Document Title:	Informed Consent Form
Protocol Title:	Menopausal Sleep Fragmentation: Impact on Body Fat Gain Biomarkers in Women
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Principal Investigator: Hadine Joffe, MD, MSc

Site Principal Investigator:

Description of Subject Population: Healthy premenopausal women ages 18-45

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.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. 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.

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 study to see how menopause and hot flash related sleep disruption affects eating behaviors and body fat gain in women. Hot flashes are a feeling of being

overheated, and often are followed by heavy sweating, skin becoming red and hot, and discomfort. Sometimes hot flashes are followed by chills. Some women experience a rapid heart rate. Hot flashes that happen at night are called night sweats, and they may interfere with sleep.

We want to cause hot flashes by giving subjects a hormone medication called leuprolide (Lupron). Hormones are chemicals that are naturally produced in the body. Leuprolide is a manufactured (artificial) hormone that will temporarily cause hormone changes similar to menopause. These changes will make your body think that you have reached menopause. Most women begin to have hot flashes within 4 weeks after taking leuprolide.

The effect of leuprolide on hormones is temporary and goes away within 3 months after leuprolide is stopped. Leuprolide has been approved by the U.S. Food and Drug Administration (FDA) to treat endometriosis (overgrowth of the lining of the uterus) and fibroids (non-cancerous growths in the uterus). It is also used to treat premenstrual syndrome (PMS), a group of symptoms and problems that some women experience on a monthly basis before their periods.

Leuprolide has not been FDA-approved for the way it will be used in this study. However, we are allowed to use this medication as part of this research study.

We are asking you to take part in this study because you are a healthy premenopausal woman, between the ages of 18 and 45 years, with regular menstrual cycles. About 130 women will take part in this research study at Brigham and Women's Hospital (BWH).

The National Institute of Health (NIH) is paying for this research to be done.

How long will I take part in this research study?

This study will take about 4 to 6 months, from the time of screening to the end of data collection. This time includes the study visits you make to the hospital, at-home study procedures, and phone calls we will make to you.

After you finish the study visits, we will contact you to check on how you are doing until the effect of leuprolide has gone away.

There are approximately 6 visits in the entire study, including 2 outpatient visits (one for screening and one to receive the leuprolide injection) and two five-night inpatient stays. Depending on scheduling, you may have an additional outpatient visit for the dual x-ray absorptiometry (DXA) scan. These visits will take place at Brigham and Women's Hospital.

The two five-night study visits will be at the BWH Clinical and Translational Science Center/Center for Clinical Investigation (CCI) inpatient unit, for a total of 10 nights. You will

also come to BWH to pick up food for the study diet on separate occasions from the scheduled visits. Food may also be delivered to you.

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.

We will look at changes in your eating habits and biomarkers of body fat gain during this study. We will use questionnaires, blood tests, and food intake to measure these changes.

During this study we may need to make changes to study visits and procedures to comply with public health efforts to address COVID- 19 (coronavirus). We may need to adjust the study visit schedule and/or research procedures as a result of study site restrictions on research visits. We may conduct study visits remotely until the restrictions are lifted. Remote visits will be conducted by Zoom or telephone. During these visits, someone from the study staff will contact you via Zoom or telephone to conduct some research activities, such as asking you questions about your general health, wellbeing, sleep, and mood, your current medications, your menstrual cycle, and your availability to participate in this study.

Study staff will provide you information on how to access the video conferencing platform. We will launch the video conferencing in a private and secure area. To protect your privacy we ask that you do not take screenshots, photographs, or recordings of any kind with any electronic equipment. We would like to remind you that a video meeting is similar to us visiting you at home. We may learn more about your home and the people living with you than we would during a visit at the hospital. For example, we may learn information from you that must be reported to public health or public safety authorities. We are required by law to report known or suspected child or elder abuse. If we make such report, the public health and safety authorities can use the information as they see fit and may end up sharing it with other government agencies. Please ask the research staff if you have any questions about this prior to your video visit.

The study procedures for each part of the study are listed below.

Screening Visit (Visit 1a)

Screening Visit 1a will be conducted remotely using video or telephone call. It will take between 60-90 minutes.

At this visit, we will:

- Review this research consent form in detail. Prior to continuing the visit, we will ask you to sign this form electronically using a secured research database accessed with a web browser and internet connection.
- Ask you about your medical, sleep, and psychiatric history, and current medications.

