University of Pittsburgh

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: Proof of Concept Study to Treat Negative Affect in Chronic Low Back Pain (TNA-LBP)

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KEY INFORMATION

You are being asked to take part in a research study. Research studies include only people who choose to take part. The study team members will explain the study to you and answer any questions you might have. You should take your time to make your decision.

- The purpose of this research is to evaluate whether antidepressants (AD), fear avoidance rehabilitation (EFAR), or the combination of the two is the better treatment for chronic low back pain patients with high negative affect.
- An optional sub-study will obtain qualitative feedback from participants that will help us better understand and address stigma in people with pain and negative affect.
- The duration of this study is 8 months (32 weeks).

Once you are enrolled into the study, you will be randomly assigned, like a flip of a coin. We cannot predict or influence the group in which you will be randomized.

Antidepressant (AD) group
Subjects will be prescribed antidepressant medication under the care of a nurse practitioner and psychiatrist. Side effects are mitigated by AD check-ins every 2 weeks.

Enhanced Fear Avoidance Rehabilitation (EFAR) group
Subjects will receive physical therapy and pain education during their 8 physical/occupational therapy sessions. Trained physical/occupational therapists will determine the activities as part of the treatment.

AD+EFAR group
Subjects will receive a combination of both antidepressants and physical therapy.

Optional Qualitative Interview
Subjects will complete two qualitative interviews, one prior to the start of treatment and one following the first phase of treatment.

Risks and side effects include those which are:

- *Antidepressant:* Antidepressants may lead to side effects, such as loss of appetite, weakness, and/or muscle pain.
- *Physical/Occupational therapy:* Physical therapy may temporarily aggravate your low back pain during the treatment sessions.
- *Opioid-weaning:* You may report increased physical and psychological withdrawal, such as craving, irritability, or more pain.
- *Collection and storage of private health information:* There is a risk of breach of confidentiality of your private health information obtained from your medical record.

The possible benefit is that the treatment you received may help you improve back pain, function, and mood and may help you wean from opioids more effectively than by standard care measures alone.

You may choose not to participate in this research and continue to have your pain and medications managed by your healthcare team.

Why is this research study being done?
Approximately 50 million Americans have Low Back Pain. One of the most common problems associated with having chronic pain is also having several mood symptoms at the same time, such as depression and anxiety. These symptoms can be called "negative affect". People with low back pain and high negative affect may have higher pain levels and worse function. Such people may avoid doing a variety of activities because of an increased concern that pain will increase to and unmanageable level, which is also known as "fear avoidance of activities."

This research study will compare three treatments for patients with chronic low back pain and negative affect:

- **Antidepressant Treatment (AD)**: Prescribing antidepressant medication under the care of a nurse practitioner and psychiatrist. We will use different medication than what you might have already been prescribed before.
- **Enhanced Fear Avoidance Rehabilitation (EFAR)**: Weekly sessions of physical or occupational therapy. This is a different type of physical therapy and what you may have already had.
- **AD+EFAR**: Combined treatment of antidepressants and physical therapy

Who is being asked to take part in this research study?
You are being invited to participate in this research study because you are 18-75 years of age and you have chronic low back pain along with depression or anxiety symptoms.

How long will I take part in this research study?
All three treatment groups will take part in the study for 8 months. Phase 1 of the study ends at Month 4 and Phase 2 ends at Month 8. During Phase 1, everyone who participates in this study will attend a total of four study visits in addition to the unique visits per treatment group over this four-month period. Additional visits may be needed for Phase 2 of the study.

AD Treatment Group:
- 7 AD visits (phone call)

EFAR Treatment Group:
- 4 physical/occupational therapy sessions at the Center for Rehabilitative Services and 4 sessions by video call.

AD+EFAR Treatment Group:
- 7 AD Visits (in-person or via phone call)
- 4 physical/occupational therapy sessions at the Center for Rehabilitative Services and 4 sessions by video call.

For subjects already prescribed opioids who agree to reduce their dose gradually:
- 4 opioid weaning visits with a study doctor, that can be done in-person or through phone call

What will happen in this research study?

