Participant's Name: _____ Date: _____

Title of Study: CBT-I Augmentation of Medications for Drinking in AUD

Principal Investigator's Name: Subhajit Chakravorty, MD

SUMMARY OF STUDY

WHAT IS THE STUDY ABOUT AND WHY ARE WE DOING IT?

We are asking you to choose whether or not to volunteer for a research study being funded by the Department of Veterans Affairs, Clinical Research & Development Service. This study is looking at how medication treatment combined with a behavioral intervention for insomnia can improve drinking problems and sleep disturbance. This initial material is to give you key information to help you decide whether to participate. We have included detailed information about this study. Ask the research team questions. Taking part in this study is completely voluntary.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

The purpose of this study is to determine whether Cognitive Behavioral Therapy for Insomnia (CBT-I) added to medications routinely prescribed to reduce alcohol consumption improves insomnia and alcohol consumption in early recovery from Alcohol Use Disorder. Actively drinking participants who are motivated to abstain or reduce their drinking will complete a screening assessment to see if the study is a good fit. No treatment will take place during this phase. If you are eligible to participate, you will be prescribed a standard VHA recommended medication treatment for problematic drinking (either topiramate, Naltrexone, or Vivitrol, or a combination of topiramate and Naltrexone or topiramate and Vivitrol) over the course of approximately 6 weeks (study Phase 1). If problematic drinking has sufficiently improved during that time (down to 2 heavy drinking days or less), you will be randomly assigned (i.e., like flipping a coin) to either treatment with Cognitive Behavioral Therapy for Insomnia (CBT-I) or to Sleep Hygiene Education on a weekly basis for 8 weeks (Phase 2). This is followed by an additional assessment session one week after completing your sleep treatment sessions. You will also be asked to return for follow-up assessments eight weeks after Phase 2. In total your participation will last up to 28 weeks. By participating in this study, we hope to learn whether the combination of medication and CBT-I is an effective treatment for veterans with alcohol use disorder and insomnia.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

You may want to participate in this study if you have a problem with drinking and difficulty sleeping at night and are interested in improving these problems. For a complete description of benefits, see the research details section of this document.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You may *not* want to participate in this study because of the time commitment of participating in a research study. You may *not* want to participate in this study because of potential side effects

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from the medication and the sleep treatment used in this study. You may *not* want to participate in this study if you have any health condition that would put your health at risk while taking the medications prescribed during this study. Also, you will be randomly assigned (like a flip of a coin) to a sleep treatment. One sleep treatment may be less effective than the other. For a complete description of risks, see the *Research Details* section of this document.

The medications prescribed for drinking in this study are also available to you from your outpatient provider in the clinic if you choose not to participate in the study. CBT-I is also available to you on an outpatient basis if you choose not to participate.

DO YOU HAVE TO TAKE PART IN THE STUDY?
If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?
The person in charge of the study is Dr. Subhajit Chakravorty at the Corporal Michael J. Crescenz VA Medical Center. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his contact information is: MIRECC, 2nd Floor, 116, Cpl. Michael J. Crescenz VA Medical Center; 215-823-5800, extension 20-6509 or 610-731-3039.

If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

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RESEARCH DETAILS

WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

In this research study we hope to learn whether providing sleep treatment in addition to drinking medications can improve the insomnia and recovery from harmful drinking. This study will determine whether a combination of medication for drinking and Cognitive Behavioral Therapy for Insomnia (CBT-I) successfully improves insomnia and strengthens recovery from drinking during early recovery. You are being invited to participate because you have indicated that you struggle with harmful drinking and problems sleeping.

HOW LONG WILL I BE IN THE STUDY? HOW MANY PEOPLE WILL BE IN THE STUDY?

Your individual participation in this study will take approximately 28 weeks (6.5 months). This research study is expected to take approximately 3 years.

WHAT IS EXPECTED IF I TAKE PART IN THIS STUDY?

The study is broken up into several parts.

Screening Procedures:

- Once you agree to take part in this study, and after by signing this informed consent document, you can begin participating in the Screening Phase.
- During the screening phase we will try to find out whether this study is a good fit for your problems from an addiction, sleep, medical and mental health perspective.
- The screening visit can take up to 4 hours and will consist of us asking questions about your sleep, addiction, and mental health.
- After this visit, you will be also sent home with a device that you wear at night while sleeping that will to determine whether you have a moderate or severe form of obstructive sleep apnea, which is a disorder in which breathing pauses can cause disturbances in sleep.
    - This device includes a sensor outside your nostril, a probe over your finger, and flexible bands over your chest and stomach and is worn for at least one night.
- You will also be using an actigraph, a wristwatch-like device, worn over your wrist, for about a week to monitor your sleep-wake patterns in your specific living situation.

