# *Collaborative Care for Chronic Pain in Primary Care (PPACT)* Pragmatic Clinical Trial

# PROTOCOL

Sponsored by

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**STUDY PROTOCOL MODIFICATIONS**

**04/21/2014:** Originally, primary care providers could opt out after clustering and randomization occurred. However, with this approach we could not include an additional PCP to take the place of the PCP who had opted out. Therefore, we would be left with fewer than the optimal number of PCPs in each cluster wave. We changed the protocol to have PCPs opt out prior to clustering and randomization.

**07/07/2015:** The target number for enrollment was changed from "up to 160 primary care providers (PCPs) and 1,200 patients with chronic pain on long term opioid treatment (CP-LOT)" to "up to 375 PCPs and 1,000 patients with chronic pain on long term opioid treatment (CP-LOT)." In addition, the number of PCP clusters changed from 120 PCP clusters to 106 clusters, with 53 receiving the intervention and 53 receiving usual care.

The description of PCP recruitment was changed to reflect that PCPs are provided an in-person presentation to the study rather than an informational letter. The detailed PowerPoint presentation covers all elements of informed consent. PCPs that are unable to attend the in-person presentation are sent an email with an overview of the study and a copy of the PowerPoint presentation.

## 1. OVERVIEW

Chronic pain affects at least 116 million adults in the United States and exacts a tremendous cost in suffering and lost productivity. While health systems offer specialized pain services, the primary care setting is where most patients seek and receive care for pain. Patients with chronic pain are seen primarily by primary care providers (PCPs) in settings where medications have become the mainstay of pain treatment for many PCPs with few other treatment options available to them. Yet rising concerns about the safety and efficacy of opioid medications for the treatment of chronic pain have heightened awareness of the need for better treatment options. Primary care-based treatment of chronic pain by interdisciplinary teams (including behavioral specialists, nurse care managers, physical therapists, and pharmacists) is one of the most promising approaches for improving outcomes and managing costs. Recent national health policy changes, in addition to the increasing recognition of the high prevalence and cost of chronic pain conditions present a unique opportunity to shift the care paradigm for patients with chronic pain.

The overarching goal of the Pain Program for Active Coping and Training (PPACT) is to test the effectiveness of integrating an evidence-based, interdisciplinary pain management intervention within a primary care environment. The trial is conducted in three health care delivery systems (Kaiser Permanente Georgia, Hawaii, and Northwest) and is anticipated to involve up to 375 PCPs and 1,000 patients with chronic pain on long term opioid treatment (CP-LOT).

The PPACT trial compares usual care services to an interdisciplinary, primary care-based approach to treating CP-LOT patients. The primary outcome for the trial is a composite of pain severity and interference as measured by the 4-item version of the Brief Pain Inventory – Short Form, known as the PEGS,[1] and administered routinely in clinical care. Secondary outcomes include patient satisfaction, potential reductions in dispensed opioid medication (measured as morphine equivalent dose), and other health service use variables extractable through patients' electronic health records (EHR).

## 2. STUDY AIMS

**Aim 1:** Conduct a cluster randomized pragmatic clinical trial in 106 PCP clusters across the three KP health plan settings (Hawaii, Northwest, Georgia) to compare the effects of the PPACT intervention to usual care on:

- Patients' pain symptoms, pain-related functioning, and satisfaction with health care services;
- Patients' use of health care services, including receipt of opioid medication; and,
- The cost of the program and economic impact of the intervention.

**Aim 2:** Conduct process and formative evaluations to understand, describe, explain, and enhance intervention Reach, Effectiveness, Adoption, Implementation, and Maintenance.

## 3. STUDY DESIGN

### 3.1. Cluster Randomized Design

The trial compares usual care services to a multidisciplinary, primary care-based approach to treating CP-LOT patients. The study team has planned for up to 1,000 patients from 106 clusters of PCPs (6-12 patients per cluster) across three KP health plans (KPNW, KPGA, and KPH) to participate in the trial, with 53 PCP clusters randomized to the PPACT intervention and 53 PCP clusters to usual care representing 9-30 PCP clusters in each of the three participating KP regions.

### 3.2. Eligibility

#### 3.2.1. Primary Care Providers

Primary care provider participants (PCPs). All PCPs (internal medicine and family practice providers [medical doctors – MD, doctors of osteopathic medicine – DO, physician assistants – PA, and nurse practitioners – NP with established panels of patients]) in the three participating KP regions are eligible to participate in the trial.

#### 3.2.2. Patients

Patient inclusionary eligibility criteria includes the following:

1. Adult (18 years of age or older) health plan members from KPNW, KPGA, and KPH who receive their primary care services from participating PCPs
2. Health plan membership of at least 180 days/6 months duration
3. Long term opioid use defined by: 90+ day supply of short acting opioid spanning at least 120 days or 2 or more long acting opioid dispense in the past 180 days
4. Pain diagnosis within the past year

Patient exclusionary criteria are limited to the following:

1. Patients currently enrolled in intensive addiction medicine services or with evidence of active substance dependence of sufficient severity to interfere with their ability to actively participate in the behavioral/lifestyle change program
2. Patients with cognitive impairment severe enough to preclude their participation in a behavioral/lifestyle change program
3. Patients with current malignant cancer diagnosis
4. Any evidence of patient having received hospice or other end-of-life palliative care within past year
5. Patients unwilling to participate in the skills training/lifestyle change elements of the program (PCPs cannot mandate that their referred patients participate in the program).

Exclusionary criteria are purposively kept to a minimum to ensure that study participants resemble those most in need of these services in the broader population.

### 3.3. Recruitment and Retention Strategies

#### 3.3.1. Recruitment

Based on the previously stated eligibility criteria, one database for each regional healthplan compiles the health record numbers (HRNs) of all PPACT eligible patients who are paneled to all participating PCPs. This database is refreshed just prior to beginning recruitment of any given cluster to ensure the most accurate PCP paneling of patients. PCPs in each clinic are invited to participate in an informational meeting held in their primary care clinic prior to recruitment efforts in that clinic. During this meeting, PCPs are informed of their option to opt out of

participation in the study. The PCP's receipt of the study overview, expectations of participating, and absence of opting out of the study constitutes that PCP's informed consent.

For half of the participating PCPs their patients are randomized to participate in the intervention while for the otherhalf their patients are randomized to the usual care condition. PCPs, other clinic, and study staff are blinded to their randomization status until all of their patients have been recruited. The number of PPACT eligible patients on a given PCP's panel ranges from 1 to 146 in the three KP healthcare systems. One goal of this project is to target the more complex patients with chronic pain; those which often place the greatest strain on PCPs and the regions as a whole. In an effort to accomplish this goal the study team 1) prioritizes recruitment of patients on ≥ 120 daily morphine equivalent dose of opioids, patients concomitantly prescribed benzodiazepines, and patients with high primary care service utilization (defined as 12 or more contacts in the prior 3 months) and 2) asks that PCPs review a list of their prioritized patients to ensure that all patients on the list are appropriate candidates for the program.

All PCP approved PPACT eligible patients are mailed a recruitment brochure summarizing the study and providing an opt out contact number.. Additionally, it states that patients might be contacted within a week to participate in the study if they have not called to opt-out. The brochure specifies that there are limited spaces in the program such that not everyone receiving a brochure will be contacted to participate.

Consistent with the pragmatic nature of this trial and the full partnership of the three KP healthcare systems in incorporating this intervention reorganizing pain-related services and enhancing pain-related assessments, patients are informed that the study represents a partnership between their KP providers and the research team to evaluate existing pain-related services within the health plan and to evaluate the impact of providing a closer coordination of pain-related services available within the primary care clinics. KP staff working in coordination with the health plan and the research center then attempt to contact by phone those patients who do not opt out. Recruitment callers invite patients to enroll in the clinic summarizing the intervention as one that provides closer coordination of pain-related services within the primary care clinics, verbally reviewing the elements of consent (waived written consent), and obtain baseline patient reported outcomes. The study's target cluster size is 10-12 patients per cluster, thus, recruitment for any given cluster stops when 10-12 patients in a given cluster have been consented. Patients on the PCP approved list who have not been contacted are not recruited for the study. When recruitment for each PCP cluster within the cluster wave has been finalized, interventionists (staff not involved in the initial recruitment calls of patients) are unblinded to the study condition of each PCP cluster and their associated patients. These interventionists contact patients in the usual carecondition to inform them of their next assessment study contact in 3 months. Patients in the intervention condition are contacted to schedule their intake evaluation sessions.

### 3.3.2. Retention

Intervention retention.There is a recognition that the target patient population for the PPACT trial is one for whom motivation and adherence to recommended treatment and self-care practices is frequently an issue.[2-4] Accordingly, everyday clinical interventions frequently embed elements of motivational enhancement techniques to encourage patient adherence and retention as does the PPACT intervention.[5] A rescue session protocol details the process interventionists undergo when individuals do not attend sessions regularly or unable to attend due to various circumstances (e.g., surgery, transportation issues). While attempts are made by interventionists to engage all individuals with the highest "dose" of intervention that is feasible, as a pragmatic trial, attention to retention is informed by what would be realistic for included healthcare systems to sustain in everyday clinical care.

Data collection retention. The study employs a tiered system (patient health record sent to patient through health plan secured e-mail system, automated telephone calls using the KP Message Center, live telephone calls by medical assistant) to enhance collection of the primary study outcome, the PEGS.[6] This approach builds off of the current clinical data collection processes available in the health care delivery systems in which the trial is conducted and, as such, represents a modest enhancement of existing clinical systems. Importantly, all participants may refuse to provide specific responses or measures or may withdraw from enhanced data collection procedures or the intervention at any time.

### 3.4. Informed Consent and HIPAA Compliance

#### 3.4.1. Patients

The study team obtains oral consent and oral review of HIPAA elements from all participants enrolled in the study, accordingly the IRBs in the three included KP healthcare organizations have granted a waiver of signed informed consent and an alteration of privacy rule authorization (HIPAA) (no signature). When study interviewers obtain oral consent from a prospective study participant over the telephone, the interviewer indicates that each element of informed consent and HIPAA privacy guidelines/study use of health data have been reviewed with the KP member by checking the requisite element within the patient record in the study electronic tracking system. This helps ensure that each element of informed consent and HIPAA privacy guidelines/study use of health data have been thoroughly reviewed with all prospective participants. Following screening and oral consent, an informational letter including all elements of informed consent, is sent to all participants recently enrolled in both intervention and usual care. For individuals randomized to the intervention arm, the letter includes details of study activities and expectations. For this study, obtaining oral rather than written consent is an appropriate consent procedure because intervention activities involve the *coordination* of clinical care services already available to most KP members (e.g., physical therapy, behavioral services, nurse care management, and pharmacy) and therefore the intervention is expected to cause no more risk of harm than what already exists for patients undergoing usual care treatment for chronic pain. Some patients participating in the intervention are expected to have worsening pain and/or other physical or emotional problems during the study period. However, these are risks inherent in the population and would occur whether or not they were enrolled in the study and the risk of adverse outcomes should not be heightened as a function of being enrolled in the study. Further, because the intervention is embedded directly in the primary care clinics and conducted in partnership with participating patients' PCPs, in the event that a patient's symptoms significantly worsen during the intervention, their PCP will be immediately contacted by a PPACT intervention team member and their PCP will work with the patient to identify and provide appropriate care. This is consistent with the standard of care provided at KP.

