Single Session Pain Catastrophizing Class: Efficacy & Mechanisms for Reducing Opioid Use Among Chronic Pain Patients.

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1. PURPOSE OF STUDY

a. Brief Summary

Untreated Pain Catastrophizing can lead to increased opioid use and facilitate the risk for misuse and overuse of medications, particularly when surgery and pharmacologics are the focal medical care plan. Despite critical need, there are no targeted interventions that efficiently address the key psychological factors that can amplify both pain, need for opioids, and increased risk for misuse. In this project, we will attempt to address this urgent need for efficient and effective solutions. Our group has developed a 2-hour targeted, single-session pain catastrophizing class (PC-class), rooted in cognitive-behavioral therapy (CBT) approaches, aimed at reducing opioid use by reducing pain catastrophizing in chronic pain.

b. Study Objectives

This project aims to identify patients who achieve a meaningful reduction in opioid use, which will enable better characterization of treatment responders and refining opioid reduction strategies. Also, the daily data will be used characterize the mechanistic influence of catastrophizing on opioid use both on the daily-level and prospectively.

c. Rationale for Research in Humans

This research necessitates human participants because there is no equivalent animal model or non-human model to answer the study questions. The interventions are designed for human participants only.

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2. STUDY PROCEDURES

a. Procedures

i. Screening of Participants: A total of 300 male and female adult patients (ages 18-80) who meet criteria for a chronic pain condition receiving care at the Stanford Pain Management Centers will be enrolled. Recruitment efforts will include targeted emails and advertisements at Stanford's pain management clinics. Screening procedures will include a phone screening by study staff, or an in-person screening. Informed consent will either be obtained in-person during the visit, or through REDCap or on the phone with a research coordinator. All participants will have the informed consent presented to them through REDCap where they can provide their digital signature. All participants will automatically be emailed a copy of their informed consent.

ii. Screening visit or call: During this first visit, after eligibility has been determined, we may ask participants to use a computer, handheld device like a tablet, or iOS/android phone to record their daily pain and take the full surveys at specified time points. During or after this visit or call, they may be randomized to one of the 2 class types described below, and we may contact them to inform them of their schedule. After randomization, patients will be emailed a schedule of their participation.

iii. Pre-Class Procedures: Participants will complete an enrollment survey online using a secure, HIPAA compliant, online system (via REDCap or Qualtrics). There is a chance that patients may present with depression, as measured by the PROMIS Depression Short Form upon enrollment. Patients exhibiting signs of depression (a raw score of 33 or greater) will be provided with a list of mental health providers/resources (attached in section 16). Patients endorsing suicidality will be offered immediate assessment and will be considered ineligible and subsequently withdrawn from the study. Responses the PROMIS Depression Short Form will be assessed within one week to assure prompt response to signs of depression and suicidality.

iv. Class sessions: Participants may be randomly assigned to one of the two educational groups described below. The classes will be in person or online via Zoom. All participants who are assigned to the online class will receive a password to join the Zoom session so it is secure. Participants in the online class will also receive all relevant documents in an email prior to the class or mailed hard copies if applicable. All documents cannot be reassigned once they are allocated to a group. Upon completion of the initial 12-month study, participants previously in the health education class will be invited to enroll in the active treatment arm of the study (pain psychology class), receive the same surveys and compensation, and if not interested in the research, are eligible to just attend the treatment class for free (no survey or compensation).

1. Pain psychology class is a 2-hour pain psychology education class. Participants will learn various information and skills to better manage important aspects of their pain. At the end of the pain psychology class, participants will be given instructions to download an app specific to the study containing a relaxation resource or be sent a link to the audio file of the relaxation resource. This application is an optional relaxation resource, and we will only collect data regarding the frequency and duration of use. Data will be stored securely in REDCap.

