Understanding and targeting stress reactivity in women Veterans with alcohol misuse

NCT04393623

April 4, 2024

Department of Veterans Affairs

RESEARCH CONSENT FORM

VA Connecticut Healthcare System

Subject Name: _____ Date:_____

Title of Study: __ Stress, Emotion Regulation, and Alcohol in Women Veterans _____

Principal Investigator: _____Dr. Cathryn Holzhauer_____ Version Date: ___2/27/2023

RESEARCH SUMMARY

You are invited to take part in a research study because you are a woman who consumes alcohol. This study is sponsored and funded by the Department of Veterans Affairs (VA). Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This initial summary is to give you key information to help you decide whether to participate. Detailed information follows this brief summary. Ask the research team questions. Taking part in this study is completely voluntary.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

The purpose of the study is to learn about the effects of negative emotion and stress on behavior (including alcohol use) among women Veterans and civilians, including women with and without posttraumatic stress disorder. Additionally, the study looks at whether a woman's use of emotion regulation techniques changes the association between stress or negative emotion and behavior. Lastly, the study examines how women's reactions to stress, and the effects of stress, vary, depending on the level of circulating hormones. Your participation in this research will last about 35-75 days (or about 1-2.5 months).

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

Because this is an experimental study, it is possible that this study will not benefit you directly. You may, however, learn an effective strategy that can be easily implemented in order to help you regulate stress and negative emotion. Participation in this study should not be understood as treatment for alcohol misuse or any other health issue. Ultimately, this research may benefit other women Veterans, as it will provide information about particular therapeutic needs of this population. For a complete description of benefits, refer to the Research Details.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

In this study, we will be asking you to describe a stressful event (a "day-to-day" type stressor, such as arguments with a loved one) in detail. We will ask you to complete daily assessments via a link that is sent to your mobile phone, for 35 days. For some participants, when applicable, we will also ask you to take urine ovulation tests daily for up to 2 weeks at home. We will ask all participants to undergo a blood draw on two days during your study participation. For a complete description of risks, refer to the Research Details.

The current study is not therapeutic in nature and should not be considered as a treatment or therapy for alcohol use. If you are concerned about your alcohol use and would like treatment recommendations, the study staff can provide you with referrals. For a complete description of alternate treatment/procedures, refer to the Research Details.

DO YOU HAVE TO TAKE PART IN THE STUDY?

VA Connecticut Healthcare System Human Studies Subcommittee
Effective Date: April 4, 2024

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

RESEARCH DETAILS

WHAT IS THE PURPOSE OF THIS STUDY?

This study will examine how negative emotions and stress impact behavior, including alcohol use, in women. Research has shown that women can have a hard time regulating their behavior when in a negative emotional state, and some women will drink alcohol in order to cope with negative emotions. This research seeks to understand the association between behavior regulation and negative emotional state more clearly, and how negative emotions are related to alcohol drinking. Additionally, the study looks at whether a woman's use of emotion regulation techniques changes the association between negative emotion and behavior. We are specifically examining the effects of an emotion regulation technique called cognitive reappraisal, which is a way of changing the way you think about a situation in order to reduce the negative emotional impact that the situation is having. Lastly, the study examines how women's reactions to stress, and the effects of stress, vary depending on the level of circulating hormones. Research has shown that progesterone and estrogen, two hormones that fluctuate across the menstrual cycle and during different life stages such as menopause, may impact women's stress and negative emotion and may, among some women, be related to alcohol use and other behaviors.

With this research we hope to learn how to make our behavioral treatments (or psychotherapies) more personalized and tailored to women Veterans. We also hope to better understand how two hormones (progesterone and estrogen) - which fluctuate a lot in women – impact women's emotions, coping abilities, and behavior. Gaining understanding of these processes can inform how we provide therapy and also will have implications for medications prescribed to women Veterans.

HOW LONG WILL YOU BE IN THE STUDY?