For the pragmatic trial, data is assessed and recorded in accordance with regular clinical care (either in the intervention arm or the comparison usual care condition), and subsequently extracted by our research staff from EHR and administrative databases in each of the KP health plans participating in the study. As such the IRBs have granted a waiver of consent to use computerized records to collect assessment data for the trial. The study team believes that the assessment portion of the pragmatic trial clearly satisfies the criteria of 45 CFR 46:116 for waiver of informed consent. Those criteria are:

- *"The research involves no more than minimal risks to the subjects"* – The only risk to participants from this procedure is violation of confidentiality, which the study protects against.
- *"The waiver or alteration will not adversely affect the rights or welfare of the subjects"* – Research use of records will have no effect on insurance coverage, access to care, or eligibility for any benefit from participating health systems. The various HMO regions already routinely permit the use of EHR records for research purposes without member consent.
- *"The research could not practically be carried out without the waiver or alteration"* – It would not be possible to meet in person with all PPACT participants to obtain written consent.

Finally, patients in the intervention arm of the study are informed that group sessions may be recorded and shared with supervising staff to evaluate the quality of services the patient is receiving and to help the PPACT providers and the health plan understand how to best improve services for health plan members. A signed release of information is obtained for the potential recording of groups. Should a patient not be willing to sign the release of information, the group they are assigned to is not audio recorded.

#### 3.4.2. Primary Care Providers

PCPs are provided a thorough presentation at their regular primary care meeting (or presentation materials when not in attendance), which includes all elements of informed consent. The PCPs have a one week opt-out opportunity after the meeting or receipt of materials. The sIRB deems this is an appropriate consent procedure given the minimal risk to the PCP posed by the study. Benefits to the PCPs who are randomized to the intervention arm of the study include assistance managing their patients with chronic pain who are on opioids, patients who often utilize primary care services at a greater capacity. The PCPs in the intervention arm are provided with a comprehensive assessment of their study patients, the intervention team's pain management recommendations, and templates for communicating with those patients who often present with challenging communication styles. All PCPs participating in the trial regardless of which study arm they (and their patients) are randomized have the benefit of the study supporting quarterly collection of patient reports of pain and pain-related functioning using the standard monitoring tool adopted in all KP region to monitor patients on long term opioid therapy. Participating providers, regardless of study arm, are free to refer their patients to any pain-related services they deem warranted.

### 3.5. Treatment Arms

#### 3.5.1. Usual Care

As noted in the earlier section 3.3.1 on "Recruitment," all potential patient participants are approached about their willingness to participate in regular quarterly assessment of their pain and related functioning and status as well as their availability and willingness to participate in the PPACT intervention if offered and oral consent is obtained before they are enrolled in the study. For those patients whose PCPs are randomized to the usual care condition, further study-related contact is limited to quarterly study data collection over the following year.

Those patients in PCP clusters randomized to either the PPACT intervention or the usual care arm of the study are able to utilize all diagnostic and treatment health plan services available to them for pain and related conditions.

#### 3.5.2. PPACT Intervention

The intervention involves (1) a comprehensive intake evaluation with periodic reevaluation (evaluations performed by a behavioral health specialist *or* nurse care manager, physical therapist (PT), and a chart based medication review by a pharmacist), (2) group coaching sessions (co-led by a behavioral specialist and nurse care manager, with consultation from the PT to support the adapted movement activities), and (3) interim care management contacts (conducted by the behavioral health specialist or the nurse care manager). Section 4 below describes the PPACT intervention in more detail.

**4. PPACT INTEGRATED INTERVENTION COMPONENTS**

The intervention consists of (1) a comprehensive intake evaluation with, (2) group coaching sessions, and (3) interim care management contacts by intervention team members as needed. The interdisciplinary intervention team includes a behavioral health specialist (most often a social worker or master's-level counselor), a nurse care manager, and a PT with additional consultation from a pharmacist.

The intervention approach integrates ancillary services—behavioral services, nursing care management, PT, and pharmacy consultation—into the primary care environment with the goal of helping patients develop the skills to increasingly self-manage their condition. Many CP-LOT patients may have received brief trials of one or more of these services, albeit in a fragmented fashion. By coordinating such services within the primary care setting and providing services consistent with evidence-based treatment protocols, CP-LOT patients receiving the intervention are expected to be better able to manage their chronic pain and reduce their reliance on opioid medication. This approach is consistent with chronic care models of care,[7-11] previous collaborative care and multidisciplinary approaches to the management of chronic pain,[12-16] and chronic pain treatment guideline criteria.[17-19] A visual depiction of participant flow through the intervention is shown in Figure 1: PPACT Intervention Description. Each segment of the intervention is described in more detail below.

