UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: HypErthermia as an Additional Treatment for the Biology and Experience of Depression: The HEAT BED Study

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This is a research study testing 4 sauna sessions and 8 cognitive behavioral therapy (CBT) sessions in patients with clinical depression. The study researchers, Ashley Mason, PhD, and Frederick Hecht, MD, from the Departments of Psychiatry and General Internal Medicine, and the UCSF Osher Center for Integrative Health, or a member of the study team, will explain this study to you.

DETAILED STUDY INFORMATION

This part of the consent form gives you more detailed information about what the study involves.
Research studies include only people who choose to take part. Please take your time to make your decision about participating and discuss your decision with your family or friends if you wish. If you have any questions, you may ask the researchers.

You are being asked to take part in this study because you have major depressive disorder.

Why is this study being done?
The purpose of this study is to test the feasibility and acceptability of 4 sauna sessions and 8 cognitive behavioral therapy (CBT) sessions in adults with clinical depression. The Clearlight Portable Sauna Dome used for the sauna sessions in this study is commercially available. It is not approved by the Food and Drug Administration (FDA) as a medical device. Its use in this study is considered experimental.

Who pays for this study?
This study is funded by the National Institutes of Health, the William H. Donner Foundation, Wilkinson Ventures, and the Aoki Foundation.

How many people will take part in this study?
About 16 people will take part in this study.

What will happen if I take part in this research study?
If you agree, the following procedures will occur:

Study Procedures:

- **Study location:** All procedures will be conducted at the UCSF Osher Center located at 1545 Divisadero Street, San Francisco, CA 94115.
- At the **baseline study visit,** you will complete screening procedures that include a study therapist interviewing you about your depression symptoms and study staff measuring your height, weight, hip

and waist size, and blood pressure. If you are female, you will also complete a urine pregnancy test. If you are eligible, you will then complete a few online questionnaires (on an iPad). Study staff will provide you with the app-enabled Oura ring to wear and will help you download the Oura ring app onto your smartphone. The Oura ring will measure your body temperature and heart rate while you sleep at night during the time you are enrolled in the study. Study staff will verify your vaccination status by viewing your vaccine card or the California website verification page. Study staff will also work with you to schedule your sauna and CBT sessions. This visit will take about 2.5 hours.

- At your **first sauna study visit**, you will first complete COVID-19 screening procedures, which includes a rapid COVID-19 test, and then complete your first sauna session in a single-person sauna device. During the sauna session, we will measure your temperature continuously using a rectal thermometer with a probe cover that you will insert using a water-soluble, non-staining jelly lubricant. Before and after entering the sauna device, you will complete brief online questionnaires (on an iPad) and a phlebotomist will collect a saliva and a blood sample from you (one sample before the sauna session and one sample after the sauna session; details below). We suggest wearing cotton underwear (briefs or boxers) and if female, a loose-fitting sports bra (optional) for during the sauna sessions. If you are female and think you might be pregnant, you will complete a urine pregnancy test before the sauna session. Staff will remain with you during the entire sauna session. This visit will take about 4 hours.
- Your **second through fourth sauna study visits** will be similar to your first sauna visit and will include COVID-19 screening and rapid COVID-19 testing. A phlebotomist will collect a saliva and a blood sample before and after your third and fourth sauna sessions. These visits will take about 4.5 hours.

- At your **cognitive behavioral therapy (CBT) study** visits, you will complete 50-minute CBT sessions with the study therapist and will answer brief questionnaires before and after each session. CBT has been shown to be an effective treatment for clinical depression in clinical trials. The therapist will follow a CBT protocol specifically designed to help people with clinical depression. A dedicated study therapist will provide the CBT sessions. Your sessions will be audio-recorded so that Dr. Ashley Mason, a clinical psychologist and one of the principal investigators of this study, can ensure that the study therapist is providing the CBT treatment according to the protocol. Researchers may also use the recordings to study whether qualities from the session, particularly on the part of the therapist, are associated with study outcomes. All recordings will be stored on a secure, UCSF passcode-protected system and will be destroyed after the study. These visits will take about 1.25 hours.

