Consent Form
Distress tolerance and benzodiazepine discontinuation in opioid agonist therapy, Phase 2
NCT04109118

PI- Tae Woo Park, MD

IRB NUMBER: H-38981
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RESEARCH CONSENT FORM

Basic Information

Title of Project: Distress tolerance and benzodiazepine discontinuation in opioid agonist therapy, Phase 2

IRB Number: H-38981

Sponsor: Boston University Clinical and Translational Science Institute & NIH/National Institute on Drug Abuse (NIDA)

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Study Related Phone Numbers: Monday-Friday, 9am-5pm: 617-638-8541
24 hours: 617-703-0043

Overview

We are asking you to be in a research study. A research study is an organized way of collecting information about scientific questions. This form will tell you what you should expect if you agree to be in the study. There are programs in place to make sure that investigators fulfill their obligations listed in this form.

It is your decision whether or not to join the study. We are doing the research to study an investigational treatment to help opioid agonist therapy (methadone and buprenorphine) patients stop benzodiazepine use. Benzodiazepines (BENZOS) include drugs like Valium, Klonopin, and other medications people take for anxiety and other reasons. If you agree, you will be assigned to the Distress Tolerance treatment (DT-BD), an investigational treatment that makes you have feelings like anxiety from breathing quickly or running in place and teaches you how to cope with those feelings. If you decide to stay for the whole study, you will be in the study for up to 13 weeks. You will find more information about what will happen in this study later in this form. Everyone in this study plans on stopping benzodiazepine use. You will be given medicines to slowly reduce your use of benzodiazepines that is usual medical treatment at Boston Medical Center.

The main risks of being in the study are loss of confidentiality answering sensitive questions and unwanted physical reactions or strain from breathing quickly or running in place to feel like you are having anxiety. You will find more information about risks later in this form.

You might benefit from being in the study because the treatments may lead to a lower risk of benzodiazepine misuse, dependence, and overdose, and other benzodiazepine-related health risks. The

study may additionally increase your understanding of distress tolerance in benzodiazepine discontinuation. You will find more information about benefits later in this form.

You could get these benefits without being in the study by seeking help stopping benzodiazepine use through the Outpatient Behavioral Health Clinic at Boston Medical Center. You will find more information about alternatives later in this form.

Your doctor may also be an investigator in this research study. Being an investigator means your doctor is interested in both you and the study. You may want to get another opinion about being in the study. You can do so now or at any time during the study. A doctor who is not part of this study could give you their opinion about being in the study. You do not have to agree to be in this study even though it is offered by your doctor.

Purpose

Stopping benzodiazepine use is hard. We are trying to find a way to help methadone and buprenorphine patients stop benzodiazepines by teaching them skills that can help them endure the discomfort of benzodiazepine withdrawal (with the help of a gradual decrease in benzodiazepine dose) AND teach skills that can help accept the reasons why people take benzodiazepines in the first place (for example, anxiety). We have created an investigational treatment (Distress Tolerance for Benzodiazepine Discontinuation or DT-BD) that we hope can help patients stop benzodiazepine use and the purpose of this study is to try it out in a small group of patients, so that we can make the investigational treatment better and more tolerable for patients.

What Will Happen in This Research Study

If you agree to take part in the research study, after an initial baseline assessment, you will begin the DT-BD treatments including the benzodiazepine taper.

Your baseline appointment will happen in person at Boston Medical Center at our research office or in a clinical office. At the baseline appointment, which will last up to 3 hours, trained research staff will review study eligibility criteria, collect information about you, your anxiety and substance use, why you take benzodiazepines, withdrawal symptoms, other drug use, distress tolerance measures, affect (mood or how you feel) and sleep symptoms, and urine for drug use and pregnant screens. You will receive a $30 prepaid card called a ClinCard for completing these baseline assessments. You will not be eligible to enroll in the study if a) your urine screen shows that you are currently pregnant, b) you report use of illicit drugs (including opioids, cocaine, barbiturates, or unprescribed amphetamines) in the past 30 days, or c) if your urine drug use screen shows use of illicit drugs (including opioids, cocaine, barbiturates, or unprescribed amphetamines). The results of the urine drug screen may take a few days to process.