All of these procedures will be conducted by research staff.

- If you continue to remain eligible for the study and motivated to reduce your drinking or abstain from drinking, the study doctor or nurse practitioner will conduct a medical examination and will include blood tests to make sure that you don't have any medical

problems that will affect your ability to take the medication or interfere with your ability to participate in the study. A urine test will check for use of a street drug other than marijuana.

- The blood tests that will be collected include routine clinical laboratory evaluations (blood counts, chemistry panel, liver function, uric acid levels), and phosphatidyl ethanol (Peth) levels to check for recent alcohol use.
- Urine tests will consist of a urine drug screen, and regular urine pregnancy test for women of child-bearing potential.

Once you have successfully completed this phase and remain eligible, you may choose to continue participation in this study. If you are a patient at the CMCVAMC and complete the Screening phase here at Philadelphia, you have the option of completing the remainder of the study at the Coatesville VAMC (CVAMC), if this is more convenient for you, but you will need to sign the informed consent document again. Please note that if you are considered to be at a high risk of health problems while coming off the alcohol, we may arrange for medically supervised detoxification from alcohol within the hospital, before you continue with other study-related procedures.

If you are a patient who completed the screening phase at the Coatesville VAMC (CMAMC) site and are still eligible for the study, you may complete the remaining phases (phases 1 through 3 of the treatment) here at the Cpl. Michael J. Crescenz VAMC (CMCVAMC) in Philadelphia after you sign this informed consent for the CMCVAMC study site. You are allowed to switch sites once, i.e., between Screening and Phase 1 treatment and you will continue with the remainder of the study procedures at the same site where you commence with treatment Phase 1. By signing this consent, you are allowing the study team at Philadelphia to access study materials from the Coatesville site.

Phase 1: Medication to treat heavy drinking

If you are eligible to participate after completing the screening procedures, you may choose to continue participation in this study, beginning with the medication phase (Phase 1).

- Phase 1 will last for about 6 weeks and will involve medication treatment for your drinking.
- During phase 1, you will be prescribed medication/s (i.e., topiramate, naltrexone either in pill or injection form, or a combination of both medications) with counseling to help you get sober or decrease your drinking. The type of medication treatment will be determined by what you and the study physician or nurse practitioner decide is best for you.

  - If topiramate is chosen for your treatment, there will be a gradual increase in dosage so that by the 6th week, you will be at a stable dose of the medication at a daily dosage of 200 mg per day or less.
  - If you are prescribed Naltrexone, you will be prescribed up to a dose of 100 mg a day or less. If you are started on the monthly injection form of naltrexone, i.e., Vivitrol®, the dose will be 380 mg every 4 weeks. The vivitrol will be prescribed in the outpatient mental health clinic by a clinic nurse.
- The initial MM session may last up to an hour and the other sessions will be about 30 minutes in duration. These sessions will be delivered weekly by the nurse practitioner or a study physician to provide medication monitoring and support you as you work to reduce your drinking to non-risky levels or stop drinking altogether. The initial MM session will be conducted in-person whenever possible. The remaining MM sessions will be done in-person if possible but can also be completed via video teleconferencing.
- During some of these visits (weeks 1, 4 and 6), you will also complete research questionnaires and be interviewed by the nurse practitioner or study physician about any other medications you are taking, adverse events, and whether you are taking your medications regularly (for Naltrexone or topiramate).
- If you are a woman of childbearing age and potential, we will have you repeat a urine pregnancy test every 4 weeks in the study to make sure that you are not pregnant while in treatment.
- At week 6 we will ask you to wear an actigraph again (the device that resembles a wrist-watch) to assess your sleep and wakefulness over the course of one week.

If your drinking has been sufficiently reduced, meaning you had no more than 2 heavy drinking days during the last week of the medication phase and you continue to report problems with your sleep, you may proceed to Phase 2, or the insomnia treatment phase.

- If you do not meet the requirements to move on to the next phase of the study, the study team will work with you to continue your medication treatment on an outpatient basis and get you the next available appointment with your outpatient provider if you are agreeable.
- Referrals to insomnia treatment through our sleep center or mental health clinic will also be available to you if you cannot proceed further in the study.

Phase 2 (Treatment of your insomnia)

- During Phase 2, you will receive sleep treatment over 8 weekly sessions that will be provided to you by the sleep medicine provider.
- You will either receive Cognitive Behavioral Therapy for Insomnia or Sleep Hygiene Education.
- The sleep therapy you get will be decided randomly, like the flip of a coin.