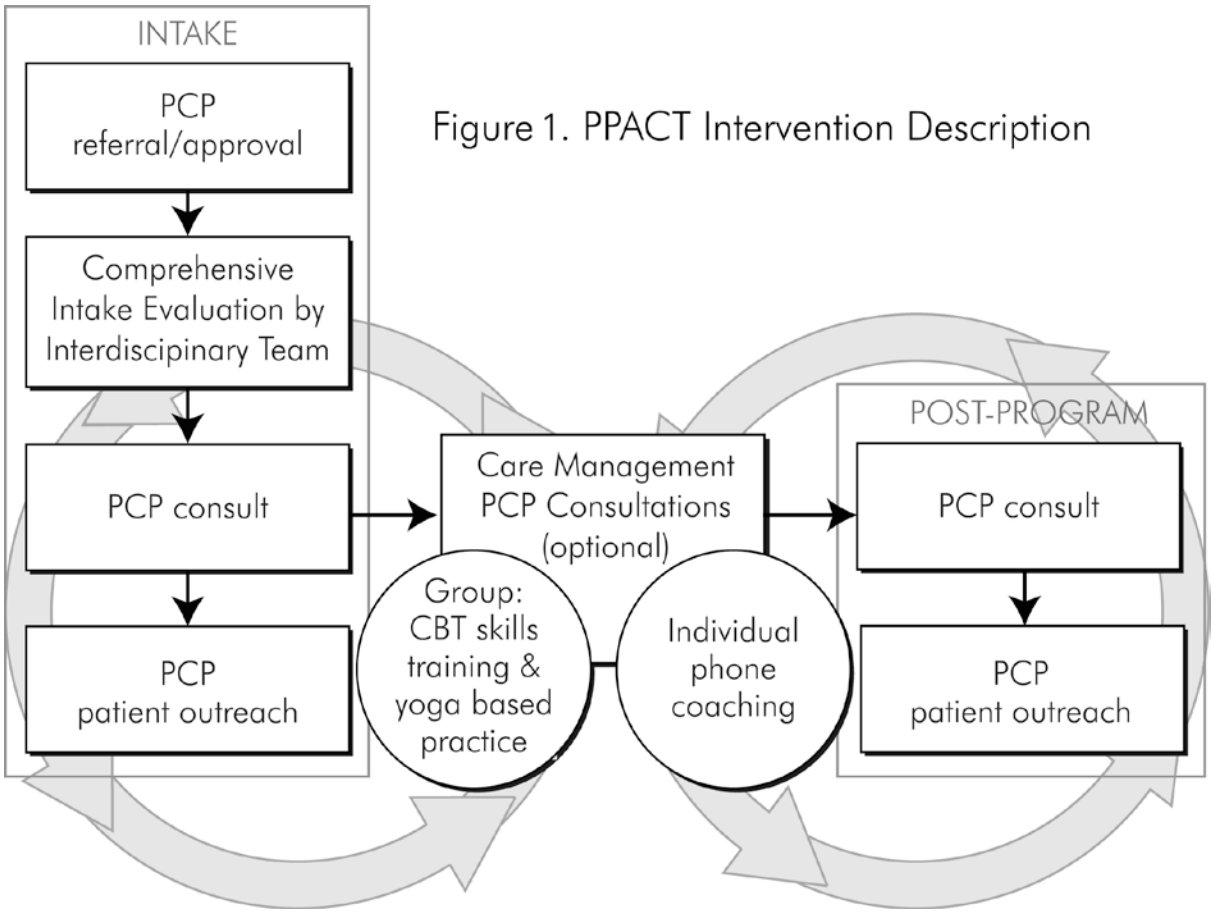


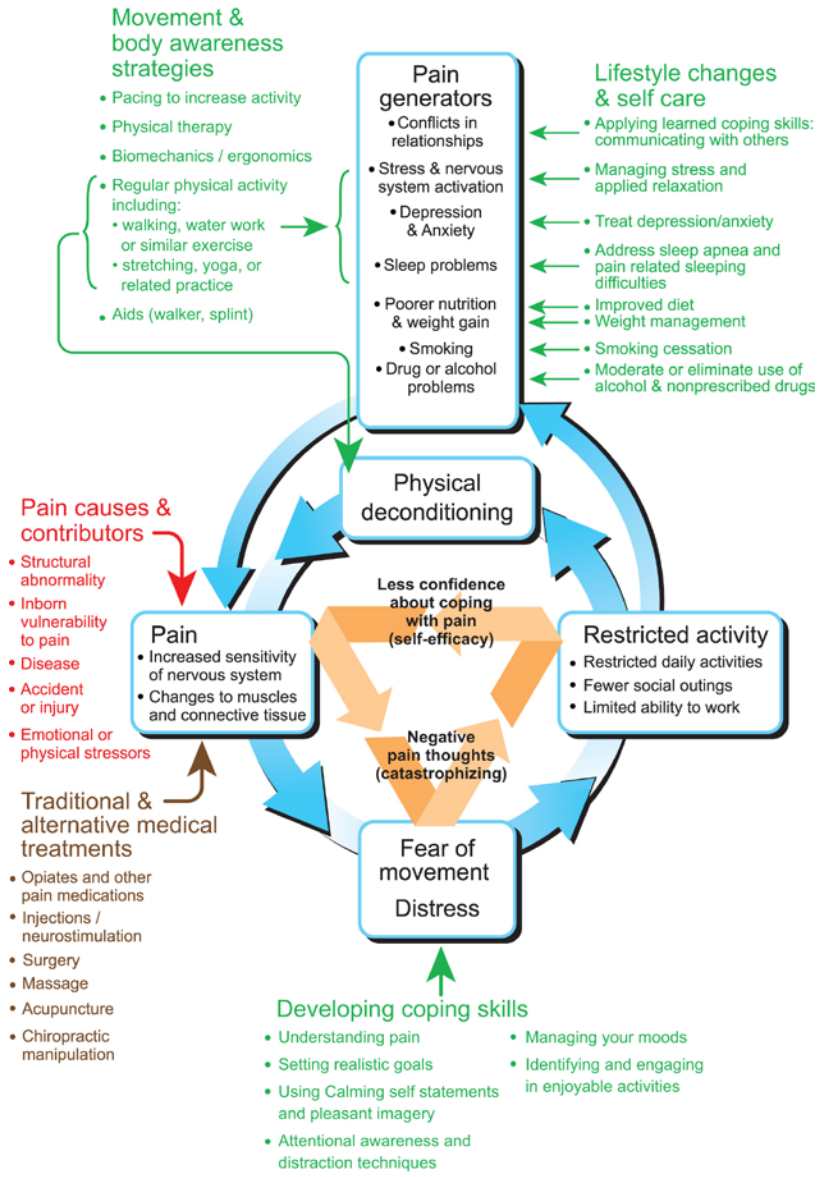

Figure 1. PPACT Intervention Description

### 4.1. Comprehensive Intake Evaluation and Re-Assessment

#### 4.1.1. Overview of Goals and Strategies

An important part of the PPACT program involves a comprehensive up-front assessment of the patients' pain and functional status to elucidate possible contributing factors to their pain and impaired functioning. The evaluation is designed to orient patients to the program approach, address any questions or concerns they have about participating in the program, and use assessment findings to develop individualized treatment plans that can then be added to the patients' EHR to guide PPACT program staff, PCPs, and other health plan providers. The "persistent pain cycle" depicted in Figure 2: Reversing the Persistent Pain Cycle provides the framework that the PPACT team uses to orient patients, PCPs, and other health care providers to the potential contributors to chronic pain and those most pertinent for a given patient. This framework is also used as a means of helping patients understand the role of pain management skills training and utilizing movement and body awareness strategies in reversing the cycle of persistent pain. Further, as the framework orients both patients and clinical providers to the many factors (the pain amplifiers in Figure 2) that may exacerbate pain and contribute to pain management difficulties, it helps motivate patients and providers alike to begin to address these factors.

**Figure 2. Reversing the Persistent Pain Cycle**




Although some of these "pain amplifiers" are addressed directly within the PPACT program or use CBT techniques useful for treating such conditions (e.g., stress, depression), other problems are outside the purview of the program but instructional materials have been developed to help patients understand the link between persistent pain and these "amplifiers" (smoking and pain, sleep problems and pain) or intervention staff work with patients and their PCPs to identify health plan and community resources for addressing their needs. Throughout the PPACT program, patients are encouraged to focus on the pain management pratices and treatments from the upper quadrants of the figure labeled as "First Line Recommendations/Active Approaches" (green and blue domains summarizing "Pain Management Skills" and "Movement & Body Awareness Strategies") to reinforce the active role patients can take in managing their pain and beginning to reverse the cycle depicted in Figure 2. Our clinical and research experience suggests that many patients focus most of their energy on trying to identify causes and contributors to pain and seeking out "Common Conventional Medical Treatment Options" (depicted in the lower right orange quadrant); patients are encouraged to view the more passive approaches to pain

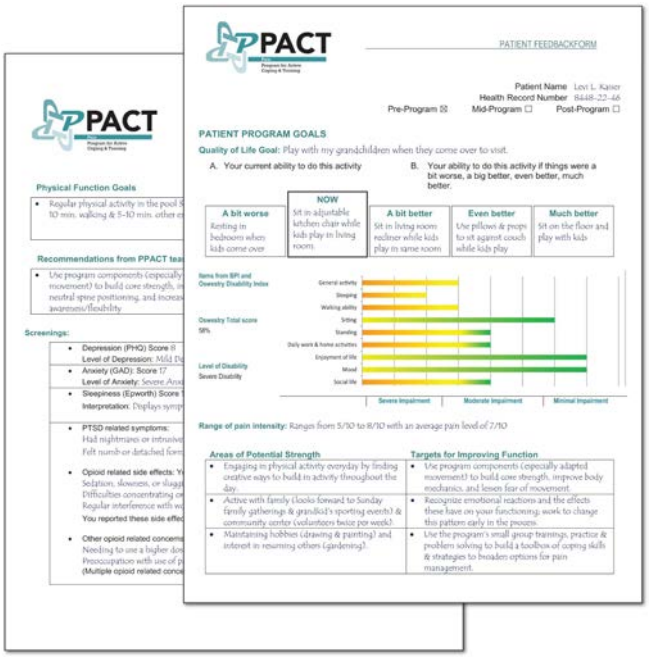
management summarized in the lower quadrants of the figure as second line treatments to be used more judiciously in augmenting the day-to-day lifestyle changes more consistent with pain management approaches summarized in the top of the figure.

With regard to the PPACT intake evaluation, all assessment instruments have been chosen for their clinical utility to help PPACT program staff, patients, and PCPs best identify targets for skills training and ancillary treatment needs and to gauge patients' functional progress in the program. Intervention assessment tools include those designed to address the following:

- Pain-related symptoms and disability. Although administered routinely through every day clinical care, the intervention team administers the complete BPI[20,21] to gauge changes in pain severity and impairment related to pain (pain interference) and to give patients and their PCPs information about patient functioning during the course of the intervention. The intervention team also administers the Oswestry Disability Index,[22-24] a psychometrically validated assessment for disability due to musculoskeletal pain conditions that is widely used by KP PTs and thus provides a metric for them to gauge PPACT patient functioning and change. Finally, a few questions are included to get a sense of the duration of participants' chronic pain, their attribution regarding the cause, and the impact of their condition on employment and/or disability status.
- Identifying treatable comorbidities and pain generators. Several clinical issues can exacerbate pain severity and contribute to functional impairment. Accordingly, the intervention team screens for depression using the Personal Health Questionnaire,[25] anxiety symptoms using the Generalized Anxiety Disorders Scale,[26] post-traumatic stress disorder using the Primary Care PTSD screen,[27,28] adverse childhood experiences using an adaptation of the ACE questions,[29] alcohol abuse using the Audit-C,[30,31] and sleep problems and sleep apnea using the Epworth Sleepiness Scale.[32-36] All selected screening measures included in our assessment battery have demonstrated strong psychometric properties and are regularly used in everyday clinical care settings, including the health plans in which the study is conducted.
- Helping patients and PCPs identify potential opioid problems and concerns. Because a primary focus of the proposed study is to help patients in the PPACT intervention identify non-opioid alternatives for pain management, the intervention team uses the Prescribed Opioids Difficulties Scale[37] to help patients identify consequences of their opioid treatment (e.g., difficulty concentrating, excess sedation or fatigue, constipation). The scale also provides an entry point for the PPACT interventionists to initiate a dialogue with participating patients about the pros and cons of using opioid medications for managing chronic pain.
- Identifying modifiable psychosocial and behavioral mediators of pain. The intervention team includes questionnaires that help underscore for patients their coping approaches to pain and their emotional and attitudinal reactions to pain, factors that can either exacerbate or help reverse the chronic pain cycle. Exacerbating factors include fear of movement (measured using an abbreviated version of the Tampa Scale for Kinesiophobia[38]) and pain catastrophizing.[39-41] Helpful factors include patients' ability to cope with their pain; e.g., by increasing physical and social activities (measured using a modified version of the CHAMPS Physical Activity Questionnaire[42,43]), increasing levels of adaptive coping (as measured using an adaptation of the Coping Strategies Questionnaire[44,45]), and improving their perceived self-efficacy beliefs about their ability to cope with the consequences of chronic pain (as measured by the chronic pain self-efficacy scale).[46]

Although data collected through the PPACT intake and follow-up evaluations (including scale scores from the instruments described above) are included in the treatment plan in the EHR and are extractable by research staff as a means to gauge patients' success in the program, these are not primary research data for the study (see Figure 3 for a fictional example of a completed patient feedback form).

**Figure 3. Example Completed Patient Feedback Form**




These feedback forms are provided to participating patients at the third intake visit and attached to an encounter in the EHR for PCP and other KP provider access. Patients are asked to complete the evaluation utilized to produce and update these feedback forms upon entry into the program and brief meetings are held with patients' PCPs to review the information. This allows the PCP and nurse care manager or behavioral health specialist to discuss areas of strength for the patient, areas of need targeted by the program, and strategic opportunities for the PCP and the program to partner in delivering a consistent message to the patient. Following this collaboration between intervention team and PCP, the PCP is encouraged to hold a scheduled telephone appointment with the participating patient to commend their participation in the program, recognize their identified strengths, and encourage their work on targeted opportunities for enhancement.

This outreach by the PCP serves to highlight for the patient the collaboration between the program and PCP and demonstrates the coordination occurring among the patient's overall team. The PCP is provided with an optional script template to use during this call. This script template and proactive nature of the PCP outreach is designed to promote enhanced collaboration between the PCP and patient.

#### 4.1.2. Schedule and Delivery

Each patient in the intervention arm is scheduled for three 60-minute intake evaluation visits in the first month:

1) Intake #1 – behavioral specialist **or** nurse care manager "new" visit
2) Intake #2 – PT evaluation
3) Intake #3 – behavioral specialist **or** nurse care manager: 60 minute "follow-up" visit

The pharmacist completes a medication chart review after the in-person medication review done during intake visit #1 or 3 and charted by the behavioral specialist or nurse care manager.

PT visits are also schedule mid-treatment to allow the PT to refine physical activity goals and to help patients utilize more advanced portions of the adapted movement yoga DVD (e.g., floor-based exercises) if warranted. Post-treatment assessment/maintenance planning with the nurse care manager or behavioral specialist is to occur shortly after the last group session (approximately four months after enrollment).

### 4.2. Core Groups for Coping Skills Training / Yoga-Based Adapted Movement Practice

#### 4.2.1. Overview of Goals and Strategies

Group coaching sessions. The group coaching sessions are based upon the approach utilized in the study team's previous studies of persistent pain[47-56] and are designed to modify psychosocial variables this team and others have found to be related to pain and functional impairment.[39,40,57-62] The variables targeted for change are (1) self-efficacy for pain and pain catastrophizing, (2) fear of movement, and (3) physical deconditioning. The group coaching portion of the intervention is designed to (1) enhance patients' self-efficacy in using coping skills to control pain, (2) decrease maladaptive pain catastrophizing, (3) decrease fear of movement, and (4) increase social and physical activities. The group sessions occur every week over 3 months for a total of 12 groups. The groups are co-led by a behavioral specialist and/or nurse care manager, with consultation from a PT to support the adapted movement activities and physical activity-relevant portions of the intervention.

