STUDY PROTOCOL

Guiding aging long-term opioid therapy users into safer use patterns

PI: Jason Doctor, PhD

Supported by:

The National Institute on Aging

Supplement to Roybal Center for Behavioral Interventions in Aging

Grant #: P30AG024968

Version date: 11/4/2025

TABLE OF CONTENTS

STUDY TEAM ROSTER

Jason N. Doctor, Ph.D. (Principal Investigator), Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, 635 Downey Way, Los Angeles, CA 90089, Office: 213.821.8142, jdoctor@usc.edu

Mark Sullivan, M.D., Ph.D. (Co- Investigator) University of Washington, Department of Psychiatry & Behavioral Sciences, 1959 NE Pacific Street, Box 356560, Room BB1644, Seattle, WA 98195-6560
sullimar@uw.edu

Daniella Meeker, Ph.D (Co-Investigator), University of Southern California, 2250 Alcazar Street Health Sciences Campus Los Angeles 90033, dmeeker@usc.edu

Stephen D. Persell, MD, MPH, .(Co-Investigator), Division of General Internal Medicine and Geriatrics, Institute for Healthcare Studies, Feinberg School of Medicine, Northwestern University, 750 N. Lake Shore Drive, 10th Floor, Chicago, IL 60611, spersell@nmff.org

Jeffrey A. Linder, MD, MPH, FACP (Co-Investigator), Division of General Internal Medicine and Geriatrics, Institute for Healthcare Studies, Feinberg School of Medicine, Northwestern University, 750 N. Lake Shore Drive, 10th Floor, Chicago, IL 60611, jlinder@partners.org

Tara K. Knight, Ph.D. (Project Manager) Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, 635 Downey Way, Los Angeles, CA 90089, Office: 213.821.7943, knight@usc.edu

PARTICIPATING STUDY SITES

University of Southern California. USC, led by Dr Jason Doctor, is prime awardee institution. Dr. Doctor will serve as the Principal Investigator and be responsible for overall design, implementation and project deliverables. USC will receive and manage HIPAA compliant limited data sets with outcome and covariate data for analysis from the clinical site, Northwestern. Dr. Doctor will lead regular project meetings with the entire study team via teleconferencing and at in person meetings and will prepare scientific publications and presentations along with the other members of the study team.

Northwestern University. Division of General Internal Medicine and Geriatrics, Institute for Healthcare Studies, Feinberg School of Medicine, Northwestern University, 750 N. Lake Shore Drive, 10th Floor, Chicago, IL 60611. Northwestern Medicine, led by Site PI Jeffrey Linder, M.D., M.P.H., FACP and Co-I Stephen D. Persell, M.D., M.P.H., will be the clinical site for Randomized Controlled Trial implementation. Drs. Linder and Persell will work with the overall study investigators to conduct the specific aims of this study. Dr. Linder and Dr. Persell will ensure the NU Analyst is able to extract necessary data from the electronic health record for analytic purposes. Throughout the project, Dr. Linder and the others will work with the overall project team to disseminate the results of such development, implementation, and evaluation. They will participate in regular project meetings with the entire study team via teleconferencing and at in person meetings and will prepare scientific publications and presentations along with the other members of the study team.

University of Washington: Dr. Mark Sullivan is Co-Investigator and subcontract PI for University of Washington. In his role on this project, he will assist in study design, provide expertise in the implementation of PainTracker, and the analysis and interpretation of outcome data. He will participate in regular project meetings with the entire study team via teleconferencing and at in person meetings and will prepare scientific publications and presentations along with the other members of the study team.

PRÉCIS

Study Title

Guiding aging long-term opioid therapy users into safer use patterns

Objectives

The main objective is to use of point-of-care randomization within the electronic health record to learn if different survey assessments lead to different medical decisions and patient care pathways that will improve the health services received by long-term opioid therapy recipients. We develop strategies for comparison for collecting clinical pain data and for assessing, preventing, and managing pain in later life. Our intent is also to elucidate at the visit, some of the psychosocial factors underlying pain experience and its consequences in aging. We utilize the UW PainTracker, a brief assessment that reframes the patient visit around improving function and identification of correlates of pain intensity to broaden the discussion around patient needs to address chronic pain in an aged population.

Design and Outcomes

Using the electronic health record, patient portal, and patient-reported outcome capabilities, we will develop programming logic for a randomized experimentation platform wherein two (or more) versions of pain surveys may be delivered to patients. In a randomized controlled trial, we will use this system to evaluate Current Opioid Misuse Measure (COMM) + PainTracker[15] delivered randomly to half of persons over 65 years of age on long-term opioid therapy within patient registries at Northwestern University's health system with at least one primary care encounter in the past 12 months. The other half of patients receive standard clinical practice at Northwestern which involves assessment with COMM only which focuses on identifying opioid misuse and abuse, but not broader problems associated with chronic pain.

Interventions and Duration. The intervention period will be 9-months in length for all participants. The following intervention arms will be compared:

Condition 1 (Current Opioid Misuse Measure) - On a monthly basis, as part of standard clinical practice, patients will receive the Current Opioid Misuse Measure, a 17-item self-report screener to identify and monitor the risk of aberrant opioid-related behavior in chronic pain patients on opioid therapy. The COMM asks patients to report their behaviors over the past 30 days using a five-point Likert-type rating scale. Multiple studies have shown that the COMM can accurately identify patients who are engaging in aberrant opioid-related behavior (defined as medication misuse, abuse, addiction, diversion, and opioid-seeking behaviors) with approximately 80% accuracy.

Much of its classification accuracy is because many of the items, while predictive of opioid misuse, do not appear to patients to be asking about opioid misuse.