- The first sleep treatment session will last for about 45 minutes, and the remaining (seven) sessions will be 30 minutes in duration.
- You will have one more additional session (week 9) after you complete the sleep treatment phase during which you will complete assessments and bloodwork.
- Treatment sessions will be conducted via videoconference or in-person, depending on you and the provider's preference and ability to meet remotely.
- Alternately, if you are uncomfortable with videoconferencing and the behavioral sleep medicine provider is unable to meet with you in person, we can arrange a videoconferencing session with the provider in our outpatient clinic.
- You will fill out the treatment-related questions on your health weekly, and research questionnaires on an every-other week basis (weeks 1, 3, 5, 7, and 9) during the first this phase 2 treatment.
- You will also get blood work to monitor your health at weeks 1 and 9, and a urine pregnancy test if you are a woman of child-bearing potential (at weeks 1, 5, and 9).
    - The blood tests will include blood counts, chemistry panel, liver function tests, and a serum phosphatidyl ethanol level to check for recent drinking.
- During Phase 2 you will also have two medical management sessions which will be completed on a monthly basis when you are due for your medication renewal every 4 weeks.
    - These medical management sessions may occur in-person or via videoconferencing.
- If you wish to continue your medications following completion of the study, we will talk to your outpatient provider and make sure you have enough medication till you see her/him in the outpatient clinic.
- If you wish to be discontinued off your medications, we will discontinue them according to procedures specific to the medication you are taking.

Audio-recording

The study team is requesting permission to make audio recordings of sleep treatment sessions for research purposes. This is commonly done in research involving sleep treatments, and the purpose is to check that the sleep treatment is given as it is recommended. The recordings are stored on the secured VA server and will contain the date and time stamp of the recording and not your name or other identifiers. Recordings are not subject to additional compensation, and access to recordings is limited to study staff and monitors. If you refuse to grant consent to audio recording, there will be no effect on any VA benefits to which you may be entitled and you will still be able to participate in this study. You may at any time decide against being recorded.

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The study team has explained that by signing this Informed Consent Document, you voluntarily and without separate compensation authorize voice recording(s) to be made of you by research staff while you are participating in this study. Voice recording is intended for the purpose of monitoring treatment fidelity.

Signature:_____ Date:_____

Post-treatment Follow-up Visit

- Following the completion of phase 2 (treatment of your sleep problems), we ask that you continue to take your medications as recommended until the end of your participation in the study.
- 8 weeks after the final treatment phase 2 session, you will need to return to the CMCVAMC for a final research visit.
- During this visit we will repeat a few of the questionnaires done during your participation in the study.
- These questionnaires will include questions about your sleep, drinking and mental health status. We will also check you for any side effects from the medication.
- Prior to your final visit, we will ask that you fill out a daily diary about your sleep and naps over the last 2 weeks before the visit.
- For women in the childbearing age, we encourage you to continue active birth control measures such as use of a condom, diaphragm, oral contraceptive pills or an intrauterine device while in the study.

Participant expectations.

Participants are expected to:

- Complete and sign this informed consent document.
- Keep your appointments. If you miss an appointment, please contact the research staff to reschedule as soon as you know you will miss the appointment.
- Stick to your commitment to stop or decrease drinking, as applicable to you.
- Attend the weekly medical management counseling sessions with the study staff.
- Take the medication (Topiramate or naltrexone pill or injection form (Vivitrol®), or a combination, as instructed by the provider.
- Collaborate with the study staff to monitor treatment side effects which will also include giving blood and urine samples as specified.
- Complete the homework given to you by the sleep medicine specialist.
- Wear the actigraphy device on your wrist for a week, as instructed by staff.
- Immediately notify the investigator or research staff if you believe you might be pregnant.

- Keep the medication(s) in a safe place for your use only and away from children.
- Fill out your diaries as instructed by staff.
- Complete your questionnaires as directed by staff.
- Ask questions as you think of them.
- Commit to taking the medication for drinking on a regular basis while in the study.
- Commit to not participate in specific individual behavioral therapy for drinking such as Cognitive Behavioral Therapy for drinking. Participating in the group therapy is allowed.
- While participating in this research study, do not take part in another research project without approval from the investigators.
    - This is to protect you from possible injury from things such as extra blood drawing, or potential drug interactions. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

Expectations for Telehealth:
When participating in virtual telehealth sessions it is important to maintain a setting that is as similar to being in the office together as possible. In order to maximize the benefit of these sessions, we ask you to please observe the following:

- Make sure that you are somewhere where you can have reasonable privacy during your session.
- The therapist may use clinical judgment to determine if it is ok to proceed with a session and may not begin therapy if you are in a public place or significantly distracted (e.g., by childcare).
- Sessions will not be conducted while you are driving.

