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NCT06836739

Consent to Participate in a Research Study

Study title: At-home feasibility trial of genital nerve stimulation to modulate neurogenic bowel dysfunction in individuals living with spinal cord injury

Sponsor: Department of Defense

Principal Investigator: Kim Anderson, PhD; 216-957-3687

Study Coordinator: Mayson Moore; 216-957-3518

KEY STUDY INFORMATION

Taking part in this study is voluntary. You do not have to participate in this study if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are already entitled.

Please read this consent form carefully and take your time making a decision. Your study doctor or a member of the study staff will discuss this form with you. Please ask questions about anything that you do not clearly understand. You can ask as many questions as you want. We also encourage you to talk with your family and friends before you decide to take part in this study.

The following is a short summary of this research study to help you decide whether you would like to take part. More detailed information is included later in this document.

Why is this study being done?

The purpose of this study is to test whether electrical stimulation of the skin in the pelvic area (near the genitals) can reduce the reflexes that cause bowel accidents in people with spinal cord injuries. Current bowel treatments either involve diet and medications or surgery. This study will evaluate whether electrical stimulation can be an alternate option for bowel management.

For the purpose of this study, electrical stimulation of the pelvic area will be achieved using a device called a Transcutaneous Electrical Nerve Stimulation (TENS) unit. The Ultima Neo TENS is a device approved by the U.S. Food and Drug Administration (FDA) for pain relief. However, the use of the device as described in this consent is considered investigational. It has not been cleared for marketing by the FDA for the purpose we are testing in this study, to reduce bowel accidents.

You are being invited to take part in this research study because you have a spinal cord injury (SCI).

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What is involved in this study?

If you choose to be in this study, you will be asked to come to the research center 3 times to participate in exams and answer questionnaires about your spinal cord injury. You will be given a TENS device to take home with you for 4 weeks of stimulation. You will be randomly assigned to one of two groups if you participate in the study. One will receive the target level of stimulation (study intervention) and the other will receive a lower level of stimulation as a placebo (sham or fake) intervention. At the very end of the study, you will be allowed to keep the TENS device.

You will be in this research study for about 6-8 weeks.

More detailed information can be found below in the section labeled “Information on the Research.”

Why might I choose NOT to participate in this study?

There are risks to joining any research study. Some of the most likely risks of participating in this study include:

- Uncomfortable sensations on your skin
- Skin irritation

More detailed information about the risks of this study can be found in the section labeled “Risks.”

Why might I choose to volunteer for this study?

Your participation in this study will help us to learn about treating individuals with spinal cord injury. We cannot know if you will have any benefit from your participation in the study. It is possible the study treatment may improve your condition, which may give you relief from some symptoms or improve your quality of life. But it is also possible that your condition could get worse.

More detailed information about the benefits of this study can be found in the section labeled “Benefits.”

Who will be my doctor on this study?

If you decide to participate, Dr. Stephen Leb will be your study doctor. Dr. Leb will communicate with your regular health care provider as needed while you are in the study and afterward.

What are my other choices if I do not take part in this study?

You do not have to participate in this study. You can always choose not to take part in the study. If you decide not to take part, you have other choices, too. For example, you

can undergo usual bowel care strategies suggested by your doctor such as diet, fluids, laxatives, suppositories, digital stimulation, antegrade enema, or colostomy. You can also participate in another study or no study at all.

More detailed information about the alternatives to this study can be found in the section labeled “Alternatives.”

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DETAILED STUDY INFORMATION

The following is more detailed information about this study.

1. INFORMATION ON THE RESEARCH

1.1 Why is the research study being done?

The purpose of this study is to test whether electrical stimulation of the skin in the pelvic area (near the genitals) can reduce the reflexes that cause bowel accidents.

The picture below shows an overview of how this study will use electrical stimulation in the pelvic area (the genital nerve) to try to reduce bowel accidents.

Genital nerve stimulation delivered at home. (A) We are testing a non-invasive surface stimulation approach to reducing bowel accidents with minimal inconvenience to the wearer. (B) For this study, a TENS device will be used to deliver electrical stimulation. (C) Women will apply electrodes (sticky pads for delivering electrical stimulation) on the skin surrounding the pubic area to target the genital nerve. (D) Men will place electrodes on the top surface of the penis.