Coping skills training modules. Table 1 provides an overview of our coping skills modules, which are summarized below.

- Session 1: Understanding pain/pain education and role of pain coping skills. Simple diagrams, including the neuromatrix and persistent pain cycle, are used to illustrate the pain cycle along with the role of the brain and other parts of the central nervous system in influencing the pain experience. The group explores pain's effect on patients' activities, feelings, and thoughts and how these changes similarly impact the pain they experience. The menu of coping skills modules is discussed, as well as the fact that these skills can be used not only for managing pain, but also for managing stressors related to pain. Patients are taught how to use a brief relaxation method (progressive muscle relaxation) that enables them to apply relaxation during daily activities that may increase their pain (e.g., walking, transferring from one position to another, prolonged sitting).

**Table 1. Coping Skills Training**

| Group Session | Skill Focus |
|---|---|
| 1 | Adaptation Model / Neuromatrix Model of Pain |
| 2 | Progressive Muscle Relaxation |
| 3 | Activity-Rest Cycling |
| 4 | Pleasant Activity Scheduling |
| 5 | Mini Practices |
| 6 | Pleasant Imagery |
| 7 | Leaning in: Emotional regulation |
| 8 | Leaning out: Distraction |
| 9 | Cognitive Restructuring |
| 10 | Positive Self Statements |
| 11 | Problem-solving / Reinforcing the Application of Learned Skills |
| 12 | Relapse Prevention / Maintenance Plan |

- Session 2: Applying progressive muscle relaxation (PMR) and adaptation model. Using the information presented in Session 1, experiential activities encourage the group to envision how application of the program's coping skills can change their pain, stress, and adaptation to challenging situations. Time is spent breaking down the PMR activity to promote a successful experience of this important skill and an overall understanding of how this directly impacts the perception of pain and stress in the brain.
- Session 3: Activity-rest cycle. Patients are taught to use a quota system to pace their activities and increase activity level. The quota system involves targeting a daily activity that the patient tends to overdo and learning to split this activity into periods of moderate activity (e.g., 10 minutes walking) followed by limited rest (e.g., 5 minutes rest). The patient will build up the activity quota over time. A range of activity options are discussed, along with benefits of gradually increasing activity. Barriers and obstacles to using this quota system are identified and solutions for overcoming them are formulated.
- Session 4: Pleasant activity scheduling. Pleasant activity scheduling is used to help patients identify and incorporate a variety of enjoyable and realistic activities in their day-to-day life that help them overcome the

deactivation common for pain patients and to address mood-related impairments common among patients with chronic pain.

- Session 5: Relaxation mini-practices. Patients are taught to use, and then practice as a group, these brief relaxation techniques that are designed for use in the midst of various daily activities. These mini-practices provide an alternative to longer relaxation methods, such as the full PMR, but still provide the mental and physiological benefits necessary to overcome instances of pain, tension, and stress.
- Session 6: Pleasant imagery. Patients are assisted in identifying an imaginary, personal scene and are then guided through pleasant imagery sessions that focus attention on pleasant experiences in the midst of pain, stress, or negative thoughts. The group then strategizes about building these imagery sessions into their day to promote relaxation.
- Session 7: Emotional regulation: leaning in. Mood modulation skills, mindfulness, and the role of acceptance are taught and practiced to assist patients in working with strong emotions.[63]
- Session 8: Emotional regulation: leaning out. In working with patients to counterbalance leaning into and away from challenging emotions, distraction techniques using physical or auditory stimuli are discussed and practiced as helpful tools in managing pain.[63]
- Session 9: Cognitive restructuring. Cognitive restructuring is used to help patients recognize overly negative thoughts that occur in response to pain. Effects of such thoughts on feelings and behaviors are discussed.
- Session 10: Use of calming self-statements. Patients develop alternative, calming/coping thoughts and self-statements that are more helpful/useful in coping with pain.
- Session 11: Problem-solving/reinforcing the application of learned skills. Following patient-stated reviews of the coping skills used throughout the program, the group works through several problem-solving scenarios to gain experience applying learned coping skills in the context of challenges faced.
- Session 12: Relapse prevention and maintenance enhancement training. Patients are taught strategies to enhance maintenance of learned coping skills. In order to pinpoint situational factors affecting maintenance, each patient is taught to identify high-risk situations that are likely to interfere with coping efforts. A rationale for anticipating and coping with setbacks is discussed. Cognitive strategies for recognizing early warning signs of pain and symptom flares and coping with setbacks are emphasized.

Adapted movement component of group. During the adapted movement component of the group, patients are instructed in yoga-based movement (stretching and strengthening). This approach to practice utilizes the "Relax into Yoga" DVD (based on the Yoga of Awareness research trials[64-67]) which offers a gentle yoga practice tailored to encourage patients to participate daily in gentle and accessible movements with the intention that these skills will begin to generalize to everyday activities requiring physical movement. In-session, yoga-based adapted movement is limited to seated and supported standing poses because the degree of deconditioning expected for this target population suggests that these practices are best suited to their current functional limitations. The "Relax Into Yoga" DVD that is used in group sessions and given to patients to support them in adopting a regular stretching/yoga practice outside of class does contain floor-based routines. Participants able to get up and down from the floor may augment their practice with the use of these routines and work with the PPACT PT to ensure that they know and have practiced safe ways of getting down to and up from the floor.

#### 4.2.2. Schedule and Delivery

Following the completion of the Comprehensive Intake Evaluation for each patient in a given cluster (estimated to take 4 weeks), all patients in the cluster begin the Core Group Series. This series of group sessions consists of one 2-hour session per week for a total of 12 weeks. Patients in a given cluster attend these 12 group sessions together. Group sessions are led by the behavioral specialist and/or nurse care manager, with consultation from the Intervention Team Pharmacist and PT. These groups are held at the patients' primary care clinic or clinic hub.

### 4.3. Individualized Care Management

#### 4.3.1. Overview of Goals and Strategies

Incorporating interim care management contacts. The nurse care manager or behavioral specialist also works with individual participants in person or by telephone on an as-needed basis. Although the formal individual evaluation and group sessions constitute a complete dose of the PPACT intervention, the study team recognizes there are instances when individuals are unavailable for group sessions and brief in-person or telephone sessions are indicated. Such contacts are focused on brief review of coping skills strategies, monitoring participants' progress in meeting their individualized goals, and helping address barriers or obstacles to meeting these goals. Such calls last no more than 10-15 minutes and are an efficient means of ensuring that any difficulties implementing planned behavioral changes are addressed quickly. Importantly, the interventionists are trained to help patients initiate their own self-care and problem-solving, rather than attempting to solve the difficulties for the patient. This is consistent with a motivational enhancement approach that the team has used successfully in other interventions.[68-71]

### 4.4. Pharmacist Chart Review

During the intake process, a pharmacist conducts a chart review targeting the following areas of the patient's current medication regimen: (1) drug therapy gaps or redundancies; (2) drug–drug or drug–disease interactions; (3) adequacy of current doses; (4) adherence concerns (based on participant's response to intake questions about pattern and frequency of medication use); and (5) adverse events. The patient's medication history is also reviewed in order to assess the success of previously tried medications and adequacy of those trials. The outcome of this review is to advise the referring PCP on potential adjustments to the patients' opioid treatment approach, provide feedback on other current pain medications (and possibly psychotropic medications) being prescribed to help the PCP identify therapeutic alternatives to opioid treatment that may best meet the patients' needs, and provide information that can assist the treating PCP in beginning to taper the patient's opioid medication.

### 4.5. Physical Therapy Consultation

During the intake process, patients meet with the PPACT PT to assess current functioning and identify movement adaptations that will help them most realistically begin to increase activity and thus most fully participate in the group coaching sessions. The PT evaluation targets the following areas: (1) history and physical exam, which inform the remaining evaluation components; (2) education regarding biomechanics to assist patients' movement during day-to-day activities; (3) development of a plan for graduated aerobic physical activity; and (4) modifications necessary for the yoga-based adapted movement component of program.

Follow-up evaluations with the PT occur at mid-program and focus on extending patients' progress with graduated aerobic physical activity and yoga-based adapted movement. Progress meeting patients' goals is evaluated, with a focus on helping them reach the next step toward those goals. The PT works with patients who are ready to progress to more advanced forms of the yoga-based adapted movement in order to review body mechanics that ensure safe use of the DVD guided poses.

## 5. MEASUREMENTS AND EVALUATIONS

### 5.2. Primary and Secondary Patient Outcome Measures

This section includes a description of primary and secondary outcomes with appropriate supportive evidence, justification, and validation. Primary and secondary outcomes are measured at the patient level unless otherwise indicated. Table 3 summarizes primary and secondary outcome measures for the study, their source, and designated analytic purpose.

#### 5.2.1. Pain Severity and Functioning

The primary outcome measure for the study is the PEGS,[1] a psychometrically validated 4-item version of the short form of the Brief Pain Inventory (BPI-SF).[72] The 4-item PEGS asks patients to report on their average pain severity as well as report on pain-related impairments in functioning in key life domains (general activity, enjoyment of life, and

quality of sleep) on an 11-point Likert scale [0 to 10]. The 3-item PEG has been widely adopted for clinical pain assessment, epidemiological studies, and studies of pain treatment effectiveness[72,73] and found to be more acceptable for use by PCPs and their support staff in the busy everyday clinical practice setting. We used the 4-item version as PCPs in the pilot were interested in to what extent patients' pain was interfering with their sleep..

Distribution of PEGS and PEGS slope. The PEGS questions are measured on a 11-point Likert scale. Question 1 measures pain severity, while the remaining three PEGS questions measure the impact of pain on functioning (general activity, sleep, and enjoyment of life). The sum of these four questions constitutes the study's primary measure of pain (PEGS-overall), while the pain severity item and the sum of three items measuring the impact of pain on functioning form subscales of severity (PEGS-severity) and impact (PEGS-impact). Based on data for KPNW members, the distributions of these scales are unimodal, centered at about the midpoint of the scale, and reasonably symmetric. The primary outcome variable for PPACT will be the slope of PEGS-overall on time (measured over the 12 months following study enrollment). Table 2 provides summary information for these measures for KPNW patients. The distributions for all three slopes are symmetrically distributed about 0. We also used these slopes to calculate intra-class correlation (ICC) estimates using the patient's paneled PCP as the cluster-level variable (mimicking the planned cluster structure for the main study). The resulting ICC was 0.0013.

