GRANT PROPOSAL

PFIZER MEDICAL EDUCATION GROUP – The Role of Appropriate Opioid Management RFP

Grant #45354, Brigham and Women's Hospital

Title: Opioid Misuse Mitigation and Practice Quality Improvement in Primary Care

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Study Proposal

D.1. Aims and Objective of Study: We plan to conduct a controlled trial with chronic pain patients who have been or will be prescribed opioids in primary care centers. Our focus is on drug misuse behaviors that can be monitored by a treating primary care physician that can signal potential problems. *The goal of tracking and changing these behaviors is to improve compliance with opioids and reduce opioid misuse.* We will develop and pilot-test a unique intervention for patients with chronic noncancer pain who show risk for or evidence of misuse of prescription opioids. A pain treatment protocol will incorporate reliable and validated screening questionnaires and tools developed at our center to accurately identify opioid medication misuse (Screener and Opioid Assessment for Pain Patients Revised, SOAPP-R; Current Opioid Misuse Measure, COMM; Pain Assessment Interview Network and Clinical Advisory System; painCAS). We intend to evaluate opioid use and changes in quality of life of patients in two types of primary care centers. This study will help determine whether primary care physician (PCP) education, careful monitoring, and incorporation of a structured opioid therapy protocol (routine urine screens, opioid agreements and compliance checklists) will improve compliance with prescription opioids and reduce opioid misuse. We intend to determine the clinical benefit of 1) electronic pain assessment programs, 2) increased communication strategies between pain specialists and primary care physicians and 3) education and use of practice guidelines to improve pain management within a busy primary care center. The results of this study will hopefully lend insight into the best pain medicine practice models for primary care physicians.

D.1.1 Specific Aim 1: We will implement the use of a software program (painCAS) to assess and track patients with chronic pain within a busy primary care clinic in the experimental group (Specialist). We will also identify PCPs in the control group (Generalist) and track progress of matched chronic pain patients over six months using paper questionnaires. We will assess patients' pain, function, medication use, mood, side effects, medical problems, and psychiatric and substance abuse risk. Hypothesis: The use of the painCAS program will improve treating PCPs' confidence in managing pain patients and positively impact the patients in reducing opioid misuse and improving their quality of life. We also plan to assess the effects the painCAS program will have in identifying those patients who would need close monitoring and in reducing healthcare utilization.

D.1.2 Specific Aim 2: We will develop pain assessment summary reports for all patients prescribed opioids for their pain and make these reports available to PCPs at the Specialist sites using the electronic Longitudinal Medical Record (LMR). The summary report, based on monthly patient interview data, will include information on pain intensity, mood level, activity interference, current medications, side effects, opioid compliance based on the Opioid Compliance Checklist, number of clinic and emergency room visits, and treatment recommendations for use by the primary care physician. Hypothesis: The implementation of a monthly summary report designed for specific use by the PCP will improve confidence in managing patients, reduce the barriers for coordination of care between specialists and the primary care center, and help establish treatment protocols for patients prescribed opioids for pain in order to minimize opioid misuse.

D.1.3 Specific Aim 3: We will provide direct support to identified PCPs in the Specialist treatment arm by offering education sessions and access to a pharmacist, addiction specialist,

pain specialty nurse practitioner and other pain medicine staff who will be available to assess patients and review medication strategies for pain management. A case manager will help to coordinate services and collect data. A standard treatment protocol for the management of opioids for pain will be presented and pain management support will be offered to the providers. Hypothesis: Based on results of post-study tests, interviews, and chart reviews, there will be evidence of improved PCP confidence in managing opioid therapy and a higher compliance in following recognized opioid prescribing guidelines. Patients will also report improved pain management and demonstrate greater compliance with opioids.

D.2. Current Assessment of Need

The usefulness of opioids in the treatment of acute and cancer-related pain has been confirmed by several studies.[1] Yet some physicians and other health care professionals are reluctant to support the use of opioid medication for patients with chronic noncancer pain because of concerns regarding adverse effects, lack of efficacy, tolerance, and addiction.[2-4] Within the past ten years the prescription of opioids for the treatment of chronic pain has increased exponentially, primarily for noncancer pain,[5] and the abuse of such medications is receiving increasing notice.[6] Unfortunately, many physicians prescribing pain medication have little training in this area and may prescribe opioids without any assessment of early signs of risk of medication misuse. The pain literature suggests that physicians are able to better provide suitable treatment and care of patients with chronic pain when they receive adequate training and necessary assessment information.[7] It has also been shown that risk of misuse behaviors of prescribed opioid medication can be mitigated by assessment and treatment protocols.[8] These protocols help to identify patients who are at risk for opioid misuse and can provide clinicians with patient's background and behavior to help make informed treatment decisions.

Although it is well known that misuse is prominent in the chronic pain population and is a clear risk factor for the development of addiction, it is also known that patients with signs of substance misuse may be inadequately treated for pain due, in part, to a reluctance of some physicians to address the risks of opioid abuse.[8-10] Chronic pain patients who show aberrant drug-related behavior are often dismissed from a primary care practice when they are noncompliant with opioid therapy, instead of being offered treatments to reduce misuse and to improve compliance. Unfortunately, there are few treatment resources for such patients. This proposal seeks to remedy that deficit, with the goal of reducing the rate of prescription opioid misuse among those patients on opioid therapy within primary care.