Payment Schedule
You will be compensated for each week of each phase, and this amount will range from $25 to $75 depending on the study visit. By the end of the study, if all phases are completed, you will receive $800 in all. You will be compensated for your time and effort in a pro-rated fashion depending on whether you completed all the required study-related procedures.

Compensation will be provided via vouchers to be cashed at the cashier's window in the CMCVAMC, direct deposit, or a mailed check. The CMCVAMC is required to report to the Internal Revenue Service any payments for participation in research studies that exceed a total of $600 in a calendar year. Your social security number and banking information must be included on VA Form 19001 for electronic funds transfer or VA contracted debit card programs. The VA Form 19001 must be presented to the agent cashier window. The study team will need to include the last 4 of your SSN for the payment voucher.

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WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

Any procedure has possible risks and discomforts. The procedures in this study may cause all, some, or none of the risks or side effects listed. Rare, unknown, or unexpected risks also may occur. Some risks are as follows including our approach to minimizing them:

Portable Home Sleep Monitoring.
Participants may experience some discomfort sleeping with the device. This test is done for a single night for most patients, and we recommend use for at least four hours for us to get reliable data on possible sleep-related breathing disorders on the study night. If for some reason the test fails and adequate data cannot be collected, we may ask that you complete the test again. The respiratory therapists at the CMCVAMC and our research team have years of experience in conducting these tests from prior studies, and we will make every attempt to minimize your discomfort by preparing you for the testing process. The data will be downloaded in the VISN-4 sleep center at CMCVAMC.

Actigraphy.
There may be discomfort wearing the actigraph (wristwatch-like device) on a 24-hour basis for 7 days at a stretch. If you notice any major inconvenience, you may take off the actigraph when showering or swimming. The straps are adjustable, and you can alter the tightness of the band. If you have difficulty wearing the actigraph for 7 days or if the band causes any irritation, you may wear it for 3 or more days, as is comfortable for you. You will be allowed to proceed with other study-related activities if you don't desire to wear the actigraph. The actigraphy data captures movements made by your body to determine activity or sleep. Data captured will include date and time stamps, brightness and movements across the 24 hours for up to 7 days. The data will be downloaded in the VISN-4 sleep center or on a VA research computer at CMCVAMC.

Blood and Urine Collection: Although these procedures are performed primarily as a safeguard for you, and to check your reported alcohol consumption, there is a possibility that you may have discomfort, pain, bleeding or bruising from the blood draw site or the inconvenience of giving a urine sample. Rarely, fainting occurs because of drawing blood. To safeguard against these outcomes, blood draws will be conducted by trained and experienced phlebotomists at the CMCVAMC clinical laboratory or on our research team. The results of the tests will be in your clinical chart except the pregnancy test that we will conduct in our office.

Data Collection during the Study:

You may have some discomfort associated with talking about your alcohol use problems, behavioral health problems, and addiction-related issues. In some cases, the use of the sleep diaries and actigraphs may lead to (or may be perceived as causing) a temporary worsening of your insomnia problems. Most of the information will be collected on a computer so you may not have to disclose it to a person in the room. Our staff are used to and experienced with the collection of sensitive information (e.g., drinking history). If, for any reason, you wish not to answer specific questions or you wish to terminate the session, you will be able to do so but we request you to let us know.

Confidentiality
There is a possibility that your identifying data and/or study information may be viewed by non-study personnel. After you sign the informed consent form, we will give you a 4-digit study number unrelated to your personally identifiable information. This 4-digit number will be used for all the study-related procedures. All the information you fill out will be stored under your 4-digit number. Any portable sleep study results will also be transferred with the 4-digit study identification number. The results of your clinical blood tests will be in the VA clinical chart, but we will enter these results into our research database with only your four-digit identification number. In addition, most of the data from the questionnaires you fill out on the VA version of the computer will be stored in secure, password protected, VA servers. These efforts make it much less likely that your identifying data and/or study information may be viewed by non-study personnel. Your personally identifiable information that we collect will be stored in the password protected online drive within CMCVAMC. Any paper forms you sign will be stored within the locked research office with restricted access.