Condition 2 (Current Opioid Misuse Measure+ PainTracker) - On a monthly basis, patients will receive both the Current Opioid Misuse Measure (described above) and PainTracker. The latter tracks multiple outcomes relevant to the treatment of chronic pain: pain severity, general activity interference, enjoyment of life interference, sleep (initiating and maintaining), depression, and anxiety. New and returning patients are asked to complete the PainTracker assessment at least one week prior to their appointment.

Outcome Measures: We will assess the primary outcome in the electronic health record: referral rate to non-opioid related care, which includes mental health, physical therapy and sleep medicine referrals. We will also measure the rate of new starts on antidepressants. Secondary outcomes include: 1) clinician aggregate monthly milligram (mg) morphine equivalent (ME) and 2) benzodiazepine prescribing.

1. STUDY OBJECTIVES

1.1 Primary Objectives

The primary objective is to assess the comparative effectiveness of PainTracker in a randomized controlled trial at Northwestern Medicine in the United States.

2. BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

Over the last two decades, prescription opioids have grown to become a public health crisis. Today, on average 1 in 5 persons with chronic noncancer pain receive an opioid prescription in the U.S.[1] Yet, despite this record level of prescribing, reports of pain in America have not gone down.[2,3] The greater availability of prescription opioids has been accompanied by an alarming rise in the negative consequences related to their use. In 2015, there were over 365,000 emergency department visits for misuse and 20,101 prescription overdose deaths, more than have ever been recorded in U.S. history.[4,5] The costs of prescription opioids are staggering. Aggregate costs for prescription opioid harm are estimated at over $78.5 billion (in 2013 dollars). One-fourth of the aggregate economic burden is publicly funded (i.e., Medicaid, Medicare, and veterans' programs).[6,7]

While there have been reductions in opioid prescribing, persons 65 years of age and older who take these medications continue to face particular risks. First, these persons are more likely to have started on long-term opioid therapy in the early 2000s for non-progressive musculoskeletal pain conditions and continue on opioids to this day. These are “legacy patients” with chronic pain who progressively escalated to high opioid doses, often over many years. Now as they age, they face additional and very serious risks resulting from continued use. Age-related changes in drug metabolism, multi-morbidity, and polypharmacy place them at risk of falls and death due to respiratory suppression.

The dominant approach to these risks is to screen for aberrant patient opioid behaviors so that clinicians can pre-empt misuse early through review of contractual opioid agreements or by lowering patient dosages.[8–11] This approach fails the patient in several ways. First, it frames the clinician's judgment task solely as one of determining if the patient is likely a misuser without examining the reasons for misuse. In older patients, control of physical pain is the most common reason for opioid misuse.[12] Labeling patients as misusers can reduce doctor and patient trust, which can hamper future interactions necessary for future care. Second, it ignores situational and

psychological factors associated with high-dose opioid use. By focusing on opioid misuse alone, it encourages forced opioid tapering that has been associated with opioid overdose and mental health crisis.[13] Many persons have mental health, trauma-related or polysubstance use disorders that need to be addressed. Directing clinician attention to these comorbid conditions associated with opioid misuse may promote safer and more effective care.

Making these situational and psychological factors more salient may reframe the problem for the physician and patient in a number of productive ways. First, psychological studies of similarity find that an increase in the measure of common features increases the perception of similarity and decreases the perception of difference.[14] The more features of misuse that the survey assessment requires, the greater the perceived similarity the patient has to a referent person who misuses or abuses drugs. Also, an increase in the measure of the distinctive features decreases similarity and increases difference. The more the physician measures the patient's activity limitation, mental health issues, and reactions to traumatic stress, the less likely physicians might be to view the patient as a wrongdoer and more likely to open up new care pathways (e.g. physical therapy, mental health referrals, and sleep medicine) that may improve their condition. In sum, understanding broadly, a patient's pain experience may help address the reasons why these patients use opioids and may prevent problem use. This is superior to simply identifying persons who misuse medication.
For 12 years, our team has redesigned choices in the electronic health record to improve patient care. We recently implemented PainTracker,[15] a patient-reported outcome system that focuses on a broad set of outcomes and causes of pain in a person's life to facilitate better health care. As a supplement to our parent grant (P30AG024968), we follow the explicit directives of NOT-AG-22-005 that task researchers with "Developing…strategies for collection of clinical pain data and for assessing, preventing, and managing pain in later life" (**Aim 1**) and the "elucidation of mechanisms underlying pain experience and its consequences in aging" (**Aim 2**). We will also compare rates of referrals and visits to mental health, physical therapy, and sleep medicine in a randomized trial that assigns older adults using long-term opioids to broader pain assessments.

2.2 **Study Rationale**

Use of point-of-care randomization within the electronic health record to learn if different survey assessments lead to different medical decisions and patient care pathways that will improve the health services received by long-term opioid therapy recipients. We develop strategies for comparison for collecting clinical pain data and for assessing, preventing, and managing pain in later life. Our intent is also to elucidate at the visit, some of the psychosocial factors underlying pain experience and its consequences in aging. We utilize the **UW PainTracker**,[15] a brief assessment that **reframes** the patient visit around improving function and identification of correlates of pain intensity to broaden the discussion around patient needs to address chronic pain in an aged population.[16]

University of Washington (UW) PainTracker is a web-based, patient-reported outcomes tool.[16] It tracks multiple outcomes relevant to the treatment of chronic pain: pain severity, general activity interference, enjoyment of life interference, sleep (initiating and maintaining), depression, and anxiety. PainTracker administers risk stratification tools once, including an Opioid Risk Tool, post-traumatic stress disorder (PTSD-PC), STOP sleep apnea screen, and fibromyalgia screen. New and returning patients are asked to complete the PainTracker assessment at least one week prior to their appointment. Between May and November 2012, PainTracker was deployed in 9 UW Neighborhood Clinics with access through a simple Epic® SmartSet, as part of a quality improvement program to better reduce opioid risk and lower high-dose use. This program included multimodal outcome tracking and encouraged reducing opioid doses below 120mg ME/day dose, documenting a treatment plan, and obtaining at least one urine drug screen per year. By 2014, these 9 clinics achieved a 57% overall reduction in opioid doses above 120 mg ME/day with the use of PainTracker. PainTracker broadens treatment targets and clinical conversations beyond a focus on pain intensity. As an example, we found in a separate sample of patients seeking outpatient pain treatment that were given PainTracker (n=2,824) that the number of post-traumatic disorder symptoms the patient has is positively related to pain intensity, pain interference in life activities and risk of opioid misuse (all $p < 0.001$).

