Document Cover Page

Study Title: Defining the Temporal Changes in the Acute Phase Response During Graded Exercise: A Prospective Study

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Vanderbilt University Institutional Review Board
Informed Consent Document for Research

Principal Investigator: Jonathan G. Schoenecker, MD **Revision Date: 08/24/2021**
Study Title: Defining the Temporal Changes in the Acute Phase Response during Graded Exercise
Institution/Hospital: Vanderbilt University Medical Center

This informed consent applies to healthy volunteers

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study.

1. What is the purpose of this study?

The purpose of this study is to document the body's acute phase response (an increase in proteins in the body in response to injury), also known as APR, to different levels of exercise, and to determine which types of exercise produce the most physiologic benefit while limiting harm.

We will enroll 50 patients in this study who will take part in three study visits (of running, walking and sitting) and 50 patients in this study who will take part in a marathon.

2. What will happen and how long will you be in the study?

You will be asked to complete a one-time survey about yourself (age, ethnicity, height, weight), your exercise frequency, and your preferred mode of exercise.

This study has a crossover design. A crossover design is a repeated measurements design such that each experimental unit (participant) receives different treatments during the different time periods, i.e., the participants cross over from one treatment to another during the course of the trial. The purpose of this is for each participant to complete an exercise session, then each participant serves as his/her own control.

You will be asked to take part in three study visits, at least 1 week apart from each other. During the visits you will be asked to participate in 20 minutes of exercise (60 minutes total). You will be asked to run and to maintain a heart rate of 70-80% maximum heart rate, to sit, or to walk to maintain 50% maximum heart rate. Your maximum heart rate is determined by the equation: maximum heart rate = 220 – (age in years). The running or walking exercise sessions will be performed on a treadmill. A dual-grip heart rate monitor that is built into the treadmill will be used to monitor your heart rate during your exercise session. You will be asked to grip the hand bar to assess your heart rate periodically throughout the 20-minute exercise sessions. The order in which you complete the different visits will be random, but each participant will complete all 3 visits (as mentioned in the above paragraph that explains the crossover study design). Prior to each study visit, you will be asked not to exercise the day of or the day prior to your exercise visit. You will be asked to fast 1 hour prior to your study visit to prevent any digestion issues while exercising.

Exercise Visit

- Upon on arrival you will be seated for 10 minutes
- After this 10 minutes, research personnel will measure your baseline heart rate
- A 4.5 mL blood sample will also be collected before you being exercising
- You will exercise or sit for 20 minutes at the Vanderbilt Orthopaedics fitness center at the prescribed intensity. The prescribed intensity exercise: moderate intensity running (goal is 70-80% maximum heart rate), walking at ~50% maximum heart rate or sitting
- Within 30 minutes after you complete exercising or sitting, a second 4.5 mL blood sample will be collected from a new site

After you have completed the 3 study visits you will have completed the study. We will not pursue you to follow up with your study results after the study has finished. However, if you are interested in seeing your study results, you can send the study investigators a written request to obtain these results. Once a written request is received, we will plan to discuss results with you virtually or through written communication in the form of a letter.

3. Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

4. Side effects and risks that you can expect if you take part in this study:

Blood draw side effects:
You may experience pain, bruising, and bleeding at the site of your blood draw. You may feel lightheaded or you may faint. All study personnel obtaining blood draws have received training to do so.

Risks associated with using a treadmill:
There is a risk to using a treadmill. The light and moderate exercise intensities and 20 minute duration of activity minimize the risk of using a treadmill. In addition, we will be constantly monitoring you while you are using the treadmill. You will be connected to the automatic stop cord and will be taught how to stop the treadmill at any time. Study personnel conducting the research will be constantly observing you on the treadmill and they will be prepared to stop the treadmill immediately if anything concerning arises during your session. You can stop the exercise session at any time if you feel like you cannot complete it or do not want to complete it.

Risks of exercise at a running intensity:
There is a risk to exercising. These risks could include: abnormal blood pressure, fainting, disorders of heart rhythm, stroke, and very rare instances of heart attack or even death. Every effort will be made to minimize these risks during your test. Emergency equipment and personnel are readily available to deal with these unusual situations should they occur. We do not expect these occurrences to arise and have planned the exercise intensities and duration to have the minimum risk that will allow us to complete the study.