If you still qualify for this study, we will schedule your in-person screening visit (Visit 1b). You will also be asked to start tracking your menstrual cycles. If you do not qualify, the study doctor will tell you why.

Screening Visit (Visit 1b)

Screening Visit 1b will be conducted in-person at the Center for Clinical Investigation at Brigham and Women's Hospital. It will take approximately 30 minutes.

At this visit, we will:

- Do a physical exam, including height, weight, and waist, hip, and neck circumference.
- Draw a blood sample.
- Test your blood for pregnancy. Pregnant women cannot take part in this research study.
- Ask you to fill out some questionnaires about your demographics and mood.

The study clinicians will receive your lab results a few days after Visit 1b and will make a final decision regarding your eligibility to participate in this study. If you do qualify, a research coordinator will inform you of the outcome. At this time, you will be asked to complete additional questionnaires about your general health and well-being, sleep, mood, and stress levels via secured, online surveys, and will be scheduled for your next study visits depending on the dates of your menstrual cycle provided previously. Sleep Block 1 will take place approximately 2 weeks prior to the leuprolide injection. If you do not qualify, you will be told why and referred to resources or your primary care doctor to follow up, if applicable.

Sleep Block 1 (Visits 2 and 3)

Sleep Block 1 will consist of 3 parts:

1) four nights at home during which you will follow some study procedures, such as a special diet, filling out some questionnaires, and completing 1 night using an at-home EEG machine (visit 2),
2) a 5-night inpatient stay at the BWH CCI inpatient unit (visit 3),

3) up to 7 days after leaving the inpatient unit during which you may complete additional study procedures.

During the first four nights at home, you will complete two diaries: a daily sleep diary that you will fill out each morning and a daily hot flash diary you will complete each evening and morning (takes about one minute each day to complete). Each morning, you will record how much sleep you got the previous night, the quality of your sleep, as well as how many hot flashes you may have experienced during the night. Each evening, you will record any hot flashes you may have experienced during the day as well as track any medications you took or alcohol you drank during the day. You should not take any sleep medications while participating in this study. We will also give you an actigraph. This is a small device that you wear on your wrist. It monitors your activity and the amount of light exposure you have.

We will ask you to bring these diaries and the actigraph with you to each study visit, so we can track your progress. We will give you new diaries at some of the study visits. You will fill out these diaries for the remainder of the study.

At-Home EEG Machine
During one night of the at-home procedures, we will ask you to wear an EEG machine at home to record your brainwaves. We will schedule an appointment with you to come to the CCI unit, and you will have one of these machines attached. We will give you instructions about how to use the machine. You will not be able to shower during the time you wear the EEG machine. Additionally, we will have you return to the unit the next day in order to remove the machine. We will schedule this in the morning and you will eat breakfast at Brigham and Women's Hospital on that day.

Study Diet
During the study, we will give you a standardized diet for some of the days you are at home, as well as some of the days in the CCI inpatient unit. The diet has been standardized so that all study participants eat similar diets; however, the foods will match a standard adult diet. You will fill out a form to tell us the foods that you like, and the Brigham and Women's Nutrition Core will prepare meals for you. If you decide partway through the study that you don't like some of the food, it is possible to change some of your selections. You may come to the hospital to pick up these study meals. We will ask you to eat all your food. You will be allowed to have as much water as you would like, but we will standardize all other beverages on these days.

On the final day of each inpatient stay, food, snacks, and beverages will be provided at your request. You will be allowed to eat and drink as much as you would like. We will measure your caloric and macronutrient intake during your stay.

After you leave the CCI, you will log your meals during the days that you are not eating the study diet . On one day during the at-home procedures of the Sleep Block, we will ask you to come to the CCI and eat breakfast here. You will order this food beforehand from a menu and it will be prepared by the Nutrition Core.

We will ask you to record food that you eat by taking pictures and writing descriptions using the MealLogger™ application on your cell phone. You will do this for up to 7 days after discharge, as well as one day before your admission day. You can uninstall or remove the mobile phone application at the end of the study. Study staff will create an account for you with an email address that is not associated with you, so that you can log in without being identified. The study staff can assist you in downloading this application on your phone and can answer questions about how to use it.

Typical Day at the CCI

Each SB includes 2 nights during which sleep is undisturbed, and 3 nights during which sleep is fragmented. You will have three consecutive nights with sleep fragmentation.

