NCT03078075

INFORMED CONSENT FORM

Title: NIDA CTN-0068 Accelerated Development of Additive Pharmacotherapy Treatment (ADAPT-2) for Methamphetamine Use Disorder

IRB# STU062016-077

Date: December 19, 2018

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System Children's
Medical Center
Retina Foundation of the Southwest
Texas Scottish Rite Hospital for Children
Texas Health Presbyterian Hospital Dallas

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	NIDA CTN-0068: Accelerated Development of Additive Pharmacotherapy Treatment (ADAPT-2)
Funding Agency/Sponsor:	National Institute on Drug Abuse (NIDA)
Principal Investigator:	Madhukar H. Trivedi, M.D.

You may call the principal investigator or research personnel during regular office hours at 214-648-0188 or 214-648-8810. At other times, you may call them at 214-648-5555.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask the researchers to explain anything that you do not fully understand. The purpose of the study, procedures, benefits, risks, inconveniences, discomforts, and other important information about the study are below. If you show you understand the study and decide to participate, you will be asked to sign and date this consent form. You will be given a copy of this form to keep.

Why is this study being done?
This study is being done to test if using two active medications will work better than using two inactive medications to help methamphetamine (meth) use disorder. The two medications to be tested are bupropion (also called Wellbutrin - a pill you take with water) and naltrexone (also called Vivitrol – injected in your buttock). These study medications were chosen based on previous research that showed these medications might work better when taken together as a treatment for meth use disorder.

Why is this considered research?
This is a research study because medication treatments are being compared to placebo (like a sugar pill) treatments. The researchers do not yet know if the medications will be effective. The two study medications being tested are not approved by the Food and Drug Administration (FDA) to treat meth use disorder. The medications have been approved by the FDA for the treatment of depression (bupropion) and alcohol or opioid dependence (naltrexone). There are no medications approved by the FDA to treat meth use disorder. Naloxone (Narcan) is a medication that may be used in the study, if clinically indicated. It is used to confirm you are opioid free before you are given naltrexone. Naloxone is FDA approved for the treatment of opioid overdose effects.

The following definitions may help you understand this study:

Double-blind means neither you nor the researchers will know which medication you are receiving.

Placebo-controlled means that some participants will get a placebo. A placebo looks like the medication we are testing, but it does not include active ingredients.

Randomization means you will be placed by chance (like a flip of a coin) in one of the two study groups: active medication or placebo. Neither you nor the researchers will be allowed to choose which group you are assigned to; a computer program will assign you to a group. About 50% of study participants will receive the active medication during the study. During the study, the computer program may change the group you are in. Neither you nor the researchers will know when or if you change groups. If you appear to respond well to your originally assigned study group, your group will not be changed. **Please note that you should not agree to take part in this study if you are not willing to be in either of the two study groups.*

Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.

Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center and its affiliated hospitals or clinics.

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you are interested in reducing or stopping your meth use.

Do I have to take part in this research study?
No. You have the right to choose whether you want to take part in this study. If you decide to participate and later change your mind, you are free to stop at any time. If you decide not to take part in this research study, it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?
Up to 70 people will take part in this study at each ADAPT-2 research site around the country. There will be around 400 people total in this research study.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. All procedures involved in this study are for research purposes only.

The Screening Phase

To help decide if you qualify to be in this study, you will be asked to come to the clinic at least twice for around 6 hours total for all the needed screening visits. You will be asked to provide urine samples and complete other assessments. You do not need to be free of meth at these visits. You will be paid for your time no matter what the results of the urine test show. You may prefer to break up screening assessments into multiple days. However, we require that all assessments be completed within 21 days. You may be required to provide 2 to 6 urine samples during the Screening Phase.

The following Screening Phase activities will help us determine if you qualify to participate in the study.

- Screening assessments will begin only after you have completed the consent process. Screening generally takes about 4 to 6 hours and includes assessments to make sure it is safe for you to be in this study.
- You will be asked about your drug and alcohol use, lifestyle, involvement with the criminal justice system, and medical and mental health.
- You will be given a physical examination including medical history and vital signs (heart rate, blood pressure, and temperature). A test of your heart functioning will be performed with an electrocardiograph (ECG).
- We will collect blood (around 1 to 3 tablespoons) for lab testing. We will also collect urine samples for drug testing.
- Females will be given a urine pregnancy test. If you are pregnant or breastfeeding, or plan to become pregnant or breastfeed while in this study, you will not be allowed to participate. We do not know how study medications will affect an unborn baby or a nursing child. Females who can have children must agree to use an acceptable birth control method during the study. If you become pregnant during the study, you must tell study staff immediately. Study staff will contact you for information on the result of your pregnancy and the health of your newborn. This information will be reported to the study sponsor.
- One of the last things done in the Screening Phase involves asking about your opioid use. If the medical clinician determines it is appropriate, there may be an additional final step in the Screening Phase called a naloxone challenge. The time for this step will vary. Because we want to help prevent any possible difficulties with naltrexone (Vivitrol), we want to make sure you do not have opioid drugs in your system. An opioid is a type of drug typically used to treat pain, like morphine, Vicodin or oxycodone. Opioids also include drugs like heroin, methadone, and buprenorphine. If you are administered a "narcan" or naloxone challenge, vital signs will be taken before and after the challenge. A naloxone challenge may be administered even if you report no opioid use in the last 7-10 days and have a urine test negative for opioids. If you

are female, another urine pregnancy test may be done prior to the challenge. If you are given a naloxone challenge, the following will occur:

- The challenge includes an injection of naloxone. A medical clinician will monitor you for opioid withdrawal symptoms. Naloxone blocks the action of opioids and lasts only for 20 to 40 minutes.
- The injection will be given under the skin, into a shoulder muscle, or into a vein. If you have no discomfort, a second and possibly third injection of naloxone may be given.
- If you experience any withdrawal symptoms, the challenge will be stopped. You may be given medication to treat your symptoms. You will be monitored until you feel better. You may be given a chance to pass the challenge again by returning for a second challenge on another day. To avoid possible discomfort, it is important for you to avoid using most short-acting opioids for 7 days and long-acting opioids such as methadone for 10 days prior to the challenge.
- If you have no negative effects from the naloxone challenge, you may be ready to be randomized and receive your first study medication injection. Additional naloxone challenges may be done during the study, if clinically indicated.

The Study Medication Phase

Below, "medication" means either the active or placebo form of the study medication.

- During the 12 week medication phase, you will be asked to come into the clinic twice a week for 20 to 90 minutes each visit. The time needed depends on the procedures done at the visit.
- You will receive your study medication, complete assessments, and provide a urine sample.
- Your vital signs will be measured each week. On study medication injection visits, vital signs will be measured before and after each injection. You will receive an injection of either naltrexone or placebo every three weeks during the study medication phase. You will receive four injections total.
- If you are female, a urine pregnancy test will be done at screening. Urine pregnancy tests may be done at other times during the study, as needed.
- You will meet with the study physician for medical management. You will be provided information about your medications and guidance on taking your medication dose.

- We will collect a blood sample to test study medication levels in your system (up to 3 tablespoons each time) prior to each study medication injection and at week 12. We will also collect blood (around 1 to 3 tablespoons) for lab testing at week 6 and week 12.
- During the study, you will be asked to take videos of yourself taking your oral study medication using an app on a smartphone device (referred to as the "app" or "study app") provided by a company working with us on this study - AiCure. An app is application software that allows a device to perform certain tasks. You will be asked to download the free app on your personal smartphone. If you do not have a device or are unable to download the app, a study smartphone device may be available for you to use during the study. You will return this device at the end of the study. If you are provided with a device, you will only be able to use it to take videos of yourself taking your medication and receive text messages about the study. You will not be able to make phone calls or access the Internet. You will receive reminder messages to take your medication through the app on your personal device or the study provided device. The app is equipped with technology that will recognize you and the study medication, and it will be able to assess whether you took the medication properly. The app interactive software will send a message to a secure server, confirming that you took the study medication. The app will record the date and time you took the study medication so that the study site can monitor your medication adherence. Before you are randomized in the study, you will be asked to review and sign a Smartphone App/Device Use Agreement. The agreement contains information about how to use the app and, if needed, the study smartphone device. The agreement also covers in more detail the importance of taking care of and securing your smartphone with the study app (personal or study provided) and bringing it with you to all study visits. It also includes information about how to notify the study staff immediately if the smartphone you are using for the study is lost, and how to use the study provided smartphone only for study related purposes (scheduling appointments, receiving study reminders, and taking study medication dosing videos).

Injectable Medication: You will receive your first study medication injection (either 380 mg of extended-release naltrexone or placebo) after you have completed all screening tests. Study medical staff will inject the medication into your buttock muscle and will monitor you for any adverse (unpleasant or harmful) events. The injection site will be checked at your clinic visits, as necessary, to monitor for any possible injection site reactions. Injections will be administered every three weeks for the remainder of the study. You will be asked to stay in the clinic for about 30 minutes for study staff to monitor possible side effects from either the injectable or oral medication. Prior to each medication injection, medical staff will need to ensure you are opioid-free, and this may include a naloxone challenge. These visits will take about 60 to 90 minutes.

Oral Medication: The oral (by mouth) medication used in this study (150 mg strength pills of long-acting bupropion or placebo) requires taking the pills once a day. Your first dose will be provided in the clinic after receiving the injectable medication. You will

receive a 300 mg daily dose for the first 3 days. From day 4 through the end of the study, the target dose is 450 mg daily. However, throughout the study, your daily oral medication dose may change. It may change because of how you are feeling and side effects you may be experiencing. Each week, you will receive your next week's supply of oral medication. For each clinic visit, you will be asked to bring your oral medication into the clinic with you. Study staff will observe you taking your dose for that day while you are in the clinic.

