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Protocol Title:	Treating Insomnia and Improving Metabolic Health in Midlife Women With Insomnia
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Mass General Brigham

Research Consent Form
General Consent Form Template
Version Date: February 2021

Subject Identification

Protocol Title: Treating Insomnia and Improving Metabolic Health in Midlife Women with Insomnia

Principal Investigator: Shadab Rahman, PhD MPH

Site Principal Investigator:

Description of Subject Population: Perimenopausal and postmenopausal women with insomnia and metabolic dysfunction ages 40-65

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. Your decision won't change the medical care you get within Mass General Brigham now or in the future.

The following key information is to help you decide whether or not to take part in this research study. We have included more details about the research in the Detailed Information section that follows the key information.

Why is this research study being done?

We are doing this research to investigate the efficacy of suvorexant on insomnia symptoms and on metabolic health in midlife women with insomnia, and to learn whether improvement in insomnia symptoms is linked with improvement in metabolic health.

This consent form is to complete the screening procedures and, if eligible, to continue with the rest of this research study. You have already signed a consent form for the initial screening procedures for this study.

How long will you take part in this research study?

If you decide to join this research study, it will take you about 13 weeks to complete the study. During this time, we will ask you to make 3-5 study visits to Brigham and Women's Hospital.

What will happen if you take part in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

This research study will compare suvorexant 20 mg pills to placebo. During this study you will get both placebo and suvorexant, each for 4 weeks during the study, with a 4-week time off study medication in between. We will assign you by chance (like a coin toss) the order that you take suvorexant or placebo. You and the Investigator will not know which one you are taking.

Why might you choose to take part in this study?

We cannot promise any benefits to you from taking part in this research study. However, possible benefits may include improvement in your insomnia symptoms while you are in the study. Others with insomnia may benefit in the future from what we learn in this study.

Why might you choose NOT to take part in this study?

Taking part in this research study has some risks and requirements that you should consider carefully.

Common side effects of suvorexant include headache, next-day drowsiness, dizziness, abnormal dreams, cough, diarrhea, dry mouth, and upper respiratory tract infection. Taking suvorexant may also cause worsening depression or suicidal thoughts.

A detailed description of side effects, risks, and possible discomforts can be found later in this consent form in the section called "What are the risks and possible discomforts from being in this research study?"

Other things to consider are that you will be asked to attend up to 4 more in-person study visits at Brigham and Women's Hospital, each of which includes a blood draw. 2 of the visits may be able to be conducted remotely, if necessary.

What other treatments or procedures are available for your condition?

Other options available to treat insomnia include Ambien, Lunesta, or Sonata, or cognitive behavioral therapy for insomnia (CBTi). You may also have the study drug, suvorexant, prescribed by your physician and not participate in this study.

If you have questions or concerns about this research study, whom can you call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Study Staff

- Shadab Rahman, PhD, MPH is in charge of this study. You can call him at 617-525-8830 (office), 978-328-4395 (cell), Monday-Friday 9 A.M. through 5 P.M.
- You can also call the following study clinicians with questions about this research study:
    - Hadine Joffe, MD, MSc – 617-732-4906 (office), Pager #32528
    - Jessica Harder, MD – 617-732-6753, Pager #36374
    - Irene Gonsalvez, MD – 617-732-6753, Pager #31736
    - Liane Hunter, MD – 617-732-6753, Pager #33759
- In case of any study-related emergency, after hours you can contact any of the study doctors by calling 617-732-6660 and asking the page operator to page the number above associated with the corresponding clinician on this study.

If you have questions about scheduling appointments, study visits, or study procedures, please call Hannah Kim, Clinical Research Coordinator, at 617-525-6303, M-F, 9am-5pm.

If you want to speak with someone **not** directly involved in this research study, please contact the Mass General Brigham IRB office. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

Detailed Information

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.

Why is this research study being done?

We are doing this research to investigate the efficacy of suvorexant on insomnia symptoms and on metabolic health in midlife women with insomnia, and to learn whether improvement in insomnia symptoms is linked with improvement in metabolic health.

Suvorexant is approved by the U.S. Food and Drug Administration (FDA) to treat insomnia.

This research study will compare suvorexant 20 mg pills to placebo. During this study you will get both placebo and suvorexant, each for 4 weeks during the study, with a 4-week time off study medication in between. The placebo looks exactly like suvorexant but contains no real medication. Placebos are used in research studies to see if the results are due to the study drug or due to other reasons.

Because this is a research study, the suvorexant or placebo will be given to you only during this study and not after the study is over. This means that even if you feel are better at the end of the study, you will not be able to get a prescription for suvorexant from the study doctor, but your own doctor may prescribe it.