You will be assigned by a random computer program to one of three study intervention groups, after signing consent. Neither you nor the study team gets to choose your group. The three groups are:

AD Treatment Group:

· 7 AD visits (phone call): If you are in this group and NOT on an anti-depressant, the study nurse practitioner or physician will first assess how you did on any previous antidepressant medication and then prescribe you a new antidepressant medication for the study. We will continue to work with you through the study visits to optimize your treatment.

EFAR Treatment Group:

· 4 physical/occupational therapy sessions which will be in-person and 4 sessions can be via telemedicine.

AD+EFAR Treatment Group:

· 7 AD Visits and 8 EFAR sessions (in-person or via phone call): If you are in this group and NOT on an anti-depressant, the study nurse practitioner or physician will first assess how you did on any previous antidepressant medication and then prescribe you a new antidepressant medication for the study. We will continue to work with you through the study visits to optimize your treatment.

The subjects assigned to AD treatment will receive antidepressants every day for 4 months. The EFAR group subjects will receive graded exposure physical therapy. Subjects assigned to the AD+EFAR treatment will receive both antidepressant and physical therapy. Subjects who were already prescribed opioids by their regular doctor will be able to continue receiving opioid prescriptions, and they will also have the option to gradually reduce their dose if they want to under the supervision of a study doctor.

You will have to complete several questionnaires at each study visit. We also ask that you complete surveys each week at home that we send to you via email or through a text message on your phone. These surveys are estimated to take 10 minutes to complete, and they can be completed on a smart phone, a tablet, or a computer.

At the end of Month 4, we will determine who has improved (responders) or not improved (non-responders) with the treatments. Responders to the AD treatment will continue their antidepressant medication for another 4 months. Responders to the EFAR treatment will continue exercise guidelines at home for another 4 months. Non-responders in the AD or EFAR treatment will be given a choice to rerandomize to either the AD or EFAR group, for another 4 months. Those in the AD+EFAR treatment group will not be rerandomized at the end of Month 4

Overview of Schedule

Week 1(baseline):	Study visit 1, Weekly survey
Week 2:	Study visit 2 (prescribe AD), Weekly survey, EFAR visit 1 (EFAR subjects only, weekly visits for 8 weeks), Sensory testing (opioid-users only), optional qualitative interview
Week 3:	Weekly survey
Week 4:	Weekly survey, AD visit 1, EFAR visit 1 (EFAR+AD subjects only, weekly visits for 8 weeks), Opioid weaning visit 1
Week 5:	Weekly survey

Week 6:	Weekly survey, AD visit 2
Week 7:	Weekly survey
Week 8:	Study visit 3, Weekly survey, AD visit 3, Opioid weaning visit 2, Sensory testing
Week 9:	Weekly survey
Week 10:	Weekly survey, AD visit 4
Week 11:	Weekly survey
Week 12:	Weekly survey, AD visit 5, Opioid weaning visit 3
Week 13:	Weekly survey
Week 14:	Weekly survey, AD visit 6
Week 15:	Weekly survey
Week 16:	Study visit 4, Weekly survey, AD visit 7, Opioid weaning visit 4, Sensory testing, optional qualitative interview
Week 17-32:	Responders of treatment will receive treatment at-home for another 4 months. Non-responders will be rerandomized to receive either AD or EFAR for another 4 months. Surveys for Phase 2 of study will be bi-weekly instead of weekly.

Study Visit 1 (Week 1)
The Screening Visit will take about 2 hours at the UPMC Pain Medicine Clinic at Centre Commons. At this visit, you will:

- Sign Consent Form
- Meet with study physician to collect demographic information, medical history and current medications.
- If you are already prescribed opioids, take a urine drug test to assess the type and amount of opioids you are using now, as well as test for certain drugs.
    - If your urine shows you have taken illegal drugs, you cannot be in this study. The results of the urine drug test will not become part of your medical record. These test results will, however, remain part of your study record.
- Given a urine pregnancy test if you are female and of childbearing age (AD or AD+EFAR group only)
- Per PI's clinical judgment, provide a blood sample if you are on a tricyclic antidepressant medication (like nortriptyline) to optimize the current dose.
- Given online questionnaires to fill out regarding your feelings about treatment and the future, prescription opioid use, recent behaviors, opioid withdrawal symptoms, attitudes, opinions, pain history and levels, stress levels, and anxiety levels.