If your urine screen shows that you are not currently pregnant and you report no use of illicit drugs in the past 30 days, you will be able to proceed to the next visit. If your pregnancy test and/or urine drug screen results show use of illicit drugs, you will not be eligible to continue with the study. If your urine drug screen showed use of illicit drugs, but you would still like to participate in the study, you will have the opportunity to return in 30 days where you will be asked to re-take the urine drug screen, pregnancy test, and report illicit drug use in the past 30 days. If at that second screen, you are not currently pregnant, report no illicit drug use, and there is no presence of illicit drugs, then you will be able to continue in the study by completing the baseline assessments again.

You will not receive compensation for completing the baseline assessments for the second time.

If you are actively prescribed benzodiazepines, we will need permission from you to contact your prescriber and inform them that we will be providing you benzodiazepine medication with the aim of tapering you off of them. You will need to provide the name and phone number of your prescriber.

After baseline assessment, you will come in weekly for a total of 13 weeks. At each visit, you will meet with the principle investigator. The therapy consists of 1-hour therapy sessions. Participants will be taught skills designed to improve their ability to tolerate distress during the benzodiazepine taper. The DT-BD investigational treatment also involves teaching interoceptive exposure therapy skills, with elements of acceptance and commitment therapy (ACT) and relapse prevention. Interoceptive exposure is a form of therapy that makes you have feelings that can come with anxiety and benzodiazepine withdrawal such as feeling out of breath or dizzy and teaches you to learn to deal with those feelings.

During the 13-weeks treatment, you will undergo a benzodiazepine taper (meaning you will gradually stop taking your benzodiazepine medicine). After the first study visit today, which includes a therapy session, there will be 4 weekly therapy sessions, then the 9-week benzodiazepine taper begins. You will meet weekly with a supervising physician for a 30-minute visit who will monitor the taper. Each week, you will receive a week of benzodiazepine medication. The benzodiazepine will be gradually tapered starting at the 5th week. In addition to being provided medication, trained research staff will collect information on your benzodiazepine withdrawal, other drug use, and affect and sleep.

We will ask you to complete a daily self-reported measure on your substance use, benzodiazepine use, and sleep quality and duration through a daily online survey link which will be sent to your email or mobile phone (depending on your preference) to be completed about the previous day. If you do not own a mobile phone, we will provide one for you. You will be asked to return the phone if you decide to withdraw from the study at any point. You will be asked to return the phone at the end of the study.

You will also receive a breathalyzer test and research staff will perform a urine drug screen at each visit. We will monitor you for oversedation during weekly physician visits which may lead to a temporary hold of benzodiazepine medication. Additionally, we will be conducting a pill count at the beginning and at the end of this study to help determine if you are taking more medication than prescribed. If the number of pills during the pill count is short of the expected amount by over 20% at both visits, you will be discharged from the study. After the start of the study, if you test positive for cocaine, synthetic cannabinoids, non-prescribed opioids, barbiturates, z-drugs (for example, Ambien), or amphetamines during the urine drug screen or report using these substances a total of 3 times during the study, you will be discharged from the study. If there is evidence of ongoing substance use of illicit substances, we may refer you to a higher level of treatment including inpatient detoxification or residential treatment. Any treatment referral or discharge from the study will be coordinated with the outpatient opioid agonist therapy OAT and/or benzodiazepine prescriber.

If during any study visit, you appear intoxicated or impaired, the research staff will reschedule the interview. If you are experiencing anxiety and insomnia during the taper, we will offer initiation of a selective serotonin reuptake inhibitor (SSRI), for example Prozac, or an SSRI dose increase if already prescribed for anxiety, and/or a sleep medication, including trazodone or mirtazapine to help you with insomnia.

You are required to attend all 13 visits after today's visit. If you miss a study visit, you will need to contact us within 14 days of your missed appointment. If we are unable to get in contact with you during those 14 days, you will be considered dropped out of the study.

At the end of the 9-week taper, you will be asked to take part in an interview to talk about what you thought about the DT-BD treatment and how it can be improved. We will audio record the interviews. These recordings will be given to a third-party transcription company so that they can transcribe the audio recordings into written words.

The ways we will protect your privacy and confidentiality are described in a separate section later in this form.

You will be one of four subjects who will be asked to be in the study.

Risks and Discomforts

There are several risks to participating in the study described below. There are risks involved with the benzodiazepine taper, but the taper is happening as part of your clinical care and not for research purposes. We will review a separate form with you that explains the risks of the taper.

