UNIVERSITY OF WASHINGTON
CONSENT FORM

Short and Long-Term Effectiveness of Existing Insomnia Therapies for Patients Undergoing Hemodialysis (Sleep-HD)

Researchers:

UW Medicine/Nephrology and the Kidney Research Institute

Business hours 8 am- 4:30 pm, or leave message - (206) 616-8574

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24-hour emergency telephone number:
UW Medical Center Operator: (206) 598-6190; ask for nephrologist on call.

Researchers' statement

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions, you can decide if you want to be in the study or not. This process is called "informed consent." We will give you a copy of this form for your records.

PURPOSE OF THE STUDY

Insomnia is difficulty falling asleep or staying asleep, even when a person has the chance to do so. Insomnia is a common and distressing symptom for patients on hemodialysis, and there is evidence for a much larger impact on the health of patients. Chronic insomnia is disrupted sleep that occurs at least three nights per week and lasts at least three months.

The purpose of the SLEEP-HD study is to compare two types of treatment for insomnia in participants who have end-stage renal disease and who have been diagnosed with chronic insomnia. The two types of treatment involved in the study are Cognitive Behavioral Therapy (CBT) or treatment with a drug for sleep or with a placebo. The researchers hope to enroll 126 participants who are undergoing hemodialysis in two study locations (Seattle, Washington and Albuquerque, New Mexico). Participation in the study will last about 25 weeks. The entire study will take about 5 years to complete.

STUDY PROCEDURES

We are inviting you to take part in this study based on responses to the Insomnia Severity Index that you recently completed. If you choose to take part we will ask you additional questions to

find out if you are suffering from insomnia and if you are eligible for the study. You may discuss taking part in this study with your family, friends, or doctor.

If you agree to participate we will obtain demographic information such as your name, age, gender and contact information. We will review your medical record and current medication list.

If you are already on a medicine called trazodone, we will ask you to taper off in order to qualify to be in the study (you will need to be off of it for 30 days). If you take it:

- as needed, you'll just stop taking it.
- 100 mg a day, then you'll reduce the dose to 50 mg daily for 5 days, then 50 mg every other day for 5 days, then stop.
- 50 mg a day, then you'll take it just every other day for 5 days , then stop.

.We will ask you to complete the following surveys:

- A Patient Health Questionnaire-2 or -9 to screen for depression, 3-5 minutes.
- The CAGE survey to screen for alcohol use/abuse, 2-3 minutes.
- The Drug Abuse Screening Tool (DAST) to screen for drug use/abuse, 2-3 minutes.
- The Cambridge-Hopkins Restless Legs syndrome questionnaire to assess Restless Leg Syndrome, 3-5 minutes.

It is possible that you will be excluded from the study based on the scores from these surveys. If you are, then we'll refer you, as needed, for treatment.

If you are eligible for the study, you will be provided with instructions to complete a sleep diary for one week prior to treatment. This diary documents information about your sleep habits and the duration and quality of your sleep. If you choose to complete the sleep diary online you will be provided with log-in details and instructions on how to enter the information in the web-portal. If you choose to use the paper-form of sleep diary, you will be provided with the sleep diary for the first week along with instructions on how to complete it. If you need help with reading, you will need to have a caregiver available to assist you with completing the sleep diary.

We will ask you to wear an Actiwatch Spectrum Plus for one week that study staff will provide for you. This is a wrist activity monitor that you will wear on the wrist opposite to the side of your HD access. The Actiwatch records sleep/wake activity.

After one week of wearing the Actiwatch and completing the sleep diary, you will be assigned to one of two treatment methods-

- A form of counseling called Cognitive Behavioral Therapy (CBT)
- Treatment with a medication

You will be randomly assigned to one of these two treatment methods. The random assignment is like the toss of a coin and you will have a chance of being in the CBT group, or the medication group. The ratio will be 1:2, which means that for every 3 people, 1 will get CBT and 2 will get medication.