The Follow-up Phase

After the medication phase, you will be tapered off (reduced gradually) the oral medication under the guidance of the study medical clinician. You will receive a 300 mg daily dose on days 85 and 86. The dose will be further reduced to 150 mg on days 87 and 88. Similar to weekly clinic visits, you will meet with the study medical clinician who is a physician, nurse practitioner, or physician assistant.

- Two follow-up visits will be scheduled after the 12 week medication phase. These follow-up visits will occur in week 13 and week 16. The follow-up visits may take around 1 to 2 hours each. You will be given assessments similar to those completed during the Screening Phase. Urine will be collected at these visits.

OPTIONAL BLOOD DRAW COLLECTION FOR GENETIC TESTING

The National Institute on Drug Abuse (NIDA) would like to help researchers learn more about the role genes play in this condition and other conditions. NIDA is gathering medical information and genetic material from people like you and storing it at Rutgers University Cell and DNA Repository or other NIDA-designated repository (a facility where genetic material can be stored safely). If you agree, study staff will collect an additional sample of blood at one of your scheduled blood draws. Approximately 2 tablespoons of blood will be drawn from a vein in your arm (or other location, if necessary) with a small sterile needle. This is the standard method used to obtain blood for routine hospital tests. Your sample will be marked with a coded identifier and will not be personally identifiable. Neither your name nor any identifying information will be given to the researchers who receive your samples.

De-identified data, including your medical history and results of tests, can be shared by releasing it into scientific databases, including those maintained by the National Institutes of Health (NIH). Sharing this information will help advance medicine and medical research by allowing other researchers to use this information in future research projects. The data will be stored and shared in a manner that would not allow someone to identify you. Please understand that this information cannot be removed once deposited in these databases.

Will my specimens be stored for future use?
Yes, your specimens will be evaluated by research scientists studying various disorders deemed appropriate by NIDA in the future. Some portion may be frozen or stored indefinitely. Stored specimens may be analyzed in the future using additional technologies without you being asked to sign another consent form.
While your direct participation in this part of the study will be brief, the DNA isolated from your blood samples may continue to be studied for many years.

Will my samples be used to study any other diseases besides my condition?
Yes. An important part of this research is to allow for associations to be made between different diseases. Your samples may be used for broad-based research for a variety of disease states.

Will my samples be used for genetic research?
Yes. Genetic research is an important part of the investigation into the causes of these diseases. The causes of many of these diseases are believed to be the result of combinations of inherited genes and possible various exposures to the environment.

There are no plans to inform you, or your relatives, about the results of genetic studies, since at this time the information is not thought to be medically useful.

What is DNA?
DNA means *deoxyribonucleic acid*. DNA is the substance in our cells which contains information we inherited from our parents and other family members. Your DNA contains "genes" which predict things like physical characteristics (eye color, hair color, height, etc.) and may also be a factor in whether you develop or are at risk of developing certain illnesses or disorders.

What is genetic testing?
Genetic tests look for naturally occurring differences in a person's genes, or the effects of specific genes. These differences could indicate an increased chance of getting a disease or condition. Genetic testing includes gene tests (DNA testing) and sometimes biochemical tests (protein testing) if it relates to a specific gene.

In gene tests, DNA in cells taken from a person's blood, body fluids or tissues is examined for differences. The differences can be relatively large - a piece of a chromosome, or even an entire chromosome, missing or added. Sometimes the change is very small - as little as one extra, missing or altered chemical within the DNA strand. Genes can be amplified (too many copies), over-expressed (too active), inactivated, or lost altogether. Sometimes pieces of chromosomes become switched, turned over or discovered in an incorrect location.

How is DNA obtained?
Cells from blood or other body materials are processed in a laboratory that has special equipment that can extract DNA and identify genes.

What will happen to the samples collected for this research?
Researchers will compare information about the health of participants with the results of research tests using their DNA.

Your blood/tissue sample will be used to isolate DNA for genetic analysis. Part of your blood/tissue sample will also be used to grow a long term cell line. This immortalized cell line, called a lymphoblastoid cell line (or fibroblast cell line) will be stored in a Cell Bank and will be available for research, both now and in the future. This also allows us to perform many tests without having to ask you for additional blood/tissue samples.

How long will my samples be kept?
The repository will keep your sample until it is all gone, becomes unusable, or until the researchers or sponsor decide to discard the sample.

If your sample remains stored beyond your lifetime, your sample will be used as described in this document.

May other researchers use my sample?
When you provide a sample for purposes of this study, your sample becomes the property of the sponsor, NIDA, and may be used for future studies or provided to other investigators at other medical research facilities without any identifiers.

Who decides which research scientists may receive samples of my DNA?
NIDA will decide which researchers at this medical center and at other medical centers may receive samples of your DNA. Your samples may be used in other research only if the other research has been reviewed and approved by an Institutional Review Board (IRB).