We will recruit 100 women – Military Veterans and non-Veterans - for this study. This research study is expected to take approximately five years. Your individual participation in the project will take about 35-75 days (or 1-2.5 months). If you have regular menstrual cycles, the time you will be engaged in the study will depend on the timing of your menstrual cycle at the time of study enrollment. For example, if you are randomized to (or assigned to, by chance) the group who begins the study on the first day of your menses (period), but you just finished your period, you will have to wait until your next menses to begin the study. In this case, you will consent to be in the today but may not start study procedures right away.
If you do not have regular menstrual cycles, your participation is expected to last 35-42 days.

WHAT WILL HAPPEN IF YOU TAKE PART IN THE STUDY?

- After establishing initial study eligibility over the phone, all participants come in for session 1 (intake session).
- Today is Session 1 (intake, 2.5 hours): In today's session we will be establishing whether you are eligible for the study and asking you to sign this consent to participate. If you are not eligible to participate, you will still be compensated for your time (see compensation information below).
  To determine if you are eligible for the study, we will ask you to complete baseline self-report measures, and to complete a clinical assessment in which study staff will interview you about your physical and mental health. You are free to skip any questions that you prefer not to answer. We will also be asking you detailed questions about your menstrual cycle.

  Before you begin any participation in the study, we will be asking you to take a urine pregnancy test if there is any possibility that you might be pregnant. If you are pregnant, you will be unable to participate in this study. You should let the research staff know immediately if there is any possibility that you might be pregnant. If there is a possibility that you are pregnant, and the pregnancy test you take today is positive, you will not proceed with the procedures as described.

  If you sign the consent and are eligible to participate, and you have regular menstrual cycles, you will be randomized to one of two groups: group A or group B. The study uses a procedure like flipping a coin so that you will have a 1 in 2 (fifty-fifty) chance of being in one group or the other. However, there is no "con" or down side to being in one group or the other in this study. The group you are randomized to will determine your "start date". You will have your start date either on:
    A. the first day of your next menses (period), OR
    B. the first day of your next ovulation (which occurs in the middle of your menstrual cycle). You will take a daily, at-home urine test to determine when ovulation occurs, OR
    C. if you do not have regular menstrual cycles, your start date will be right after (1-2 days) today's session.

That will complete Session 1 (intake).

The rest of the study activities are as follows:

- For 35 days (with day 1 being your "start date", as described above):
  1. You will complete an electronic daily questionnaire, or a daily log, which asks you to report on your alcohol use, mood, and menstrual cycle. The questionnaire will be sent to your smartphone via a link that will be texted to your cell phone. Once

received, these questionnaires can be forwarded and completed on a computer as well.

2. You may be given weekly homework assignments, or strategies to practice, in between our meetings.
3. Unless you are already scheduled to come in for that week, you will receive a once-a-week phone call from your assigned study staff member. (S)he will ask about daily log completion, answer questions, and generally check in with you.
4. During the 35-day period, you will also be asked to come in for 4 in-person sessions (sessions 2-5) which will be scheduled around your menstrual cycle:
   - Session 2 (2 hours):
     - During this session, you will be asked to describe the details of a recent, day-to-day stressful (but not traumatic) experience. This story is then developed into a 6-minute script that will be played back to you over headphones in sessions 3 and 4.
     - In session 2 you will be randomized, by chance, to one of two sub-groups, Group A(1) or Group A(2) if you are part of Group A, or Group B(1) or Group B(2) if you are part of Group B. Again, there is no "con" or down side to being in any particular group in this study. Regardless of which group you are in, you will then learn about life skills and healthy living while meeting one-on-one with study staff during this session 2. The information that you learn will be different for different groups.
   - In Sessions 3 and 4 (experimental sessions, 1.5-2 hours), you will do many of the same things and a few new things:
     - You will provide a blood sample at the VA phlebotomy lab on the Leeds or Worcester campus, or at the Springfield Outpatient Clinic.
     - You will fill out additional self-report questionnaires about your mood
     - You will listen to the story that you told us in session 2 over head phones
     - Throughout this process, you will be asked questions about your emotional state and questions about alcohol
     - We will be monitoring your physiological arousal (e.g., your heart rate) during these sessions. This will be done via non-invasive pads that stick onto your skin (onto your chest, around your heart, and on your hands/fingers) and via saliva samples that measure changes in your hormone levels throughout the sessions

