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Prescription Opioid Taper Support for Outpatients with Chronic Pain: A Randomized Controlled Trial

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Abstract

Patients receiving long-term opioid therapy for chronic pain and interested in tapering their opioid dose were randomly assigned to a 22-week taper support intervention (psychiatric consultation, opioid dose tapering, and 18 weekly meetings with a physician assistant to explore motivation for tapering and learn pain self-management skills) or usual care (N=35). Assessments were conducted at baseline and 22 and 34 weeks after randomization. Using an intention-to-treat approach, we constructed linear regression models to compare groups at each follow-up. At 22 weeks, adjusted mean daily morphine-equivalent opioid dose (MED) in the past week (primary outcome) was lower in the taper support group, but this difference was not statistically significant (adjusted mean difference = −42.9 mg; 95% CI: −92.42, 6.62; p= 0.09). Pain severity ratings (0–10 NRS) decreased in both groups at 22 weeks, with no significant difference between groups (adjusted mean difference = −0.68; 95% CI: −2.01, 0.64; p = 0.30). The taper support group improved significantly more than usual care in self-reported pain interference, pain self-efficacy, and prescription opioid problems at 22 weeks (all p-values <0.05). This taper support intervention is feasible and shows promise in reducing opioid dose while not increasing pain severity or interference. [ClinicalTrials.gov Identifier: NCT01883882]

Keywords

Chronic Opioid Therapy; opioid dose taper; pain intensity; pain interference; pain self-management

Introduction

The number of opioid prescriptions written annually in the United States (U.S.) now approximates the number of adults in the U.S. population. The percent of Medicare Part D recipients receiving opioid prescriptions for more than 90 days in a year increased from

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4.6% in 2007 to 7.4% in 2012, with large variation among states, suggesting a lack of consensus about the indications for long-term opioid therapy. The Medicare patients more likely to have prolonged use were characterized by older age, female gender, White race, low income, living in a lower-education area, and comorbidity of drug abuse, rheumatoid arthritis, or depression.[17] These populations are also at high risk for opioid adverse events such as overdose and abuse.[20] In 2011, half of all veterans with chronic non-cancer pain (CNCP) received an opioid prescription during the year. Over half (57%) of these veterans received at least 90 days' supply of opioids and 10% received at least 350 days' supply. The median daily dose was 21 mg morphine-equivalent dose (MED), with 4.5% receiving more than 120 mg MED.[9]

Exposure to prescription opioids increases the risks for opioid abuse, overdose, and other adverse events in a dose- and duration-dependent manner.[11,19] There were almost 19,000 overdose deaths in the U.S. associated with prescription opioids in 2014.[3] These now exceed the number of deaths caused by motor vehicle accidents in the U.S. In 2013, prescription opioids were also involved in more deaths than were all illicit drugs combined.[5] The prescribing of opioids for chronic pain also appears to contribute to the nonmedical use of opioids. Data from the National Survey of Drug Use and Health suggest that prescribers are, directly or indirectly, the source of most misused opioids.[28]

It is possible that decreasing doses of opioids prescribed to patients with chronic pain may reduce these risks to patients and the general population.[23] Opioid tapering after years of therapy may be difficult for the patient and is feared by many patients. It is possible that opioid taper may be accomplished without significant worsening of pain, mood, and function, given data concerning opioid taper within multidisciplinary pain rehabilitation programs.[30] However, no protocol for taper of long-term opioid therapy (LtOT) among outpatients treated for chronic pain has been tested. The effects of tapering LtOT dose on pain, function, and mood remain unknown. This information would be helpful to patients contemplating opioid taper and their physicians, and possibly also in understanding the value of LtOT for CNCP given the absence of randomized controlled trials (RCTs) of LtOT.

The objectives of this pilot study were to (1) demonstrate the feasibility of a prescription opioid taper support intervention for patients receiving moderate- or higher-dose LtOT for CNCP who had no evidence of current substance abuse and (2) conduct a pilot RCT to evaluate the effectiveness of this intervention. We hypothesized that patients randomized to the opioid taper support intervention, as compared with patients randomized to usual opioid prescribing care, would have lower opioid doses (primary outcome) at 22 weeks (primary endpoint and end of intervention period) and 34 weeks after randomization. We explored effects of the intervention on opioid misuse, pain severity, pain-related activity interference, pain self-efficacy, depressive symptoms, opioid-related problems, and opioid-related concerns.

Materials and Methods

Study design, participants, and setting

This non-blinded RCT was conducted at the UW Medicine Center for Pain Relief in Seattle, Washington. The study was approved by the University of Washington Institutional Review Board and overseen by an independent data and safety monitoring committee. All participants provided written informed consent. Study enrollment occurred from May 2013 to September 2015. The Figure shows participant flow through the study.

Study participants were recruited through clinician referrals and clinic advertisements at the UW Medicine Center for Pain Relief and via referrals from other UW Medicine specialty and primary care clinics and other Seattle pain clinics. Recruitment was initially limited to the Center for Pain Relief, but was expanded to other pain clinics and primary care clinics due to slow enrollment. Study inclusion criteria at study initiation were CNCP, defined as pain on more than half the days in the past six months; use of opioid medication on more than half of the previous 90 days; willingness to taper opioid dose by at least 50% (or to 120 mg MED, whichever was less); daily MED >50 mg; recent urine drug test with no aberrancy; and future visits scheduled at the Center for Pain Relief. After enrollment began, the requirements for a 50% (or 120 mg) taper goal, recent urine drug test, and future visits scheduled at the Center for Pain Relief were removed and the required opioid dose at study entry was lowered to >25 mg MED in order to increase enrollment.

