Dietary Prevention of Heart Failure in Hypertensive Metabolic Syndrome

NCT03170375

August 11, 2022

Department of Veterans Affairs Research Consent Form	VAAAHS Research IRB Approved 08/11/2022

Title of Study:	Dietary Prevention of Heart Failure in Hypertensive Metabolic Syndrome	
Principal Investigator:	Scott Hummel, MD, MS	**VAMC**: VA Ann Arbor Healthcare System

PURPOSE OF RESEARCH STUDY:

You have been asked to participate in the study because you have high blood pressure and "metabolic syndrome." These conditions are risk factors for developing cardiovascular disease, including certain types of heart failure. Our research group is studying whether following recommended dietary guidelines can improve heart and blood vessel function. We hope that this could eventually prevent heart failure in people who are at risk. Current dietary guidelines recommend that people who have high blood pressure eat less salt (sodium). We are studying two parts of this recommendation.
First, we want to understand more about why some people see a big improvement in blood pressure on a low sodium diet (salt-sensitive persons), but others do not see much change (salt-resistant persons). Second, we want to study what effect dietary change guidance has on the function of your heart and blood vessels.

The name of the eating plan we will use in this study is the sodium-restricted DASH diet. The DASH diet is also known as the Dietary Approaches to Stop Hypertension diet. Besides being low in sodium (salt), this eating plan is also rich in fruits, vegetables, and low-fat or non-fat dairy. This diet is recommended by current guidelines to improve blood pressure in people with hypertension.

DESCRIPTION:

This study will be done at the VA Ann Arbor Healthcare System. We will consent up to 130 people.

Duration of the Research

The entire study is expected to last about 4 years. Your main participation in the study takes place over a 7 month period in 2 phases. You will have 3 visits in Phase 1 and 2 visits in Phase 2. Your in-person visits for the study will be complete at the end of the Phase 2 6-month visit. We will then call you after 6 months to ask you about your health history, medicines, and ask you to do a food survey. You may be asked if you would like to come in-person for an optional follow-up visit appointment for an additional blood pressure check and arterial tonometry procedure.

Study Procedures

If you decide to take part in this study, this is what will happen:

The overall study starts with Phase 1. This phase includes an in-person Screening visit that will last up to an hour, a 2-week run in when you will monitor your blood pressure at home and eat your usual diet, after which you have an in-person 2-week visit, lasting up to 3 hours. Over the next 2 weeks you'll start receiving refrigerated home-delivered meals that are low in salt. Next is your in-person 4-week visit with us, again lasting up to 3 hours.

After that you start Phase 2. In Phase 2 you will begin by seeing a dietitian who will help you toward the goal of maintaining a low salt diet for the long term. This visit will occur on the same day as the Phase 1, Week 4

RESEARCH SUBJECT IDENTIFICATION: (Required information)

Last Name	First Name	Mid. Init.	Last-4 SSN	Todays Date (mm/dd/yy)
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visit, or on a day that is convenient for you within the next 2 weeks. Half of the people in the study will see the study dietitian at the 1 Month point of Phase 2 and then again in person at 6 months. The dietitian will also talk with you by phone up to three times to continue the dietary counseling. The other half will see and speak with the study dietitian at the same time points, and will also use a smartphone application that is designed to help you follow the low sodium DASH diet. The application provides helpful dietary reminders and tips each morning – kind of like a health coach by phone. If you use the application, you will also be asked to answer brief surveys on how closely you are following the diet, as well as on your dietary knowledge and your feelings about the diet and the advice the application is providing. You will be assigned to a group randomly, like flipping a coin.

Study Visit Table

	Screening	Phase 1		Phase 2	
		Week 2	Week 4	Month 1	Month 6
Length of Time per Visit	1 hour	3 hours	3.5 hours	1 hour	3 hours

Specific Procedures:

Phase 1

Screening Visit:
At this visit there will be a physical assessment including blood pressure, height, weight, and waist and hip circumference (distance around), a blood draw, and a questionnaire about your eating patterns. Your average, resting systolic blood pressure (the top number of your blood pressure reading) must be less than 160 at this visit for your blood pressure reading to qualify for the study.