2. Health education class is an approximately 2-hour class that will cover information important to their health and pain.

v. Throughout the study: Daily questionnaire about their pain and mood, to be completed daily during 2 four-week periods from their baseline visit until 2 months after the class. This typically takes less than 5 minutes to complete each day and will be entered via a hand-held device, such as a tablet or

smart phone, or through a secure website. The research team will provide participants with instruction on how to use this device or complete their questionnaires. If they are provided with a tablet or android phone, they will be asked to return these devices at the end of their study participation. Participants will also fill out questionnaires at several time points during the study: before treatment start, after-treatment, once a month during the 3 months following their class, and once more 6 months after the class, and one last time 12 months after the class. These questions may take approximately 30-60 minutes to complete and include questions about their symptoms, mood, function, medication use, and other treatments being used. This may occur via secure web survey, regular mail, the handheld device, or by phone interview.

The PROMIS Depression Short Form will be administered for the pre-class, 3-, 6-, and 12-month questionnaires detailed above. PROMIS Depression Short Form scores will be monitored in real time and suicidality will be assessed with the same procedures as with the enrollment survey for these following questionnaires.

Patients will be sent thank you emails with enclosed amazon codes for compensation.

Additional visits to our lab may be scheduled in order to help participants with downloading the data from their handheld device, should you need such help.

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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 completing the questionnaires or undergoing proposed interventions. Participants will be informed that they have the right to refuse to answer questions and they can withdraw from the study at any time.

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c. Use of Deception in the Study

Deception will not be used.

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d. Use of Audio and Video Recordings

Recording for the treatment sessions may occur so that the study team can review the session to confirm instructor adherence to the treatment protocols. After treatment fidelity has been confirmed, recordings will be permanently deleted.

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e. Alternative Procedures or Courses of Treatment

No standard treatment is being withheld. Participants are encouraged to continue with their current course of treatment for their pain under the care of their regular physician. Participant's alternative is to not participate.

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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 after the study. If participants are exhibiting signs of depression (PROMIS depression raw score of 33 or greater), a research coordinator or study psychologist will provide the participant with a list of mental health resources/providers attached in section 16.

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g. Study Endpoint(s)

Each participant will meet the study endpoint once he/she completes the last set of questionnaires at the final time point. The study will end once the target enrollment is reached.

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3. BACKGROUND

a. Past Experimental and/or Clinical Findings

There is an urgent need to better integrate targeted effective treatment for opioid use by reducing pain catastrophizing. Cognitive behavior therapy (CBT) has demonstrated preliminary promising results for opioid-treated chronic pain, with reductions in opioid use (1), misuse (1), aberrant opioid-related behaviors (3), and discontinuation of opioid use by four patient participants in a small pre-post clinical trial (4). Similarly, pain catastrophizing is typically treated with 8-sessions of group Cognitive Behavioral Therapy (pain CBT; 16 hours of treatment time) (5), and the efficacy of pain CBT appears to be mediated by changes in pain catastrophizing (6-9). However, while existing pain CBT modalities are effective, patients incur many barriers with the typical 6-8 sessions of treatment including substantial cost, time and travel burden, lack of skilled clinicians, insurance coverage, and copayments (10-12). These barriers to care reduce patient access and may foster reliance on pharmacologic and interventional modalities, thereby illustrating the need to develop targeted, efficient, low-cost treatment strategies that will dismantle current barriers and improve patient access to care and ultimately treatment outcomes. In addition, an identified lack of skilled pain psychologists in the U.S. has underscored the need to develop effective treatment approaches that are highly efficient (13). For this proposal, we aim to utilize the single session, 2-hour patient class for the first time to focally target opioid use through reducing pain catastrophizing. The class is rooted in cognitive behavioral principles, includes education about opioid reduction and pain management, in addition to specific skills acquisition. Participants develop personalized plans to identify and stop pain catastrophizing using a variety of psychological tools, including an already developed smartphone audio app (Relaxation Response). We aim to give all patients rapid access to low-risk care that empowers them to self-manage their pain and reduce reliance on opioids.