- At your **final study visit**, you will complete online questionnaires (on an iPad) and return the Oura ring. A study clinician will interview you about your depression symptoms. If you are unable to attend your final sauna visit, a phlebotomist will collect a blood and a saliva sample from you at this final study visit. This visit will take about 1.5 hours.
- **Blood drawing (venipuncture):** A phlebotomist will collect blood samples from you by inserting a needle into a vein in your arm. Each sample will be approximately 4 teaspoons. you would provide a maximum of about 11 tablespoons (4 teaspoons before and also after the first, third, and fourth sauna sessions, and if you do not complete your fourth sauna visit, at your final study visit). Researchers will use the blood samples to examine how immune factors and other blood markers may be altered in individuals with depression change over the course of treatment.
- **Saliva sampling:** At your sauna study visits, (and if you do not complete your fourth sauna visit, at your final study visit) we will collect a small amount of saliva from you. This will allow researchers to

examine how the sauna sessions impact levels of the hormone cortisol, which may be altered in individuals with clinical depression.
- **Daily surveys via text messages**: Each day during the study you will receive a text message with a link to 2-minute survey asking about your mood.

How long will I be in the study?
Participation in the study takes place over about 10 weeks. Attending a baseline visit (~2.5 hours), four sauna sessions (~16.5 hours), eight cognitive behavioral therapy (CBT) sessions (~10 hours), and a final visit (~1.5 hours) in addition to completing text-based mood assessments (~3 hours) will take a total of about 33.5 hours.

Can I stop being in the study?
Yes. You can decide to stop at any time. Tell the study researcher or staff person right away if you wish to stop being in the study.

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

What side effects or risks can I expect from being in the study?
Possible Risks: There are risks to taking part in a research study. Some of the risks of participation in this study include:

Likely:
- Physical discomfort: You may feel discomfort related to feeling hot in the sauna, but we will place cool towels on your forehead as often as you wish and you will be able to stop the sauna session at any time. You may find the rectal probe uncomfortable, but it is made of silicone and is designed to fit in the rectum. It is unlikely, but possible, that you may experience increased heart rate or shortness of breath. It is also possible that you will experience dizziness, lightheadedness, and/or fainting when trying to stand up after the sauna session. Study staff will be available during the entire sauna session to help if you have these symptoms.
- Thirst: You may feel thirsty during the sauna session, but we will provide you with bottled water as often as you wish. Although unlikely, you may experience a decrease in electrolytes, and we will provide you with electrolyte replacement beverages, such as Pedialyte and others, as often as you wish.
- Time: Participating in this research study will use approximately 33.5 hours of your time over about 10 weeks, but we will schedule your study visits as conveniently for you as possible.
- Emotional discomfort: You may feel emotionally uncomfortable at times during the cognitive behavioral therapy (CBT) sessions with the therapist. Like other types of psychotherapy, CBT can involve exploring difficult feelings, emotions, or experiences. However, our skilled study therapist will help you with this discomfort.

Less Likely:
- Claustrophobia: The sauna sessions can take up to 140 minutes, during which you will be in a relatively small space, but your head will be outside of the sauna the entire time.
- Tachycardia: It is possible that you will feel your heart rate increase during your sauna session, much like your heart rate increases during exercise like running.
- Confidentiality: Participating in research may involve a loss of privacy, but information about you will be handled as confidentially as possible.

Rare but Serious:
- There may also be risks that we do not know about.

Other Possible Risks:

- **Blood drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and/or fainting.
- **Unknown Risks:** The sauna sessions may have side effects that no one knows about yet. The researchers will let you know if they learn anything that could change your mind about participating in the study.
- **Reproductive risks:** The procedures in this study may affect an unborn baby or infant. You should not become pregnant or breastfeed during your participation. If you can become pregnant, you must have a pregnancy test before you enter this study. If you are female and you have sexual intercourse with males, you must use contraception the entire time you are in the study. If you think you may be pregnant at any time during the study, tell the study staff right away. Acceptable methods of contraception are:
  - Condoms (male or female) must be used with another method, other than spermicide
  - Intrauterine devices (IUDs)
  - Hormone-based contraceptives (birth control pills)
  - Complete abstinence from sexual activity that could result in pregnancy

For more information about risks and side effects, ask one of the researchers.

