Effect of Pain Catastrophizing on Prescription Opioid Craving

NCT04097743

February 14, 2024

1. PURPOSE OF THE STUDY

a. Brief Summary

Adherence to prescription opioid and opioid tapering as indicated are critical for safe chronic opioid therapy for chronic pain, but this can be difficult for patients experiencing prescription opioid craving.

Because pain catastrophizing is proposed as a possible treatment target by our and others' preliminary results, the proposed study aims to determine whether pain catastrophizing is a treatment target to reduce prescription opioid craving and to investigate whether negative affect and stress hormones are potential mediators.

b. Objectives

We hope to learn whether a psychology intervention to lower pain catastrophizing will reduce opioid craving, and whether psychological and physical distress will be potential mediators of the treatment effect.

c. Rationale for Research in Humans

The purpose of this study is to examine the effect of a psychological intervention on opioid craving and medication misuse in patients taking prescription opioid for pain management.

2. STUDY PROCEDURES

a. Procedures

Potentially eligible patients will complete an online prescreening survey. Based on the responses to the online prescreening survey, potentially eligible patients will be contacted via phone for additional explanation about the study to the patient, the brief phone screening to ensure the eligibility, and scheduling a laboratory experiment visit. As recommended not to ask a sensitive question (I.e., suicidal thought) during the phone screening, we will inform participants over the phone that their eligibility can be fully determined only after the full consent in the laboratory and we will pay their travel ($25

for those living within an 1-hour driving distance and $50 for those living beyond it).

Potentially eligible patients will be invited for a laboratory experiment (Study 1, 1.5 hours). After obtaining a consent and determining the eligibility, participants will participate in the Study. We will utilize the suicide protocol if a participant is ineligible due to a suicidal ideation. Arm 1 study consists of two Studies; Study 1 will be a laboratory experiment and Study 2 will be a daily home practice. For Study 1, participants will be randomized to three conditions using previously validated protocols (Roditi et al., 2009, Taub et al., 2017): control, pain catastrophizing induction, and reduction. For Study 2, participants will be randomized again to two conditions: control and pain catastrophizing reduction.

During the Study 1 laboratory experiment, patients will undergo 1) vital sign checks (heart rate, blood pressure, body temperature), 2) blood draw(7 ml) and salivary sample collection, 3) a pain catastrophizing protocol with a cold pressor testing, and 4) FOUR salivary sample collections (immediately after pain catastrophizing
protocol, 10 min, 20 min, & 30 min after the cold pressor test). Patients' physiological states will be
continuously monitored such as Heart Rate, Skin Conductance, skin temperature, Respiration Rate, facial EMG, and blood pressure.

This study will use previously validated two pain catastrophizing protocols (Taub et al, 2017 and Roditi et al, 2009). Briefly, the induction procedures are; first, ask participants to think and write about their past pain flare up episode for 10 minutes and then, read 10 pain catastrophizing statements. Secondly, participants will read a pain catastrophizing statement of their choice out loud while putting their non-dominant hand in a cold water. The reduction procedures are; first, ask participants to think and write about their best pain management case for 10 minutes and then, read 10 pain coping statements. Secondly, participants will read a coping statement of their choice out loud while putting their non-dominant hand in a cold water.

After completing Study 1, the participants will receive instruction about Study 2, which includes daily home practice of coping statement for 7 days (delivered via REDcap system), completing a daily survey for 14 days (5 minutes, delivered via REDcap system), and donate salivary cortisol (at the time of waking up, 30-min after waking up, and 9pm) at Day 1, 7, and 14. The collected salivary cortisol will be mailed to the lab with a pre-stamped envelope and an ice pack.

If patients need to take certain medications (Steroid or Benzodiazepines) within 3 days of a saliva sample collection, saliva samples will not be collected.

Added study 3 (arm 3)----------
Due to the unexpected event of COVID-19 pandemic, the study 3 (arm 3, online only) was added to examine the effect of pain catastrophizing on prescription opioid craving. Participants enrolled in the study 1 and 2 will NOT be allowed to participate in the study 3. Different from study 1 and 2, participants in study 3 do not need to have a lab visit (all remote study tasks).

