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## Research Paper

# Efficacy of motivational-interviewing and guided opioid tapering support for patients undergoing orthopedic surgery (MI-Opioid Taper): A prospective, assessor-blind, randomized controlled pilot trial

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## ARTICLE INFO

## Article History:

Received 2 July 2020

Revised 24 September 2020

Accepted 2 October 2020

Available online 16 October 2020

## Keywords:

Persistent postoperative opioid use

Chronic opioid use after surgery

Motivational interviewing

Opioid tapering

Opioid cessation

Opioid tapering support

Orthopedic

Surgery

Total hip arthroplasty

Total knee arthroplasty

Pain cessation

Surgical recovery

Randomized trial

pilot study

## ABSTRACT

**Background:** Postoperative opioid use can lead to chronic use and misuse. Few studies have examined effective approaches to taper postoperative opioid use while maintaining adequate analgesia.

**Methods:** This randomized, assessor-blinded, pilot trial of postoperative motivational interviewing and guided opioid tapering support (MI-Opioid Taper) added to usual care (UC) enrolled patients undergoing total hip or knee arthroplasty at a single U.S. academic medical center. MI-Opioid Taper involved weekly (to seven weeks) and monthly (to one year) phone calls until patient-reported opioid cessation. Opioid tapering involved 25% weekly dose reductions. The primary feasibility outcome was study completion in the group to which participants were randomized. The primary efficacy outcome, time to baseline opioid use, was the first of five consecutive days of return to baseline preoperative dose. Intention-to-treat analysis with Cox proportional hazards regression was adjusted for operation. ClinicalTrials.gov registration: NCT02070003.

**Findings:** From November 26, 2014, to April 27, 2018, 209 patients were screened, and 104 patients were assigned to receive MI-Opioid Taper (49 patients) or UC only (55 patients). Study completion after randomization was similar between groups (96.4%, 53 patients receiving UC, 91.8%, 45 patients receiving MI-Opioid Taper). Patients receiving MI-Opioid Taper had a 62% increase in the rate of return to baseline opioid use after surgery (HR 1.62; 95%CI 1.06–2.46;  $p = 0.03$ ). No trial-related adverse events occurred.

**Interpretation:** In patients undergoing total joint arthroplasty, MI-Opioid Taper is feasible and future research is needed to establish the efficacy of MI-Opioid Taper to promote postoperative opioid cessation.

**Funding:** National Institute on Drug Abuse

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## 1. Introduction

Prescription opioid use has increased worldwide over the past decade [1]. With reports of prescription opioid misuse and an epidemic of opioid overdose deaths, opioid prescribing has fallen under

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## Research in context

### *Evidence before this study*

A meta-analysis examined studies published after 2000 that included a behavioral intervention associated with postsurgical opioid prescribing, with outcomes of discharge opioid prescriptions and postoperative opioid use. Of eight studies identified, only one randomized trial of preoperative opioid counseling, compared to usual care, in patients undergoing carpal tunnel release surgery demonstrated reduced opioid consumption during the first three postoperative days with comparable pain. We did not find any randomized trials of postoperative opioid tapering interventions.

### *Added value of this study*

This is the first randomized pilot trial of a longitudinal postoperative opioid tapering support intervention with patient-reported opioid cessation as an outcome. This trial was designed to test the feasibility of a motivational-interviewing based intervention focused on providing opioid tapering recommendations to promote faster return to preoperative opioid doses and definitive opioid cessation. This is the first trial to examine the effects of an opioid tapering intervention for up to one year after surgery and included patients with pre-existing chronic pain and opioid use.

### *Implications of all the available evidence*

Currently, there are insufficient data delineating methods for opioid tapering and the promotion of opioid cessation after surgery. This trial demonstrates feasibility of delivering MI-Opioid taper, and supports the need for a larger, fully-powered study to establish the efficacy of MI-Opioid taper, delivered by front-line clinicians, to promote opioid cessation.

Motivational interviewing (MI) is a patient-centered interaction that aims to help individuals reflect on and change behaviors by enhancing intrinsic motivation. MI has proven effective for reducing substance use and increasing engagement in substance use disorder treatment. Although MI has been studied in patients with chronic pain, it has not been used to encourage postoperative opioid cessation.

We planned a randomized controlled pilot trial to assess a Motivational Interviewing and guided opioid tapering support (MI-Opioid Taper) intervention designed to promote opioid cessation after orthopedic surgery without increasing postoperative pain duration. The main goals of the study were to establish feasibility in terms of recruitment, follow-up rates, and completion of assessments. The planned pilot study was intended to provide estimates on effect size and variance in opioid cessation rates created by the intervention. The study also aimed to provide an estimation of the potential efficacy of the intervention.

The two primary outcome hypotheses were 1) that MI and guided opioid tapering support (MI-Opioid Taper) added to usual care (UC) would result in a clinically meaningful increase in the rate of opioid cessation compared to UC alone and 2) that elevated depressive symptoms would decrease the efficacy of the intervention. Secondary hypotheses included reduced time to pain resolution and patient-reported surgical recovery with MI-Opioid Taper added to UC.

## 2. Methods

### 2.1. Study design and patients

This prospective, assessor-blinded, randomized controlled pilot study was completed at Stanford Hospital, an academic medical center in the U.S. Patients scheduled for total knee arthroplasty (TKA) or total hip arthroplasty (THA) were considered for inclusion. Inclusion criteria were patients aged 18 years and older; scheduled for TKA or THA; English-speaking; willing to complete longitudinal assessments; and continuing prescription opioid use 14 days after surgery (to target higher risk patients). Exclusion criteria were inability to complete longitudinal assessments (e.g. cognitive ability, mental status, medical status); suicidality as assessed by an answer of 2 or greater on question 9 of the Beck Depression Inventory-II [7]; pregnancy; receiving care from a pain management doctor; and patients using prescription opioids in the 30 days preceding surgery. Due to gradual recruitment, the exclusion criteria for preoperative prescription opioid use was amended mid-study to only exclude patients taking around-the-clock prescription opioids in the 30 days preceding surgery and those taking opioids for non-surgical site pain in the 30 days preceding surgery. Participant enrollment was completed by the study coordinator.

The trial received Human Subjects Research approval from the Stanford Institutional Review Board, and all patients provided written informed consent. The trial was registered in February 2014 on ClinicalTrials.gov (NCT02070003). The study protocol is attached in the supplement.

