

University of Wisconsin-Madison Consent to Participate in Research and Authorization to Use Protected Health Information for Research

Study Title: Cognitive Behavioral Therapy Study for Depression (CBT+ Study)

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Key Information

The information in this section is to help you decide whether or not to be a part of this study. You can find more detailed information later on in this form.

Why are researchers doing this study?

Depression is common and affects a person's ability to function in many ways, including impairing mood, sleep, appetite, energy, concentration, and more. Therapy is a standard and common treatment for depression. However, only half of patients feel significantly better with therapy and many people experience another episode of depression shortly after receiving therapy, so there is a need to figure out how to make therapy more effective. What people do before therapy might influence therapy but this is understudied. Therefore, the purpose of this study is to understand how pre-therapy structured routines (such as resting quietly while watching a nature video or being active while watching a nature video) influence cognitive behavioral therapy (CBT). This study will provide the necessary first step for future research aimed at improving behavioral treatments for depression.

We invite you to participate in this study because:

- You are between 18-65 years old
- You suffer depression
- You are either not taking any mental health medications or seeking other mental health treatment (e.g., behavioral, psychological) OR have been on a stable mental health medication and/or treatment regimen for the past 8 weeks, and are encouraged to maintain that regimen during the CBT intervention (8 weeks)
- You have either never done CBT-based psychotherapy before OR have not done CBT-based psychotherapy within the last 5 years
- You can safely exercise if randomized to the active group, based on a physical activity screening survey or approval from your primary care physician

Due to the potential impact of certain conditions on study outcomes, potential participants will be excluded from participation if they:

- Are currently pregnant, nursing, or planning to become pregnant during the study
- Are currently diagnosed with Substance Use Disorder
- Are diagnosed with lifetime or current Psychosis, Mania, or Bipolar Disorder
- Have Class III+ or greater level of obesity (Body mass index ≥ 40)
- Have high active suicidal ideation
- Exhibit behavioral disturbance or relationships with study team members that would significantly interfere with study participation

If you have any questions about the inclusion and exclusion criteria for this study, please ask the study staff now. Research staff will make inclusion/exclusion decisions regarding your participation based on your responses to questions during this Intake Visit. You will be excluded from participation if you are deemed ineligible to participate based on your responses.

What will I need to do in this study?

If you decide to participate, you will complete an initial Intake Visit (today's visit), and then begin 8 weeks of CBT, where you will have therapy for 50-minute sessions once a week, with either 30 minutes of a quiet rest routine ('CalmCBT') or 30 minutes of an active routine cycling on a stationary bike ('ActiveCBT') immediately before therapy. These visits take 1.5-2 hours each week. After, you will complete a Post-Intervention Visit and 2 Follow Up Visits, with procedures identical to today, including questionnaires and a mental health clinical interview.

The group you get (Calm or Active) will be chosen by chance; like flipping a coin. Neither you nor the study team will choose what group you get. Your group assignment will be determined by an automated module on the study data collection platform, called REDCap. You will be told what your group is when you arrive at your first therapy session.

We expect that you will be in this research study for one year. This includes the 8-week intervention period and follow-up assessment visits completed at 20 weeks and 1 year. You can find detailed information about the study procedures in the section called '*If I take part in the study, what will I do?*'

What are some reasons I might – or might not – want to be in this study?

Possible reason you might want to participate	Possible reasons you might not want to participate
• I will receive 8 weeks of Cognitive Behavioral Therapy with a trained therapist for the treatment of depression. • I will receive personalized activity data. • I want to help researchers find out how to improve therapy effectiveness. • I am comfortable with the confidentiality measures in place, knowing that my personal information will not be disclosed.	• I want to decide which group I am assigned and don't want to leave it to chance. • I won't be able to dedicate the time to go to all the study visits. • I am not sure if I will be comfortable with the physical demands if in the active group. • I am not sure if Cognitive Behavioral Therapy is right for me.

Do I have to be in the study?