<u>Opioid Weaning</u>
This part of the study is completely voluntary. You do not have to decide now and you can decide within the first four weeks of the study. If you agree to gradually reduce your prescribed opioid dose the study physician will work with you to reduce the daily opioid dose by 10-15% over the course of each month, for a total of four months. You can stop the opioids altogether over the course of the four months if you wish. The study doctor will prescribe the opioids for you during the study. You can halt the weaning at any time. You will receive weekly text messages or emails to complete online surveys about your opioid use, any cravings, pain,

anxiety, and stress levels. Research staff will be available via email, phone, and text messaging to provide support during regular business hours.

Study Visit 2 (Week 2)
At this visit, we will:

- Meet with study physician or nurse practitioner to follow-up about side effects, your progress with treatment, and to answer any questions you have.
- Prescribe antidepressants (AD or AD+EFAR Treatment group only)
- Administer the Columbia-Suicide Severity Rating Scale (CSSRS)
- Give you online questionnaires to fill out
- Perform sensory testing (opioid-users only)

Quantitative Sensory Testing
Quantitative sensory testing is tested by having subjects rate a painful stimulus such as heat pain. Subjects on opioids will be asked to do the quantitative sensory testing at study visit 2 (Week 2), visit 3 (Week 8), and visit 4 (Week 16). Those subjects who undergo the re-randomization procedure will be asked to do the sensory testing again for the last 4 months of the study according to the same schedule.

Study Visit 3 (Week 8)
At this visit we will:

- Meet with study physician or nurse practitioner to follow-up about side effects, your progress with treatment, and to answer any questions you have.
- Collect a urine drug screen test (opioid-users only)
- Administer the Columbia-Suicide Severity Rating Scale (CSSRS)
- Give you online REDCap questionnaires to fill out
- Perform sensory testing (opioid-users only)

Study Visit 4 (Week 16)
At this visit we will:

- Meet with study physician or nurse practitioner to follow-up about side effects, your progress with treatment, and to answer any questions you have.
- Collect a urine drug screen test (opioid-users only)
- Administer the Columbia-Suicide Severity Rating Scale (CSSRS)
- Give you online REDCap questionnaires to fill out
- Perform sensory testing (opioid-users only)

After this final visit, subjects that did not respond to the treatment they had the first 4 months will be given the option to rerandomize. Those who are non-responders and receive another treatment may receive additional AD or EFAR visits following the timeline on page 4. They may also continue opioid weaning for the second half of the study upon request. Subjects who are placed in the new treatment will continue with study visits and AD or EFAR visits for another 4 months. Subjects in the AD or EFAR treatment group that responded to the treatment will transition to at-home treatments or activities without the need to attend additional study visits or in-person visits. However, upon request, the study psychiatrist/nurse practitioner, therapist, and study coordinator will be available to answer any questions and concerns.

AD Visits 1-7
The nurse practitioner will meet with or contact the participant every 2 weeks for medication adjustment parameters. The nurse practitioner will discuss about symptoms and side effects to determine potential dose adjustment or medication change.

EFAR Visits 1-8
EFAR visits consist of 8 graded exposure PT/OT sessions per week. During these sessions, participants will complete the Fear of Daily Activities Questionnaire (FDAQ) administered by the therapist. Trained therapists will carry out the fear avoidance PT/OT sessions at each study site. The degree of graded exposure to functional activities for EFAR visits is determined by using the FDAQ. The components of the activity are introduced at a basic level that elicit minimal amounts of fear, and then is gradually increased to higher levels of activity. During the sessions, participants will also receive verbal and written educational material regarding chronic low back pain and fear of movement.

Opioid Weaning Visits 1-4
Opioid weaning visit 1 is required to be completed for those prescribed opioids. Participants will meet with the study physician to discuss and develop an opioid weaning guideline. Participants will share symptoms and concerns during these visits, while allowing the study physician to make necessary dose adjustments. If the participant decides that they don't want opioid tapering, opioid weaning visits 2-4 will not be necessary.