Drinking alcohol while being treated with a Medication for you drinking
In clinical trials of topiramate or Naltrexone, individuals who consumed alcohol did not report ill effects of the combination. However, alcohol consumption may cause sleepiness, topiramate may also cause drowsiness in some, and the risk of drowsiness may be theoretically increased when both alcohol and topiramate are taken together. Thus, we recommend that you abstain or minimize your alcohol use while taking prescribed medications. Further, we recommend that you avoid driving after consuming alcohol and medications, especially topiramate.

Drinking during the treatment study visit
There is a possibility that you may sometime drinking while on the study medication for drinking. We recommend you avoid driving an automobile if you have consumed alcohol. We also recommend that you avoid risks of tripping on the floor after drinking by avoiding clutter on the floor, cables that you may trip on, and wear sensible shoes in slippery areas. We will monitor your drinking. If you have a resumption of sustained heavy drinking and this sustained heavy

drinking places you at risk of medical, psychological, or physical harm, then you may be withdrawn from the study on a temporary basis or for the remainder of the study, and a referral to the clinic or the inpatient unit will be offered, as deemed necessary.

Sleep Restriction
You may experience a temporary increase in your daytime problems related to CBT-I treatment, when the time you spend in bed is made the same as the amount of sleep you actually get at nighttime. In the first few days of treatment this mild sleep deprivation (about 1 hour less sleep than is normal for you) may result in a temporary increase in daytime sleepiness, fatigue, concentration problems, and irritability. We will be monitoring your sleepiness through the study. Also, just like our clinical care, we will monitor you at each behavioral sleep treatment visit for excessive daytime sleepiness and we ask you to avoid driving if you feel drowsy.

Suicidal/Homicidal Ideation with CBT-I treatment:
There is no evidence that CBT-I increases suicidal or homicidal thoughts, and CBT-I treatment has been shown to decrease suicidal thoughts in prior research. It is possible that temporary sleep deprivation that can occur with CBT-I may make it more difficult to cope with suicidal or homicidal thoughts. We will actively monitor suicidal or homicidal thoughts throughout the study, and if you are ever at imminent risk of harming yourself or others, we will take steps to protect your safety (e.g., connecting you with emergency services within the CMCVAMC).

Medical Management (MM) sessions:
MM sessions may feel burdensome while you are being counseled to abstain or decrease your alcohol use. MM has been safely used in our prior topiramate studies. Psychological risks of MM are minimal and do not differ from those of similar non-study treatments.

Topiramate Side Effects:
Topiramate is non-habit-forming substance; therefore, it is not a drug with abuse risk. Although topiramate treatment is associated with some serious side effects, none such serious side events were seen in a recently completed study of topiramate. The most common side effects of topiramate as compared to placebo are numbness and tingling (49% vs. 6%). The other most common side effects (experienced by 10-31% of patients in clinical studies) include: change in sense of taste, tiredness/sleepiness, fatigue, dizziness, loss of appetite, nausea, diarrhea, weight loss, difficulty concentrating and difficulty with memory. We discuss these treatment-related adverse events below:

- **Nonphysical side effects:** (e.g., confusion, psychomotor slowing, difficulty with concentration/attention, difficulty with memory, speech or language problems, particularly word-finding difficulties) that were found during the 6-month migraine treatment studies

(28% vs. 10% for placebo) were of mild-to-moderate in severity. We will check for these side effects during the treatment phase of the study and decrease your topiramate dose, if necessary.

- **Other side effects** (experienced by 5-9% of patients) in some studies: nervousness, slow thinking, abnormal vision, confusion, decreased sensitivity or numbness (hypoesthesia), anxiety, belly pain, dry mouth, involuntary muscle spasms, and language problems. Depression and mood problems have also been reported (5-9%). Some patients have reported suicidal thoughts or behaviors (<1%). Should you feel a change in your mood, feel depressed, or feel you may harm yourself, you should contact our study staff or study physician.
- **Kidney Stone:** A side effect of topiramate which is less common but potentially serious is a kidney stone (approximately 2%). If you have a history of kidney stones, you will not be eligible for this study. In addition, you will be repeatedly counseled to drink an adequate volume of water or liquids while taking TOP, and this may reduce the risk of a kidney stone.
- **Metabolic Acidosis:** Biochemical changes in your blood (decreased bicarbonate levels) may be associated with topiramate treatment (3-7%). If you are taking certain medications (called carbonic anhydrase inhibitors) you will be excluded from this study, due to the added risk for this condition. Further, we will repeat your serum bicarbonate level test at the midpoint and at the end of your treatment, to identify if you are developing this condition.
- **Glaucoma:** Rarely, severe glaucoma has been described in patients taking topiramate, usually occurring at the beginning of treatment (less than 1%). This side effect is rare. If you have been diagnosed with narrow angle glaucoma you will be excluded from this study. You will contact the study doctor immediately if you have sudden worsening of vision, blurred vision, or eye pain.
- **Overdose:** Overdoses of topiramate have been associated with convulsions, drowsiness, speech disturbance, blurred vision, diplopia (double vision), impaired mental activity, abnormal coordination, numbness, hypotension, belly pain, agitation, dizziness, and depression. Deaths have been reported in overdoses. Therefore, we will give you weekly prescriptions till you stabilize on the topiramate, and we will have you answer some questions on medication side effects and suicidal behavior, at each treatment visit.
- **Liver failure/Hepatitis:** Rare and isolated cases of liver failure/hepatitis and blistering skin rashes (bullous skin eruptions) have been reported with topiramate (less than 1% for both). We will instruct you to use topiramate carefully, and give you limited quantities. These steps will serve to decrease the risk of any accidental overdose.
- **Decreased Effectiveness of Contraceptives**: It is possible that some hormonal contraceptives (birth control pills, hormonal implants, or hormonal injections) may be