Patient exclusion criteria at the time of study entry were: 1) currently receiving treatment for cancer (other than non-melanoma skin cancer); 2) medical comorbidity with life expectancy less than one year or otherwise considered medically unstable (as judged by the referring physician); 3) use of parenteral, transdermal, or transmucosal opioids or naltrexone within the previous month; 4) currently residing in a skilled nursing or long-term care facility; 5) currently using any implanted device for pain control (e.g., intrathecal pump, spinal cord stimulator, peripheral nerve stimulator); 6) surgery within the previous month or planned during the next 6 months; 7) report of suicide attempt or psychiatric hospitalization in the past 10 years or current suicidal ideation with specific plan or intent; 8) significant cognitive impairment, as assessed using the 6-item screener;[4] 9) report of psychotic symptoms on the Modified MINI interview;[27] and 10) report of current abuse of substances other than nicotine or marijuana according to the National Institute on Drug Abuse Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST)[12] (marijuana was allowed because it is legal under Washington State law). The exclusion for psychiatric hospitalizations within the past 10 years was changed to within the past year after study enrollment began in order to increase enrollment. Patients agreed not to initiate buprenorphine treatment while enrolled in the study. All other concurrent pain treatment was allowed.

Procedures

After clinician or self-referral to the study, potential participants were screened by telephone. Patients who were provisionally eligible and interested in study participation then completed an in-person screening visit with the study physician assistant (PA). At that visit, potential participants were shown a 14-minute video of interviews with patients who had

successfully tapered off opioids concerning what they had gained by this. Patients also provided demographic information and rated their expectations of the intervention. Patients who met all study inclusion criteria and remained interested in participating in the study then provided written informed consent and were enrolled. All measures used to assess outcomes were administered by research staff by telephone at baseline (after the screening visit and prior to randomization) and at 22 weeks (primary study endpoint; after completion of the taper support intervention for those randomized to this intervention) and 34 weeks post-randomization. If participants preferred to complete measures at home and return them by mail, this was permitted. Participants received $15 for completing the baseline assessment, $30 for the 22-week follow-up, and $50 for the 34-week follow-up.

Intervention

Opioid Taper Support—The taper support intervention began with a visit to the principal investigator, an experienced pain medicine/psychiatry physician, to evaluate whether adjustment or initiation of non-opioid psychotropic medication was indicated. This physician then adjusted or provided a prescription for new medication as indicated and supervised the study PA in monitoring patient response over the course of the intervention period.

Patients next met with the study PA for a Motivational Interviewing-based session concerning opioid tapering that included: 1) eliciting the patient's history related to pain, opioid therapy, and related difficulties; 2) eliciting change talk related to tapering; 3) education about dose-related health risks; 4) identifying practical and psychological barriers to tapering opioid dose and problem-solving ways to overcome these; and 5) developing a commitment to change with respect to opioid therapy. Patients were also shown a short video of interviews with the same patients who were in the first video concerning coping with challenges of tapering off opioids.

The taper support intervention protocol included an additional 17 weekly 30-minute sessions with the PA. Patients were provided with an opioid medication prescription for the week at each visit. Patients were encouraged to attend all sessions in person, but were allowed to complete up to every other session by telephone. At the sessions, patients reported on pain, withdrawal, and mood/anxiety symptoms. Each session included pain self-management training modeled after empirically-supported cognitive-behavioral therapy (CBT) interventions for chronic pain. The sessions included: (1) rationale for pain self-management and education about the neurophysiology of pain and the role of cognitive and behavioral variables in chronic pain and adjustment to it; (2) behavioral goal setting; (3) education about, training in, and practice of various relaxation techniques (diaphragmatic breathing, progressive muscle relaxation, body scans, applied relaxation); (4) behavioral activation techniques, activity scheduling, and instruction in activity pacing; (5) education regarding the role of cognitions in negative affective responses to pain and instruction in positive pain coping self-statements and distraction techniques; (6) sleep hygiene education; and (7) education about and training in ways to maintain gains, reduce the risk of pain flare-ups, and cope with pain flare-ups if they do occur. Motivational Interviewing was used periodically to address ambivalence about tapering as needed. Patients completed "personal action plans" at

each session for home activities to perform between sessions (e.g., practice of relaxation techniques, personal goal-related activities). The content of each session is summarized in Table 1.

The taper support intervention protocol also included booster phone calls from the PA at 24, 28, and 32 weeks after randomization. At each call, patients were asked to review their experiences with their personal action plans for pain self-management and activity participation and with relapse prevention plans they had created. These plans were modified and pain management skills were reviewed as needed.

We developed a detailed protocol for each session for the PA to follow and a patient workbook for the 18 weekly sessions that included educational content related to each session. Participants randomized to the taper support intervention were given this workbook and asked to read each session's section between sessions and bring the workbook to each session. Patients were also given CDs with relaxation exercises for home practice and a book about pain self-management (D.C. Turk and F. Winter, *The Pain Survival Guide*, American Psychological Association, 2005). They were asked to read specific chapters in the book between sessions.

Prior to seeing any study patients, the study PA was trained by two clinical psychologists (JAT, KAS) in motivational interviewing adapted for use with patients considering opioid tapering and in the pain self-management training intervention. The PA was supervised in delivery of the pain self-management training intervention per protocol in regular individual sessions with the study clinical psychologists as well as in weekly sessions with the pain medicine/psychiatry physician and the psychologists. These group supervision sessions included a review of each PA session with each participant, including a review of opioid dosing; pain, depression, and anxiety symptoms; and delivery of the pain self-management training protocol.