Once the study staff and you decide you will join the study, you may begin weaning off of some or all of your blood pressure medicine. Some blood pressure medicines can interfere with the study measurements. If you typically take these medicines, Dr. Hummel may recommend reducing or stopping them during Phase 1 of the study. If your blood pressure medicines are reduced or stopped temporarily, your blood pressure may increase above its usual range. This is not generally expected to cause health problems over the four weeks of study Phase 1. During these weeks, you will monitor your blood pressure every day (we will provide a blood pressure monitor for you if you do not have an approved, calibrated one you already use). If you develop new or concerning symptoms, or your blood pressure is consistently running above 160 systolic (top number), or 90 diastolic (bottom number), please call the study team (see last page of this form, plus the business cards we will give you). The study staff will talk to your study doctor, who may adjust your blood pressure medicines or advise you not to continue in the study. If your systolic blood pressure is 180 or higher more than once, you will go back to taking your usual blood pressure medicines and you will not be able to continue in the study.

During the first 2 weeks of the study you will eat your normal diet. During this time you will complete a 3-day food diary to record your food intake.

Week 2 Visit

At this visit the following happens:

- Your weight will be measured
- Your blood pressure will be taken
- Study staff will ask you questions about your health history and medicines

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- We will ask you to complete surveys about quality of life and how you feel
- You will have a blood draw (a total of 43 mLs, about 3 tablespoons)
    - We will measure your personal salt-sensitivity level using a small amount of blood. We will obtain the blood sample from either a blood tube (mentioned above) that you have already had drawn as a part of the study, or a finger prick (similar to a blood glucose check).
- A 24-hour urine collection will be arranged
- A 24-hour blood pressure measurement for at home will be arranged
- You will have an arterial tonometry (blood pressure measurement by a sensor placed on your skin)
- A two and three-dimensional (3D) echocardiography (ultrasound of your heart) will be taken,
- A sublingual dark field microscopy (movie images of the blood vessels under your tongue) will be taken.
- A study staff person will review your 3-day food diary with you to make sure the information is accurate. Your 3-day food diaries will be sent to the UM-MNORC (Michigan Nutrition Obesity Research Center) as coded data for analysis using a NDSR (Nutrition Database System for Research). The researcher who enters this data is a VA contracted employee who is approved to work on this study.

After the Week 2 visit you will consume DASH/SRD refrigerated meals delivered to your house for the next 14 days. During this time you will complete a 3-day food diary to record your food intake.

You will select from a menu of meal options that was designed by [redacted] in collaboration with Dr. Hummel and University of Michigan research dietitians. [redacted] is a company that specializes in home delivery of nutritious meals. Your first week of food will be delivered 24-48 hours after ordering. After the first week, you will receive a home food delivery once or twice to cover the next week. The food will be specially packaged for storage in the refrigerator or freezer. Once you start the DASH/SRD home-delivered meals, we will ask you to eat no other food for the next 2 weeks. We will provide you with all of the nutrients that your body needs, including three meals and two snacks per day.

Week 4 Visit
This in-person visit will be just like the Week 2 visit, however we will not include the surveys about your quality of life and how you are feeling.

Phase 2
Visit 1 – In Person
This visit will occur on the same day as the Phase 1, Week 4 visit, or on a date that is convenient for you within 2 weeks of the end of phase 1. You will meet with the study dietitian to talk about changing your dietary habits. If you were on any blood pressure medicine before you started the study, you will be placed back on it under Dr. Hummel's guidance.

Before this visit you will be randomized into one of two groups, like a 50/50 chance of flipping a coin. You will either be in the group that has dietitian phone and in-person visits about your diet or you will be in the group that has the dietitian visits plus you will use a smartphone app called WHEELS which will send you helpful diet-related messages and will provide education about the types of foods you eat on the DASH/SRD diet, number of servings. On WHEELS you record some diet information and the general theme of this is how well you feel you are doing with the DASH/SRD diet and also share emotions you have related to your specific diet goals.

Visit 2 (Week 2) – By Phone
You will have a phone appointment with the study dietitian to continue discussing your dietary changes.

Visit 3 (Month 1) – In Person
This visit will include a physical assessment, blood draw, 24-hour urine collection, you will begin a 24-hour blood pressure measurement, and 3 day food diary. You will meet in person with the study dietitian to continue discussing your dietary changes.

Visit 4 (Month 2) – By Phone
You will have a phone appointment with the study dietitian to continue discussing your dietary changes.

Visit 5 (Month 4) – By Phone
You will have a phone appointment with the study dietitian to continue discussing your dietary changes.
If you have been using the WHEELS mobile app, you will have the opportunity to take feedback survey.