made less effective by topiramate. If you are a woman of child-bearing potential who is either pregnant, nursing or not using effective methods of birth control, you will be excluded from the study. If you are a woman of childbearing potential and are using hormonal contraceptives, we urge you to also use barrier contraception (a condom or a diaphragm) as a second method of contraception while participating in this study. We also urge you to notify the study nurse or doctor immediately when you notice any changes in your menstrual bleeding patterns during treatment. As a safeguard, we will also conduct urine pregnancy testing of women with child-bearing capacity prior to entering the study and every four weeks during treatment phases of the study (i.e., at week 4 in phase 1, and weeks 1, 5, and 9 in phase 2), to minimize the risk of topiramate exposure to the fetus.

- **Reproductive risks:** Pregnancy and birth defects. A nursing mother may not participate in this study. The safe use of topiramate in pregnant women and nursing mothers has not been established. So, there may be risks to you (or to your embryo or fetus) if you are or may become pregnant. Effects on the baby from topiramate may include, smaller weight of newborn babies (19.7%), mouth defects (cleft lip or cleft palate, 1.1%), and metabolic acidosis (its rate of occurrence is unclear). Topiramate is also released in breast milk of mothers' breast-feeding their babies. You must weigh the potential benefit to you as a female planning to participate in the study for drinking and insomnia treatment against the potential damage to your fetus. As a woman of childbearing potential enrolling in this study you must (i) have been using a birth control before starting the study, (ii) must have a negative pregnancy test, and (iii) must agree to continue to use a birth control measure for the duration of the study. We recommend you to strictly use contraception during the study (an intrauterine device (IUD), birth control pills, a condom, diaphragm), and we will check for urine pregnancy test, as mentioned above. We urge you to immediately notify us when you notice any change in your menstrual bleeding patterns. If you are found to be pregnant while being treated in the study, we will immediately stop the topiramate and refer you to your VA primary care provider for further evaluation and management.

Oral Naltrexone Side Effects

Oral Naltrexone is a non-habit-forming substance; therefore, it is not a drug with abuse risk. The most common side effects of oral naltrexone are nausea, headaches, and nervousness. We will monitor you for these side effects and if clinically indicated, we will decrease the dose of naltrexone to 25 mg daily, or switch the dosing to nighttime or daytime, based on when you are taking the medication. We discuss serious treatment-related adverse events below:

- **Depression and suicidal ideation:** Depression has been reported by 0-15% of subjects in previous clinical trials and suicidal behavior has been reported by 0-1% of subjects in previous clinical trials. We will monitor you carefully for these side effects during the

medication stabilization phase (phase 2) of the study. If you notice the emergence of these side effects, please notify the study team as soon as possible, and we may try to decrease the dosage of naltrexone, switch you to a different medication, or maintain your treatment without medication, as is the best option for your health.

- **Increased liver transaminase levels:** As a safeguard, we will conduct liver function testing during the screening phase of the study, midpoint of the study, and end of treatment to identify if you are developing this condition. Based on your individual needs, we may decrease the dosage of naltrexone, switch you to a different medication, or maintain your treatment without medication as is clinically appropriate.

Depot Naltrexone Injection (Vivitrol®) Side Effects:

- **Pain at the injection site:** This adverse event may be seen in up to 45% of the patients receiving this injection. The clinic nurses at the CVAMC have experience in dispensing depot naltrexone injections and will make every attempt to minimize your discomfort. The other side effects listed above for oral naltrexone are also applicable for depot naltrexone injections. If the vivitrol injections partly help you with your drinking we may consider adding TOP if you are struggling with reducing your drinking or craving to have a drink, as is clinically considered appropriate for your clinical care.

