IRB APPROVED PROTOCOL

Study Title: Strategies to Improve Pain and Enjoy Life (STRIPE)

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INSTRUCTIONS:

- Complete this Protocol Template only when there is **no** existing authored protocol provided for this study.
- If you are doing a data-only study with no prospective or interventional components, use the Data Only Protocol Template instead.
- This Protocol Template is to be used in conjunction with the SMART KP IRB Core Data Form.
- Enter your responses to each question directly below the BLUE text in the fillable field.
- When completing this Protocol Template, if a section does not apply to your study then enter "N/A."

1. Protocol

Protocol Title
Pain Self-Management Training for Opioid Taper

Principal Investigator
Denise Boudreau, PhD

Version Date
April 7, 2021

Form Author
Rachel Hays

2. Objectives

Describe in plain language the purpose, specific aims, or objectives and indicate the primary goal(s) of the study (e.g. safety, tolerability, effectiveness, feasibility, pilot study, etc.). State the hypotheses to be tested. State primary and any secondary study endpoints.

This study will adapt and test a University of Washington (UW) developed/piloted pain self-management training for prescription opioid taper intervention at Kaiser Permanente Washington (KPW). To address patients' fears of opioid taper that limited recruitment into our pilot study, we will begin with randomization to pain self-management training and then offer the option of self-paced opioid taper: *Pain Self-Management Training for Opioid Taper* (PSMOT). The optional taper will occur through recommendations from the research interventionist the patient's primary care provider (PCP). This study aims to enroll 250 participants and randomize them into either 1) a nurse or physician assistant research interventionist guided PSMOT or 2) regular care (no intervention). Specifically, we will test the effectiveness of this intervention, compared with control group on opioid dose and pain outcomes among patients on high dose (≥ 40 mg morphine equivalent dose) long-term opioid therapy (LtOT) for chronic non-cancer pain (CNCP) in a pragmatic randomized trial.

The objectives of this study are:

- To adapt our previously developed prescription opioid taper support intervention by a physician assistant into a telephone-delivered pain self- management training that provides the option for supported opioid taper (PSMOT) through the patient's PCP. We will recruit participants who receive care from multiple primary care clinics. The intervention will be administered by a KPWA research interventionist (a physician assistant or registered nurse) who will be trained and supervised by a UW pain psychiatrist and UW research clinician and will include guidance in opioid and non-opioid medication prescribing. This training and guidance will be consistent with KPWA guidelines.

- To test in a randomized trial the effects of this PSMOT intervention on: a) opioid outcomes: daily opioid dose *(primary outcome)*, percent dose reduction from baseline, problem opioid use (interview, questionnaire, and electronic health record text indicators), and patient-reported opioid problems; and b) pain-related outcomes: PEG (self-report of Pain intensity, Enjoyment of life interference, General activity interference - *primary outcome*), pain self-efficacy, and depression symptoms

We will test the effectiveness of this intervention, compared with control group, on opioid dose and pain outcomes among patients on high dose (≥ 40 mg morphine equivalent dose) LtOT for CNCP in a pragmatic randomized controlled trial. This intervention will have two components:

- telephone-delivered evidence-based pain self-management training with supplemental materials including:
  - A participant workbook
  - *The Pain Survival Guide* book
  - Audio files of relaxation techniques (these will be available both as in a CD format and we are working with Eagles to create a study website that will host these files. : **www.stripestudy.org**
  - A web-based video of successfully tapered patients with motivational *interviewing* debriefing: www.stripestudy.org
- Voluntary, self-paced opioid taper through recommendations to the PCP
  - Including opioid and non-opioid prescribing guidance from the research interventionist to the patient's PCP.

Hypotheses pertaining to opioid use: Patients receiving LtOT for chronic non-cancer pain (CNCP) randomized to the PSMOT intervention, as compared with those randomized to a control group, will have lower opioid doses, greater percent reduction of opioid dose, lower proportions with problem opioid use, and lower levels of patient-reported opioid-related problems at 6 and 12 months after randomization.

Hypotheses pertaining to pain outcomes: Patients receiving LtOT for CNCP randomized to the PSMOT intervention, as compared with those randomized to the control arm, will have lower PEG scores, higher levels of pain self-efficacy, and lower levels of depressive symptoms at 6 and 12 months after randomization. The proposed trial will determine whether pain self-

management training can promote prescription opioid taper in higher-dose long-term opioid therapy patients without increasing pain levels or activity interference. If this trial is successful, *then prescribers and patients may be able to pursue supported opioid taper without fear of escalating pain*.

3. Background

a. Scientific Background

Provide the scientific or scholarly background for, rationale for, and significance of the research based on the existing literature and how will it add to existing knowledge. A list of references or bibliography must be included as part of this document or uploaded separately.

The evidence that LtOT improves chronic pain and function in patients with CNCP is weak, but there is strong evidence of dose-dependent risk for serious harms such as opioid abuse, Opioid Use Disorder (OUD), overdose, and death. LtOT patients are a high-risk group with high rates of substance use, mental disorders, problem opioid use, and adverse effects of opioids, including OUD, overdose, and death. Rapid opioid detoxification of these LtOT patients may lead to illicit opioid use, but gradual, supported opioid taper may reduce risks of opioid adverse events. While many LtOT patients are interested in opioid taper or discontinuation, they also fear increased pain. In a previous, NIDA-funded R34 pilot study of prescription opioid taper support, this study PI demonstrated that over 18 weeks opioids can be tapered more effectively than in control arm (43% vs 19% dose reduction) with no increase in pain intensity and significantly reduced activity interference for those receiving taper support. We have been funded by the National Institute on Drug Abuse (NIDA) to study this intervention in the KPWA delivery system. See grant proposal for bibliography.

b. Preliminary Data

Describe any relevant preliminary data.

In a previous, NIDA-funded R34 pilot study of prescription opioid taper support, this study PI (Sullivan) demonstrated that over 18 weeks opioids can be tapered more effectively than in control arm (i.e., only usual care) (43% vs 19% dose reduction) with no increase in pain intensity and significantly reduced activity interference scores at 22 and 34 weeks ($p<0.05$ and $p=0.05$, respectively) for those receiving taper support compared to controls. Those in the taper support group had significantly higher self-efficacy for managing pain and significantly lower levels of perceived opioid-related psychosocial problems (e.g., loss of interest in usual activities, trouble concentrating, feeling down or sluggish) at 22 weeks. This pilot also adds to growing literature that cognitive behavioral therapies (CBT) for pain can be provided successfully by health professionals other than psychologists.

The primary barrier to feasibility of this intervention is recruiting and enrolling patients in the trial. We surveyed 31 current KP LtOT patients concerning their willingness to participate in such a trial: 74% said they would participate in “a study that offered training in skills for chronic pain management done over the phone”, 71% said they would be willing to “try tapering your daily dose of opioid pain medication if you were promised that the dose reduction would only continue if your pain level did not get a lot worse.” This “pledge of non-abandonment” by PCPs to patients undergoing opioid taper is a crucial component of our intervention. It has proven to be a

powerful tool to promote opioid taper in other integrated care settings that have tried it. Few of the previous pilot study participants experienced significant pain exacerbation with opioid taper.

Our proposed strategy of recruitment and treatment through phone contact will minimize costs and inconvenience to patients. Drs. Sullivan and Turner successfully administered the pain self-management training over the phone to patients in the pilot study (44% of pilot study participants had at least one phone session). Among participants randomized to taper support who completed the 22-week assessment, 81% rated the intervention as very or extremely helpful. Among the participants who completed this rating at the 34-week assessment, 73% rated the intervention as very or extremely helpful

Additionally, using KPWHRI's JIFFI tool, the study programmer identified that the clinics with the largest number of LtOT users on high dose opioids are Olympia, Everett and Capitol Hill Medical Centers. Therefore, we will target the intervention in those clinics first but may need to expand to other clinics to meet our targeted enrolment.

4. Study Design

Describe the overall approach of the study (e.g. prospective, interventional, observational, retrospective, etc.). If your study includes more than one group, arm, or subject population, describe that here (for example, a study of both subjects and their caregivers, or a study with both a prospective interventional arm and a retrospective chart review arm).

This study is a pragmatic randomized trial that includes data collected from electronic health records (EHR – KPWHRI Virtual Data Warehouse),patient self-report, and data on the training sessions. There are two arms in the trial: a research interventionist guided Pain Self-Management Opioid Taper (PSMOT) or control group (no intervention, usual care). In addition, the education intervention has a sub-arm which involves an opportunity to taper opioid medication dosing. The goal of the tapering is to gradually decrease opioid dosing by ~ 10% per month.

<u>Pre-intervention Clinic Visit</u>

Preliminary data suggests that the KP Washington Clinics with the most LtOT users are: Olympia, Everett and Capitol Hill Medical Centers. Prior to rolling out the intervention at these or other clinics (clinics to be decided upon with KPWA Drs. Levy and Mehta), Drs. Sullivan and Boudreau along with the research interventionist will 1) present the intervention to the Primary Care Providers and care teams at those clinics and 2) attend at least two morning team huddles at the clinics. The purpose of this presentation and attendance at morning huddles is not only to be awareness of the intervention taking place at the clinic, but also to get buy-in from the care teams and answer any questions they may have. It is important for providers to be supportive of this intervention because the study team may be communicating to them prescribing recommendations for their patients and the implementation of those recommendations (tapering) is an important outcome of this study. The study team will also send letters to PCPs informing them when one of their patients is randomized to the intervention arm of the study (see letter to PCP). Dr. Boudreau is working closely with the delivery system on the trial. She meets and corresponds regularly with Dr. Khushboo Mehta (Family Medicine provider and Program Chief of Family Medicine), Dr. Sarah Levy (Medical Director, Continuum of Care), Dr. Angela Sparks (Family Medicine Physician and Medical Director, Clinical Knowledge

Development and Support), and Melissa Sturgis, PharmD, BCACP (Clinical Pharmacy Operations Coordinator, Quality and Clinical Operations). They will all be clinical champions of the trial.

Screening, Randomization, and Follow-up

Potentially eligible participants will be identified by the study programmer using KPWA EHR data that located in the KPWHRI Virtual Data Warehouse. Potentially eligible patients will then be screened by phone twice for additional eligibility requirements before being consented and enrolled into the study. Eligible participants will be randomized based on their primary care clinic and baseline opioid dose into one of the trial arms. Both groups will be surveyed on physical health, pain, medication use, and mental health at baseline (prior to randomization), 6 months and 12 months. The total length of enrollment/follow-up in the trial for both groups is one year. See Figure 1 for the study process.