The PA assumed all opioid medication prescribing during the intervention taper period for patients randomized to the taper support intervention. For patients remaining on opioid medication at the end of this period, their prior prescriber resumed prescribing. These transitions were coordinated through communication of the PA with the prescriber. The opioid taper protocol specified a 10% reduction of the original dose per week until 30% of the original dose was reached. At that point, the 10% was recalculated on the basis of this dose and the taper then proceeded by 10% of this new dose per week. However, patients were allowed to pause the taper and hold their opioid dose steady at any point. Patients were not allowed to increase their opioid dose; those wishing to do so were withdrawn from the visits with the PA but retained in the study for data collection.

Usual Care—Patients randomized to usual care received care for their pain, including opioid prescriptions from their usual prescribers, as they would as if they were not in the study, with no restrictions other than avoiding buprenorphine for the duration of the study.

Measures

Descriptive measures—At baseline, information was obtained regarding participant age, race, ethnicity, gender, and education. Additionally, patients were asked how long they had been experiencing pain on a daily or near-daily basis and about the duration of the current episode of opioid therapy and their goals for opioid taper (discontinuation or dose reduction).

Outcome measures

Opioid dose: The primary outcome was mean daily opioid dose in the past week at 22 weeks after randomization. This was assessed by patient self-report or obtained from electronic medical records if self-report data were unavailable. Opioid use was converted to MED using the Washington State Agency Medical Directors' Group Opioid Dose Calculator (http://agencymeddirectors.wa.gov/mobile.html). Secondary outcomes were opioid dose 34 weeks after randomization and percent reduction (from baseline) in opioid dose at 22 weeks and 34 weeks.

Additional secondary outcome measures included:

Brief Pain Inventory (BPI) pain severity and pain interference subscales.[7] These subscales have been shown to have satisfactory internal consistency.[29]

Prescription Opioid Difficulties Scale (PODS). The PODS assesses problems and concerns related to opioid use from the patient's perspective (in the past 2 weeks for common problems and in the past month or year for less common problems). The PODS has one 8-item sub-scale that assesses psychosocial problems (e.g. lose interest in usual activities, trouble concentrating) attributed to opioids and another 8-item sub-scale that assesses patients' opioid control concerns (e.g., preoccupied with use of opioids, worried unable to control use). The PODS has been validated among LtOT recipients, with satisfactory internal consistency and demonstration of a two-factor structure: psychosocial problems and opioid control concerns.[1]

Prescription Opioid Misuse Index (POMI). This 6-item measure has been validated among patients receiving opioid therapy for pain and those receiving treatment for opioid abuse. Endorsing ≥2 items reliably classified a person as at risk for medication misuse.[14]

Patient Health Questionnaire-9 (PHQ-9). This 9-item self-report measure is a well-validated, widely used measure of depressive symptom severity.[15] Scores can range from 0–27, with higher scores indicating greater depressive symptom severity.

Generalized Anxiety Disorder-7 (GAD-7). This 7-item index of anxiety symptom severity has been shown to be reliable and valid.[18] Scores can range from 0–21, with higher scores indicating greater levels of anxiety symptoms.

Insomnia Severity Index (ISI). This self-report measure of sleep difficulties has demonstrated reliability, validity, and sensitivity to change.[2] Scores range from 0–28, with higher scores indicating more severe sleep problems.

Pain Self-Efficacy Questionnaire (PSEQ). This 10-item measure assesses confidence in ability to do tasks and activities despite pain. Scores can range from 0 to 60, with higher scores indicating greater self-efficacy for managing pain.[24]

Patient Health Questionnaire-15.[13] The PHQ-15 assesses somatic symptom severity. Cut points of 5, 10 and 15 represent mild, moderate, and severe symptom levels.[16]

Opioid Craving. Study participants rated their craving for opioids in the past week from 0 (not at all) to10 (extremely) at each assessment. Measures of prescription opioid craving have predicted relapse to prescription opioid abuse among individuals in substance abuse treatment.[21]

Patient Global Impression of Change (PGIC). At 22 and 34 weeks, patients were asked to rate "the change in activity limitations, symptoms, emotions, and overall quality of life" related to their pain since beginning the study on a scale from 1 to 7 (1 = no change, 2 = almost the same, 3 = a little better, 4 = somewhat better, 5 = moderately better, 6 = better ["and a definite improvement that has made a real and worthwhile difference"], 7 = "a great deal better, and a considerable improvement that has made all the difference"). This scale has been validated for use in chronic pain treatment trials.[26]

Perceived Helpfulness of Opioid Taper Support. Participants randomized to the taper support intervention were asked to rate the helpfulness of the intervention on a scale from 1 (not helpful) to 5 (extremely helpful).

Feasibility measures—To assess feasibility of the intervention, we monitored the number of sessions attended among patients randomized to the taper support intervention and whether these were in-person or by telephone.

Randomization procedures

Study participants were randomized 1:1 to receive either the opioid taper intervention or usual care according to a computer-generated randomization list in sealed envelopes. To ensure approximately equal numbers of men and women in the intervention and control groups, a gender-stratified randomization procedure was used, with patients randomized in five-patient blocks.

Statistical power/sample size calculations

The primary purpose of the study was to demonstrate feasibility and potential efficacy of the intervention. Statistical power was estimated to test the hypothesis that the adjusted (for baseline) daily opioid dose (the primary outcome) would be significantly lower in the taper support group than in the usual care group at 22 weeks. Using power calculations based on the normal approximation with a 5% significance level for a 2-sided test, we determined that a sample size of 25 patients in each study arm would provide adequate power (0.70–0.93) to detect a 40%–50% difference in opioid dose. The trial was stopped after 35 patients were randomized due to funding constraints.