Visit 6 (Month 6) – In Person

- Your weight, waist and hips will be measured
- Your blood pressure will be taken
- Study staff will ask you questions about your health history and medicines
- You will complete the same food questionnaire you did at the screening visit
- We will ask you to complete surveys about quality of life and how you feel
- You will have a blood draw (a total of 43 mLs, about 3 tablespoons)
    - We will measure your personal salt-sensitivity level using a small amount of blood. We will obtain the blood sample from either a blood tube (mentioned above) that you have already had drawn as a part of the study, or a finger prick (similar to a blood glucose check).
- A 24-hour urine collection will be arranged
- A 24-hour blood pressure measurement for at home will be arranged
- You will have an arterial tonometry (blood pressure measurement by a sensor placed on your skin)
- A two and three-dimensional (3D) echocardiography (ultrasound of your heart) will be taken
- A sublingual dark field macroscopy (photos of the blood vessels under your tongue) will be taken.
- We will ask you to complete a 3-day food diary to record your food intake.

We will mail you the same food questionnaire you did at the screening visit 6 months after you complete Phase 2 of the study. A study staff member will call you to remind you to complete the questionnaire and to see if you have had any heart related medical events. You may be asked if you would like to come in for an optional in-person visit at this time to complete an additional blood pressure check and arterial tonometry procedure.

Echocardiogram: The echocardiogram is a type of scan that uses sound waves (ultrasound) to measure the strength and effectiveness of your heart muscle. There is a rare likelihood of mild discomfort related to the pressure of the hand-held ultrasound probe on the skin or the placement and removal of skin electrodes used for heart rate monitoring. Echocardiography is an ultrasound of the heart that provides information about the heart's size, structure, and function. Temporary heart monitoring leads will be placed (stickers with attached wires) on your chest and a small ultrasound probe will take images of your heart in several different locations

while you are lying on your side or back. The probe has a blunt tip and is not painful; ultrasound jelly is used to improve the quality of the images that we will wipe off after the test. This test will take 30 minutes.

Arterial Tonometry: Artery tonometry measures the stiffness of the arteries (blood vessels carrying blood away from the heart). While lying on your back, you will have a small blunt probe shaped like a pencil placed over the artery on the underside of your wrist. The probe will press against your skin but is not painful. A computer will estimate the stiffness of your arteries based on the measurements from the probe. Next, we will briefly place the same probe over your carotid artery (in your neck), then the femoral artery (near your groin area) to measure the timing of blood flow between these two locations. These tests will take about 10-15 minutes.

24 Hr Blood Pressure Measurement: This is an automatic blood pressure cuff that you wear for the entire 24 hours. This cuff is attached to a small device (in a bag like a "fanny pack") that inflates the cuff and records the measurements. Your blood pressure is automatically measured every 30 minutes while you are awake and every 1 hour while you are sleeping.

Sublingual Dark Field microscopy: This is a camera that takes movie images of the small blood vessels under your tongue. A blunt-tipped probe (like the cap of a marker) that gives off a specialized bright green light will be placed under your tongue for 1-3 minutes. We will ask you to keep your tongue still during the procedure to get clear pictures.

RISKS:

Any treatment or test has possible risks and discomforts. The procedures in this study may cause all, some, or none of the risks or side effects listed. Rare, unknown, or unexpected risks also may occur. The known or expected risks are:

Blood draw:

- The needle stick for drawing blood is mildly painful and involves a small risk of developing a bruise or skin infection at the site of the needle stick. This risk is minimized by strict adherence to clean technique.
- Blood drawing may cause you to feel faint or actually faint, but this is very rare.
- The amount of blood drawn each visit is about 3 tablespoons. This amount of blood loss is not expected to cause problems to you. Some of the blood work may already be obtained as part of your usual care.

Echocardiogram: We do not expect this test to cause risk to you.

Arterial Tonometry: The arterial tonometry testing is entirely non-invasive with no known risks.

24 Hr Blood Pressure Measurement: The most common complaint is that the instrument is an annoyance due to being unable to shower for 24 hours and the experience of a cuff inflating frequently. The cuff inflating is not painful.

Sublingual Dark Field microscopy: You will feel mild pressure under your tongue but should not feel pain; you may have mild discomfort from not being able to swallow your saliva as easily while the test is going on.