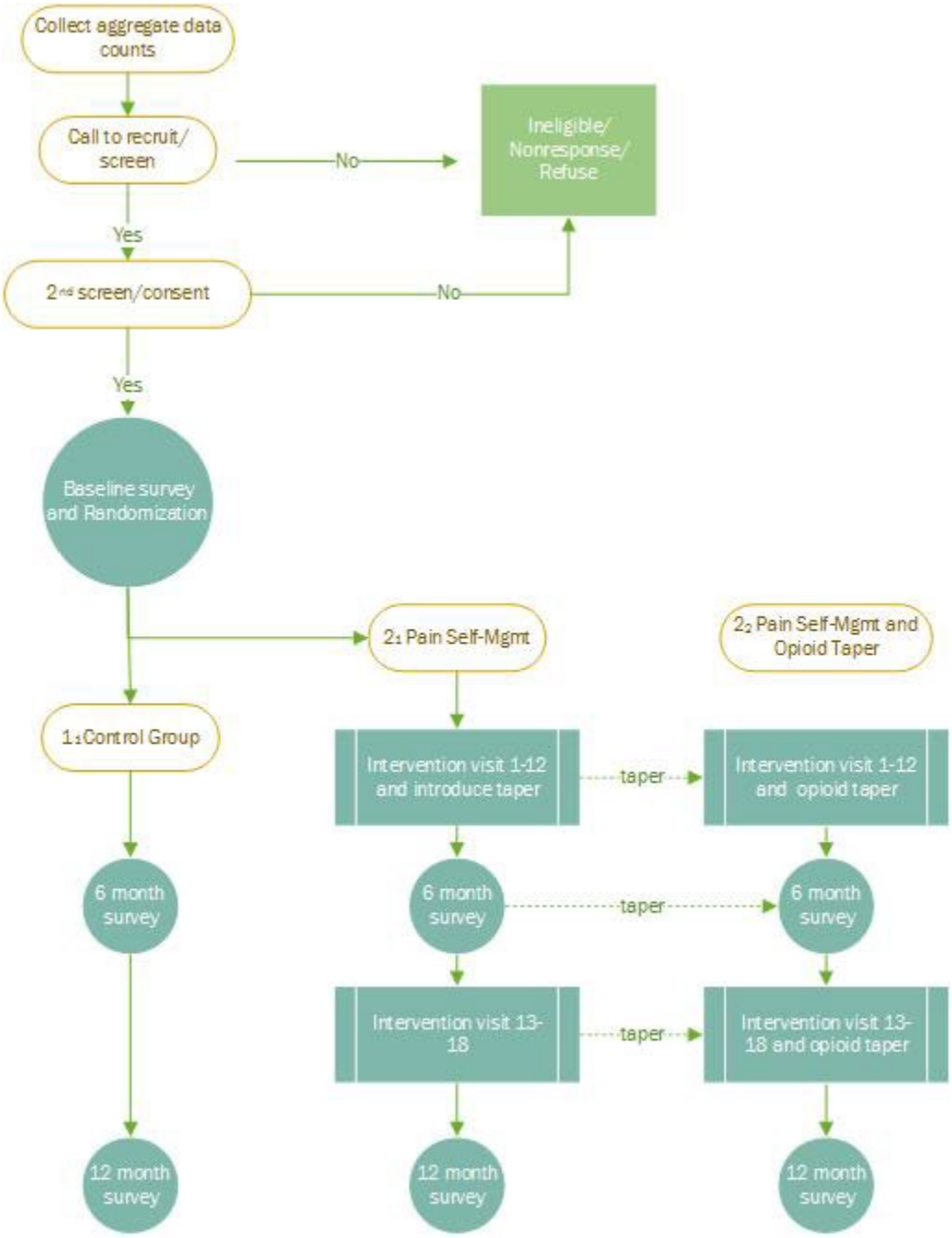
Control Arm (i.e., usual care only)
The control arm subjects will not participant in any additional study activities other than the screenings, baseline, and follow-up data collection (6 and 12 months post randomization) as described above. Usual care is the standard of care at KPWA.

Intervention Arm
The intervention arm subjects will talk with the clinical research interventionist up to 18 times over a year on the phone. The research interventionist will:

- Train participants on methods to self-manage their pain
- Introduce and offer an optional opioid taper support
- Work with the participant's PCP to suggest medication dosage recommendations
    - Difficult cases may need to be reviewed with Dr. Sullivan, the research physician, who may need to review pieces of the participant's medical record, specifically medication list and active diagnosis list to ensure the recommended medication dosing changes are appropriate. The research physician will not be abstracting information from the chart. Dr. Sullivan has Epic read only access until 12/2021, when all participants will have completed the intervention.
- Monitor, track and respond to adverse events (AE's) and Critical Incidents (CIs). CI's are a type of adverse event where a participant spontaneous reports risk behavior such as intent to harm oneself or others.

While teaching participants how to manage their pain is not part of usual care at KPWA, gradually tapering and/or discontinuing opioids are considered standard of care at KPWA and included in KPWA's "Patients on Chronic Opioid Therapy for Chronic Non-Cancer Pain Safety guidelines (September 2016). However, PCP's often do not initiate tapering due to numerous barriers such as lack of support, lack of expertise, the need to educate patients, and time constraints. As such, our trial is endorsed by the KPWA delivery system and is viewed as a mode to improve uptake of KPWA's standard of care around opioid tapering.

Figure 1. Study process



5. Study Population

a. Number of Subjects

State the number (or approximate number, if appropriate) of subjects you plan to include at the KP region to which this study is being submitted. If applicable, distinguish between the number

of subjects who are expected to be enrolled/screened and the number of subjects needed to complete the research procedures (e.g. numbers of subjects excluding screen failures).

As appropriate, consider different populations of subjects within the same study (e.g. subject/caregiver, parent/child, patient/physician). If this is a multicenter study, indicate the total number of subjects to be accrued across all sites.

This study is an educational intervention with two arms: a research interventionist guided PSMOT (with a sub-arm of patients who decide to taper their medications) or control group (no intervention, usual care). We plan on enrolling 250 participants. 125 participants in each arm. Eligible participants will be randomized based on their KPW primary care clinic and baseline opioid dose into either arm.

	Invited (contacted)	Enrolled
KP Washington	825	250
Other sites	-	-
Total	825	250

b. Inclusion and Exclusion Criteria

- Describe the criteria that define who will be included or excluded in your final study sample.
- Describe how individuals will be screened for eligibility.
- Describe the plan for disposition of data collected during recruitment/screening in the event of a screen failure or when a potential subject is contacted but declines participation (e.g. destroyed immediately, destroyed at end of study, retained for separate analysis or so that subjects are not contacted repeatedly about participation after they have declined, etc.).

Inclusion Criteria:

KPW enrollees:

- age 18-80 years *(from KPWHRI Virtual Data Warehouse (VDW))*
- receiving care at a KPWA primary care clinic *(from VDW)*
- with chronic non-cancer pain (CNCP), defined as patient-reported pain on more than half the days in the past 6 months *(from eligibility screening)*
- currently on higher-dose LtOT, defined as >90 days' supply in the past 180 days with a mean daily dose of40 mg morphine equivalent dosing (MED) or greater in the past 90 days, as first identified via KPW's pharmacy dispensing data and opioid use subsequently validated by patient self-report during screening for the trial *(from VDW)*
- who can consent to participate in the study arm to which they are randomly assigned *(from eligibility screening)*
- who are able to read, speak, and write English adequate for outcome measures *(from eligibility screening)*

- enrolled in KPW for at least 6 months prior and no plans to disenroll over the next year *(from eligibility screening)*

Exclusion criteria
We will exclude participants who:

- are receiving treatment for cancer *(from VDW and eligibility screening)*
- are enrolled in palliative or hospice care *(from VDW and eligibility screening)*
- have use in past month of parenteral, transdermal, or transmucosal opioids *(from VDW)*
- are residing in nursing home or assisted living *(from VDW and eligibility screening)*
- are using any implanted device for pain control *(from VDW and eligibility screening)*
- are taking buprenorphine formulations (Suboxone) used to treat OUD, *(from VDW, self-report and eligibility screening)*
- have psychotic symptoms, psychiatric hospitalization or suicide attempts in the past year (*from VDW and pre-randomization screening)*
- have current suicidal ideation with plan or intent *(from VDW and pre-randomization screening)*
- psychiatric hospitalization or suicide attempt in the past year (*from pre-randomization screening*)
- have cognitive impairment *(from VDW)*
- do not have regular access to a phone *(from eligibility screen)*
- are pregnant (*from VDW or self-report*)
- KPWA employees and members who are on the “do not contact” list
- are enrolled in the KPWA COMET initiative; a pharmacy based initiatve to lower opioid dosing

Secondary data sources used to identify potentially eligible subjects are listed in the table below. This data will be collected from the VDW on potential subjects at each sample pull (every 2 weeks).

Sources (specify) (I.e., from KPWA, from an approved or previous study, from another site, etc.)	List any electronic data that will be used to identify potential subjects	Date Range
KPWHRI Virtual Data Warehouse (VDW)	Demographics such as age, sex, race, ethnicity, marital status, education	2017-2021
KPWHRI Virtual Data Warehouse (VDW)	Enrollment	2017-2021
KPWHRI Virtual Data Warehouse (VDW)	Primary care clinic location: e.g., Everett, Capital Hill, Olympia)	2017-2021
KPWHRI Virtual Data Warehouse (VDW)	Diagnoses (ICD	2017-2021
KPWHRI Virtual Data Warehouse (VDW)	Medications	2017-2021
KPWHRI Virtual Data Warehouse (VDW)	Health care utilization including: outpatient, inpatient, hospice care, palliative care, emergency department	2017-2021
KPWHRI Virtual Data Warehouse (VDW)	Procedures	2017-2021

After potential subjects are identified using the electronic data in the VDW listed above, there are two steps for screening participants into the study:

1. Recruitment screening where the Survey Research Program interviewers call to recruit participants and screen them into the study with simple screening questions.
2. Pre-randomization screening where a research specialist will screen for sensitive ineligibility criteria such as psychiatric hospitalization and recent suicidal ideation.

Both screening scripts and screening questions are included in this packet.

All participant contact information (name, address, telephone number) and their study disposition (non-responder, refuser, or ineligibility reason) remains in the study recruitment database for the duration of the study to ensure that the participant isn't contacted for recruitment again.

The aggregate table below will be populated each time a potentially eligible sample is pulled from the VDW (twice per month) and prior to attempting any contact (i.e., mailing of letters and phone calls) with subjects. This table will be used for sample monitoring and a future non-reponder bias analysis. The table will be updated twice a month with potentially eligible subjects moving into columns of enrolled, non-responder, active refuser, or ineligible.

Table 1. Characteristics to be summarized and updated every two weeks when new potentially eligible subjects are identified from the KPWHRI Virtual Data Warehouse (VDW).

	Potential eligible (VDW data only)	**Enrolled**	**Not enrolled (active and passive refusers)* (**
	n=	n=	n=
		%	
Mean age (SD), years			
% Male			
Race			
White			
Black			
Asian			
Other			
Missing			
Hispanic			
Prior health plan enrollment, years			
1-2			
3-9			

10+			
Mean number (SD) of visits with a pain diagnoses, past year			
Multifocal pain (pain arising from >1 location)			
Mean daily opioid dose, past 90 days (MEQ - morphine equivalent dose)			
<40 MEQ			
40-49 MEQ			
50-89 MEQ			
90-119 MEQ			
120+ MEQ			
Primary Care Clinic			
Clinic 1			
Clinic 2			
Clinic 3			
Etc.			
Charlson co-morbidity index, past year			
0			
1			
2+			
Depression diagnosis, past year			
Anxiety diagnosis, past year			
Substance use disorder, past year			
Smoking status, past year			
Current			
Past			
Non-smoker			

c. Vulnerable Populations

Indicate whether you will include or exclude each of the following special populations. This refers to subjects who are known members of these populations upon enrollment or at any time during the study. Justify the inclusion of any of these populations. Describe additional safeguards to protect the rights and welfare of these subjects.

- Children
- Pregnant Women
- Neonates of uncertain viability or nonviable neonates (up to 28 days post birth)

- Prisoners (NOTE: The KP IRB does not have the appropriate membership to review research involving prisoners. Consultation with KFRI will be required.)

We are not including children, pregnant women, neonates or prisoners.

Pregnancy is an exclusion criteria (VDW and screening), and a reason for withdrawal from the entire study for participants in both arms of the trial (data source: VDW for both arms and EMR or patient report for the intervention arm). Data collection and the intervention will stop if the PA learns a participant is pregnant (EMR or patient reports). VDW data on diagnosis codes for pregnancy will be ascertained on all participants (intervention and control arm) at the end of the study and prior to analyses. Pregnant women will be excluded from the analyses.