Behavioral insights: We hypothesize that the aspects of the patient's health that are assessed and discussed at the visit affect the type of care received. Evidence for this comes from two sources in the field of psychology: 1) similarity research and 2) linguistic labels. Similarity is an organizing principle for statements and judgments about patients.[23,24] "This patient is like … [*some referent*]" is a type of task ubiquitous in medicine. For high scorers on the Current Opioid Misuse Measure, the measure promotes a response from the treating clinician that "this patient is behaving like a misuser of opioids". Whereas, broader assessments such as Pain Tracker may produce more varied similarity statements, such as "This patient is behaving like a person who has experienced psychological trauma". Further, linguistic labels may play a role in the stability of judgments about persons. Nouns such as "misuser" may have a stronger and more lasting effect on the person's identity than verbs (e.g., "misuses").[25,26]

3. STUDY DESIGN

We will conduct a 9-month randomized trial where persons age 65 or older on long-term opioid therapy (N= 1451 persons within the Northwestern Medicine Chronic Opioid Use registry system with at least one primary care encounter in the past 12 months ending 8/08/2023) receiving care from 286 clinicians will receive either the 1) Current Opioid Misuse Measure alone (Standard clinical practice /Control) or 2) COMM + Pain Tracker (intervention). We will assess the primary outcome in the electronic health record: referral rate to non-opioid related care, which includes mental health, physical therapy and sleep medicine referrals. We will also

measure the rate of new starts on antidepressants. Secondary outcomes include: 1) clinician aggregate monthly milligram (mg) morphine equivalent (ME) and 2) benzodiazepine prescribing.

SELECTION AND ENROLLMENT OF PARTICIPANTS

3.1 Inclusion Criteria

Clinicians. The subjects involved in this trial are clinicians from outpatient clinics at Northwestern Medicine in Chicago, Illinois. Each study clinic is required to have an electronic health record (EHR) system in place and have its own physical building (as opposed to multiple clinics sharing the same space, such as the floor of a hospital, where interactions between providers assigned to different intervention groups would be more likely).

The target group of physicians is fully inclusive and representative. Clinicians will be eligible if they treat patients age 65 or older on long-term opioid therapy within the Northwestern Medicine Chronic Opioid Use registry system with at least one primary care encounter in the past 12 months ending 8/08/2023. We will request a waiver of consent for physician participation.

Patients. Patients will be eligible if they are ages 65 or older on long-term opioid therapy within the Northwestern Medicine Chronic Opioid Use registry system with at least one primary care encounter in the past 12 months ending 8/09/2022-8/08/2023. We will request a waiver of consent for patient participation.

3.2 Exclusion Criteria

Clinicians. There are no exclusion criteria for clinicians.

Patients. Visits will be excluded from the primary analysis when they have active cancer. Cancer exclusions (ICD-10 codes) are listed in Appendix A.

3.3 Study Enrollment Procedures

We will seek a waiver of consent for clinician and patient participation. All clinicians treating patients who meet the inclusion criteria in participating practices will be contacted by email to inform them that their patients will be receiving the following assessments: COMM or COMM+PainTracker, depending on clinician study arm assignment.

The COMM is already being delivered as part of standard clinical care. Our study proposes to randomize half of the patients to also receive the PainTracker, which poses no additional risk.

We are requesting a waiver of consent under the Common Rule. The Common Rule (§46.116) specifies that informed consent can be waived when: "(1) The research involves no more than minimal risk to the subjects; (2) The research could not practicably be carried out without the requested waiver or alteration; (3) If the research involves using identifiable private information, the research could not be practicably carried out without the identifiable information; (4) The waiver or alteration will not adversely affect the rights and welfare of the subjects; [and] (5) Whenever appropriate, the subjects will be provided with additional pertinent information after participation."

Withdrawal of subjects: Patients receive COMM as part of their standard of care at Northwestern Medicine. Patients will not be required to respond to the additional PainTracker surveys, and will continue to receive the same standard of care. After the 9 month intervention, PainTracker surveys will no longer be delivered to patients.

STUDY INTERVENTIONS

3.4 Interventions, Administration, and Duration

The intervention period will be 9-months in length for all participants.

3.5 Handling of Study Interventions

The following study arms will be compared:

Condition 1 (COMM) - On a monthly basis, as part of standard clinical care, patients will receive the Current Opioid Misuse Measure, a 17-item self-report screener to identify and monitor the risk of aberrant opioid-related behavior in chronic pain patients on opioid therapy. The COMM asks patients to report their behaviors over the past 30 days using a five-point Likert-type rating scale. Multiple studies have shown that the COMM can accurately identify patients who are engaging in aberrant opioid-related behavior (defined as medication misuse, abuse, addiction, diversion, and opioid-seeking behaviors) with approximately 80% accuracy. Much of its classification accuracy is because many of the items, while predictive of opioid misuse, do not appear to patients to be asking about opioid misuse.

Condition 2 (COMM+PainTracker) - On a monthly basis, patients will receive both the Current Opioid Misuse Measure (described above) and PainTracker. The latter tracks multiple outcomes relevant to the treatment of chronic pain: pain severity, general activity interference, enjoyment of life interference, sleep (initiating and maintaining), depression, and anxiety. New and returning patients are asked to complete the PainTracker assessment at least one week prior to their appointment.