The procedures for each of the Sleep Blocks are described here, and will be similar for both sleep blocks.

You will stay in a special suite of rooms in the inpatient CCI unit. Some of the rooms do not have radios or televisions, but you will be allowed to bring your computer, cell phone, reading materials, and any other materials you would like for entertainment. For about an hour before your scheduled bedtime each night and up to 2 hours after you wake up each morning, you may not have access to your personal electronic devices.

During the time you are staying in the CCI, we will schedule all your daily activities (eating, sleeping, etc.). A typical day will include breakfast, shower, lunch, dinner and a snack. We will also do some study procedures, like:

- Answering questions on mood and appetite on the computer or on paper.
- Participating in computer-based probability tasks during each stay. These tasks will take about 20 minutes each.
- Participating in computer-based learning tasks during each stay.
- Drawing blood samples through an IV catheter (a very thin plastic tube inserted into your vein) several times throughout the day. We will run a sterile salt solution with small amounts of a drug that prevents clotting (porcine-derived heparin) through the line between blood draws.
    - The blood samples will be used to determine the level of reproductive and appetite hormones, as well as measures of immune function related to sleep and menopause.

- Monitoring and recording your brain waves (EEG), eye movement (EOG), muscle activity (EMG), and your heart rhythm (ECG) monitored when you are asleep. To prepare for the recordings, we will ask you to wash your face with special soap and then cleanse your skin with an alcohol swab. We will place small electrodes (wires with little pads attached) on the skin of your scalp, face, and chin. The electrodes will be held in place by a special glue.
- Taking vital signs once a day, including heart rate and blood pressure
- Measuring core body temperature with an oral thermometer.
- Measuring 24-hour skin conductance twice during the 2nd Sleep Block using a Biolog skin conductance monitor. The hot flash monitor is a computer (about the size of a cell phone) that is attached to a small skin patch that sticks to your chest, like a band-aid. Since the hot flash monitor is small, you can do all of your normal activities while you are wearing it. Because of the sensitivity of the equipment, you will not be able to shower during the time you wear the monitor. However, the staff can provide wet wipes at your request.
- Collecting all the urine that you produce and at times we may ask you to provide a urine sample.
    - Urine will be collected via a urine collection hat or a bedpan
    - Urine samples will be used to determine the level of hormones and other biological substances. All samples will be identified by your alphanumeric study code.

We will keep track of your activity and light exposure patterns with an actigraph, like in the weeks before you entered this part of the study. We will ask you to wear an actigraph and fill out sleep diaries before you come to the CCI, and for up to 7 days after your discharge from the CCI.

Monitoring

Throughout the time in the CCI, you will be monitored by a study staff member on a closed circuit television. The study staff will be able to hear you through an audio/intercom system. We will watch and listen to you to make sure you are safe in the room. We will not make any video or audiotape recordings of you.

Study Rules

- You will have access to our library of recorded movies, books, magazines and newspapers. You are also allowed to bring your own materials for entertainment.
- During your scheduled sleep sessions you will need to stay in bed in the dark for the entire time. We will give you a bedpan during that time, if you need it.
- Exercise will be limited to light stretching only during your wake times.

There are some sleep procedures which are specific to undisturbed nights and experimentally fragmented nights. Those procedures are described below:

Sleep Procedures on Undisturbed Nights
During the two nights when your sleep will be undisturbed, we will standardize your bedtime and wakeup time such that you can get up to 8 hours of total sleep time.

Sleep Procedures on Experimentally Fragmented Nights
During the 3 nights when your sleep will be experimentally fragmented, you will be awakened using sounds throughout the night. You will be asked to stay in bed long enough to be able to get 8 hours of total sleep while still being awakened throughout the night. You will not be permitted to get out of bed or eat in the middle of the night.

Visit 4 – Leuprolide injection

We will try to schedule this appointment about 1 week prior to the start of your menstrual cycle after your first Sleep Block. If you start your menstrual cycle before receiving the leuprolide injection, you will wait until your next menstrual cycle to resume the study. It will last about 1 hour, but we may also try to schedule your DXA scan appointment for the same day. We will ask you to:

- Let us take a urine sample for a pregnancy test to make sure that you are not pregnant. We will do this the immediately before the leuprolide injection.
- Have a blood test of your hormone levels. This will be done the day of the injection.
- Take your vital signs, including heart rate, blood pressure, and weight
- Do a DXA Scan.*

At the very end of the visit we will give you the leuprolide injection in your buttock.

