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Changes in pain intensity after discontinuation of long-term opioid therapy for chronic noncancer pain

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Abstract

Little is known about changes in pain intensity that may occur after discontinuation of long-term opioid therapy (LTOT). The objective of this study was to characterize pain intensity after opioid discontinuation over 12 months. This retrospective U.S. Department of Veterans Affairs (VA) administrative data study identified N = 551 patients nationally who discontinued LTOT. Data over 24 months (12 months before and after discontinuation) were abstracted from VA administrative records. Random-effects regression analyses examined changes in 0 to 10 pain numeric rating scale scores over time, whereas growth mixture models delineated pain trajectory subgroups.

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Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at <http://links.lww.com/PAIN/A600>.

Supplemental video content

Video content associated with this article can be found online at <http://links.lww.com/PAIN/A601>.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Conflict of interest statement

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Mean estimated pain at the time of opioid discontinuation was 4.9. Changes in pain after discontinuation were characterized by slight but statistically nonsignificant declines in pain intensity over 12 months after discontinuation ($B = -0.20$, $P = 0.14$). Follow-up growth mixture models identified 4 pain trajectory classes characterized by the following postdiscontinuation pain levels: no pain (average pain at discontinuation = 0.37), mild clinically significant pain (average pain = 3.90), moderate clinically significant pain (average pain = 6.33), and severe clinically significant pain (average pain = 8.23). Similar to the overall sample, pain trajectories in each of the 4 classes were characterized by slight reductions in pain overtime, with patients in the mild and moderate pain trajectory categories experiencing the greatest pain reductions after discontinuation ($B = -0.11$, $P = 0.05$ and $B = -0.11$, $P = 0.04$, respectively). Pain intensity after discontinuation of LTOT does not, on average, worsen for patients and may slightly improve, particularly for patients with mild-to-moderate pain at the time of discontinuation. Clinicians should consider these findings when discussing risks of opioid therapy and potential benefits of opioid taper with patients.

Keywords

Chronic noncancer pain; Prescription opioid discontinuation; Pain intensity; Veterans; Long-term opioid therapy

1. Introduction

U.S. epidemiologic data characterize rising trends in opioid prescribing nationally from the early 1990s through 2012 with subsequent modest year-over-year declines from 2013 through 2016.^{11,26} Declining rates of overall and unsafe opioid prescribing are the result of fewer new opioid initiations and, in large part, discontinuation of existing opioid therapy.²⁰ Although prescription opioids have demonstrated short-term efficacy in placebo-controlled clinical trials at reducing pain intensity in patients with some chronic pain conditions,¹ little evidence exists for their efficacy beyond 3 months,² and even less is known about changes in pain after discontinuation of long-term opioid therapy (LTOT).

For patients with chronic pain, pain intensity may follow distinct trajectories over time.^{4,9,17,29} Results from a recent systematic review of pain trajectories in patients with low back pain found that, overall, chronic low back pain is characterized by slight reductions in pain after initial presentation for treatment in ambulatory outpatient settings, followed by stable levels of pain over time.¹⁷ A minority of patients (<15%) have pain characterized as fluctuating over time. Notably, within-patient variability of pain scores over time is high, with scores for some patients fluctuating across the entire 0 to 10 pain intensity numeric rating scale (NRS).⁹ These findings have been extended to other chronic musculoskeletal pain conditions including knee and hip pain, and over continuous longitudinal follow-up of 5 to 6 years.^{4,29}

Despite evidence that chronic pain, on average, remains consistent overtime, few studies have examined pain trajectories after important therapeutic changes to patients' pain management plans, such as tapering or discontinuing prescription opioid therapy. A recent systematic review examined patient outcomes after interventions aimed to taper or

discontinue LTOT.¹⁰ Thirty-six studies, the majority (n = 28) of which were rated as “poor” quality observational studies, assessed pain intensity outcomes. In the 8 studies rated at least “fair” quality based on U.S. Preventive Services Task Force rating criteria, interventions for tapering or discontinuing LTOT resulted in overall reductions in pain intensity.