### 2.2. Randomization and masking

Patients were randomized in blocks of 5, stratified by operation (TKA or THA) to enroll similar numbers in each group. A randomization schedule was created using SAS PROC PLAN, and patients were assigned to intervention or UC sequentially as stated in the schedule. Participants were randomized 14 days after surgery and contacted with new instructions on opioid use after confirmation of continued prescription opioid use for surgical pain. Patients not meeting this additional inclusion were not eligible for randomization. The study coordinator informed patients of the randomization outcome to maintain allocation concealment. Research staff assessing outcomes were masked to group allocation. Separate research staff assessing outcomes did not have access to study coordinator documents, patient clinical notes or treatment allocation.

increased scrutiny. Excessive postoperative opioid prescribing, particularly in the USA and Canada, may initiate persistent or chronic opioid use, and undergoing certain operations such as total joint arthroplasty further increase the risk [2]. With an aging population and an increasing number of operations, the incidence of persistent postoperative opioid use (PPOU) is likely to increase if targeted interventions and risk mitigation strategies are not in place.

Preoperative opioid use is most commonly associated with PPOU [3]. Over 60% of patients presenting for surgery are prescribed opioids already [4]. This is particularly concerning in the context of elective surgery, often performed with the expectation of resulting pain relief and opioid cessation. In addition, higher preoperative doses, longer durations of preoperative opioid use, and depressed mood can incrementally increase risk of chronic use after surgery [5].

Concerns regarding PPOU and its associated consequences have led to numerous efforts to decrease the risks of postoperative opioid prescribing. However, research often excludes patients with chronic pain and those receiving chronic preoperative opioid therapy [6]. Limiting opioid prescribing reduces over-prescribing to patients experiencing typical postoperative pain. However, for those higher-risk patients presenting to surgery with co-morbid pain and chronic opioid use, these restricted opioid prescribing patterns may lead to suboptimal postoperative pain management. As the gap between clinician expectations of minimal opioid use and the realities of post-surgical opioid use among patients at-risk for PPOU widens, clinical pathways and personalized, targeted interventions are urgently needed. Also, extended follow-up is necessary to understand the long-term impact of curbing postoperative opioid consumption on the development of persistent postsurgical pain and surgical recovery.

### 2.3. Procedures

The MI-Opioid Taper intervention was provided via phone calls by a single pain medicine physician (JH). The MI-Opioid Taper intervention involved adaptation of MI principles for enhancing motivation to change in pain treatment by Jensen to postoperative opioid cessation [4]. Key MI tools were tailored from Miller and Rollnick's textbook [5]. Of note, the pain medicine physician solely provided advice regarding opioid medications, and the exchange remained patient-centered. (See Supplement Table 1 for further details). Concepts of individual MI were adapted to this intervention based on prior research [8] and the structures of calls included 1) review of medication adherence prior to the phone call, 2) review of response to medication, 3) advice concerning opioid weaning, 4) support for patient's efforts, 5) education on pain management and drug misuse, and 6) discussion of non-adherence (greater than recommended opioid use according to the opioid tapering protocol) when relevant. Calls for the MI-Opioid Taper intervention were conducted weekly starting two weeks after surgery through week seven, and then monthly up to one year after surgery as-needed. Calls were discontinued as soon as patients reported opioid cessation.

The guided opioid tapering protocol centered on dose reductions of 25% of the total opioid dose every seven days. The physician conducting MI-Opioid Taper calls monitored for adverse effects of tapering including worsening pain and opioid withdrawal. Withdrawal symptoms were monitored through administration of the Short Opiate Withdrawal Scale (SOWS), which included 10 items rated on a 4-point scale, over the phone [9]. A mean score of greater than two prompted recommendations to hold the opioid dose at the current level for seven days. Once patients reached one opioid pill per day, they were instructed to discontinue opioid use after seven days. Similarly, a numeric rating scale (NRS) of pain intensity greater than seven prompted recommendations for an opioid dose increase of 25% for seven days followed by re-assessment [10]. Participants were instructed that they could always use less medication than suggested. With simultaneous report of a mean SOWS score greater than two and an NRS score greater than seven, the physician recommended an opioid dose increase of 25% for seven days with re-assessment.

The study physician received MI training through a combination of online and in-person workshops for skills development as recommended in "Motivational Interviewing Assessment: Supervisory Tools for Enhancing Proficiency" [11]. The physician received individual coaching sessions every six months to ensure MI proficiency and proper application of MI techniques. To assess treatment fidelity, three random sessions were taped with patient consent and reviewed by an independent MI trainer. All tapes were evaluated using global ratings from the MI Treatment Integrity coding system [12] with goal ratings  $\geq 3$  on all global scores.

All participants received standardized verbal and written instructions on the proper analgesic use of opioids before surgery. Those randomized to UC received the same instructions two weeks after surgery: "Following your surgery, you are going to have a certain amount of pain for a short period of time. Your doctor will either prescribe pain medication or instruct you to take over-the-counter pain medication. You should take these pain medications only when you are in pain. You should stop taking the medications when you no longer have pain. If you do not require the entire amount of medication prescribed, you should dispose of the remainder. It is alright for you not to finish all the medication you are given."

### 2.4. Assessments

Prior to surgery, participants completed an online questionnaire assessing pain and opioid use with a modified Brief Pain Inventory (BPI) [13]. Subjects completed the BPI twice, first referencing pain at the upcoming surgical site and second referencing pain elsewhere. In

**Table 1**

Demographic and preoperative characteristics of patients according to treatment group<sup>1</sup>.