COMM and PainTracker surveys will be delivered through the patient portal and survey responses will be recorded in the patient electronic health record, and will be visible to the patient's doctor at the time of their next visit. USC will not receive patient survey data, only completion rates.

3.6 Adherence Assessment

In order to ensure that the study interventions are being reliably delivered we will create testing scripts that cover logical and coding variation in EHR-based interventions. Study staff will conduct assessments regularly during the intervention to ensure that tests do not fail.

4. STUDY PROCEDURES

4.1 Schedule of Evaluations

Assessment	Screening: Baseline	Enrollment, Randomization: (Day 1)	Intervention start (Month 1)	Continuously Measured or monitored	Intervention end: (Month 9)	Follow-up period
Clinician-level Assessments						
Demographics		X				
Inclusion/Exclusion Criteria						
Prescribing: Monthly morphine milligram equivalents	X			X		X
Visit-level assessments						
Demographics		X				
Inclusion/Exclusion Criteria		X				
ICD-10 codes	X	X	X	X	X	X

Ordering Data	X	X	X	X	X	X
Pain Tracker/COMM completion rates			X	X	X	
Referral rates to non opioid care			X	X	X	X
Adverse Events			X	X	X	

4.2 Description of Evaluations

4.2.1 Screening Evaluation

Consenting Procedure

We will seek a waiver of consent and HIPAA authorizations for participating physicians and use of patient data for the trial. This approach expedites the implementation phase, maximizes clinician observations and prevents selection bias associated with clinician enrollment.

4.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

This study involves a randomized trial with 286 clinicians to inform the best approaches to patient assessments for opioid at clinical visits. Long-term opioid recipients complete the Current Opioid Misuse Measure as standard clinical practice. PainTracker will appear as part of these required assessments randomly for half the patients of clinicians randomized to the intervention (COMM+PainTracker). If a waiver is granted, enrollment date (RCT implementation date) will be recorded for each clinic.

Assessments

Baseline: At baseline, we will assess clinician baseline prescribing monthly morphine milligram equivalents (MMEs), ICD-10 codes, and ordering data.

Enrollment and Randomization (Day 1). Demographics, inclusion/exclusion criteria, ICD-10 codes, and ordering data.

Intervention start (Month 1). ICD-10 codes, and ordering data, Pain Tracker/COMM completion rates, Referral rates to non-opioid care, adverse events

Continuously measured or monitored. ICD-10 codes, and ordering data, Pain Tracker/COMM completion rates, Clinician

monthly MMEs, Referral rates to non-opioid care, adverse events

Intervention end (Month 9): ICD-10 codes, and ordering data, Pain Tracker/COMM completion rates, Referral rates to non-opioid care, adverse events

Follow-up (Month 10-12): ICD-10 codes, ordering data, Clinician MMEs, Referral rates to non-opioid care.

Randomization

We will use cluster randomization at the physician level to avoid contamination that might occur if individual providers are randomized to multiple interventions. We will carry out block randomization of physicians with respect to historical referral rate (high vs. low) by using a random permutation of physician lists in the statistical computing language R. Patients of clinicians in the first half of the permuted list will receive the PainTracker survey intervention in addition to COMM. The second half will receive the control condition (COMM standard clinical practice). The same intervention (PainTracker survey) will be implemented throughout the 9 month study period. No intervention will occur during the 3 month follow-up period; it will be for outcomes assessment only.

5. SAFETY ASSESSMENTS

For patients who were noted to have opioid prescriptions abruptly stopped, emergency room visits or hospitalizations with a diagnosis that could represent a serious complication of untreated pain will be extracted from study site EHRs and reported to the Data and Safety Monitoring Board. Relative rate of ED visits between study conditions will also be evaluated.

5.1 Specification of Safety Parameters

Data elements from qualifying visits for providers enrolled in the study will be collected from the electronic health record. Aggregate counts of total visits across sites for which the intervention was implemented, for high dose opioid patients, if abrupt changes to dose (> 20% morphine equivalent daily dose) were made. Such cases will be examined closely to determine if unsafe drops in opioids occurred.

5.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

The Roybal Standing Data and Safety Monitoring Board will be providing oversight for this study, and has determined the cadence of our reporting (6 and 12 months). The data analyst at Northwestern University will pull the required patient data for analysis from the NU electronic health records one month prior to the 6 and12 month report due dates. The PIs and Co-Is will review in our team

meeting before delivering to the Data and Safety Monitoring Board. When necessary, our NU Site PI (Jeffrey Linder) will conduct chart reviews to investigate any safety concerns.

5.3 Adverse Events

Per CDC guideline clarification, adverse events are defined as an abrupt discontinuation of opioids for persons whose most recent prescription exceeds > 49 morphine equivalent daily dose; or as reported to study staff.[1] Emergency department visits will also be evaluated as well as *increases* in prescribing > 20% presumably in response to reports of worsening pain.

5.4 Reporting Procedures

The Principal Investigator will report any unanticipated events to the IRB as well as the Data and Safety Monitoring Board (DSMB) assembled for this study. When notified of an unanticipated event, the DSMB will convene and make a decision as to whether the study should continue. The IRB will also be notified of the DSMB's decision. Please see detailed Data and Safety Monitoring Plan.

5.5 Safety Monitoring

This study will leverage the standing Roybal Data and Safety Monitoring Board (DSMB) established by NIH. Reports of our safety measures will be delivered to our Data and Safety Monitoring Board at 6 and 12 months.

6. INTERVENTION DISCONTINUATION

Following each DSMB report, the board will make recommendations to the IRB as to whether the study should continue or if changes to the protocol are necessary for continuation.