1.2 Who can take part in the study?

People who are eligible for this study are:

- At least 18 years old
- Living with a spinal cord injury caused by trauma
- Living with a spinal cord injury for at least 6 months
- Living with a spinal cord injury between neck level C1 (the base of your skull) and back level T12 (the bottom of your back)
- Living with any severity of spinal cord injury
- Living with severe bowel dysfunction based on a questionnaire of your symptoms

People who are not eligible for this study are:

- Currently participating in another electrical stimulation study
- Pregnant or planning on becoming pregnant during the study
- Living with an implanted device that might interact with stimulation of the pelvic area (such as an implanted sacral neuromodulation device)
- Living with a health problem that might interfere with the study

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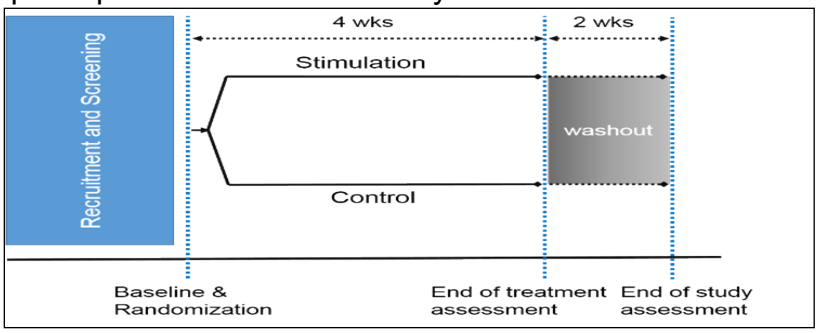
1.3 How many people will take part in this study?
Approximately 12 people will take part in this study at MetroHealth.

1.3 How long will my participation last in this study?
Your study participation is expected to last between 6-8 weeks.

1.4 What is involved if I decide to take part in this study?
In this study, you will be asked to come to the MetroHealth Rehabilitation Institute 3 times over the next 2 months. Each visit will last about 6 hours. The picture below shows the timeline of your participation in the whole study.



SCREENING/BASELINE:
Day 1 (will last up to 6 hours)

If you agree to participate, you will read and sign this consent document before any study related procedures take place. A member of the study team will review your medical history to make sure you are eligible, and it is safe for you to participate. You will have the following procedures and assessment done solely for research purposes:

1. Questions about your spinal cord injury, medical history, bowel routine, and quality of life.
2. Spinal cord exam – This will test your arm and leg muscles and your ability to feel light touch and pinprick. This will confirm information about your spinal cord injury.
3. Bowel and genital exam – This will confirm the reflexes you have in the genital area and whether you can feel or move your anal sphincter.
4. Genital nerve stimulation – This will confirm your genital nerve responds to electrical stimulation.
5. Anorectal manometry (also called ARM) – This test will tell us a lot about how your bowels are working or not working on the inside (in your rectum). During this test you will lay on your side on an exam table. A small tube will be inserted into your rectum. This tube is called a catheter, and it can measure the pressures in your rectum. Trained study staff will give you instructions about when to relax, when to try to squeeze, and when to try to push. Measurements will be recorded by the catheter during all of these activities. Your blood pressure will be monitored during this ARM test. You will also receive stimulation of the genital nerve at various times during this test so that we can measure the response in your rectum.

If the results of your procedures show that you can be in the study, and you choose to take part, you will continue with study procedures.