Statistical Analyses

We used descriptive statistics to characterize the sample at baseline. Using an intention-to-treat strategy, we conducted a series of linear regression analyses, with separate models for each outcome at each time point, to test whether the two study groups differed at 22 and 34 weeks on the outcome measures, adjusting for the baseline value of the outcome measure. For each outcome, we report the adjusted mean difference between treatment groups at each time point and its 95% confidence interval. All reported p-values are two-sided and considered significant at < 0.05. We did not correct for multiple comparisons, given the exploratory nature of the analyses and the pilot nature of the study. All analyses other than the test of the primary outcome at 22 weeks are considered exploratory and hypothesis-generating.

Results

Baseline characteristics of the sample

As can be seen in the Figure, 144 patients were referred to the study. Among these, 76 were eligible but declined to participate and 33 were ineligible. The remaining 35 patients enrolled, completed the baseline assessment, and were randomized (18 to taper support and 17 to usual care).

Table 1 shows the sociodemographic characteristics of study participants and baseline information on pain and opioid therapy duration, history of attempts to taper or discontinue opioid therapy, and goals for the opioid taper intervention. There were no statistically significant differences between the taper support and usual care groups on these measures. Overall, the mean (SD) age of the study participants was 54.4 (10.1) years. The mean (SD) duration of their pain was 13.8 (8.2) years and the mean (SD) duration of their current use of opioid medication was 10.2 (4.3) years. Mean (SD) daily opioid dose at baseline was 207.2 mg MED (269.3) in the taper support group and 245.2 mg (347.3) in the usual care group. At baseline, 11/18 (61%) participants randomized to taper support and 9 (53%) participants randomized to usual care scored 10 or more on the PHQ-9 (moderate or greater depressive symptom severity).

Primary and secondary outcomes at 22 and 34 weeks

Table 2 shows the observed values for the primary and secondary outcome measures in each group and the adjusted mean differences between groups at 22 and 34 weeks. At 22 weeks, opioid dose was reduced from baseline in both the taper support and usual care groups, with no significant difference between groups in dose (adjusted mean difference = −42.9 mg MED; 95% CI: −92.42, 6.62; p= 0.09) or in percent reduction from baseline in dose (mean, 43% vs 19%; adjusted mean difference = −0.25; 95% CI: −0.52, 0.02; p= 0.07). Statistically significant differences between groups at 22 weeks favoring the taper support group were observed for the BPI Pain Interference scale (adjusted mean difference = −1.39; 95% CI: −2.78, −0.01; p= 0.049), the Pain Self-efficacy Scale (adjusted mean difference = 7.86; 95% CI: 1.22, 14.50; p= 0.02), and the PODS Problems scale (adjusted mean difference = −4.90; 95% CI: −8.40, −0.80; p= 0.02). The groups did not differ significantly on the other outcomes at 22 weeks. More than twice as many patients in taper support (56%, n = 9) than

in usual care 3 (23%, n = 3) rated themselves as at least moderately better since the study began on the patient global impression of change (PGIC) rating at 22 weeks, but this difference was not statistically significant (p=0.13).

At 34 weeks, opioid dose was reduced from baseline in both the taper support and usual care groups, with no significant difference between groups in daily dose (adjusted mean difference = −26.7 mg MED; 95% CI: −83.04, 29.62; p= 0.34) or in percent reduction from baseline in daily dose (mean, 52% in the opioid taper support group vs 31% in the usual care group; adjusted mean difference = −0.22%; 95% CI: −0.52, 0.08; p= 0.14). Also at 34 weeks, the opioid taper support group continued to show lower BPI Interference scores as compared with the usual care group, although there was only a trend towards a statistically significant difference (adjusted mean difference = −1.21; 95% CI: −2.43, 0.02; p = 0.053). The differences between the taper support and usual care groups were no longer statistically significant for pain self-efficacy (adjusted mean difference = 7.26; 95% CI: −2.14, 16.66; p = 0.12) or PODS Problems (adjusted mean difference = −4.74; 95% CI: 10.13, 0.64; p = 0.08). The groups also did not differ significantly on the other outcomes at 34 weeks. Ten (62%) patients in taper support vs. 6 (37%) patients in usual care rated themselves as at least moderately better on the PGIC at 34 weeks (p = 0.29).

Among the 16 participants randomized to taper support who completed the 22-week assessment, 13 (81%) rated the intervention as very or extremely helpful. Among the 15 participants who completed this rating at the 34-week assessment, 11 (73%) rated the intervention as very or extremely helpful.

At 22 weeks, four (22%) randomized to the taper support intervention and eight participants (47%) randomized to the usual care group had not reduced their opioid dose at all. Six participants (33%) randomized to taper support and five participants (29%) randomized to usual care and decreased their opioid dose 0–49%, while seven (39%) in taper support and two participants (12%) in usual care and had decreased by 50% or more. One taper support participant and one usual care participant had completely discontinued opioids. At 34 weeks, nine participants in taper support and five in usual care had tapered opioid dose by at least 50%. At 34 weeks, two participants in taper support and two in usual care had completely discontinued opioids.

Adverse events

No adverse events were reported in the usual care group. One adverse event was reported in the taper support group and was classified as severe and study-related. A patient prescribed nortriptyline by the study psychiatrist/PI during the patient's initial psychiatric evaluation developed an allergic reaction (difficulty breathing, a swollen uvula, redness in neck, and flushed face) two days later. The patient saw his primary care physician and discontinued the medication, and his symptoms resolved.

Co-interventions

At baseline, 10 taper support and 8 usual care participants were taking antidepressant medication. Among the 18 patients randomized to taper support, medication changes were recommended for 12 by the study PI/psychiatrist. For 10 of the 12 patients, these changes

involved initiation or dose increase of antidepressant medications. For two of these patients, the change was a reduction in baclofen doses. Antidepressants recommended to be initiated or increased included: nortriptyline (5), venlafaxine (2), trazodone (2), citalopram (2), and bupropion (1). The PI/psychiatrist generally handled titration of antidepressants or other psychotropic medications during the weekly phone supervision of the physician assistant. On three occasions, he met a second time with taper support participants who were having difficulty with their antidepressants and/or opioid taper.