Pregnancy will be rare in this population. The average age of patients on COT at KPWA is 57 years. Opioid use during pregnancy issues are complex and need special consideration beyond the limits of this study. It also introduces considerable heterogeneity into the study.

IMPORTANT NOTE: Consider whether subjects will be in a vulnerable category at the time of data collection or during analysis. For instance, if you collect data about children who were ages 12 – 15 from years 2000 – 2002, you know that now those individuals are no longer children.

d. Identification of Subjects

Describe how you will identify subjects. If you plan to use private records (EHR, Dept. of Licensing) complete 5.e, 5.f., and 5.g below as relevant.

A KPWHRI research programmer will identify eligible subjects from the KPWHRI Virtual Data Warehouse (VDW) using the variables described in Item 5b. At the time of identification (every 2 weeks), Table 1 will be generated/updated with all potentially eligible subjects.

e. Waiver of Informed Consent for **Identification** from EHR or Other Private Records

Provide rationale and justification for the Waiver of Informed Consent for identification of subjects, including:

- Does the proposed research present no more than minimal risk to the study participants?
- How the waiver of informed consent will not adversely affect the rights and welfare of the participants.
- Why this research cannot practically be carried out without a waiver of informed consent.
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

We believe that the proposed research presents no more than minimal risk to the study participants for the following reasons. Only persons directly involved in the study will have access to data. Each KP Washington enrollee will be assigned a unique study identification number linked to his or her medical record number at KP Washington. The crosswalk between the study identification number and each subject's medical record number is maintained in electronic form, but separate from the analysis files. To create project analytic files the crosswalk between the study identification number and each subject's unique medical record number will be re-established by the KP Washington research project programmer. We will use existing procedures to ensure that individual patient identifiers are kept separate from analysis

files. All data necessary to complete this research will be created and stored in secure computers to which only project team participants will have access. No participant will be identified from any published manuscripts, tables, or reports generated from the proposed study.

The waiver will not adversely affect the rights and welfare of the subjects. Neither care nor benefits will be impacted. Furthermore, safeguards are in place to protect the confidentiality of all potential research subjects.

We could not practicably identify all potential subjects without identifying them through KP Washington Virtual Data Warehouses. We could not practicably approach all participants for their consent prior to that data pull.

Subjects will not be provided with additional pertinent information after participation.

f. Waiver of HIPAA Privacy Rule Authorization for **Identification** from EHR

If you will not obtain a signed HIPAA Privacy Rule Authorization or if you want to eliminate any required language from the authorization, provide the following rationale and justification.

- Why the research could not practicably be conducted without the waiver.
- Why access to and use of the PHI is necessary for the research.
- Why the use or disclosure of PHI for the research poses no more than minimal risk to the subjects' privacy (must have an adequate plan to protect the PHI from improper use or disclosure, a plan to destroy identifiers at the earliest opportunity consistent with the purpose of the research, and when applicable, written assurances from collaborators that PHI will not be reused or re-disclosed to any other entity).

We are requesting a waiver of HIPAA authorization of Identification from EHR because we could not practicably identify and approach all potential subjects without identifying them through KP Washington Data Warehouses.

Access to and the use of PHI for this research is necessary because we need participant contact information to approach participants by mail and telephone. We also need dates (medication and enrollments) to correctly identify the sample. Finally, once on the phone, we need information such as name and birth date to confirm we have the correct person on the phone.

The use and disclosures of PHI poses no more than minimal risk to the subject's privacy because of the following protections: Only persons directly involved in the study will have access to data. Each KPW enrollee will be assigned a unique study identification number linked to his or her medical record number. The crosswalk between the study identification number and each subject's medical record number is maintained in electronic form at each site, but separate from the analysis files. To create project analytic files the crosswalk between the study identification number and each subject's unique medical record number will be re-established by the project programmer. We will use existing procedures to ensure that individual patient identifiers are kept separate from analysis files. All data necessary to complete this research will

be created and stored in secure computers to which only project team participants will have access. When these files are created, the crosswalk will be erased from all files and kept only by the programmer. No participant will be identified from any published manuscripts or reports generated from the proposed study.

Once all data has been collected for this study, the crosswalk between the study identification number and each subject's unique medical record number will be erased from all analysis files and stored in a file kept by each site's project programmer. The project manager maintains a calendar that tracks destruction date information and will notify the programmer prior to the scheduled date for destruction.

All linkages will be destroyed as early as is consistent with the research and no later than December 31, 2026

g. RCW 70.02 Requirements to Access HIPAA Covered Data without Consent for **Identification** from EHR (WA State Law)

If you will not obtain written HIPAA Authorization provide the following rationale and justification. Explain how the research:

- Is of sufficient importance to outweigh the intrusion into the privacy of the patient that would result from the disclosure;
- Is impracticable without the use or disclosure of the health care information in individually identifiable form;
- Contains reasonable safeguards to protect the information from redisclosure;
- Contains reasonable safeguards to protect against identifying, directly or indirectly, any patient in any report of the research project; and
- Contains procedures to remove or destroy at the earliest opportunity, consistent with the purposes of the project, information that would enable the patient to be identified, unless an institutional review board authorizes retention of identifying information for purposes of another research project.

This research is of sufficient importance to outweigh the intrusion into the privacy of the participant that would result from the disclosure because although some study participants may not benefit directly from this study, their participation may eventually be of help in understanding whether pain self-management training and optional taper support helps patients reduce their prescribed opioid medications, which is currently an important public health priority.

We could not practicably identify potentially eligible patients or approach participants for their written authorization prior to the automated data (i.e., VDW) pull.

Access to and the use of PHI for this research is necessary because we need participant contact information to approach participants by mail and telephone. We also need dates (medication and enrollments) to correctly identify the sample. Finally, once on the phone, we need information such as name and birth date to confirm we have the correct person on the phone.

The use and disclosures of PHI poses no more than minimal risk to the subject's privacy. Only persons directly involved in the study will have access to data. Each KPWA enrollee will be assigned a unique study identification number linked to his or her medical record number. The crosswalk between the study identification number and each subject's medical record number is maintained in electronic form at each site, but separate from the analysis files. To create project analytic files the crosswalk between the study identification number and each subject's unique medical record number will be re-established by the project programmer. We will use existing procedures to ensure that individual patient identifiers are kept separate from analysis files. All data necessary to complete this research will be created and stored in secure computers to which only project team participants will have access. When these files are created, the crosswalk will be erased from all files and kept only by the programmer. No participant will be identified from any published manuscripts or reports generated from the proposed study.

Once all data has been collected for this study, the crosswalk between the study identification number and each subject's unique medical record number will be erased from all analysis files and stored in a file kept by each site's project programmer. The project manager maintains a calendar that tracks destruction date information and will notify the programmer prior to the scheduled date for destruction. All linkages will be destroyed as early as is consistent with the research and no later than December 31, 2026

h. Decisionally Impaired Adults

State whether decisionally impaired adults will be included and explain the extent of cognitive impairment (complete, fluctuating, progressive, or temporary). Justify their inclusion, and explain any protections to mitigate risk (such as the involvement of a caregiver or authorized representative). Describe consent/assent procedures.

N/A we will not include decisionally impaired adults.

i. Other Populations Targeted for Recruitment

If you are targeting a population that may be vulnerable to coercion or undue influence based on the specific circumstances of the study, describe how you will ensure that participation is voluntary and minimize any added risk. (Common examples include employees, students, people of low socioeconomic status, etc.)

N/A we will not be targeting or including vulnerable populations. We will not actively be excluding KPWA employees, but we will exclude patients including KPWA employees, who have pro-actively requested to not be included in research.

j. Setting

Describe the sites or locations where your research team will conduct the research.

We will sample participants from KPWA clinics that have high the highest proportion of high dose LtOT users. Preliminary data exploration suggests that Olympia, Capitol Hill and Everett

Medical Centers have the highest counts of LtOT users but we are working with leaders in the delivery system (Sarah Levy and Melissa Sturgis) to determine the best clinics to target.

We will recruit participants by mail and telephone. All study visits will be conducted on the telephone.

k. Recruitment Methods

Describe how study participants will be recruited and enrolled. Indicate whether you will openly recruit using advertisements, websites, or brochures. Indicate if you plan to do targeted recruitment using existing records or referral. (Upload all recruitment materials to your submission to the IRB.)

Describe, by position/title, who will be recruiting and enrolling participants (providing the specific names of research team members is not necessary).

Describe any plans for the participants in the currently proposed study to be re-contacted or recruited for future follow-up studies. (Note that participants should be informed of this potential for re-recruitment during the current study's consent process.)

Potential participants will be identified using the KPWHRI VDW (see inclusion/exclusion criteria). Survey Research Program staff will then mail potential participants an advance invitation letter describing the study along with an information sheet, study insert and $2 pre-incentive.

Approximately 5 business days after sending the invitation packet, the Survey Research Program phone room staff will call participant to conduct the first round of eligibility screening and, for subjects who remain eligible, schedule the pre-randomization screening with the study research specialist. After the call, we will send these potentially eligible participants a cover letter and a copy of the consent form for the next round of screening.

At the pre-randomization, second round of screening, the study research specialist with further screen potential participants with two more screening questions. If eligible, the participant will then be consented, enrolled, and asked to take the baseline survey by phone or web.

Once the baseline survey is complete (by phone or web), the participant will receive a thank you letter (including $20 incentive) with their randomization status (PSMOT intervention arm or control arm) and next steps. Participants in the intervention arm will also receive a welcome cover letter with the materials needed for the training sessions. Their provider will also receive a letter informing them of their patient's enrollment into the intervention arm of the trial (see letter to PCP that informs them of their patient's participation in the intervention arm of the trial).

Participants may be recruited for future supplements to this study. Drs. Sullivan and Boudreau are exploring the feasibility of conducting a supplement to this project where participants

enrolled in the intervention arm would be offered the opportunity to participate in two (one at baseline and one at 12 month) 2 hour, in-person, neuropsychology tests to examine the cognitive and social aspects of patients as they taper down their opioid dosage. While all intervention arm participants would/could take the baseline assessment, only those who chose to taper would be approached to do a 12 month assessment. At this time, Dr. Sullivan is merely exploring the feasibility of doing this type of supplement and no definitive plans are in place for moving this research forward. We would like to request permission at this time to contact the intervention arm participants for this potential, future research if it comes to fruition.

Description of Recruitment Methods, Randomization and Mailings

When	Task	Who	Description
Day 0	Send Invitation Packet	Survey Research Program	Mail hardcopy invitation letter, study insert, information sheet and $2 bill
Day 5	Call to recruit and first eligibility screen	Survey Research Program	Eligibility screen
Day 5	Mail Consent Packet	Survey Research Program	Mail cover letter and copy of consent form
Day 10	Pre-randomization screen and consent	Study Research Specialist	2nd eligibility screen, obtain oral consent, confirm PCP information, obtain web survey mode preference
Day ~10-28	Baseline survey	Participant/ Survey Research Program	Participant takes baseline survey by web or phone
Day ~10-28	Randomization	Study Programmer	Study team randomizes participants who complete their survey to either the intervention arm or the control arm
Day ~14-32	Thank you letter	Survey Research Program	Mail thank you letter with randomization status and $20 incentive
Day ~14-32	Letter to PCP	Study Team	Mail letter to intervention participant's PCP informing them of enrollment into intervention arm of STRIPE study

Day ~14-32	Intervention Welcome	Study Team	Mail intervention packet containing cover letter, participant workbook with appendices, audio files on CD and "The Pain Survival Guide."