STUDY PROCEDURES

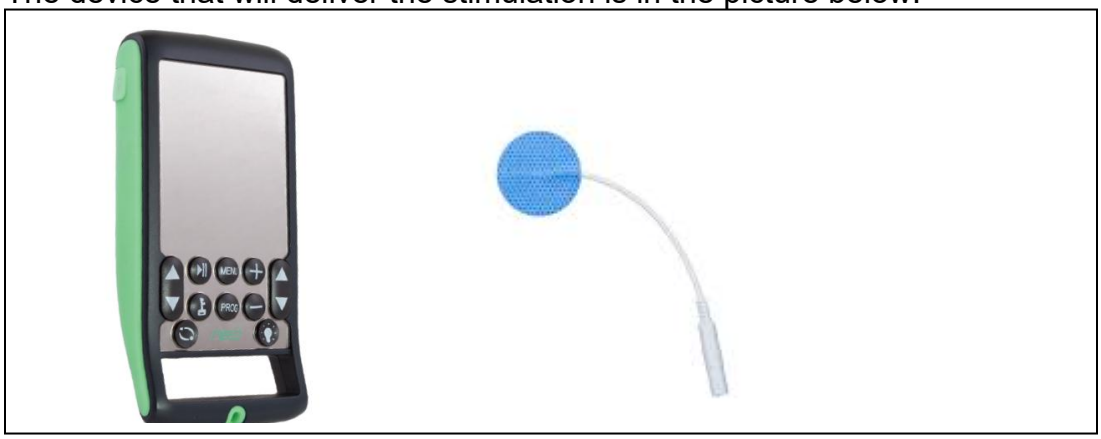
You will be randomized to one of two study groups. Randomization means that you are put into a group by chance (like the flip of a coin or drawing numbers from a hat). A computer program will place you in one of the groups. This will allow your study doctor to compare different treatments or procedures. If you decide to be in this study, you need to be comfortable not knowing which study group you will be in. Neither you nor your study doctor can choose the group you will be in. You will have an equal chance of being placed in any group. You will not know which group you are in until you are finished with the study. However, this information can be obtained if you have a medical emergency.

GROUP 1: If you are in group 1 you will receive a higher level of stimulation – this is called the experimental group.

GROUP 2: If you are in group 2 you will receive a lower level of stimulation – this is called the control group.

The only difference between the two groups is the pattern and strength of electrical stimulation delivered by the device.

The device that will deliver the stimulation is in the picture below.



The stimulation pattern will be set up by the research team depending on the group to which you are randomized. You will be shown how and where to place each electrode, how to turn the device on/off, how to select the correct stimulation pattern, how to store the electrodes when not in use, and what particular cautions to watch for.

You will be given a supply of electrodes to take home with you for the next 4 weeks. You will be given a diary to complete every day with information about your bowel activities. You will fill this out every day until the end of the study.

You will perform stimulation every day for 6-8 hours for 4 weeks. In the daily diary you are keeping, you will also include how many hours of stimulation you complete each day.

TELEPHONE CONTACT: The study coordinator will check-in with you every week to see how you are doing, if you have any questions, and if you have had any problems.

When you are finished with the 4 weeks of at-home stimulation:
End-of-study treatment – This visit will occur as soon as the 4 weeks of study treatment are complete. The End-of-treatment visit will be an exact repeat of the Screening/Baseline visit except there will not be a spinal cord exam or bowel/genital exam. After this visit you will return home for 2 weeks without the device. The study team will hold on to your device.

End-of-study – This visit will occur after the 2-week period where you do not use the device ends (as noted above). The End-of-study visit will be an exact repeat of the End-of-study treatment visit. After this visit your participation in the study will be complete.

1.5 Will I be notified of the results of the tests/studies?

You will receive a summary report of your results about one month after the end of your participation. The study team will review this report and let you know if anything requires follow up with your regular doctor. The report is for you to learn more about your body and your participation in this study.

1.6 Can I stop being in the study?

Yes. You can decide to stop at any time. It is important to tell the study doctor if you are thinking about stopping so he or she can help you stop safely. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

2. RISKS

2.1 What are the risks of participating in the research study?

<u>Risks and Side Effects Related to electrical stimulation with the TENS device</u>:

The most common side effects (happen in more than 10% of patients) are:

- *Uncomfortable Sensation (common)* – Participants that have sensation in the genital area, may feel the electrical stimulation. This sensation may feel like a

slight buzzing, tickling, tingling, or could be painful. During the screening test for genital nerve stimulation, lower levels of stimulation will be used first to see if you feel anything, then higher levels of stimulation will be tested. If you cannot tolerate sensations you experience during this testing, you will not continue with the study.

- *Skin Irritation (common)* – There is a risk of skin irritation from the sticky electrodes applied to the skin for stimulation or from the gel adhesive used to secure them. This is a common risk. This will be minimized by using electrodes that are not known to be allergenic, removing the electrodes for several hours each day, and by using gel that is commonly used for other types of electrical stimulation. Additionally, if open wounds in the genital region are discovered during baseline, your participation will be put on hold until any such wounds are healed.