Are there benefits to taking part in the study?

Cognitive behavioral therapy (CBT) is an established effective treatment for clinical depression. The study will provide you with CBT without charge. You may benefit from participating in the study, but this cannot be guaranteed. Additionally, the information that you provide may help health professionals learn more about the feasibility and acceptability of providing both sauna sessions and cognitive behavioral therapy (CBT) sessions to patients with clinical depression. This may help develop treatments for people with clinical depression.

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

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you. You will not lose any of your regular benefits, and you can still get your care from UCSF the way you usually do. If you choose not to take part in the study, your other choices are:

- Getting treatment or care for your depression without being in a study
- Taking part in another study
- Getting no treatment

How will my specimens and information be used?

Researchers will use your specimens and information to conduct this study. Specimens and information gathered during this research study will only be used for this study. We will save blood to analyze markers of immune aging (e.g., telomere length, epigenetic patterns, gene expression). Telomeres and epigenetic patterns are parts of the cell that can serve as a rough proxy measure of the immune cells age. Telomeres are protective caps at the ends of chromosomes and epigenetic patterns surround the chromosomes. Gene expression is the proteins genes make. We will not be conducting genetic analyses. We may share these results with other researchers with whom we collaborate on analyses. We will not share your name or any other personal information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information. There may be times when researchers using your information may learn new information. The researchers may or may not share these results with you, depending on a number of factors.

- **Research results:** There may be times when researchers using your information and/or specimens may learn new information. The researchers may or may not share these results with you, depending on a number of factors.

How will information about me be kept confidential?
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. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. In this study, we collect information about depression and suicidal thoughts. If we determine that you are at high risk of harming yourself, we will conduct a risk assessment and may direct you to the nearest emergency room and/or to call 911. If you decline, we will call your local emergency services number to ensure your safety. Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the University of California
- Representatives of the National Institutes of Health
- Representatives of the Food and Drug Administration (FDA)

Under California law, we must report information about known or reasonably suspected incidents of abuse or neglect of a child or elder including physical, sexual, emotional, and financial abuse or neglect. If you disclose actual or suspected abuse, neglect, or exploitation of a child or elder, members of the study staff may be required to report such information to appropriate authorities such as Child or Adult Protective Services.

Are there any costs to me for taking part in this study?
No. The sponsor has agreed to pay for all items associated with this research study; you or your insurer will not be billed.

Will I be paid for taking part in this study?
In return for your time and effort, you will be paid $15 for each sauna session, $15 for the baseline visit, and $15 for the final visit, for a total of up to $90. There is no compensation for receiving cognitive behavioral therapy (CBT). We will reimburse you for round trip Muni, BART, or other public transportation, or will be provided with parking stickers for validation at the nearby UCSF parking garage at Sutter Street.

What happens if I am injured because I took part in this study?
It is important that you tell the study doctor, Frederick Hecht, MD, if you feel that you have been injured because of taking part in this study. You can tell the study doctors, Ashley Mason, PhD and Rick Hecht, MD, by calling the study at 415-514-8445 or emailing Dr. Ashley Mason (ashley.mason@ucsf.edu) or Dr. Rick Hecht (rick.hecht@ucsf.edu).

Treatment and Compensation for Injury
If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

What are my rights if I take part in this study?
Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?
You can talk to the researcher(s) about any questions, concerns, or complaints you have about this study. You can contact the study principal investigators, Dr. Ashley Mason (ashley.mason@ucsf.edu; 415 514 6820) or Dr. Rick Hecht (rick.hecht@ucsf.edu; 415 353 9743) or reach the study coordinators at heatbed@ucsf.edu or 415 514 8445.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

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

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CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____	_____	_____
Date	Participant - Printed Name	Participant - Signature for Consent

_____	_____	_____
Date	Person Obtaining Consent - Printed Name	Person Obtaining Consent - Signature