- Within 5 days of the end of the 35-day period, you will be asked to return for Session 5 (30 minutes) to:
  - Complete end-of-study questionnaires, and
  - Receive a full study de-briefing

Throughout your participation in the study, your participation and study staff will be overseen by the Principal Investigator, Dr. Cathryn Holzhauer. During the study, you will be interacting with Dr. Holzhauer and/or other study staff who are trained in the research procedures. Blood samples in sessions 3 and 4 will be drawn by a phlebotomist in the VA laboratory. Aside from the blood draws, all study procedures will take place in Building 12 of the Leeds campus, or in the Springfield or Worcester outpatient clinic. The days and times of your appointments will be scheduled based on your availability.You will be in communication with study staff throughout the course of your participation in the study, and these staff members will be checking in with you regularly about your safety and any concerns you may have.

By signing this consent, you voluntarily and without separate compensation authorize voice recording(s) to be made of you by the study team while you are participating in this study. Specifically, we will use audio recording in the in-person sessions. The voice recording is intended for training purposes, and so that the study team may assess the quality of study staff's delivery of study methods. The recordings will be labeled with your study ID number only, will be kept on the VA secure network, and will only be accessible to study staff. You have the option to verbally refuse having your sessions audio-recorded but still participate in the study.

Option for Virtual Sessions: You have the option to participate in sessions 1, 2, and 5 virtually, or over the internet. This is intended to reduce your risk for exposure to illness (including the COVID-19 virus) and to reduce burden you may experience with regard to travel or childcare. This is optional, and it is important that you consider whether you are able to attend sessions virtually. For example, to meet with study staff virtually you will need reliable internet connection in a private space, reliable mail service, ability to download the VA virtual meeting platform (Webex), and there should be no chance of pregnancy (precluding the need to take a pregnancy test). We will speak to you more about whether this option is a good one for you. Because sessions 3 and 4 involve biological assessments, you will still need to attend these sessions in-person. As will be described for you, precautions (including wearing masks, sanitization, and social distancing) will be maintained during the sessions to protect your safety and health.

WHAT IS EXPECTED OF YOU IF YOU TAKE PART IN THIS STUDY?

If you agree to participate in the study, study staff will have the following expectations:

- Keep your study appointments. If you miss an appointment, please contact the investigator or research staff to reschedule as soon as you know you will miss the appointment.
- Tell the investigator or research staff if you believe you might be pregnant.
- Submit your daily logs and complete daily urine screens for ovulation as instructed.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.

- While participating in this research study, do not take part in any other research project without approval from the investigators. This is to protect you from possible injury from things such as extra blood drawing. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT YOU HAVE IF YOU TAKE PART IN THIS STUDY?

Any procedure 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.

Questionnaires:

Some people become uncomfortable being asked questions about their physical and mental health and/or their substance use; if, for any reason, you wish not to answer specific questions or you wish to terminate the session, you will be able to do so.

Blood draw and physiological measures:

There may be some discomfort, bruising, or bleeding at the site where the blood is drawn. Rarely, fainting occurs because of drawing blood.

Physiological monitors (e.g., to measure your heart rate) are commonly used without posing any risk to the patients. In order for the monitor to work, we will use sticky pads which go on your hands and fingers and on your chest, around your heart. These are non-invasive, as they simply stick onto the skin. In the unlikely case that you become uncomfortable during these procedures despite providing consent, you can stop the study at any time.

Mobile device use:

Use of smartphones for data collection purposes in this study introduces a degree of risk as your phone number will be stored on University of Massachusetts Medical School's REDCap servers. These risks will be reduced by limiting personal data collected using the smartphone; for instance, we will not ask for any additional identifying information beyond your cell phone number via REDCap. In addition, your cell phone number will not be attached to the data we keep.