I. Informed Consent Process

Describe how you will obtain and document consent, including:

- Where, when and how the consent process will take place.
- A process to ensure ongoing consent.
- Steps that will be taken to minimize the possibility of coercion or undue influence.
- Any steps that will be taken to ensure the subjects' understanding.
- If you will conduct screening or any other research procedures before obtaining full informed consent, describe this.

For this study we will be collecting data and requesting different forms of consent and a waiver of HIPAA authorization for the following data collection activities.

OVERVIEW OF CONSENT PROCESS:

Please see the table below for an overview of the proposed consent and waiver of informed consent for this study.

Data collection timepoint	**Informed Consent**			**HIPAA Authorization**	
	Informed Consent	Waiver of documentation of informed consent	Waiver of informed consent	HIPAA authorization	Waiver of HIPAA authorization
Sample identification via VDW			X		X
Recruitment screening		X			No EMR data if ineligible
Pre-randomization screening		X			No EMR data if ineligible
Study enrollment		X			X

All project activities are conducted through the mail, on the telephone or using a web-link for survey data collection. There are no in-person study activities, therefore this project is requesting a waiver of documentation of informed consent to:

- Screen potential participants in two rounds for eligibility during recruitment. VDW data will be used to identify the potentially eligible sample.
- Enroll participants into our study by sending a copy of the consent form and obtaining verbal consent (instead of signed consent)

For the screening steps (both for eligibility during recruitment calling and pre-randomization screening) the consent process will be as follows:

- The study team will send potential participants a single invitation letter and an information sheet that describes **both** screening activities
- For each screening telephone call, the study team will confirm the participant's identity, provide an opportunity to answer any questions and obtain oral consent

For study enrollment the consent process will be as follows:

- Consent will occur during the pre-randomized second screening telephone call
  - Prior to the call, the study team will send the participant a paper copy of the consent form and a cover letter
  - After and if the participant has screened eligible, the study research specialist will go over the consent form with the participant (using a script which will highlight all the key points) and obtain:
    - Oral consent to participate in the study
    - Approval/disapproval to allow the use of email for study communication
    - Approval/disapproval to allow the study team to audio record telephone sessions (if the participant is chosen to be in the intervention arm)
  - The study team will track the consent outcomes (consented yes/no, use of email yes/no, and audio recording yes/no) in the project tracking database

m. Waiver of Informed Consent

Provide rationale and justification for the Waiver of Informed Consent for this study, including:

- Does the proposed research present no more than minimal risk to the study participants?
- How the waiver of informed consent will not adversely affect the rights and welfare of the participants.
- Why this research cannot practically be carried out without a waiver of informed consent.
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

We are requesting a waiver of documention of informed consent to screen and enroll subjects into the study. See below.

n. Waiver of Documentation of Informed Consent

Provide rationale and justification for the Waiver of Documentation of Informed Consent by identifying which of these two conditions applies and how.

1) The research involves no more than minimal risk to participants AND involves no procedures for which written consent is normally required outside of the research context.
2) The signed consent document would be the only record linking the participants to the research, and the principal risk to participants would be potential harm resulting from a breach of confidentiality.

We are requesting a waiver of documentation of informed consent to:

- Screen potential participants for two rounds of eligibility during recruitment by sending an information sheet and obtaining verbal consent
- Enroll participants into our study by sending a copy of the consent form prior to the pre-randomization screening call and obtaining verbal consent (instead of signed consent) during that pre-randomization screening call after the participant has screened eligible.

We believe that the proposed research presents no more than minimal risk to the study participants. Only persons directly involved in the study will have access to data. Each KPWA enrollee will be assigned a unique study identification number linked to his or her medical record number at KPWA. The crosswalk between the study identification number and each subject's medical record number is maintained in electronic form, but separate from the analysis files. To create project analytic files the crosswalk between the study identification number and each subject's unique medical record number will be re-established by the KP Washington research project programmer. We will use existing procedures to ensure that individual patient identifiers are kept separate from analysis files. All data necessary to complete this research will be created and stored in secure computers to which only project team participants will have access. No participant will be identified from any published manuscripts or reports generated from the proposed study.

Additionally, all study activities are being conducted on the telephone and written consent cannot be obtained, we will do the following: For eligibility screenings, we will send an information sheet and obtain verbal consent. For enrollment into the study, we will send a copy of the consent form for participant's review, obtain oral consent and track documentation of consent in our project tracking database.

o. Alteration of Informed Consent

Identify the required elements of informed consent that you wish to remove or alter. Provide justification for their removal or alteration.

N/A

p. Non-English-Speaking Subjects

If subjects who do not speak English will be enrolled, describe how the consent discussion will take place and indicate if translated consent forms or short forms will be used. Confirm that an interpreter will assist with the initial consent process and subsequent study visits.

N/A

q. Assent of Children and Parent Permission

IMPORTANT NOTE: Consent may be obtained in certain situations. For example, conducting family planning or sexually transmitted disease (STD) research. In addition, for older children ages 16 and up who participate in an adult study, the consent document can be used in place of the assent document.

Describe how you will obtain and document assent/parental permission, including:

- Describe your plan for obtaining parent permission. The permission of one parent is generally sufficient for minimal risk research, or for greater than minimal risk research if there is the potential for direct benefit to the child.
- Note that for studies involving greater than minimal risk with no prospect of direct benefit to the child, permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
- Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission.
- Indicate whether assent will be obtained and documented from all, some, or none of the children. If assent will only be obtained from some children (because of very young age, severe cognitive impairment, etc.), indicate which children will be required to assent and which will not.
- When assent of children is obtained, describe whether and how it will be documented.
- When subjects might reach the age of majority during the study, describe the plan to obtain consent from these subjects at that time using an adult consent form.

N/A

r. Adults Unable to Consent/Decisionally Impaired

Describe the consent/assent process for Adults Unable to Consent/Decisionally Impaired, including:

- Describe the process to determine whether an individual is capable of consent.
- List the individuals from whom permission will be obtained in order of priority. (E.g., durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and adult child.
- Describe the process for assent of the subjects. Address the following:
    - Whether assent will be required of all, some, or none of the subjects. If assent will be obtained from some subjects, indicate which subjects will be required to assent and which will not.
    - If assent will not be obtained from some or all subjects, an explanation of why not.
    - When assent is obtained, describe how it will be documented.
- Describe the plan to obtain consent if subjects might regain capacity to consent during the study.

N/A

s. HIPAA Privacy Rule Authorization – if study will use or disclose Protected Health Information (PHI)

Describe the plan to obtain a signed Privacy Rule Authorization from each subject.

All participant contact will occur by mail, telephone or web (for those who elect to take their surveys on the internet) and we will not have the opportunity to obtain a signed HIPAA authorization form from each subject. We are requesting a waiver of HIPAA authorization.

t. Waiver of HIPAA Privacy Rule Authorization

If you will not obtain a signed HIPAA Privacy Rule Authorization, or include HIPAA authorization in the consent form, or if you want to eliminate any required language from the authorization, provide the following rationale and justification.

- Why the research could not practicably be conducted without the waiver.
- Why access to and use of the PHI is necessary for the research.
- Why the use or disclosure of PHI for the research poses no more than minimal risk to the subjects' privacy (must have an adequate plan to protect the PHI from improper use or disclosure, a plan to destroy identifiers at the earliest opportunity consistent with the purpose of the research, and when applicable, written assurances from collaborators that PHI will not be reused or re-disclosed to any other entity).

All study activities will take place over the telephone, mail or internet and we will not be able to obtain signed HIPAA authorization.

For the following activities we are requesting a waiver of HIPAA authorization to:

- Enrolling participants into the study by sending a copy of the consent form which contains the required HIPAA authorization language

For the above activities, research could not practicably be conducted without a waiver because there are no plans for contacting participants in person. Additionally, we cannot practicably identify the sample without a waiver.

Access to and the use of PHI for this research is necessary because we need participant contact information to approach participants by mail and telephone. We also need dates (medication and enrollments) to correctly identify the sample. Finally, once on the phone, we need information such as name and birth date to confirm we have the correct person on the phone.

The use and disclosures of PHI poses no more than minimal risk to the subject's privacy. Only persons directly involved in the study will have access to data. Each KPW enrollee will be assigned a unique study identification number linked to his or her medical record number. The crosswalk between the study identification number and each subject's medical record number is maintained in electronic form at each site, but separate from the analysis files. To create project analytic files the crosswalk between the study identification number and each subject's unique medical record number will be re-established by the project programmer. We will use existing procedures to ensure that individual patient identifiers are kept separate from analysis files. All data necessary to complete this research will be created and stored in secure computers to which only project team participants will have access. When these files are created, the

crosswalk will be erased from all files and kept only by the programmer. No participant will be identified from any published manuscripts or reports generated from the proposed study.

Once all data has been collected for this study, the crosswalk between the study identification number and each subject's unique medical record number will be erased from all analysis files and stored in a file kept by each site's project programmer. The project manager maintains a calendar that tracks destruction date information and will notify the programmer prior to the scheduled date for destruction.

All linkages will be destroyed as early as is consistent with the research and no later than December 31, 2026

u. RCW 70.02-Requirments to Access HIPAA Covered Data without Consent

If you will not obtain HIPAA Authorization or Consent provide the following rationale and justification. Explain how the research:

- Is of sufficient importance to outweigh the intrusion into the privacy of the patient that would result from the disclosure;
- Is impracticable without the use or disclosure of the health care information in individually identifiable form;
- Contains reasonable safeguards to protect the information from redisclosure;
- Contains reasonable safeguards to protect against identifying, directly or indirectly, any patient in any report of the research project; and
- Contains procedures to remove or destroy at the earliest opportunity, consistent with the purposes of the project, information that would enable the patient to be identified, unless an institutional review board authorizes retention of identifying information for purposes of another research project.

This research is of sufficient importance to outweigh the intrusion into the privacy of the participant that would result from the disclosure because although some study participants may not benefit directly from this study, their participation may eventually be of help in understanding whether taper support helps patients taper their prescribed opioid medications, which is currently an important public health priority.

We will have the following safeguards in place to protect the information from re-disclosure:

Physical Controls: KPWA policies and procedures ensure controlled access to computers and physical space for secure storage of data and confidentiality information. Access to the KPWHRI building is restricted by locked doors and requires a key card to enter KPWHIR facility

always. Any paper files with identifiers are required to be kept in locked filing cabinets. Keys are only provided to study staff once they are approved by the facilities and project managers.

Technical Controls: Administrative, physical, and technical safeguards are employed to ensure the confidentiality, integrity, and security of electronic health information (45 CFR Part 160 and Subparts A and C of Part 164; 44 U.S.C. § 3541, et seq). At KPWA data will be stored on password protected computers in a network folder where only authorized study personnel are granted access. All access by staff person, date and time is logged. All computers are loaded with anti-virus software and security patches are deployed to staff computers automatically. Data will never be transferred to laptops, memory sticks or other mobile devices; our policy does not permit the storage of PHI on these devices.

Administrative Controls: At KPWA, files are backed up on an hourly basis to a disk system and are not encrypted. Backup media are stored within KPWA data centers in Tukwila, Quincy and Liberty Lake (all within Washington State) to which only authorized staff have access. Data will be accessed via KPWA desktop computers which require staff to log on using their password. Data will be stored on KPWA's SAN system, secured using NTFS file permissions. members. The data will be kept in a dedicated secure folder, separate from administrative datasets/records and will only be accessed by study team members. Collected data will be used only for this IRB approved study and will not be combined with any non-study administrative datasets/records. At project completion, the data will be archived with an automated, mandatory deletion date the sooner of 5 years from receipt of the data or December 31, 2026. Published data will not contain any individual identifiers.