	Usual Care (n = 55)	MI-Opioid Taper (n = 49)	P-value
Age (years)	66.2(8.6)	64.8(8.8)	0.4
Sex			0.3
Male	24(43.6%)	26(53.1%)	
Female	31(56.4%)	23(46.9%)	
Hispanic or Latino/Latina	3(5.6%)	4(8.2%)	0.7
Ethnicity			0.3
Asian	2(3.6%)	3(6.1%)	
White	47(85.5%)	35(71.4%)	
Black or African-American	1(1.8%)	4(8.2%)	
Other	5(9.1%)	7(14.3%)	
Approximate Household Annual Income			0.5
Less than or equal to \$50,000	17 (30.9%)	12(24.5%)	
Greater than \$50,000	38 (69.1%)	37(75.5%)	
Education Level			0.1
Any education from grade school, high school diploma or GED, some college (No Degree), to Associate Degree/Vocational Certificate	25(45.5%)	15(30.6%)	
Bachelor's Degree, Master's Degree, Professional School Degree, or Doctoral Degree	30(54.6%)	34(69.4%)	
Employment Status			0.08
Full-time employed	19(34.6%)	22(44.9%)	
Part-time employed	4(7.3%)	1(2.0%)	
Other	2(3.6%)	0(0.0%)	
Unemployed	0(0.0%)	3(6.1%)	
Retired	24(43.6%)	19(38.8%)	
Disabled, permanently or temporarily	6(10.9%)	2(4.1%)	
Marital Status			0.5
Never Married	3(5.5%)	3(6.3%)	
Married	37(67.3%)	38(79.2%)	
Domestic Partnership	1(1.8%)	1(2.1%)	
Separated or Divorced	9(16.4%)	3(6.3%)	
Widowed	5(9.1%)	3(6.3%)	
Preoperative Pain			0.7
Average pain at surgical site in past 24 h, NRS	4.3(2.3)	4.4(2.1)	
Average pain other than surgical site in past 24 h, NRS	4.0(3.3)	4.2(3.6)	0.6
Preoperative Opioid Use in the Two Weeks before Surgery	13(23.6%)	12(24.5%)	0.9
Preoperative Daily Oral Morphine Equivalent Use (mg)	2.4(6.1)	8.6(16.2)	0.01
Mood Assessments			
Beck Depression Inventory-II Score	8.6(7.2)	8.1(7.5)	0.7
NIH PROMIS Anxiety T-Score	52.1(8.9)	51.0(6.8)	0.5
NIH PROMIS Depression T-Score	48.2(7.7)	47.2(7.9)	0.5
NIH PROMIS Anger T-Score	45.9(8.5)	46.2(9.1)	0.9
Positive Affect Score, mean (SD)	32.8(8.1)	33.4(7.7)	0.7
Negative Affect Score, mean (SD)	16.5(14.5)	15.9(14.2)	0.6
Pain Catastrophizing Score, mean (SD)	11.2(8.0)	9.4(6.5)	0.4
Operation			0.6
Total Hip Replacement	21(38.2%)	21(42.9%)	
Total Knee Replacement	34(61.8%)	28(57.1%)	

NRS = Numeric rating scale of pain (0–10).

<sup>1</sup> Data are mean (SD) or n (%), unless otherwise indicated. There were no significant differences between the treatment groups ( $P \leq 0.002$  was considered to indicate significance in these between-group comparisons).

addition, several mood assessments were administered. Three NIH PROMIS measures of emotional distress (depression, anxiety, anger) were assessed before surgery via computerized adaptive testing [14]. NIH PROMIS measures are reported as T-scores calibrated to a mean score of 50 and standard deviation of 10 representing the average healthy population. The Beck Depression Inventory-II [7] (21 items measuring depressive symptoms on a 4-point scale, score range,

0–63, with 0–13 indicating minimal depression, 14–19 indicating mild depression, 20–28 indicating moderate depression, and 29–63 indicating severe depression), (2) the Positive and Negative Affect Schedule (20 items measuring positive affect and negative affect on 5-point scales [15–19], score range, 10–50, with higher scores for either positive or negative affect representing higher levels of positive or negative affect respectively), and (3) the Pain Catastrophizing Scale (13 items rated on a 5-point scale, score range, 0–52, with higher scores indicating more catastrophic thinking and emotional responses to pain) [20].

After surgery, the modified BPI was administered over the phone to assess pain related to the surgical site, pain medication use, and pain interference. For trajectories of pain, opioid use, and surgical recovery, calls continued until patients had 5 consecutive days of no opioid use, 5 consecutive days of 0 out of 10 average pain at their surgical site, and patient-reported full recovery after surgery. The modified BPI was assessed daily for 3 months, weekly thereafter up to 6 months, and monthly thereafter up to 1 year after surgery.

### 2.5. Outcomes

As a pilot study, the prespecified primary feasibility outcome was the proportion of people who completed the study in the group to which they were randomized. Study completion specific to the feasibility endpoint was defined as opioid cessation or continued opioid use two months after surgery.<sup>21</sup> Secondary feasibility outcomes included the proportion of study non-completers censored due to competing risks or loss to follow-up, and the proportion of completers reaching opioid cessation or continued opioid use 2 months after surgery.

The primary prespecified efficacy outcome was time to baseline opioid use. This was defined as the first of five days of zero opioid use for those not taking opioids prior to surgery or return to baseline preoperative dose for those taking opioids prior to surgery. Secondary prespecified efficacy outcomes included time to complete opioid cessation, defined as the first of five days of zero opioid use for all patients, time to pain cessation, defined as the first of five consecutive days of 0 out of 10 average pain, and time to patient-reported surgical recovery, defined as the first report of a patient answering “Yes” to the question, “Would you say that you are fully recovered from your surgery?” The BDI-II was included for the purposes of mediation analysis.

All adverse events that came to the attention of research staff during calls and assessments were recorded. The electronic medical record was also checked to accurately record the nature and outcome of the adverse events.

### 2.6. Statistical analysis

The trial statisticians (BN and JMH) prepared a fully detailed statistical plan prior to analysis. PK was the trial statistician lead for conducting the statistical analysis. JMH provided confirmatory statistical analysis. BN, PK, and JMH were responsible for the trial outcome analyses. Time to baseline opioid use was the prespecified primary endpoint of intervention efficacy. Power, set to 80%, was calculated using SAS Power and Sample Size 3.12. To detect a favorable effect for reducing time to baseline opioid use to 30 days in the MI-Opioid Taper group compared with 40 days in the UC group. With a 2-sided type I error rate of 0.1, 110 participants were required. Post-hoc power analysis was conducted to confirm the rationale for the significant effect sizes calculated. The original power analysis was conducted with TWOSAMPLESURVIVAL, and the post-hoc analysis was completed with the more appropriate COXREG option. With a 2-sided type I error rate of 0.05, event probability of 0.85, R-square of the primary outcome predictor of 0.4, Hazard ratio of 1.35, standard deviation of 27, and total sample size of 104, we had greater than

99.9% power for our primary outcome of interest (See Supplement section on Post-Hoc Power Analysis).

Statistical analyses were performed with SAS software (Version 9.4, SAS Institute Inc., Cary, NC, USA). We completed a formal analysis of factors leading to failure to complete the study based on baseline preoperative variables. Patients were dichotomized according to the primary feasibility outcome. We examined differences in baseline variables between groups using the *t*-test for continuous variables and chi-square test for categorical variables. Logistic regression was used to identify factors associated with failure to complete the study.