Risks of the usual care you receive are not risks of this study. 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 your usual care.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

We do not know if you will get any benefits from taking part in this research study. You may, however, learn an effective strategy that can be easily implemented in order to help you regulate distress and negative emotion. All participants will receive a brief intervention with study staff that may provide helpful information about your health.

Participation in this study should not be understood as treatment for alcohol use or any other health issue.

Additionally, this research may ultimately benefit other women Veterans, as it will provide information about women Veterans and their alcohol use.

WHAT OTHER CHOICES DO YOU HAVE IF YOU DO NOT WANT TO JOIN THIS STUDY?
The current study is not therapeutic in nature and should not be considered as a treatment or therapy for alcohol use or any other condition. If you decide not to take part in the research, it will not affect your usual care in any way. If you are concerned about your alcohol use and would like treatment recommendations, the study staff can provide you with referrals. You may also discuss these options with your doctor.

HOW WILL YOUR PRIVATE INFORMATION BE PROTECTED?
Participation in research may involve a loss of confidentiality. Your research records will be kept as confidential as possible. One of the risks of being in this study is that your personal information could be lost or exposed.

To protect against this, only a participant number will identify all research records, and all copies of hard-copy (paper) records will be kept in locked files at Central Western Massachusetts VAMC (VACWM) in Leeds, MA, and electronic records will be stored on a secure VAMC network accessible only to study research personnel. We will collect your personal contact information for scheduling purposes, but it will be kept separately from the other information we collect from you (e.g., separate from any of the health information that you provide during the study, which will be identified only by your participant number).

Mobile device use*:* You will not be asked for any protected health information on the mobile device surveys in this study. Participants will only be identified by their study ID number on the mobile devices and likewise, data transmitted from the smartphones to study staff will be identified by study ID number only. This ID number will be different from your VA study ID number, and will only be stored in association with your phone number. This adds an additional layer of security to protect your privacy. On the surveys, you will be asked questions about daily stress levels, emotional states, alcohol use, if you took any new medications, and whether you started your menses or ovulation. If you lose your smartphone, you will not be at added risk of your identity or highly sensitive information being revealed to individuals outside of the study.

Also, mobile surveys will use a multiple-choice format so that you will not be asked to write in any free text. This eliminates the chance that any responses could identify you.

All research information will be secured in locked files. Your identity will not be revealed in any reports or publications resulting from this study. Only authorized persons will have access to the information gathered in this study. Authorized persons may include regulatory agencies such as the Food and Drug Administration (FDA), the Government Accountability Office (GAO), the Office for Human Research Protections (OHRP), Office of Research Oversight (ORO), and VA Connecticut Healthcare System Research Office.

The Department of Veterans Affairs (VA) requires some information to be recorded in the VA electronic medical record for veteran and non-veteran research subjects. Therefore, if you participate in this study, a medical record will be created if you do not already have one. Notes reflecting your participation in this research and your laboratory tests (i.e., progesterone and estradiol levels at the time of sessions 3 and 4) will be included in this record, however confidential information that you provide to us during the study (in the interviews and self-reports) will not be put into your medical record. In addition to the research team, and the VA staff who provide clinical services, other researchers may be granted approval to access this information in the future. Federal laws and regulation that protect privacy of medical records will apply to your VA record.

Your information or biospecimens collected as part of the research, even if identifiers removed, will not be used or distributed for future research studies.

Clinical Trial
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.