Dr. Joffe, a co-investigator of this study, has a financial interest in Merck & Co., Inc., the study sponsor. In accordance with Mass General Brigham's conflict of interest policies, the Mass General Brigham Office for Interactions with Industry has reviewed Dr. Joffe's financial interest in the company and has determined that the interest creates no significant risk to the welfare of participants in this study or to the integrity of the research. If you would like more information about this, please contact the Mass General Brigham Office for Interactions with Industry at 857-282-2024 or PHSOIIRESEARCH@PARTNERS.ORG.

Who will take part in this research?

Women between 40 and 65 years old with insomnia and who are at risk for cardiovascular disease can take part in this research.

About 61 participants will take part in this research study at Brigham and Women's Hospital (BWH).

Merck & Company is paying for this research to be done.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

If you are eligible to continue with the study, we will assign you by chance (like a coin toss) to take suvorexant or placebo for the first 4 weeks. You and the study doctor cannot choose whether you will take suvorexant or placebo first and neither you nor the study staff will know which you are taking. You will have a 1 in 2 chance of being assigned to take suvorexant first. When you complete the first 4 weeks of treatment, you will take no study medication for 4 weeks. Then you will start taking the other study medication for another 4 weeks. If you took suvorexant first, you will take placebo second; if you took placebo first, you will take suvorexant second.

Study Visits

Visit 1b (Research Consent Visit)
The Research Consent Visit will take 1-2 hours. At this visit, we will ask you about your sleep patterns and related symptoms and do some tests to see if you qualify to take part in this research study. The study doctor will review the results of these evaluations and tests.
At this visit, we will:

- Review and sign the Informed Consent Form.
- Ask you about your medical history.
- Review any medications you are currently taking and have taken recently.
- Ask you to fill out some questionnaires about your sleep, general health, and mood.

We will let you know if you do not qualify for the study, and you will be referred to resources or your primary care doctor to follow up, if applicable.

At Home, Between Visits 1b and 2
If you are eligible and still interested in participating in the study, you would complete the following tasks at home before Visit 2:

- Complete 1 week of sleep, hot flash, and food diary.
- Wear an activity watch to track you sleep patterns for 1 week immediately leading up to your Visit 2.

Visit 2 (Start of Treatment Block 1)
Visit 2 will take place about 1 week after the Research Consent Visit and will take about 1 hour at Brigham and Women's Hospital. At this visit, we may complete the following procedures:

- Complete questionnaires about your sleep and other symptoms.
- Draw a fasting blood sample for your blood sugar, diabetes, and cholesterol lab tests.
- Collect a urine sample to test for pregnancy. Pregnant women and women who are breastfeeding cannot take part in this study.
- Take vital signs and body measurements.
- Initiate wearing a small glucose monitor, which you will wear for 3 days on the skin of your upper arm.
- Initiate tracking the food you eat using an application on your phone called MealLogger ™ for 3 days
- Receive a one-month supply of study medication to take one pill each night before bedtime.

At Home, before Visit 3
Before Visit 3, you would complete the following procedures:

- Complete 1 week of sleep, hot flash, and food diary.
- Wear an activity watch for 1 week immediately leading up to your Visit 3.
- Track the food you eat using an application on your phone called MealLogger ™ for 3 days immediately leading up to your Visit 3.
- Wear a glucose monitor for 3 days immediately leading up to your Visit 3.

Visit 3 (End of Treatment Block 1)
Visit 3 will take place 4 weeks after Visit 2 and may take place at Brigham and Women's Hospital or may be remote via video call. At this visit, you may complete the following procedures:

- Complete questionnaires about your sleep and other symptoms.
- Be asked about how you are feeling on the study medication.
- Draw a fasting blood sample for blood sugar, diabetes, and cholesterol lab tests.

- Take vital signs and body measurements.
- Return the activity watch, glucose monitor, and any unused study medication.

If this visit is conducted remotely, we would ask that you visit a phlebotomy lab at a local Quest laboratory near you to have your blood drawn. You would be provided mailing materials to send the activity watch, glucose monitor, and any unused study medication back to the research team

Between Visit 3 and 4
After finishing the first 4 weeks on study medication, you would not take any study drug for the next 4 weeks, but would

- Complete 1 week of sleep, hot flash, and food diary.
- Wear an activity watch to track you sleep patterns for 1 week immediately leading up to your Visit 4.