For efficacy, we planned intention-to-treat analyses. We included all patients who were randomized. We examined the distribution of baseline covariates among groups to establish adequacy of randomization. We used Kaplan Meier analyses to identify a difference in time to opioid cessation. We used Cox proportional hazards regression to adjust for type of operation. All HR and 2-sided 95% confidence intervals (CIs) based on Cox proportional hazards models included adjustment by operation as prespecified in our analytic plan. This controlled for the different degrees of tissue injury and healing associated with each operation as well as the operation-specific multimodal analgesia protocols followed at our institution. Similar analyses were conducted to determine a difference in time to pain cessation and patient-reported surgical recovery. Adverse events were summarized for all randomized patients.

### 3. Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. JMH and SM had full access to all the data in the study and had final responsibility for the decision to submit for publication.

### 4. Results

Between November 26, 2014 and April 27, 2018, 318 patients were referred from the tertiary orthopedic clinic (Fig. 1). Of the 209 patients screened, 18 patients did not meet inclusion criteria as most were taking preoperative around-the-clock opioids. Of the 191 participants assessed for randomization 14 days after surgery, 46 were no longer using prescription opioids and were therefore not randomized, 40 participants did not complete preoperative assessments, and 1 participant enrolled in another study. We randomly assigned 104 patients to receive MI-Opioid Taper plus UC ( $n = 49$ ) or UC alone ( $n = 55$ ). All 104 patients completed baseline preoperative assessments, provided follow-up data for the primary efficacy outcome, and were included in the intention-to-treat analysis. 3.6% ( $n = 2$ ) of patients in the UC group and 2.0% ( $n = 1$ ) of patients in the intervention group were lost to follow-up between 21 and 34 days after surgery. 9.1% ( $n = 5$ ) of patients in the UC group were lost to follow-up at greater than 60 days after surgery while none of the patients in the intervention group were lost to follow-up after 60 days. The mean number of MI-Opioid Taper sessions administered was 2.6 (SD 1.5). Counting at least one call as a minimum therapeutic dose, 42 (85.7%) of 49 patients had at least one MI-Opioid Taper session. The actual number of MI-Opioid Taper calls completed ranged from one ( $n = 13$ ), two ( $n = 10$ ), three ( $n = 9$ ), four ( $n = 4$ ), five ( $n = 3$ ), or six ( $n = 3$ ) calls.

Baseline and demographic characteristics were similar between groups (Table 1). Overall, mean (SD) age was 65.6 (8.7) years. The majority of study participants were white, either employed full-time or retired, and married. Preoperative pain and preoperative opioid use were similar between groups. However, the average daily preoperative oral morphine equivalent use was slightly higher in the MI-Opioid Taper group at 8.6 (SD 16.2)mg than the UC group at 2.4 (SD 6.1)mg. Mood assessments were similar across groups with patients exhibiting minimal depressive symptoms. Both groups reported

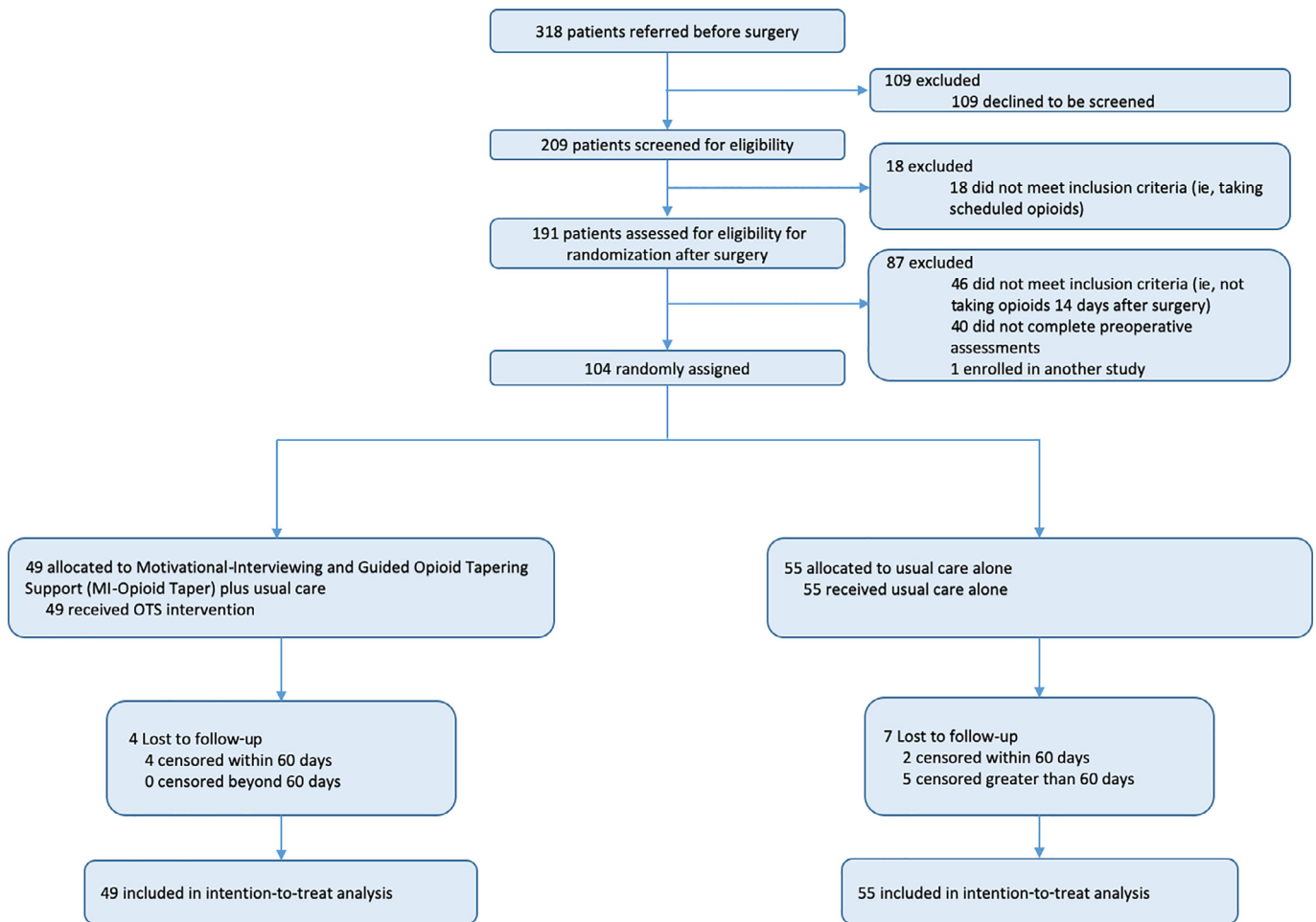


Fig. 1. Study flowchart.

minimal elevations in NIH PROMIS anxiety T-scores representing a slight elevation compared to the U.S. general population T-score of 50. Both groups reported less anger symptoms compared to the U.S. general population. Pain catastrophizing scale (PCS) scores were much lower in both groups than those previously reported for orthopedic patients [22].