No, you do not have to be in this study. Taking part in research is voluntary. If you decide not to be in this study, your choice will not affect your healthcare or any services you receive. There will be no penalty to you. You will not lose medical care or any legal rights. You can ask all the questions you want before you decide.

Instead of being in this research study, you could find a local mental health care provider, such as a therapist or psychiatrist, and our lab website (<https://wellex.labs.wisc.edu/>) lists local options under the 'Resources' tab if you are interested. The CBT provided in this study is like the CBT that would be available from a clinical provider.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

How is research different from health care?

When you go to a health provider for care, the provider focuses on how to help you as an individual. When you take part in a study, you are helping to answer a research question, like how safe or effective a treatment is, or what dose to use. Treatment is based on a study plan, not on you as an individual.

Who can I talk to about this study?

If you have questions, concerns, or complaints, or think that participating in the research has hurt you, please talk to the research team. You can reach out to any of the following research personnel whenever necessary.

- Jacob Meyer, PhD - Principal Investigator: jdmeyer3@wisc.edu
- Jeni Lansing, PhD - Research Scientist: jlansing3@wisc.edu
- Madeleine Connolly, PhD – Research Associate: mconnolly5@wisc.edu
- Ruby Rogers, BA – Research Specialist: rrogers24@wisc.edu

Please note, email is generally not a secure way to communicate sensitive or health related information as there are many ways for unauthorized users to access email. You should avoid sending sensitive, detailed personal information by email. Email should also not be used to convey information of an urgent nature. If you need to talk to someone immediately or would prefer not to receive study communication by email, please contact Ruby Rogers, Research Specialist, at 608-893-2973.

If you have concerns about your rights as a research participant or have complaints about the research study or study team, call the confidential research compliance line at 1-833-652-2506. UW staff, not part of the study team, will work with you to address concerns and assist in resolving any complaints.

If I take part in the study, what will I do?

If you agree to participate, you will be asked to complete an initial Intake Visit (today's visit), 8 sessions of weekly therapy sessions, a Post-Intervention Visit and two Follow Up Visits, with further descriptions of each visit listed below.

Intake Visit (~2.5-3 hours)

During the Intake Visit, you will read, ask questions, and sign the informed consent document (this document), verbally verify you continue to meet the inclusion/exclusion criteria, and complete a structured clinical interview for depression with a trained Clinical Interviewer. This interview ranges in time but usually lasts about 2 hours. If eligible to participate, you will complete several other questionnaires about your health, wellbeing, and activity level that take around 30 minutes. Your height, weight, blood pressure, and heart rate will be measured. You will also be given an activity monitor to wear for one week and return it during your first CBT session. At the end of this visit, you will be randomized into CalmCBT (quiet rest routine prior to CBT) or ActiveCBT (exercise routine prior to CBT).

CBT Sessions (~2 hours)

During the 8-weekly CBT Sessions, we will ask you to arrive 45 minutes prior to therapy. You will begin each session with a few brief questionnaires (~5 minutes) about how you are feeling, and blood pressure/heart rate will be recorded. On sessions 1, 4, and 8, we will also collect a blood sample.

You will then begin a Calm or Active routine (depending on randomization). In both routines, you will watch a nature documentary series ("Blue Planet"). If randomized to CalmCBT, you will rest quietly for 30-minutes while viewing the video. If randomized to ActiveCBT, you will complete 30-minutes of moderate or 'somewhat hard' exercise on a stationary bicycle while viewing the video. The exercise session will begin with a 3–5-minute warm up and include a built-in cool-down (during the last 3 minutes of the 30-minute exercise session). During both routines, we will continuously monitor your heart rate, rating of exertion, and how you are feeling. During this time, we will ask that you refrain from using other devices (e.g. cell phone) and sources of entertainment (e.g. music).

After, you will again complete a few brief questionnaires about how you are feeling. At session 1, 4, or 8, we will collect another blood sample.

