Subject Name:_____

First Name MI Last Name

Title of Study: Optimal Treatment of Veterans with PTSD and Comorbid Opiate Use Disorder

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(v.04.12.2022)

SECTION I: THE PURPOSE OF THE STUDY AND HOW LONG IT WILL LAST.

You are invited to participate in a research study designed to evaluate the use of a standard psychotherapy for post-traumatic stress disorder (PTSD) in Veterans and civilians who also suffer from an opiate use disorder (OUD). You have been invited to participate because you have been diagnosed with PTSD and OUD. Your participation will last for approximately 30 hours spread over 14 weeks with additional follow-up visits scheduled approximately 1 and 3 months after study completion.

In order to decide whether or not you wish to be a part of this research study, you should know enough about its risks and benefits to make an informed judgment. This consent form gives you detailed information about the research study which a member of the research team will discuss with you. This discussion will go over all aspects of this research; its purpose, the procedures that will be performed, any risks of the procedures, and possible benefits. Once you understand the study, you will be asked if you wish to participate, if so, you will be asked to sign this form.

SECTION II: DESCRIPTION OF THE STUDY INCLUDING PROCEDURES TO BE USED.

This study will evaluate two types of counseling, Cognitive Processing Therapy (CPT) and Individual Drug Counseling (IDC), among participants diagnosed with both PTSD and an opiate use disorder (OUD) who are on buprenorphine maintenance. Several studies have shown that CPT is effective in reducing PTSD symptoms and is a standard therapy that is used among individuals with PTSD. IDC is the standard treatment for individuals who are participating in buprenorphine maintenance. Buprenorphine maintenance with buprenorphine/naloxone (BUP/NLX) is a standard line of treatment for individuals with an opiate use disorder. In order to participate in this study you must be willing to take BUP/NLX or already be participating in a buprenorphine maintenance program with BUP/NLX or BUP. We anticipate that approximately 160 people will be enrolled in this study.

Screening: If you agree to participate in this study you will be asked to provide a thorough medical and psychiatric history and participate in a detailed psychiatric interview. You will also have urine tests done at in-person visits, which will become part of your medical record. This screening appointment will take approximately four hours The screening visit may also be done over several shorter visits, instead of all at once. The purpose of this visit is to make sure it is safe for you to participate in this study.

You will have the option to complete part of this screening visit remotely using a VA approved video platform. If you choose this option a member of the research team will contact you to set up an appointment to go over this consent with you. If you would still like to participate in the study after reviewing the consent, we will obtain verbal consent to continue and this will be documented in your medical record. You will need to sign written consent at your first in-person study visit, prior to starting any study treatment/therapy.

Treatment Assignment:

Buprenorphine/Naloxone (BUP/NLX)

Everyone who participates in this study will be taking the medication buprenorphine. If you have already started buprenorphine/naloxone (BUP/NLX) treatment with a healthcare provider, you will continue to take the medication, as prescribed.

If you are taking standalone Buprenorphine, including injectable buprenorphine, you will continue to take the medication, as prescribed.

Medication Dosing: If you are not already taking BUP/NLX, you will meet with a study nurse to start the medication. You will be asked to stop taking any opiates for 24 hours before you are scheduled to start taking BUP/NLX and you may be asked to stay in the clinic for up to 2 hours after your first dose of BUP/NLX. A nurse will go over what medications/drugs you need to stop taking. Examples of opiates include (this is not a complete list): hydromorphone (Dilaudid), demerol, oxycodone (OxyContin, Percocet), hydrocodone (Vicodin, Lorcet, Lortab), fentanyl, methadone, heroin, morphine, and codeine.

During induction into buprenorphine, you will be started at a dose of 2mg, and this dose will be increased as needed until your withdrawal symptoms have been stabilized, up to 32mg per day. This will take approximately 7 days. You will be seen on a daily basis (excluding weekends) for the initial 5-7 days.

