STUDY INFORMATION:

Study Title: CRAMP Study - Characterizing Resilience and Menstrual Pain Study

Principal Investigator (Head Researcher): Erwin Bottinger, MD

Physical Address: Icahn School of Medicine at Mount Sinai, 1468 Madison Ave, Annenberg building, 11th floor, New York, NY 10229

Mailing Address*:* Hasso Plattner Institute for Digital Health at Mount Sinai, 1 Gustave L. Levy Place, NY, NY 10029

Email: ehivecramp@mssm.edu

SUMMARY OF THIS RESEARCH STUDY:

In medicine there are many unanswered questions. A research study is when scientists try to answer a question about something that we don't know enough about. Participation in a research study may or may not directly help you or others. Participation is entirely voluntary. It is completely up to you whether or not you take part. You can also change your mind at any time, and it will not affect your ability to get medical care within the Mount Sinai Health System.

Menstruation related symptoms are widespread among women with many affected by menstruation related pain also known as dysmenorrhea. Dysmenorrhea and other menstrual symptoms affect the quality of life including physical, mental and social functioning.

Dysmenorrhea is also known to increase feelings of stress. People have different levels of stress resilience, that is their ability to stand up to and bounce back from stressful experiences. The purpose of this research study is to understand the relationship between the level of menstrual symptoms, specifically dysmenorrhea and stress resilience. We will also study the effect of social networks and social interactions on resilience to stress.

If you choose to participate, you will be asked to download the study app (ehive) and complete surveys on your iPhone. A resilience test, involving audio and video recording, will be administered on ehive 14 to 7 days before the beginning of your menstruation. We will follow your health for an entire menstrual cycle length with surveys about your mood, stress, pain, and menstrual symptoms. We will ask you to share data from your iPhone and Apple watch. You must own an iPhone and Apple watch to participate in this study. A portion of Mount Sinai Participants who own an iPhone, but no wearable device, may be provided with an Apple Watch for the duration of the study per availability.

The main risk to you if you choose to participate is loss of private information. Participating in this research will not benefit you. If you are interested in learning more about this study, please continue to read below.

PARTICIPATION IN THIS RESEARCH STUDY:

This research study will be fully explained to you by a member of the study team. Feel free to ask all the questions you want before you make a decision about whether or not to participate. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

You may qualify to take part in this research study because 1) you are a healthy female 18 – 40 years of age 2) with a regular menstrual cycle length (first day of one period to the first day of the next) between 21 and 40 days. 3) You own an Apple iPhone. You should not participate in this study if you are pregnant or lactating, taking hormonal contraception now or in the past 3 months, had surgery in the past 3 months or have a current acute illness (e.g., cold, cough)

Funds for conducting this research are provided by Hasso Plattner Institute at Mount Sinai.

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE:

Your participation in this research study is expected to last until data from one full menstrual cycle length is collected. The number of people expected to take part in this research study throughout the United States is 870.

DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved. This study is remote, meaning there are no in person study visits required.

- You will download the study app, ehive, on your Apple iPhone
- You will complete an eligibility questionnaire on ehive
- You will complete the consent process on ehive
- You will be asked to link your wearable device (like Apple watch) with the ehive app
- You will complete questionnaires and surveys
- You will complete a resilience test 14 to 7 days before the beginning of your menstrual cycle. The test will involve audio and video recordings.

You will receive notifications and reminders through the study app to complete surveys. These can be turned off by disabling App notifications. If there are any issues obtaining the data from your surveys or the ehive app, a research coordinator may reach out to you to assist in troubleshooting the issue. Since this study is completely remote, research coordinators may reach out to you to check in on how the study is going. This may occur once a week or not at all.

Screening and enrollment:
On study day 1, you will download the ehive app and complete an eligibility questionnaire to ensure you qualify to participate in this study. The questionnaire will ask about your demographic information, and medical history. If you are eligible, you will complete the consent process on the app and electronically sign the document to enroll. The study team contact information is in the contacts section of the app. You can pause the consent process at any time and contact the study team for additional information. The signed consent document will be available on the app to view and download.