Visit 4 (Start of Treatment Block 2)
Visit 4 will take place 4 weeks later at Brigham and Women's Hospital. Procedures are the same as Visit 2 (Start of Treatment Block 1). You will

- Complete questionnaires about your sleep and other symptoms.
- Draw a fasting blood sample for blood sugar, diabetes, and cholesterol lab tests.
- Collect a urine sample to test for pregnancy. Pregnant women and women who are breastfeeding cannot take part in this study.
- Take vital signs and body measurements.
- Initiate wearing a small glucose monitor, which you will wear for 3 days on the skin of your upper arm.
- Initiate tracking the food you eat using an application on your phone called MealLogger™ for 3 days
- Receive a one-month supply of study medication to take one pill each night before bedtime.

At Home, before Visit 5
Before Visit 5, you would complete the following procedures:

- Complete 1 week of sleep, hot flash, and food diary.
- Wear an activity watch for 1 week immediately leading up to your Visit 5.
- Track the food you eat using an application on your phone called MealLogger™ for 3 days immediately leading up to your Visit 5.
- Wear a glucose monitor for 3 days immediately leading up to your Visit 5.

Visit 5 (End of Treatment Block 2)

Visit 5 will take place 4 weeks after Visit 4 and may take place at Brigham and Women's Hospital or may be remote via video call. Procedures are the same as Visit 3 (End of Treatment Block 1). You will

- Complete questionnaires about your sleep and other symptoms.
- Be asked about how you are feeling on the study medication.
- Draw a fasting blood sample for blood sugar, diabetes, and cholesterol lab tests.
- Take vital signs and body measurements.
- Return the activity watch, glucose monitor, and any unused study medication.

If this visit is conducted remotely, we would ask that you visit a phlebotomy lab at a local Quest laboratory near you to have your blood drawn. You would be provided mailing materials to send the activity watch, glucose monitor, and any unused study medication back to the research team.

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example, list of allergies, results of standard blood tests done at the hospital labs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

Mass General Brigham has an electronic system that lets your study doctors know if you are admitted to a Mass General Brigham Hospital, or if you visit a Mass General Brigham Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study

How may we use and share your samples and health information for other research?

At the completion of this research study, we would like to store and be able to use and share your samples and health information with researchers at Mass General Brigham for other research related to menopause, sleep, diabetes, and metabolism. All samples and data would be labeled with your deidentified study ID. A key that connects your name and other identifiers to your deidentified study ID will be kept in a password-protected computer file, only accessible by research staff on this study. Because these samples and/or health information could be linked back to your identifiers, we are asking your permission to store, use and share these samples for future research. You can still take part in the research study whether or not you give permission for the storage, use, and sharing of these samples and health information for future research.

Do you agree to let us store and use your samples and health information for future research related to menopause, sleep, diabetes, and metabolism?

☐ YES ☐ NO Initials _____

Will you get the results of this research study?

You and your doctor should not expect to get information about the results of the research study or the results of your individual participation in the research study. We will study samples and information from many people. It could take many years before anyone knows whether the results have any meaning. There is a small chance that we could find out something from the study that might be important to your health. If this happens, we may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted.

What are the risks and possible discomforts from being in this research study?

Risks of taking suvorexant
Taking suvorexant may cause you to have one or more of the side effects listed below:

Common side effects:

- Headache (7 out of 100 people reported this side effect)
- Next-day drowsiness (7 out of 100 people reported this side effect)
- Dizziness (3 out of 100 people reported this side effect)
- Abnormal dreams (2 out of 100 people reported this side effect)
- Cough (2 out of 100 people reported this side effect)
- Diarrhea (2 out of 100 people reported this side effect)
- Dry mouth (2 out of 100 people reported this side effect)
- Upper respiratory tract infection (2 out of 100 people reported this side effect)

Suvorexant may cause serious side effects that you may not know are happening to you. These side effects include:

- Sleepiness during the day
- Not thinking clearly
- Acting strangely, confused or upset

- "Sleep-walking" or doing other activities when you are asleep like eating, talking, having sex, or driving a car.
- Depression and/or suicidal thoughts

Call the study doctor right away if you find out that you have done any of these activities after taking the study drug.

Taking suvorexant may cause worsening depression or suicidal thoughts. Please contact the study doctor right away if you are experiencing thoughts of self-harm.

Suvorexant can cause next-day mental impairment, and this risk is increased with higher doses or if instructions are not carefully followed.