WHAT ARE THE COSTS TO YOU IF YOU TAKE PART IN THIS STUDY?
You will not be charged for any part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

IS THERE PAYMENT TO YOU IF YOU TAKE PART IN THIS STUDY?
You will be compensated for all steps of the study. Specifically, you will receive gift cards for participating in the intake ($25), and sessions 2-5 ($25 for sessions 2 and 5, and $30 for in-person sessions 3 and 4). Additionally, you will receive $4 per day for each of the 35 days that you complete a daily log (for a total possible of $140) and a $25 “bonus” for completing all laboratory sessions. Additionally, if you must drive 20 miles or more to get to the Leeds,

Springfield, or Worcester Campus for sessions three and four, we will compensate you in the form of gas gift cards based on gas mileage up to 150 miles (75 miles one way) total. We will pay in increments of $5 at a rate of $0.13 per mile, based on the average price of gas and gas mileage. This compensation is applicable to participants driving or being driven in a personal automobile to sessions. Thus, total compensation for completing all elements of the study is $300, plus travel compensation if applicable. You will receive payment in the form of gift cards, for the study in the mail at the completion of your study participation. If you decide to withdraw from the study or if you are withdrawn by the investigator, you will be compensated for all the study procedures that you did complete at the time of study withdrawal. Payments will be disbursed by the VACWM Research Office.

WHAT WILL HAPPEN IF YOU ARE INJURED BECAUSE OF YOUR BEING IN THE STUDY?
If you are injured as a result of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury is due to non-compliance by a study subject with study procedures. Emergency and ongoing medical treatment will be provided as needed. This medical treatment will be provided in a VA Medical facility. There are no plans to provide compensation for disability or other losses occurring over the long term or if an injury becomes apparent after your participation in the study has ended. However, by agreeing to participate in this research study, you are not waiving or giving up any legal rights to seek compensation.

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call:

DURING THE DAY:

The VA Central Western MA Research Coordinator at 413-328-0577, OR

[redacted] and

AFTER HOURS:
[redacted]

WHO ELSE MAY YOU CONTACT IF YOU HAVE QUESTIONS?
If you have any complaints, concerns or pertinent questions regarding the conduct of this study, or if you have any questions about compensation for injury, you may contact the Human Studies Coordinator in the Research Office at [redacted]

If you have any questions about the research or the use of private information or your biospecimens, you may contact [redacted]

If you have questions about your rights as a study subject, or you want to make sure this is a valid VA study, you may contact the Chairman of the Human Studies Subcommittee at 203-932-5711 x3350.

If you have questions, complaints or concerns about the study or if you would like to obtain information or offer input you may call Dr. Cathryn Holzhauer at 413-584-4040 x 2057.

DO YOU HAVE TO TAKE PART IN THE STUDY?
Your participation in this study is voluntary. Refusal to take part in the study will involve no penalty or loss of benefits to which you are otherwise entitled.

If you are a VA employee or student, refusal to take part in the study will in no way influence your employment, ratings, subsequent recommendations, or academic progress, as applicable. You may discontinue taking part at any time without any penalty or loss of benefits.

If you choose to discontinue the study, the study team will reach out at the end of the 35-day study phase to ask some follow-up questions. However, you may choose not to answer these questions. If you request we do not contact you at the time of study withdrawal or discontinuation, we will not attempt to contact you at that time. If you choose to withdraw, we may continue to review any data that has already been collected; however, we will not collect further information, except from public records. Specimens already used (e.g., blood samples) cannot be withdrawn.

RIGHT OF INVESTIGATOR TO TERMINATE YOUR PARTICIPATION
Your participation in this study may be terminated if:

1. The investigator decides that continuing in the study would be harmful to you, or is too emotionally distressing.
2. You fail to keep your appointments with study staff.
3. The Institutional Review Board/HSS at the VA cancels the study.

Department of Veterans Affairs	**RESEARCH CONSENT FORM** **VA Connecticut Healthcare System**

Subject Name: _____ Date:_____

Title of Study: __ Stress, Emotion Regulation, and Alcohol in Women Veterans _____

Principal Investigator: _____Dr. Cathryn Holzhauer_____ Version Date: ___2/27/2023_

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr./Mr./Ms_____ _____has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study You also confirm that you have read this consent document, or it has been read to you. You will receive a copy of this consent document after you sign it.

I agree to participate in this research study as it has been explained in this document.		
_____ Subject's Name	_____ Subject's Signature	_____ Date

_____ Person Obtaining Consent	_____ Person Obtaining: Signature	_____ Date