Rare side but serious effects (fewer than 1% of patients) are:

- *Tissue burns (rare)* – There is a very small risk that the skin electrodes for stimulation could cause a tissue burn. This risk is very low because of the level of electrical stimulation and safety testing of the device as well as the low levels of stimulation being used in this study. Stimulation should not be applied while you are sleeping or bathing.
- *Autonomic Dysreflexia (rare)* – There is a very low risk that genital nerve or the lower intensity sham stimulation may trigger autonomic dysreflexia (AD) in individuals with SCI (risk< 1%). There is the possibility that the ARM procedure may trigger AD in some participants. This condition may be characterized by excessively high blood pressure, headache, sweating, flushing, and goose bumps. AD is easily recognized and treated immediately. In the unlikely event that you develop AD during the ARM test, you will be promptly treated. Most times treatment consists of the removal of the triggering element like draining of a full bladder, relieving pressure over an area under constant pressure, or removal of painful stimuli like stimulation. In the very unlikely event that you develop AD at home, you will follow the same process that you normally use to stop AD (removing the triggering element by draining your full bladder, relieving pressure over an area under constant pressure, or removing stimulation).

<u>Other Risks of Study Participation</u>:

Emotional and Psychological Risks (rare) – Some of the questions we ask 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.

Breach of Confidentiality (rare) – As part of study participation, information about you will be collected and then kept on paper and in computer files. There is a risk that this information could be stolen. Great care will be taken to safeguard all forms of such information, for example using locks for files with paperwork, using passwords for computer files, and by following HIPAA regulations.

Unknown Risks: There may be risks or side effects related to the study procedures that are unknown or unforeseeable at this time. You will be notified if we learn about any important new findings that may affect whether you wish to continue in the study.

Ask your study doctor for more information about any of these risks and side effects.

3. BENEFITS

3.1 What are possible benefits of participating in the research?

There is no guarantee that you will personally benefit by participating in this research study. Taking part in this study may or may not help to improve your condition. It is also possible that your condition may get worse. While doctors hope electrical stimulation of the pelvic area will be useful in treating your condition, they do not know for sure. Your participation in this study will help doctors learn more about risk-benefit profile of daily stimulation on bowel activity. This information may help other people who have a similar medical problem in the future.

4. ALTERNATIVES

4.1 What other choices do I have if I do not take part in this study?

Your participation in this study is voluntary. You may choose not to participate in this study.

If you do not wish to participate in this study, the following alternative treatments are available: Usual bowel care strategies suggested by your doctor such as diet, fluids, laxatives, suppositories, digital stimulation, antegrade enema, or colostomy. You can also participate in another study or receive no bowel care.

5. Financial Information

5.1 Are there any costs to me if I participate in this study?

There is no cost to you or your insurance company for you to be in this research study. All the procedures/assessments that are done during the three in person study visits are being provided to you at no cost.

The study device will be provided free of charge while you are participating in this study. It is possible that the study device will need to be replaced or have its batteries changed. During the study, the sponsor will pay for the costs associated with replacements.

At the conclusion of your study participation, you will be allowed to keep the TENS device that you used during the study. If you continue with the use of the TENS device, you will do so without study team oversight and you or your insurance will be responsible for the costs associated with replacement and any required maintenance of the device.

5.2 What happens if I am injured while taking part in this study?

It is important that you tell your study doctor, Dr. Stephen Leb, if you think that you have been injured because of taking part in this study. You can tell the doctor in person or call him at 216-957-6255.

If you are injured as a result of being in this study, the costs for medical treatment may be billed to you or your health insurance plan. Health insurance plans may or may not cover costs for treatment of research-related injuries. If you have insurance, you should check with your health insurance plan before deciding to participate in this research study. If your health insurance plan covers some or all of the treatment costs, you may still be responsible for any co-pays or deductibles required by your plan.