Taper support session attendance and dosing reduction pauses

Among the 18 participants randomized to the taper support intervention, 12 (67%) attended all 18 self-management training sessions, 3 (17%) attended 10–17 sessions, 2 (11%) attended 1–5 sessions, and 1 (6%) attended no sessions. Most patients (10/18, 56%) attended all sessions in person, with the remainder (8/18, 44%) attending 1–5 sessions by telephone. Sixteen (88%) paused the taper at least once. One patient withdrew from the taper support sessions to have her opioid dose increased due to escalating levels of pain, anxiety and depression, but she provided complete outcome data.

Discussion

In this study, we demonstrated the feasibility of a prescription opioid taper support intervention and its promise for efficacy in reducing opioid dose without worsening pain intensity, pain interference, and other important pain-related clinical outcomes. On our primary outcome, daily opioid dose at 22 weeks, those randomized to the intervention had an adjusted (for baseline) mean daily MED 43 mg lower than that of patients randomized to usual care, although this difference was not statistically significant (95% CI: −92.42, 6.62; $p = 0.09$). The taper support group achieved more than double the percent reduction in MED achieved in the usual care group at 22 weeks (43% vs 19%), although this difference also was not statistically significant ($p = 0.07$). We did not reach our target enrollment goal of 50 participants and our study was under-powered to detect even moderate to large differences in dose between groups. The differences observed between groups in our study are clinically meaningful. It will be important to determine whether these findings are replicated in a larger study with sufficient statistical power to detect meaningful differences between intervention and usual care groups.

It is of note that patients randomized to the taper support intervention, as compared with those randomized to usual care, had lower pain interference scores at 22 and 34 weeks ($p < 0.05$ and $p = 0.05$, respectively). Furthermore, those in the taper support group had significantly higher self-efficacy for managing pain and significantly lower levels of perceived opioid-related psychosocial problems (e.g., loss of interest in usual activities, trouble concentrating, feeling down or sluggish) at 22 weeks. These findings suggest that training in CBT-based pain self-management skills is effective in decreasing pain interference with activities and in increasing patients' confidence that they can manage their pain. These findings are consistent with those of other studies of CBT and CBT-based therapies for chronic pain,[10, 6,31] but the current findings extend these other studies by demonstrating these benefits while opioid doses are reduced. Our study also adds to growing

literature indicating that CBT-based therapies for pain can be provided successfully by health professionals other than psychologists.[10] To our knowledge, this is the first study demonstrating successful administration of CBT-based pain self-management training by a physician assistant, trained and supervised by clinical psychologists.

It is important to note that the opioid dose reduction in both the taper support and usual care groups was achieved without a significant increase in pain severity. In fact, pain severity decreased on average from baseline to 22 weeks by approximately 1 point on the 0–10 scale in the taper support group and approximately a half-point in the usual care group. This finding is consistent with those in studies of inpatient pain rehabilitation programs, which have documented pain reduction with opioid dose reduction.[8,30,25, 22]

There is a striking lack of previous research evaluating the efficacy of outpatient opioid dose reduction interventions. A 2013 Cochrane review of randomized trials of interventions to reduce prescription opioid dose found only two small trials (one of electro acupuncture that showed no benefit over sham and one of computerized CBT that showed benefit over usual care) and was unable to draw conclusions concerning effectiveness.[33] To our knowledge, our study is the first to suggest that opioid dose can be reduced in the outpatient setting without an increase in pain. In our clinical experience, patients' fears of dramatic increases in their pain are their primary reasons for avoiding opioid dose tapering. Furthermore, many patients report that opioid medication is "all they have" to manage pain. Thus, our findings may be reassuring to patients who are contemplating tapering their opioid dose.

Patients randomized to the opioid taper support intervention, as compared with patients randomized to usual opioid prescribing care, did not differ in levels of reported opioid misuse, depressive symptoms, or opioid control concerns at 22 and 34 weeks. Other secondary outcomes assessed, including insomnia severity, PHQ-15 somatic symptoms, and the GAD-7 anxiety scale also did not differ significantly between the taper support and usual care groups at either follow-up. However, adjusted mean differences between groups consistently favored the taper support group over usual care on measures of insomnia, somatic symptom severity, depression, and anxiety, especially at 22 weeks.

Our findings indicate the need for a larger, adequately-powered trial to evaluate the efficacy of this taper support intervention in producing clinically and statistically significant reductions in prescription opioid dose, as well as improvement on measures of other important outcomes such as pain severity, pain interference, insomnia, depression, and anxiety, among patients receiving long-term opioid therapy for chronic pain. Further research is also needed to identify patient subgroup differences associated with treatment response.

The primary barrier to feasibility of this intervention was recruiting and enrolling patients in the trial. It took three years to recruit the 35 patients who were randomized. Among 144 patients referred to the trial, only 35 were eligible and enrolled. In any future trial of an opioid taper support intervention, we believe that an enhanced engagement strategy will be necessary. For example, future trials might offer pain self-management training for patients on LtOT with an option for opioid taper. Other options include a two-stage consent

procedure whereby patients initially consent only to exploring the pros and cons of long-term opioid use and subsequently are offered an opportunity to be randomized to receiving opioid taper support or a control condition. Alternatively, randomization could occur at the clinic or provider level, with a waiver for obtaining individual patient consent.