*The DXA can be performed at a time that is convenient for you. This test will take place at BWH at 221 Longwood Ave.

DXA Scan
This test will help us determine your total body relative amounts of fat and muscle by taking a special type of x-ray called dual x-ray absorptiometry (DXA). This test involves lying on your back for 5 to 10 minutes while your body composition is measured with low dose x-rays.

Study Medication: Leuprolide

We will give you one injection of leuprolide in the buttock. We will give you a standard dose of the drug that is routinely used for the treatment of endometriosis and uterine fibroids in women.

Leuprolide affects your hormones for 3 months. If you withdraw early from the study after receiving the leuprolide injection, this hormone medication will continue to affect your hormones for up to 3 months. *Four out of five women who receive this drug* experience hot flashes nearly every day within a few weeks of getting the leuprolide injection. You may experience an average of 1 to 6 hot flashes per day for up to 3 months.

Before your next visit, we may ask you to:

- Complete a daily diary for 7 days to record any hot flashes (takes about 1 minute a day).
- Complete a daily sleep diary for 7 days (takes about 1 minute a day).

Sleep Block 2 (Visits 5 and 6)

Sleep Block 2 will be similar to Sleep Block 1. Twice, you may be asked to wear a 24-hour skin conductance monitor to help measure any hot flashes you may experience.
Visit 5 will be approximately 4 weeks after visit 4.

Follow-up Phone Calls

About 4 weeks after the final study visit, we will give you a short telephone call (takes about 5 minutes). We will ask if your menstrual periods have restarted and if you are still having hot flashes. If you tell us you have not had a period and that you continue to have hot flashes, we will continue to call you every 4 weeks to make sure that your menstrual periods resume and that you stop having hot flashes.

Within 3 months after we give you the leuprolide injection, menstrual periods usually restart and hot flashes stop happening. If your menstrual periods do not restart or you continue to have hot flashes 4 months after we give you the leuprolide injection, we will suggest that you see one of your health-care providers. If your health-care providers are unable to help you with this, we will refer you to the Endocrinology Division to get care.

Stopping the Study Early

You may decide to stop taking part in this study for any reason. If you withdraw from the study before having the leuprolide injection, we will **not** ask you to come in for a final study visit or give you any phone calls. However, if you withdraw after receiving a leuprolide injection, we will contact you by phone every 4 weeks to make sure that your menstrual periods resume and that you stop having hot flashes.

Also, the study doctor may take you out of the study without your permission. This may happen because:

- you develop any severe medical problems or severe psychiatric symptoms,
- start taking hormone medications (such as birth control pills),
- become pregnant, or
- are unable to follow the study procedures.

If this happens, the study doctor will explain why you need to stop taking part in the study. We may continue to contact you as described above.

Sending Study Information to Research Collaborators Outside Partners

We will send your study information to researchers working with us at University of Massachusetts. We will label all your study materials with a code instead of your name. The key to the code connects your name to your study information. We will keep the key to the code here at Partners and will not share it with our research collaborators. No one outside of Partners will know which study information or samples are yours.

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.

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

Risks of Taking Leuprolide acetate (Lupron Depot®)

Leuprolide will make you skip a menstrual period for 2-3 months after the injection is given. However, irregular menstrual bleeding and spotting can occur during this time period. We will keep close track of your menstrual-cycle patterns during the study. Through its effects on female hormones, leuprolide reduces your ability to get pregnant for up to 3 months after the injection is given.

You should NOT consider the leuprolide injection a method of birth control. You should use a barrier contraceptive while enrolled in this study and after completion of this study until your

period starts again. Barrier contraceptives are forms of birth control such as condoms, diaphragms with spermicidal foam, intra-uterine devices (IUDs), a sponge, or spermicide (a gel that kills sperm and helps prevent pregnancy.

Taking hormone medications like leuprolide for 6 months or longer can cause bone loss and osteoporosis (thinning of the bones). However, we do not expect that your bones will be affected by leuprolide because leuprolide will be used for only 1 month in this study.