We could not practicably approach all participants for their written authorization because we are not conducting any study visits in-person.

While aggregate data can be appropriate for certain study questions, collecting individual level data is necessary to conduct analyses that look at the relationship among variables.

The use and disclosures of PHI poses no more than minimal risk to the subject's privacy. Only persons directly involved in the study will have access to data. Each KPW enrollee will be assigned a unique study identification number linked to his or her medical record number. The crosswalk between the study identification number and each subject's medical record number is maintained in electronic form at each site, but separate from the analysis files. To create project analytic files the crosswalk between the study identification number and each subject's unique medical record number will be re-established by the project programmer. We will use existing procedures to ensure that individual patient identifiers are kept separate from analysis files. All data necessary to complete this research will be created and stored in secure computers to which only project team participants will have access. When these files are created, the crosswalk will be erased from all files and kept only by the programmer. No participant will be identified from any published manuscripts or reports generated from the proposed study.

Once all data has been collected for this study, the crosswalk between the study identification number and each subject's unique medical record number will be erased from all analysis files and stored in a file kept by each site's project programmer. The project manager maintains a

calendar that tracks destruction date information and will notify the programmer prior to the scheduled date for destruction.
All linkages will be destroyed as early as is consistent with the research and no later than December 31, 2026

6. Study Procedures

Describe and explain the study design, including:

- Procedures to monitor subjects for safety, including who will review the data and at what frequency for safety issues.
- Procedures performed to lessen the probability or magnitude of risks.
- All drugs and devices used in the research and the purpose of their use, and their regulatory approval status.
- The source records that will be used to collect data about subjects. (Attach all surveys, scripts, and data collection forms.)
- What data will be collected including long-term follow-up.
- The duration of an individual subject's participation in the study.
- The duration anticipated to enroll all study subjects.
- The estimated date for the investigators to complete this study (complete primary analyses)

NOTE: It should be clear exactly which procedures will be conducted for the research as opposed to procedures the subjects would undergo (in the exact manner described in the protocol) even if they were not participating in the study.

Describe procedures that will be followed when subjects withdraw from the research, including withdrawal from intervention but continued data collection.

Describe any anticipated circumstances under which subjects could be withdrawn from the research without their consent.

Describe any procedures for orderly termination.

If the study involves genetic testing or collection of genetic information, describe this.

Study Procedures – Intervention Arm and Control Arm
Sequential description

As described in the recruitment section of this application, potential research participants are identified via the KPWHRI VDW by the KPWA programmer and sent a letter of invitation, a study information sheet, study insert, and a $2 incentive. Five days after the invite letter is sent, the KPWA survey team calls subjects for the first screening. Participants will be screened twice. First, they will be screened on basic eligibility criteria when the survey research program calls them to recruit. (See STRIPE screening

script for screening questions.) If the participant passes the first round of screening and is still interested, they will be scheduled for a second round of screening with a study research specialist.

Prior to the call, the study team will mail the participant a copy of the consent form and a cover letter. During the second screening call, the research specialist will ask sensitive eligibility questions regarding recent intent to harm and recent psychiatric hospitalization. (see "Pre-randomization script" for sensitive eligibility screening script and questions). If the participant passes this round of screening, the research specialist will administer and obtain oral consent. The participant will then be offered the baseline survey via phone or web. If phone is chosen, the participant will be asked if they would like to do the baseline survey now or schedule a time to complete it. If web is chosen, the research specialist will confirm the participants email address and email them a link to the survey. Reminder emails and/or phone follow-up will occur if subjects do not complete the baseline survey.

Once the baseline survey is complete, we will randomize the participant into the intervention arm or the control arm. The study team wants participants to be randomized after the baseline survey out of concern that knowledge of status could affect a subject's responses to questions and participation in the baseline assessment. We will send participants a thank you letter with their incentive upon completion of the baseline assessment that details which arm they were assigned to and next steps.

We anticipate the time from the letter being mailed to time of enrollment to be between 2-4 weeks. All invitation materials, consent forms, HIPAA authorization forms and scripts are attached in this package.

After the baseline assessment and randomization, all participants will be asked to take two more surveys; 6 months after enrollment and 12 months after enrollment. The survey can be taken either in web form or on the telephone, administered by a survey research program telephone interviewer. With the 12 month phone or web survey reminder letter, all participants wil receive a $2 pre-incentive. The survey will ask questions about physical health (including any experience with pain), mental health (depression and anxiety), and medication use. All baseline, 6-month, and 12-month surveys including script are included in this packet. See Master Survey document for a list of the surveys to be administered at the three-time points.

Additionally, all subjects enrolled in the intervention who choose to taper their opioids arm will be asked to complete the two item Graded Chronic Pain Scale (GCPS) and the fourteen item Hospital Anxiety and Depression Scale (HADS) before each intervention telephone session. (See Measures for Intervention Arm only doc.). Surveys are attached in this package. The pre-visit GCPS and HADS will be completed on paper (mailed with intervention packet materials) prior to the visit and read their score to the research interventionist at the beginning of the session.

Activity	**Time Commitment**

Read invitation packet	5 minutes
1st screening call	10 minutes
Read consent packet and answer any questions	10 minutes
2nd screening call including consent and randomization	20 minutes
Baseline survey	30 minutes
Pre-visit GCPS and HADS for particpants who choose to taper	5 minutes each visit 5-18
Intervention arm study visit 1-18	30-60 minutes each visit
6 month survey	20 minutes
12 month survey	20 minutes

We anticipate it will take 18 months to enroll all 250 study participants. Each participant will be followed for 12-months post randomization.

Device/drug information
N/A

Secondary data: data, sources, and date range

In addition to the primary data described above, secondary data to be collected on participants enrolled in both arms of the study are listed in the table below.

Data from KP Washington

Source (specify) (i.e., from KPWA, or from an existing or previous study)	Key Information/Description of Variables	Date Range
KPWA data sources (VDW)	Diagnoses via ICD codes and dates of code: Comorbidities (comorbidity indices and the individual constituent diseases), mental health disorders (e.g. depression, anxiety), substance use disorders (e.g. opioid use disorder, alcohol use disorder, tobacco use disorder, cannabis use disorder, stimulant use disorder),	2016-2022

	cancer, suicidal ideation, and pain including site of pain	
KPWA data sources (VDW)	Social history table variables for alcohol use and tobacco use	2016-2022
KPWA data sources (VDW)	Health plan enrollment information (start and stop dates)	2016-2022
KPWA data sources (VDW)	Health care utilization including: outpatient, inpatient,, emergency department	2016-2022
KPWA data sources (VDW)	Medication orders and pharmacy dispensings including dates	2016-2022
KPWA data sources (VDW)	Laboratory tests and results	2016-2022

DIRECT IDENTIFERS		
☒ Names	☐ Social Security Numbers	☐ Web URLs
☒ Dates	☒ Medical record numbers	☐ IP address numbers
☒ Postal address	☒ Health plan numbers	☐ Biometric identifiers (e.g., finger prints, voice prints, retina scans)
☐ Geocode	☐ Account numbers	
☒ Phone numbers	☐ License/Certificate numbers	
☐ Fax numbers	☐ Vehicle ID numbers	☐ Facial Photos/Images
☒ Email address	☐ Device identifiers/Serial numbers	☐ CHS ID
		☐ Other unique identifier(s):

Alternative treatment(s) and/or denied treatment
N/A
Deception/incomplete disclosure
N/A
Incidental findings
N/A

Procedures to monitor, lessen or mitigate risk
There are several study design features that lessen or mitigate risk:

- Participants assigned to the control group may be disappointed with their assignment. We are providing incentives for completing 6 and 12 months surveys for both groups to improve retention in the trial.
- Participants may be embarrassed or psychologically distressed at the survey questions, they are told that they can skip any questions they do not want to answer
- Breach of confidentiality is a potential risk. See section 5u for a description of the various controls set in place to safeguard data security. Additionally, staff are trained on best practice privacy and confidentiality measures.
- The study will have a plan in place to handle Critical Incidents, when a participant endorses intent to harm themselves or others. Although, we anticipate this to be rare, we would like to be prepared in the event that a participant spontaneously endorses intent to harm. The research specialist and research interventionist will administer the Columbia Suicidality Severity Rating Scale. After determining the score, the research interventionist will take the appropriate steps to triage the participant per the study protocol. (see CI procedures for Columbia Suicidality Severity Rating Scale and general CI procedures). Additionally, the research specialist and research interventionist will be supervised by a KPW licensed clinical psychologist. Dr. Ben Balderson is KPWA mental health provider. All critical incidents will be reviewed by the study psychologist.
- A data use agreement will be in place to share study data with investigators at the University of Washington

Subject drop out or withdrawal procedures

If a subject drops out or we withdraw them from the study, the study team will:

- Update the tracking database to indicate that no further patient-self report data collection or participant contact will occur. They will not be asked to complete any more surveys. If we withdraw the participant from the study, we will send them a letter notifying them that they are no longer enrolled in the study.
- We will continue to use the data they have already contributed/agreed to allow us to use per their consent for analyses
- All participants using buprenorphine for treatment of OUD will be withdrawn from the entire study. We may learn about buprenorphine use from the screening survey or as indicated in VDW medication dispensing data ascertained prior to the analyses. Primary data collection will cease and they will not be included in analyses. This is an exclusion criteria.
- All pregnant women will be withdrawn from the study entirely. Primary data collection will cease and they will not be included in analyses. Pregnancy status will be determined via a screening question and diagnosis codes from the VDW for subjects in both study arm prior to analyses. We expect very few young women to be in the study due to the average age of chronic high dose opioid users at KP.

Anticipated study end date

The anticipated study end date for the completion of primary analyses will be on or before December 31, 2021

Study Procedures – Intervention Arm

Sequential description

After subjects are randomized into the intervention arm, they will receive a letter with their randomization status, intervention packet, and then begin having telephone visits with the study research interventionist . The study team will send a letter to the participants PCP noting their participation in the pain self-management training arm of the trial. Prior to their first telephone call we will send participants a packet containing, "The Pain Survival Guide" https://www.amazon.com/Pain-Survival-Guide-Reclaim-LifeTools-ebook/dp/B0029KHTK8, a CD containing audio files of relaxation techniques and participant workbook that includes the various exercises for each visit along with GCPS and HADS questionnaires to administer before each telephone visit. Participants can opt to receive and take the GCPS and HADS questionnaires on the web if they choose. The workbook, CD and questionnaires are included in this package. Additionally, we are working on creating a study website that will host the audio files.

A description of each telephone visit, the timing of the visit and the duration of the visit is described in the following table. See the "Clinician Manual" for details on the content for each session.