Could my sample be used for other purposes?
No. Your samples or your DNA will only be used for research.

Research tests using your sample may possibly result in inventions or procedures that have commercial value and are eligible for protection by a patent.

Compensation for any future commercial developments is not available from the University of Texas Southwestern Medical Center at Dallas, its researchers or other facilities or researchers whose research may benefit from the use of your sample.

By agreeing to the use of your sample in research, you are giving your sample without expectation of acknowledgment, compensation, interest in any commercial value or patent, or interest of any other type. However, you retain your legal rights during your participation in this research.

Will the results of research tests be reported to me?
No. Researchers will use samples of your DNA only for research. The samples will not be used to plan your health care.

You will be able to indicate your choice regarding participating in the optional blood genetic component of the study at the end of this consent form.

The urine and blood tests in this study are designed for research, not for medical purposes. They are not useful for finding problems or diseases. Even though the researchers are not looking at your urine or blood to find or treat a medical problem, you will be told if there is something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the urine and blood test results in this study are not for medical purposes, the research results will not be sent to you or to your regular doctor.

STAYING IN TOUCH DURING THE STUDY

To help us keep in touch with you during the study, we will ask you for different ways to contact you so we can remind you of upcoming study visits. We will also ask you to let us know about other people who can pass you a message to contact us. If we need to contact those people, we will not reveal any information about the study, unless you have signed a release for us to do so. We will ask you for your social security number (SSN) and similar information that may be used with public databases to locate you. We ask for this number because it can help us get in touch with you if we have trouble finding you. Your SSN will also help us with paying you for your study participation. We will only use your SSN for locating and paying you. We will always use the contact information you provide us first, before using your SSN. Keeping in touch with the researchers is required for study participation.

If we have trouble finding you, we may also search local jails, prisons, or other settings to locate you. If you become incarcerated or detained within the criminal justice system during the study, we will attempt to contact you and ask to conduct assessments. The study team will facilitate contact with the proper authorities to obtain permission for your research participation while incarcerated. We may need to disclose that you are participating in the study, if the facility requires this information. Any assessment or procedure scheduled for your visit will be completed unless not allowed by the facility. However, any research visits conducted while you are incarcerated may not be confidential.

How long can I expect to be in this study?
This study includes up to a 21 day screening phase, a 12 week medication phase, a medication taper, and follow-up assessments in weeks 13 and 16. The total duration of the study is about 19 weeks.

What are the risks of the study?
Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

Study Medications:
The medications may cause some, all, or none of the side effects listed below.

Bupropion: Most common/less serious side effects (approximately 3-26% of people may experience these symptoms): Sleep problems, dry mouth, dizziness, irritated or runny nose, nausea, vomiting, trouble concentrating, constipation, joint pain, muscle pain, diarrhea, nervousness, ringing in the ears, headache, changes in appetite, weight loss or gain, mild itching or skin rash, increased sweating, loss of interest in sex, stomach/abdominal pain, flushing, changes in taste, weakness, drowsiness, blurry vision, shakiness, sore throat, frequent urination, or anxiety.

Less common but potentially serious side effects (approximately 1-2% of people may experience these symptoms): Seizures, depression, suicidal thoughts or behaviors, severe agitation, irritability, anxiety, confusion, restlessness, engaging in unusual or dangerous behavior, hallucinations, delusions, paranoia, rapid heart rate or chest pains, swollen glands, severe headache/migraine, difficulty urinating, increased blood pressure, and signs or allergic reactions including unexplained rash, blistering or peeling, itching, unexplained swelling, fever, difficulty breathing or swallowing, or severe dizziness.

There may be a higher risk of a person having a seizure on this study's bupropion dose. At doses of 450 mg daily, there are around 4 chances in 1000 that a person taking bupropion will experience a seizure. You cannot participate if you have a seizure disorder or are taking certain medications. Meth misuse can also increase the risk of seizures. Studies suggest bupropion may slow down metabolism and clearance of meth from the body. Some people taking bupropion also have an increased risk of developing eye pain and vision changes requiring emergency treatment to reduce pressure in the eye. Preventive treatment is available if an eye exam shows that you are at risk of this condition. Although bupropion is used to treat depression, a small percentage of people who take antidepressants have increased thoughts of suicide, particularly during the early weeks of medication. Combining bupropion with alcohol, other medications, meth, or other street drugs may have dangerous side effects. Always discuss other prescriptions, over-the-counter medications, and recreational drug use with the study doctor.

If you experience any physical symptoms, let your doctor know so he or she can determine whether they might be caused by the medication and what to do about them. If you should develop daytime drowsiness, you should not drive at the times of the day that this occurs. If you develop dizziness, you should use extra care using stairs and carrying things.

Three tablets are considered one dose, and you should only take one dose per day. Always follow the dosing schedule. For safety reasons, do not take extra tablets.