b. Findings from Past Animal Experiments

N/A

4. RADIOISOPES OR RADIATION MACHINES

a. Standard of Care (SOC) Procedures

Identify Week/Month of study	Name of Exam	Identify if SOC or Research
N/A	N/A	N/A

b. Radioisopes

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

N/A

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

N/A

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

N/A

c. Radiation Machines – Diagnostic Procedures

i. Examination description (well-established procedures)

N/A

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

N/A

iii. Setup and techniques to support dose modeling

N/A

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

N/A

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)

N/A

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

N/A

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5. DEVICES USED IN THE STUDY

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

N/A

b. IDE Exempt Devices

N/A

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

a. Investigational Drugs, Biologics, Reagents, or Chemicals

N/A

b. Commercial Drugs, Biologics, Reagents, or Chemicals

N/A

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

N/A

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8. PARTICIPANT POPULATION

a. Planned Enrollment

We plan to enroll up to 300 patients with chronic pain, all of them at Stanford. Sample Size Estimation was conducted: a sample size of 116 completers (58 per group) was estimated to produce 80% power to

detect medium-large treatment effects on the primary outcome (opioid use). The main effect of PC treatment on opioid use will be compared against the HE control condition using a 2-samples t-test. However, given the attrition rate in behavioral treatments, namely pain CBT literature, is typically 18-25%, we plan to over enroll to account for attrition.

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b. Age, Gender, and Ethnic Background

Men and women, ages 18-80 of any race or ethnicity may be recruited.

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c. Vulnerable Populations

None

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d. Rationale for Exclusion of Certain Populations

This study is looking at a class structured for an adult population; therefore, children will not be included.

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e. Stanford Populations

We expect this research to be accessible to any adult patient with chronic pain who is taking opioid medication, some of whom may be students, employees, or lab personnel. We will afford them the same opportunity as any other participant.

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f. Healthy Volunteers

N/A

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g. Recruitment Details

We may be recruiting through our existing database of patients who are interested and willing to be contacted about future studies, through physician referrals for the Stanford Pain Management Center and outside providers, and through internet advertising using sites such as Craigslist, Google, and social media ads. Recruitment may also be done through an online survey available to interested potential participants through our study-specific online screening form (attached in Section 16), through our lab website (protocol 33436), through the National Pain Report, and from screen failures or participants who will conclude their future participation in other studies taking place in the lab. Additional recruitment avenues for this project may include:

- Hardcopy and screen advertising with flyers, brochures, and postcards at physicians' offices and community locations
- Online and Social Media Ads (e.g., Facebook, Stanford Report, Craigslist, Reddit, lab website) - Newspaper Ads
- Radio Ads
- Research networking sites such as Researchmatch.org and patientslikeme.com - Registration on Clinicaltrials.gov We are not planning to mail any advertisements.

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h. Eligibility Criteria

i. Inclusion criteria:

1) 18-80 years of age

2) Diagnosis of chronic non-cancer pain (> 3 months in duration)

3) Currently using prescription opioids ≥ 10mg morphine equivalent daily dose (MEDD) for ≥ 3 months

4) Ability and willingness to complete study procedures

ii. Exclusion Criteria

1) Open litigation regarding a medical condition

2) Inability to provide informed consent and complete study procedures

3) Active suicidality

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i. Screening Procedures

Potential participants will be screened using the attached phone script to determine eligibility prior to consent. We are obtaining a limited waiver of authorization to collect initial eligibility information in the phone screen, which may include questions about their pain and opioid use.

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j. Participation in Multiple Protocols

Participants will be asked whether they are enrolled in any other research studies. If another study's procedures interfere with our own or places the subject at increased risk, he/she will not be enrolled in our study.

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k. Payments to Participants

Participants will be compensated $25 for completing assessments at enrollment, baseline, and at 1, 6 and 12-month time points, and $35 at 3-month follow-up. Therefore, total potential compensation per participant is $160.

l. Costs to Participants

No costs will be charged to the participants.

m. Planned Duration of the Study

The entire study is estimated to take 5 years. For each participant:

(i) Phone screening will take about 10 minutes.