Session number	Week (from random-ization)	Session content	Duration
1	1	Overview of intervention and sessions, education regarding benefits of pain coping skills training and collaborative nature of treatment. Identification of treatment goals. Instruction and practice in diaphragmatic breathing. Personal action plan introduction. Review of study team contacts Review pre-visit GCPS and HADS assessments to be done prior to each subsequent session	60 mi
2	2	Diaphragmatic breathing review and practice. Education regarding rationale for and benefits of relaxation techniques, introduction to 7-muscle group tense-release progressive muscle relaxation.	30 min
3	3	Pain neuroscience education and rationale for cognitive and behavioral techniques for managing pain. Education about and discussion of harm and fear-avoidance beliefs. Home assignment: watch two videos and read article about patient opioid taper experiences.	30 min
4	4	Motivational interviewing: elicit history of opioid use and views about tapering, provide education about long-term opioid therapy risks and scientific evidence for benefits, discuss and problem-solve barriers to tapering. Education about withdrawal symptoms. --debriefing of subject after viewing videos at home of patient experiences tapering off opioids. --If interested in taper, subject instructed to make appointment with primary care provider at the time of their next opioid refill to discuss taper and subject informed interventionist will communicate with PCP about this, as well as with the study PI, a psychiatrist with expertise in pain, who will review their medications and may make suggestions about their medications. To be asked at subsequent sessions if patient is not interested in tapering starting at session 4. -- If pt interested in taper, interventionist provides to Study PI information on EHR diagnoses, pain rating (graded chronic pain scale - GCPS), anxiety and depression score	45 min

		(HADS). After consultation with Study PI Dr. Sullivan, interventionist provides guidance to primary care provider about taper discussion, opioid taper plan, and initiation or adjustment of non-opioid medications to relieve pain, anxiety, depression, insomnia. See Taper Guidelines for details. --If not interested, interventionist will ask about interest at subsequent sessions as deemed appropriate.	
5	5	Education about relationship between sleep and pain, sleep hygiene, and cognitive and behavioral strategies for improving sleep.	30 min
6	6	Review of cognitive and behavioral skills taught to date, and application to daily life to manage pain and stress. Concept that hurt ≠ harm.	30 min
7	8	Education about benefits of activity pacing. Development of individual activity pacing plan for the participant.	30 min
8	10	Coping with pain flare-ups: development of personal pain coping plan.	30 min
9	12	Instruction and practice in 4-muscle group tense-release progressive muscle relaxation	30 min
10	14	Instruction in and practice of 4-muscle group progressive muscle relaxation without tensing.	30 min
11	18	Education about coping self-statements and identification of helpful coping self-statements for the individual participant.	30 min
12	22	Distraction as a pain coping skill.	30 min
13	26	Instruction and practice in body scan technique.	30 min
14	30	Instruction and practice in mini-relaxations.	30 min
15	34	Review and practice of mini-relaxation, and application to daily situations of increased pain or stress.	30 min
16	38	Education about importance of pleasurable activities, identification of pleasurable and meaningful activities for the individual participant, education about goal setting, pleasurable activity goal-setting. Review of daily plan and pain coping flare-ups plan; refinement and revision as necessary. Pain coping skills review.	30 min
17	42	Review of pain coping skills learned in this program. Education about maintenance of gains and relapse prevention.	30 min
18	46	Skills summary, final plan for maintaining gains and managing setbacks and pain flare-ups. Discussion of participant's thoughts about this being the last session, and reminders of next steps in the research.	30 min

Note: The first 6 sessions are weekly. The next 4 sessions are biweekly. The remaining sessions are monthly. For participants who are tapering their opioid dose, each session will include discussion of how that is going and how the pain coping skills might be used to manage pain and any other symptoms experienced. Each session includes home activity assignments for reading (The Pain Survival Guide and participant workbook) and coping skills practice (personal action plan) and review of experiences with the previous week's assignments. Each session also includes identification of obstacles or challenges to completing the home activity assignments and problem-solving ways to overcome these. Intervention participants will be provided a workbook, The Pain Survival Guide, access to audio files of relaxation exercises, and access to two videos of patient interviews.

Primary Data Collected on the Intervention

During each telephone session, the research interventionist will track the phone sessions into the project REDCap tracking data base hosted at KPWA. The information captured at the visits includes:

- Date of the phone visit

- Whether or not the participant attended their scheduled appointment
- Check boxes for session content that was covered during the visit
- Any critical incidents (intent to harm oneself or other)
- Any adverse events
- Detailed notes on the visit
- Amount of time spent on each visit
- HADS and GCPS score (score read to interventionist and entered into REDCap at the beginning of each session for participants who choose to taper)

At the fourth study visit, the research interventionist will ask participants if they want to taper their opioid dosing. If the participant declines to taper, they will proceed with the rest of their pain self-management sessions and follow-up surveys. If a participant expresses interest in tapering, the interventionist will recommend medication taper suggestion to the participant's PCP using Epic Telephone Encounters. We will provide taper support at a later date if they prefer to delay the taper or resume paused tapers. Patients will be allowed to pause tapers (i.e., put the taper on hold) for any reason including the need to escalate opioid dose (e.g., surgery requiring additional pain management). Patients delaying or pausing tapers will still continue to receive the pain self-management training. Participants will be informed of the risk of stock-piling opiates during the taper process. The research interventionist may need to consult with Dr. Sullivan, the study research physician on complicated tapering scenarios. Dr. Sullivan will have Epic read only access to review the medical records of any difficult tapering sessions to provide guidance to the research interventionist. The guideline for tapering was developed by Dr. Sullivan (UW psychiatrist and Principal Investigator),and is attached. The guidelines were reviewed by Dr. Sarah Levy (KP Medical Director, Continuum of Care), Dr. Angela Sparks (Family Medicine Physician and Medical Director, Clinical Knowledge Development and Support), Dr. Khushboo Mehta (Family Medicine provider, Program Chief of Family Medicine, study Co-Investigator) and Melissa Sturgis, PharmD, BCACP (Pharmacy Clinical Coordinator, Quality and Clinical Operations). This taper guideline is consistent with KPWA guidelines for COT tapering.

Prior to opioid tapering, the research interventionist will follow the Communication Plan for points to cover with both the patient and provider.

A random sample of the intervention visits will be chosen for quality assurance activities. We will send audio files of the visit to Dr. Turner at the University of Washington using the KPW secure file transfer site. The purpose of the QA is to ensure the research interventionist is conducting the telephone visits correctly according to protocol. During the telephone visit, the research interventionist will inform the participant that they will not use the participant's full name in session and the recordings will be labeled with a study id and date; not their name.

<u>Primary Data Collected on Opioid Tapering for a Subgroup of Patients Electing to Taper</u>

During the opioid taper, Dr. Sullivan will be responsible for managing the tapering plan.

The research interventionist will meet with Dr. Sullivan weekly and together they will track specifics about the taper into the project REDCap tracking data base hosted at KPWA. This data will come from the patient and provider interactions and the electronic medical record. The information captured in REDCap at the visits that are specific to tapering includes:

- Details on the taper each week

- Taper start date
- Current opioid medication(s) name and dose per day in morphine equivalents
- Taper recommendations: opioid taper plan, specific opioid taper recommendations (see Taper Guidelines)
- Other medication recommendations: drug name and dose (see Taper Guidelines and KPWA guidelines)
- Provider implemented recommendations for taper: yes, no, no response
- Provider implemented recommendations for supportive medications for the taper: yes, no, no response
- Taper paused (i.e., put on hold) (yes, no)
  - Reason for pause (dose escalation, patient preference, provider preference, pain, other symptoms, etc.)
- Taper resumed (yes, no, date)

Device/drug information
N/A

Secondary data: data, sources, and date range

Additional secondary data other than what is described in the "Study Procedures – Intervention Arm and Control Arm" will be collected and entered into REDCap on participants enrolled in the intervention arm as outlined in the table below.

Data from KP Washington

Source (specify) (i.e., from KPWA, or from an existing or previous study)	Key Information/Description of Variables	Date Range
KPWA data sources (Epic)	Current problem list	2018-2021
KPWA data sources (Epic)	Current medication list	2018-2021

DIRECT IDENTIFERS

☐ Names	☐ Social Security Numbers	☐ Web URLs
☒ Dates	☐ Medical record numbers	☐ IP address numbers
☐ Postal address	☐ Health plan numbers	☐ Biometric identifiers (e.g., finger prints, voice prints, retina scans)
☐ Geocode	☐ Account numbers	☐ Facial Photos/Images
☐ Phone numbers	☐ License/Certificate numbers	☐ CHS ID
☐ Fax numbers	☐ Vehicle ID numbers	☐ Other unique identifier(s):
☐ Email address	☐ Device identifiers/Serial numbers	

Alternative treatment(s) and/or denied treatment
N/A
Deception/incomplete disclosure
N/A
Incidental findings
N/A

Procedures to monitor, lessen or mitigate risk
There are several study design features that lessen or mitigate risk:

- Participants may be embarrassed or psychologically distressed at some of the survey questions, they are told that they can skip any questions they do not want to answer
- Breach of confidentiality is a potential risk. See section 5u for a description of the various controls set in place to safeguard data security. Additionally, staff are trained on best practice privacy and confidentiality measures.
- Participants may feel increased pain while they are tapering. If the participant experiences increased pain due to the condition for which they are on COT, the research interventionist may consult with Dr. Sullivan and the participant's PCP to evaluate and provide assistance.
- While very unlikely with the planned gradual taper, participants may experience opioid withdrawal and can call the research interventionist to discuss these symptoms. The research interventionist will consult with Dr. Sullivan (PI) and work closely with the participant's PCP to recommend medications to provide comfort from withdrawal symptoms.
- The study will have a plan in place to handle Critical Incidents, when a participant endorses intent to harm themselves. The research interventionist (PA) will administer the Columbia Suicidality Severity Rating Scale. After determining the score, the research interventionist will take the appropriate steps to triage the participant per the study protocol and KPWA guidelines. Additionally, the research interventionist will be supervised by a KPW licensed clinical psychologist. All critical incidents will be reviewed by the study psychologist. The protocol for handling critical incidents is including in this package.
- A data use agreement will be in place to share study data with investigators at the University of Washington

Subject drop out or withdrawal procedures

If a subject drops out or we withdraw them from the study, the study team will:

- Update the tracking database to indicate that no further patient-self report data collection or participant contact will occur.
- We will continue to use the data they have already contributed/agreed to allow us to use per their consent for analyses
- We will not ask them to complete any additional surveys or attend study visits (if applicable)

In rare instances, the study PI's may decide to withdraw a participant from the study and analyses. The reasons for removing participants from the study and analyses would be:

- Concern about data validity. Examples of the types of scenarios are when a participant's behavior indicates that they may not be answering questions truthfully either due to deceit, they are high on drugs during their scheduled visit or there is a medical condition like narcolepsy that makes it difficult for them stay awake during their scheduled appointment.
    - The research interventionist would bring concerns about data validity to the study team and the PI would make the determination on whether to withdraw or not. The study team will send them a letter informing them of their withdrawal.

- All participants using buprenorphine for treatment of OUD will be withdrawn from the entire study. Primary data collection will cease and they will not be included in analyses. While buprenorphine is a partial opioid, it is indicated for the treatment of opioid use disorder and rarely if ever used to treat pain at KPWA. Patients treated with buprenorphine for OUD are complicated and are either no longer on other opioids or being tapered off other opioids by the provider treating their OUD. They are not part of our study population of interest and thus buprenorphine use is both an exclusion criteria and reason for being withdrawn from the study.
    - If the research interventionist learns that the participant is taking buprenorphine for OUD, they would bring that information to the study team and the PI would withdraw the participant from the study. The study team will send them a letter informing them of their withdrawal.
    - Similarly, patients in both the intervention and control arm will be removed from the entire study and analyses if they are using buprenorphine as indicated in VDW medication dispensing data ascertained prior to the analyses.
- All pregnant women will be withdrawn from the study entirely. Primary data collection will cease and they will not be included in analyses. Pregnancy status will be determined via diagnosis codes from the VDW for subjects in both study arm prior to analyses. The research interventionist may also learn of pregnancy through the EMR, PCP, or self-report from the participant. We expect very few young women to be in the study due to the average age of chronic high dose opioid users at KP.

Anticipated study end date

The anticipated study end date for the completion of primary analyses will be on or before December 31, 2021

Study Procedures –Control Arm

Sequential description
Participants randomized to the control arm (i.e. usual care only) will not receive any intervention visits. They will only complete the three surveys described above in the "Study Procedures – Intervention Arm and Control Arm" section.