Naltrexone/Vivitrol: Most common/less serious side effects (approximately 4-33% of people may experience these symptoms): Nausea, vomiting, diarrhea, abdominal pain, headaches, dizziness, insomnia, dry mouth, sore throat, irritated or runny nose, joint stiffness, muscle cramps, back pain, skin rash, changes in appetite, anxiety, tiredness, sleepiness, toothache, or depressed mood.

In rare cases, people who received naltrexone developed suicidal thoughts, or a type of pneumonia (lung inflammation) caused by an excess of a certain type of white blood cells in the lungs. The most serious side effect of naltrexone is liver injury, which has almost always occurred with oral doses of 1400 to 2100 mg per week. Recent study findings show that no evidence of liver injury was found in people receiving once monthly 380 mg Vivitrol injections. Vivitrol is being used every 3 weeks in this study rather than every 4 weeks as currently approved, so there may be additional unknown side effects. For your safety, you will not be allowed to participate in the study if you have acute symptomatic hepatitis or liver failure.

Vivitrol injections will be performed using safe and sterile techniques but may cause pain, tenderness, hardening or damage of body tissues, swelling, redness, bruising, itching, or infection at the injection site. Such injection site reactions have been the most common side effects associated with Vivitrol. The injection site will be monitored after each of the injections. You should report any injection site reactions immediately to the study team. Any participants showing signs of injection site reactions such as a localized infection (abscess), skin infection (cellulitis), body tissue damage, or extensive swelling will be monitored by the study medical staff and treated accordingly.

- Vivitrol may block the effects of opioid pain medications. If you need medications for pain relief while on this study, it is important that you tell your doctor that you are in a study and may be on Vivitrol. Vivitrol will not affect response to non-opioid pain medications such as aspirin or acetaminophen.

Overdose Risks:

Attempts to overcome opioid blockade due to Vivitrol may result in a fatal overdose. Because your tolerance is decreased, you may be more sensitive to the effects of opioids when you stop taking Vivitrol. Use of opioids after discontinuing Vivitrol may result in a fatal overdose because you may be more sensitive to lower doses of opioids.

Naloxone: You may receive naloxone prior to study medication injection, to help ensure it is safe to receive the study medication. Immediately let the study medical team know if you have any of these signs of an allergic reaction so that they may obtain emergency assistance: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

Most common/less serious side effects (approximately 5-15% of people may experience these symptoms): Dizziness; weakness; tired feeling; nausea; vomiting; diarrhea; feeling nervous, restless, or excited; sweating; runny nose; abdominal pain; or trembling.

Less common but potentially serious side effects (approximately 0.5-1% of people may experience these symptoms): Chest pain or fast or irregular heartbeats; feeling lightheaded, fainting; seizure (convulsions); or difficulty breathing.

Let the study medical team know if you have any of these serious side effects.

Withdrawal from Opioids: For anyone who has opioids in their system, naloxone and naltrexone may cause opioid withdrawal symptoms such as agitation, muscle aches, insomnia, nausea, or abdominal cramping.

Allergic Reaction: As with any medication, there is also the possibility of an allergic reaction. You will be monitored for about one hour following your naloxone challenge (if conducted), study medication injection, and oral study medication dose to see how you are responding.

Placebo: If you receive a placebo, you will not receive active medication for your health problem. If your problem becomes worse, your participation in the research will stop. If this happens, your study doctor can discuss other care options with you.

ECG Risk: ECG patch adhesive may be cold and sticky; shaving of hair to get the patch to stick may be required. You may develop a rash or redness where the patches were attached. This mild rash often goes away without treatment.

Urine Samples: You may experience some inconvenience or embarrassment related to providing urine samples.

Blood Draw: You may have around 18 tablespoons of blood total collected because you are in this research study. You may be asked to provide additional blood sample(s) if needed. Risks associated with drawing blood from your arm include minimal discomfort and/or bruising, infection, excess bleeding, or swelling of the vein and surrounding tissue. Clotting and/or fainting also are possible, although unlikely. The trained staff drawing your blood will seek to minimize these potential risks.

Psychological Stress: Some of the questions we will ask you may make you feel uncomfortable, upset, embarrassed, or disappointed. Questions will cover your personal habits, lifestyles, and drug or alcohol use. You may refuse to answer any of the questions, take a break, or stop your participation in this study at any time.

Loss of Confidentiality: Any time information is collected, there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed. You may also experience unanticipated encounters with friends or acquaintances while in the study.

Social Media: If you gave permission to be contacted through social media, the use of social media may pose an increased risk to privacy, but staff will take every effort to minimize that risk.

Study Smartphone App/Device: You will be asked to take a video of yourself taking study medication through an app on a smartphone device. All of your videos and data will be protected to help safeguard your identity. You should also take steps to secure your smartphone. The study staff can tell you more about the app/device and how they will be used.