Interventions, however, were predominantly specialty multidisciplinary pain rehabilitation programs delivered in outpatient or inpatient settings to patients who volitionally presented with goals of tapering LTOT. Reviewed studies did not examine patient outcomes in the context of discontinuations initiated in primary care settings where the majority of LTOT prescribing decisions are made, or for patients whose discontinuation was involuntary.

The purpose of this study was to characterize trajectories of pain intensity in the year after discontinuation of LTOT among patients with chronic noncancer pain. We hypothesized that pain would remain unchanged after discontinuation of opioid therapy, after accounting for sociodemographic, clinical, and nonopioid pain treatment factors. However, pain would vary across patients, such that some would experience consistently low levels of pain, others consistently moderate pain, and others consistently severe pain.

2. Methods

Study procedures were approved by the institutional review board at the VA Portland Health Care System.

2.1. Sample selection

Data for the current study were obtained from a research project where the goal was to examine reasons for discontinuation of LTOT between patients with and without substance use disorders (SUDs) based on a comprehensive electronic health record review.²⁰ Data were collected from the VA Corporate Data Warehouse (CDW), a collection of relational databases containing national VA patient electronic health record data, including demographic characteristics, clinical diagnoses, treatment utilization, pharmacy, and other data. We used the CDW to identify a national cohort of VA patients prescribed continuous opioid therapy in 2011, allowing for gaps of up to 30 days between prescription opioid fills to account for delayed scheduled refills due to travel, prescription mail order delays, or other circumstances. The average number of days prescribed opioids in the year before discontinuation in this sample was 351 of 365 days. Patients were included in our study if they discontinued opioid therapy for at least 12 consecutive months beginning in 2012. We defined an index discontinuation date as the last date of a prescription opioid pharmacy fill. Patients were excluded if they received opioid agonist therapy for opioid use disorder (ie, buprenorphine or methadone maintenance therapy), had cancer diagnoses (other than non-melanoma skin cancer), or surgeries in the 12 months before discontinuation. We also excluded patients with no VA contact or who died in the 12 months after opioid discontinuation because our goal was to evaluate pain intensity scores for 1 year after discontinuation.

A total of 7247 patients met our criteria for discontinuation of LTOT. Of these, 1868 patients had an SUD diagnosis documented in the electronic health record in the 12 months before discontinuation, whereas 5379 patients did not. We randomly sampled 300 patients with an

SUD diagnosis and propensity score-matched 300 patients without an SUD diagnosis. Details about the matching procedures have been described, along with the parent study method description and sample characterization.²⁰

2.2. Data sources and study variables

2.2.1. Administrative data—The primary outcome of interest for this study was current pain intensity, as measured by the NRS score where 0 = “no pain” and 10 = “worst possible pain.” Numeric rating scale pain ratings are assessed in VA as part of routine clinical care along with other vital signs obtained from patients during outpatient and inpatient encounters. Numeric rating scale pain scores collected as part of routine clinical care have been shown to be moderately correlated with NRS pain scores obtained by trained research staff.^{12,15,19} For the current study, we obtained NRS pain scores over 24 months for each patient (12 months before discontinuation of opioid therapy through 12 months after discontinuation). We excluded pain scores for which multiple scores were recorded on a single day, as this may be indicative of multiple same-day appointments for acute conditions associated with above-average pain ratings for an individual.⁶