### 5.2.2. Use of Opioids and Other Medications

An important secondary outcome for this study is the level of opioid medication used by participants as measured by their daily morphine equivalents of short-acting (U.S. Drug Enforcement Agency Schedule II or Non-Schedule II) or long-acting opioids. Morphine equivalents per dispensing (MEDs) is calculated by first multiplying the quantity dispensed times the milligram strength per dosage unit dispensed, times the opioid-specific morphine equivalents conversion factor.[74,75] Next, total daily morphine equivalents are calculated by dividing the total morphine equivalents per dispensing by the days' supply dispensed. Finally, daily morphine equivalents are applied across the corresponding days. If an individual had opioids available from multiple dispensings on the same day, morphine equivalents are summed for that day. This method of calculating MED has been widely used and applied to EHR data.[181;182]

Benzodiazepine and opioid polydrug use is common and of increasing concern to our clinical delivery systems because of potential adverse events. Research suggests that benzodiazepines and opioids alter the pharmacokinetic effects of one another and that benzodiazepines may increase the rewarding and reinforcing effects of opioids, thereby placing patients at an increased risk for abuse.[76-78] Because our health plans have prioritized reducing benzodiazepine and opioid polydrug prescribing and identifying appropriate nonpharmacotherapy treatment to support patients with such use, receipt of benzodiazepines is a secondary outcome we will track in the study.

### 5.2.3. Utilization of Health Care Services

Planned secondary outcome analyses include examination of the utilization of health care services of specific relevance for the PPACT target patient population that are hypothesized to be reduced for those randomized to the intervention when compared to their usual care counterparts. These utilization variables include both aggregated and disaggregated primary care contacts (outpatient visits, e-mail contacts, telephone contacts), use of specialty pain services (including physiatry, pain medicine, physical therapy, and occupational therapy services), inpatient services related to the participant's pain condition (e.g., surgeries, implementation of pain-related devices), and overall outpatient utilization. Utilization of other health services for which directional hypotheses are not indicated but for which data will be collected include the receipt of acupuncture or chiropractic care for pain reimbursed by the health plan. Resource and time permitting, analyses will be conducted with these additional secondary health service utilization variables. Validation of these utilization variables is reviewed in section 7.1 above.

### 5.2.4. Other Secondary Outcomes

While patient satisfaction information is routinely collected by the health plan in each of the KP regions participating in PPACT, each region uses its own distinct survey. That information is not sampled consistently and frequently among our target population, nor is it necessarily available in a manner that can be linked to a KP member's record,

given the anonymous format used to collect the information in both KPGA and KPH. Accordingly, we worked with our regional stakeholders to identify the critical patient satisfaction questions that they believed to be of importance in evaluating the intervention. These included two questions assessing patients' satisfaction with their primary care services as well as their satisfaction with overall pain-related services provided by the health plan. The questions assess satisfaction over the past three months on a 5-point Likert scale ("very dissatisfied" to "very satisfied"). Because satisfaction measures are not routinely collected in the EHR, these data will be collected directly by study personnel and stored apart from the patients' EHR. The data will be collected twice: at the time the patient initially enrolls in the study and at 6 months after enrollment, when those randomized to the intervention condition will have completed the study intervention.

#### 5.2.5. Clinical Covariates

Patient-level clinical covariates that are extracted from either the EHR or other existing clinical information systems include demographics (age, gender, race/ethnicity) and diagnostic variables that are important in categorizing the patient population, including the presence of concomitant psychiatric diagnoses, evidence of substance use disorder history, and number of pain disorder conditions. These variables are be extracted from the EHR for the six months preceding study enrollment for each participant to better characterize the patient as he/she enters the study.

### 5.3. Quantitative Data Collection Schedule

Table 2 lists quantitative data collection measures and procedures and indicates the schedule for data collection.

**Table 2. PPACT Outcome Variables**

| Measure | Source | | Schedule of Assessment: Up to 12 months preceding patient enrollment | Study Month 0 | 3 | 6 | 9 | 12 |
|---|---|---|---|---|---|---|---|---|
| **Patient-Reported Outcomes** | | | | | | | | |
| PEGS | Primary outcome | Study survey | | ✓ | ✓ | ✓ | ✓ | ✓ |
| Roland Morris Disability Questionnaire | Secondary outcome | Study survey | | ✓ | ✓ | ✓ | ✓ | ✓ |
| Patient Satisfaction Survey | Secondary outcome | Study survey | | ✓ | | ✓ | | |
| **Medication-Related Outcomes** | | | | | | | | |
| Opioids dispensed | Secondary outcome | EHR | ← | — | — | — | — | → |
| Benzodiazepines dispensed | Secondary outcome | EHR | ← | — | — | — | — | → |
| **Health Service Utilization** | | | | | | | | |
| Primary care utilization (outpatient visits, emails, telephone contacts and total) | Secondary outcome | EHR | ← | — | — | — | — | → |
| Emergency and urgent care services | Secondary outcome | EHR | ← | — | — | — | — | → |
| Use of specialty pain services (physiatry, pain clinic, physical and occupational therapy) | Secondary outcome | EHR | ← | — | — | — | — | → |
| Overall outpatient service utilization | Secondary outcome | EHR | ← | — | — | — | — | → |
| Inpatient services related to pain condition | Secondary outcome | EHR | ← | — | — | — | — | → |

### 5.4. Supporting the Clinical Collection of Patient Reported Outcomes

To ensure adequate PEGS data for primary outcome analyses, additional processes are in place to ensure quarterly PEGS data availability for all enrolled patients. This approach extends the current clinical data collection processes. Every quarter, a message is sent to PPACT patients asking them to complete the PEGS via the **kp.org** web-based patient health record system. One week after the message is sent to the PPACT patients, local analysts extract a data file of all patients' PEGS data. The lead analyst uploads the non-completers to the KP Message Center, an automated calling vendor service that the study uses to conduct the PEGS over the telephone. This service also allows for a message to be left; the patient can call back at a later date and still do the brief automated interview. Five days after the KP Message Center pushes out their automated phone calls, the results from those interviews is extracted and a list of PEGS non-completers is again generated and uploaded into the tracking system. In the last step of this three-phase process, a medical assistant will call the non-completers to attempt to conduct the brief interview with a live person. This multi-step process takes advantage of what data is already captured via the individual regions' clinical processes while still trying to get as much data as possible in a cost-effective manner.

### 5.5. Process Evaluation

The PPACT process evaluation assesses *fidelity* of intervention delivery (the extent to which the intervention is delivered as intended), the intervention *dose* (how much of the intended intervention is delivered), and the *reach* to the groups targeted by the intervention (the proportion of intended recipients who actually participate in an intervention) using the RE-AIM framework as a guide.[79,80]

For the study's formative evaluation framework, we use PRISM,[81] created to complement RE-AIM and focused on delineating criteria for successful implementation of interventions in health systems. Further, the structure, staffing, and analysis of formative evaluation data is guided by the Rapid Assessment Process (RAP),[82,83] which employs ethnographic assessment by teams to gather and analyze information quickly to build an evolving understanding of conditions related to a planned or existing intervention. Data used for the process evaluation include: journal entries compiled by the study team (to document the conversations, current practices, and PPACT-related concerns that arise in the course of their interactions with stakeholders, project staff and teams) as well as patient surveys and telephone interviews with patients, clinicians and operational leaders. As part of RAP, the qualitative team meets regularly to review data collection and incremental data analyses to compile an emerging picture of the progress of the intervention, and the results of these analyses become part of debriefing meetings and progress reports to the larger research team.

**Reach** is an individual-level measure reflecting the percentage and characteristics of persons who receive or are affected by a program—in this case, patients and PCPs. For patients, the project uses EHR data to examine:

1. The percentage of patients excluded from the trial and the rationale for exclusion (diagnostic criteria, patient availability, level of pain)
2. The percentage of patients who participate in the program based on the denominator of all patients who were approached for participation in each health plan, as well as all potentially eligible patients in the health plan regardless of whether or not they were approached for participation
3. The characteristics of participating patients compared to non-participating patients in the health plan (both those refusing participation, and those never approached for recruitment)

To describe the reach as it applies to participating PCPs, the project uses health plan administrative data to examine:

1. The percentage of PCPs who participate in the program based on the denominator of all PCPs approached for participation in the health plan, as well as all potentially eligible PCPs in the health plan regardless of whether or not they were approach for participation.
2. The characteristics of participating PCPs compared to those of non-participating PCPs (both those declining participation as well as those never approached for participation).

3. In addition to the quantitative data described above, the qualitative data collected as part of the formative evaluation is critical for understanding the reach and recruitment findings.

**Effectiveness** comprises individual-level measures focused on the impact of the intervention on important outcomes. This includes the following:

1. Broader outcomes of importance include patient satisfaction, shifts in patient utilization of health services and medication use, and overall intervention cost and potential cost offset associated with the program.
2. Resource and time permitting, the team may conduct exploratory analyses examining the robustness of the intervention across patient subgroups (e.g., gender, age, ethnicities, pain type(s), comorbid conditions).
3. Short-term attrition in the intervention will be examined as well as differential rates by patient characteristics such as those described above.

In addition to the quantitative data described above, the qualitative data collected as part of the formative evaluation will better allow the study team to best understand the reach and recruitment findings.

**Adoption.** No primary care clinics in any of the participating health plan regions have declined to participate, nor has the study team identified conditions that would restrict a given clinic from participating. However, the team will continue to monitor adoption as the intervention is more broadly rolled out in each of the regions, identifying clinics who do not participate and the reason for non-participation. The study team will also compare the characteristics (e.g., size, location type, demographics of patients served) of those clinics who participate compared to those who don't.

**Implementation** is assessed both at the individual and organization level. Each is described in turn below.

Individual implementation adherence. Individual implementation measures the adherence of patients to the intended intervention level as measured through attendance at intervention-related sessions (assessment intake evaluations and reassessments, group sessions, scheduled telephone contacts) and completion of intended home practice. As each intervention visit is scheduled using a PPACT program-specific identity code and visit type, this can be easily extracted from the EHR to evaluate degree of implementation.

Organization implementation adherence. Organization implementation measures how closely the intervention staff follow the intended intervention program as well as the consistency of the program over time. To examine intervention staff's adherence to the intervention protocol, all intervention individual and group sessions are digitally recorded, and sections of these tapes are reviewed in the supervision sessions (see section 8.1) to ensure that study procedures are closely followed. Remedial training is provided for any clinicians who deviate from the established protocol. Treatment adherence and therapist competence ratings are obtained as part of the supervision process. Treatment adherence refers to the extent to which a therapist uses the interventions prescribed by the protocol. Protocol adherence criteria are used for each session, with satisfactory adherence defined as 90% or more of the maximum possible score on the adherence rating scale. Ratings of therapists' competence in delivering the interventions is used to evaluate digital recordings of the sessions reviewed in supervision sessions.[84]

**Maintenance** is measured at the organization level, evaluating the extent to which the intervention program becomes part of the routine organizational practices and policies in a given primary care clinic and across participating regions. The team will interview operational leaders in each region regarding the sustainability of the intervention and fit with organizational priorities.

