questionnaire to be filled out. Instead, questionnaires will be filled out on a computer and the data will be stored on a password-protected folder (on ISU's secure cloud-based storage system) with only subject ID codes linking each set of questionnaire answers to the participant. The individual information that you provide as part of this experiment will not be disseminated in any manner that may identify you. However, information from this experiment may be disseminated in journal articles, theses, and conference presentations.

Potential Use of Data, Including Blood Samples

De-identified data (i.e., data that has been anonymized to protect your identity) may be used in research papers and presented at conferences by the research team. There is a possibility of sharing de-identified information with other researchers and/or using the information for future research projects. These studies may be similar to this study or completely different. Further, there is also a possibility that individual level de-identified data may be shared for journal publication or in a data repository. We will make sure that your identity cannot be linked to the information we share. We will not ask you for additional permission before sharing the information.

Your blood samples will have your identity removed and will be securely and confidentially stored for potential future analyses of biomarkers, such as a protein or hormone when new research indicates it may be relevant (in treatment of epilepsy or physiological response to exercise) after you have finished the study. In some cases, we may ask a collaborator or lab outside of the Iowa State research team to analyze the blood samples for us. We will not perform genome sequencing of your samples. Whole genome sequencing is a process that maps out your specific DNA. You will not receive results for any analysis of blood samples. Please be aware that we will not obtain additional permission from you for the uses of your de-identified data or blood samples described above.

Questions

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You are encouraged to ask questions at any time during this study. For further information ***about the study,*** contact the project coordinator, Sydney Churchill at (515) 294-5230 or wellex@iastate.edu. You may also contact Dr. Jacob Meyer, who is supervising this research, at (515) 294-1386 or jdmeyer3@iastate.edu.

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Consent and Authorization Provisions

Your signature indicates that you voluntarily agree to participate in this study. When you sign this document, you are stating that the experiment has been fully explained to you, and that you understand that the data obtained from this study are to be used for research purposes only, not for the evaluation or diagnosis of any disorder, and that such data will remain confidential, except as required by law. You are also stating that you have been given the time to read the document, had the opportunity to ask questions concerning all aspects of the procedures, and that your questions have been satisfactorily answered. Your signature indicates that you are aware that participation is voluntary, and that you may withdraw your consent at any time.

I, the undersigned, hereby consent to be a participant in the project described above conducted in the Department of Kinesiology at Iowa State University.

Participant's Name (printed) _____

Participant's Signature_____ Date_____

Investigator Statement

I certify that the participant has been given adequate time to read and learn about the study and all of their questions have been answered. In my opinion the participant understands the purpose, risks, benefits and procedures included in this study and has voluntarily agreed to participate.

(Signature of Person Obtaining Informed Consent)_____ (Date)_____

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Pregnancy

This study does not allow the participation of female subjects who are pregnant. Female subjects are therefore asked to sign the following statement before proceeding. Please sign this statement only if you are certain you are not pregnant and do not plan on becoming pregnant during your inclusion in this study. If you are not certain or are trying to become pregnant, please do not sign this statement.

I confirm that I am not pregnant and do not plan on becoming pregnant during my inclusion in this study. If I become aware that I am or was pregnant during my inclusion in this research, I will promptly inform the investigators.

Signature of Subject: _____

Date: _____

Maintain Contact Information

Aside from the present research study, Dr. Meyer's laboratory and others in the Kinesiology department routinely conduct research on physical activity, exercise and wellbeing. If you are interested in being contacted about studies in the future, please indicate so below.

____ Yes, please keep my contact and demographic information and contact me regarding future studies that I may be eligible to participate in

_____No, I would not like to be contacted regarding future research opportunities, please destroy my contact information at the conclusion of the study