Qualitative Interview Visits 2 and 4,
A subset of 60 participants from the trial will be recruited to participate in two qualitative interviews. Participants will complete two 60–90-minute audio recorded interviews, one prior to the initiation of treatment and the second in the two weeks following completion of phase one of the study. The interviews will be conducted using open-ended, inductive questioning organized around broad topics identified and piloted among the research team. Topics for the baseline interview will include participants' experiences of public stigma, their own stigmatic beliefs, perceived causes and sources of stigma, and how they believe stigma can be addressed. Topics for the follow-up interview will include changes in stigma over the course of the intervention, if and how the intervention improved their stigma, and what they would like to see in future interventions that address the impact of stigma on patients with CLBP and high NA.

Will I receive any results from participation in this research study?
Individual research results from the urine pregnancy testing and urine drug toxicity screen will be disclosed to subjects prior to the completion of Study Visit 2 (Week 2).

What are the possible risks, side effects, and discomforts of this research study?
(1) Risks of Taking Study Antidepressants

If you are assigned to the Antidepressant Treatment group, you will most likely only be prescribed one medication at a time. The study psychiatrist or nurse practitioner will only prescribe you the medication that best suits you.

Side Effects of Taking Bupropion (Wellbutrin):

Common Side Effects

- Loss of appetite
- Dry mouth
- Skin rash
- Sweating
- Shakiness
- Stomach pain
- Agitation
- Anxiety
- Dizziness
- Insomnia
- Muscle pain
- Nausea
- Fast heartbeat
- Frequent urination
- Hyponatremia (low sodium levels)

Uncommon Side Effects

- Suicidal thoughts of actions
- High blood pressure
- Seizures
- Manic episodes
- Increased energy
- Racing thoughts
- Reckless behavior
- Severe trouble sleeping

Side Effects of Taking Duloxetine (Cymbalta):

Common Side Effects

- Loss of appetite
- Dry mouth
- Mild nausea
- Drowsiness
- Constipation
- Hyponatremia (low sodium levels)

Uncommon Side Effects

- Stomach pain
- Itching
- Loss of appetite
- Dark urine
- Light-headedness, weakness
- Agitation
- Hallucinations
- Fever
- Fast heartbeat
- Vomiting
- Diarrhea
- Stiff muscles
- Difficulty in urinating

Side Effects of Taking Escitalopram (Lexapro):

Common Side Effects

- Nausea

Uncommon Side Effects

- Suicidal thoughts or actions

- Drowsiness
- Weakness
- Dizziness
- Anxiety
- Sweating
- Shaking
- Dry mouth
- Constipation
- Diarrhea
- Weight gain or weight loss
- Trouble sleeping
- Hyponatremia (low sodium levels)
- Sweating
- Fever
- Manic episodes
- Agitation
- Stiff muscles
- Hallucinations
- Agitation
- Seizures

Side Effects of Taking Mirtazapine (Remeron):

Common Side Effects

- Drowsiness
- Increased Appetite
- Weight gain
- Dry mouth
- Constipation
- Dizziness

Uncommon Side Effects

- Suicidal thoughts or actions
- Sweating
- Fever
- Manic episodes
- Agitation
- Stiff muscles
- Hallucinations
- Increased cholesterol levels

Side Effects of Taking Aripiprazole (Abilify):

Common Side Effects

- Difficulty with speaking
- Loss of balance control
- Stiff muscles
- Restlessness
- Uncontrolled movements
- Nausea
- Vomiting
- Anxiety
- Constipation
- Dizziness
- Headache

Uncommon Side Effects

- Blurred vision
- Fever
- Fast or slow heartbeat
- Trouble breathing or swallowing
- High or low blood pressure
- Agitation
- Seizures

Side Effects of Taking Sertraline (Zoloft):

Common Side Effects

- Nausea

Uncommon Side Effects

- Suicidal thoughts or actions

- Diarrhea
- Insomnia
- Sleepiness
- Sexual problems
- Agitation
- Weight gain or weight loss
- Dry mouth
- Constipation
- Sweating
- Fever
- Fast heartbeat
- Twitching
- Stiff muscles
- Hallucinations
- Seizures
- Abnormal bleeding
- Low salt levels in blood