D.2.1 Preliminary Studies. We conducted a randomized trial in patients prescribed opioids for noncancer back pain who showed risk potential for or demonstration of opioid misuse to see if close monitoring and cognitive behavioral substance abuse counseling could increase overall compliance with opioids.[8] Forty two patients meeting criteria for high risk for opioid misuse were randomized to either standard control (High-Risk Control; N=21) or experimental compliance treatment consisting of monthly urine screens, compliance checklists, and individual and group motivational counseling (High-Risk Experimental; N=21). Twenty patients who met criteria indicating low potential for misuse were recruited to a low-risk control group (Low-Risk Control). Patients were followed for 6 months and completed pre- and post-study questionnaires and monthly electronic diaries. Outcomes consisted of the percent with a positive Drug Misuse Index (DMI), which was a composite score of self-reported drug misuse

(Prescription Drug Use Questionnaire), physician-reported abuse behavior (Addiction Behavior Checklist), and abnormal urine toxicology results. Significant differences were found between groups with 73.7 % of the High-Risk Control patients demonstrating positive scores on the DMI compared with 26.3% from the High-Risk Experimental group and 25.0% from the Low-Risk Controls ($p<0.05$). The results of this study demonstrated the benefits of a brief behavioral intervention in the management of opioid compliance among chronic back pain patients at high-risk for prescription opioid misuse at a pain management center. We plan to use this information to investigate how similar interventions can be used within primary care.

To gain some knowledge of pain management practices within primary care, we recently conducted a survey of 60 primary care physicians within the Boston area to assess the degree to which they agreed or disagree with 10 statements related to the assessment and treatment of chronic pain patients.[11] The findings showed that chronic pain is perceived to be a problem for the PCPs (89.9% agreed), that there is a reluctance to prescribe opioids for chronic pain even after other treatments were ineffective (64.4% agreed), and many lacked confidence in managing patients with chronic pain (62.7% agreed). Also, we found that only a minority followed accepted opioid therapy practice guidelines (23.7%) and many were dissatisfied with their communication with the pain specialists (84.7%). Importantly, the majority of the physicians agreed that they would be willing to prescribe opioids if they were given adequate support and direction (64.4%). This survey information is the basis for this proposed study. The intent is to improve the comfort of PCPs to prescribe opioids for chronic noncancer pain, to reduce risk of opioid misuse, and to measure the impact of an education and tracking program on patient-reported pain and healthcare utilization.

D.2.2. Definitions of Terms. Concise definitions of terms are important to minimize confusion and help to clarify the objectives of this study.[12, 13] For purposes of this investigation, *substance misuse* is defined as the use of any drug in a manner other than how it is indicated or prescribed. *Substance abuse* is defined as the use of any substance when such use is unlawful, or when such use is detrimental to the user or others. *Prescription opioid addiction* is a primary, chronic, neurobiologic disease that is characterized by behaviors that include one of more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. *Addiction* is a behavioral pattern of substance abuse characterized by overwhelming involvement with the use of a drug that, once manifested, is believed to persist. *Aberrant drug-related behaviors* are any behaviors that suggest the presence of substance abuse or addiction. Determining an individual's potential for aberrant drug behaviors and preventing misuse of prescription opioids is important in the evaluation and management of patients with chronic pain.

D.3. Technical Approach, Intervention Design and Methods

One hundred patients (N=100) and 20 PCPs will be recruited for this study. All patients will be followed for 6 months. Patient outcomes and provider ratings will be compared between those in the Specialist treatment arm (N=50) and the Generalist treatment arm (N=50). Those providers in the Specialist Centers (N=10) will receive periodic updated information about their patients including electronic assessments using painCAS, monthly reports that consist of assessments of pain, mood, activity level, current medications, side effects, healthcare utilization, including number of clinic and emergency room visits, and hospitalizations, and

results of the Opioid Compliance Checklist. Those patients determined to be high-risk for opioid misuse will be offered evaluations at the Pain Clinic and close monitoring including monthly urine screens as well as individual motivational counseling. All of these interventions have been used previously by us and were found to be successful in managing substance misuse among high-risk chronic pain patients.[8]

Chronic pain patients in the Generalist treatment arm who are considered for or are prescribed opioids for pain will be identified and asked to participate in the study by their primary providers. These patients will receive *standard of care,* which will consist of risk assessment using paper versions of the SOAPP-R, opioid prescribing by the primary care provider and monthly patient monitoring without feedback to the providers or support from pain specialists. The intent of the study for the Generalist condition will be to carefully track those patients who are prescribed opioids for their pain. Additional outcome information will be obtained through chart monitoring. Providers in the Generalist condition (N=10) will **not** have access to the electronic Pain Assessment Program, monthly Summary Reports, or direct assess to a specialty pain center. All Centers will be offered pain treatment guidelines and opioid risk assessment. The centers will be independent of each other and at different locations.

All providers will be compensated $200 for completion of the initial questionnaires and paid $200 for completion of the post-study questionnaires and interview. All patient participants will be given a $50 gift card for completion of the initial questionnaires and a $50 gift card for completion of the post-study questionnaires and interview.