Psychological Stress and Discomfort: During the study, you may feel distressed from the study's focus on your benzodiazepine and other drug use and behaviors. You may additionally feel frustration and stress from the investigational treatment procedures and administration of laboratory tasks (breath-holding and mirror tracing persistence task – computerized version [MTPT-C]) including temporary discomfort, such as frustration and other temporary symptoms of psychological stress. Your responses are confidential. You can refuse to answer any particular question you do not want to answer, discontinue any laboratory task, and are free to withdraw from the study at any time. In addition, referrals will be available upon request if you experience distress related to the study. The PI and research staff will be available to respond to any concerns and distress that may result from the study visits or investigational treatment. The results of these urine drug tests could potentially be psychologically stressful. This information will be delivered by a trained physician.

Loss of confidentiality: As with any research study, there is always a risk of loss of confidentiality. However, we will employ measures described later in this form how we will minimize the risk of breach of confidentiality.

Interoceptive Exposure Risk: As part of the Interoceptive exposure therapy, you may be asked to perform tasks (e.g. hyperventilating, jogging in place) that may unwanted physical reactions or strain. Hyperventilating may cause dizziness, light headedness, numbness, blurred vision, and/or hot flashes or sweating. Jogging in place may increase heart rate and cause joint or muscle strain. The exercises will be very low impact and done for short periods of time. We ask that you inform the research staff if you have any pre-existing health conditions, such as high blood pressure, heart problems, or joint/muscle injuries, so that we may personalize your tasks. The research staff will stop any task if the burden on your body becomes too great.

There may be unknown risks or discomforts involved.

If you decide that you want to stop being in the study, we ask that you let us know. If you stop the study early during the benzodiazepine taper, you may experience symptoms of benzodiazepine withdrawal listed above. You are free to stop at any time, but if you tell us, we can do some things to help keep you safe. These things include making a referral to the Boston Medical Center's Project ASSERT, which can help connect you with an inpatient detoxification facility.

If you get pregnant while you are in this study, it could be bad for the fetus. You must use birth control if you are a woman having sex with men while you are in this study. You should also keep using birth control for three months after the study ends. Only some birth control methods work well enough to be safe while you are in this study. These methods are oral contraceptives (the pill), intrauterine devices (IUDs), contraceptive implants under the skin, contraceptive rings or patches or injections, diaphragms with spermicide, and condoms with foam. You should not be in this study if you are a woman who has sex with men and cannot use one of these birth control methods.

Potential Benefits

The benefits of being in this study may be: a lowered risk of benzodiazepine misuse or dependence, overdose death, and opioid agonist therapy treatment failure as a result of stopping benzodiazepine use. Discontinuation of benzodiazepines may reduce health risks of benzodiazepine use. Throughout the study, you may develop a more thorough understanding of the roles of distress tolerance in benzodiazepine discontinuation. Learning distress tolerance-related skills may help with underlying problems of anxiety or reduce risk of relapse to benzodiazepine use. You may not benefit directly but your participation in this research study may have a broader impact by helping to develop a distress tolerance-based treatment for opioid agonist therapy patients who regularly use who use benzodiazepines. This distress tolerance investigational treatment may help people discontinue benzodiazepine use, treat underlying symptoms of anxiety, and decrease risk of relapse to benzodiazepine use.

Alternatives

The following alternative procedures or treatments are available if you choose not to be in this study:

- If you are seeking help to stop benzodiazepine use, you can be seen at the Outpatient Behavioral Health Clinic at Boston Medical Center
- For urgent care, you can be seen at the Faster Paths to Treatment center at Boston Medical Center

Costs

Items and services done only for study purposes will be provided at no cost to you. They won't be billed to your health insurance either. These items and services include the psychotherapy treatment, pregnancy test (if applicable), and a mobile phone (if needed). You or your health insurance will be billed for all costs that are part of normal medical care. These costs include co-payments and deductibles for the benzodiazepine taper, pregnancy test, urine-drug screens, and physician visits. You can ask any questions now about insurance coverage for this study or about the research activities paid for by the sponsor. You can also ask the investigator later, using the number on the first page of this form. There may additionally be costs associated with transportation to the study visits. The payment for participating will cover the cost of transportation. Bus vouchers will be additionally be available, if desired.

Payment

You will earn $30 in a prepaid card called a Clincard by completing your baseline assessment, regardless of the results of your pregnancy test and urine drug screen.

- If you are found to not be eligible due to a urine pregnancy screen or drug use self-report, you will have the opportunity to return in 30 days to re-take the self-report, at which you will be asked to complete the basement assessment again. There will be no compensation for completing the baseline for the second time.
- If you are found to not be eligible due to self-reported illicit drug use, pregnancy screen, or urine drug screen, you will not be able to continue with the study to receive the additional payments mentioned below. However, if you return after 30 days and you are not currently pregnant, report no illicit drug use in 30 days, and your urine drug screen is negative for illicit drugs, you may continue with the study and have the opportunity to receive the payments mentioned below.