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks of the usual care you receive are not risks of this study. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care.

WHAT ARE THE POSSIBLE BENEFITS OF THE STUDY?

We do not know if you will get any benefits from taking part in this research study. However, possible benefits of the treatments may include an improvement of your drinking, insomnia, or both. Participation in the study may also help you understand more about your health problems. The research will benefit future Veterans by providing information on how to treat drinking and sleeping problems.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

- One of the choices is not to participate in this research study. Participation is voluntary and you do not have to participate if you do not want to.

- If you decide you do not wish to participate in this study, we will refer you to the Addiction Recovery Unit (ARU) or the Mental Health Clinic for further assessment and treatment.
- You do not have to participate in a research study to get treatment with medication.
- You don't have to participate in a research study to get treatment with CBT-I, sleep hygiene education, or medications for your sleep problems.
- Other treatments for alcoholism may include other medications approved by the Food and Drug Administration, such as acamprosate and disulfiram. Other treatment options for drinking also include behavioral treatments such as counseling, group therapy, participation in Alcoholics Anonymous groups, or intensive treatment in a residential rehabilitation program. Treatment options can be coordinated by your primary health care provider or mental health treatment counselor.
- Alternative treatments for sleep problems may include behavioral interventions like CBT-I, or education about appropriate sleep hygiene. These treatments can be provided to you by your clinic provider in the CMCVAMC outpatient clinic. Alternative medication treatment options for sleep problems include, ramelteon, mirtazapine, doxepin, or gabapentin.
- You may discuss all these options with your healthcare provider.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

During the participation in this study, you will be assigned a 4-digit unique identification number or code. This code will NOT include any variation of your social security number or date of birth but, will represent your recruitment number in the study (e.g., 2001). We will keep the code that links your 4-digit study identification number to your identifying information such as name, social security number or address in a secure location on the VA's password protected online drives or consent forms in locked cabinets within the restricted access research clinics. Coded information that we collect electronically or on paper will be kept in a secure location in the VA. These efforts make it very less likely that your identifying data and/or study information may be viewed by non-study personnel. For statistical analysis purposes, we will be transferring your data to the University of Pennsylvania data management team where the team will identify your information from the study using the 4-digit study identification code assigned to you, although the data may have a date and time stamp when the information was collected.

We will include information about your participation in this study in your VA medical record. Your research records may be reviewed by the regulatory agencies such as the CMCVAMC Institutional Review Board, VA Data Management Committee, or the VA Clinical Science Research and Development staff member, as and when needed.

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A description of this clinical trial will be available on www.ClinicalTrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

All research records, including the investigator's research records, must be retained according to the National Archives and Records Administration VHA's Records Control Schedule. The data from the assessment measures may be used for future studies and/or analysis, but the data used will not be linked your personal health information.

Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization,' for the use and disclosure of information protected by the HIPAA Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records such as your contact address, telephone number, telephone number of your next of kin, telephone number of your emergency contact person, telephone number of a person who can locate you when we are unable to (patient locator), electronic mail address, social security number/medical record number, medical history, allergies, lab results, HIV status, drug, alcohol or STD treatment, and mental health treatment.

The research team may also need to disclose your health information and the information it collects to others as part of the study progress. Others may include the VA Clinical Science Research and Development organization, CMCVAMC laboratory services, CMCVAMC pharmacy services, CMCVAMC Institutional Review Board, CMCVAMC agent cashier's office (for payment vouchers for your reimbursement), Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO), and the Government Accountability (GAO). In addition, if you are transferred to the Coatesville VA Medical Center for treatment in their rehabilitation program, we will coordinate with their health center staff for you to attend your appointments here at our medical center as needed. Information shared with them will include but not limited to your name, social security number, date of birth, your contact number, your medical, psychiatric and

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addiction treatment information, allergies, and date and time of transport on the shuttle van to and from Coatesville VA Medical Center.

Your health information disclosed pursuant to this authorization may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization, in writing, at any time. To revoke your authorization, you must write to the Release of Information Office at this facility or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Release of Information Office receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

If you revoke this authorization, Dr. Subhajit Chakravorty and his research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?

You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call:

DURING THE DAY:

Dr. Chakravorty at (215) 823-5800, extension 206509 or (610)-731-3039, and

AFTER HOURS:

Dr. Chakravorty at (610)-731-3039.

- The VA will provide treatment for research related injury in accordance with applicable federal regulations (38 CFR 17.85).
- There is no additional compensation available if any injury occurs during your participation in this study.
- Emergency and ongoing medical treatment will be provided as needed.