MetroHealth has not committed to pay you or to pay for your treatment if you suffer an injury as a result of being in the study. There are no plans for MetroHealth to provide other forms of compensation (such as lost wages, pain and suffering, or other direct or indirect losses) to you for research-related injuries. However, you are not waiving any legal rights by signing this form, including the right to seek compensation for an injury.

5.3 Will I be paid for taking part in this study?

You will receive up to $360 for your participation in this research study. It will be paid using a ClinCard which is a reloadable debit card. You will receive payments after each study visit as described below:

- Baseline visit – $120
- End of treatment visit – $120
- End of study visit – $120

If you withdraw from the study, you will be paid for the portions of the study that you have completed.

If you live in the region serviced by local transportation companies and need assistance with transportation to get to and from the research site for a visit, the study team will make these arrangements at no cost to you. If you live outside of the region, the study team will reimburse your transportation expenses up to a maximum of $556 per visit. It will be paid by a check mailed to you approximately 6-8 weeks after each visit.

If you live a distance away from the research site for which it would be easier for you to spend the night closer for a research visit, accessible lodging is available at the Zubizarreta House. This house is right next door to the MetroHealth Rehabilitation Institute and is designed for people with spinal cord injuries. The overnight stay will be provided at no cost to you. If you need a caregiver to stay with you, he/she can stay at the Zubizarreta House as well for no cost. The study team does not provide caregivers, however, so identifying one is your responsibility.

The Accounting Department at MetroHealth will be given your name, address, and Social Security number to process payment for your study participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

5.4 Who pays for this study?

This study is being sponsored by a grant from the Department of Defense. Portions of Dr. Anderson's and her research team's salaries are paid for by this grant.

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5.5 Could MetroHealth or the researchers profit or financially benefit from the study results?

Neither MetroHealth nor the researchers involved with this study have a conflict of interest that would allow them to profit or financially benefit from the study results.

6. PRIVACY AND CONFIDENTIALITY

6.1 Authorization to Use and Disclose Your Protected Health Information

Your medical information and billing records are protected health information ("PHI"). By signing this form, you allow the researchers for this study to obtain, use, and share your PHI as described more below. Your permission to allow the use and disclosure of your PHI is required if you want to take part in this study. MetroHealth has rules and procedures to protect information about you. Federal and state laws also protect your privacy. Your decision to allow the use and disclosure of your PHI is voluntary and will have no impact on your treatment at MetroHealth or any benefits to which you are already entitled. You will receive a copy of this form for your records.

- **What PHI will be obtained, used, or disclosed?**

Your health information may be used or disclosed in connection with this research study. Health information that may be collected, used, or disclosed for this study includes the following:

- date of birth, date of spinal injury, name, medical record number (social security number), address, email, and phone number

- **How will my PHI be used in the study?**

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- To make sure you can take part in the study
- To analyze the results of the study
- To pay your medical bills or other costs of your participation

- **Do I have to sign this Authorization?**

You do not have to sign this form. However, if you do not sign this Authorization, you will not be able to participate in this research study. Your decision whether to sign this Authorization will not affect your ability to receive medical care outside the study.

- **When does the Authorization end? If I sign the Authorization, can I revoke it?**

Your permission to use and disclose your PHI does not expire. However, if you decide to participate in the study, you are free to withdraw your Authorization regarding the use and disclosure of your PHI (and to discontinue your participation in the study) at any time. If you revoke your Authorization, the researchers will continue to use the information that they previously collected, but they will not collect any additional information. If you wish to revoke your Authorization for the research use or disclosure of your PHI in this study, you must write to: Dr. Kim Anderson, 2500 MetroHealth Drive, Room OBC SM2-006 Cleveland, OH 44109.

- **Who may use or disclose my PHI?**

Generally, only people on the research team will know your identity and that you are in the research study. However, sometimes other people at MetroHealth may see or give out your information. These include people who review research studies such as the Institutional Review Board (IRB) and other MetroHealth staff authorized to access your information.

- **Who may receive or use my PHI?**

The parties listed in the last paragraph may disclose your PHI to the following parties for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The Department of Defense
- The Food and Drug Administration

We will do our best to ensure your information is kept confidential and that the least amount of health information required to conduct the study is used or disclosed to people outside MetroHealth. Please know that people outside MetroHealth who receive your information may not be covered by this promise and the information disclosed to them may no longer be protected.