Embryo or Fetus

Females: If you are part of this study while pregnant or breastfeeding, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant or nursing females cannot participate in the study. A urine pregnancy test will be done prior to your participation in the study and may be repeated later, if needed. If you take part in this study and you are sexually active, you and any person that you have sex with must use medically-acceptable birth control (contraceptives) during the study. Medically acceptable birth control (contraceptives) includes:

(1) surgical sterilization (such as hysterectomy or "tubes tied"),
(2) approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),
(3) barrier methods (such as condom or diaphragm) used with a spermicide(a substance that kills sperm),
(4) an intrauterine device (IUD), or
(5) complete abstinence from sexual intercourse with a male partner.

If you do become pregnant during this study, you must tell the researchers immediately. The research staff follow the outcome of any pregnancy and condition of any newborn and report this to the study sponsor.

Males: There are no known risks for children male participants might father. There are no expected risks to male partners of female study participants.

Other Risks: There may possibly be other side effects that are unknown at this time. If you are concerned about other unknown side effects, please discuss this with the researchers. There may be risks that are unforeseeable.

How will risks be minimized or prevented?

You will be closely monitored by study staff. Trained study staff will do everything possible to prevent or minimize possible risks. You will be referred for appropriate medical treatment if you are injured in the study. After the study is completed, you will be given a list of referrals for continued treatment.

What will my responsibilities be during the study?

While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.
- Report to the researchers any injury or illnesses while you are in the study even if you do not think they are related to your participation in the study.

- Store study medication in a secure place at home away from anyone who is unable to read and understand labels, especially children.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Carry information about the possible study medications you might be on in your purse or wallet.

If I agree to take part in this research study, will I be told of any new risks/findings that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, and show them your medication card from the study.

What are the possible benefits of this study?
If you agree to take part in this study, there may or may not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research, since people respond differently to medications. Various tests will be performed, including a physical exam and laboratory tests, which may show an illness you did not know you had. You may experience a decrease in your drug use. The researchers hope the information learned from this study will benefit others with drug use problems in the future. The study treatments may provide new treatment strategies to reduce meth use. Information gained from this research could lead to better care for people like you who are looking for treatment in the future.

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options:

- You can receive standard care for your condition at this facility.
- You can attend other standard treatment programs in your area, including counseling and self-help programs.

- Please talk to the researchers or your personal doctor about options.

Will I be paid if I take part in this research study?

Yes. You will be given study medication, receive medical management, and use a medication adherence app on your own device at no cost. You may also be able to use a study smartphone device, if needed, during the study. You will be paid for your time, travel, and related costs at the end of each clinic visit as described below:

Visit/Assessment	Amount	# of Possible Payments	Maximum Total
Screening Assessments	$50	1	$50
Screening Phase Clinic Visits (4 possible)	$10	4	$40
Medication Injection Visits	$25	4	$100
Clinic Visits (12 week Medication Phase)	$10	23	$230
In-clinic dosing/medication card return (twice per week)	$5	24	$120
Dosing videos (5 times per wk + 4 taper days)	$5	64	$320
Mid-Treatment (Week 6) and End-of-Treatment (Week 12) Visits	$40	2	$80
Bonus payment for attending all expected visits in each 2-week block during Medication Phase	$20	6	$120
Follow-up Visits (Weeks 13 and 16)	$30	2	$60
Additional data service for dosing app on personal device (to help with data plan costs) OR smartphone device return (if provided by researchers)	$40	1	$40
Maximum Compensation Possible			**$1,160**

A total of up to $50 will be provided for completion of Screening Phase assessments (typically divided among multiple screening visits). Ten dollars ($10) will be provided for each additional Screening Phase clinic visit to provide a urine sample. During the medication phase, $10 will be provided for completion of assessments including a urine sample ($5 will be provided for assessments without a urine sample). You will receive

$25 for each study medication injection visit. You will receive $5 each time you bring the study medication on clinic days and take a self-dosing video via the smartphone while staff observe (up to $120 total). In addition, you will be paid $5 for each video confirming self-dosing, including the taper in week 13 (up to $320 total). You will be paid $40 each for the mid-treatment visit (week 6 visit 2) and the end-of-treatment visit (week 12 visit 2). Additionally, you will receive a bonus of $20 each time you attend all expected visits in each 2-week block during the medication phase (i.e., perfect attendance for Weeks 1-2, 3-4...through Weeks 11-12). You will receive $30 for each follow-up visit in weeks 13 and 16. You may receive up to $40 to help with the cost of additional data needed (if you downloaded the app on your personal smartphone device) OR for the safe return of the study smartphone device (if you received a study device). The total maximum monetary compensation possible is $1,160.

Please note, you may not receive payment for research assessments completed while detained or incarcerated within the criminal justice system.

There are no funds available to pay for parking expenses, lost time away from work and other activities, lost wages, or childcare expenses. Bus passes or other transportation arrangements may be available, if needed.

How will I be paid?