Within 10 minutes, you will begin your CBT session with a trained therapist in a private room in the Medical Sciences Center. Each CBT session will last approximately 50 minutes. Audio from these sessions will be recorded to ensure the therapist is applying the CBT techniques in a standardized way across all participants. The therapist and CBT session supervisors (co-investigators of this study, Simon Goldberg, PhD, University of Wisconsin-Madison and Nathaniel Wade, PhD, Iowa State University) will be the only study team members who listen to these sessions.

After therapy, we will ask you to complete a few more brief questionnaires and schedule your next appointment. Again, at sessions 1, 4 or 8 we will collect a final blood sample (3 total on each visit). Additionally, on sessions 4 and 8, you will be asked to re-wear the activity monitor for one week.

Please note, prior to sessions that involve a blood draw, we will ask you to refrain from caffeine containing drinks and using tobacco/nicotine products 4 hours prior to sessions, refrain from consuming alcohol and from fatiguing exercise 24 hours prior to sessions, and refrain from changing regular medications or treatments during the 8-week intervention period. These lifestyle considerations are important to limit the variability in the blood biomarkers we are looking at and how that may then influence the therapy sessions.

Post-Intervention and Follow-Up Visits (~1 hour each)

Your final visit will take place within one week of your final therapy session. During the Post-Intervention Visit, you will first undergo the structured clinical interview for depression by a clinical interviewer. You will then complete several other questionnaires about your health. Next, height, weight, blood pressure, and heart rate will be taken. You will return for two Follow-up Visits 3 months and 1 year after the end of therapy and these visits will be identical to the Post-Intervention Visit, including re-wearing the activity monitor for one week.

Remote visits may be considered in limited, exceptional situations in consultation with the research team; participants are otherwise expected to attend visits in person.

If I take part in the study, what are the tests that will be done?

Questionnaires:

You will be asked to complete several questionnaires about your health, physical activity, how you are feeling and other psychological factors. Most questionnaires will be completed electronically, and all data that will be used from your responses to the questions will only be associated with your study ID number. You will be able to skip any questions that you do not feel comfortable responding to.

Mental Health Interview:

You will meet with a Clinical Interviewer (trained and supervised by Dr. Simon Goldberg, a licensed psychologist in the state of Wisconsin and Dr. Nathaniel Wade, a licensed psychologist in Iowa) to complete a mental health interview. A mental health interview is a face-to-face conversation between a mental health professional and a person in which the professional ask questions and gathers information about a person's behavior, attitudes, current situation, personality, and life history. This interview will be used to determine if you meet eligibility criteria (e.g., currently have Major Depressive Disorder) and to assess mental health symptoms throughout the study.

As part of the study, we will collect audio recordings of you during the interview procedures for supervision and quality assurance. Audio recordings from the clinical interviews and therapy sessions will also be kept confidential. The Lyssn platform (Lyssn AI, Seattle Washington) will be used for collection and storage of recordings from clinical interviews and therapy sessions for supervision and quality assurance. Lyssn is an artificial intelligence (AI) software that has been trained to accurately evaluate evidence-based practices, including clinical interview and CBT session fidelity. Lyssn meets the highest industry security standards, as the platform is HIPAA, FERPA, and GDPR compliant. All data rest in the Lyssn cloud, available only to authorized study personnel (e.g., Dr. Simon Goldberg, clinical interviewers, therapists) via password protected account log in. Audio recordings will not be used for purposes outside of the study or in any papers or publications.

Blood Sample:

A trained phlebotomist will collect approximately 4 teaspoons of blood before your routine, after your routine and after your therapy session during weeks 1, 4, and 8. These samples will be drawn via venipuncture. Blood samples will be collected to examine the response of blood biomarkers before and after exercise.

What protected health information is used in this study?

Protected health information, also called PHI, is information about your physical or mental health that includes your name or other information that can identify you, like your date of birth or medical record number. To do this study, we will use the following kinds of PHI: contact information for scheduling purposes (e.g., name, email, phone),

information related to your birth (e.g., name, date, sex, location), results of tests or procedures done as part of the study, and things you tell the researchers about your health.