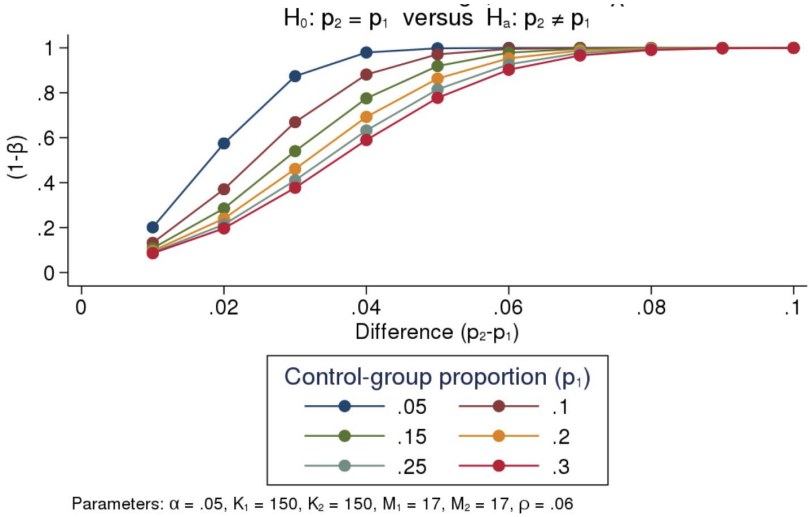
7. STATISTICAL CONSIDERATIONS

7.1 Sample Size and Randomization

Sample Size: We conduct power on the discrete outcome of the referral. The rate of referrals for mental health and pain treatment is low at Northwestern, but if combined with sleep and physical therapy will be at least 5%. There are 300 clinicians who treat patients at the Northwestern outpatient clinics. There are also 5,159 persons over 65 years of age on long-term opioid therapy within patient registries at Northwestern University's health system with at least one primary care encounter in the past 12 months. Assuming 150 clinicians per condition, each treating 17 patients (i.e., 2,500 patients per condition), alpha = 0.05 for a two-sided

test, an intraclass correlation coefficient of 0.06, and an 80% chance of detecting an effect, requires a 3% difference between groups when the baseline referral rate is 5% and 4% difference between groups when the baseline referral rate is 10% (see **Figure 2**).

Figure 2



7.2 Interim analyses and Stopping Rules

No interim analysis will be conducted on primary or secondary outcomes. The DSMB is granted full power to recommend discontinuation of the study to the consolidated IRB if safety concerns are found. The study team will send the board a biannual report providing data on our safety measures. Following each report, the board will make recommendations to the IRB as to whether the study should continue or if changes to the protocol are needed.

7.3 Outcomes

7.3.1 Primary outcome

The primary outcome is the referral rate to non-opioid related care. This includes: mental health, physical therapy and sleep medicine referrals. We will also measure the rate of new starts on antidepressants.

7.3.2 Secondary outcomes

Secondary outcomes include: 1) clinician aggregate monthly milligram (mg) morphine equivalent (ME) and 2) benzodiazepine prescribing. We will estimate the daily milligram morphine equivalent for each clinician by summing the total number of daily morphine equivalents written within a monthly observation period divided by the number of 30 days. For example, suppose a clinician has three qualifying visits over three days in one month and prescribed as follows: Patient #1 is prescribed 200mg ME/day x 30 days, Patient #2 has tapered from 200 mg ME/day to now 100mg ME/day x 30 days and Patient # 3 is on a tapering plan from 60 to 30 mg ME/day and receives 50 mg ME/day x 15 days. The clinician's outcome for that month then equals:

$$[(200 \text{ mg/day x } 30 \text{ days}) + 100 \text{ mg/day x } 30 \text{ days}) + (50 \text{ mg/day x } 15 \text{ days})] \text{ x } [1 \text{ Month}/30 \text{ days}]$$
$$= (300 \text{ mg x } 1 + 100 \text{ mg x } 1 + 50 \text{ mg x } (½)) = 425 \text{ mg MED/[Month]}.$$

Oral buprenorphine will be excluded from the calculations as it relates to opioid use disorder treatment. Morphine equivalent dose will be computed by standard means described elsewhere.[28] Benzodiazepines will be handled similarly to monthly milligram morphine equivalents but with valium morphine equivalents. Qualifying pain visits will be captured by including all ICD-10 pain diagnostic codes and excluding active cancer diagnoses.

7.4 Data Analyses

For inferential analysis, our *primary hypothesis* is that the proportion of non-opioid referrals will be greater among physicians treating patients who receive PainTracker. We evaluate this with a zero-inflated Poisson model to estimate the number of referrals to non-opioid related care which is then divided by the average number of referrals for each group to estimate the proportion. Our *secondary hypothesis* is that milligram morphine equivalent dose will decrease for persons on high doses of opioid therapy receiving PainTracker. We assume a linear mixed-effects hierarchical knotted spline regression model which offers a flexible way to accommodate non-linear trends before and after the introduction of the intervention.[20] This model places a knot at the intervention start date allowing slopes before and during treatment to vary for intervention and control. For our two-group study evaluating this outcome, monthly mean milligram morphine daily dose prescribed for intervention and control, we will place a knot at t*, the start of the intervention, and evaluate for each comparison between groups:

$$Y = \beta_1 + \beta_2\text{Time} + \beta_3(\text{Time} - t^*)_+ + \beta_4\text{Group} + \beta_5\text{Time x Group} + \beta_6(\text{Time} - t^*)_+ \text{ x Group} + \eta + \text{error} \quad [1]$$

where $(z)_+$ is a truncated line function that equals z when z is positive and is equal to zero otherwise, and η is the clinic random effect.

8. DATA COLLECTION AND QUALITY ASSURANCE

8.1 Data Collection Forms

Data will be collected from electronic medical and billing records and completion rates of PainTracker and COMM surveys.