Additional data were abstracted from the CDW for the 12 months before discontinuation of LTOT for use in our descriptive and multivariable analyses as prespecified model covariates. These variables were selected based on their associations with longitudinal pain trajectories in previous studies.^{9,17,29} Demographic characteristics included age, sex, and race/ethnicity. Medical comorbidities were obtained and used to compute an Elixhauser Comorbidity Index score for each patient, where higher scores indicate a greater number of comorbidities.⁸ VHA service-connected disability status, which is disability granted to veteran patients as a result of military service-related injuries or traumas, was also obtained. Other diagnoses included mental health disorders (depressive disorder, bipolar disorder, posttraumatic stress disorder, other anxiety disorders, and psychotic disorders), SUDs, and chronic pain-related diagnoses. We also computed patients’ average daily dose of opioids in milligrams of morphine equivalents for the year before opioid discontinuation by summing the total milligrams of morphine equivalents over the year and dividing by the number of days a patient was prescribed opioids, which could be fewer than 365 days if a patient had gaps between prescription opioid fills.²¹

2.2.2. Electronic health record review—A trained research associate experienced with reviewing and coding VA electronic health records for opioid- and pain-related studies performed all record reviews. Additional details about the training and quality assurance procedures are described in the parent study.²⁰ Review of patients’ electronic health records identified patient reasons (15% of the sample) and clinician reasons (85% of the sample) for discontinuation of opioid therapy. Discontinuations were coded as patient-initiated when the patient requested to be discontinued from opioids due, for example, to opioid-related side effects, ineffectiveness of opioids at managing pain, preference for the use of nonopioid pain treatments, and concern about developing addiction to opioids. Clinician-initiated discontinuations were not requested by the patient. Rather, the initial decision was made by the clinical team to discontinue opioid therapy. We were unable to ascertain from the electronic health record the extent to which clinician-initiated tapers involved patients in a

collaborative decision-making process. The majority of clinician-initiated discontinuations were due to patients engaging in aberrant behaviors (75%) such as abuse of opioids or other substances as determined by urine toxicology screen, opioid diversion, and other opioid misuse behaviors (eg, obtaining opioids from multiple sources, repeatedly requesting early opioid refills). Patients could be coded as having multiple patient- or clinician-initiated discontinuation reasons (eg, a patient may have been discontinued due to an aberrant urine toxicology screen and for safety concerns after an opioid overdose). However, no patients in this sample had documentation in the medical record suggesting that both the patient and clinician simultaneously initiated conversations leading to discontinuation of opioid therapy. Thus, all reasons for discontinuation for each patient were classified as either patient-initiated or clinician-initiated in this sample.²⁰

2.3. Statistical analyses

This investigation focused on pain score trajectories for 1 year after opioid discontinuation. We used random-effects growth modeling²⁴ to capture and quantify both fixed and random effects of pain intensity at the time of discontinuation (ie, the model intercept, which estimates pain at the time of opioid discontinuation) and change in pain over time (ie, the model slope, which characterizes the trajectory of pain intensity over 12 months after discontinuation). Notably, pain at the time of discontinuation (ie, the model intercept) is an estimate based on the trajectory of an individual's pain scores over the entire postdiscontinuation period and does not necessarily represent an actual pain score measured at the time of discontinuation. Although several types of change were explored for the 12-month postdiscontinuation period of observation—including quadratic, cubic, and piecewise change—a linear model for change in pain over time fit the data best based on the Bayesian Information Criterion (BIC) and parsimony of model parameters.¹³ We report estimates of change in pain over time in monthly intervals for ease of interpretation (ie, beta coefficients represent estimated change in pain score per month). However, to most accurately capture pain score changes overtime, we used all individual pain scores rather than computing monthly pain score averages when more than one pain score was available within a month, as has been suggested in previous studies.⁶ This makes optimal use of all the available data and allowed us to explore within-patient variability in pain scores, which has been shown to be high in patients with chronic pain⁹ and represents clinically meaningful information about patients' pain intensity experiences. We regressed both random effects (intercept and slope) onto the same set of prespecified covariates that have been shown to be associated with longitudinal pain trajectories,^{9,17,29} adding a block of covariates with each step. All covariates were measured over the 12 months before opioid discontinuation. The models, at each step, included (1) patient demographic characteristics; (2) VA service-connected disability status, medical comorbidities as measured by the Elixhauser Comorbidity Index score, number of pain diagnoses, average NRS pain score and average daily opioid dose in milligrams of morphine equivalents in the 12-month prediscontinuation period, and mental health and SUD diagnoses; (3) nonpharmacologic pain treatment utilization, including number of specialty pain clinic, rehabilitation medicine (including physical therapy), and occupational therapy encounters; and (4) reason for discontinuation of opioid therapy coded as patient-initiated vs clinician-initiated discontinuation.