D.3.1 Study sites

D.3.1.1 Specialist Centers. Two proposed sites are being considered for this study. Brigham and Women's Hospital within the Partners Heathcare System has two centers that could be participating in this study: 1) Phyllis Jen Center (PJC) for Primary Care, Francis Street, Boston, and 2) The Brigham Advanced Primary Care Associates, South Huntington in Jamaica Plain (www.partners.org). Both centers are located near each other and share staff and have access to the same electronic medical record (LMR) system. The combined practices include 40 internal medicine physicians. The PCPs provide routine health screening as well as complex diagnostic work-ups and treatment. In the Specialist condition, 50 chronic noncancer pain patients will sign a consent form and may be referred to be seen by at least one of a number of specialists in pain management who will be available to assess patients and review medication strategies for pain management. The study pain nurse practitioner will serve as case manager and will be available to the PCPs to help coordinate services for the patients. Pain specialists located at the BWH Pain Management Center, will offer evaluations and treatment services when indicated and a research assistant will conduct the monthly interviews and collect and enter study data. Attempts will be made to enhance communication between the pain specialists and primary care providers using the Longitudinal Medical Record (LMR) system. An electronic assessment program (painCAS) will be used to assess opioid risk potential that contains electronic versions of the SOAPP-R and COMM, and the results will be posted on the LMR. All patients will be managed using a team approach of primary care providers and pain management specialists. While this model is seen as more costly and less efficient, it has the

potential to greatly improve the management of complicated pain patients and improve the confidence of the PCPs.

D.3.1.2 Generalist Centers. The Manet Community Health Center is a public healthcare system serving the North Quincy, Quincy and Hull Massachusetts areas and located within and around Quincy Medical Center. It is affiliated with the Mass League of Community Health Centers (www.massleague.org). This proposed study will include primary care providers mostly from the Manet Community Health Center on Whitwell Street, Quincy. The faculty will include internal medicine physicians, physician assistants, and nurse practitioners. The facility also has a multidisciplinary staff who are available to assist the providers. If recruitment becomes a problem, we would also consider collaborating with The Cambridge Health Alliance, which is an independent healthcare system serving the Cambridge, Somerville, and Boston areas. Fifty patients with chronic noncancer pain who have either been prescribed opioids or may be candidates for opioids for their pain will be identified and asked to participate in the study. They will sign a consent form and be managed on opioids prescribed by their primary care provider (physician or nurse practitioner). All patients will complete a risk evaluation (paper version of the Screener of Opioid Abuse for Pain Patients, Revised - SOAPP-R), sign an opioid agreement, and will be tracked over the course of 6 months with periodic urine screens and compliance checklists. All physicians and providers will be offered limited pain management education including treatment guidelines in the best ways to manage pain patients on chronic opioid therapy. In the Generalist condition, all patients will be managed by the provider alone. This model is seen as most efficient and cost-contained, but lacks outside support for the providers compared with the Specialist centers.

D.4. Evaluation Design

Three service delivery models will be examined: 1) electronic assessment 2) ongoing patient monitoring, and 3) education and support from pain medicine specialists.

D.4.1. PainCAS. We will investigate the use of an electronic software program called “Pain Assessment Interview Network and Clinical Advisory System” or ***painCAS.*** We are currently partnering with a software development company, Infexxion in Newton, MA, who has received NIH support to develop this program. This software program offers a computerized ‘live’ interview of the patient and can generate a provider report with summarized assessment. It has the potential to present treatment algorithms or care paths and can be integrated with the hospital’s electronic medical record system (LMR). The program offers pain screening, assessment, tracking, and decision support and can identify those patients who are at risk for opioid misuse through the use of electronic versions of the SOAPP-R and the COMM.[14-17] Assessment summary in dash-board like format will be available to the providers with treatment recommendation strategies and summary feedback for the pain patients. PainCAS has been successfully used in a Phase I trial.[18] Funds from this grant will cover the costs of leasing this program and for IT support in running the program.

D.4.2. Summary Reports. We will develop an electronic interdisciplinary patient summary report to assist the PCPs in decision making and in using practice guidelines. Summary information will be obtained by the RA, through regular phone interviews.
Although collected for all patient participants, summary reports will be made available only to those providers in the Specialist clinics. The monthly report will summarize results from the

patient interview on 1) pain intensity, 2) mood, 3) activity interference, 4) medication usage, 5) side effects, 6) hospital and emergency room visits, and 7) results of the Opioid Compliance Checklist. This monthly summary report will be electronically transmitted to the PCPs and communicated to those providers responsible for that patient's care.

D.4.3. Pain Education Seminars. The PCPs and other providers in the Specialist clinics will be offered three didactic seminars on best practice guidelines for the management of chronic pain. The sessions will primarily follow case-based learning using both didactic and interactive discussion formats. Topics will include opioid assessment, opioid prescribing practices, prescription monitoring, interventions for pain, urine toxicology screening, frequent medical comorbidities, psychiatric and psychological assessment and treatment, and substance misuse assessment. The sessions will be repeated for the physicians over the 2-year study period.

D.4.4 Provider Measures

D.4.4.1 Opioid Therapy Provider Survey.[11] This is a 10-item questionnaire created and administered through our center in a preliminary survey of 60 physicians designed to assess practice behavior and confidence related to opioid therapy for the treatment of noncancer pain. Each item consists of a statement and each provider will rate the item on a scale between 1 = strongly agree to 5 = strongly disagree.