The primary feasibility outcome, study completion after randomization was similar between groups with 96.4% ( $n = 53$ ) of patients in the UC group and 91.8% ( $n = 45$ ) of patients in the MI-Opioid Taper group reaching study completion (Table 2). There was no significant difference in the odds of study completion, rates of censoring among study non-completers, and rates of opioid cessation among study completers. Every 3-point increase in the NRS was associated with an almost 9-fold increased likelihood of study completion (OR 8.92; 95%CI 1.35–59.20;  $p$ -value=0.02). Every 10-point increase in the NIH PROMIS Anger T-score (representing 1 standard deviation above the average referenced population) resulted in a significantly decreased likelihood of study completion (OR 0.24; 0.08–0.77;  $p$ -value=0.02).

Administration of UC was similar between groups and stable during the trial including intraoperative management, postoperative management, and medications prescribed at hospital discharge (Table 3). None of the patients received postoperative intravenous ketamine.

Mean time to baseline opioid use was 67.8 days in the UC group and 34.6 days in the MI-Opioid Taper group (Fig. 2). Mean time to complete postoperative opioid cessation was 76.4 days in the UC group and 41.1 days in the intervention group (Fig. 3). Persistent post-surgical pain was common, and both groups reported pain long

after opioid cessation (Table 4). Similarly, patient-reported recovery occurred long after opioid cessation.

In the prespecified analyses (multivariable Cox regression model adjusted for type of operation), compared to UC alone, patients receiving MI-Opioid Taper had a 62% increase in the rate of return to baseline opioid use after surgery (HR 1.62; 95%CI 1.06–2.46;  $p = 0.03$ ). Similarly, MI-Opioid Taper resulted in a 53% increase in the rate of complete postoperative opioid cessation (HR 1.57; 95%CI 1.01–2.44;  $p = 0.05$ ). There was no effect of MI-Opioid Taper on time to pain cessation or patient-reported recovery from surgery (Table 5). Patients undergoing THA had a significant decrease in time to baseline opioid use and complete postoperative opioid cessation after surgery compared to those undergoing TKA, and median days to baseline opioid use and opioid cessation (Table 4) indicate that MI-Opioid Taper may be more effective among patients undergoing THA. As a sensitivity analysis, patients who received at least one MI-Opioid Taper session were included in a per-protocol analysis which similarly demonstrated a significant effect of MI-Opioid Taper on time to baseline opioid use (HR1.57; 95%CI 1.01–2.44;  $p$ -value=0.04). In addition, after controlling for preoperative daily oral morphine equivalent, both MI-Opioid Taper and operation type remained significant (See Supplement Table 2 for further details).

In total, four patients, three in the UC group and one in the intervention group, had a total of four adverse events: three hospitalizations (two from the UC group and one from the intervention group) for accidental injuries or falls, and one elevated BDI-II score indicating severe depression. No adverse events were considered related to the study intervention. There were no deaths or complaints about the intervention.

**Table 2**  
Primary and secondary feasibility outcomes.

Outcome	Usual Care (n = 55)	MI-Opioid Taper(n = 49)	Odds Ratio (95% CI)*	P value
Primary Feasibility Outcome: Study Completion after Randomization <sup>1</sup>	53 (96.4%)	45 (91.8%)	0.43 (0.07–2.43)	0.33
Secondary Feasibility Outcomes				
Study Non-completers				
Censored-Competing Risk	0(0.0%)	3(6.1%)		0.10 <sup>2</sup>
Censored-Loss to Follow-up	2(3.6%)	1(2.0%)		1.00 <sup>2</sup>
Study Completers				
Reached Opioid Cessation	48(87.3%)	45(91.8%)		0.5 <sup>2</sup>
Duration of Postoperative Opioid Use >60 days	5(9.1%)	0(0.0%)		0.06 <sup>2</sup>
Multivariate Analysis of Factors Associated with Study Completion				
Average pain at surgical site in past 24 H <sup>3</sup>			8.92(1.35–59.20)	0.02
NIH PROMIS Anger T-score <sup>4</sup>			0.24(0.08–0.77)	0.02

\*Odds Ratio of MI-Opioid Taper vs. Usual Care group.

<sup>1</sup> Study completion was defined as return to preoperative opioid dose or continued opioid use for at least 2 months after surgery.

<sup>2</sup> Chi-square or Fisher's Exact Test p-value.

<sup>3</sup> Every 3-point increase in the Numeric Rating Scale of Pain.

<sup>4</sup> Every 10-point increase in T-score representing 1 standard deviation above the average referenced population.

## 5. Discussion

This is the first randomized controlled trial testing the effects of a longitudinal, postoperative motivational interviewing and guided opioid tapering support intervention to promote opioid cessation in patients undergoing total hip or knee replacement surgery. The study demonstrates feasibility of testing the efficacy of this intervention. We demonstrated effective participant recruitment, enrollment, randomization, retention, and detailed longitudinal follow-up to one year after surgery with a total of 16,378 follow-up calls recorded during the course of the trial. Phone assessments were preferred with almost no request to transition to web-based assessments of the modified BPI. In addition, our findings demonstrate preliminary efficacy of MI-Opioid Taper in reducing the duration of postoperative opioid use that exceeds preoperative opioid doses. MI-Opioid Taper also reduced the total duration of postoperative opioid use by promoting definitive opioid cessation without prolongation of time to postoperative pain resolution or recovery. Patients undergoing THA experienced significantly faster return to baseline opioid use and