Other common side effects related to short-term use of leuprolide include:

- Hot flashes,
- headache,
- vaginal bleeding,
- vaginal dryness,
- infection in the vagina,
- loss of body hair,
- body/joint pain,
- changing emotions,
- depression symptoms,
- memory problems,
- nausea/vomiting, and
- swelling of the arms and legs,
- muscle aches,
- unwanted hair growth,
- acne (skin problems),
- weight gain or weight loss,
- a loss of sexual interest,
- painful intercourse (sex),
- numbness and tingling,
- skin reactions,
- dizziness, and
- breast tenderness/pain.

Hot flashes: Once hot flashes start, there is no proven way to stop them. However hot flashes usually stop by themselves within 3 months after a leuprolide injection is given.

You may experience some irritation at the injection site, such as burning, itching, and swelling. These side effects are mild and usually go away quickly.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant

Leuprolide may cause growth abnormalities and death in an unborn fetus. Because of these risks, you cannot take part in this study if you are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study and until your normal periods resume.

Acceptable birth control methods for use in this study are:

- Barrier methods such as condoms, diaphragms with spermicidal foam, intra-uterine devices (IUDs,) a sponge, or spermicide (a gel that kills sperm and helps prevent pregnancy).
- Other than hormonal intra-uterine devices (IUDs), you may NOT use any birth control methods that include hormones (no birth control pills or patches, Depo-Provera).

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking part in this study.

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, lightheadedness, and/or fainting. For the frequent blood draws during sleep, a long intravenous line will be placed to minimize blood loss and discomfort associated with repeated venipuncture. All blood draws and IV placements will be performed by trained personnel that use standard sterile techniques.

There may be some discomfort or bruising on initial insertion of the catheter into a vein, but wearing the catheter should not be painful. Occasionally, mild discomfort may occur from the tube in the vein. If this happens, it can be repositioned or removed. We will ask your permission before reinserting the IV. Occasionally, there is a bruise at the site of the IV insertion, which may last a few weeks; and, rarely, a small scar may remain permanently at the blood draw site. There may be a minor skin rash or reaction to the sterile tape used to hold the catheter in position.

A total of 1 ¾ cups of venous blood will be drawn throughout the study. Federal guidelines allow for up to 2 1/3 cups of venous blood per 2-month period in healthy non-pregnant adults weighing >110 pounds. There is a risk of becoming anemic from frequent blood sampling. We will check your hemoglobin at the end of the study to check if you are anemic.

Risks of Heparin

The medicine we use to flush out the catheter and prevent clotting, Heparin, can cause bleeding and, 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, tell the study staff right away.

Risks of Polysomnography

The tape and special glue used to attach the recording devices may cause some minor discomfort or skin irritation. Very small amounts of the glue used to hold the devices to your scalp may stick in your hair for several days. You may not sleep as well during the sleep recordings because you are wearing the recording devices.

Risks of Actigraphy

There is a risk of skin irritation while wearing the actigraphy watch. It looks and feels like a typical wristwatch.

Risks of Inpatient Sleep Study Procedures

You will be admitted to the BWH Clinical and Translational Science Center/Center for Clinical Investigation (CCI) inpatient unit. Admissions of this length may be psychologically stressful and inconvenient or disruptive to daily routines. During some of the admissions, you will experience experimentally induced sleep fragmentation. You will be woken up from sleep throughout the night. This can make you feel sleepier during the study and also at the end of the study. You may also experience headache, nausea, dizziness, light headedness, excessive sleepiness, muscle soreness or weakness. It is not safe to operate heavy machinery or drive when sleepy, because it can cause accidents.

After each of your inpatient study visits, you will not be allowed to drive home. We will offer you reimbursement (up to $25) to travel home by taxi or private car (e.g., Uber or Lyft) from the inpatient unit after each visit.

You will have increased sleepiness and fatigue on the day of your discharge (final day of each 5-night stay). This may increase the chance of errors and accidents on that day. Since you will likely be very sleepy at the end of the study, you should not return to work on the day you finish the study.

You may become sleepy during some parts of the study. We will ask you to stay awake during the times you're not asked to be in bed, even though you may feel like sleeping. You can stop the study at any point you want. If you stop the study early you will have the opportunity to sleep before leaving the unit. After completing the study, you may have some difficulty sleeping and waking at your usual times for several days.

Risks of Hot-flash Monitor

There is a minor risk of skin irritation from the sticky pad that attaches the electrodes of the hot-flash monitor to the skin on your chest.