6.2 How will researchers protect my information?

Research records will be kept in a separate research file that does not include names, registration numbers, or other information that is likely to allow someone other than the researchers to link the information to you. Your research information will be stored in a locked cabinet or on a password protected secure network computer drive in a locked office or a locked file in a locked office. Only research staff will have access to these files.

6.3 What will happen to my information that is collected for this study?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law. MetroHealth has no control over the use of your information once it is released. This information may be used for purposes unrelated to this research and could potentially be used to identify you.

Sharing data is part of research and may increase what we can learn from this study to help scientific purposes. Often, data sharing is required as a condition of funding or for publishing study results. It also is needed to allow other researchers to validate study findings and to come up with new ideas. Your data may be stored and shared for future research projects without further consent if identifiable private information, such as your name and medical record number, are removed. If your identifying information is removed from your data, no one will know that it is related to you specifically, and we will no longer be able to identify and destroy them. Your data, after being stripped of all identifiers, may

be shared with other researchers at The MetroHealth System, other academic institutions, for-profit companies, sponsors, government agencies, and other research partners.

Study results may be shared in medical journals, at scientific meetings, and in other forums, but these results will not include your identifying information. Your records will be confidential, and your identity will not be shared in these forums without your express consent. If your name or other information that might identify you will be used in any publication or presentation, the researchers will ask for your separate written permission.

Your data may also be put in government or other databases/repositories if required by law.

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

7. RESEARCH PARTICIPATION

7.1 What are my rights as a research participant?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you do not take part in the study, your doctor will still take care of you.

If you chose to take part, you have the right to stop at any time. We will tell you about any new findings from this or other studies that may affect your health, welfare, or willingness to stay in this study.

If you are an employee or student, whether or not you take part in this study will not affect your job, current or future medical care, or academic studies.

7.2 What happens if I stop participating in the study?

You are free to leave the study at any time. Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled and will not affect your access to health care at MetroHealth. If you withdraw from the study, with your written permission, clinical data will continue to be collected from your medical records.

If you do decide to withdraw, we ask that you contact Dr. Kim Anderson in writing and let her know that you no longer wish to participate in the study.

7.3 Could researchers take me out of the study even if I want to participate?

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, if you become ineligible to participate, if you do not follow the instructions of study staff, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. Reasons why this might occur include finding unexpected

safety concerns. If this occurs, you will be notified, and your study doctor will discuss other options with you.

8. Contact Information

8.1 Whom do I call if I have questions or problems?

If you have questions about any part of the study now or in the future, or if you wish to communicate concerns or a complaint, you should contact Dr. Kim Anderon, who may be reached at (216) 957-3687. If you experience any side effects or injuries while participating in this study, please contact Dr. Stephen Leb, who may be reached at (216) 957-6255. For after hours, weekends and/or holidays, page Dr. Stephen Leb at (216) 207-1048. To use the pager system, after the beep, enter your phone number followed by the pound (#) sign, and someone will return your call momentarily. Any written communications with the study team may be sent to 2500 MetroHealth Drive, Room OBC SM2-006, Cleveland, OH 44109.

If you have any questions about your rights as a research participant, or if you wish to express any concerns or complaints, please contact The MetroHealth System's Institutional Review Board—a group of people who review the research to protect your rights—at (216) 778-2021.

9. Signatures

Statement of Participant

I have read this form (or someone has read it to me), and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions about the purpose of the study, and the study procedures, risks, benefits, and alternatives, and all of my questions so far have been answered. By signing below, I voluntarily agree to participate in this research study.

I understand that am not giving up any legal rights by signing this form. I also understand that I will receive a copy of this form when I sign it and later if I so request.

_____
Printed name of Participant

_____ _____
Participant Signature Date

Statement of Person Conducting Informed Consent Discussion

I have discussed the information contained in this document with the participant, and it is my opinion that the participant understands the risks, benefits, alternatives, and procedures involved with this research study.

MetroHealth

_____
Printed name of person obtaining consent

_____ _____
Signature of person obtaining consent Date

For individuals who cannot physically sign, but are able to provide informed consent:

_____ _____ _____
Signature of Witness Date Printed Name of Witness