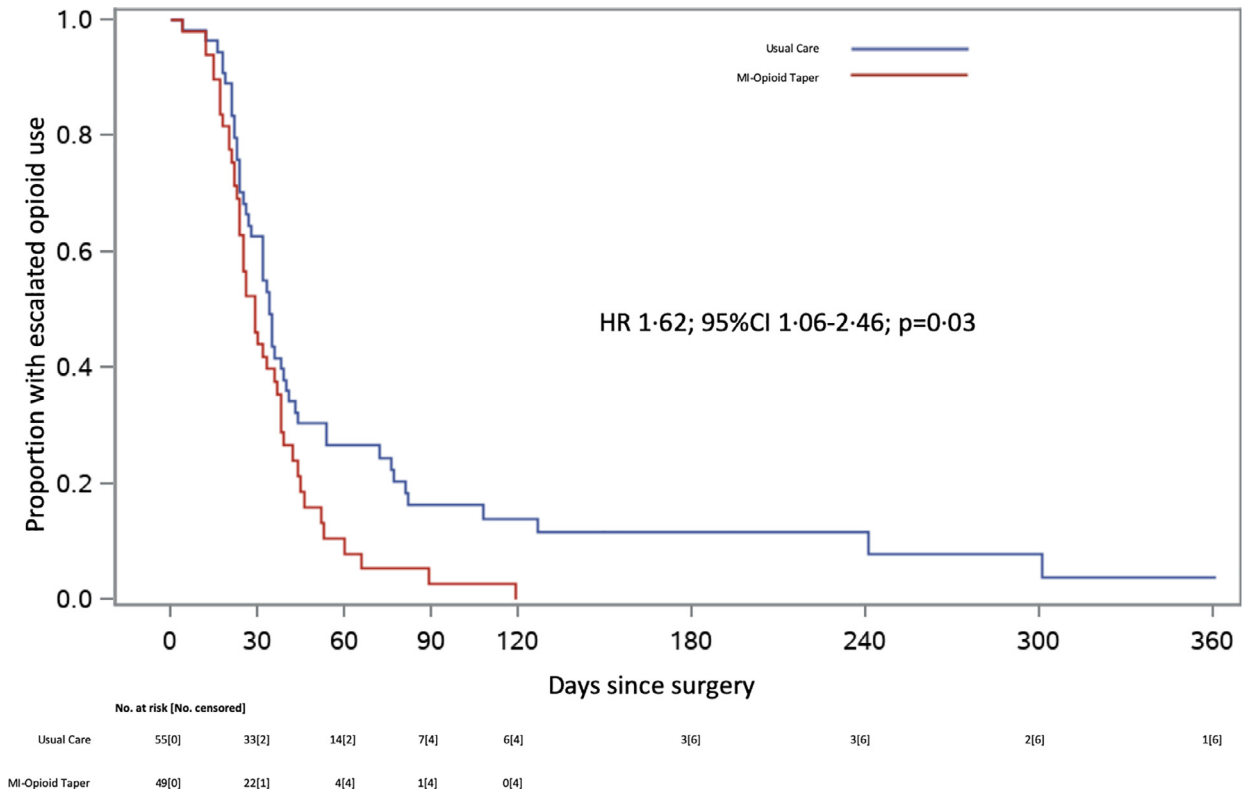
reduced total duration of postoperative opioid use. Examination of estimated median survival times from Kaplan-Meier curves indicate the efficacy of MI-Opioid Taper may be limited to those undergoing THA. However, Cox regression allows for simultaneous assessment of multiple covariates, and demonstrates a significant effect of the intervention after controlling for operation. Future research is needed to determine the relative effects of MI-Opioid Taper based on the type of operation. It is important to note that only 54% of participants were eligible for study randomization and were taking opioids 2 weeks after surgery. Combined with the resource-intensive nature of MI-Opioid Taper, the generalizability of intervention effects may be limited to those at highest risk for continued postoperative opioid use rather than all patients undergoing surgery.

Approaches to curb postoperative opioid use have been reported [6], but few interventions have been studied in the context of a randomized trial [6]. Within these trials, patients with chronic pain, substance abuse, and preoperative opioid use are often excluded [6], and trial results cannot be translated to those at highest risk for PPOU [23]. In patients undergoing arthroscopic rotator cuff repair, preoperative opioid education reduced opioid consumption three months after surgery with no difference in pain [24]. Although patients using opioids prior to surgery were included, patients unable to tolerate multimodal analgesic medications and oxycodone were excluded [24]. A pilot trial of a one-day, preoperative acceptance and commitment therapy workshop demonstrated trends towards faster pain and opioid cessation. However, the findings were non-significant, and the results were not adjusted for type of operation [25]. Our trial extended follow-up to one year rather than three months after surgery and was controlled for operation type, both factors which may account for our significant findings. A trial of preoperative opioid counseling compared to usual care demonstrated reductions in opioid consumption during the first 3 postoperative days after carpal tunnel release surgery in the setting of uniform postoperative opioid prescribing [26]. During that time, patients in both groups reported comparable pain. Our research adds to these findings by demonstrating the efficacy of a postoperative longitudinal intervention in limiting opioid consumption long after hospital discharge without worsened pain. Smith et al. describe a randomized trial of a pharmacist-led intervention compared to usual care in patients undergoing total hip or knee arthroplasty at increased risk for persistent postoperative opioid use [27]. Patients randomized to the intervention received pre- and postoperative opioid education brochures. If they filled opioid prescriptions in the 28 to 90 days after surgery, the pharmacist completed one follow-up call using motivational enhancement principles. Overall, there was no significant reduction in the amount of opioid dispensed [27]. Our trial better demonstrated the efficacy of an MI-based intervention likely due to repeated and

**Table 3**  
Intraoperative, postoperative, and discharge non-opioid pain management, No./total No. (%)<sup>1</sup>.

	Usual Care (n = 55)	MI-Opioid Taper (n = 49)	P-value
Intraoperative Management			
Intravenous ketamine	23 (41.82%)	17(34.7%)	0.5
Local anesthetic infiltration at the surgical site	31 (56.4%)	26 (53.1%)	0.7
Spinal analgesia	24 (43.6%)	27 (55.1%)	0.2
Epidural analgesia	1 (1.82%)	0 (0%)	1.0
Regional anesthetic technique	27 (49.1%)	23 (46.9%)	0.8
Postoperative Management			
Intravenous Lidocaine	1 (1.8%)	0 (0%)	1.0
Gabapentin	42 (76.4%)	34 (69.4%)	0.4
Celecoxib	19 (34.6%)	18 (36.7%)	0.8
Acetaminophen	51 (92.7%)	45 (91.8%)	0.9
Discharge Medications			
Gabapentin	21 (38.2%)	18 (36.7%)	0.9
Celecoxib	6 (10.9%)	5 (10.2%)	0.9
Acetaminophen	35 (63.6%)	27 (55.1%)	0.4