You will be issued a UT Southwestern Greenphire ClinCard, which can be used as a credit or debit card. You will also receive instructions on how use the card. In order to receive study payments, your name, address, date of birth, and Social Security Number (SSN) will be collected from you by the research staff. All information will be stored securely and will be deleted from the UT Southwestern Greenphire ClinCard system once the study has been completed.

Important Information about Study Payments

1. Your SSN is needed in order to process your payments. Should you decide not to provide your SSN, your study participation payment will be decreased at the current IRS tax rate. Study payments are considered taxable income and are reportable to the IRS.
2. An IRS Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.
3. Your ClinCard payment information will not be shared with any third parties and will be kept completely confidential.

This information will remain confidential unless you give your permission to share it with others, or if we are required by law to release it.

UT Southwestern, as a State agency, will not be able to make any payments to you for your participation in this research if the State Comptroller has issued a "hold" on all State payments to you. Such a "hold" could result from your failure to make child support payments or pay student loans, etc. If this happens, UT Southwestern will be

able to pay you for your taking part in this research 1) after you have made the outstanding payments and 2) the State Comptroller has issued a release of the "hold."

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., study procedures described above).However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care.

If you gave permission to be contacted by text messages, you will be responsible for any applicable costs.

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the sponsor, University of Texas Southwestern Medical Center, Parkland Health & Hospital System, or affiliated clinics.

You retain your legal rights during your participation in this research.

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern clinic staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

Your doctor may be a research investigator in this study. If so, s/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

Are there procedures I should follow after stopping participation in the research?
You may decide to stop your participation at any time. There are no consequences for early withdrawal. If you decide to stop taking part in the research study:

- Let your study staff know immediately that you wish to withdraw from the research, so that stopping can be done safely.
- Return study materials no longer needed.
- Discuss your future medical care options (appropriate follow-up care and testing) with your study doctor and/or your regular doctor.
- If you are willing, you may be asked to complete some final study questionnaires, tests, or procedures.

If I agree to take part in this research study, can I be removed from the study without my consent?

Yes. You should know that the study doctor may take you out of this study if it is deemed necessary, even if you would like to continue. The decision may be made to protect your health and safety. You may also be removed because it is part of the research plan that people who develop certain conditions may not continue to participate. Your participation may also be terminated for reasons such as not following study-related directions, going to jail, or because the study is stopped early. If you are asked to end participation early, you will be compensated for any research activities that you have completed.

Will my information be kept confidential?

Every effort will be made to maintain the confidentiality of your study records, but it cannot be guaranteed. Confidentiality and the protection of study participants' privacy is critical and of the utmost importance at all times.

Some information may be shared with medical staff. This information might include the fact that you are in the study, your study visit dates, and any information necessary to treat you in the event of a medical or psychological emergency. Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company. None of the other information that you give us during the study will be part of your medical record; it will only be part of your research record.

Privacy and the AiCure Study App/Smartphone Device:

This study will use an AiCure smartphone app (also referred to as the "app" or "study app") on your personal device or a study-provided smartphone device to take videos of you taking your oral study medication. AiCure is the company providing the app or study device. You should be aware that:

- Personal data will be collected by AiCure for study purposes only. This may include email address, phone number, medication adherence information, and video information (e.g., images of the user's face and audio information).
- Personal data is collected and processed electronically through the AiCure app.

- AiCure is committed to ensuring that all personal data collected is secure at all times. Physical, administrative, and technical safeguards are put in place to protect the security of personal data obtained through the AiCure app. This includes controlled access through the use of individual user identification and password, firewall protection, and encryption of data before transmitting to a secure server.
- For people who use their own smartphone devices or the study-provided smartphone devices: You understand that the study site may contact you at this number.
- By submitting your personal telephone number, you understand that AiCure may contact you at this number (e.g., SMS text message) if you are late taking the study medication. Your collected data may be used by AiCure during the study in order to improve the software and/or report high level statistics. No identifiable data will be disclosed by AiCure.

You should know that certain organizations that may look at and/or copy your medical records/clinic treatment records for research, quality assurance, and data analysis include:

- The National Institute on Drug Abuse (NIDA) (the study sponsor and its agents)
- NIDA's independent Clinical Trials Network's Data and Safety Monitoring Board
- Representatives of government agencies, like the U.S. Food and Drug Administration (FDA), involved in keeping research safe for people
- The UT Southwestern Institutional Review Board
- Researchers at the University of Texas Southwestern Medical Center (Study Lead Team), Parkland Health & Hospital System, and affiliated clinics
- Lifeline, Inc.
- PHARMout Laboratories
- ICON Central Laboratories
- Quest Diagnostics
- Study medications manufacturers – Naltrexone (Vivitrol®) provider Alkermes, Inc. and bupropion (Wellbutrin) provider VA Cooperative Studies Program (CSP) (for safety reporting)
- AiCure (for study videos of oral medication dosing)
- The National Drug Abuse Treatment Clinical Trials Network Clinical Coordinating Center (CCC) – The Emmes Corporation (for data and safety monitoring)
- The National Drug Abuse Treatment Clinical Trials Network Data and Statistics Center (DSC) – The Emmes Corporation (for data management)

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

A description of this research study is available on http://www.ClinicalTrials.gov, as required by U.S Law. ClinicalTrials.gov is a registry and results database of clinical trials conducted in the U.S. and around the world. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This website will not include information that can identify you. You can search this website at any time. At most, the website will include a summary of the results. Data from this study will be available to researchers on another website, https://datashare.nida.nih.gov/, after the study is complete and the data is analyzed. This website will not include information that can identify you. You can view this website at any time.