What happens if I say yes, but I change my mind later?

You can leave the study at any time. If you choose to leave the study, your choice will not affect your healthcare or any services you receive. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights. If you decide to leave the study, contact the investigator so that the investigator can remove you from the study.

Your authorization for researchers to use your protected health information (PHI) does not have an end date. However, information that could identify you (like your name) will be destroyed at study closure. However:

- You can choose to take back your authorization for researchers to use your health information. You can do this at any time before or during your participation in the research.
- If you take back your authorization, information that was already collected may still be used and shared with others, but the researchers will no longer be able to collect NEW information about you.
- If you take back your authorization, you will not be able to take part in the research study.
- To take back your authorization, please contact Ruby Rogers, Research Specialist, at 608-893-2973. The research team will need to acquire a written note (email or by mail) that you take back your authorization, and the research team will work with you to do so.

Will being in this study help me in any way?

By participating in the study, you will receive 8 weeks of cognitive behavioral therapy with a trained therapist for treatment of depression. Cognitive behavioral therapy is currently a frontline treatment for depression, so enrollment in this study will actively treat depression and may help reduce symptoms and improve quality of life.

What are the study risks?

There are some risks and/or discomforts you may experience during participation in this research study. Each risk is detailed below, along with a description of how the research team will attempt to minimize their occurrence.

Psychological stress from mental health questions and therapy sessions. There may be limited psychological stress related to discussing mental health questions during the clinical interview or therapy sessions. Dr. Meyer and Dr. Goldberg have supervised the training of the personnel who administer the clinical mental health interviews and CBT sessions. Dr. Goldberg, a licensed psychologist in the state of Wisconsin, will

provide guidance to the person performing the clinical interviewer and CBT sessions to help them in minimizing any psychological distress that may be experienced while discussing mental health issues. For participant safety, during the Intake Visit or first therapy session, you will collaboratively create a safety plan with the clinical interviewer or therapist (respectively) to provide support if dealing with suicidal thought any time throughout or after the study.

Social risk due to stigmatization. There may be some social risk regarding the disclosure of mental health information. The main risks are harm to reputation, embarrassment, or stigmatization if participation in the study becomes known, but given the study procedures, this risk is low. Nonetheless, strategies to reduce this risk include:

- Using a strategic study name that does not disclose the clinical outcome being evaluated in the study
- Having all assessment visits on an individual basis to minimize contact with other participants
- Having assessment visits performed in closed rooms to minimize the chance of being noticed by others

Breach of confidentiality. Confidentiality will be a central value of this study. However, there are situations in which confidentiality might need to be breached. Research staff will contact local authorities or other health service providers if you reveal (a) that a child or older adult is being abused or severely neglected, or (b) that you are an imminent threat to yourself or someone else. If a report is made, this may be a breach of your confidentiality. We are making you aware of this potential need to breach your confidentiality by informing you here, as well as having this specifically discussed with the clinical interviewer during the Intake Visit.

Digital Health Technology. Digital health technology is required for study participation and may relate to risks described above. Specifically, we will ask you to wear an activPAL activity tracker. This is a research grade fitness tracker that will measure sitting and activity patterns. We will set up the device and provide clear instructions with how you will use it. This device measures your leg position, if you're moving, and how quickly you are moving. You may experience skin discomfort or irritation from the tape used to adhere the activity monitor to your leg. If this occurs, we will provide instructions for switching legs, advise shaving your leg where the tape adheres, and changing the tape less frequently. After you wear the monitor for one week, the research team will download the data from the device to get data regarding your sitting time, walking time, and exercise time (like average steps per day). This data will be erased from the device and stored on a HIPAA-compliant restricted research drive, only accessible to senior research personnel.

Exercise in Active Routine. Moderate exercise is generally very safe and tolerable. Most complications are minor and may include shortness of breath, feeling dizzy, feeling fatigued, experiencing muscle soreness or experiencing joint pain. Very rarely a heart

rhythm abnormality or heart attack may occur during exercise, requiring resuscitation and hospitalization. However, this is extremely uncommon even during maximal exertion and you will be closely supervised by trained personnel throughout the moderate exercise session.