Diet: The sodium-restricted DASH diet meets recommended guidelines for persons who have hypertension. However, persons with hypertension may have other medical problems such as diabetes or kidney failure, and also often take blood pressure medicine, diuretic ("water pill") medicine or electrolyte supplements (such as potassium pills). In such persons, dietary changes may have certain risks, such as:

- Dehydration
- Low blood pressure
- Fluid retention
- Abnormal blood sugar levels
- Abnormal blood levels of electrolytes, such as potassium, calcium, and/or phosphorous – risks of these abnormal levels may include:
    - Abnormal heart rhythms, which can cause fainting or even death in rare cases
    - Painful calcium salt deposition in the muscles

We expect a very low chance of these more serious risks to your health in this study. We will minimize these risks by choosing only participants who we believe will tolerate the sodium-restricted diet safely. Dr. Hummel, the head doctor on this study, is a cardiologist and he will review and approve each participant for the study. In addition to the 24 hour blood pressure monitoring you will do, you will also check your blood pressure at least once every day. Also, you will not be able to continue in the study if we (the researchers) feel that you are at high risk of any of the complications listed above. In addition, we will check blood tests for your electrolyte levels to make sure that the diet is safe for you to continue.

There is a rare risk of breach of confidentiality where your information would be accessed by someone not associated with the study. There are 4 ways your study information is shared and each has some risk that you could be identified and shared inadvertently with people outside the study.

1. You will have blood and urine samples analyzed. Some of this will be done at the VA Ann Arbor and the results will be in your electronic medical record. Your loss of confidentiality risk is therefore the same as when you get regular clinical care at the VA Ann Arbor.

   The rest of your research blood and urine will be labeled with your unique study number, the date of the sample, what kind of sample it is, and study visit (for example Phase I, Week 2) and sent to the CLASS laboratory at [redacted] This is a University of Michigan affiliated lab where Dr. Scott Hummel has lab space dedicated only to him. Your samples will be frozen and stored here until they are analyzed. This sample collection and storage is required to participate in the study.

   We may share these de-identified samples and research data with other scientists at the University of Michigan or other institutions, but we will not give them any information that would personally identify you. We will not put the results of any tests conducted on these samples in your medical record.

2. When we collect research information from you, we will enter it into a website called VA REDCap. The REDCap data base is kept within the VA computer system. You will not be identified by more than your unique study number, your age and whether you are male or female.

3. When we collect your 3-day food diaries, we will send them to the UM-MNORC for analysis. Your 3-day food diaries will contain coded data including: your study ID, date of birth, sex, and date of record. There is a small risk that your 3-day food diary data could be handled by non-approved research staff while the data moves from the VA to the UM-MNORC and back to the VA. Your 3-day food diary will be kept in a locked cabinet in a locked research office only accessible by approved research staff. Your 3-day food diaries will be hand carried by approved research staff from the VA to the UM-MNORC to be entered by approved research staff. Your 3-day food diaries will be transferred back to the VA only by approved staff and stored on a private and secure VA computer network, only accessible by research staff.

4. Last, if you are in the group participating in the WHEELS smartphone app program your data will be identified by only a unique study number. In addition, the information you share will not be sensitive – it is information about foods, diet changes, and how you feel about these. As this app will be downloaded from the Apple or Google store (no charge) to your IP address, neither this consent nor the VA can assure you that your information will be secure. By signing this consent you will be agreeing that you accept the risks inherent in downloading a smartphone application.

   In addition, the information you provide thru WHEELS will be available by only unique study number to The University of Michigan Center for Health Communications Research (CHCR) who will provide consultation to the research team and is the software developer for all technical development and implementation activities for the study's interventions, associated technical systems and data management.

As with any research study, there may be additional risks that are unknown or unexpected. Risks of the usual care you receive are not risks of the research. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care. The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell Dr. Scott Hummel (contact info below) about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

You may not receive any personal benefits from being in this study. It is possible that you may receive personal benefit from the meals and/or instruction given throughout the study. Possible benefits to society include a better understanding of the eating patterns heart failure patients should follow after they leave the hospital.

ALTERNATE COURSES OF ACTION:

Your participation in this study is voluntary. You may refuse to participate in or withdraw from the study at any time without penalty or loss of benefits to which you may otherwise be entitled. Your other option is to continue with your current course of treatment and not participate in the study.

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STATEMENT OF RESEARCH RESULTS:

Taking part in this study will involve collecting private information about you. This information will be protected in the following ways: your research information will be stored on password-protected computers or in a locked cabinet in a locked office. The records will be kept confidential to the extent provided by state, federal and local law. Only approved research staff will have access to this data. The information collected for this study will be kept confidential. Any reports of the results of this study will not identify you.