For the medication group, some will get trazodone and some will get placebo. This is also a random assignment with a chance of getting either. The ratio will be 1:1, which means that for every 2 people getting medication, 1 will get trazodone and 1 will get placebo.

A placebo is an inactive substance that looks just like the investigational drug but does not have any medical effects. Neither you nor the research team, nor your doctors will know whether you are receiving the trazodone or the placebo.

Description of Treatment Arm:

Cognitive Behavioral Therapy (CBT) using Telehealth

What is individual CBT?

It is one-on-one psychotherapy or "talk therapy" that involves changing the way you behave and the way you think about a problem. In this study CBT is focused on improving sleep. You will talk with a therapist about your sleep-related habits and behaviors, about your thoughts about your sleep, and about the things you can be doing to make sure that problems with sleep are not interfering with your living a meaningful life. An example of a question the therapist might ask are "what are 3 things that are important for your quality of life"?

You will be provided with a booklet of educational material about sleep and the therapist will ask you to try some things to improve your sleep over the course of the treatment.

What is Telehealth?

Telehealth is the remote provision of healthcare, health education or support, using telecommunication technologies. In this study participants will meet one-on-one with a therapist once a week for 6 weeks, using a confidential video telehealth platform called Zoom. The telehealth sessions will each last about 20-30 minutes. You can use a personal smart phone, tablet, laptop or desktop computer, and can schedule sessions at a time that is convenient for them. If you choose to have your session while at the dialysis unit and need a telehealth device, the study team can provide a tablet for use. The sessions will be audio-recorded with your permission, for quality purposes.

Sleep Diary

If you are in the CBT arm, you will also keep the sleep diary throughout the 6 week treatment phase. You will do it just like you did previously.

Drug Therapy using Trazodone or Placebo

What is Trazodone drug therapy?

This treatment involves taking pills of a medicine called Trazodone, or an identical looking pill that is a placebo, by mouth once a day. A member of the study team make sure that you get the supply of the drug each week. At the end of each treatment period you will be asked to return any unused drug and/or the empty bottle before you are given a fresh supply of the drug. This will occur in your dialysis facility while you are receiving hemodialysis.

The medicine will be started at a dose of 50 mg for the first week. You will continue on this dose if you are satisfied with your sleep over the previous 7 days. You have the option to increase the dose to 100 mg at week 2 or week 3 of treatment, if you have persistent problems with sleep in the previous 7 days. Based on your satisfaction with sleep and tolerability of the medication, you will continue on either the 50 mg or 100 mg dose after week 3, and will be provided with a two-week supply of the medication.

For women who are of child bearing potential, we will collect about 3.5 ml (about ½ teaspoon) blood from your dialysis line before you take any Trazodone. We will test it to make sure you are not pregnant. If the test is positive, you will not receive any Trazodone, but you will continue with the other procedures in the study (unless you decide to withdraw from it).

If necessary, we may repeat the pregnancy test for confirmation as agreed on by you and the study doctor. The same amount of blood will be taken for additional tests.

For all Study Participants:

You will be asked to wear the Actiwatch again for one week at week 6 and for one week at week 24. Study staff will deliver the Actiwatch to you and you will return it after each one week time period, while you are at the dialysis unit. The Actiwatch gives the study team information about whether your sleep has improved over the treatment phase. You will also keep a sleep diary for the week you are wearing the Actiwatch. You will do it just like you did previously.

Phone Calls to Check Your Response to Treatment:

Whether you are getting CBT or taking a pill for the treatment of insomnia, a member of the research team at the University of New Mexico or at the UW will call you at five different times – once before the start of any treatment, at 4 weeks from the start of treatment, at 7 weeks from the start of treatment, at 13 weeks, and at 25 weeks. The call will happen either Tuesday if you are on a Mon-Wed-Fri dialysis schedule, or Wednesday if you are on the Tues-Thurs-Sat schedule. If for some reason the call cannot be completed on Tuesday or Wednesday, we will try to complete it on the next day that you do not go for dialysis. If you are unavailable to take the call on a non-dialysis day, then you can do the call during the first hour of your dialysis session. We will ask that you do the other two calls the same way (either a dialysis or non-dialysis day). The person from the research team will not know what form of treatment you are getting. He/she will ask you to answer questions about your sleep, fatigue, pain, depression, anxiety and quality of life. These phone calls will take about 30 minutes each time.