Study 1, 2, and 3 will use the same inclusion criteria, but exclusion criteria for study 3 will be different because study 3 will not do cold pressor testing on the non-dominant hand and will not collect blood and saliva samples. Therefore, we removed the following exclusion criteria in the study 1 and 2: needle phobia, skin condition on the non-dominant hand, daily use of cortisol or benzodiazepine. However, we added ineligibility criteria for inability to use heart rate monitoring device and app because Study 3 will collect resting heart rate daily. During the phone screening, we will ask all eligibility questions except one sensitive question (I.e., suicidal ideation). We will inform participants that we have one more eligibility question, which can be asked only after they sign the phone consenting.

After the phone screening, we will do a phone consenting. A research coordinator will send the consent document to a participant via the REDCap system, which is a HIPPA compliant database. When sending the consent link, we will not include any PHI in the subject line. Then, the research coordinator will go over the consent over the phone and answer any questions. Participants will have a plenty of time to read the consent and can indicate whether they agree to participate or not on their own at home. Participants type their name and date if they agree to participate. After signing their consent, participants can download the consent and keep the copy for their own record. Once we obtain their consent, we will ask about suicidal ideation to determine their eligibility. Only the eligible participants will participate in Arm 3 study. We will use a suicide ideation protocol if a participate is ineligible due to suicide thought.

Participant in the study 3 will do the baseline survey and be randomized into two conditions: daily coping statement practice (50%) and no coping statement (50%). The participants in the daily coping condition will be asked to choose the coping statement of the day and rehearse throughout the day for the 15 days. Except this difference, participants in the both conditions will do a daily survey and check the resting HR for five minutes for the 15 days. The participant will receive a wrist heart rate device (i.e., a heart rate measuring device) before the baseline survey and heart rate will be anonymously collected. Also, participants in the both conditions will do a cognitive testing at day 1 (baseline), day 8, and day 15 (final study). Different from the study 1 and 2, study 3 will examine resting sympathetic cardiac levels and cognitive function as a mediator of the effect of the pain catastrophizing on craving.

Stanford is the only study site, University of Oklahoma will only conduct EDTA sample analysis

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b. Procedure Risks

All members of the study team have been trained to conduct the research procedures in the safest manner possible. There are no known risks to complete the study procedures as all the procedures and questionnaires are validated in this patient population and this medical setting. However, patients may feel temporarily uncomfortable for blood draw, laboratory pain testing, and completing some questionnaires. To minimize the risk, we will exclude patients with a needle phobia and history of vasovagal syncope for blood draw. Additionally, vital signs will be assessed prior to the blood draw and throughout

the laboratory procedures. During the inform consent procedure, the patients will be informed that they can withdraw their consent anytime without penalty and their time will be compensated. Patient will have an option to not to answer any questions that make them feel uncomfortable. Finally, we will obtain the certificate of confidentiality to protect the privacy of research subjects by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the subject consents or in a few other specific situations.

c. Use of Deception in the Study

The exact study hypothesis and study procedures of part 1 are not completely described in the consent, but will be debriefed at the end of Experiment 1.**Use of Audio and Video Recordings**

No audio or video recording will occur.**Alternative Procedures or Courses of Treatment**

Participants are free to pursue the treatment of their choice at any time during and/or after the study.

f. Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

Participants are free to pursue the treatment of their choice at any time during and/or after the study

g. Study Endpoint(s)

Each participant will meet the study endpoint once he/she completes the daily survey for 14 days after Study 1 laboratory visit. The study will end once the target enrollment is reached.

3. BACKGROUND

a. Past Experimental and/or Clinical Findings

Chronic pain and opioid overdose are two critical public health problems in the US. About 25 million adults (11%) suffer from chronic daily pain and up to 8 million use opioids to manage chronic pain. Unfortunately, 46 people die daily from overdose of prescription opioids. For safe chronic opioid therapy for chronic pain, physicians monitor patients' adherence to prescription opioids, and reduce or discontinue the prescription as indicated. Yet, adherence and cessation are not easy for some patients and one reason is opioid craving, a strong desire or urge to use opioids. Our preliminary data show about 34% of patients on chronic opioid therapy report craving. Craving is strongly associated with opioid misuse and negative health outcomes. To date, we do not fully understand the underlying mechanisms of prescription opioid craving in chronic pain sufferers, and psychological treatment targets to reduce craving. Based on our pilot survey, patients endorsing craving reported greater pain catastrophizing than those endorsing no craving. Our other survey study also reported a positive link between pain catastrophizing and opioid craving in patients on chronic opioid therapy for chronic pain conditions. Although these findings propose a possibility that lowering pain catastrophizing may decrease opioid craving, cross-sectional observational studies are limited in investigating a causal association. Potentially, pain catastrophizing enhances stress-induced opioid

craving because stress-induced opioid craving is a well-established phenomenon in studies of addiction, and pain catastrophizing is associated with greater pain and emotional distress in patients with chronic pain. Therefore, the proposed project seeks to determine: a) the effect of pain catastrophizing on prescription opioid craving in patients on chronic opioid therapy for chronic pain and b) psychological (negative affect) and physiological (cortisol, norepinephrine) distress as potential mediating variables.