Participants will receive $30 at baseline visit. Participants will be paid $2 for each daily mobile assessment from week 2 to week 13 (earning up to $168). They will additionally receive a $50 ClinCard for a post-intervention interview. Participants can earn up to $248 for participating in the study.

Confidentiality

We must use information that shows your identity to do this research. Information already collected about you will remain in the study record even if you later withdraw.

We will store your information in ways we think are secure. We will store urine samples in a refrigerator in a locked room and take them the same day to be processed in the BMC laboratory. We will store paper files in locked filing cabinets. We will store electronic files in computer systems with password protection and encryption. However, we cannot guarantee complete confidentiality.

This study is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. All studies funded by the National Institutes of Health that involve identifiable information or biological samples are covered by a CoC**.** The CoC provides how we can share research information or biological samples. Because we have a CoC, we cannot give out research information or biological samples that may identify you to anyone that is not involved in the research except as we describe below. Even if someone tries to get your information or biological samples in connection with a legal proceeding, we cannot give it to them. The CoC does not prevent you from sharing your own research information. We will record information from this study in your medical record, such as information related to your medical care. Please ask us if you have any questions about what information will be included in your medical records. You should know that once information has been put into your medical records, it is not covered by the CoC. However, information in your medical records is protected in other ways.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. This includes the urine drug screens which we are conducting as standard of care for benzodiazepine discontinuation. The results of the drug screens will be part of your medical

record. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

If you agree to be in the study and sign this form, we will share information that may show your identity with the following groups of people:

- People who do the research or help oversee the research, including safety monitoring.
- People from Federal and state agencies who audit or review the research, as required by law. Such agencies may include the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and the Massachusetts Department of Public Health.
- People who see your medical records. Please ask us if you have any questions about what information will be included in your medical records.
- Any people who you give us separate permission to share your information.

Some study staff members are mandated reporters, including the study's Principal Investigator, Dr. Park. You should know that we are required to report information such as child abuse or neglect; elder abuse; specific reportable diseases; harm to self or others.

If you are in immediate danger of hurting yourself at any time in the study, the study team will try to work with you on a plan to keep you safe. Because study staff will be trying to protect you, it is possible that your information will be shared with others as part of a plan for safety.

We will share research data where we have removed anything that we think would show your identity. There still may be a small chance that someone could figure out that the information is about you. Such sharing includes:

- Publishing results in a medical book or journal.
- Adding results to a Federal government database.
- Using research data in future studies, done by us or by other scientists.
- Using biological samples in future studies, done by us or by other scientists.

The daily mobile assessment will be sent to your email or mobile phone (depending on your preference) using a Boston Medical Center sponsored survey management program. We will also use a third-party web service program called Twilio, which will allow us to text survey links to your mobile phone number. Twilio will access your mobile phone number to send the text with the survey link. However, Twilio is set up so that your phone number does not get saved on Twilio's servers. Additionally, Twilio will not have access to your protected health information.

Additionally, audio files will be sent to a commercial transcription company to be transcribed in order for the research team to better study your responses.

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.

Use and Sharing of Your Health Information

The research team has to use and share your health information to do this study, including information that may identify you. By agreeing to be in this study and signing this form, you are giving us your permission where needed to use and share your health information as described in this form.

Health information that might be used or shared during this research includes:

- Information that is in your hospital or office health records. The records we will use or share are those related to the aims, conduct, and monitoring of the research study.
- Health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.
- The health information specifically includes:
    - Mental health communications (with a psychiatrist, psychologist, clinical nurse specialist, marriage-, family-, rehabilitation-, or mental-health-counselor, or educational psychologist)
    - Results of urine drug screens which will be part of your medical record at Boston Medical Center

The reasons that your health information might be used or shared with others are:

- To do the research described here.
- To make sure we do the research according to certain standards set by ethics, law, and quality groups.
- To comply with laws and regulations. This includes safety-related information.
- To protect you. As we explained above, if you are in immediate danger of hurting yourself, it is possible that your information will be shared with others as part of a plan for safety.