8.2 Data Management

Each of the participating sites will create an extract from their Electronic Medical or Billing Records of the Data Elements. These records will be transferred to the coordinating center as a one time HIPAA compliant limited data set at the end of the study. The CC has created programs and quality control queries for transforming all of the data into a standard model (Observational Medical Outcomes Partnership Common Data Model, version 5.3.1).
The electronic data system, Epic, will have native data capture formats.

Data will be recorded with SSL-protected websites to a data warehouse, and transferred over a secure network protocol. Data will be kept in encrypted files on a secure research computing cloud at USC Schaeffer Center facilities. Study investigators will have access to a list of study ID codes that will be traceable back to actual subject contact identifiers for clinicians. These codes will be kept in locked offices at USC Schaeffer Center facilities. USC and Northwestern University have a fully executed Data Use Agreement in place.

8.3 Quality Assurance

8.3.1 *Training*

Staff will be trained on the permissible values present in Electronic Records, frequency of update, and expected volumes of data.

8.3.2 *Quality Control Committee*

The quality control committee will consist of practicing clinicians from Northwestern Medicine.

8.3.3 *Metrics*

Quality control metrics will be based on reports verifying visits were not for cancer exclusions. All drugs prescribed at these visits will be categorized as “opioid” or “non-opioid”.

8.3.4 *Protocol Deviations*

Our task tracking systems, JIRA and Monday.com will be used to track and document issues. Each issue will include both an assignee and a reviewer.

8.3.5 *Monitoring*

In addition to data quality reviews, we will also review the integrity of the interventions. On an approximately quarterly basis, staff will verify functionality of decision support tools. Additionally, practicing clinicians on our study team will have the ability to monitor electronic medical record interventions in their own health systems.

9. PARTICIPANT RIGHTS

9.1 Institutional Review Board (IRB) Review

The study protocol for clinic sites will be reviewed and approved by the University of Southern California's Institutional Review Board (IRB) as the IRB of record. Northwestern University will rely on the USC IRB through the SMART IRB online reliance system.

9.2 Informed Consent Forms

Not applicable - we will seek a waiver of consent for clinicians and patients in the randomized trial.

9.3 Study Discontinuation

Following each DSMB meeting/report, the board will make recommendations to the IRB as to whether the study should continue or if changes to the protocol are necessary for continuation.

10. PUBLICATION OF RESEARCH FINDINGS

Publication of results from our research will follow the NIH Public Access Policy, which requires that we submit to the National Library of Medicine's PubMed Central an electronic version of final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication.

11. REFERENCES

1. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. JAMA. 2016;315(15):1624. PMCID: PMC6390846 DOI: 10.1001/jama.2016.1464

2. Daubresse M, Chang H-Y, Yu Y, Viswanathan S, Shah ND, Stafford RS, Kruszewski SP, Caleb AlexanderG. Ambulatory Diagnosis and Treatment of Nonmalignant Pain in the United States, 2000–2010. Med Care. 2013;51(10):870–878. DOI: 10.1097/MLR.0b013e3182a95d86

3. Chang H-Y, Daubresse M, Kruszewski SP, Alexander GC. Prevalence and treatment of pain in EDs in the United States, 2000 to 2010. Am J Emerg Med. 2014 May;32(5):421–431. PMID: 24560834 DOI: 10.1016/j.ajem.2014.01.015

4. CDC [Internet]. [cited 2017 Jan 7]. Available from: CDC WONDER

5. Stein BD, Taylor EA, Sheng F, Dick AW, Vaiana M, Sorbero M. Change in Per Capita Opioid Prescriptions Filled at Retail Pharmacies, 2008-2009 to 2017-2018. Ann Intern Med. 2022 Feb;175(2):299–302. PMID: 34958601 PMCID: PMC9175092 (available on 2022-08-01) DOI: 10.7326/M21-3042

6. Krueger, Alan B. 2016. Where have all the workers gone? Paper preapred for "The Elusive 'Great' Recovery: Causes and Implications for Future Business Cycle Dynamics," 60th Annual Economic Conference, Federal Reserve Bank of Boston, Boston, October 14. https://www.bostonfed.org/-/media/Documents/economic/conf/great-recovery-2016/Alan-B-Krueger.pdf

7. Florence CS, Zhou C, Luo F, Xu L. The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013. Med Care. 2016 Oct;54(10):901–906. PMID: 27623005 PMCID: PMC5975355 DOI: 10.1097/MLR.0000000000000625

8. Butler SF, Budman SH, Fernandez KC, Houle B, Benoit C, Katz N, Jamison RN. Current Opioid Misuse Measure [Internet]. PsycTESTS Dataset. 2012. Available from: https://psycnet.apa.org/record/9999-11953-000?doi=1

9. Buckley PF. Identifying prescription opioid use disorder in primary care: Diagnostic characteristics of the Current Opioid Misuse Measure (COMM) [Internet]. Yearbook of Psychiatry and Applied Mental Health. 2012. p. 136–137. Available from: http://dx.doi.org/10.1016/j.ypsy.2011.07.069

10. Meltzer EC, Rybin D, Saitz R, Samet JH, Schwartz SL, Butler SF, Liebschutz JM. Identifying prescription opioid use disorder in primary care: Diagnostic characteristics of the Current Opioid Misuse Measure (COMM) [Internet]. Pain. 2011. p. 397–402. Available from: PMID: 21177035 PMCID: PMC3027065 DOI: 10.1016/j.pain.2010.11.006

11. Butler SF, Budman SH, Fernandez KC, Houle B, Benoit C, Katz N, Jamison RN. Development and validation of the Current Opioid Misuse Measure [Internet]. Pain. 2007. p. 144–156. https://doi.org/10.1016/j.pain.2007.01.014

12. Schepis TS, Wastila L, Ammerman B, McCabe VV, McCabe SE. Prescription Opioid Misuse Motives in US Older Adults. Pain Med. 2020 Oct 1;21(10):2237–2243. PMID: 31816076 PMCID: PMC7593793 doi: 10.1093/pm/pnz304