Side Effects of Taking Venlafaxine/Venlafaxine Extended Release (Effexor/Effexor Extended Release):

Common Side Effects

- Mild nausea or changes in appetite
- Drowsiness
- Strange dreams
- Dizziness
- Increased sweating
- Dry mouth
- Constipation

Uncommon Side Effects

- Seizure
- Sweating
- Fever
- Fast heartbeat
- Overactive reflexes
- Vomiting
- Diarrhea
- Loss of coordination
- Headache
- Trouble concentrating
- Memory problems
- Weakness
- Hallucination
- Trouble breathing, chest tightness
- Easy bruising

Side Effects of Taking Nortriptyline (Pamelor):

Common Side Effects

- Suicidal thoughts or actions
- Sudden changes in mood, behaviors, thoughts, or feelings
- Nausea
- Drowsiness
- Weakness or tiredness
- Excitement or anxiety
- Nightmares

Uncommon Side Effects

- Jaw, neck, and back muscle spasms
- Slow or difficult speech
- Shuffling walk
- Fever
- Uncontrollable shaking of a part of the body
- Difficulty breathing or swallowing
- Rash
- Yellowing of the skin or eyes
- Irregular heartbeat

Side Effects of Taking St. John's Wort

Common Side Effects

- Stomach upset
- Hives or other skin rashes
- Fatigue
- Restlessness
- Headache
- Dry mouth
- Diarrhea
- Feelings of dizziness or mental confusion

Uncommon Side Effects

- Increased sensitivity to sunlight (photodermatitis)

Serotonin Syndrome for example agitation, hallucinations, coma ,coordination problems or muscle twitching, muscle rigidity, tremor, seizures is a possible risk for all serotonergic antidepressants used in this study like escitalopram, sertraline, venlafaxine, and duloxetine. The study team will follow up every 2-3 days with subjects reporting symptoms consistent with serotonin syndrome until symptoms are resolved.

There may be other infrequently or rarely seen side effects to any of these drugs. Please speak with the study team at any time if you have any concerns.

For your safety during this study, call your study doctor BEFORE you take any over-the-counter or new medications prescribed by your own doctor. It is advised that you do not drink alcoholic beverages while taking the study medications due to interactions that may occur.

(2) Risks to an Embryo or Fetus, or to a Breastfeeding Infant (Medication Treatment Group Only)

The effects of antidepressants on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant or trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a period for the past 12 months or more, you will not need to have a pregnancy test. Also, you will not need to have a pregnancy test if you have had a hysterectomy (surgical removal of your uterus and/or ovaries). All other female subjects must have a negative pregnancy test before starting the study drug.

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and stop taking part in the study.

(3) Opioid Weaning May Lead to Increased Physical and Psychological Withdrawal
The study physicians taking over your opioid prescribing will advise you about managing common side effects of opioid use, such as constipation and sedation. Your opioid medication may be reduced (weaned) slowly according to a shared decision between you and the study physician. Thus, the following withdrawal symptoms will probably be minimal and occur infrequently. You may report increased physiological and psychological withdrawal, which will generally be craving, increased pain, or feeling restless. While these symptoms are uncomfortable, they are not dangerous, and you may choose to stop the weaning at any time and still remain in the
study.

Some of the symptoms of physical and psychological withdrawal are:

Restlessness	Joint pain
Watery eyes	Weakness
Runny nose	Abdominal cramps
Yawning	Trouble sleeping
Sweating	Nausea (upset stomach)
Chills	Decreased appetite
Muscle pain	Vomiting
Dilated pupils	Diarrhea
Irritability	Increased blood pressure
Anxiety (nervousness)	Increased heartbeat
Backache	Faster breathing

(4) Risks of Physical Therapy
Physical therapy may temporarily aggravate your low back pain during the treatment sessions; anxiety.

(5) Risks of Sensory Testing
You will experience mild, temporary pain during this test session. Your skin may become slightly red or sore in the area tested. This should go away in less than an hour after testing.

(6) Risks of Questionnaires
There is a risk of personal discomfort while answering questions about opioid use, stress, anxiety, and other sensitive topics. You do not need to answer any question that you do not wish to. You may take breaks or stop at any time.