Risks of Psychological Questionnaires

Answering questions on the questionnaires used to evaluate mental health symptoms can be upsetting to some women. You may skip over any questions that you choose not to answer.

Risks of Radiation Exposure

As a result of your participation in this study you will be exposed to radiation from DXA procedures. Please note that this radiation is not necessary for your medical care and is for research purposes only.

The total amount of radiation exposure you will get from taking part in this study is equal to a whole body exposure of 3-10 microsieverts. This compares to about 5-8 microsieverts that you receive daily in normal background radiation, or the 50-150 microsieverts you would receive during a chest x-ray.

Scientists disagree on whether radiation doses at these low levels are harmful. A possible effect that could occur at doses used in this study is a slight increase in the risk of developing cancer later in life.

Risks of Study Diet

You will receive the study diet during each Sleep Block. Because you may eat some foods that you are not used to, there is a small risk of stomachache, abdominal bloating, or nausea.

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

You will not benefit from taking part in this research study. However, other women with hot flashes may benefit in the future from what we learn in this study.

If any of the routine testing (e.g., hormone levels, psychological questionnaires) that is done during your screening visit is considered abnormal, we will provide that information to you so that you can discuss it with your doctor. Additionally, you may request a copy of the routine health information that we collect during the study. You will be provided with a copy of this information after you complete the study procedures.

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners 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.

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. 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 I do if I 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 I be paid to take part in this research study?

You will begin accumulating compensation after the screening visit. If you complete the entire study, you will receive up to $8,055 by check. You will be paid at the end of the study, or at your final visit if you do not complete the study. Your compensation will accumulate according to the following schedule:

Screening visits: up to $100 ($25 for completing remote Visit 1a and $75 for completing in-person Visit 1b)
DXA Scan: $55
Lupron Administration Visit: $250
Inpatient Data Collection: $275 per night spent in the lab
Outpatient data collection: Up to $700 per Sleep Block ($50 per day; up to 7 days prior to and 7 days after each Sleep Block
Bonus for completion of all study visits and procedures: $3,500

If you do not complete the study, you will be paid for the parts of the study you have completed, but you will not get any study bonus.

If you park at the BWH parking garages using valet parking for outpatient visits, we will give you a voucher to cover your parking costs. If you are unable to arrange your own transportation after each of your 5-night stays in the hospital, we will reimburse taxi fare for you to return home

(up to $25 each time). In order for us to cover your transportation costs, you must provide us with receipts of your travel expenses.

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

Study funds will pay for the study medication and all of the tests and procedures that are done only for research. You and your health insurance company will not be billed for any study procedures.

What happens if I am 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 next section of this consent form.

If I have questions or concerns about this research study, whom can I 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

- Hadine Joffe, MD, MSc is in charge of this study. You can call her at [redacted] Monday-Friday 9 A.M. through 5 P.M.
- [redacted] – co-investigator
- [redacted] – co-investigator

- [redacted] – project manager, [redacted]
- Study physicians
  - [redacted]
- Research Coordinators
  - [redacted]

After routine business hours or for any study-related emergency, you can page the study staff by calling [redacted] and asking the page operator to page ID [redacted]

If you have questions about the scheduling of appointments or study visits, call [redacted] the study coordinator, at [redacted] Monday-Friday from 9 A.M. through 5 P.M.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at [redacted]

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

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

If I take part in this research study, how will you protect my privacy?

Federal law requires Partners 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:

- Partners 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 Partners ethics board or an ethics board outside Partners that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Partners 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)
- Other researchers within or outside Partners, for use in other research as allowed by law.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate, unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain completely 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 information does not expire.

The results of this research 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 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.

Storing Samples and Health Information at BWH for Future Use

We would like to store some of your samples and health information for future research related to menopause and sleep disturbance. We will label your samples and health information with a code instead of your name. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password protected computer.

Do you agree to let us store your samples and health information for future research related to menopause and sleep disturbance?

☐ Yes ☐ No Initials_ _____

If later you change your mind and want your samples destroyed, contact the study doctor.

Future Studies

Do you give the study team permission to contact you in the future about additional studies in which you might be interested in participating? Please check the appropriate box.

☐Yes ☐No Initials _____

Signature of Subject:

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

_____	_____	_____
Subject	Date	Time

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

Consent Form Version Date: 09/14/2021