Findings from Past Animal Experiments

NA

4. RADIOISOTOPES OR RADIATION MACHINES

a. Standard of Care (SOC) Procedures

b. Radioisotopes

i. Radionuclide(s) and chemical form(s)

NA

ii. Total number of times the radioisotope and activity will be administered (mCi) and the route of administration for a typical study participant

NA

iii. If not FDA approved: dosimetry information and source documents (package insert, Medical Internal Radiation Dose [MIRD] calculation, and peer reviewed literature)

NA

c. Radiation Machines – Diagnostic Procedures

i. Examination description (well-established procedures)

NA

ii. Total number of times each procedure will be performed (typical study participant)

NA

iii. Setup and techniques to support dose modeling

NA

iv. FDA status of the machine and information on dose modeling (if procedure is not well-established)

NA

d. Radiation Machines – Therapeutic Procedures

i. Area treated, dose per fraction/number of fractions, performed as part of normal clinical management or due to research participation (well-established procedures)

NA

ii. FDA status of the machine, basis for dosimetry, area treated, dose per fraction and number of fractions (if procedure is not well-established)

NA

5. DEVICES USED IN THE STUDY

a. Investigational Devices (Including Commercial Devices Used Off-Label)

NA

Investigational Device 1	
Name:	NA
Description:	NA
Significant Risk? (Y/N)	NA
Rationale for Non-Significant Risk	NA

b. IDE-Exempt Devices

IND-Exempt Device 1	
Name:	NA
Description:	NA

6. DRUGS, BIOLOGICS, REAGENTS, OR CHEMICALS USED IN THE STUDY

a. Investigational Drugs, Biologics, Reagents, or Chemicals

Investigational Product 1	
Name:	NA
Dosage:	NA
Administration Route:	NA

b. Commercial Drugs, Biologics, Reagents, or Chemicals

Commercial Product 1	
Name:	NA
Dosage:	NA
Administration Route	N A
New and different use? (Y/N)	NA

7. DISINFECTION PROCEDURES FOR MEDICAL EQUIPMENT USED ON BOTH HUMANS AND ANIMALS

NA

8. PARTICIPANT POPULATION

a. Planned Enrollment

(i) 156 participants (50% female) will be recruited at the Stanford Systems Neuroscience and Pain Lab.
(ii) All participants will be enrolled at Stanford. Patients with chronic pain and opioid medication use will be enrolled.

(iii) Patients, aged at least 18 years old, visiting our pain clinic for chronic pain treatment will be recruited because we want to identify a psychological treatment target for prescription opioid craving and misuse in patients with chronic pain conditions.
(iv)We will partner with the Research Participant Engagement Program (RPEP) team for Honest Broker outreach. Potential participants are identified via STARR and invited by RPEP team (honest broker) on behalf of study team. See Section 16 for Honest Broker study invitation letters. We will be using Postal Mail and Research Registry honest broker outreach. For Postal Mail, study team may support the process by sticking pre-printed address labels (created by RPEP, the honest broker) on the envelopes.

b. Age, Gender, and Ethnic Background

Participants, aged at least 18 years old of both genders and all racial and ethnic backgrounds will be included.

c. Vulnerable Populations

NA

d. Rationale for Exclusion of Certain Populations

The pain catastrophizing protocols (Taub et al, 2016, Roditi et al, 2009) have been validated only for adults with chronic pain. This study will be the first to use this protocol in patients taking opioid pain medications for chronic pain management. If this study finds no safety concerns in adult patients with chronic pain and chronic opioid therapy, a future study can include children.

e. Stanford Populations

Laboratory personnel, employees, and/or students will not be specifically recruited, although they will be able to participate if they visit our clinic.

f. Healthy Volunteers

NA

g. Recruitment Details

We will use the Collaborative Health Outcomes Information Registry (CHOIR) system. Patients on the CHOIR OK-to-Contact list will be invited to complete the online screening survey. Additionally, our lab is affiliated with the Stanford Pain Management Center, through which providers can inform interested patients of our research study. If needed, we will be able to recruit participants through our existing Stanford research databases where participants have agreed to be contacted for future research and recruit through community advertisements (Facebook/Instagram, Reddit, Stanford Report, Craigslist).