(7) Risks of Collection of Assessment Data and Protected Health Information
There is a risk of breach of confidentiality of your private health information obtained from your medical record. That is, in very rare cases, people not associated with this research study may inadvertently see your identifiable research results. We will do everything in our power to prevent this from happening by keeping all paper research records in locked files and identifying all specimens and medical information by a subject ID number, rather than by your name. The codebook containing your name and subject ID number will be kept secure by the Study Team.

(8) Risks of Qualitative interviews

There is a risk of personal discomfort while answering questions about stigma and being recorded. You do not need to answer any questions that you do not wish to answer. All the recording will be deleted after they are transcribed. The transcribed notes will be kept in a secure, locked file cabinet and be accessible to approved study staff only.

The text messages you will receive as part of this study are sent from a secure, encrypted system, and all of your responses are stored in this secure system. However, the text messages you send are not encrypted or secure during transmission and could be intercepted. These text messages will include information about pain medication that you may be currently taking. Therefore, it is important to understand your text message response is not protected, and it is possible that it may be viewed by others. It is important to note that depending on your cell phone carrier, even if you delete the text message from your phone, your cell phone carrier will retain those messages for an extended period of time. Additionally, depending on your specific device or carrier, copies of those messages may be stored on multiple devices and/or related cloud storage services. You are responsible for the security of any information that is stored on your cell phone or mobile device. We suggest you periodically check for and delete any sensitive information that may be contained in these text messages.

Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study.

(9) Unknown Risks
As with any experimental procedure, there may be adverse events or side effects that are currently unknown, and certain of these unknown risks could be permanent, severe or life-threatening.

What are the possible benefits from being in this research study?
You may find that the treatment you received may help you improve back pain, function, and mood. You may also find that the treatment helped you wean from opioids more effectively than by standard care measures alone.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
You will be promptly notified if any new information is discovered that suggests you were put at any increased risk as a result of your participation in this research study.

Will I be paid to take part in this research study?
Antidepressant Group will receive up to $ 370, detailed as follows:
Week 1 (Study Visit 1): $30
Week 2 (Study Visit 2): $30
Week 1-2 (Qualitative Interview 1): $25
Week 8 (Study Visit 3+AD visit 3): $30
Week 16 (Study Visit 4 +AD visit 7): $70

Week 16-18 (Qualitative Interview 1): $25
Week 17-32 (8 Online Surveys): $10 per completion of a weekly survey; up to $80
Week 20 (Completion of Month 5 events): $20
Week 24 (Completion of Month 6 events): $20
Week 28 (Completion of Month 7 events): $20
Week 32 (Completion of Month 8 events): $20

EFAR Group will receive up to $490, detailed as follows:
Week 1 (Study Visit 1): $30
Week 2 (Study Visit 2): $30
Week 1-2 (Qualitative Interview 1): $25
Week 8 (Study Visit 3): $30
Week 16 (Study Visit 4+completion of PT visits): $70 + $120
Week 16-18 (Qualitative Interview 1): $25
Week 17-32 (8 Online Surveys): $10 per completion of a weekly survey; up to $80
Week 20 (Completion of Month 5 events): $20
Week 24 (Completion of Month 6 events): $20
Week 28 (Completion of Month 7 events): $20
Week 32 (Completion of Month 8 events): $20

SUBJECTS MUST ATTEND ALL WEEKLY STUDY EVENTS TO RECEIVE FULL COMPENSATION FOR THAT WEEK.

AD+EFAR Group will receive up to $490, detailed as follows:
Week 1 (Study Visit 1): $30
Week 2 (Study Visit 2): $30
Week 1-2 (Qualitative Interview 1): $25
Week 8 (Study Visit 3): $30
Week 16 (Study Visit 4+completion of PT visits): $70 + $120
Week 16-18 (Qualitative Interview 1): $25
Week 17-32 (8 Online Surveys): $10 per completion of a weekly survey; up to $80
Week 20 (Completion of Month 5 events): $20
Week 24 (Completion of Month 6 events): $20
Week 28 (Completion of Month 7 events): $20
Week 32 (Completion of Month 8 events): $20

You will be paid on a reloadable debit card or check mailed to you. All study compensation is taxable income regardless of the amount. If you receive $600 or more in a calendar year from one organization, that organization is required by law to file a Form 1099 – Miscellaneous with the IRS and provide a copy to the taxpayer. Individuals who do not provide a social security number may still participate in the research, but the IRS requires that 26% of the payment be sent by the institution to the IRS for 'backup withholding;' thus you would only receive 74% of the expected payment.