We believe that the option to pause the taper was crucial to our ability to retain patients in the taper support intervention. Only one patient in the taper support group stopped the taper support sessions in order to increase opioid dose after experiencing increasing pain, depression, and anxiety. However, the option to pause the taper meant that some patients receiving the taper support intervention did not taper their opioid dose at all. One patient randomized to taper support attended no intervention sessions and stated that she did not want to taper her medications but enrolled in the study to please her referring doctor. Another patient randomized to taper support attended 18 treatment sessions but declined to reduce his opioid dose, explaining that he enrolled only to satisfy his prescribing doctor.

Only 13 of the 18 patients (72%) assigned to taper support received at least 80% of the sessions. Further research is needed to identify ways to increase participant engagement with and adherence to the intervention protocol. Attending sessions in person once a week was a challenge for many participants and would likely be a challenge in primary care settings. We did allow completion of up to half of the sessions by telephone. Further research is needed to examine the efficacy of telephone- or video-call-based treatment.

We excluded patients with current substance use disorders, but allowed past substance use disorders. In the Prescription Opioid Addiction Treatment Study, over 90% of patients with prescription opioid dependence who were tapered off opioids relapsed to opioid use despite adjunctive counseling during brief or extended buprenorphine-naloxone treatment.[32] This suggests that it is not appropriate to attempt complete opioid taper in patients with moderate to severe Opioid Use Disorder, even if they have used only prescription opioids. We did not use buprenorphine-assisted taper in our trial because we wanted to test a taper strategy useable by the majority of primary care providers who do not have the buprenorphine waiver. We also recruited only patients who were voluntarily tapering their opioids because we did not believe that patients being compelled to taper their opioids (for whatever reason) would engage in the taper support intervention. However, these inclusion criteria may have resulted in a misalignment of our trial with the most pressing needs in current clinical practice. Clinicians in primary and specialty care are seeking ways to reduce opioid doses and risks in patients demonstrating aberrant opioid behaviors. Many of these patients have substance use problems of various types, involving licit, illicit, and prescription drugs. A more broadly aimed and flexible opioid taper support program that can provided to these patients may be more useful to clinicians.

Our study had several limitations in addition to lack of statistical power to detect differences between groups. Neither patients nor clinicians were blinded. The generalizability of our results to other patient populations and settings is unknown. A single physician assistant delivered the intervention and the extent to which results might differ if the intervention is delivered by other clinicians is unknown. It is possible that ecological trends affecting opioid prescribing in the Seattle area influenced opioid dose reductions observed in both study

groups. However, the Washington State requirement of pain specialist consultation for patients receiving more than 120 mg of morphine or equivalent without clear improvement in pain and function was implemented in 2012, prior to the start of recruitment for this study, and we are not aware of other opioid reduction initiatives in the health systems from which the study participants were recruited.

In summary, this pilot study supports the feasibility of this opioid taper support intervention and its promise for efficacy in reducing prescription opioid doses without increases in pain intensity or pain interference. Opioid taper support thus may offer an important patient care strategy in combatting the opioid epidemic.

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Perspective

In a pilot randomized trial comparing a prescription opioid taper support intervention to usual care, lower opioid doses and pain severity ratings were observed at 22 weeks in both groups. The groups did not differ significantly at 22 weeks in opioid dose or pain severity, but the taper support group improved significantly more in pain interference, pain self-efficacy, and perceived opioid problems. These results support the feasibility and promise of this opioid taper support intervention.

Highlights

- A taper strategy for outpatients receiving long-term opioid therapy for chronic pain is needed
- Thirty-five subjects were randomized to a 22-week taper support intervention or usual care
- Subjects randomized to taper support achieved lower opioid daily doses without an increase in pain