Breach of confidentiality:
Because your information is being collected there is a slight risk of breach of confidentiality. To reduce this risk, the study will utilize a REDCap database, a secure web application for data capture. Only research personnel will have access to your study information to ensure confidentiality. Your record will be assigned a unique ID# that will be used to identify your record when data is sent for analysis. All blood specimens will be stored in the Schoenecker Lab at Vanderbilt University Medical Center.

5. Risks that are not known:

If we discover an unknown risk to this study not listed in Item# 4 we will let you know about it.

6. Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

7. Good effects that might result from this study:

a) The benefits to science and humankind that <u>might</u> result from this study: This study may benefit people in the future by allowing physicians to maximize the benefits of exercise based on changes to acute phase response (APR). The information may also be useful to the larger population, as this type of information will be invaluable to planning future studies on the harms and benefits of certain types of exercise with respect to acute phase response. Additionally, characterizing this system will build a foundation for the study of changes in the APR of exercise in participants with chronic diseases.

b) The benefits you might get from being in this study: There is no direct benefit to you by participating in this study.

8. Other treatments you could get if you decide not to be in this study:

You do not have to take part in this study if you do not want to.

9. Payments for your time spent taking part in this study or expenses:

You will not be paid for your time spent in this study.

10. Reasons why the study doctor may take you out of this study:

You may be taken out of this study if it is determined that you no longer meet inclusion criteria. You may also be removed from the study if you are unable to follow study guidelines. If you are taken out of this study, you will be told why.

11. What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell the research investigator or research coordinator. There is no penalty if you decide you no longer want to take part in the study.

12. Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact **Breanne Gibson at 615-936-3080 or at Breanne.H.Gibson@Vanderbilt.edu.**

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

13. Confidentiality:

During this study every attempt will be made to keep your protected health information (PHI) private. To reduce the risk of a breach of confidentiality, all study data will be maintained in a password-protected Vanderbilt Redcap database. A Vanderbilt Redcap database is a secure, web-based application for building and managing online databases. The data obtained and stored in this database will only be accessible by research personnel. All blood specimens will be stored in the Schoenecker Lab at Vanderbilt University Medical Center. Only research personnel will have access to your study information to ensure confidentiality. Your record will be assigned a unique ID# that will be used to identify your record when data is sent for analysis.

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Schoenecker and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

14. Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Dr. Schoenecker and his study team may share the results of your study, as well as parts of your medical record, to the groups named below. These groups may include people from the: Federal Government Office for Human Research Protections and the Vanderbilt University Institutional Review Board. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Schoenecker in writing and let him know that you withdraw your consent. His mailing address is 1215 21st Avenue South, Ste. 3200, Nashville, TN, 37232-8828. His mailing address is 4202 Doctors Office Tower, 2200 Children's Way, Nashville, TN 37212. At that time, we will stop collecting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_____ _____
Date Signature of volunteer

Consent obtained by:

_____ _____
Date Signature

_____ _____
Printed Name and Title Time

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Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
The purpose of this study is to document the body's acute phase response (an increase in proteins in the body in response to injury), also known as APR, to prolonged exercise during a marathon to determine how long the response lasts following this type of exercise. We will enroll 50 patients in this study who will take part in three study visits (of running, walking and sitting) and 50 patients in this study who will take part in a marathon.

You will be asked to complete a one-time survey about yourself (age, ethnicity, height, weight), your exercise frequency, and your preferred mode of exercise. Prior to your previously schedule marathon, a 4.5mL blood sample will be collected. Three more 4.5mL blood samples will be collected after the marathon: one immediately following the marathon, one 1 day following completion of the marathon and a final blood draw 2 days following completion of the marathon. The first two blood samples will be collected on site at the marathon by study personnel, but the blood draws at 1 and 2 days after the marathon will require a study visit to the Schoenecker Lab. After you have completed these 4 blood draws, you will have completed the study.

There are no direct benefits to you by participation in the study. This study may benefit people in the future by allowing physicians to maximize the benefits of exercise based on changes to acute phase response (APR). The information may also be useful to the larger population, as this type of information will be invaluable to planning future studies on the harms and benefits of certain types of exercise with respect to acute phase response. Additionally, characterizing this system will build a foundation for the study of changes in the APR of exercise in participants with chronic diseases.

There are risks from blood draws (pain, bruising, bleeding, etc.), risks of exercise at a running intensity (abnormal, blood pressure, fainting, etc.), risks associated with outdoor endurance running (dehydration, injury, heat exhaustion, etc.) and a breach of confidentiality. There is not cost to you for taking part in the study. You do not have to take part in the study if you do not want to.