Once you reach the maintenance dose you will remain on that dose for the rest of the study. Your symptoms will be monitored on a regular basis (see "Study Schedule" below) and your dose will be modified if needed. At the end of the 12-weeks of treatment you will be referred to a buprenorphine clinic.

The BUP/NLX will be prescribed to you by either your current provider or a study provider. The research team will work with you and your provider to decide which option is best for you prior to starting the study. The amount of medication dispensed to you at one time (daily, weekly, or monthly supply) will be determined by your provider and may change during the study at the discretion of your provider. Medication will be dispensed by either the VA Pharmacy or the VA Research Pharmacy.

Medication Storage: You will be given a pill bottle at each visit that indicates how you should take your study medication. We will review with you how you should take your study medication each visit. You should keep all medication containers out of the reach of children.

Counseling: You will have a 50% chance of being assigned to CPT, and a 50% chance of being assigned to IDC. The study uses a procedure like flipping a coin, so that you will have a 1 in 2 chance of receiving CPT or IDC. You will participate in either CPT or IDC for the entire study (the type of counseling you are receiving will not change during the 12 weeks of treatment). After the study is completed, you will be given a referral to continue treatment for PTSD (if you choose) and if you were not assigned to receive CPT in this study, you will be given a referral to a provider that can provide you with CPT therapy.

Study Schedule: Your participation will last for approximately 30 hours spread over 14 weeks with additional follow-up visits scheduled approximately 1 and 3 months after study completion. Visits will be broken into four different parts: (1) induction to BUP/NLX; (2) counseling visits; (3) medication visits; and (4) follow-up.

Once you have completed the BUP/NLX induction, the counseling and medication visits will begin. Counseling visits will occur once a week for weeks 1-12. Medication visits will occur on weeks 1-4, 6, 8, 12. On weeks where you have both a counseling visit ***and*** medication visit (weeks 1-4, 6, 8, and 12), we will try and schedule your appointments on the same day. However, this will depend on your schedule and may not always be possible. This means you may have to come in for study related visits approximately 1-2 times a week.

Induction: If you are not already taking BUP/NLX, you will be started on it. This will take place over approximately 7 days and is described earlier under "Medication Dosing". If you are already taking BUP/NLX, you will skip the induction phase of the study.

Counseling visits: You will be asked to attend 12 therapy sessions of CPT or IDC (described below). These sessions will occur once a week for 12 weeks, and they will be approximately 60-90 minutes long. At each session you will talk one on one with a therapist and also be asked to fill out surveys asking you about your feelings, PTSD symptoms and drug use. These sessions will be audio (voice) recorded. In order to maintain social distancing we will ask you to complete the counseling visits using a VA approved video platform (eg. VA Video Connect or VVC). If this is not possible you can complete the counseling session by telephone or in person.

Cognitive Processing Therapy (CPT): CPT is a 12-session therapy that has been found to be effective for PTSD. CPT aims to give you new ways of handling distressing thoughts and feelings and to gain an understanding of traumatic experiences. Throughout the course of CPT, you will be asked to discuss various aspects of the traumatic event, including its details and consequences. CPT has four main parts: 1) learning about PTSD symptoms, 2) becoming aware of thoughts and feelings, 3) learning skills to help you have more adaptive beliefs about your trauma(s), and 4) understanding how your trauma(s) may have impacted your beliefs about yourself, others, and the world. You will be asked to complete daily practice assignments.

Individual Drug Counseling (IDC): IDC is the standard treatment used with individuals who are receiving buprenorphine maintenance. The main focus of this counseling is to help individuals achieve and maintain abstinence by encouraging behavioral changes (avoiding triggers, adding structure, engaging in healthy behaviors such as exercising).