(ii) Active participation in the intervention is one session, with 12 months of post-treatment follow-up. There may be additional wait time before treatment starts.

(iii) Data analysis is expected to take 2-3 years.

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9. RISKS

a. Potential Risks

i. Investigational Devices

N/A

ii. Investigational drugs

N/A

iii. Commercially available drugs, biologics, reagents or chemicals

N/A

iv. Procedures

N/A

v. Radioisotopes/radiation-producing machines

N/A

vi. Physical well-being

N/A

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 any question(s). Patients endorsing suicidality will be offered immediate assessment. There are no expected risks from the treatments in this study.

viii. Economic well-being

N/A

ix. Social well-being

N/A

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b. International Research Risk Procedures

N/A

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c. Procedures to Minimize Risk

Risks of discomfort due to the questionnaires will be minimized by allowing the participant to refuse to answer particular questions.

All participant information will be stored in a locked cabinet and on an encrypted, password-protected computer.

Surveys will be monitored in real time by the study coordinator. If patients exhibit signs of depression as measured by the PROMIS Depression Short Form (raw score of 33 or greater), they will be offered a list of mental health providers/resources and if endorsing suicidality, they will be offered an immediate assessment. These responses will be assessed within one week to assure prompt response to signs of depression and suicidality.

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d. Study Conclusion

The experiment will terminate when all participants have completed participation. If an individual participant chooses to withdraw, or the researcher determines it is unsafe or scientifically invalid for him/her to continue, his/her participation will end. We do not anticipate the study will directly result in adverse effects to the participants, but we have physicians on staff should a medical intervention become necessary in the event of an adverse event.

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10. BENEFITS

Participants may experience benefits from the interventions offered to them. Knowledge gained from this study may inform future research studies and clinical treatments aimed at reducing catastrophizing in patients with chronic pain.

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11. PRIVACY AND CONFIDENTIALITY

a. Privacy Protections

Interactions will occur at the Redwood City location and/or our research offices at 1070 Arastradero, Palo Alto. Interactions may also occur via a secure, online platform called Zoom. In such instances, participants would need to enter a password before joining the Zoom session. Interactions will also

occur via email through a secure Stanford address, online via the secure REDCap, or via the phone from a private location. All necessary precautions will be taken to ensure privacy for the participants.

b. Specify PHI

The following information may be collected to determine eligibility, including but not limited to: Name, contact information, date of birth, demographics, medical and pain history, psychological history, pain intensity, pain catastrophizing scale scores, and medication use. We may also collect responses to questionnaires, and treatment satisfaction measures. COVID-19 related questions on the questionnaire No PHI will be disclosed outside Stanford.

c. Data Security

Data will be maintained on paper records, which will be stored in locked cabinets. Electronic data will be stored on password protected computers and password protected servers, to which only the study team has access (REDCap). Electronic data on the handheld device will not contain PHI. It will nonetheless be stored on a secure server when downloaded to our lab.

d. Data De-identification

Data will be labeled with the participant's study ID number. Study ID numbers will be linked with patient name via a master key, which will be stored on an encrypted, password-protected computer.

e. Data Access

The research team will have access.

f. Data Code

Study ID numbers will be linked with patient name via a master key, which will be stored on a password-protected computer. The ID number will not be derived from the patient's name or any other PHI.

g. Data Code Key

Study personnel will maintain the key to the code on password protected computers to which only the study team has access.

h. Sharing, Transferring, or Transmitting Data

No PHI will be shared outside our research team.

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i. How will you educate research staff to ensure they take appropriate measures to protect the privacy of participants and the confidentiality of data or specimens collected?

All research staff have completed the human subjects' training. Research guidelines and confidentiality are emphasized at team and lab meetings.