The stored samples of blood and urine will be kept in a secure freezer at the CLASS Lab until the end of the study when they will be analyzed. Your samples will not be placed in a biorepository for future research. Samples will be coded in a secure way and will not have personally identifiable information on them. The key to the code will be kept secure by the Principal Investigator. If the Principal Investigator should move to another institution, the study information will move with him. When the study ends, there will be no links back to your identity.

We will include information about your study participation in your medical record. There are times when we might have to show your records to other people. For example, someone from the Office of Human Research Protections, the Government Accountability Office, the Office of the Inspector General, the VA Office of Research Oversight, the VA Central IRB, our local Research and Development Committee, the Food and Drug Administration and other study monitors may look at or copy portions of records that identify you.

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 website at any time.

SPECIAL CIRCUMSTANCES:

Right of Investigator to Terminate Participation
The investigator reserves the right to terminate your participation if, in the judgment of the investigator, your continued participation represents a potential for harm. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

Significant New Findings
Sometimes during the course of a research study, new information becomes available that might change a person's decision to stay in the study. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your research doctor will arrange for your medical care to continue. If you decide to continue in the study, you might be

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asked to sign an updated informed consent form. Your research doctor could also decide it to be in your best interests to withdraw you from the study. If so, he will explain the reasons and arrange for your usual medical care to continue.

COMPENSATION:
You will receive up to $525 if you complete all parts of the study. Compensation will be provided via cash or check after the appointment. Compensation for your participation will be given in the following amounts:

Screening Visit	$25
Week 2 Follow-up	$100
Week 4 Follow-up with Dietitian Visit	$100
Dietitian Call Week 2	$25
1 month Follow-up with Dietitian Visit	$75
Dietitian Call Month 2	$25
Dietitian Call Month 4	$25
6 month Follow-up	$100
Post Phase 2, 6 month FU	$25
Post Phase 2, 6 month FU in-person visit	$25

Note: those who have completed the majority of the screening assessment but are determined ineligible during the Week 2 visit will still receive $100 compensation.

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RESEARCH SUBJECT'S RIGHTS:

_____ has explained this research study and answered all questions. The risks or discomforts and possible benefits of the study have been described. Other choices of available treatment have been explained. Some veterans are required to pay co-payments for medical care and services provided by VA. These co-payment requirements will continue to apply for VA care and services that are not part of this study.

Participation in this study is entirely voluntary. You may refuse to participate. Refusal to participate will involve no penalty or loss of rights to which individuals are entitled. Participants may withdraw from this study at any time without penalty or loss of VA or other benefits. VA will provide treatment for research related injury in accordance with applicable federal regulations. The VA will provide necessary medical treatment should you be injured by participation in this study. You will be treated for the injury at no cost to you, but no provisions have been made for additional compensation. No reimbursement, compensation or free medical care is offered by (name of any non-VA project sponsor here). You may be among the veterans required to pay co-payments for medical care and services provided by VA. These co-payment requirements will continue to apply to medical care and services provided by VA that are not part of this study. You have not waived any legal rights or released the hospital or its agents from liability for negligence by signing this form.

In case there are medical problems, an injury, or if you have questions, concerns or complaints about the research study, you can contact member(s) of the research study team: [redacted] can be called at [redacted] during the day for nonemergent issues and Scott Hummel, MD can be called at [redacted] during the day or paged by calling [redacted] during after hours. The sponsor of this research study is the VA.

You may contact the VA Human Studies coordinator at [redacted] to ask questions about your rights as a research subject and to verify this study is reviewed and approved by the VA. You may also call when research study staff are not available or to discuss your questions or concerns with someone other than study staff. You may learn more about research at the VA Ann Arbor Healthcare System at www.annarbor.research.va.gov

I have been informed about my rights as a research subject, and I voluntarily consent to participate in this study. I will receive a signed copy of this consent form.

X_____	X_____	X_____
Signature of Subject	(Print Name)	**Todays Date (mm/dd/yy)**
X_____	X_____	X_____
Signature of person obtaining consent (Study personnel must be approved by VA IRB)	(Print Name)	**Todays Date (mm/dd/yy)**

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IF MORE THAN ONE PAGE IS USED, EACH PAGE (VAF 10-1086) MUST BE CONSECUTIVELY NUMBERED.