How much will I have to pay to take part in this research study?
The study is provided at no cost to you during the 8-month study. All AD medication and physical therapy sessions will be covered. We will provide remuneration for your parking in the

clinic parking lot during study visits and transportation to and from the study site of $100 for Phase 1 and $100 for Phase 2.

Neither you nor your insurance provider will be charged for the costs of any of the procedures performed for the purpose of this research study, such as urine testing, antidepressant medications, or the physical therapy. You will be charged in the usual manner for any procedures performed as part of your standard medical care (care you would receive even if you were not participating in this research study, such as the prescribing of opioids).

If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff.

What happens if I am injured as a result of taking part in this research study?
If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You do not give up any of your legal rights by signing this form.

Who will know about my participation in this research study?
Any information about you obtained from this research will be kept as confidential (private) as possible. All records related to your involvement in this research study will be stored in a locked file cabinet. Your identity on these records will be indicated by a case number rather than by your name, and the information linking these case numbers with your identity will be kept separate from the research records. You will not be identified by name in any publication of the research results. We will attempt to preserve your medical record and participation in this study as confidentially as possible, but breach of confidentiality is a risk of participation.

In addition to the investigators listed and their research staff, the following individuals may have access to your information related to your participation in this research study:

- Authorized representatives of the study sponsor, federal regulatory agencies, and the University of Pittsburgh Office of Research Protections may review your identifiable research information for purposes of monitoring the conduct of this research study.
- If investigators learn that you, or someone with whom you are involved is in serious danger or potential harm, they will need to inform the appropriate agencies, as required by Pennsylvania law.
- Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to your identifiable information (which may include your identifiable medical record information) for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (such as laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and (3) for internal hospital operations (i.e. quality assurance).

- Information collected from this study may be shared with other investigators; however, this information will be shared in a de-identified manner (i.e., without identifiers).

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings; if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Per University of Pittsburgh policy, all research records must be maintained for at least 7 years following final reporting or publication of a project.

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

How will my information be transmitted, stored, and used in this research study?

(1) Surveys Will Use a Unique ID to Your Data Instead of Your Name

You will receive weekly questionnaires about opioid cravings and pain, anxiety, and stress levels via email or text message. This data will be accessible by University of Pittsburgh research staff and by REDCap software developers. All usage and transference of data will be HIPAA compliant. A unique identifier will be attached to your data instead of your name.

(2) Text Messages Received in this Study Will be Sent and Stored in a Secure System

The text messages you will receive as part of this study are sent from a secure, encrypted system, and all of your responses are stored in the Mosio system. However, the text messages you send are not encrypted or secure during transmission and could be intercepted. Therefore, it is important to understand that your text message response is not protected, and it is possible that it may be viewed by others. It is important to note that depending on your cell phone carrier, even if you delete the text message from your phone, your cell phone carrier will retain those messages for an extended period of time. You are responsible for the security of any information that is stored on your cell phone or mobile device. We suggest you periodically check for and delete any sensitive information that may be contained in these text messages.

(3) Urine Drug Testing Results Will be Processed and Stored Safely by Quest Diagnostics

When you take a urine drug test during your clinic visits, your sample will be processed by Quest Diagnostics. This company requires the following identifiable information in order to process the sample:

- Your printed name and signature on the specimen collection form
- Your study ID number on the sample cup and specimen collection form

- Your date of birth on the sample cup

Quest Diagnostics will receive all the information listed above. Test results will only be accessible by the study doctor or University of Pittsburgh research staff in determining your eligibility for the study.

There are security measures in place to protect your data at all of the organizations listed above. Although we will do everything in our power to protect your data, absolute confidentiality cannot be guaranteed.