Sharing health records: *(optional)*
At enrollment, you will be asked to share your medical records with the ehive study app. If you accept, we will prompt you to connect your electronic health record from your healthcare provider to your Apple Health App and share this information with ehive. This is optional. You can choose not to share your medical records and still participate in this study. You can choose to stop or start sharing your records anytime during the study. The data we collect includes past diagnoses, medical and surgical procedures, and current medications.

Day 1 Study assessments:
On study day 1, you will complete surveys on the ehive app about your demographic information, and health history. You will also be asked to provide information about your menstrual cycle length and current menstrual cycle day. Starting from the 1st day of the study, questionnaires about your personality, stress events in your lifetime, stress resilience, social network and loneliness, and social exclusion will become available in ehive. You have a choice to complete these questionnaires when it is more convenient to you.

Smartphone and Wearable device:
We will collect the following information from your iPhone (iPhone will not be provided by the study): screen unlocks, screen wakes, duration social media app usage, duration of music app usage, number of messages, phone calls and unique contacts with whom you interacted, smartphone keyboard usage statistics including number of words written with a specific sentiment, location. No information that may identify you or your contacts will be collected or stored. Information regarding time spent in a specific location (home, work, school, gym or other) and its distance from home will be determined by Apple algorithm. Location information will not include any address or GPS location information.

You will be asked to link your Apple watch with the ehive app to share data with the study team. The following information will be collected from your device: Heart rate, heart rate variability, activity, oxygenation (depending upon model) and sleep duration and pattern. A portion of Mount Sinai

Participants who own an iPhone, but no wearable device, may be provided with an Apple Watch for the duration of the study per availability. If you are not a Mount Sinai participant, you must own an Apple watch to participate.

Pre-resilience test survey:
The day before you will be prompted to perform the resilience test, we will ask you to answer a brief questionnaire regarding stress, depression, anxiety, and symptom burden in the last seven days.

Resilience test:
14 to 7 days before the beginning of your menstrual cycle, the ehive app will prompt you to complete a resilience test. The session will include cognitive and verbal performance test consisting of two tasks. In one task, you will be asked to perform simple math calculations. In the other task, you will be asked to do brief presentations simulating a job interview. The test will take about 15 mins to complete. Audio and video recording will be collected from the front microphone and camera on your iPhone during the test. This will be used to analyze your resilience to stress. The perceived stress from this test will not go beyond the stress in daily life like school exams. If you feel uncomfortable or overstrained, you can cancel the test at any time by closing the browser.

Daily surveys:
Starting the day after the resilience test, every day for one full menstrual cycle length (number of days between first day of one period to the first day of the next), you will complete surveys on the ehive app 3 times a day at 9 am, 12 pm and 8 pm. The surveys will ask about your mood, pain, and stress. An additional daily symptoms survey asking about your menstrual symptoms will be included at the 8 pm survey.

Post-menstruation survey:
The first day without bleeding after your menstruation, we will ask you to answer a short questionnaire regarding the stress, depression, anxiety, symptom burden and interference of pain with your daily life activities you experienced over the last seven days.

WhatsApp and Facebook data sharing: ***(optional)***
On the last day of the study, you have an option to share your WhatsApp and Facebook Messenger meta-data through our anonymizing platform called Dona. Dona locally removes all personal identifying information from the messaging data and just collects the number of words used in your messages, the timestamps, and replaces sender and receiver names with fake names to protect your privacy. No information regarding the content of the message is retrieved. The data will be used to gather information on your social interaction.

Returning study results:
At the end of your study participation, you will receive a report of your data including:

- Graph of your mood, pain and stress across your menstrual cycle
- Your average pain, stress and mood levels
- The maximum and minimum pain, stress and mood levels during your menstrual cycle
- Your stress response to the resilience test
- Change in your heart rate (HR) and heart rate variability (HRV) upon stress induction
- Your average HRV and HR across pain, stress and mood levels
- Graph of your social interactions and their change across the menstrual cycle and across mood, stress and pain levels

This report does not represent a medical report. The report will only serve as a description of the data you provided through surveys and collected from your wearable device.