- Suvorexant should be taken at night within 30 minutes of going to bed.
- Only take suvorexant when you can get a full night's sleep (at least 7 hours).
- Do not take suvorexant if you drank alcohol that evening or before bed. Taking suvorexant with alcohol increases the risk of dangerous side effects.
- Do not drive, operate heavy machinery, do anything dangerous or other activities that require clear thinking after taking suvorexant.
- You may still feel drowsy the next day after taking suvorexant. Do not drive or do other dangerous activities until you feel fully awake. In the first week of study you should be careful about driving in the morning, because there is individual variation in people's sensitivity to suvorexant.
- Before taking the study drug, please read the FDA-approved Medication Guide.

There may be other risks of suvorexant that are currently unknown.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think you are having an allergic reaction, call the study doctor right away. If you are having trouble breathing, call 911 immediately.

Risks of taking suvorexant with other medications

There are some medications that you cannot take at the same time as the study drug, suvorexant. Study staff will review all of your current medications to determine if you can safely remain in this study. In particular, you cannot remain in the study if you are currently taking digoxin (common brand names include Lanoxin, Lanoxicaps, Cardoxin, and Digitek). Also, you should let study staff know if you are currently taking any of the following types of medications: antibiotics, anti-fungal medications, HIV medications, heart medications, or anti-seizure

medications. Women who are currently taking medication to help them sleep will be asked if they are willing to refrain from taking sleep medications during the tracking period and duration of the study. Refraining from taking sleep medications may, however, cause discomfort. Taking the study drug while also taking any of these types of drugs may cause serious side effects. You will be closely monitored for any side effects associated with taking suvorexant while enrolled in this study.

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

Unknown risks of taking suvorexant
There may be other risks of suvorexant that we don't yet know about. During this study, we may learn something new about suvorexant. We will tell you as soon as possible if we find out anything that might affect your decision to be in this study.

Risks of blood draws
You may have a bruise (a black and blue mark) or pain on your arm where we take the blood samples (up to 160 mL = 32.5 teaspoons total). There is also a small risk of infection, lightheadedness, or fainting.

Risks of glucose monitoring
The sensor is small (about the size of 2 stacked US quarters) and generally comfortable to wear. A very thin filament sits just under the skin to measure glucose levels. You may find the monitor uncomfortable at first or feel a slight prick when initially placing the sensor in your skin. In some cases, with sensitive skin, irritation is possible. If you report discomfort or skin irritation at the site the sensor is applied then we will ask you move the sensor to a nearby different part of the upper arm.

Risks of wearing the activity watch
There is a risk of skin irritation while wearing the activity watch. The watch can be removed during the daytime to reduce irritation if it emerges.

Risks of collecting data using MealLogger and glucose monitor
MealLogger and the 24-hour glucose monitor does not collect identifiable information through the software application, and you will be required to provide information only about your meals for MealLogger. The research team will create credentials for you to use when using these applications, so that your data are not associated with a real person.

What are the possible benefits from being in this research study?

You may not directly benefit from taking part in this research study. It is possible that your insomnia symptoms may improve while you are in the study. Others with insomnia may benefit in the future from what we learn in this study.

What other treatments or procedures are available for your condition?

You do not have to be in this study to receive treatment for your sleep disturbance. For your insomnia, you may choose to receive available medications, such as Ambien, Lunesta, or Sonata, or cognitive behavioral therapy for insomnia (CBTi) or a combination of medications and therapy for insomnia.

The study doctor will discuss with you the risks and benefits of the alternative treatments. You may also talk to your doctor anytime about other treatments for sleep patterns and hot flashesbut we ask that you not take any other treatments for these conditions while you are in the study.

Can you still get medical care within Mass General Brigham if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Mass General Brigham now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

You will be paid up to $800 upon completion of the study. If you do not complete all study procedures, you will be paid for what you completed:

- $100 – Visit 1a & V1b (Screening and Consent)
- $100 – Visit 2 (Start of Treatment Block 1)
- $200 – Visit 3 (End of Treatment Block 1)
- $100 – Visit 4 (Start of Treatment Block 2)
- $300 – Visit 5 (End of Treatment Block 2, completion of all study procedures, and after returning all study equipment)

We will also provide vouchers for valet parking or reimbursement, with receipts, up to $25/each way for taxi or ride-share for in-person visits.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

Study funds will pay for study-related procedures that are done only for research. Merck is providing study drug at no cost.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why they may need to do so:

- Mass General Brigham researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records

- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)

Some people or groups who get your identifiable information might not have to follow the same privacy rules that we follow and might use or share your identifiable information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your identifiable information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your identifiable information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your identifiable information for any mailing or marketing list. However, once your identifiable information is shared outside Mass General Brigham, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____	_____	_____
Subject	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____	_____	_____
Study Doctor or Person Obtaining Consent	Date	Time (optional)

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