D.4.4.2 Concerns About Analgesic Prescriptions.[19] This is a 22-item measure previously developed for primary care physicians in England and adopted for the United States.[19] For each item the physicians will be asked to rate how true each statement is from 0 = never to 5 = always true. The measure includes four subscales derived from factor analyses (1) Adverse Behavioral Effects, (2) Profession Scrutiny, (3) Other Adverse Effects, and (4) Efficacy Beliefs. In previous research, scores from this measure have been found to predict both frequency of prescribing opioids and reluctance to prescribe opioids.

D.4.4.3 Test of Opioid Knowledge (TOK). This is a 15-item multiple choice quiz derived from consensus practice guidelines on good practice of opioid management for persistent pain.[20, 21] It was developed with input from psychologists and anesthesiologists knowledgeable about chronic pain and opioids prescribing. It contains questions about how to manage prescription opioids for patients with chronic pain, and both the physical and behavioral effects of opioids. Each item has a choice of four responses with only one response being correct.

D.4.4.4. Training Evaluation. A five-item training evaluation survey will be administered to the physicians to assess their views of the training seminars. It is based on a widely used treatment credibility measure developed by Borkovec and Nau.[22] The physicians will be asked to rate their interest in the training, how satisfied they were with the quality of training, how logical the training was, how confident they were that the training would help their practice, and how confident they would be in recommending the training to a colleague on an 11-point scale from 0 = not at all to 10 = completely.

D.4.4.5 Physician and Patient Satisfaction Ratings. We will track the effectiveness of chronic pain management within the primary care practice using the following qualitative assessments: 1) physician satisfaction survey and structured interview, 2) patient satisfaction survey and structured interview from a select group of patients (N=10). Pre- and post-study

physician satisfaction ratings and post-study patient interviews will help to determine perceived benefit.

D.4.4.6 Addiction Behaviors Checklist (ABC).[23] This is a 20-item instrument completed by the treating physician at the end of the study designed to track behaviors characteristic of addiction related to prescription opioid medications in chronic pain populations. Items are focused on observable and reported behaviors during and between clinic visits. This checklist was found to have adequate validity and reliability. A cutoff score of 3 or greater showed optimal sensitivity and specificity in determining whether a patient is displaying inappropriate opioid use. An additional question, not used in the scoring, asks whether there is suspicion of pseudoaddiction.

D.4.4.7 Chart review. Pre- and post-study chart reviews will be conducted to determine the rates of use of: 1) pain assessment tools, 2) standardized opioid treatment agreements, 3) opioid misuse and abuse risk screening tools, and 4) urine drug screens. We will also document evidence of compliance and potential changes in healthcare utilization, including ED visits and hospitalizations. As part of this proposed study, we will also determine whether the study intervention will reduce unscheduled clinic visits. This information will be obtained through a thorough chart review of clinic notes and patient data on the electronic medical record system.

D.4.5 Patient Measures

The following measures will be administered to all the patients who participate in this study at baseline and at 6-month follow-up.

D.4.5.1 Demographic Questionnaire.[24] This baseline questionnaire will collect basic demographic information about patients, including: 1) age, 2) gender, 3) racial background, 4) education level, 5) marital status, 6) history of medical problems, 7) history of substance abuse (including treatment experience, activity in AA/NA, etc.), 8) history of psychiatric treatment and trauma, and 9) active litigation and disability or worker's compensation payments.

D.4.5.2 The Brief Pain Inventory (BPI*).*[25] This self-report questionnaire, formerly the Wisconsin Brief Pain Questionnaire,[26] is a well-known measure of clinical pain and has shown sufficient reliability and validity. The questionnaire provides information about pain history, intensity, and location as well as the degree to which the pain interferes with daily activities, mood, and enjoyment of life. Scales (rated from 1 to 10) indicate the intensity of pain in general, at its worst, at its least, and pain "right now." A figure representing the body is provided for the patient to shade the area corresponding to his or her pain. Test-retest reliability for the BPI reveals correlations of .93 for worst pain, .78 for usual pain, and .59 for pain now. Research suggests the BPI has adequate validity. BPI scores correspond with clinical judgments of pain as reflected in pain medication use and the amount of patient-reported activity interference.

D.4.5.3 Pain Catastrophizing Scale (PCS).[27] The PCS is a 13-item instrument that examines three components of catasrophizing: Rumination, Magnification, and Helplessness. The PCS is found to predict levels of pain and distress among clinical patients and scores have been related to thought intrusions.[28] It has good psychometric properties with adequate reliability and validity[27] and is associated with levels of pain, depression and anxiety.

D.4.5.4 The Pain Disability Index (PDI).[29] This inventory consists of seven questions designed to measure the degree to which patients believe that their pain interferes with their

functioning in family/home responsibilities, recreation, social activities, occupation, sexual behavior, self-care, and life-support (eating and sleeping) activity. Patients respond to each item on 0- to 10-point scales anchored with descriptors ranging from "no disability" to "total disability." This measure has adequate internal consistency (Cronbach alpha = .86) and test-retest reliability (0.91) and is a valid measure of disability.[30]

D.4.5.5 The Hospital Anxiety and Depression Scale (HADS).[31] The HADS is a 14-item scale designed to assess the presence and severity of anxious and depressive symptoms. Seven items assess anxiety, and seven items measure depression, each coded from 0 to 3. The HADS has been used extensively in clinics and has adequate reliability (Cronbach's Alpha = .83) and validity, with optimal balance between sensitivity and specificity.[32] It has been translated into many languages and is widely used around the world in clinical and research settings.