Medication visits: Medication visits are conducted by a Registered Nurse (RN) and/or research staff member during weeks 1-4, 6, 8, and 12. These appointments will be approximately 60 minutes each and are for medical management, symptom evaluation, and medication refill (if study physician is providing). You will be asked to come into the research clinic for an in-person visit during weeks 1, 4, 8, and 12; this may be conducted by telephone (including video call). The other visits (weeks 2, 3, and 6) will be conducted by telemedicine using a VA approved video platform (e.g. VA Video Connect or VVC) or by telephone.

At each in-person visit you will be asked to provide a sample of urine for drug screening and to take a breathalyzer test (which involves blowing into a tube to estimate your blood alcohol level). Females will have a urine pregnancy test done on weeks 4, 8, and 12. During each visit (in-person or telemedicine/telephone), you will also be asked to complete several questionnaires asking about your mood, drug and alcohol use, and PTSD symptoms. You will receive a reminder call before each visit and you will be asked to bring in the bottle with the study medication, regardless of whether any medication is left over.

Follow-up: Follow-up sessions will be scheduled with a research staff member following the completion of the study, and will take place at approximately 1 and 3 months after your last visit. You will meet with the study staff and be asked to complete several questionnaires asking about your mood, drug and alcohol use, and PTSD symptoms. These visits will be approximately 60-90 minutes each and will be conducted by telemedicine or telephone.

For all in-person visits you will be required to follow current COVID-19 local guidelines. This may include wearing a cloth face covering during your visits, participating in a temperature check, and passing a screening before entering the hospital. If you have a scheduled appointment and have a fever (99.9 F or higher) or any symptoms of COVID-19 you will need to contact us to reschedule your appointment.

SECTION III: DESCRIPTION OF ANY PROCEDURES THAT MAY RESULT IN DISCOMFORT OR INCONVENIENCE.

At any point in the study, you will be discharged if study personnel are concerned that continued study participation may cause you physical or psychological harm. If you are discharged from the study, you will be referred back to your regular clinician. The procedures that may result in discomfort or inconveniences include: attending appointments, completing evaluations/surveys, and attending psychotherapy (CPT or IDC).

Attending Appointments: Attending appointments weekly for evaluations may be inconvenient for you.

Evaluations/ Surveys: Talking about your trauma and drug use history can be stressful and can sometimes increase anxiety, craving, or PTSD symptoms.

CPT: Previous research shows that PTSD symptoms increase somewhat during the early part of CPT before they decrease. This is expected because you are thinking more about your traumatic experience(s). It is also possible that CPT will not help you.

IDC: PTSD symptoms are not typically addressed during IDC. If you are assigned to this type of therapy, it is possible that your PTSD symptoms may increase.

SECTION IV: EXPECTED RISKS OF STUDY:

The risks in this study include: side effects from BUP/NLX, BUP/NLX detoxification, increased PTSD symptoms/anxiety/craving, loss of confidentiality, causes for early discharge, and unanticipated risks. These risks are described below:

Buprenorphine/naloxone (BUP/NLX): Side effects associated with BUP/NLX include: abdominal pain, constipation, nausea, vomiting, headache sweating, sedation, and allergic reaction. BUP/NLX can also cause physical addiction or dependence. Uncommon but more serious adverse side effects of BUP/NLX include liver abnormalities, feeling dizzy when you suddenly get up, and a possibility that your breathing could significantly slow down. You are asked not to use alcohol throughout the study because it may interact with buprenorphine/naloxone and increase the risk of side effects and serious life-threatening breathing problems. Use of benzodiazepines, sedatives, or tranquilizers also increases these risks.

Buprenorphine/naloxone Detoxification: Detoxification from BUP/NLX can produce signs and symptoms of opiate withdrawal, including nasal congestion, abdominal symptoms, anxiety, muscle pain, insomnia, sweating, and diarrhea. You should take BUP/NLX as prescribed and should not suddenly stop taking the medication.

Increased PTSD Symptoms, anxiety, and craving: You will be asked to talk about your PTSD symptoms, anxiety and craving at most appointments. This may cause all of these symptoms to become worse. If you are uncomfortable at any point, you should let a member of the research team know. If your symptoms bother you after you go home, you should contact the numbers listed on the last page of this consent document. A study doctor will be contacted to evaluate you by phone or in person, if necessary, to see if any further treatment is needed.