Device/drug information
N/A

Secondary data: data, sources, and date range
N/A – no additional data other than what is described in the "Study Procedures – Intervention Arm and Control Arm" will be collected.

Alternative treatment(s) and/or denied treatment
N/A
Deception/incomplete disclosure
N/A
Incidental findings
N/A
Procedures to monitor, lessen or mitigate risk
N/A
Subject drop out or withdrawal procedures
If a subject drops out or we withdraw them from the study, the study team will:

- Update the tracking database to indicate that no further patient-self report data collection or participant contact will occur.

Anticipated study end date
The anticipated study end date for the completion of primary analyses will be on or before December 31, 2021

a. Data Analysis

Describe the data analysis plan, including:

- Statistical procedures.
- When applicable, the power analysis.
- Any procedures that will be used for quality control of collected data.

We will use descriptive statistics to characterize the sample at baseline. To address the trial's effectiveness aims, we will use an intent-to-treat approach (i.e., individuals will be analyzed according to randomized group regardless of participation in any opioid taper support sessions). We will also use a complete case analysis (i.e., that includes those participants who have observed follow-up outcome data) since we expect at least 85% follow-up at 12 months (primary time-point).

To compare each of the primary outcome measures (opioid dose and PEG score) between intervention groups the following linear regression model will be constructed: $E(Y_{ij}) = \beta_0 + \beta_1 Trt_i + \beta_2 Time_j + \beta_3 Trt_i x Time_j + \alpha_z \boldsymbol{Z}_i$, where Y_{ij} is the outcome for person *i* at time *j* (*j*=6 or 12 months), Trt_i is the dichotomous intervention effect of interest (with control arm as the referent group), $Time_j$ is the dichotomous variable indicating the 6- or 12-month time point, $Trt_i x Time_j$ is the interaction between the treatment and time point indicators and $\boldsymbol{Z}_i$ is a vector of baseline covariates that we a priori plan to adjust for including age, gender, baseline opioid dose group, whether they were referred to COMET, and KPWA clinic. We will include both 6- and 12-month time-points in a single model to improve statistical efficiency, but the12-month time point is considered primary. We will fit the linear regression model using GEE with robust standard errors to account for the multiple time points in a single model. We will use two-sided tests at the 0.05 level. Arguments against adjusting for multiple comparisons for two co-primary outcomes have been made by Rothman and others.(Rothman KJ. No adjustments are needed for multiple comparisons. Epidemiology. 1990;1:43–46) For each outcome, we will report the adjusted mean difference between treatment groups and its 95% confidence interval.

A set of comparable linear regression models will be fit for continuous secondary outcomes. For dichotomous secondary outcomes**,** similar models will be built using a modified Poisson regression framework with a robust sandwich estimator to estimate adjusted relative risks and 95% confidence intervals. In addition, for each outcome, we will conduct a sensitivity analysis that further adjusts for baseline factors that are predictive of the outcomes, predictive of the probability of being missing at follow-up, or found to be significantly different between treatment groups. If more data are missing than expected (i.e., <85% with follow-up), we will also conduct a sensitivity analysis using an imputation method for non-ignorable non-response to evaluate whether our results are robust to different missing data assumptions. Selection bias analyses will compare demographic and clinical data of non-responders (potentially eligible per VDW and unreachable for recruitment) with responders (enrolled) using chi square and t-tests. This will allow us to identify factors associated with non-response. Secondary analyses will be conducted to assess for subgroup heterogeneity of treatment effects across levels of these pre-specified baseline variables: SUD+ vs SUD-, MH+ vs MH-, <90mg. vs >90mg MED, opioids with sedatives vs without, and focal pain vs multifocal pain. Heterogeneity will be indicated by a significant test of the interaction between treatment and each baseline variable, and subgroup-specific treatment effects with confidence intervals will be reported. In light of multiplicity and reduced power, these results of these analyses will be interpreted cautiously.

Sample Size:

Our sample size is designed to ensure that we are highly powered to detect a clinically meaningful difference in the co-primary outcomes of opioid dose and pain (PEG) at 12 months. With 172 participants (86 per intervention arm) we will have >90% power to detect a 20mg mean difference in opioid dose between intervention groups assuming a 34 mg SD (based on data from KPWHRI participants meeting entry criteria) and a two-sided, two-sample equal-variance t-test. Assuming the mean baseline dose in our study population to be 67mg MED, this 20mg difference represents a clinically meaningful 30% reduction. Further, given our

sample size of 172 participants we will have approximately 90% power to detect a 1.2 point difference in the PEG between intervention groups, assuming a standard deviation of 2.5. To ensure adequate power given potential loss to follow-up we inflated our final sample size by 25% yielding a target randomization of 215 participants. This will also allow some pre-specified sub-group analyses to look for heterogeneity of treatment effect, as described below. Sample and power calculations were conducted using PASS software Version 14.

b. Sharing of Results with Subjects

Describe whether results (study results or individual subject results, such as results of standard or research lab tests and genetic tests) will be shared with subjects or their providers.

If the study carries a risk of incidental findings, describe your plan for evaluating these and determining whether and how subjects or their providers will be given this information.

If laboratory results will be shared with subjects or their healthcare providers, verify that the laboratory conducting the test is Clinical Laboratory Improvement Amendments (CLIA) certified.
We will not be sharing study results with participants

We will be communicating some study information with providers, however we will not be sharing study results with the provider

- If a participant is enrolled in the intervention arm, the provider will be notified of their participation by the study team
- The research interventionist will pass provide a medication recommendation to the PCP using Epic Telephone Encounters. Additionally, any study information that is collected as part of the telephone visit which the research interventionist feels may be important to either support the taper or supplements clinical care may be shared with the provider. This will continue through the course of the taper for patients electing to try the taper support.

c. Data and/or Specimen Banking

Indicate if specimens may be used for future research and whether that may include genetic research.

State if data or specimens will be sent to a separate repository. If data or specimens will be banked in a repository for future use as part of this protocol submission address the following questions:

- What will be banked and what identifiers will be associated with the data or specimens?
- Where and how will the data or specimens be stored?
- For what purpose will the data or specimens be used?
- How will the data or specimens be accessed, and who will have access?
- Describe the procedures to release data or specimens, including the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

N/A we will be not banking data or specimens for this project

7. Privacy, Confidentiality and Data Security

Describe the steps that will be taken to protect subjects' privacy during recruitment, consent and study procedures.

Recruitment, Screening and Consent

During all recruitment, screening and consent telephone calls, the study team will confirm the identity of the participant by asking for their full name and DOB. All recruitment and screening calls will take place in the Kaiser Permanente Washington Health Research Institute (KPWHRI) offices; this ensures that work computers are secure and assumes that surrounding colleagues are trained in standard research privacy and confidentiality procedures. We will use REDCap hosted at KPWA to collect patient reported data and intervention visit data; it is 21 CFR Part 11, FISMA, and HIPAA-compliant.

Intervention

All intervention telephone visit calls will be made at KPWHRI offices (see above). Intervention study visit information will be collected using REDCap which is 21 CFR Part 11, FISMA, and HIPAA-compliant.

a. Describe the plan for storage of data and/or specimens.
   - Who will have access and how.
   - Where the data/materials will be stored and for how long.
   - What identifiers will be included.
   - Any other steps that will be taken to ensure security (e.g., training of staff, authorization of access, password protection, encryption, physical security, and separation of identifiers from data and specimens, certificates of confidentiality).
   - Describe the plan to deidentify data, destroy data, or retain/archive data at the end of the study.

Analytic study data will be stored at KPWA indefinitely. The linking file and files with PII needed for recruitment and participant contact (names, DOB, address, telephone number, email) will be stored at KPWA on the project G: drive and then destroyed by 12/31/2026. Analytic data files will be stored on the project G: drive. REDcap will be stored on KPWA servers while data collection is ongoing. When REDCap data collection has been completed, QA'ed and cleaned, that data will be exported to the project G: drive and merged with other data sources to create the analytic dataset. Data will be accessible to the study team whose access is controlled by the study project manager and Dr. Boudreau.

Additional steps to ensure data security include:
- All KPWA staff are required to have current Human Subjects Research Training
- All KPWA staff are required to have privacy and confidentiality training when they onboard employment
- All KPWA computers are password protected in secure office building where workspace is accessible by key cards

- REDCap access requires a study specific URL to access it and requires a user login/password to authenticate and login
    - REDCap is 21 CFR Part 11, FISMA, and HIPAA-compliant.
- The project has a Certificate of Confidentiality from the National Institutes of Health

b. Collection of data from subjects electronically

If you will collect any data from participants electronically (including email, website, etc.), explain:

- How the data will be collected.
- How the information will be secured (encryption, password protection, etc.; may require consultation with IT department).
- Any risks to the participants' privacy posed by using these methods (describe in consent, as applicable).
- How you will verify the participant's identity.

Participants who elect to take their surveys (at baseline, 6 and 12 months) on the internet will complete their survey in REDCap.

When the participant's survey is due (at baseline, 6 and 12 months) the system will trigger an email that sends a link that is specific to the individual recipient.

Similarly, in the intervention arm, participants who elect to take their pre-visit GCPS and HADS surveys on the internet will be emailed a link to take the surveys online. (See "Master Survey Doc")

There will be no further authentication steps to verify the participant's identity.

As stated in above sections, there are many technical, physical and administrative safeguards in place for both REDCap and the servers that REDCap is stored at KPW.

The consent form adequately explains the risks of using email for study research and asks participants to opt-in or out of receiving study emails for web survey administration.

c. Does this study involve the disclosure of PHI to a collaborator?

If any data will be sent outside of this site, list each recipient (may list by role or category if the information is the same for several different entities). For each recipient, describe:

- What will be sent.
- Whether the information will be fully identifiable (PHI, if health information), a Limited Data Set, de-identified, or aggregate.
- How the data/materials will be transferred securely (for instance, Secure File Transfer).

This study will disclose PHI to the University of Washington; Drs. Sullivan and Turner.

We will send audio files of intervention sessions to Dr. Turner and these files may contain PHI.

Additionally, Drs. Sullivan and Turner will receive dates, such as medication dispensing dates, intervention visit dates, and diagnosis dates.

The information sent to Drs. Sullivan and Turner will be in the form of 1) a limited data set during analyses and 2) the participant tracking database in REDCap, where Dr. Sullivan will be able to view the intervention visit information for each participant and PII will not be displayed/made visible to him. He can view the data in REDCap, but cannot export it.

Dr. Sullivan will have EPIC read only access. He will access EPIC from the KPWHRI hotel stations, inside the KP firewall.

With regard to data transfer security, analytic datasets and audio files will be transferred to Drs. Sullivan and Turner using the KPWA secure file transfer site (SFTS). This SFTS is housed on KPWA servers. Main analyses will occur at KPWHRI.

When the audio files are transferred to Dr. Tuner at UW, she will store the files on a UW network drive on her UW office computer. This resides inside the UW firewall. Physically, this computer resides at Dr. Turner's personal office which is kept locked when she is not present. The computer is password protected and meets all UW Medicine and UW regulations and policies. The UW has security controls in place to prevent the unauthorized access and monitors for unauthorized access.

With regard to the participant tracking database, REDCap is also housed on KPWA servers.

8. Provisions to Monitor Data to Ensure the Safety of Subjects

This is required when research involves more than Minimal Risk to subjects.

The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.
Describe:

- Who will monitor the study data for safety?
- The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.
- What data are reviewed, including safety data, untoward events, and efficacy data.
- How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).
- The frequency of data collection, including when safety data collection starts.
- The frequency or periodicity of review of cumulative data.
- Criteria for taking action on monitoring findings (for instance, stopping rules, immediate suspension, reporting, protocol changes, changes to monitoring frequency or plan).
- For studies monitored by a DSMB/C, describe the committee membership and structure, meeting format, and quorum requirements. Upload the board/committee charter, if one exists.