DO I HAVE TO TAKE PART IN THE STUDY?

Participation in this study is on a voluntary basis. Your refusal to take part in the study will not involve any fine or loss of benefits to which you are otherwise entitled. If you are a VA employee, your refusal to take part in the study will in no way influence your employment, ratings, or subsequent recommendations, as applicable.

You may discontinue taking part in the study at any time without any penalty or loss of benefits, and you will still receive the same standard of care that you would otherwise have received.

It should be noted that most of the treatments offered in this study are easily available in the outpatient clinic, although they may not be provided together in the same clinic.

If you decide to withdraw from the study, we will coordinate with your current outpatient provider to set up the next available appointment in the clinic with him/her, so that you may discuss the option of receiving similar or other treatment outside of the research study.

It should be noted that the investigators may continue to review the information we have already collected from you during the study before you decided to withdraw, but we cannot collect any new information, except for what is available from publicly available records.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION

Your participation may be terminated from the research study by the investigator, without regard to your consent, under certain conditions. Some of these conditions may include the following:

- Any condition which the study psychiatrist finds topiramate, naltrexone, Vivitrol or CBT-I to be a hazard to you (such as it makes you very anxious, suspicious, or you are unable to follow through with the recommendations and/or homework related to this treatment).
- Relapse to sustained heavy drinking during treatment that makes your participation in the study risky or difficult for you.
- You develop a mental health problem that prevents you from functioning or is dangerous for you.

- You develop a medical problem that requires you to be admitted to the hospital for a few weeks, thus making your continued participation in this study difficult.
- You develop another substance abuse problem for which you need to be admitted to the hospital or need a higher level of treatment than what we give you in this study.
- If you are unable to follow the recommendations of the research staff or complete research procedures in a timely fashion
- You are jailed or imprisoned for more than one week
- Any other unanticipated situation where the Principal Investigator decides that your continued participation in the study may be more harmful than of benefit to you.

Your study participation can be restarted after discussing with the study physician if you, 1) return to treatment after a period of brief absence of 4 weeks or less in total, or 2) return to treatment within 4 weeks, after a brief inpatient hospitalization or additional outpatient treatment. Restarting study procedures may also depend on your need to be in treatment.

If we determine that your further participation in our research study is not in your best interests, you will be withdrawn from the research treatment, but we will try to follow you in the study, if you are willing, till your participation in the study ends.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

If you have questions about your rights as a study participant, or you want to make sure this is a valid VA study, you may contact the Institutional Review Board (IRB). This is the Board that is responsible for overseeing the safety of human participants in this study. You should contact the Research Compliance Officer at 215-823-7847 or the Patient Representative at 215-823-5803 from 8:00 AM to 4:30 PM, Monday through Friday if you have questions, complaints or concerns about the study or if you would like to obtain information or offer input.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

If there are any new findings that may affect your participation in the study, we will disclose them to you before or during your treatment part of the study.

WHO COULD PROFIT FROM THE STUDY RESULTS?

No payment is being made to the research team that can be considered that they are making cash profit from this study. If any possible commercial product is developed in the future as part of this research, you will not profit from any products or tests that might result from this research.

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DOES THIS STUDY INVOLVE GENETIC RESEARCH? HOW WILL MY GENETIC INFORMATION BE PROTECTED?

There will be no genetic research conducted in this study.

FUTURE USE OF DATA AND RE-CONTACT

Any blood or urine samples taken during this study will not be used for future research. Once the recruitment ends, we will remove any identifiable private information from the data that is collected in this study. We may use the information collected from the research study for additional future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative. None of this data was be linked in a way that can identify you. We will not contact you after the end of your study participation. If we have any reason to contact you after the study, we will obtain permission from the CMCVAMC IRB to contact you again.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr. Chakravorty or another research team member has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study and authorize the use and disclosure of your health information for this study. You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it. A copy of this signed consent will also be put in your medical record.

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I agree to participate in this research study as has been explained in this document.		
Print Participant's Name	**Participant's Signature**	**Date Signed**

☐ **Subject was consented in-person**

Individual Obtaining Consent (required)		
Print Individual's Name Obtaining Consent	**Signature of Individual Obtaining Consent**	**Date Signed**

☐ **Subject was consented via a telemedicine portal**

Individual Obtaining Consent (required)			
Print Individual's Name Obtaining Consent	**Signature of Individual Obtaining Consent**	**Date individual was Consented via Video Portal**	**Date Signed**

Participant's Name: _____ Date: _____

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