If the research staff is concerned about your safety during the study, you may be evaluated by a study clinician and if necessary referred for further evaluation and/or treatment. If it is determined that you are a danger to yourself or others, or are so ill you can't take care of your basic needs at home, you may be held in the hospital against your will.

Loss of Confidentiality: Participation in research may involve a loss of confidentiality. Your research records will be kept as confidential as possible. Only a code number will identify your research records. The code number will not be based on any information that could be used to identify you (for example, social security number, initials, birth date, etc.) The master list linking names to code numbers will be kept separately from the research data. All urine drug screens will become a part of your medical record.

All research information will be secured in locked files. Your identity will not be revealed in any reports or publications resulting from this study. Only authorized persons will have access to the information gathered in this study. Authorized persons may include regulatory agencies such as the Food and Drug Administration, (FDA), the Government Accountability Office (GAO), the Office for Human Research Protections (OHRP), Office of Research Oversight (ORO), and VA Connecticut Healthcare System Research Office.

The Department of Veterans Affairs (VA) requires some information to be recorded in the VA electronic medical record for Veteran and non-Veteran research subjects. Therefore, if you participate in this study, a medical record will be created if you do not already have one. Notes from your visits, procedures, and laboratory tests will be included in this record. In addition to the research team, and the VA staff who provide clinical services, other researchers may be granted approval to access this information in the future. Federal laws and regulation that protect privacy of medical records will apply to your VA record.

Causes for Early Discharge: At any point in the study, you will be discharged: 1) If your behavior is too disruptive 2) If you experience serious side effects due to the study medication, 3) If you regularly miss medications, 4) if urine toxicology screens show frequent use of benzodiazepines or barbiturates, 5) If the investigator has evidence that your health or well-being may be threatened by continuation in the study, 6) (**Females only)** Should a pregnancy test become positive, you will be withdrawn from the study and referred to an appropriate treatment program.

Unanticipated risks: If at any time during the study you observe any unusual or uncomfortable feelings, you should contact the research staff by coming in to the research office or calling (203) 932-5711 ext. 3121 during weekdays from 8:00 a.m. to 4:00 p.m. After hours, you may call the Psychiatric Emergency Room at the VA Connecticut Healthcare System (West Haven, CT) at (203) 932-5711, extension 4472 and ask for the substance abuse research psychiatrist on call. If you become suicidal, hospitalization is possible.

Females Only: Since this research may have bad or unforeseen effects on a fetus and should not be done during pregnancy, it is necessary that a pregnancy test be done first. You will have pregnancy test during

the screening and at weeks 4, 8, and 12. To your knowledge, you are not pregnant at the present time. You also agree to avoid becoming pregnant (to use contraceptives, to take precautions against becoming pregnant, etc.) during this study. You will be given counseling about acceptable forms of contraception that include barrier (diaphragm and condom) methods and birth control pills. You will also be counseled about the implications of opiate use while pregnant. You will be discharged from the study if you become pregnant at any time during the course of the study.

SECTION V: EXPECTED BENEFITS OF STUDY.
Potential benefits may include a reduction in PTSD symptoms. However, there is no guarantee or promise that you will receive any benefit from participation in this study. Your participation may help to develop more effective treatment approaches for indivuduals with PTSD and Opiate Use Disorder that may help others.

SECTION VI: ALTERNATIVE THERAPY OR DIAGNOSTIC TEST.
The alternatives to being in this research study are to not be in this research study and, if you are not already in substance abuse or PTSD treatment, to enter treatment at a general facility. If you do not wish to be in this study, your condition will be treated according to standard medical practice, and we will provide you with referral information for PTSD or substance abuse treatment, if you wish. If your drug or psychiatric symptoms require further care, you may be referred for either inpatient or outpatient services under the guidance and recommendation of the study psychiatrist. A decision not to be in the study or to withdraw from the study will not affect your future interactions with the VA Connecticut Healthcare System, West Haven and/or Newington.