## 6. STUDY INTERVENTION STAFF TRAINING AND SUPERVISION

All core PPACT interventionists (behavioral specialists, nurse care managers, physical therapists, and pharmacists) receive training prior to conducting treatment sessions with study participants. The initial training consists of a 3-day didactic and experiential course conducted by Drs. Keefe, DeBar, and Benes with participation from the KPNW PT (Gabriel), and pharmacist (Thorsness).

Interventionists are provided with a detailed outline of the intake and reassessment process as well as detailed outlines for each group treatment session, and the treatment strategies taught through didactic instruction, taped illustrations of techniques from model cases, and role-play of common scenarios. All instruction sessions are videotaped for reference and/or education of new interventionists and retraining as need.

Procedures to ensure consistency of treatment. To ensure that the interventionists consistently follow the appropriate treatment protocol, (1) the interventionists follow a detailed intervention manual, (2) telephone-based supervision sessions are conducted with all interventionists, (3) each treatment session is audiotaped to provide opportunities for review during the weekly supervision meetings, where study investigators give feedback on interventionists' performance, and (4) ratings of treatment adherence are conducted. Protocol adherence criteria have been developed for each session with satisfactory adherence defined as 90% or more of the maximum possible score on the adherence rating scale. Ratings of interventionists' competence in delivering the intervention[85] are used to evaluate 10% of the sessions. Sessions to be evaluated are randomly selected. However, the intensity of supervision will be decreased over the course of the trial as PPACT providers gain more experience delivering the intervention mimicking the way supervision is often provided in everyday care settings. We anticipate supervision occurring weekly for the first four months, bi-weekly for the next four months, and monthly thereafter. In addition, we have planned for annual "booster" training to ensure that any new staff are fully trained and to refresh skills among interventionists. We considered carefully the intensity and frequency of training and supervision that is most appropriate for this intervention. While some simple and most systems-level interventions in pragmatic trials may call for little in the way of specific training for implementing the protocol nor systematic review of practitioner efforts,[86] the complicated problems of CP-LOT patients call for more systematic training and clinical supervision. This level of oversight is consistent with what regularly occurs in clinical settings. Importantly, many CP-LOT patients have had many treatment failures, due in part to the fragmented nature of their care; our approach is designed to address this with strong initial support and training for the interventionists working with these patients. While the increasing reliance in health care on less highly specialized and trained providers (e.g., nurse care managers, masters-level behavioral specialists) represents an exciting new direction for behavioral science in ensuring the sustainability of evidence-based interventions in everyday practice settings, it is imperative to determine the level of training and supervision necessary to ensure that the treatment is both effective for patients and feasible for providers.

## 7. SAFETY REPORTING AND MONITORING

### 7.1. Adverse Events and Serious Adverse Events

NIH guidelines indicate that an adverse event is any untoward medical occurrence in a study participant. We have operationally defined a serious adverse event as a death or hospitalization during a patient's participation in the trial. Because patients with chronic pain are anticipated to have fluctuating physical and emotional symptoms as part of the natural course of their condition (and would be expected to occur regardless of patients' enrollment in the trial), such symptoms will not be systematically monitored as part of the trial. However, because the intervention is embedded directly in the primary care clinics and conducted in partnership with participating patients' PCPs, in the event that a patient's symptoms significantly worsen during the intervention, their PCP will be immediately contacted by a PPACT intervention team member and their PCP will work with the patient to identify and provide appropriate care. This is consistent with the standard of care provided at KP.

### 7.2. Data Safety Monitoring Plan (DSMP)

As the intervention aspect of this study is based on best available evidence and constitutes a reorganization of currently available clinical services, we do not foresee any new risks above and beyond standard clinical care. Nonetheless, patients with complex chronic pain conditions are vulnerable to clinical outcomes that constitute serious adverse events, and while such events are unlikely to occur as a consequence of study participation, we are obliged to investigate and respond appropriately to these events. Consequently, we will implement a safety monitoring plan based on those used successfully in other, similar interventions. This plan involves EHR monitoring of all study participants every 6 months to assess the rate of death and hospitalization. Given the minimal risk posed by the study, however, we do not propose formal safety stopping rules and hence do not plan to conduct formal statistical analyses comparing these rates between treatment arms. In addition to calculating overall rates of occurrence of these events, an independent KP clinician in each region will conduct chart reviews of all deaths of intervention participants to identify any connection to study participation. All potential study-related deaths will be promptly reported to each of our IRBs and to our NINDS Project Officer. Because the number of hospitalizations in this group may be high and the study poses only minimal risk, we do not plan to chart-review hospitalizations as a matter of course. However, if our reports suggest a possible increased risk of hospitalizations associated with the intervention, we will work with our monitoring groups to develop a plan to do chart reviews on all or a subset of hospitalizations. All of this information will be reviewed by experienced clinicians on the investigative team and by an NINDS-appointed independent monitor.

## 8. STATISTICAL METHODS

### 8.1. Sample Size and Power

We calculated power using the PASS software program, which applies the formulas from Donner and Klar[87] and assumes a simple ANOVA framework with no covariate adjustment. Based on direct estimates of the intraclass correlation coefficient (ICC) of PEG slopes clustered within provider groups that we derived from historical data from the KPNW region, we estimate the ICC to be .0013. In the calculations presented below we conservatively use ICCs of .002, .005 and .01. From the literature, we also expect standardized effect sizes to range from .022 to 0.54,[88-92] and therefore conservatively calculated power for effect sizes ranging from .16 to .24 standard deviation units (SDUs).

Our initial study design nominally called for 120 total clusters of 10 patients each. In practice, however, we randomized 106 PCP clusters, and cluster sizes varied from 3-13, with a mean of 8 and interquartile range of 6-10. As seen in Table 3, we constructed our power calculations to accommodate the possibility of such smaller cluster sizes. With the likely ICC of .002 and 106 clusters with an average cluster size of 8, we should have 93% to detect a standard effect size of 0.24 and 88% power to detect an effect size of 0.22.

**Table 3. Power for detecting given effect sizes under various design scenarios**

| Number of Clusters | Patients per Cluster | ICC=.002 | | | | | ICC=.005 | | | | | ICC=.01 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Effect Size (in SDUs) | | | | | Effect Size (in SDUs) | | | | | Effect Size (in SDUs) | | | | |
| | | .16 | .18 | .20 | .22 | .24 | .16 | .18 | .20 | .22 | .24 | .16 | .18 | .20 | .22 | .24 |
| 120 | 8 | 68% | 78% | 86% | 92% | 96% | 68% | 78% | 86% | 91% | 95% | 66% | 76% | 84% | 90% | 95% |
| 106 | 8 | 63% | 73% | 82% | 88% | 93% | 62% | 72% | 81% | 88% | 93% | 61% | 71% | 80% | 87% | 92% |

### 8.2. Randomization

Given the lagged nature of the intervention rollout, even within a given clinic, it is necessary to randomize all providers in a given clinic at the outset of intervention activities in that clinic. However, the assignments are not revealed to either patients or providers until all of the patients for a given PCP have been recruited. To preserve blinding, recruitment staff are totally distinct from the intervention staff and remain blinded during the entire course of the study as they collect follow-up assessments.

### 8.3. Dropout and Withdrawal

Primary Care Provider. If an enrolled PCP leaves their KP practice, changes clinics, or asks to withdraw from the study, every effort will be made to collect process data from the PCP before their departure and to document the reason for leaving. We will continue to collect data on the provider's enrolled patients and will analyze them according to the group to which they were originally assigned (i.e., per intention to treat, ITT).

Patients. If an enrolled patient discontinues KP coverage or changes providers during the study, we will continue to collect data on them and will analyze them according to the group to which they were originally assigned. Such patients who are in clusters randomized to the intervention arm of the study will continue to be offered individual or telephone contact with the study interventionists throughout the time that their enrolled cohort is in the active phase of the intervention so as to provide as much therapeutic benefit to these patients as is possible.

We will document the extent to which either of the above events occurs and will compare the frequency of such occurrences between intervention and control participants.

### 8.4. Quantitative Data Methods and Analysis

The following analytic framework will be used for our primary and secondary outcome analyses. All analyses will be performed using an intention-to-treat framework, and tests will be evaluated at a two-tailed alpha level of .05. Because of the nested structure of the data (observations nested within patients nested within provider groups), we will use a three-level hierarchical linear model (HLM: mixed models, random effects regression, and multilevel models) to account for the intraclass correlation that results from the nesting.[93-95] An advantage of multilevel modeling is that unlike repeated measures analysis of variance, it does not require the same number of data points from all patients, thus all patients with at least a baseline measure can be included in the analysis. The first level of the model will include time as a predictor (five timepoints, representing the number of weeks since baseline), thus modeling the within-person trajectories across time. We will use two parameters (linear and quadratic slope) to characterize change across time, with linear slope capturing initial rate of change and quadratic slope reflecting the degree to which the change slowed (or increased) over time. The second level of the model may include patient-level covariates as predictors of the baseline PEGS score and the slope parameters for time. Randomization is expected to balance most potential patient-level covariates, however, in the case of remaining residual imbalances, covariates will be included in the model. These may include variables such as substance use problems/history, number of pain conditions and type, and other comorbid medical and mental health conditions. The third level will include a dummy variable for arm as the predictor of the patient-level intercept and slope parameters for time. A significant coefficient for arm on the slope(s) of time would indicate that there are different trajectories across time for each arm. A pattern in which those in PPACT demonstrate a greater reduction in pain impact over time than those in the usual care arm would provide support for the effectiveness of PPACT. We will use the same analytical framework for the RMDQ. Because there are only two timepoints available for satisfaction, we will be limited to a two-level model of the difference scores between 6 months and baseline of patients nested within provider groups.