Follow-up Phase

You will participate in the study treatment (either CBT or medication) for six weeks. After that, there is an 18 week (4 ½ month) follow up phase. You will no longer receive any treatment through the study, though you will continue with study follow-up procedures as described in this form.

If you were in the medication group, and you have improved by 6 weeks, you and your doctor may choose to continue the pills for insomnia. You will then pay for the drug yourself or through your insurance, since it will now be a part of your regular health care, rather than a study procedure. If you decide that you do not want to continue treatment with the drug or if you are not feeling better with the drug, we will slowly reduce the dose of the medicine over a few weeks until it is stopped completely.

If you were in the CBT group, you are free to address insomnia as you wish with your care provider, including taking trazodone. Whatever means you choose, you or your insurance will pay for it, since it will now be a part of your regular health care, rather than a study procedure.

Medical Records

We will check your clinical medical records periodically throughout the study. We will check them to confirm that you are eligible for the study, including current medications and health problems, any updates to your contact information, dialysis schedule or unit, to help monitor for any side effects if you're on the medication.

RISKS, STRESS, OR DISCOMFORT

During CBT and the study phone calls, we will ask questions about your health and habits. You may find some of these questions uncomfortable or inconvenient. You do not have to answer any question you do not want to or stop the surveys at any time.

There is a risk of discomfort from lack of privacy when we talk to you at the dialysis unit during research visits. You may request that our discussions take place in a private setting, though this will be outside of the time of your dialysis session.

There is a risk of discomfort from lack of privacy if you choose to complete CBT sessions at the dialysis unit. You may request that the sessions take place in a private setting, though this will be outside of the time of your dialysis session. Using Zoom CBT is University of Washington HIPAA compliant.

People that receive trazodone pills for the treatment of insomnia may suffer some side effects of the drug:

- Common side effects (>5%) are drowsiness, nervousness, dizziness, fatigue, dry mouth, nausea, and vomiting.
- Extremely rare side effect is priapism, an erection that lasts more than 4 hours. If you experience this, you should call 911 and go to the nearest emergency room for treatment.
- If you taper off trazodone that you were already on in order to be in the study, you may experience worsening of your insomnia.
- Young adults may experience suicidal ideas. We will monitor you closely so that we can refer you to someone who can help you, if you experience this. If you have thoughts of harming yourself, call 911 or let us know right away so that we can find help for you.
- Do not use alcohol or take other medications that make you sleepy or dizzy while taking study medication.

There is minimal risk with the use of the Actiwatch. The Actiwatch band may cause mild irritation to the skin.

<u>Pregnancy</u>
We do not know for sure how safe trazodone is during pregnancy and breast feeding. For all women in this study whom we randomize to take study medication: if have not had a hysterectomy or tubal ligation, or have not gone through menopause at least one year ago, you must use a method of preventing pregnancy during the study. This can be birth control pills or implant, an intrauterine device (IUD), or a barrier method (male or female condom, diaphragm with intravaginal spermicide, cervical cap).

If you are in the study medication arm of the study and suspect that you have become pregnant, you must stop taking study medication. You should immediately notify the study investigator or study staff and they will instruct you how to taper off of the study medication. If you become pregnant, you will not be able to continue taking study medication. You may work with your

doctors to find another way to treat insomnia. However, you will continue to participate in the study, unless you decide to withdraw from it. We will follow you throughout your pregnancy and child-birth (including medical record access), even after you are done with the study, in order to check for any problems that may be related to the study medication.