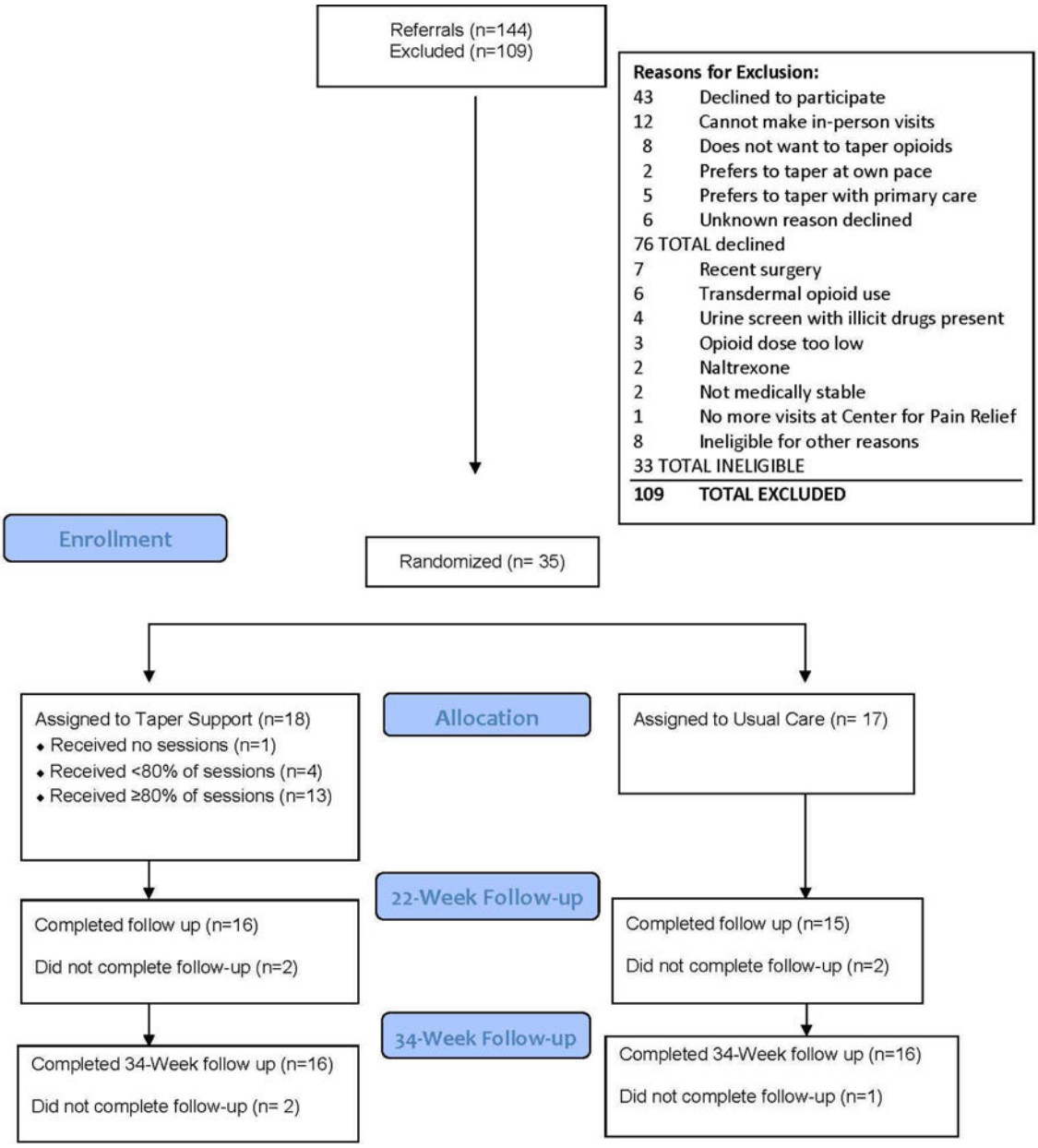

Figure 1.
Study Flow

Table 1

Opioid taper support intervention: summary of session content.

Session number	Session content
1	Motivational interviewing and engagement: elicit history of opioid use and hopes and expectations for tapering, provide education about opioid therapy, discuss and problem-solve barriers to tapering, elicit commitment to tapering
2	Overview of sessions, education regarding benefits of pain coping skills training and collaborative nature of treatment
3	Taper initiation. View and discuss video of a patient discussing opioid taper experiences. Education about withdrawal symptoms. Instruction and practice in diaphragmatic breathing. Personal action plan introduction and completion.
4	Diaphragmatic breathing review and practice. Sleep hygiene education.
5	Pain neuroscience education and rationale for managing negative thoughts, negative feelings, and stress.
6	Education regarding rationale for and benefits of relaxation techniques, instruction and practice in 7-muscle group tense-release progressive muscle relaxation.
7	Activity pacing
8	Coping with pain flare-ups
9	Diaphragmatic breathing and 4-muscle group tense-release progressive muscle relaxation practice
10	Diaphragmatic breathing and 4-muscle group progressive muscle relaxation without tensing practice
11	Coping thoughts
12	Distraction as a pain coping skill
13	Body scan
14	Mini-relaxations
15	Mini-relaxation practice; education about and discussion of harm and fear-avoidance beliefs
16	Pain coping skills review, education about importance of pleasurable activities, pleasurable activity goal-setting
17	Pain coping skills review
18	Skills summary, plan for maintaining gains and managing setbacks and pain flare-ups

Note: The first half of each 30-minute session focused on medications and symptoms; the second half focused on education and pain and symptom coping skills training. Each session included home activity assignments for reading and coping skills practice (personal action plan) and review of experiences with the previous week's assignments. Each session also included identification of obstacles or challenges to completing the home activity assignments and problem-solving ways to overcome these.

Table 2

Sample demographic, pain, and opioid therapy characteristics

	Taper Support (n=18) n (%)	Usual Care (n=17) n (%)
Age, years		
<50	4 (22.2)	4 (23.5)
50–64	7 (38.9)	9 (53.0)
65+	7 (38.9)	4 (23.5)
Gender		
Female	12 (66.7)	13 (76.5)
Male	6 (33.3)	4 (23.5)
Race and ethnicity		
White	13 (72.2)	16 (100)
Black	1 (5.6)	0
Asian	2 (11)	1 (5.6)
Native American, Alaska Native, or Pacific Islander	1 (5.6)	0
Hispanic	1 (5.6)	0
Education		
High school	2 (11.1)	4 (23.5)
Some college	8 (44.4)	8 (47.1)
College graduate	5 (27.8)	4 (23.5)
Graduate or professional school	3 (16.7)	1 (5.9)
Pain duration, years		
<10	4 (22.2)	7 (43.8)
10 – <20	9 (50.0)	5 (31.2)
20+	5 (27.8)	4 (25.0)
Opioid therapy duration, years		
<0.5	0	0
0.5 – <1	3 (16.7)	1 (6.3)
1 – <10	5 (27.8)	8 (50.0)
10 – <15	4 (22.2)	3 (18.7)
15+	6 (33.3)	4 (25.0)
Opioid daily dose, past week (MED)		
< 50 mg	5 (27.8)	1 (5.9)
50–<200 mg	7 (38.9)	11 (64.7)
200–<500 mg	4 (22.2)	3 (18.7)
500 – <1000 mg	1 (5.6)	1 (5.9)
≥1000 mg	1 (5.6)	1 (5.9)
Since starting opioids, have you tried to stop taking opioids altogether?		
No	10 (55.6)	11 (64.7)
Yes	8 (44.4)	6 (35.3)

	Taper Support (n=18) n (%)	Usual Care (n=17) n (%)
Since starting opioids, have you tried to reduce your opioid dose?		
No	4 (22.2)	3 (17.7)
Yes	14 (77.8)	14 (82.3)
What are your goals for opioid taper?		
Opioid discontinuation	12 (67)	11 (65)
Opioid dose reduction	6 (33)	6 (35)

Note. One patient in the usual care group had missing information on race, ethnicity, pain duration, and opioid therapy duration.