We will partner with the Stanford Research Registry to invite potential arm 1, 2, and 3 participants from the following cohort lists:
Individuals 18 and over indicating a pain condition with local zip codes (starting with 94 or 95) = 211

Individuals 18 and over indicating a pain condition with all zip codes (for arm 3) = 465 Participants will receive an email invitation (attached in section 16) and then will be directed to complete our screening survey.

Potential participants will complete the online screening survey. Based on the screening survey results, we will invite eligible participants to a laboratory experiment.

We will partner with the Research Participant Engagement Program (RPEP) team for Honest Broker outreach. Potential participants are identified via STARR and invited by RPEP team (honest broker) on behalf of study team. See Section 16 for Honest Broker study invitation letters. We will be using Postal Mail honest broker outreach. For Postal Mail, study team may support the process by sticking pre-printed address labels (created by RPEP, the honest broker) on the envelopes.

For both the Postmail and Registry, the patient can either reach out to the research coordinator or complete the screening survey. If they reach out to the research coordinator, they will send our screening survey link. If they are eligible after completing the screening survey, a research coordinator will reach out to conduct a phone screening and confirm eligibility. If they complete the screening survey, if they are eligible, a research coordinator will reach out to conduct a phone screening and confirm eligibility.

Update 6/6/24: We will use the Pain Division Newsletter, a new IRB approved recruitment method for SNAPL, to recruit current and past participants, patients, and members of the public who are interested in research on chronic pain.

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h. Eligibility Criteria

i. Inclusion Criteria

For study 1, 2, and 3,
1. At least 18 years old
2. Chronic opioid therapy at least 3 months
3. Any chronic pain conditions at least 3 months

ii. Exclusion Criteria

For study 1 and 2,
1. Current diagnosis of cancer
2. Other severe psychiatric and cognitive conditions (schizophrenia, delusional disorder, psychotic disorder, dementia, Parkinson's or dissociative disorder)
3. An skin conditions on the non-dominant hand (pain testing site)
4. Non-English speaker
5. No access to email or smart phone
6. (For saliva collection) Daily use of cortisol or benzodiazepines
7. Being pregnant
8. Needle phobia for blood draw
9. Current suicide thoughts

added for study 3----------

For study 3,
1. Current diagnosis of cancer
2. Other severe psychiatric and cognitive conditions (schizophrenia, delusional disorder, psychotic disorder, dementia, Parkinson's or dissociative disorder)
3. Non-English speaker
4. No access to email or smart phone
5. Being pregnant
6. Current suicide thoughts
7. Concurrent psychological treatments during the 15-day study period.

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i. Screening Procedures

New recruitment method will be used, the Research Participant Engagement Program (RPEP). RPEP will use coded diagnoses and procedures, clinical records, demographics with embedded identifiers, medications, names, telephone numbers, home address, date of birth, date of service, date of diagnosis, emails, and MRNs to recruit via postal mail.

Potentially eligible patients will complete an online prescreening survey. The online screening survey will assess patients' chronic pain and other health conditions, pain medication use, and prescription misuse, and craving. For prescription misuse and craving, the PROMIS item bank for the misuse of prescription pain medication and the COMM will be administered. This study will invite people endorsing chronic pain at least 3 months, taking opioid pain medications at least 3 months, and no craving or craving at any frequency on the PROMIS craving item (i.e., I experienced cravings for pain medication). Name, email, and phone number will be collected to invite eligible participants for the study.