SECTION VII: USE OF RESEARCH RESULTS.
You will be informed of any important discoveries made during this study, which may affect you, your condition, or your willingness to participate in this study. If the research staff is concerned about your safety during the study, you may be evaluated by a study clinician and if necessary referred for further evaluation and/or treatment. If determined that you are a danger to yourself or others you may be held in hospital against your will. If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. Your medical records will be maintained according to VA requirements. The Food and Drug Administration or designated individuals from the National Institute of Health may inspect the records.

SECTION VIII: SPECIAL CIRCUMSTANCES.
Participants can receive up to $330 for participating in the study. Payment is outlined below:

Visit	**Payment Amount**
Screening	$30
Medication- week 1	$30
Medication- week 2	$30
Medication- week 3	$30
Medication- week 4	$30
Medication- week 6	$30
Medication- week 8	$30
Medication- week 12	$30
1 month follow-up	$45
3 month follow-up	$45
Counseling visits (weeks 1-12)	No payment
Total Payment	**$330**

Payment for your participation (for your visit(s)) will be made through electronic funds transfer (EFT). You will need to provide us with your banking information by completing a special payment form. If your banking information changes while you are still participating in the study, you will need to fill out the form again. It is your responsibility to notify us if your banking information changes. Alternatively, if you do not have a bank account, a check will be mailed to you instead. This check(s) will be mailed to the address you provide us with. You may choose to receive gift certificates issued to you for use at the VCS canteen (retail store) or VCS cafeteria here at the VACHS, instead of EFT or check payment. If you choose to receive payment by gift certificate you will be paid for the telemedicine/telehealth visits you participated in at your next in-person visit (e.g. if you complete weeks 2 and 3 by telephone you will receive gift certificates for weeks 2, 3, and 4 at your week 4 visit). Please note, study payments are subject to withholding for outstanding federal debts (i.e., defaulted student loans, interstate child support, back taxes etc.) without notification.

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.

There will be no charge for care received as part of your participation in this study. However, some Veterans are required to pay a co-payment for medical and other services provided by the VA Connecticut Healthcare System that are not part of the study. These co-pay requirements will continue to apply to medical care and services provided by VA that are not part of this study. This may include co-pays for Buprenorphine/Naloxone and/or CPT, if you choose to receive these treatments after your study participation has ended.

If you are injured as a direct result of your participation in this research study, VA will provide necessary medical treatment at no cost to you. Except in very limited circumstances, this medical treatment will be provided in a VA Medical facility. There are no plans to provide compensation for disability or other losses occurring over the long term or if an injury becomes apparent after your participation in the study has ended. However, by agreeing to participate in this research study, you are not waiving or giving up any legal rights to seek compensation. If you have any questions about your rights as a participant, you may contact the Chairman of the Human Studies Subcommittee at 203-932-5711, extension 3350. If you have any complaints, concerns or pertinent questions regarding the conduct of this study, or if you have any questions about compensation for injury, you may contact the Human Studies Coordinator in the Research Office at 203-937-3830**.**

RESEARCH SUBJECTS' RIGHTS

I have read or have had read to me all of the above and I voluntarily consent to participate in this study. The study has been explained to me and my questions have been answered. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled. I will receive a signed copy of this consent form.

The results of this study may be published, but my records will not be revealed unless required by law.

In case there are medical problems, a research related injury or complaints, concerns, or pertinent questions about the research. I have been told I can call Dr. Petrakis at (203) 932-5711 ext. 2244 during the day and the on-call physician at (203) 932-5711, ext. 4471 after hours.

_____ _____

Signature of Subject Date

_____ _____ _____

Signature of Person Obtaining Consent Name of Person Obtaining Consent (Print) Date

_____ _____

Signature of Principal Investigator Date