USE OF YOUR DATA:

In the future, your identifiable information may be removed from the private information that is collected as part of this research. After this removal, the information could be used for future research studies or shared with other research teams for future research studies. You will not be informed of the details of specific research that is done with your medical information. That means that a research project might be done that you would not consent to if provided with the details of that research project.

To do more powerful research, it is helpful for researchers to share information they get from studying data. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. Researchers can then study the combined information to learn even more about health and disease. If you agree to take part in this study, some of health information might be placed into one or more scientific databases. There are many different kinds of scientific databases; some are maintained by Icahn School of Medicine at Mount Sinai or another institution, some are maintained by the federal government, and some are maintained by private companies. For example, the National Institutes of Health (an agency of the federal government) maintains a database called “dbGaP.” A researcher who wants to study the information must apply for permission to use the database. Different databases may have different ways of reviewing such requests. Researchers with an approved study may be able to see and use your information, along with that from many other people.

Researchers will always have a duty to protect your privacy and to keep your information confidential, but there are risks associated with data collection and sharing. They are described in more detail in the risks section.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things: Downloading the ehive app, connecting wearable devices, completing the resilience test involving audio and video recordings, and answering survey questions.

If you are a Mount Sinai Participant with an iPhone but no Apple watch, email the study team at ehivecramp@mssm.edu to request a device. You will receive a return label to ship the Apple watch back at the end of your participation.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

You will not be paid for participating in this research study. Being in this research study will not lead to extra costs to you.

POSSIBLE BENEFITS:

You are not expected to get any benefit from taking part in this research study. Others may not benefit either. However, the data generated from this study will be used to support development of stress resilience interventions to improve symptoms in patients with dysmenorrhea (menstruation related pain).

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

The study involves no more than minimal risk. The possible risks related to participating in the study include:

- Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk. Your name and other information that could directly identify you (such as address, date of birth or social security number) will never be placed into a scientific database.
- The resilience test may be uncomfortable.
- Some survey questions may be uncomfortable. You have an option to skip any task/question.
- There is no additional risk to using your iPhone and Apple watch for study participation.
- For Mount Sinai participants: If you receive an Apple watch from the study, you will complete a user agreement when setting up the device. This will involve agreeing to Apple's data sharing and privacy policies. This agreement would be the same if you bought the device yourself.

Your name and other information that could directly identify you (such as address, date of birth or social security number) will never be placed into a scientific database.

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you believe that you have suffered an injury related to this research as a participant in this study, you should contact the Principal Investigator.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff.

If you decide you don't want your data to be used for research anymore, you can contact the researcher and ask to have your data removed from future use. You can decide to have your audio and video recordings, collected as part of the resilience test, destroyed anytime. If you withdraw from the study your audio and video recordings will be destroyed. If any data has already been shared without your identity, it won't be possible to retrieve them because no one will know who you are. Data that has already been used will not be affected by your decision. Any data that is still linked to your identity by a code the researcher has will be withdrawn so that no future sharing of your data will take place.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If data has been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns, or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Principal Investigator at ehivecramp@mssm.edu.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be shared with others?
As part of this research project, the research team at the hospital(s) involved in the research will collect your name, email, address and medical record number. The resilience test will collect audio and video recordings. The researchers will also get information from your medical records in the Mount Sinai Health System.

During the study the researchers will gather information by asking survey questions through the ehive app and collecting data from your wearable devices.

Why is your protected health information being used?
Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not

include any information that would let others know who you are, unless you give separate permission to do so. The Principal Investigator may also use and share the results of these tests and procedures to treat you in collaboration with others in the Mount Sinai Health System.

The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects is responsible for overseeing research on human subjects and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your protected health information?
As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- The United States Department of Health and Human Services and the Office of Human Research Protection.

In all disclosures outside of Mount Sinai, you will not be identified by your name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, *the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document, you are authorizing this access.* We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information?

Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?
NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?
You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State

Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

ADULT PARTICIPANT:
Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

Signature of subject	Printed Name of Subject	Date	Time

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

Signature of consent delegate	Printed Name of consent delegate	Date	Time

WITNESS SECTION:
When a witness is required to observe the consent process, it should be documented below (for example, when subject is illiterate, visually impaired, or this document accompanies a short form consent).

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of Witness	Printed Name of Witness	Date	Time