MED, morphine-equivalent dose

Table 3

Primary and Secondary Outcomes by Intervention Group: Observed (unadjusted) means (SD) and adjusted (for baseline values) mean differences between groups

	Taper Support (n=18) Mean (SD)	Usual Care (n=17) Mean (SD)	Adjusted mean difference	95% CI		p-value
MED /day						
Baseline	207.17 (269.38)	245.19 (347.35)				
22 weeks	111.94 (153.63)	169.85 (201.31)	−42.90	−92.42	6.62	0.09
34 weeks	99.51 (151.99)	138.24 (155.85)	−26.71	−83.04	29.62	0.34
Proportion change from baseline in MED/day						
Baseline						
22 weeks	−0.43 (0.36)	−0.19 (0.41)	−0.25	−0.52	0.02	0.07
34 weeks	−0.52 (0.34)	−0.31 (0.49)	−0.22	−0.52	0.08	0.14
BPI Pain Severity (0–10)						
Baseline	5.68 (1.36)	6.26 (1.49)				
22 weeks	4.72 (1.62)	5.77 (1.92)	−0.68	−2.01	0.64	0.30
34 weeks	4.67 (1.79)	6.16 (2.64)	−0.91	−2.30	0.48	0.19
BPI Interference (0–10)						
Baseline	6.03 (1.88)	6.60 (2.36)				
22 weeks	4.55 (2.39)	6.38 (2.11)	−1.39	−2.78	−0.01	0.049
34 weeks	4.49 (2.08)	6.05 (2.72)	−1.21	−2.43	0.02	0.05
Pain Self-efficacy (PSEQ)						
Baseline	30.56 (10.98)	31.94 (8.52)				
22 weeks	36.13 (12.21)	30.00 (13.87)	7.86	1.22	14.50	0.02
34 weeks	35.25 (13.92)	29.75 (16.64)	7.26	−2.14	16.66	0.13
Opioid Problems (PODS)						
Baseline	12.72 (10.97)	12.00 (10.47)				
22 weeks	2.94 (3.89)	7.53 (6.69)	−4.90	−8.40	−0.80	0.02
34 weeks	3.44 (5.54)	9.25 (10.23)	−4.74	−10.13	0.64	0.08
Opioid Concerns (PODS)						
Baseline	11.56 (6.27)	13.25 (6.15)				

	Taper Support (n=18) Mean (SD)	Usual Care (n=17) Mean (SD)	Adjusted mean difference	95% CI		p-value
22 weeks	10.00 (7.30)	11.47 (6.91)	0.16	−3.74	4.06	0.93
34 weeks	10.00 (8.00)	10.75 (7.26)	1.62	−3.27	6.51	0.50
Opioid craving						
Baseline	1.56 (2.71)	3.41 (2.85)				
22 weeks	0.88 (2.28)	1.60 (2.97)	−0.36	−2.42	1.69	0.72
34 weeks	0.81 (1.05)	1.69 (2.36)	−0.46	−1.93	1.00	0.52
Opioid misuse (POMI)						
Baseline	1.00 (1.08)	1.24 (1.09)				
22 weeks	0.56 (1.03)	0.67 (1.11)	0.08	−0.58	0.75	0.80
34 weeks	0.63 (0.96)	0.88 (1.09)	0.06	−0.45	0.57	0.81
Insomnia severity (ISI)						
Baseline	15.56 (7.52)	17.12 (6.62)				
22 weeks	12.44 (6.44)	16.80 (7.14)	−3.13	−7.22	0.96	0.13
34 weeks	13.38 (6.74)	15.50 (7.11)	−1.19	−5.49	3.11	0.58
Somatic symptoms (PHQ-15)						
Baseline	10.22 (4.41)	12.35 (4.44)				
22 weeks	9.81 (5.28)	12.80 (4.55)	−1.47	−4.72	1.78	0.36
34 weeks	10.31 (3.30)	11.38 (4.47)	−0.43	−3.33	2.47	0.76
Depression (PHQ-9)						
Baseline	12.56 (8.33)	12.29 (6.93)				
22 weeks	8.88 (7.49)	11.27 (6.58)	−2.21	−6.62	2.21	0.32
34 weeks	9.00 (5.80)	11.13 (7.53)	−1.89	−6.23	2.44	0.38
Anxiety (GAD-7)						
Baseline	8.39 (7.18)	8.82 (7.34)				
22 weeks	5.94 (5.59)	9.07 (7.31)	−2.73	−5.99	0.53	0.10
34 weeks	6.00 (4.38)	8.75 (6.97)	−2.39	−5.79	1.01	0.16

CI: confidence interval; MED: morphine-equivalent dose; BPI: Brief Pain Inventory; PODS: Prescription Opioid Difficulties Scale; POMI: Prescription Opioid Misuse Index; PSEQ: Pain Self-Efficacy Questionnaire; ISI: Insomnia Severity Index; PHQ: Patient Health Questionnaire; GAD: Generalized Anxiety Disorder.

Missing data are as follows: 1 patient had missing information on MED at 22 weeks and 34 weeks; 4 patients and 3 patients had missing information on the BPI, Craving, POMI, PSEQ, ISI, PHQ-15, and PHQ-9 measures at 22 weeks and 34 weeks, respectively; information was missing for the PODS for n=1 at baseline, n=4 at 22 weeks, and n=3 at 34 weeks; and information was missing for the GAD-7 for n=5 at 22 weeks and n=3 at 34 weeks.