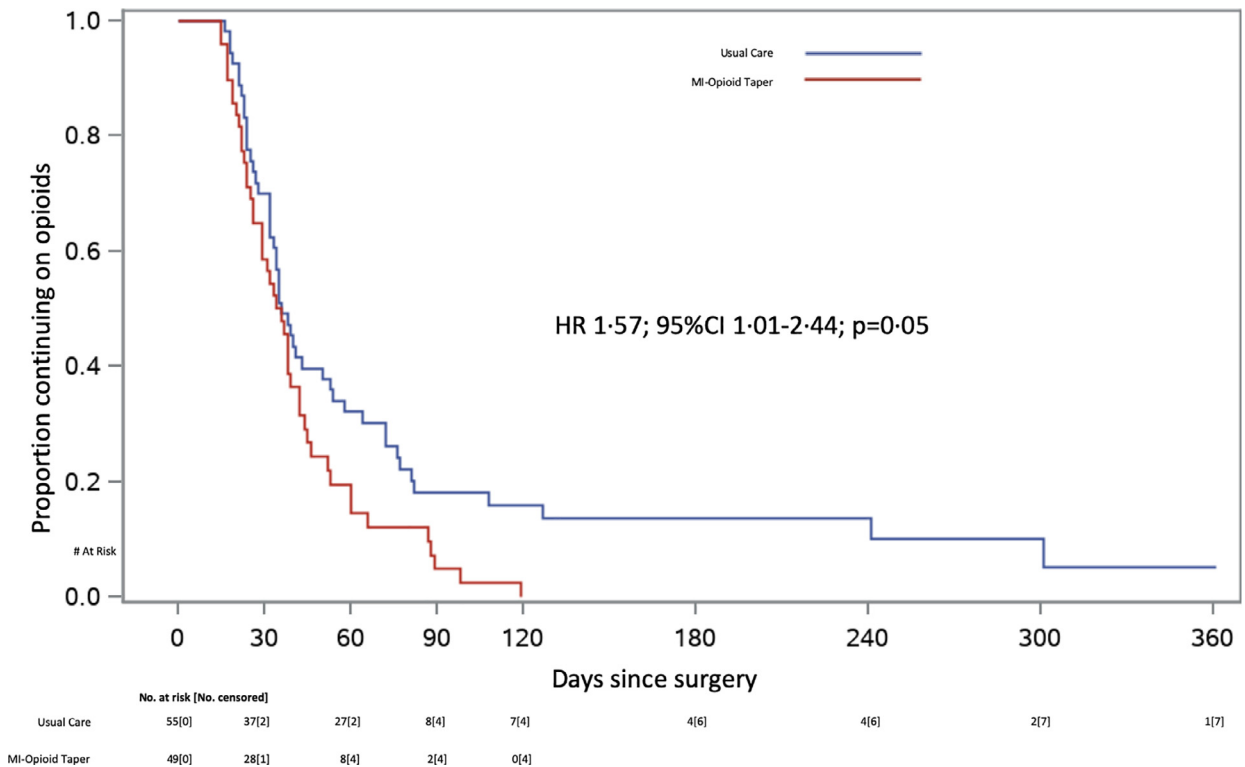
<sup>1</sup> Categories are not mutually exclusive, and patients may have received multiple treatments simultaneously. Among those randomized to usual care, 3 of 55 (5.5%) did not receive any of the treatments listed above. Among those randomized to opioid tapering support, 2 of 49 (4.1%) did not receive any of the treatments listed above.



**Fig. 2.** Kaplan-Meier plot for time to baseline opioid use by treatment group, in days. The number of patients at risk (have not yet reduced their postoperative opioid use to preoperative levels) is given below the bottom axis.

personalized participant contact after surgery, with an average of 2.6 physician-led phone calls prior to opioid cessation. Increased attention and interaction time may lead to non-specific MI-Opioid Taper

intervention effects. However, given that the UC group continued to receive daily calls for regular follow-up assessments, which likely reduced these effects. Rather than a follow-up phone call 4 to 13



**Fig. 3.** Kaplan-Meier plot for time to complete opioid cessation by treatment group, in days. The number of patients at risk (have not yet discontinued postoperative opioid use) is given below the bottom axis.

**Table 4**

Median days to opioid cessation, pain resolution, or recovery, and persistent opioid use<sup>1</sup>.

	UC	MI-Opioid Taper
Time to Baseline Opioid Use, overall	34(24–72)	29(22–42)
Time to Baseline Opioid Use, THR only	32(22–44)	24(17–30)
Time to Baseline Opioid Use, TKR only	36(24–81)	37(24–45)
Time to Opioid Cessation, overall	36(26–76)	36(26–46)
Time to Opioid Cessation, THR only	35(26–68)	29(20–42)
Time to Opioid Cessation, TKR only	38(27–81)	38(26–52)
Time to Pain Cessation, overall	167(90-*)	153(56-*)
Time to Pain Cessation, THR only	167(48-*)	111(42–321)
Time to Pain Cessation, TKR only	211(90-*)	167(80-*)
Time to Recovery, overall	150(71–271)	118(68–271)
Time to Recovery, THR only	160(104–241)	139(61–280)
Time to Recovery, TKR only	118(50–333)	118(68–155)
Opioid Use at 3 months-Overall	7 of 55 (12.7%)	1 of 49 (2.0%)
Opioid Use at 6 months-Overall	3 of 55 (5.5%)	0 of 49 (0%)
Opioid Use at 3 months- Preoperative opioid naïve	4 of 42 (9.5%)	1 of 37 (2.7%)
Opioid Use at 6 months- Preoperative opioid naïve	1 of 42 (2.4%)	0 of 37 (0%)
Opioid Use at 3 months- Preoperative opioid use	3 of 13 (23.1%)	1 of 12 (8.3%)
Opioid Use at 6 months- Preoperative opioid use	2 of 13 (15.4%)	0 of 12 (0%)

<sup>1</sup> Time is reported as median (interquartile range) in days.

weeks after surgery, MI-Opioid Taper involved earlier follow-up starting 2 weeks after surgery. This implies that earlier intervention may have a greater effect in altering postoperative opioid use trajectories. In addition, our main outcome focused on actual patient-reported opioid consumption rather than opioid dispensing, which is partly determined by clinician opioid prescribing. By extensive postoperative longitudinal follow-up, our trial was able to more accurately assess opioid use over time and the point of opioid cessation, affording more granularity in the outcomes of our intervention beyond electronic health records or administrative data.

The MI-Opioid Taper intervention did not significantly prolong postoperative pain or delay recovery after surgery while limiting postoperative opioid consumption. Although not significant, the overall direction of effects suggests MI-Opioid Taper shortens pain duration and promotes surgical recovery. A larger clinical trial will allow for better estimates of MI-Opioid Taper effects on these outcomes.