To monitor risks of the interventions and any need to stop the trial early, we have will create a Data Safety Monitoring Committee (DSMC). This committee will be composed of Dr. David

Tauben (general internist and Head of the Pain Division of the Department of Anesthesiology and Pain Medicine at the University of Washington), Dr. Jane Ballantyne (anesthesiologist and pain medicine expert practicing at Harborview Medical Center in Seattle) and Dr. Joan Russo, a biostatistician and Associate Professor, Psychiatry and Behavioral Sciences, University of Washington, with experience in data analysis and design of RCTs. Dr. Tauben will serve as the chair of the committee while Drs. Ballantyne and Russo will be members. This committee will meet during the pre-intervention phase and annually to review the protocol, data collection and data completeness. A quorum is defined as all three members of the committee being present.

The research specialist and research interventionist and project manager will monitor AEs and severe adverse events (SAEs) as they interact with study participants. They will be documented in the study tracking database. These will be reviewed with Drs. Sullivan and Boudreau during monthly study meetings. AEs and SAEs will be reported to the KPW IRB according to the timing summarized above. AEs will be forwarded monthly and SAEs will be forwarded weekly to the DSMC.

Progress in enrollment and data collection will be reviewed on a bi-weekly basis using study status reports and status report meetings with study personnel. Any difficulties in enrollment or data collection will be discussed by the research team in order to resolve any problems and ensure complete data.

The KPWHRI biostatisticians, will review all study data, including AE and CI data, once per year to determine if there are substantially more adverse events in one intervention group compared to another or if one group demonstrates a markedly superior or more negative effect on the outcome variables than the other groups. The biostatistician will provide a summary report of this review to the DSMC. If the DSMC agrees that there is a markedly superior or negative effect in one group vs. another or if there are substantially more adverse events in one group vs. another, Dr. Sullivan will notify the NIDA Project Officer and the KPW IRB and follow their advice about how to proceed. If the DSMC agrees that such effects are not present, no further action will be taken.

The KPW IRB will review the study protocol. The IRB will maintain ongoing oversight of the risks and benefits of the study and ensure compliance with institutional and NIH guidelines. Drs. Sullivan and Boudreau will be responsible for notifying the KPW IRB of all adverse events. The IRB will work with the Drs. Sullivan and Boudreau to ensure additional agencies (e.g., NIDA) are notified as required. Temporary or permanent suspension of an NIH funded protocol will be reported to the NIH grant program director directly responsible for the grant.

The following events will be reported to the KPW IRB within 10 business days: unanticipated medical problem, serious non-compliance, continuing non-compliance, emergency deviation from IRB approved procedures, continuation of research after IRB approval has lapsed, complaint of a subject that cannot be resolved by the study team, audit or inspection or safety-related inquiry by a federal agency, new information that indicates a new or increased risk or safety issue.

If it becomes necessary to change the proposed study protocol, amendments will be filed with the IRB at KPW seeking approval for these. These changes will be made only after receiving

approval from the IRBs. Following approval and implementation of these changes, the DSMC and NIDA program officer will be notified.

The trial may be stopped because the intervention poses unacceptable risk to participants. We will not perform interim efficacy analyses or develop related stopping rules because: 1] it is highly unlikely that the intervention will have such dramatic positive effects on both opioid dose and pain primary outcomes, 2] the comparison group receives usual care and cannot thus be harmed relative to usual care, 3] stopping early may preclude analyses of secondary outcomes and subgroup effects. The DSMC (Drs. Tauben, Ballantyne, and Russo) will be kept informed of AEs and SAEs encountered in the conduct of the study. They will review these yearly to determine if the intervention is posing unacceptable risks to participants. Review may occur more frequently if there are unexpectedly frequent or severe AEs. If they believe stopping the trial is appropriate, they will notify Drs. Sullivan and Boudreau and the NIDA program officer. Decisions about stopping the trial will be made in consultation with the NIDA program officer.

9. Risks and Benefits

a. Risks to Subjects

List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Describe the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks.

- If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.
- If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.
- If applicable, describe risks to others who are not subjects and risks to Kaiser Permanente

For both intervention arms potential risks to subjects include breach of confidentiality and embarrassment from some of the study questions.

For the intervention arm, subjects electing to taper may experience withdrawal symptoms. These symptoms can include: increase in pain, insomnia, anxiety, restlessness, agitation, sweating, diarrhea nausea, vomiting or abdominal pain. However, our study of voluntary, self-paced and supported opioid taper will use a very gradual withdrawal schedule over a period of 46 weeks. This gradual withdrawal will minimize, if not eliminate, these withdrawal symptoms. These symptoms will be closely monitored during and after taper by the research interventionist . Subjects will be cautioned not to abruptly discontinue their opioids. However, it is still possible that subjects will become impatient with the taper process and abruptly stop their opioids on their own. If participants have an AE's the research interventionist may recommend medications to the participant's PCP to help alleviate the abstinence syndrome symptoms. During the taper, participants may hoard any non-used opioids. The study consent form reminds participants that all non-used opioids should be disposed of properly. Participants will be informed of the risk of stock-piling opiates during the taper process. All medical care treatment and decisions are the responsibility of the primary care provider.

For the control arm, participants may be disappointed with the intervention condition to which they are assigned when they are randomized to the control arm. An incentive is being provided to both groups to improve retention in the trial.

b. Potential Benefits to Subjects

Describe the potential benefits that individual subjects may experience from taking part in the research. Include as may be useful for the IRB's consideration, the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit. You may include benefits to society or others.

In the intervention arm, some individuals may benefit from reduced dependency on prescription opioids and/or decreased pain and improve quality of life.

10. Economic Burden to Subjects

Describe any costs that subjects may be responsible for because of participation in the research study (for example, co-pays; paying for treatment, therapies, or other interventions, or the delivery of these) and how you will inform participants of these costs prior to their enrollment in this study.

Subjects will be financially responsible for the treatment of physical injuries resulting from study procedures. Recommended (not required) in-person visits with the PCP and medication costs will result in standard co-pays, co-insurance and deductibles. This is outlined in the informed consent form.

11. Compensation to Participants

Describe any compensation provided to participants, for example, for time inconvenience, discomfort, travel, or in the event of research related injury. If applicable, describe how you will inform participants of this prior to their enrollment in the study, including if payment will be prorated if the subject withdraws early from the study.

NOTE: payment may not be withheld as an incentive for participants to complete the study.

Both intervention and control arm will receive: $20 for completion of baseline assessment, $40 for completion of the 6 month assessment, $50 for completion of the 12 month assessment

12. Resources Available

Describe any special resources or expertise required to conduct the study.

Dr. Boudreau, Senior Scientific Investigator at KPWHRI, will spend .20 FTE conducting and completing this research. She will oversee all aspects of the study at KPW.

The project will use REDCap to collect data from participants and to track participant progress through the study.

Additionally, Dr. Boudreau is working closely with Dr. Kushboo Mehta. Dr. Mehta is a Family Medicine provider and Program Chief of Family Medicine at KPW who assisted with developing and rolling out KPW's newest guidelines on chronic opioid therapy. She will serve as the liaison between the study team the KPW delivery system and KPW leadership. She will be the Study

Clinic Champion directly involved with educating providers, promoting the study, recruitment and retention.

Dr. Boudreau meets and touches based regularly with others in the KPWA delivery system including Dr. Sarah Levy (Medical Director, Continuum of Care), Dr. Angela Sparks (Family Medicine Physician and Medical Director, Clinical Knowledge Development and Support), and Melissa Sturgis, PharmD, BCACP (Pharmacy Clinical Coordinator, Quality and Clinical Operations). Dr. Boudreau keeps them apprised of the trial aims, design, and methods while they provide feedback on trial and keep her up to date on of KPW initiatives around safe opioid prescribing and tapering.

Finally, the taper portion of the study functions by working in conjunction with the participant's primary care provider. The research interventionist use Epic Telephone Encounters to pass on medication dosing recommendations to the primary care provider and any other research information that may be pertinent for the provision of health care.

13. Prior Approvals

Describe any approvals that will be obtained prior to commencing the research. (e.g., school, external site. funding agency, laboratory, radiation safety, or biosafety approval.)

See attached:

- Systems Engagement Review
- KPW Delivery System letters of support

14. Drugs or Devices

NOTE: see the ICH-GCP guidance for a summary of investigator and sponsor responsibilities in clinical trials.

a. Drug Studies

If the research involves drugs and is investigator-initiated, indicate whether there is any possibility that the results will be reported to FDA (e.g. as part of a new drug application [NDA]).

- If the drug is investigational (has an IND), confirm that you will comply with all applicable FDA requirements for investigators.
- Confirm that you will follow applicable KP pharmacy policies and procedures.
- Describe your plan for drug storage, handling, and accountability, including distribution, return, and destruction of the drug(s).

N/A we are not studying any drugs or devices

b. Device Studies:

If this is a device study and you think the device is Non-Significant Risk, include justification here or upload it as a separate document along with any available device information (instructions for use, etc.).

If the research involves devices and is investigator-initiated, indicate whether there is any possibility that the results will be reported to FDA (e.g. as part of a premarket approval application [PMA]).

- If the device has an IDE or a claim of abbreviated IDE (Non-Significant Risk device), confirm that you will comply with all applicable FDA requirements for investigators.
- Describe the device, the manufacturing process, and the device labeling, including safety instructions or warnings. If available, this may be addressed in separately uploaded device information (such as instructions for use).
- Describe device storage, handling, and accountability, including how access to the device will be limited to appropriate personnel and how you will ensure the device will be used only for appropriate study subjects.

N/A we are not studying any drugs or devices

15. Multi-Site Research

a. If this is a multi-site study and you are the lead investigator or this site will be the coordinating center for any activity, describe the processes to ensure communication among sites, such as:
   - All sites have the most current version of the protocol, consent document, and HIPAA authorization.
   - All required approvals have been obtained at each site (including approval by the site's IRB of record).
   - All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.
   - All engaged participating sites will safeguard data as required by local information security policies.
   - All local site investigators conduct the study appropriately.

b. Describe the method for communicating to engaged participating sites the following:
   - Problems.
   - Interim results.
   - The closure of a study.

c. Describe any special resources or expertise required to conduct the study.

This study is a multi-site study consisting of two sites: KPW and the University of Washington. All recruitment, participant interaction and data analysis will occur at KPWA.

KPW will be the IRB of record for this project. We have already received confirming from the University of Washington that authority of their submission has been granted to KPW's IRB. (see attached letters from UW IRB)

The KPW project manager will communicate to sites, all modifications before the modification is implemented.

All data for this study will be stored at KPW. Data safeguards have been explained in detail in previous sections. Data will be transferred to UW and all engaged participating sites (KPWA and UW) will safeguard data as required by local information security policies.

Dr. Boudreau will be responsible for ensuring that all site investigators and project staff conduct the study appropriately.

Problems on this study will be communicated to all sites by email or telephone from any of the study investigators or the project manager.

Interim results will be discussed during monthly project team meetings, as results are made available. The KPW/UW study leads meet bi-monthly and can discuss interim results at those meetings when results are made available.

When it is time to close the study, the project manager will inform the UW investigators that the project is coming to an end and ask them to complete the administrative paperwork/processes on their end to close the study.

16. Community-Based Participatory Research

Describe involvement of the community in the design and conduct of the research.

Describe your plan for ensuring that community research partners are appropriately trained in human subjects' protection.

NOTE: "Community-based Participatory Research" is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. Community-based Participatory Research begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

N/A this is not community-based participatory research