13. Agnoli A, Xing G, Tancredi DJ, Magnan E, Jerant A, Fenton JJ. Association of Dose Tapering With Overdose or Mental Health Crisis Among Patients Prescribed Long-term Opioids. JAMA. 2021 Aug 3;326(5):411–419. PMCID: PMC8335575 doi: 10.1001/jama.2021.11013

14. Tversky A. Features of Similarity [Internet]. Readings in Cognitive Science. 1988. p. 290–302. Available from: https://doi.org/10.1016/B978-1-4832-1446-7.50025-X

15. Tran C, McReynolds J, Theodore B, Lober W, Sullivan M, Tauben D. (188) PainTracker: development and implementation of a web-based pain assessment and outcomes tracking tool for primary and specialty clinical care. J Pain. 2015;16(4):S23. DOI: https://doi.org/10.1016/j.jpain.2015.01.102

16. Schorn MM, Doorenbos AZ, Gordon D, Read-Williams P. Survey of Primary-Care Providers on Perceived Benefits of and Barriers to PainTracker. J Nurse Pract. 2014 Dec;10(10):781–786. PMID: 25580098 PMCID: PMC4287260 DOI: 10.1016/j.nurpra.2014.08.003

17. Meeker D, Knight TK, Friedberg MW, Linder JA, Goldstein NJ, Fox CR, Rothfeld A, Diaz G, Doctor JN. Nudging guideline-concordant antibiotic prescribing: a randomized clinical trial. JAMA Intern Med. 2014 Mar;174(3):425–431. PMCID: PMC4648560 doi: 10.1001/jamainternmed.2013.14191

18. Persell SD, Friedberg MW, Meeker D, Linder JA, Fox CR, Goldstein NJ, Shah PD, Knight TK, Doctor JN. Use of behavioral economics and social psychology to improve treatment of acute respiratory infections (BEARI): rationale and design of a cluster randomized controlled trial [1RC4AG039115-01]--study protocol and baseline practice and provider characteristics. BMC Infect Dis. 2013 Jun 27;13:290. PMID: 23806017 PMCID: PMC3701464 doi: 10.1186/1471-2334-13-290

19. Linder JA, Doctor JN, Friedberg MW, Reyes Nieva H, Birks C, Meeker D, Fox CR. Time of day and the decision to prescribe antibiotics. JAMA Intern Med. 2014 Dec;174(12):2029–2031. PMID: 25286067 PMCID: PMC4648561 doi: 10.1001/jamainternmed.2014.5225

20. Meeker D, Linder JA, Fox CR, Friedberg MW, Persell SD, Goldstein NJ, Knight TK, Hay JW, Doctor JN. Effect of Behavioral Interventions on Inappropriate Antibiotic Prescribing Among Primary Care Practices: A Randomized Clinical Trial. JAMA. 2016 Feb 9;315(6):562–570. PMID: 26864410 PMCID: PMC6689234 DOI: 10.1001/jama.2016.0275

21. Tannenbaum D, Doctor JN, Persell SD, Friedberg MW, Meeker D, Friesema EM, Goldstein NJ, Linder JA, Fox CR. Nudging physician prescription decisions by partitioning the order set: results of a vignette-based study. J Gen Intern Med. 2015 Mar;30(3):298–304. PMID: 25394536 PMCID: PMC4351289 doi: 10.1007/s11606-014-3051-2

22. Pineros DB, Doctor JN, Friedberg MW, Meeker D, Linder JA. Cognitive reflection and antibiotic prescribing for acute respiratory infections. Fam Pract. 2016;33(3):309–311. PMID: 27006411 PMCID: PMC4931815 doi: 10.1093/fampra/cmw015

23. Sales CMD, Wakker PP. The metric-frequency measure of similarity for ill-structured data sets, with an application to family therapy. Br J Math Stat Psychol. 2009 Nov;62(Pt 3):663–682. PMID: 19195426 DOI: 10.1348/000711008X376070

24. Tversky A. Features of Similarity [Internet]. Readings in Cognitive Science. 1988. p. 290–302. Available from: https://doi.org/10.1016/B978-1-4832-1446-7.50025-X

25. Walton G, Banaji M. Being what you say: The effect of linguistic labels on preferences [Internet]. PsycEXTRA Dataset. 2004. Available from: https://doi.org/10.1521/soco.22.2.193.35463

26. Gelman SA, Heyman GD. Carrot-Eaters and Creature-Believers: The Effects of Lexicalization on Children's Inferences About Social Categories [Internet]. Psychological Science. 1999. p. 489–493. Available from: https://doi.org/10.1111/1467-9280.00194

27. McCaffrey SA, Black RA, Villapiano AJ, Jamison RN, Butler SF. Development of a Brief Version of the Current Opioid Misuse Measure (COMM): The COMM-9 [Internet]. Pain Medicine. 2019. p. 113–118. PMID: 29237039 PMCID: PMC1163279 DOI: 10.1093/pm/pnx311

28. Vieweg WVR, Carlyle Lipps WF, Fernandez A. Opioids and Methadone Equivalents for Clinicians. Prim Care Companion J Clin Psychiatry. 2005;07(03):86–88. PMID: 16027761 doi: 10.4088/pcc.v07n0301