Based on the responses on the online prescreening survey, potentially eligible patients will be contacted via phone for additional explanation about the study and to assess eligibility. During the screening phone call, potentially eligible participants will be asked questions to ensure inclusion criteria have been met and with the exception of assessing for current suicidal thoughts, potential participants will be asked questions to ensure exclusion criteria are not met. Participants who are otherwise willing and eligible will be notified that there is one sensitive eligibility question that will need to be asked after they have provided informed consent. If the potential participant inquires about the eligibility question, the research staff will notify the participant that the question is on the topic of suicidal ideation and that no response is needed at this time.
Participants recruited for the Arm 1 and 2 (in-person) study will be invited to the laboratory and will receive informed consent. Once the participant has signed the informed consent form, the research staff will assess the participant for the exclusion criteria of current suicidal thoughts. If the participant reports current suicidal ideations, they will be ineligible for the study and the Suicidal Ideation Protocol will be followed (included in section 16). Participants found to be ineligible will be withdrawn from the study.
Participants recruited for the Arm 3 (on-line only) study will receive an electronic copy of the consent form and will receive information about the study over the phone. Once the participant has signed the consent form, the research staff will assess the participant for the exclusion criteria of current suicidal thoughts. If the participant reports current

suicidal ideations, they will be ineligible for the study and the Suicidal Ideation Protocol will be followed (included in section 16). Participants found to be ineligible will be withdrawn from the study.

j. Participation in Multiple Protocols

Participants will be okay to participate in other clinical trials except for clinical trials including pain self-management or psychological interventions. If a patient is interested in participating in other clinical trials including pain self-managements or psychological interventions, a patient will be informed of two options : the one will be participating in other studies after completing this study for 14 days and the other option will be not to participate in this study.

k. Payments to Participants

Participants will be compensated $30 for Study 1, $5 for daily survey for 14 days, $5 for three at home saliva samples, and $5 for completion of all study requirement. Therefore, when completing the whole study requirements, a participant receive a total of $120.

Travel cost will be compensated: $25 for people living within 60 miles and $50 for people living beyond 60 miles.

Added for the Study 3, ----------
For study 3, participants will be compensated $25 for completing the baseline tasks (the 30 or 40-min survey, cognitive testing and blood pressure and HR measure), $60 for completing the short-daily survey and blood pressure ($5x12 days = $60), and $10 for completing a 10-min survey and HR measure at day 8, and $20 for completing the final survey. When completing all the tasks, the participant will receive additional $5. Therefore, the total compensation is up to $120 (=25+60+10+20+5). Participants will receive check as compensation.

l. Costs to Participants

NA

m. Planned Duration of the Study

Participants will complete (i) the initial 2.5 hour-laboratory experiment (Study 1) and daily home practice of coping statement and daily survey (3-5 minutes, Study 2) for 14 days. (iii) This study estimates 3 years of data collection and 1 year of data analysis.

Added for study 3,----------
Participants will completed (i) the initial 45-60min baseline survey, cognitive testing, and resting blood pressure and HR measure, (ii) a brief daily survey, resting blood pressure and HR measure for 15 days and practicing a 5-min daily coping statement 15 days (only for the 50% of people who are assigned to the coping statement condition), (iii) a 10 min survey at Day 8 and blood pressure and HR measure, and (iv) 20 min-final survey and cognitive testing, and blood pressure and HR measure.

9. RISKS

a. Potential Risks

i. Investigational devices

NA

ii. Investigational drugs

NA

iii. Commercially available drugs, biologics, reagents or chemicals

NA

iv. Procedures

Participants may experience discomfort from blood draw such as bleeding, soreness, bruising and stinging at the site of the blood draw. Participants may experience physical discomfort in undergoing cold water pressor test. To minimize the risk of physical discomfort, we will use our standard laboratory protocol (4 Celsius, 2 minutes), which is shown to induce "temporary" discomfort.

Online only Arm 3 study----------
No risk of physical discomfort in Arm 3 study

v. Radioisotopes/radiation-producing machines

NA

vi. Physical well-being

NA

vii. Psychological well-being

None of the questionnaires pose a risk to the participants. It is possible that subjects may feel uncomfortable answering some questions on the questionnaires; this risk will be minimized by allowing participants to refuse to answer a question. Additionally, some participants undergo pain catastrophizing induction protocol. We will use a validated pain catastrophizing protocol (IRB 11689, Taub et al., 2017, and Roditi et al., 2009), which is proven to "temporarily" induce catastrophic thinking about pain. For daily practice of pain coping statement, we will have only pain catastrophizing reduction and control condition. Finally, we will obtain certificate of confidentiality to protect the privacy of research subjects by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the subject consents or in a few other specific situations.

Arm 3 (online only) study----------
None of the questionnaires pose a risk to the participants. It is possible that subjects may feel uncomfortable answering some questions on the questionnaires; this risk will be minimized by allowing participants to refuse to answer a question. Also, we will collect the heart rate data anonymously and heart rate data will be recorded only with research email account and study id.