Risks of the Blood Draws. There is a rare risk of fainting or dizziness. There is also a small risk of bruising or bleeding at the site of the needle (about 1 in 10 cases), and an extremely small risk (about 1 in 1000 cases) of infection. The total quantity of blood collected across all visits will be about 180 mL (about $\frac{3}{4}$ cup), much less than that taken during a single donation at the Red Cross Center or a blood drive (500mL or a little more than 2 cups). On rare occasions, the needle may damage a nerve or the vein, causing the vein to become blocked. Additionally, there is a small risk of fainting or dizziness during and after the blood draws. These risks will be minimized by using trained phlebotomists to draw the blood and using sterile equipment in an area designed for the collection of blood samples. Two research staff members will be present in case you begin to feel faint or dizzy.

Mobile charges. Taking part in this research study may lead to added costs to you, such as mobile charges for phone calls or texts made with the study team. We attempt to minimize this risk by notifying you now that you are responsible for all mobile charges related to communications made with the study team.

Who has access to the information collected for the research?

We have strict rules to protect your personal information and protected health information (PHI). We will limit the use and disclosure of your personal information, including research study and medical records, as described in this consent form. However, we cannot promise complete confidentiality. We will share information with individuals or organizations identified in this consent form. Federal or state laws may also permit or require us to show information to university or government officials responsible for carrying out or monitoring this study. This includes University of Wisconsin and its representatives and affiliates, including those responsible for ensuring compliance, such as the Human Research Protection Program, and the Department of Health and Human Services.

The study is protected by a Certificate of Confidentiality from the National Institutes of Health. This means we will not share any information that would identify you as a participant in the study, even if the police or courts ask to look at the data we have collected.

We may have to tell appropriate authorities, such as child protective services or health care providers, if we learn during the study that you or others are at risk of harm (for example, due to child or elder abuse, or suicidal thoughts).

Authorizing the research team to use your PHI means that we can release it to the people or groups listed in this form for the purposes described in this form. Once we

share your identifiable health information outside UW-Madison, the HIPAA Privacy Rule may no longer protect it. However, we try to make sure that everyone who sees your health information keeps it confidential.

We will share information collected for this study with researchers (i.e., Co-Investigators) or organizations outside UW-Madison, including the University of Minnesota, Iowa State University, and the University of Iowa. This is necessary to complete the planned statistical analyses, safety reporting requirements, and for the clinical team to conduct training and ongoing fidelity checks.

A description of this clinical trial will be available on clinicaltrials.gov. This web site will not include information that can identify you. At most, the web site will include a summary of the study results. You can search this Web site at any time.

Will information from this study go in my medical record?

None of the information we collect for this study will go in your medical record. The researchers are not required to release health information to you if it is not part of your medical record.

Will my information and samples be used in other research?

With appropriate confidentiality protections, we might use information and samples that we collect during this study for other research or share it with other researchers without additional consent from you.

This study is collecting information and samples from you. We would like to make your information and samples available for other research studies that may be done in the future without additional consent from you. The research may be about similar diseases or conditions to this study. However, research could also be about unrelated diseases, conditions, or other types of research. These studies may be done by researchers at this institution or other institutions, including commercial entities. Your information and samples may be shared with researchers around the world. Our goal is to make more research possible. We plan to keep your information and samples indefinitely. To get your information and/or samples, future researchers must seek approval from this institution and review by an IRB may be required.

Your name and other information we think could identify you, such as your date of birth or medical record number, will be removed from any information and samples you provide before they are shared with other researchers. Researchers cannot easily link your identifying information to the information and samples. However, there remains a possibility that someone could identify you. There is also the possibility that people who are not supposed to might access your information and samples. In either case, we cannot reduce the risk to zero.

Participating in this study means you agree to share your information and/or samples. You can change your mind later, but researchers might still use your information and/or samples if they have already been shared or have been de-identified and can't be

removed. If you do not want your information and/or samples used for other research studies, you should not participate in this study.