An important caveat when discussing the efficacy of MI-Opioid Taper is that this pilot study has numerous limitations to be

addressed in a future clinical trial before there is adequate data to inform clinical practice. The study allowed for greater type I error. In addition, our sample size of 104 patients was slightly less than our target (110 patients) as many participants were not taking opioids 14 days after surgery, or did not have time to complete the preoperative assessments. These factors will be taken into consideration in a future, larger efficacy-testing trial. In addition, the protocol was amended during the course of the pilot trial to include patients who were taking prn, as-needed, prescription opioids to treat pain at the future surgical site. Nonetheless, baseline demographics demonstrate higher preoperative daily opioid doses in patients randomized to MI-Opioid Taper. As preoperative opioid use is associated with prolonged postoperative opioid use, this would bias the trial to demonstrate a lack of intervention efficacy. Despite this, we still found significant efficacy in the MI-opioid Taper. The rates of persistent postoperative opioid use among patients receiving UC were comparable to prior research that used high frequency of postoperative longitudinal assessments [21]. When compared to larger surgical cohorts, only 2.4% of patients randomized to UC were using opioids 6 months after surgery, which is much lower than previously reported rates of opioid use 9–12 months after surgery (9.9% and 6.3% of opioid naïve TKA and THA patients respectively) [28]. Providing instructions on opioid use before and after surgery may have reduced opioid consumption in both groups. Although assessors were blinded to randomization status, repeated contact over time may have increased the possibility of unblinding from study participants. Combined with lack of assessor blinding validation, the possibility of unblinding is an important consideration. Further, the sheer volume of follow-up calls required for this pilot trial limit scalability and feasibility of this assessment method, and a future trial should consider alternative methods of data collection such as web-based surveys. Another important limitation was the delivery of the MI-Opioid Taper intervention by the study PI due to the pilot nature of the study, a future trial will need to train clinicians in MI and the MI-Opioid Taper intervention to truly determine efficacy. At present, given the numerous limitations of the current pilot study we have outlined, future research is needed to determine the efficacy of MI-Opioid Taper to definitively inform clinical practice.

Individuals with higher levels of preoperative pain were more likely to complete the trial, while patients with higher levels of anger were less likely to complete the study. Addressing postoperative pain management is likely a priority among patients with preoperative pain and can serve to promote treatment engagement and retention. Patients with elevated anger may benefit from exploration of perceived barriers to continued trial participation.

**Table 5**

Primary and secondary efficacy outcomes.

Outcome	Usual Care Number of Events	MI-Opioid Taper Number of Events	Hazard Ratio (95% CI)	P value
Primacy Efficacy Outcome: Time to Baseline Opioid Use <sup>1</sup>	48 of 55	45 of 49		
MI-Opioid Taper vs. UC			1.62 (1.06–2.46)	0.03
THR vs. TKR			1.88(1.23–2.87)	0.004
Secondary Efficacy Outcomes:				
Time to Baseline Opioid Use Per-Protocol Analysis				
MI-Opioid Taper vs. UC	48 of 55	38 of 42	1.57(1.01–2.44)	0.04
THR vs. TKR			1.93(1.24–3.01)	0.004
Time to Complete Opioid Cessation <sup>1</sup>	47 of 55	45 of 49		
MI-Opioid Taper vs. UC			1.53(1.00–2.33)	0.05
THR vs. TKR			1.22(0.80–1.86)	0.4
Time to Pain Cessation <sup>1</sup>	29 of 55	29 of 49		
MI-Opioid Taper vs. UC			1.26(0.75–2.12)	0.4
THR vs. TKR			1.25(0.74–2.12)	0.4
Time to Recovery <sup>1</sup>	38 of 55	32 of 48		
MI-Opioid Taper vs. UC			1.12(0.69–1.81)	0.6
THR vs. TKR			1.22(0.75–1.98)	0.4

<sup>1</sup> Intention-to-treat analysis, adjusted by operation.



MI combines empathic counseling and strategies for eliciting client self-motivational statements to build intrinsic motivation and commitment to positive behavioral change. MI has been researched extensively in the context of substance use to improve treatment engagement and outcomes, decrease alcohol use, increase medication adherence, and decrease illicit drug use. Our trial represents a novel application of MI for reduced prescription opioid use in the post-operative setting and postoperative opioid cessation. MI used to enhance prescription opioid adherence among older adults with chronic pain also decreases opioid misuse and depression levels [29]. MI bolsters autonomous motivation, in turn improving satisfaction with therapy and reducing depression severity among depressed patients. It is possible that the MI-Opioid Taper intervention strengthens motivation and improves depressive symptoms to promote postoperative opioid cessation. Future work to illustrate these mechanistic changes are needed.

The MI-Opioid Taper intervention did not aim to influence opioid prescribing, but rather actual patient opioid consumption. By simultaneously minimizing postoperative opioid prescribing, identifying patients at high-risk for persistent opioid use after surgery, and providing MI-Opioid Taper to those at highest risk to encourage opioid cessation, the risks of postoperative opioid prescribing can be minimized for all patients. As multiple countries now aim to curb postoperative opioid use through clinical care initiatives and health policy [2], our promising pilot study findings support the need for a larger trial to establish the effects of MI-Opioid Taper, delivered by front-line clinicians, on minimizing postoperative opioid use.

### Contributors

JMH, JT, IC, and SM designed the study. JMH was the principal investigator and had the main responsibility for drafting the study protocol and report. JMH was the trial therapist. HH and YS were research coordinators. JMH, BN, and PK were responsible for the trial outcome analyses. JMH, BN, PK, and SM take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to, read, and approved the final report.

### Funding

This trial was funded by grants from the National Institutes of Health (NIH), National Institute on Drug Abuse (NIDA) (K23DA035302, R01DA045027, K24DA029262). The views and opinions expressed herein are those of the authors and do not necessarily reflect those of the NIH or NIDA. JMH and SM had full access to all the data in the study and had final responsibility for the decision to submit for publication.

### Data Sharing Statement

Due to institutional review board restrictions associated with the trial, participant data is not available to external sources. Proposals to access the de-identified individual participant data that underlie the results reported in this article will be considered 12 months after publication of the Article. Proposals should be directed to the corresponding author, with approval by JMH, IC, and SM. Requesters will need to sign a data access agreement. JMH and SM had full access to all the data in the study and had final responsibility for the decision to submit for publication.

### Declaration of Competing Interests

Dr. Hah reports grants from NIH NIDA, during the conduct of the study.

Dr. Trafton reports other interests from Institute for Brain Potential outside the submitted work.

Dr. Maloney reports other interests from Stryker, Zimmer, and grants from NIH outside the submitted work.

Dr. Goodman reports personal fees from board membership, personal fees from consultancy, grants from NIH, grants from Omega, from Coulter, personal fees from payment for development of educational presentations, personal fees from stock/stock options outside the submitted work.

Dr. Mackey reports grants from NIH NIDA, during the conduct of the study.

All other authors have nothing to declare.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2020.100596.

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