If you need a pregnancy test for this study, we will use a blood sample drawn from your dialysis line, as described above. This will introduce a small risk of infection when we access the line. The dialysis staff is trained in how to draw blood from the line in a way that minimizes this risk.

ALTERNATIVES TO TAKING PART IN THIS STUDY

If you choose not to take part in the study, the same options for treatment of insomnia will be available to you. These include therapy and a variety of medications, including trazodone and others. Your care will not be affected by your decision to take part in this study.

BENEFITS OF THE STUDY

If you choose to participate in this study, you may not receive any benefit. Your symptoms of insomnia may get better or worse or stay the same. Society may benefit if the study shows that the treatment is effective and safe. This study is the first large-scale comparison of benefits and safety of CBT and pills for the treatment of insomnia among hemodialysis patients. You may help contribute to knowledge about insomnia in hemodialysis patients that my help patients in the future. You may benefit from learning about different options for treatment of insomnia.

SOURCE OF FUNDING

The study team and/or the University of Washington are receiving financial support from the National Institute of Diabetes, Digestive, and Kidney Disease (NIDDK) of the National Institutes of Health (NIH).

CONFIDENTIALITY OF RESEARCH INFORMATION

All the information you provide will be considered confidential. Your name and other identifying information will be linked to a unique study ID. Your study ID will not display any information that can identify you. All of the data we collect from you will be coded with your study ID and kept in a locked cabinet, and/or password protected computer files. The master list linking your identifying information to your study data will be kept in a separate, secure location. The study team will have access to the master list. We will keep the link between your identifying information and study data until the end of the research study.

The Center for Biomedical Statistics at the University of Washington will be the Data Collection Center (DCC) for this study. For those enrolled in the treatment phase of this study, we will send all study information to the DCC, including your identifying information and contact information. The master list linking your identifying information to your study data will be available to the DCC and the local study team at the Kidney Research Institute.

An interview team at the either the University of New Mexico or the UW will make the 5 phone calls to you for the follow up evaluations. The DCC will give the interview team your name and contact information so that they can call you. Your name and contact information will only be

available to the interview team on the day of your call. They will not use it for any other purpose.

Your responses on the surveys will be kept strictly confidential and staff members at your dialysis unit will not have any knowledge of your answers to the questions. During the course of the study, if we learn that you intend to harm yourself or others, we will try to get immediate help for you.

The certified therapists will also follow a strict code of confidentiality. The CBT sessions and will only be audiotaped with your permission. The audiotapes will be encrypted and coded with your study ID so as to not reveal your identity or any personal information. These recordings will be stored at the DCC along with your other study information.

A Data Safety and Monitoring Board (DSMB) will monitor the conduct of the study at least twice yearly to check for safety.

Government or university staff sometimes review studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk or harm.

The study information will be available to the study doctors here at the University of Washington and the University of New Mexico. Only study staff here at the UW will have your identifying information. After this study is over, the study doctors may share study information with other researchers. If they do, they will not share your identifying information. Only coded information will be shared (the information will be anonymous). Also, we will never release any information that anyone could combine to identify an individual participant or study site. Any researcher to whom we may release anonymous study data is bound to strict confidentiality and data-use guidelines.

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.

We will not use your name or other information that could identify you in any published reports. A copy of this consent form will be placed in your medical record.

A copy of this consent form and the HIPAA authorization form will go into your medical records.

We have a Certificate of Confidentiality from the federal National Institutes of Health. This helps us protect your privacy. The Certificate means that we do not have to give out identifying information about you even if we are asked to by a court of law. We will use the Certificate to resist any demands for identifying information.

We can't use the Certificate to withhold your research information if you give your written consent to give it to an insurer, employer, or other person. Also, you or a member of your family can share information about yourself or your part in this research if you wish.

There are some limits to this protection. We will voluntarily provide the information to:

- a member of the federal government who needs it in order to audit or evaluate the research;
- individuals at the University of Washington, the funding agency, and other groups involved in the research, if they need the information to make sure the research is being done correctly;
- the federal Food and Drug Administration (FDA), if required by the FDA;
- local authorities, if we learn of child abuse, elder abuse, or the intent to harm yourself or others.