To help us further protect the information, the investigators have obtained a Certificate of Confidentiality from the U.S. Department of Health and Human Services (DHHS). This Certificate adds special protections for research information that identifies you and will help researchers protect your privacy. With this Certificate of Confidentiality, the researchers cannot be forced to disclose information that may identify you in any judicial, administrative, legislative, or other proceeding, whether at the federal, state, or local level, even in response to a court order or subpoena. There are situations, however, where we will voluntarily disclose information consistent with state or other laws, such as:

- to DHHS for audit or program evaluation purposes;
- information regarding test results for certain communicable diseases to the Texas Department of State Health Services, including, but not limited to HIV, Hepatitis, Anthrax, and Smallpox;
- if you pose imminent physical harm to yourself or others;
- if you pose immediate mental or emotional injury to yourself;
- if the researchers learn that a child has been, or may be, abused or neglected; or
- if the researchers learn that an elderly or disabled person has been, or is being, abused, neglected or exploited.

The researchers will not, in any case, disclose information about you or your participation in this study unless it is included in the Authorization for Use and Disclosure of Protected Health Information for Research Purposes or as stated above.

The Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about your involvement in this research study. In addition, the researchers may not use the Certificate to withhold information about your participation in this research study if you have provided written consent to anyone allowing the researchers to release such information (including your employer or an insurance company). This means that you or your family must also actively protect your privacy.

A Certificate of Confidentiality does not represent an endorsement of this research project by the Department of Health & Human Services or any other Federal government agency, but it adds special protection for the research information about you.

Is there anything else I should know before I decide?

Dr. Trivedi, who is part of a team of researchers at UT Southwestern overseeing the study, has a financial interest in Alkermes, Inc., the maker of Vivitrol®. You should feel free to ask questions about this.

Whom do I call if I have questions or problems?

For questions about the study, contact Madhukar H. Trivedi, M.D. at (214) 648-0188 during regular business hours and at (214) 648-5555 after hours and on weekends and holidays. You may also contact study staff at 214-648-8810. For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

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COMPREHENSION QUESTIONS

1.	My participation in this study is entirely voluntary.	☐ True	☐ False
2.	Information about me or provided by me during the course of this study will NOT be disclosed to others under any conditions.	☐ True	☐ False
3.	I will be asked to attend clinic visits 2 times per week during the 12 week medication phase.	☐ True	☐ False
4.	There are no possible risks or discomforts associated with my participation in this research study.	☐ True	☐ False
5.	There are no other possible treatment options if I choose not to be in this study.	☐ True	☐ False
6.	Information such as my name will be included in future publications and presentations.	☐ True	☐ False
7.	All pills and injections that I could possibly receive in this study (in either study group) will have active ingredients that will definitely help me with my drug use problem.	☐ True	☐ False
8.	I will use a smartphone app to video me taking my oral medication dose.	☐ True	☐ False
9.	The study doctor may end my participation in this research study to protect my health and safety, even if I would like to continue.	☐ True	☐ False
10.	The study is guaranteed to help me stop using methamphetamine.	☐ True	☐ False

GENETICS

BLOOD

You are being asked to have around 30 mL (2 tablespoons) of blood drawn once during the course of this study. This is completely optional and would add approximately 10 minutes to your study visit. You may still participate in this study even if you choose not to provide a blood sample.

Yes____initials. I agree to have a sample of my blood drawn, and researchers may use my genetic material and medical information for future genetic research.

No_____initials. I do not agree to have a sample of my blood drawn for future genetic research.

PERMISSION FOR FUTURE CONTACT

Permission to allow study staff to contact me about future research is completely VOLUNTARY. If I agree, the study team may contact me in the future about new opportunities to take part in studies. At that time, I can decide whether or not I am interested in participating in a particular study.

Yes____initials. I request that study staff contact me about future studies for which I may be eligible.

No_____initials. I do NOT want study staff to contact me about future studies for which I may be eligible.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.

_____

Participant's Name (Printed)

_____ _____ _____ AM / PM

Participant's Signature Date Time

_____

Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM

Signature of Person Obtaining Consent Date Time

DO NOT DISCLOSE

DO NOT FILE OR SCAN THIS CONSENT INTO THE MEDICAL RECORD