D.4.5.6 Screener and Opioid Assessment for Pain Patients-Revised (SOAPP-R)[33]. The SOAPP-R is a 24-item, cross-validated, self-administered screening instrument revised from the original SOAPP v.1.[34] used to help determine risk potential for aberrant drug-related behavior. Items are rated from 0=never to 4=very often, and their sum is the total SOAPP-R score. The SOAPP-R has been shown to have good predictive validity, with an area under the curve ratio of 0.88 (95% confidence interval [CI], .81-.95). Test-retest reliability was .71 with a coefficient alpha of 0.74. A cutoff score of 18 shows adequate sensitivity (.86) and specificity (.73). A combined factor analysis of the SOAPP v.1 revealed five factors: 1) history of substance abuse, 2) legal problems, 3) craving medication, 4) heavy smoking, and 5) mood swings. Support has been found for the internal reliability and predictive validity of the SOAPP-R. An accumulated score of 18 or higher is considered positive. The cross validation study of 302 patients from 5 centers revealed a mean score on the SOAPP-R of 20.5 (SD=10.7; range 1-62).[17] The SOAPP-R will be used as part of the initial evaluation.

D.4.5.7. Current Medication Misuse Measure (COMM).[35] This 17-item self-reported questionnaire helps to track current aberrant medication-related behaviors during opioid treatment. All items are rated from 0=never to 4=very often, with a total maximum score of 68. Construct validity has been shown to be adequate, with positive correlates with urine toxicology results ($p<0.05$). Test-retest reliability was .86 with a 95% CI ranging from .77 to .92. The overall accuracy of the COMM for predicting current aberrant drug-related behavior, as measured by the area under the curve ratio, was .81 (95% CI, .74-.86; $p < .001$) and coefficient α (.86) for the 17 items suggests adequate reliability. A cutoff score of 8 yielded a sensitivity of 0.75 and specificity of 0.65. An accumulated cutoff score of 9 or higher is considered positive. The COMM will be administered as a follow-up measure.

D.4.5.8 Compliance Checklist.[36] Participants will complete a compliance checklist every month and this information will be included in the summary report for the Specialist centers. On the checklist the participants answer yes/no questions about their use of opioids that reflect items on the opioid agreement to: 1) take the opioid medication as prescribed, 2) use only one pharmacy, 3) receive opioid prescriptions from only one provider, 4) take precaution not to lose or misplace their pain medication, 5) not run out early, 6) keep all scheduled medical appointments, 7) not "borrow" opioid medication from others, and 8) avoid use of any illegal or unauthorized substances. Any responses which suggest noncompliance will be documented.

D.4.5.9 Treatment Helpfulness Questionnaire (THQ).[37] This 8-item rating scale was adapted from the original THQ and will be completed by the patients at the end of the study. The items

reflecting different aspects of treatment will be rated from 0 = extremely harmful to 10 = extremely helpful. It has been shown to have good test-retest reliability and validity and to assesses how helpful specific and overall treatments for pain have been from the various centers.[38]

D.4.5.10 Prescription Drug Use Questionnaire (PDUQ).[39] This 42-item self-report measure of opioid misuse will be administered at the end of study and is probably the most well-developed abuse-misuse assessment for pain patients. The PDUQ is a 20-minute interview during which the patient is asked about his or her pain condition, opioid use patterns, social and family factors, family history of pain and substance abuse, and psychiatric history. In an initial test of the psychometric properties of the PDUQ, the standardized Cronbach's alpha was 0.79, suggesting acceptable internal consistency. Compton and her colleagues suggested that subjects who scored below 11 did not meet criteria for a substance use disorder, while those with a score of 11 or higher showed signs of a substance use disorder.

D.4.6 Drug Misuse Index (DMI)

At posttreatment, patients will be categorized on the Drug Misuse Index, which relates positively to opioid medication misuse. The DMI is based on positive scores on (1) the PDUQ (>11),[39] (2) the ABC (>2),[23] and (3) abnormal urine toxicology results.[40] A positive rating from the urine screens is given to anyone with evidence of having taken an illicit substance (e.g., cocaine) or an additional opioid medication that was not prescribed. All urine screen results will be confirmed based on chart review of prescription history and a comparison between self-report at the time of the urine screen and the toxicology report. At post-treatment, those with positive scores on any of the three measures are given a positive DMI. Those with negative scores on all three scales (minimal risks or indicators of misuse) are given a negative DMI. This will allow for triangulation of data to identify those patients who admit to risk factors of medication misuse, and those who may underreport risk factors (e.g., low PDUQ scores, but still present with a drug misuse profile, including positive ABC and/or abnormal urine screen result). In using this scoring plan for the DMI in our previous studies (previously called Aberrant Drug-related Behavior Index, or ADBI), we found that 32% met criteria for aberrant drug-related behavior based on the results of self-report behavior (PDUQ), physician ratings (ABC), and abnormal urine toxicology results. Forty-three percent of the patients followed for over 6 months in our original study[40] showed aberrant drug-related behavior.

D.5 Inclusion/Exclusion Criteria

Patients with a diagnosis of chronic noncancer pain will be recruited to participate in this 6-month trial. Patients will be included if they (1) have chronic pain for > 6 months' duration, (2) average 4 or greater on a pain intensity scale of 0 to 10, (3) are able to speak and understand English, (4) have been prescribed or will be eligible to be prescribed opioid therapy for pain, and (5) are under the care of a primary care physician.