We will share the data from this study in a database that requires researchers to request access and receive permission to use the data for a specific research project. This is called “controlled access.” Only summary results, a summary of the information generated from all of the research participants in this study, would be shared in a database that does not require permission. When sharing, we will remove any personal information that could directly identify you (like name, birthdate, address, phone number) and replace it with a code number. We will share this code number, dates information was collected, your age, your sex, and your responses to questionnaires in the study. In using the coded number, we believe there is a low risk that study data could be used to re-identify you. However, it’s possible that data that cannot be used to identify you today could be used to identify you in the future. It is also possible that you will participate in more than one study that sends data to the database. The database and other researchers can connect your data from different studies by matching the code number on your data from each study.

Will I receive the results of research tests?

Most tests done as part of a research study are only for research and have no clear meaning for health care. In this study, you will not be informed of any test results or unexpected findings. However, we will provide you with a personalized report of your activity.

The questionnaires you will complete in this study may show that you are experiencing symptoms of emotional distress such as depression, suicidal thoughts, and/or anxiety. If the questionnaires show that you are experiencing depression, suicidal thoughts, or anxiety, please utilize the mental health resources provided by the research team.

Can I be removed from the research without my agreement?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include:

- You do not follow the study rules or no longer meet the requirements to be in the study
- The research team determines you need a higher level of professional mental health treatment (e.g., severe suicidality or imminent threat to others or yourself)
- The study is stopped by the sponsor or researchers

What happens if I am injured or get sick because of this study?

If you are injured or get sick because of this study, medical care is available to you through UW Health, your local provider, or emergency services, as it is to all sick or injured people.

If it is an emergency, call 911 right away or go to the emergency room. For non-emergency medical problems, please contact the study team to report your sickness or injury by phone at 608-890-0154 to document the event, and follow up with your regular healthcare provider.

Here are some things you need to know if you get sick or are injured because of this research:

- If sickness or injury requires medical care, the costs for the care will be billed to you or your insurance, just like any other medical costs.
- Your health insurance company may or may not pay for this care.
- No other compensation (such as lost wages or damages) is usually available.
- UW-Madison and UW Health do not have a program to pay you if you get sick or are injured because of this study.
- By signing this consent form and taking part in this study, you are not giving up any legal rights you may have. You keep your legal rights to seek payment for care required because of a sickness or injury resulting from this study.
- In emergency situations, your personal information (like your name, contact information) may be shared with emergency services (like EMS), building safety officers, or others if needed to provide help or document the event.

Will I receive anything for participating?

There are no payments or compensation associated with this study.

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

How will I be contacted?

By consenting to participate in this study, you opt in to receive study related texts, calls and emails for visit reminders and scheduling. You will need to provide your phone number or email address to participate. Your contact information will be used for visit reminders and scheduling, and it is important so we can send you reminders of your study visits, communicate about schedule changes, and provide you links to surveys when necessary. Email and text messaging are generally not secure ways to communicate about your health as there are many ways for unauthorized users to access them. You should avoid sending sensitive, detailed personal information by email or text message. Email and text messages should also not be used to convey information of an urgent nature. If you need to talk to someone immediately and/or about your health information, please call Ruby Rogers, Research Specialists, at 608-893-2973.

How many people will be in this study?

We expect about 100 people will be in this research study.

Who is funding/supporting this study?

This research is being funded by the National Institute of Mental Health (NIMH), a sub-agency of the National Institutes of Health (NIH).

Agreement to participate in the research study

You do not have to sign this form. If you refuse to sign, however, you cannot take part in this research study. If you sign the line below, it means that:

- You have read this consent and authorization form.
- You have had a chance to ask questions about the research study, and the researchers have answered your questions.
- You want to be in this study.
- You give authorization for your protected health information to be used and shared as described in this form.

Signature of participant

Date

Printed name of participant

Signature of person obtaining consent

Date

Printed name of person obtaining consent