OTHER INFORMATION

You may refuse to participate and you are free to withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled.

If you do join and want to drop out later, please inform us. Please contact Dr. Mehrotra or a member of the study staff using the contact information listed at the front page.

You may also ask to have your information no longer used for research. If studies have already been done on your information, the results of the study will be kept, but your identity will be removed and no further studies will be done on them.

You will not have to pay for the CBT or drug therapy while in the treatment phase of the study. If you decide to continue therapy after the 6 week treatment phase is over, then you (or your insurance company) will have to pay for it.

We will give you $100 for completing the whole study. You will receive the payment in the form of a Visa cash card at the end of your participation. If you only do part of the study, we will give you $50 if you did at least 3 study phone calls before you stopped, $75 if you did 4, and the full $100 if you did all 5 phone calls.

You may also elect to receive the payment in installments: $50 after you complete 3 study phone calls, another $25 after you complete the 4th, and another $25 after the 5th phone call."

RESEARCH-RELATED INJURY

What to do. For a life-threatening problem, call 911 right away or seek help immediately. Contact Dr. Mehrotra at (206) 744 – 4933, when the medical emergency is over or as soon as you can.

For all other problems: contact Dr. Mehrotra (206) 744 – 4933, or Lori Linke (206) 720 – 3835 right away. They will treat you or refer you for treatment.

Who will pay. The costs of the treatment may be billed to you or your health insurance just like other medical costs, or it may be covered by the UW's discretionary Human Subjects Assistance Program (HSAP), depending on a number of factors. The researcher may request HSAP coverage by following established procedures. If you wish to request HSAP coverage yourself, contact the researcher or the UW Human Subjects Division at hsdinfo@uw.edu or 206-543-0098. You may also call collect to the UW Human Subjects Division at 206-221-5940 if you do not otherwise have access to a telephone. Ask the researcher if you would like information about the limits and conditions of the HSAP. The UW does not normally provide any other form of

compensation for injury. However, the law may allow you to seek payment for injury-related expenses if they are caused by malpractice or the fault of the researchers. You do not waive any right to seek payment by signing this consent form. We will bill your health insurance for treating problems that result from your kidney disease, insomnia, or from standard clinical care. If you have no health insurance or your insurance refuses to pay, we will bill you.

Printed name of study staff obtaining consent Signature Date

Subject's statement

This study has been explained to me. I volunteer to take part in this research. I have had a chance to ask questions. If I have questions later about the research, or if I have been harmed by participating in this study, I can contact one of the researchers listed on the first page of this consent form. If I have questions about my rights as a research subject, I can call the Human Subjects Division at (206) 543-0098 or call collect at (206) 221-5940. I give permission to researchers to use my medical records as described in this consent form. I will receive a copy of this consent form.

- If selected for Cognitive Behavioral Therapy, I give permission for my sessions to be audiotaped:

  Yes ☐ **No** ☐

Printed name of subject Signature of subject Date

When the consent form is read to a subject, an impartial witness must be present and sign here:

:

Printed name of witness Signature of witness Date

Copies to: Researcher
Subject
Subject's Medical Record

	Pre-Screen	Screen	Baseline		Treatment						Follow-up from Randomization		
WEEK			-1	0	1	2	3	4	5	6	7	13	25
Insomnia Severity Index (ISI)	x			x				x			x	x	x
Inclusion/Exclusion Criteria		x											
Randomization				x									
Sleep Diary for CBT arm					x	x	x	x	x	x			
CBT-I Arm Visits					x	x	x	x	x	x			
Trazodone/Placebo Visits					x	x	x	x			x		
Treatment Adherence Assessment						x	x	x		x	x		
Phone call to check treatment response				x				x			x	x	x
Actigraphy with sleep diary			x							x			x
Concomitant Sedatives/Hypnotics				x				x			x	x	x