Patients were excluded from participation if they meet any of the following criteria: (1) current diagnosis of cancer or any other malignant disease, (2) acute osteomyelitis or acute bone disease, (3) present or past DSM-IV diagnosis of schizophrenia, delusional disorder, psychotic disorder, or dissociative disorder that would be judged to interfere with study participation, (4) pregnancy, (5) any clinically unstable systemic illness judged to interfere with

treatment, (6) a pain condition requiring urgent surgery, and (7) an active addiction disorder, such as cocaine or IV heroin use, (positive on the Mini International Neuropsychiatric Interview; M.I.N.I. v.5.0)[41] that would interfere with study participation.

D.6 Statistical Analyses

The primary endpoints for this study would be overall ratings on the Opioid Therapy Provider Survey and the differences among centers on the patient Drug Misuse Index. We also will include secondary measures in order to gain some understanding of the factors that might have the greatest effect on improving provider confidence and patient compliance. Total scores and average values will be calculated for the baseline measures, the pre- and post-study questionnaires (BPI, PCS, PDI, and HADS) and Pearson Product Moment correlations will be run between the variables. A Wilcoxon two-sample test will be used to compare results from the two types of treatment centers (Specialist and Generalist) for continuous variables. For categorical variables, chi-square or Fisher exact tests will be used to compare groups. Preliminary stepwise discriminant function analyses will be conducted with those explanatory variables that showed differences between groups in order to identify those items that were best in classifying participants in the experimental and control centers.

We anticipate that the monitoring program and patient support will contribute to higher opioid compliance, particularly among the subjects in the Specialist centers. We also expect to identify behavioral indicators of opioid misuse through the outcome measure of the Drug Misuse Index (DMI). In a recent randomized trial of substance misuse treatment for chronic pain patients on opioid therapy,[8] we found that 73.7% of high-risk control patients met criteria for aberrant drug behavior (positive DMI) using the triangulation data of self-report, physician ratings, and urine toxicology results. As a preliminary study, this proposed clinical research is powered based on the expected post-treatment outcomes of the trial after 6 months of tracking in the clinic. We predict that physicians in the Specialist clinics will demonstrate a difference in overall rated confidence in prescribing opioids (Opioid Therapy Provider Survey, 1=strongly agree; 5=strongly disagree) from 2.3 (SD=0.5) in the Specialist treatment arm to 3.0 (SD=0.5) in the Generalist treatment arm, and patients in the Specialist clinics will demonstrate 30% lower DMI percentage compared with the Generalist clinics (60% vs. 30%).

Based on these assumptions, with 50 patients per center (100 total) at a significance level of 0.05, we believe that there is adequate power (86.6% and 83.8% respectively) to detect the difference between the Specialist and Generalist treatment groups. Standard deviations used for power calculations were obtained based on our previous opioid compliance study. Power calculations were completed using proc glmpower in SAS Version 9.2 (SAS Institute, Inc., Cary, NC). We assume an attrition rate of 15%, so 58 total patients will need to be recruited in each treatment arm to obtain the intended goal of 50 in each group.

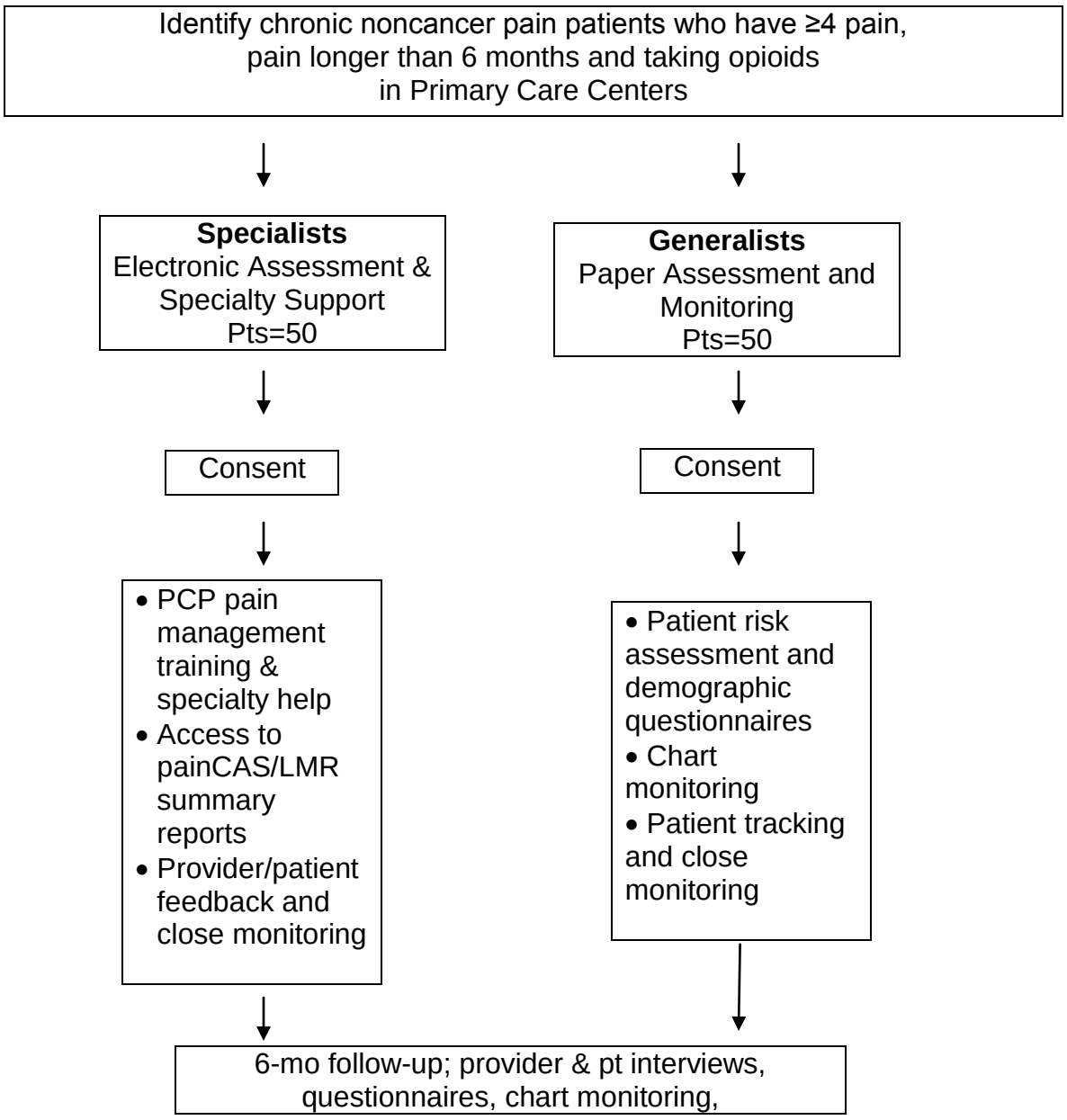
E. Detailed Work Plan and Deliverables Schedule