The people and groups that may use or share your health information are:

- Researchers involved in this research study from Boston Medical Center, Boston University, and/or other organizations
- Other people within Boston Medical Center and Boston University who may need to access your health information to do their jobs such as for treatment, research administration, payment, billing, or health care operations
- People or groups that the researchers use to help conduct the study or to provide oversight for the study
- The Institutional Review Board that oversees the research and other people or groups that are part of the Human Research Protection Program that oversees the research
- Research monitors, reviewers, or accreditation agencies and other people or groups that oversee research information and the safety of the study
- Public health and safety authorities who receive our reports about child abuse or neglect; elder abuse; specific reportable diseases; harm to others.
- Other care providers and public safety authorities who may be involved in helping to protect you if you express thoughts about hurting yourself.

We ask anyone who gets your health information from us to protect the privacy of your information. However, we cannot control how they may use or share your health information. We cannot promise that they will keep it completely private.

The time period for using or sharing your health information:

- Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

Your privacy rights are:

- You have the right not to sign this form that allows us to use and share your health information for research. If you do not sign this form, you cannot be in the research. This is because we need to use the health information to do the research. Your decision not to sign the form will not affect any treatment, health care, enrollment in health plans, or eligibility for benefits.
- You have the right to withdraw your permission to use or share your health information in this research study. If you want to withdraw your permission, you must write a letter to the Principal Investigator at the address listed on the first page of this form. If you withdraw your permission, you will not be able to take back information that has already been used or shared with others. This includes information used or shared to do the research study or to be sure the research is safe and of high quality. If you withdraw your permission, you cannot continue to be in the study.
- When the study has been completed for everyone, you have the right to request access to the health information that we used or shared to make your treatment or payment decisions. If you ask for research information that is not in your medical record, we might not give it to you, but we will explain why not. You may use the contact information on the first page of this form to find out how to get your health information. You may also contact the HIPAA Privacy Officer at Boston Medical Center at DG-privacyofficer@bmc.org

Compensation for Injury

If you think that you have been injured by being in this study, please let the investigator know right away. Use the phone number on the first page of this form. You can get treatment for the injury at Boston Medical Center or at any healthcare facility you choose. There is no program to provide compensation for the cost of care for research related injury or for other expenses. Other expenses might be lost wages, disability, pain, or discomfort. You or your insurance will be billed for the medical care you receive for a research injury. You are not giving up any of your legal rights by signing this form.

Re-Contact

We would like to ask your permission to contact you again in the future. This contact would be after the study has ended. Please initial your choice below:

____Yes_____No You may contact me again to ask for additional information related to this study

____Yes_____No You may contact me again to ask for additional biological samples related to this study

____Yes_____No You may contact me again to let me know about a different research study

Subject's Rights

By consenting to be in this study you do not waive any of your legal rights. Consenting means that you have been given information about this study and that you agree to participate in the study. You will be given a copy of this form to keep.

If you do not agree to be in this study or if at any time you withdraw from this study you will not suffer any penalty or lose any benefits to which you are entitled. Your participation is completely up to you. Your decision will not affect your ability to get health care or payment for your health care. It will not affect your enrollment in any health plan or benefits you can get.

During this study, we may find out something that might make you not want to stay in the study. If this happens, we will tell you as soon as possible.

We may decide to have you stop being in the study even if you want to stay. Some reasons this could happen are if staying in the study may be bad for you, or if the study is stopped.

Questions

The investigator or a member of the research team will try to answer all of your questions. If you have questions or concerns at any time, contact Imme Kobayashi at 617-414-1940. Also call if you need to report an injury while being in this research.

You may also call 617-358-5372 or email medirb@bu.edu. You will be talking to someone at the Boston Medical Center and Boston University Medical Campus IRB. The IRB is a group that helps monitor research. You should call or email the IRB if you want to find out about your rights as a research subject. You should also call or email if you want to talk to someone who is not part of the study about your questions, concerns, or problems.

Subject: _____
Printed name of subject

By signing this consent form, you are indicating that

- you have read this form
- your questions have been answered to your satisfaction
- you voluntarily agree to participate in this research study
- you permit the use and sharing of information that may identify you as described, including your health information.

_____ _____
Signature of subject Date

Researcher: _____
Printed name of person conducting consent discussion

I have personally explained the research to the above-named subject (who has read this consent form) and answered all questions. I believe that the subject understands what is involved in the study and freely agrees to participate.

_____ _____
Signature of person conducting consent discussion Date

BMC and BU Medical Campus IRB
IRB NUMBER: H-38981
IRB APPROVAL DATE: 06/30/2021