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Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you are participating in a marathon.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:

Blood draw side effects:
You may experience pain, bruising, and bleeding at the site of your blood draw. You may feel lightheaded or you may faint. All study personnel obtaining blood draws have received training to do so.

Risks of exercise at a running intensity:
There is a risk to exercising. These risks could include: abnormal blood pressure, fainting, disorders of heart rhythm, stroke, and very rare instances of heart attack or even death. Every effort will be made to minimize these risks during your test. Emergency equipment and personnel are readily available to deal with these unusual situations should they occur. We do not expect these occurrences to arise, and have planned the exercise intensities and duration to have the minimum risk that will allow us to complete the study.

Risks associated with outdoor endurance running:
There are additional risks to intense outdoor endurance running in marathons, including dehydration, injury, and heat exhaustion. While study personnel cannot continuously monitor participants during a marathon other than by heart rate, participants will be reminded of appropriate fluid, electrolyte, and carbohydrate replenishment during the marathon. The participant can stop the marathon or slow the pace at any time if they feel like they cannot complete it or need to reduce intensity.

Breach of confidentiality:
Because your information is being collected there is a slight risk of breach of confidentiality. To reduce this risk, the study will utilize a REDCap database, a secure web application for data capture. Only research personnel will have access to your study information to ensure confidentiality. Your record will be assigned a unique ID# that will be used to identify your record

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when data is sent for analysis. All blood specimens will be stored in the Schoenecker Lab at Vanderbilt University Medical Center.

Risks that are not known:
If we discover an unknown risk to this study that is not listed in this form we will let you know about it.

Good effects that might result from this study:
The benefits to science and humankind that might result from this study: The benefits to science and humankind that might result from this study: This study may benefit people in the future by allowing physicians to maximize the benefits of exercise based on changes to acute phase response (APR). The information may also be useful to the larger population, as this type of information will be invaluable to planning future studies on the harms and benefits of certain types of exercise with respect to acute phase response. Additionally, characterizing this system will build a foundation for the study of changes in the APR of exercise in participants with chronic diseases.

The benefits you might get from being in this study: There is no direct benefit to you by participating in this study.

Procedures to be followed:
You will be asked to complete a one-time survey about yourself (age, ethnicity, height, weight), your exercise frequency, and your preferred mode of exercise.

Prior your previously schedule marathon, a 4.5mL blood sample will be collected. Three more 4.5mL blood samples will be collected after the marathon: one immediately following the marathon, one 1 day following completion of the marathon and a final blood draw 2 days following completion of the marathon. The first two blood samples will be collected on site at the marathon by study personnel, but the blood draws at 1 and 2 days after the marathon will require a study visit to the Schoenecker Lab.

After you have completed these 4 blood draws, you will have completed the study. We will not pursue you to follow up with your study results after the study has finished. However, if you are interested in seeing your study results, you can contact the study investigators at the contact provided to you during study enrollment. We will plan to either meet in person to hand you the results or we will mail you the results. We will include a letter explaining your study results.

Payments for your time spent taking part in this study or expenses:
You will not be paid to take part in the study. Participants will receive a small charm for their finisher's medal as a thank you.

Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

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Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Breanne Gibson at 615-936-3080 or at Breanne.H.Gibson@Vanderbilt.edu.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
You may be taken out of this study if it is determined that you no longer meet inclusion criteria. You may also be removed from the study if you are unable to follow study guidelines. If you are taken out of this study, you will be told why.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell the research investigator or research coordinator. There is no penalty if you decide you no longer want to take part in the study.

Clinical Trials Registry:
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Confidentiality:
During this study every attempt will be made to keep your protected health information (PHI) private. To reduce the risk of a breach of confidentiality, all study data will be maintained in a password-protected Vanderbilt Redcap database. A Vanderbilt Redcap database is a secure, web-based application for building and managing online databases. The data obtained and stored in this database will only be accessible by research personnel. All blood specimens will be stored in the Schoenecker Lab

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at Vanderbilt University Medical Center. Only research personnel will have access to your study information to ensure confidentiality. Your record will be assigned a unique ID# that will be used to identify your record when data is sent for analysis.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:
We will not pursue you to follow up with your study results after the study has finished. However, if you are interested in seeing your study results, you can send the study investigators a written request to obtain these results. Once a written request is received, we will plan to discuss results with you virtually or through written communication in the form of a letter.

Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?

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You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

_____ _____
Date Signature of patient/volunteer

Consent obtained by:

_____ _____
Date Signature
Time: _____
_____
Printed Name and Title