This is a proposed 2-year controlled trial designed to determine the benefit of interventions to improve opioid prescribing practices among PCPs. This study will aim to assess how improved care coordination, electronic monitoring, and provider education will advance the quality of care of patients with chronic pain within primary care. We fully intend to present the results of this study at scientific meetings (APS, AAPM, etc.) and to submit the study results for publication. We also believe that the results of this study will supply sufficient preliminary data to help support an application for a controlled, multi-centered, NIH-funded clinical trial (e.g., RO1) to investigate interventions to improve opioid practice guidelines and reduce chronic pain patient healthcare utilization within primary care.

Below is the study timeline that outlines the work plan.

Months of Study	0	3	6	9	12	15	18	21	24	End of study
Develop measures and Software										
Recruit providers/subjects										
Baseline measures										
Pain management training										
Clinic-based assessment										
Post-study measures										
Data Analyses										

STUDY SCHEMA



Outcomes:
1. Provider pain treatment confidence ratings
2. Patient treatment satisfaction
3. Opioid protocol compliance
4. Healthcare utilization

References

1. American Academy of Pain Medicine, The American Pain Society, The American Society of Addiction Medicine. Definitions related to the use of opioids for the treatment of pain: a consensus document from the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine. American Society of Addiction Medicine. Chevy Chase, MD; 2001.
2. Ballantyne JC, LaForge KS. Opioid dependence and addiction during opioid treatment of chronic pain. Pain 2007;129:235-55.
3. Fleming MF, Balousek SL, Klessig CL, Mundt MP, Brown DD. Substance use disorders in a primary care sample receiving daily opioid therapy. J Pain 2007;8:573-82.
4. Turk DC, Swanson KS, Gatchel RJ. Predicting opioid misuse by chronic pain patients: a systematic review and literature synthesis. Clin J Pain 2008;24:497-508.
5. Olsen Y, Daumit GL, Ford DE. Opioid prescriptions by U.S. primary care physicians from 1992 to 2001. J Pain 2006;7:225-35.
6. Substance Abuse and Mental Health Services Administration. Results from the 2009 National Survey on Drug Use and Health: Volume I. Summary of National Findings (Office of Applied Studies, NSDUH Series H-38A, HHS Publication No. SMA 10-4586 Findings). Rockville, MD, 2010.
7. Gilson AM, Ryan KM, Joranson DE, Dahl JL. A reassessment of trends in the medical use and abuse of opioid analgesics and implications for diversion control: 1997-2002. J Pain Symptom Manage 2004;28(2):176-88.
8. Jamison RN, Ross EL, Michna E, Chen LQ, Holcomb C, Wasan AD. Substance misuse treatment for high-risk chronic pain patients on opioid therapy: a randomized trial. Pain 2010;150:390-400.
9. Jamison RN, Raymond SA, Slawsby EA, Nedeljkovic SS, Katz NP. Opioid therapy for chronic noncancer back pain: a randomized prospective study. Spine 1998;23(23):2591-600.
10. Michna E, Ross EL, Hynes WL, Nedeljkovic, SS, Soumekh, S, Janfaza D, Palombi D, Jamison, RN. Predicting aberrant drug behavior in patients treated for chronic pain: importance of abuse history. J Pain Symptom Manage 2004;28(3):250-8.
11. Matthews ML, Jamison RN, Ross EL, Scanlan EM, Tishler LW. An interdisciplinary approach to reducing opioid analgesic misuse inpatients with chronic noncancer pain in the primary care setting. Presented at the American College of Clinical Pharmacy Annual Meeting. Pittsburgh, PA; November, 2011.
12. Webster LR, St. Marie B, McCarberg B. Current status and evolving role of abuse-deterrent opioids in managing patients with chronic pain. J Opioid Manage 2011;7:235-45.
13. Wasan AD, Ross EL, Michna E, Chibnik L, Greenfield S, Weiss R, Jamison RN. Characterizing craving of prescription opioids in patients with chronic pain: a longitudinal outcomes trial. J Pain 2012;13:146-54.
14. Butler SF, Budman SH, Fernandez K, Jamison RN. Validation of a screener and opioid assessment measure for patients with chronic pain. Pain 2004;112(1-2):65-75.