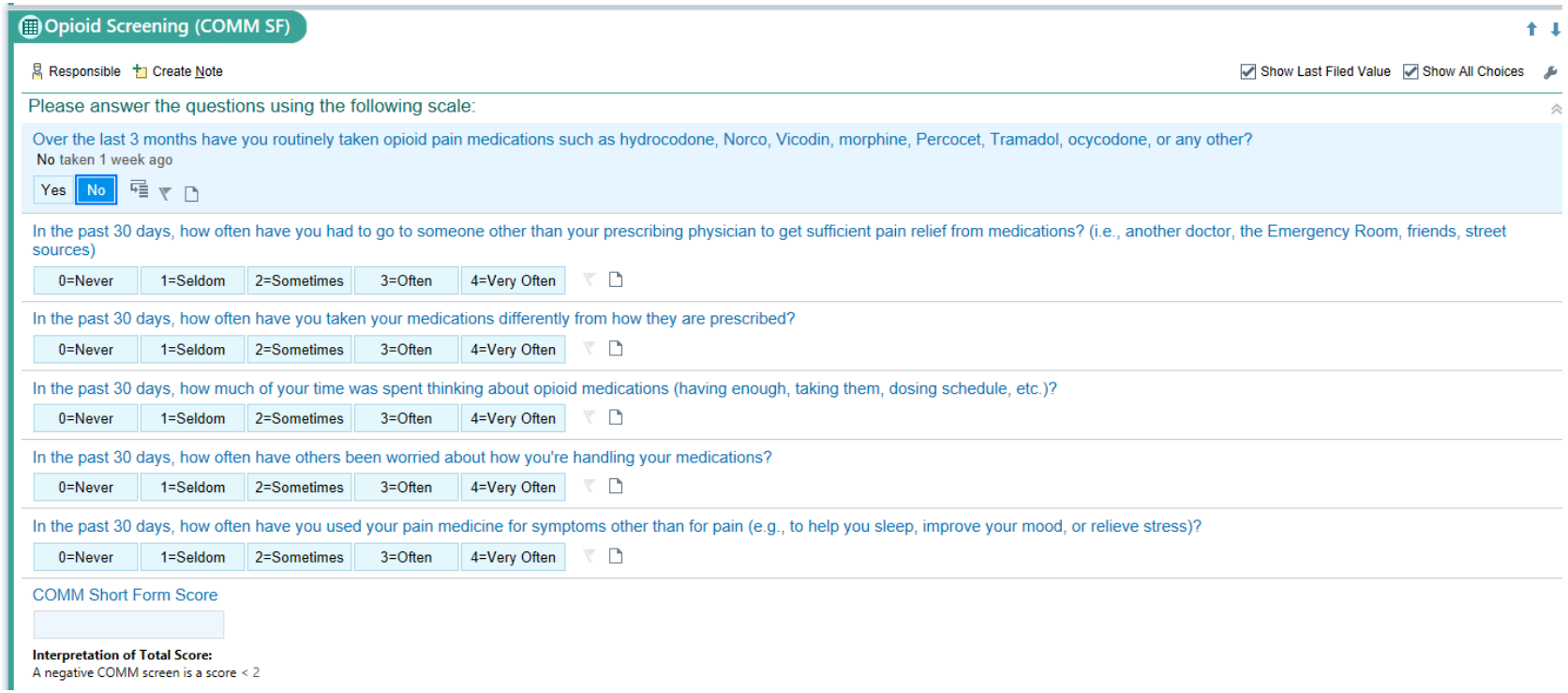
29. Ohno-Machado L, Agha Z, Bell DS, Dahm L, Day ME, Doctor JN, Gabriel D, Kahlon MK, Kim KK, Hogarth M, Matheny ME, Meeker D, Nebeker JR, pSCANNER team. pSCANNER: patient-centered Scalable National Network for Effectiveness Research. J Am Med Inform Assoc. 2014 Jul;21(4):621–626. PMID: 24780722 PMCID: PMC4078293 doi: 10.1136/amiajnl-2014-002751

12. SUPPLEMENTS/APPENDICES

Appendix A.

[Cancer exclusions]

Appendix B



PainTracker™

University of Washington

Below is a list of locations of pain. In the first column, please indicate one or more areas where you have felt pain over the past week. In the second column, please indicate the ONE location of your most severe pain:

LOCATION	**ANY PAIN?** (√ ALL THAT APPLY)	**WORST PAIN?** (√ ONE ONLY)
Head		
Neck		
Chest		
Stomach		
Back		
Arm		
Hand		
Buttocks		
Genital/Urinary		
Leg		
Knee		
Foot		

Please rate your pain by filling in the circle of the one number that best describes your pain on the **average** in the last week?

○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

No Pain — Pain as bad as you can imagine

Fill in the circle of the one number that describes how, during the past week, **pain has interfered** with your:

General activity

○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

Enjoyment of life

○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

Falling asleep

○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

Staying asleep

○ 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10

Does not interfere — Completely interferes

Chronic pain may limit activities that are very important to you (e.g., caring for children, walking, working). We hope your pain treatment will make it easier for you to do these important activities. **Please list one important activity that is difficult for you to perform** so that we can monitor it during your pain treatment.

Activity (describe): _____

How would you rate the **difficulty** you have had **doing this activity** over the past week? Can do with…

○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10
No difficulty										Extreme difficulty

Over the past 2 weeks, have you been bothered by these problems?

	Not at all	Several days	More days than not	Nearly every day
	0	1	2	3
Feeling nervous, anxious, or on edge	○	○	○	○
Not being able to stop or control worrying	○	○	○	○
Feeling down, depressed, or hopeless	○	○	○	○
Little interest or pleasure in doing things	○	○	○	○

Are you having any **side effects** from any of the medications you take for pain? ○ Yes ○ No

If yes, what is the most bothersome side effect? _____

Please circle the number that best shows the **severity of the most bothersome side effect**:

○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10
None										Severe

In the past month, how many "**bad days**" have you had where you **needed to take more pain** medication than your doctor is currently prescribing?

○ None	○ 1 - 2	○ 3 – 5	○ > 5

Please fill in the circle of the one number that best shows how **satisfied** you are with the **results of your pain treatment**:

○ 0	○ 1	○ 2	○ 3	○ 4	○ 5	○ 6	○ 7	○ 8	○ 9	○ 10
Extremely Dissatisfied										Extremely Satisfied

PainTracker™