HIPAA Authorization for Disclosure of Protected Health Information (PHI)
As part of this research study, we are requesting your authorization or permission to review your medical records to determine your eligibility for this study and to follow your care once you are enrolled in the study. This authorization is valid for an indefinite period of time. We will obtain the following information: diagnostic information, lab results, medications, demographics, and medical history.

As part of this research study, some information that we obtain from you will be placed into your medical records held at UPMC, including the medications prescribed as part of this study and the prescribe opioid taper, if applicable.

This identifiable medical record information will be made available to members of the research team for an indefinite period of time.

Your medical information, as well as information obtained during this research study, may be shared with other groups, possibly including authorized officials from the study sponsor, federal regulatory agencies, and the University of Pittsburgh Office of Research Protections, for the purpose of monitoring the study. Authorized representatives of UPMC or affiliated health care providers may also have access to this information to provide services and addressing billing and operational issues.

We will protect your privacy and the confidentiality of your records, as described in this document, but cannot guarantee the confidentiality of your research records, including information obtained from your medical records once your personal information is disclosed to others outside UPMC or the University.

You can always withdraw your authorization to allow the research team to review your medical records by contacting the investigator listed on the first page and making the request in writing. If you do so, you will no longer be permitted to participate in this study. Any information obtained from you up that point will continue to be used by the research team.

Data Storage and Sharing with the National Institutes of Health (NIH)
Your study data and will also be stored securely at *the National Institutes of Health BACPAC Data Repository.* Your data will be stored indefinitely. We will do our best to protect your personal information. Your name and other personally-identifying information will not be kept with the data. Your data will either be stored without a code linking them to you or they will

have a code that links to your identifying information. If your data has a code, the key to the code will be kept at in a separate, secure area and will not be shared outside of the BACPAC Data Repository.

This study is part of the NIH HEAL Initiative focused on understanding and developing new treatments for addiction and pain. Research gives us the best information and progresses more quickly when data is available from many studies and many individuals, and when many researchers can work with the data and analyze them in different ways. Therefore, your data will be used for this and other NIH HEAL Initiative studies. Your stored data will also be made widely available to other researchers. The shared data may be used indefinitely for research not related to this study or the HEAL Initiative, without asking you for additional consent.

If you withdraw from this research study before it is done, we will keep and continue to use data that have already been collected.

What are the possible benefits of sharing data and samples?
There is no direct benefit to you from the storage and sharing of your data and samples, but sharing may help researchers learn more about low back pain and other diseases, which may help you or others in the future.

What are the risks of sharing data and samples?
Even though we will protect your privacy as much as possible, there is a very small chance that the data and samples could be identified as yours. The risk of this happening is very small but may increase in the future as technology changes.

Research using data and samples from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your samples and data.

Is my participation in this research study voluntary?
Your participation in this research study is completely voluntary. Whether or not you provide your consent for participation in this research study will have no effects on your current or future relationship with the University of Pittsburgh, your current or future medical care at a UPMC hospital or affiliated health care provider, or your current or future relationship with a health care insurance provider.

Your doctor might be involved as an investigator in this research study. As both your doctor and a research investigator, she/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor.

You may withdraw, at any time, your consent for participation in this research study. Any identifiable research or medical record information recorded for, or resulting from, your

participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw your consent for participation in this research study, you should provide a written and dated notice of this decision to the principal investigator at the address listed on the first page of this form.

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

It is possible that you may be removed from the research study by the researchers for the following reasons:

- if you are unable to follow the daily tasks required by the study
- if any safety concerns arise
- if information is obtained that indicates you do not meet eligibility requirements for inclusion in the study
- for any other administrative reasons

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VOLUNTARY CONSENT

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by a qualified individual or by the principal investigator listed on the first page of this consent document at the telephone number given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator.

I understand that I may contact the **Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668)** to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable.

Are you interested in the participating in the optional qualitative interviews?

☐ YES ☐ NO Initials:_____

By signing this form, I agree to participate in this research study and provide my authorization to share my medical records with the research team. A copy of this consent form will be given to me.

_____	_____	_____
Participant's Signature	Printed Name of Participant	Date/Time

CERTIFICATION of INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be

available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

Printed Name of Person Obtaining Consent	Role in Research Study
Signature of Person Obtaining Consent	Date/Time