15. Butler SF, Budman SH, Fernandez KC, Houle B, Benoit C, Katz, N, Jamison RN. Development and validation of the Current Opioid Misuse Measure. Pain 2007;130(1-2):144-56.
16. Butler SF, Fernandez K, Benoit C, Budman SH, Jamison RN. Validation of the revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R). J Pain 2008;9(4):360-72.
17. Butler SF, Budman SH, Fernandez K C, Fanciullo GJ, Jamison RN. Cross-validation of a screener to predict opioid misuse in chronic pain patients (SOAPP-R). J Addict Med 2009;3:66-73.
18. Zacharoff K, Butler S, Jamison RN, Budman S, Charity S, Yiu E. Development of the pain assessment interview network – clinical advisory system (painCAS), a systematic computer-administered assessment of chronic pain patients. Presented at the Annual Scientific Meeting of the American Pain Society. Baltimore, MD; 2010.
19. McCracken LM, Velleman SC, Eccleston C. Patterns of prescription and concern about opioid analgesics for chronic non-malignant pain in general practice. Prim Health Care Res Develop 2008;9:146-56.
20. Chou R, Fanciullo GJ, Fine P, et al. Clinical Guidelines for the Use of Chronic Opioid Therapy in Noncancer Pain. J Pain 2009 2009;10:113-30.
21. The British Pain Society. Opioids for persistent pain: good practice. January, 2010, http://www.britishpainsociety.org/book_opioid_maon.pdf. Accessed on October 30, 2012.
22. Borkovec TD, Nau SD. Credibility of analog therapy rationales. J Behav Ther Exper Psychia 1972;3:257-60.
23. Wu SM, Compton P, Bolus R. The Addiction Behaviors Checklist: validation of a new clinician-based measure of inappropriate opioid use in chronic pain. J Pain Sym Manage 2006;32:342-52.
24. Jamison RN. Mastering Chronic Pain: A Professional's Guide To Behavioral Treatment. Sarasota, FL: Professional Resource Press; 1996.
25. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singapore 1994;23:129-38.
26. Daut RL, Cleeland CS, Flanery RC. Development of the Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases. Pain 1983;17:197-210.
27. Sullivan MJ, Pivik J. The Pain Catastrophizing Scale: development and validation. Psychol Assessment 1995;7(4):524-32.
28. Sullivan MJ, Stanish W, Waite H, Sullivan M, Tripp DA. Catastrophizing, pain, and disability in patients with soft-tissue injuries. Pain 1998;77:253-60.
29. Tait RC, Pollard CA, Margolis RB, Duckro PN, Krause SJ. The Pain Disability Index: psychometric and validity data. Arch Phys Med Rehab 1987;68:138-441.
30. Turk DC, Melzack R, eds. Handbook of Pain Assessment. 2nd ed. New York: The Guilford Press; 2001.
31. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatrica Scandinavica 1983;37:361-70.
32. Bjelland I, Dahl AA, Huag TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: an updated literature review. J Psychosom Res 2002;52(2):69-77.

33. Butler SF, Fernandez K, Benoit C, Budman SH, Jamison RN. Validation of the Revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R). J Pain 2008;9:360-372.
34. Butler SF, Budman SH, Fernandez K, Jamison RN. Validation of a Screener and Opioid Assessment Measure for Patients with Chronic Pain. Pain 2004;112:65-75.
35. Butler SF, Jamison RN, Fernandez KC, Benoit C, Villapiano A. Validation of the Current Opioid Misuse Measure (COMM) for chronic pain patients. Presented at the Annual Scientific Meeting of the American Pain Society May 5, 2006.
36. Ross EL, Holcomb C, Jamison RN. Opioid misuse among chronic pain patients: risk assessment issues. J Musculo Med 2008;25:268-77.
37. Chapman SL, Jamison RN, Sanders SH. Treatment Helpfulness Questionnaire: a measure of patient satisfaction with treatment modalities provided in chronic pain management programs. Pain 1996;68(2-3):349-61.
38. Chapman SL, Jamison RN, Sanders SH, Lyman DR, Lynch NT. Perceived treatment helpfulness and cost in chronic pain rehabilitation. Clin J Pain 2000;16(2):169-77.
39. Compton P, Darakjian J, Miotto K. Screening for addiction in patients with chronic pain and "problematic" substance use: evaluations of a pilot assessment tool. J Pain Symptom Manage 1998;16(6):355-63.
40. Michna E, Jamison RN, Pham LD, Ross EL, Janfaza D, Nedeljkovic SS, Narang S, Palombi D, Wasan AD. Urine toxicology screening among chronic pain patients on opioid therapy: frequency and predictability of abnormal findings. Clin J Pain 2007;23(2):173-9.
41. Sheehan D. The MINI International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59:S22-33.