Level-1 Model

$$Y_{tij} = \pi_{0ij} + \pi_{1ij}*(LIN\_TIME_{tij}) + \pi_{2ij}*(QUAD\_TIME_{tij}) + e_{tij}$$

Level-2 Model

$$\pi_{0ij} = \beta_{00j} + \beta_{01j}*(Patient\_covariates_{ij}) + r_{0ij}$$
$$\pi_{1ij} = \beta_{10j} + \beta_{11j}*(Patient\_covariates_{ij}) + r_{1ij}$$
$$\pi_{2ij} = \beta_{20j} + \beta_{21j}*(Patient\_covariates_{ij}) + r_{2ij}$$

Level-3 Model

$$\beta_{00j} = \gamma_{000} + \gamma_{001}(ARM_j) + u_{00j}$$
$$\beta_{01j} = \gamma_{010}$$
$$\beta_{10j} = \gamma_{100} + \gamma_{101}(ARM_j) + u_{10j}$$
$$\beta_{11j} = \gamma_{110}$$
$$\beta_{20j} = \gamma_{200} + \gamma_{201}(ARM_j) + u_{20j}$$
$$\beta_{21j} = \gamma_{210}$$

where: $Y_{tij}$ is the outcome for person i under provider j at time t, $\pi$ are level 1 (occasion) regression coefficients, $e_{tij}$ is the random error associated with person i under provider cluster j at time t, Lin_Time is the number of weeks since baseline and Quad_Time is the number of weeks since baseline squared, $\beta$ are level 2 (patient) regression coefficients, r are level 2 random effects, $\gamma$ are level 3 (provider cluster) regression coefficients, u are level 3 random effects, and arm is an indicator variable.

Hierarchical generalized linear modeling (HGLM) will be used to test the secondary outcomes: opioids dispensed, pain treatment and diagnostic procedures, emergency/urgent care visits, primary care visits, and specialty care visits over 12 months. These will be two-level models, with patients forming the first level of the model and clinics the second level. Patient-level covariates will be included in the first level, and PPACT versus a usual-care dummy variable will form the second level of the model. This will allow us to test whether the secondary outcomes differ for the two groups, controlling for differences in patient characteristics. Because the utilization variables are likely to follow non-

normal distributions, we will use Poisson, Negative Binomial, or Gamma distributions as appropriate for the distribution of each secondary outcome variable.

Level-1 Model

$$\eta_{ij} = \beta_{0j} + \beta_{1j}*(\text{Patient\_covariates}_{ij})$$

Level-2 Model

$$\beta_{0j} = \gamma_{00} + \gamma_{01}*(\text{ARM}_j) + u_{0j}$$
$$\beta_{1j} = \gamma_{10}$$

where: $\eta_{ij}$ is the outcome defined by the identity link (log) and distribution (gamma, Poisson, or Negative Binomial), β are level 1 (person) regression coefficients, γ are level 2 (provider cluster) regression coefficients, u is the level 2 random effect for the level 1 intercept, and arm is an indicator variable.

**8.5. Economic Data Methods and Analysis**

In our economic analysis of the PPACT intervention, we will assess the resources and costs necessary to deliver the PPACT intervention in routine clinical practice, and the cost-effectiveness of the PPACT intervention compared with usual care. Costs will be reported at three levels: 1) costs related to the intervention delivery, 2) medical care costs related to pain control, and 3) the total cost of medical care. Intervention costs will be estimated using EHR data, supplemented with data collected directly from intervention team staff. A sampling of clinical visits and interviews with intervention delivery staff will be used to determine the time needed to deliver the intervention. We will also consider costs related to the administration of the PPACT intervention in practice, including project management, training, and additional team meetings.

Using EHR data, we will aggregate medical care events related to pain control and total costs at meaningful levels in order to demonstrate how the intervention impacts medical care resource use, specifically inpatient stays, outpatient procedures, clinic visits, and pharmacy dispenses. We will identify medical care utilization events that are related to pain control and the intervention using ICD-9CM, ICD-10CM, and CPT codes. To facilitate costing, we will examine the number and type of health care encounters participants receive over the course of their 12-month participation in the study. We will capture inpatient stays by extracting the information in the discharge abstract, including ICD-9 and ICD-10 codes and procedures and length-of-stay information necessary to cost the event.

Medical care utilization events will be analyzed using mixed effects Poisson regression analysis, with primary care provider cluster as a random effects factor and follow-up time as an offset variable. We will estimate quantities of medical care events (i.e., inpatient stays, outpatient procedures, clinic visits, and pharmacy dispenses) using separate regression models.

## 9. LITERATURE CITED


1. Krebs EE, Lorenz KA, Bair MJ, et al. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. *J Gen Intern Med.* 2009;24(6):733-738.
2. Jensen MP, Nielson WR, Kerns RD. Toward the development of a motivational model of pain self-management. *The Journal of Pain.* 2003;4(9):477-492.
3. Jensen MP, Nielson WR, Turner JA, Romano JM, Hill ML. Changes in readiness to self-manage pain are associated with improvement in multidisciplinary pain treatment and pain coping. *Pain.* 2004;111(1-2):84-95.
4. Vong SK, Cheing GL, Chan F, So EM, Chan CC. Motivational enhancement therapy in addition to physical therapy improves motivational factors and treatment outcomes in people with low back pain: a randomized controlled trial. *Archives of physical medicine and rehabilitation.* 2011;92(2):176-183.
5. Rollnick S, Miller WR, Butler C. Motivational interviewing in health care: helping patients change behavior. Guilford Press; 2008.
6. Owen-Smith A, Mayhew M, Leo MC, et al. Automating Collection of Pain-Related Patient-Reported Outcomes to Enhance Clinical Care and Research. *J Gen Intern Med.* 2018;33(Suppl 1):31-37.
7. Wagner EH. The Chronic Care Model. 2006; http://www.improvingchroniccare.org/.
8. Wagner EH, Austin BT, Davis C, Hindmarsh M, Schaefer J, Bonomi A. Improving chronic illness care: translating evidence into action. *Health affairs.* 2001;20(6):64-78.
9. Coleman K, Austin BT, Brach C, Wagner EH. Evidence on the chronic care model in the new millennium. *Health affairs.* 2009;28(1):75-85.
10. Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? *Effective clinical practice: ECP.* 1998;1(1):2.
11. Wagner EH, Austin BT, Von Korff M. Organizing care for patients with chronic illness. *The Milbank Quarterly.* 1996:511-544.
12. Dobscha SK, Corson K, Perrin NA, et al. Collaborative care for chronic pain in primary care: a cluster randomized trial. *Jama.* 2009;301(12):1242-1252.
13. Kroenke K, Bair M, Damush T, et al. Stepped Care for Affective Disorders and Musculoskeletal Pain (SCAMP) study: design and practical implications of an intervention for comorbid pain and depression. *General hospital psychiatry.* 2007;29(6):506-517.
14. Loeser JD, Turk DC. Multidisciplinary pain management. Paper presented at: Seminars in Neurosurgery2004.
15. Turk DC. 2 Efficacy and Cost-Effectiveness Treatment for Chronic Pain: An Analysis and Evidence-Based Synthesis. *Chronic pain management: Guidelines for multidisciplinary program development.* 2007:15.
16. Von Korff M, Moore JE, Lorig K, et al. A randomized trial of a lay person-led self-management group intervention for back pain patients in primary care. *Spine.* 1998;23(23):2608-2615.
17. Chou R, Huffman LH. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Annals of internal medicine.* 2007;147(7):492-504.
18. Chou R, Loeser JD, Owens DK, et al. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: an evidence-based clinical practice guideline from the American Pain Society. *Spine.* 2009;34(10):1066-1077.
19. Management ASoATFoCP. Practice guidelines for chronic pain management: an updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. *Anesthesiology.* 2010;112(4):810.
20. Cleeland C, Ryan K. Pain assessment: global use of the Brief Pain Inventory. *Annals, Academy of Medicine, Singapore.* 1994.
21. Keller S, Bann CM, Dodd SL, Schein J, Mendoza TR, Cleeland CS. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. *The Clinical journal of pain.* 2004;20(5):309-318.
22. Roland M, Fairbank J. The Roland–Morris disability questionnaire and the Oswestry disability questionnaire. *Spine.* 2000;25(24):3115-3124.

23. Vianin M. Psychometric properties and clinical usefulness of the Oswestry Disability Index. *Journal of chiropractic medicine.* 2008;7(4):161-163.
24. Wittink H, Turk DC, Carr DB, Sukiennik A, Rogers W. Comparison of the redundancy, reliability, and responsiveness to change among SF-36, Oswestry Disability Index, and Multidimensional Pain Inventory. *The Clinical journal of pain.* 2004;20(3):133-142.
25. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. *Journal of affective disorders.* 2009;114(1-3):163-173.
26. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of internal medicine.* 2006;166(10):1092-1097.
27. Kimerling R, Ouimette P, Prins A, et al. Brief report: Utility of a short screening scale for DSM-IV PTSD in primary care. *Journal of general internal medicine.* 2006;21(1):65-67.
28. Ouimette P, Wade M, Prins A, Schohn M. Identifying PTSD in primary care: Comparison of the Primary Care-PTSD screen (PC-PTSD) and the General Health Questionnaire-12 (GHQ). *Journal of Anxiety disorders.* 2008;22(2):337-343.
29. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. *American journal of preventive medicine.* 2019;56(6):774-786.
30. Berner MM, Kriston L, Bentele M, Härter M. The alcohol use disorders identification test for detecting at-risk drinking: a systematic review and meta-analysis. *Journal of studies on alcohol and drugs.* 2007;68(3):461-473.
31. Kriston L, Hölzel L, Weiser A-K, Berner MM, Härter M. Meta-analysis: are 3 questions enough to detect unhealthy alcohol use? *Annals of internal medicine.* 2008;149(12):879-888.
32. Beaudreau SA, Spira AP, Stewart A, et al. Validation of the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale in older black and white women. *Sleep medicine.* 2012;13(1):36-42.
33. Hayes AL, Spilsbury JC, Patel SR. The Epworth score in African American populations. *Journal of Clinical Sleep Medicine.* 2009;5(04):344-348.
34. Heaton K. A psychometric analysis of the Epworth Sleepiness Scale. *Journal of nursing measurement.* 2007;15(3).
35. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *sleep.* 1991;14(6):540-545.
36. Nguyen ATD, Baltzan MA, Small D, Wolkove N, Guillon S, Palayew M. Clinical reproducibility of the Epworth sleepiness scale. *Journal of Clinical Sleep Medicine.* 2006;2(02):170-174.
37. Banta-Green CJ, Von Korff M, Sullivan MD, Merrill JO, Doyle SR, Saunders K. The prescribed opioids difficulties scale: a patient-centered assessment of problems and concerns. *The Clinical journal of pain.* 2010;26(6):489.
38. Shelby RA, Somers TJ, Keefe FJ, et al. Brief fear of movement scale for osteoarthritis. *Arthritis care & research.* 2012;64(6):862-871.
39. Keefe FJ, Brown GK, Wallston KA, Caldwell DS. Coping with rheumatoid arthritis pain: catastrophizing as a maladaptive strategy. *Pain.* 1989;37(1):51-56.
40. Keefe FJ, Lefebvre JC, Egert JR, Affleck G, Sullivan MJ, Caldwell DS. The relationship of gender to pain, pain behavior, and disability in osteoarthritis patients: the role of catastrophizing. *Pain.* 2000;87(3):325-334.
41. Sullivan MJ, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. *Psychological assessment.* 1995;7(4):524.
42. Mills KM, Stewart AL, King AC, et al. Factors associated with enrollment of older adults into a physical activity promotion program. *Journal of Aging and Health.* 1996;8(1):96-113.
43. Sepsis P, Stewart A, McLellan B, et al. Seniors' ratings of the helpfulness of health promotion program features in starting and maintaining physical activity. *Journal of Aging and Physical Activity.* 1995;3(2):193-207.
44. Jensen MP, Keefe FJ, Lefebvre JC, Romano JM, Turner JA. One-and two-item measures of pain beliefs and coping strategies. *Pain.* 2003;104(3):453-469.