In this Arm 3 protocol, we have pain catastrophizing reduction and control condition. So, the intervention arm may help to reduce catastrophic thinking related to pain. We will also ask people to report opioid craving and misuse. As a part of NIH study, certificate of confidentiality also apply to this protocol. Therefore, we can protect the privacy of research subjects by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the subject consents or in a few other specific situations.

viii. Economic well-being

<Enter text or "NA">

ix. Social well-being

NA

x. Overall evaluation of risk

Minimum

b. International Research Risk Procedures

NA

c. Procedures to Minimize Risk

We are minimizing risks of physiological discomfort by excluding someone with a history of vasovagal syncope from blood draw and a needle phobia. We will also check vital signs before the blood draw. We are minimizing risks of psychological discomfort by allowing participants to refuse to answer any questions. Additionally, we will monitor physiological states throughout the study procedures. An experimenter will monitor physiological states and make sure their values are all within normal limits by the end of the experiment. We will also obtain the certificate of confidentiality to protect the privacy of research subjects by prohibiting disclosure of identifiable and sensitive research information to anyone not connected to the research except when the subject consents or in a few other specific situations. Finally, this study use validated and standard laboratory procedures.

For both the in-person study (Arm 1 and 2) and the online-only study (Arm 3), participants will be assessed for current suicidal thoughts by research staff after the participant has signed the consent form. For the in-person study, the consent procedure occurs in-person and participants endorsing current suicidal thoughts will be ineligible for the study and the Suicidal Ideations Protocol (included in section 16) will be followed accordingly. For the online-only study, participants will be consented over the phone and participants endorsing current suicidal thoughts will be ineligible for the study and the Suicidal Ideations Protocol (included in section 16) will be followed accordingly. If a suicidal thought is expressed anytime even before the consent, we will activate "the suicidal ideation protocol."

Added 10/17/2024: In response to the adverse event at the end of September, the research

team will be available to accompany in-person participants to their cars after appointments to help ensure their safety.

A research coordinator and research assistant will review all the responses in free text-format questions daily and activate "The suicide Ideation protocol" as needed.

d. Study Conclusion

The experiment will terminate when all data has been collected from participants. An individual's participation will terminate at the point that all data is collected from that individual, if the protocol director decides to withdraw the subject, or if the patient wishes to withdraw from the study.

e. Data Safety Monitoring Plan (DSMC)

i. Data and/or events subject to review

Self-reported adverse events were collected at the study endpoint for Aim 1, 2, and 3 studies. Adverse events were reviewed as soon as participants reported any events on the REDCap, which sent automatic email notification to Dr. You, PI and Clinical Research Coordinator.

ii. Person(s) responsible for Data and Safety Monitoring

Dokyoung Sophia You, PhD

iii. Frequency of DSMB meetings

Yearly

iv. Specific triggers or stopping rules

Any SAEs that are probably or possibly related to this study

v. DSMB Reporting

Sent a yearly DSMB reporting to NIH

vi. Will the Protocol Director be the only monitoring entity? (Y/N)

Y

vii. Will a board, committee, or safety monitor be responsible for study monitoring? (Y/N)

N

f. Risks to Special Populations

NA

10. BENEFITS

There is no direct benefit to the participants. Knowledge gained from this study may help to identify a psychological treatment target to reduce prescription opioid craving and misuse, and

therefore,
psychological treatments to reduce prescription opioid craving can help patient with chronic pain to use pain medication as prescribed or successfully taper the medication as recommended by a doctor. This study also has the potential to inform that other psychological interventions (cognitive and behavioral therapy for pain and mindfulness), which are known to reduce pain catastrophizing, will be effective in improving medication compliance and success of prescription opioid tapering.

11. PRIVACY AND CONFIDENTIALITY

All participant information and specimens are handled in compliance with the Health Insurance Portability and Accountability Act (HIPAA) and privacy policies of Stanford University, Stanford Health Care, and Stanford Children's Health.

Analysis Plan

We will conduct two-way repeated-measures ANOVAs (Condition × Time) to test whether reductions in pain catastrophizing are associated with decreases in craving, cortisol levels, and psychological distress (depression and anxiety).

If a significant effect of Condition is observed, we will conduct mediation analyses to test whether the intervention's effects on craving are mediated by reductions in cortisol and psychological distress.