45. Rosenstiel AK, Keefe FJ. The use of coping strategies in chronic low back pain patients: relationship to patient characteristics and current adjustment. *Pain.* 1983;17(1):33-44.
46. Anderson KO, Dowds BN, Pelletz RE, Edwards WT, Peeters-Asdourian C. Development and initial validation of a scale to measure self-efficacy beliefs in patients with chronic pain. *Pain.* 1995;63(1):77-83.
47. Emery CF, Keefe FJ, France CR, et al. Effects of a brief coping skills training intervention on nociceptive flexion reflex threshold in patients having osteoarthritic knee pain: a preliminary laboratory study of sex differences. *Journal of pain and symptom management.* 2006;31(3):262-269.
48. Keefe FJ, Ahles TA, Sutton L, et al. Partner-guided cancer pain management at the end of life: a preliminary study. *Journal of pain and symptom management.* 2005;29(3):263-272.
49. Keefe FJ, Blumenthal J, Baucom D, et al. Effects of spouse-assisted coping skills training and exercise training in patients with osteoarthritic knee pain: a randomized controlled study. *Pain.* 2004;110(3):539-549.
50. Keefe FJ, Caldwell DS, Baucom D, et al. Spouse-assisted coping skills training in the management of osteoarthritic knee pain. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology.* 1996;9(4):279-291.
51. Keefe FJ, Caldwell DS, Baucom D, et al. Spouse-assisted coping skills training in the management of knee pain in osteoarthritis: Long-term followup results. *Arthritis Care & Research.* 1999;12(2):101-111.
52. Keefe FJ, Caldwell DS, Williams DA, et al. Pain coping skills training in the management of osteoarthritic knee pain: a comparative study. *Behavior Therapy.* 1990;21(1):49-62.
53. Keefe FJ, Caldwell DS, Williams DA, et al. Pain coping skills training in the management of osteoarthritic knee pain-II: follow-up results. *Behavior Therapy.* 1990;21(4):435-447.
54. Keefe FJ, Shelby RA, Somers TJ, et al. Effects of coping skills training and sertraline in patients with non-cardiac chest pain: a randomized controlled study. *PAIN®.* 2011;152(4):730-741.
55. Naylor MR, Helzer JE, Naud S, Keefe FJ. Automated telephone as an adjunct for the treatment of chronic pain: a pilot study. *The Journal of Pain.* 2002;3(6):429-438.
56. Naylor MR, Naud S, Keefe FJ, Helzer JE. Therapeutic Interactive Voice Response (TIVR) to reduce analgesic medication use for chronic pain management. *The Journal of Pain.* 2010;11(12):1410-1419.
57. Buckelew SP, Parker JC, Keefe FJ, et al. Self-efficacy and pain behavior among subjects with fibromyalgia. *Pain.* 1994;59(3):377-384.
58. Geisser ME, Robinson ME, Keefe FJ, Weiner ML. Catastrophizing, depression and the sensory, affective and evaluative aspects of chronic pain. *Pain.* 1994;59(1):79-83.
59. Keefe FJ, Kashikar-Zuck S, Robinson E, et al. Pain coping strategies that predict patients' and spouses' ratings of patients' self-efficacy. *Pain.* 1997;73(2):191-199.
60. Keefe FJ, Lipkus I, Lefebvre JC, et al. The social context of gastrointestinal cancer pain: a preliminary study examining the relation of patient pain catastrophizing to patient perceptions of social support and caregiver stress and negative responses. *PAIN®.* 2003;103(1-2):151-156.
61. Somers TJ, Keefe FJ, Carson JW, Pells JJ, LaCaille L. Pain catastrophizing in borderline morbidly obese and morbidly obese individuals with osteoarthritic knee pain. *Pain Research and Management.* 2008;13(5):401-406.
62. Sullivan MJ, Thorn B, Haythornthwaite JA, et al. Theoretical perspectives on the relation between catastrophizing and pain. *The Clinical journal of pain.* 2001;17(1):52-64.
63. Turk DC, Meichenbaum D, Genest M. *Pain and behavioral medicine: A cognitive-behavioral perspective.* Vol 1: Guilford Press; 1983.
64. Carson JW, Carson KM, Jones KD, Bennett RM, Wright CL, Mist SD. A pilot randomized controlled trial of the Yoga of Awareness program in the management of fibromyalgia. *PAIN®.* 2010;151(2):530-539.
65. Carson JW, Carson KM, Porter LS, Keefe FJ, Seewaldt VL. Yoga of Awareness program for menopausal symptoms in breast cancer survivors: results from a randomized trial. *Supportive care in cancer.* 2009;17(10):1301-1309.
66. Carson JW, Carson KM, Porter LS, Keefe FJ, Shaw H, Miller JM. Yoga for women with metastatic breast cancer: results from a pilot study. *Journal of pain and symptom management.* 2007;33(3):331-341.

67. Wren AA, Wright MA, Carson JW, Keefe FJ. Yoga for persistent pain: new findings and directions for an ancient practice. *Pain.* 2011;152(3):477.
68. DeBar LL, Ritenbaugh C, Aickin M, et al. YOUTH: a health plan–based lifestyle intervention increases bone mineral density in adolescent girls. *Archives of pediatrics & adolescent medicine.* 2006;160(12):1269-1276.
69. DeBar LL, Stevens VJ, Perrin N, et al. A primary care–based, multicomponent lifestyle intervention for overweight adolescent females. *Pediatrics.* 2012;129(3):e611-e620.
70. DeBar LL, Striegel-Moore RH, Wilson GT, et al. Guided self-help treatment for recurrent binge eating: Replication and extension. *Psychiatric Services.* 2011;62(4):367-373.
71. DeBar LL, Wilson GT, Yarborough BJ, et al. Cognitive behavioral treatment for recurrent binge eating in adolescent girls: A pilot trial. *Cognitive and behavioral practice.* 2013;20(2):147-161.
72. Kroenke K, Theobald D, Wu J, Tu W, Krebs EE. Comparative responsiveness of pain measures in cancer patients. *The Journal of Pain.* 2012;13(8):764-772.
73. Krebs EE, Bair MJ, Damush TM, Tu W, Wu J, Kroenke K. Comparative responsiveness of pain outcome measures among primary care patients with musculoskeletal pain. *Medical care.* 2010;48(11):1007.
74. Boudreau D, Von Korff M, Rutter CM, et al. Trends in long-term opioid therapy for chronic non-cancer pain. *Pharmacoepidemiology and drug safety.* 2009;18(12):1166-1175.
75. Von Korff M, Saunders K, Ray GT, et al. Defacto long-term opioid therapy for non-cancer pain. *The Clinical journal of pain.* 2008;24(6):521.
76. Gudin JA, Mogali S, Jones JD, Comer SD. Risks, management, and monitoring of combination opioid, benzodiazepines, and/or alcohol use. *Postgraduate medicine.* 2013;125(4):115-130.
77. Jones JD, Mogali S, Comer SD. Polydrug abuse: a review of opioid and benzodiazepine combination use. *Drug and alcohol dependence.* 2012;125(1-2):8-18.
78. Webster LR. Considering the risks of benzodiazepines and opioids together. Blackwell Publishing Inc Malden, USA; 2010.
79. RJ B-W, PJ C, CL T, BD L. The use of the eating disorder examination with children: a pilot study. *Int J Eat Disord.* 1996;19(4):391-397.
80. Campbell CI, Weisner C, LeResche L, et al. Age and gender trends in long-term opioid analgesic use for noncancer pain. *American journal of public health.* 2010;100(12):2541-2547.
81. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Annals of internal medicine.* 2010;152(2):85-92.
82. Kuehn BM. Opioid prescriptions soar. *Jama.* 2007;297(3):249-251.
83. Sullivan MD, Von Korff M, Banta-Green C, Merrill JO, Saunders K. Problems and concerns of patients receiving chronic opioid therapy for chronic non-cancer pain. *PAIN®.* 2010;149(2):345-353.
84. Waltz J, Addis ME, Koerner K, Jacobson NS. Testing the integrity of a psychotherapy protocol: assessment of adherence and competence. *Journal of consulting and clinical psychology.* 1993;61(4):620.
85. Borkovec TD, Nau SD. Credibility of analogue therapy rationales. *Journal of behavior therapy and experimental psychiatry.* 1972;3(4):257-260.
86. Thorpe KE, Zwarenstein M, Oxman AD, et al. A pragmatic–explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *Journal of clinical epidemiology.* 2009;62(5):464-475.
87. Von Korff M, Kolodny A, Deyo RA, Chou R. Long-term opioid therapy reconsidered. *Annals of internal medicine.* 2011;155(5):325-328.
88. Dixon KE, Keefe FJ, Scipio CD, Perri LM, Abernethy AP. Psychological interventions for arthritis pain management in adults: a meta-analysis. *Health Psychology.* 2007;26(3):241.
89. Goldenberg DL. Multidisciplinary modalities in the treatment of fibromyalgia. *Journal of Clinical Psychiatry.* 2008;69(Suppl 2):30-34.
90. Sarzi-Puttini P, Atzeni F, Salaffi F, Cazzola M, Benucci M, Mease PJ. Multidisciplinary approach to fibromyalgia: what is the teaching? *Best Practice & Research Clinical Rheumatology.* 2011;25(2):311-319.
91. Scascighini L, Toma V, Dober-Spielmann S, Sprott H. Multidisciplinary treatment for chronic pain: a systematic review of interventions and outcomes. *Rheumatology.* 2008;47(5):670-678.

92. Smith BH, Torrance N. Management of chronic pain in primary care. *Current Opinion in Supportive and Palliative Care.* 2011;5(2):137-142.
93. Hox JJ. *Multilevel analysis: techniques and applications.* Routledge; 2010.
94. Raudenbush SW, Bryk AS. *Hierarchical linear models: Applications and data analysis methods.* 2nd ed. Thousand Oaks, CA: Sage Publications Inc; 2002.
95. Snijders T, Bosker R. *Multilevel analysis: An introduction to basic and advanced multilevel modeling.* Thousand Oaks, CA: Sage; 1999.