After this initial model was fit, we used growth mixture modeling to examine our second hypothesis concerning the possibility of multiple subgroups, or “classes,” of pain score levels at the time of discontinuation and over the subsequent 12 months. Mixture modeling is an increasingly used approach for identifying trajectory subgroups within a given sample.^{18,22} For the current investigation, we examined a 1- through 6-class solution and compared the relative fit using the BIC, as this has been repeatedly shown to be the best measure of nonnested model fit.²⁵ When using the BIC, both in this analytic situation and in our original modeling approach, smaller BIC indicates better fit.^{22–24,27} In all models, both the intercept and the linear slope random effects were regressed onto the same full list of covariates.

We set our alpha threshold at $P < 0.05$ to determine statistical significance, and all regression coefficients are reported in unstandardized format. All analyses were conducted in Mplus 7.2²⁴ and we used robust maximum likelihood to estimate model parameters.

3. Results

A total of 551 out of the 600 patients in this sample had valid pain intensity scores that were included in analyses. Similar to the general VA population of patients prescribed LTOT, patients were, on average, 55 years old, predominantly male (95%), and non-Hispanic white (71%). By design, approximately half of the patients (51%) had an SUD diagnosis and 61% had one or more mental health diagnoses. Eighty-seven percent of patients were diagnosed with chronic musculoskeletal pain, 6% with neuropathic pain, and 11% with headache pain, including migraine. Average daily dose of opioids in milligrams of morphine equivalents was 75.76. Table 1 provides additional descriptive statistics for the sample.

3.1. Pain at the time of opioid discontinuation

The unadjusted estimated average pain score at the time of opioid discontinuation was 4.90 (on the 0–10 NRS pain intensity measure); this value represents the estimated level of pain averaged across the entire sample at the time of discontinuation. However, variability about this intercept was high (SD of 2.19 on the NRS measure, $P < 0.01$), suggesting that estimated pain scores at the time of discontinuation varied widely between patients. Table 2 represents the covariate effects on estimated pain at the time of discontinuation. The average pain score reported by a patient before discontinuation was a significant predictor of pain at the time of discontinuation, with an effect of $B = 0.60$ ($P < 0.01$) in the final, fully adjusted model (Table 2, model 4). This indicates that higher prediscontinuation pain levels were associated with higher pain levels at the time of opioid discontinuation. In addition, patients who discontinued opioid therapy of their own volition (vs being discontinued by the opioid-prescribing clinician) had significantly lower pain immediately after discontinuation of LTOT ($B = -1.15$, $P < 0.01$ in the fully adjusted model; Table 2, model 4). No other covariate effects were associated with pain scores immediately after opioid discontinuation across any of the 4 models analyzed.

3.2. Longitudinal changes in pain after discontinuation of opioid therapy

The unadjusted linear slope describing the 12-month postdiscontinuation pain trajectory was -0.07 points ($P < 0.01$), indicating that pain scores decreased, on average across all patients,

by approximately one-tenth of a point on the NRS per month for the year after opioid discontinuation. Table 3 presents the covariate effects on the linear slope of pain in the 12 months after opioid discontinuation. Similar to pain scores at the time of discontinuation, patients' average prediscontinuation pain scores were significantly related to pain score slope after LTOT discontinuation across all the reported models, with an effect of $B = -0.02$ ($P = 0.03$), in the final, fully adjusted model. This indicates that the higher an individual's average pain before discontinuation, the less reduction in pain the patient experienced over time after opioid discontinuation. No other covariates were associated with change in pain across the 12-month postdiscontinuation period. In the final, fully adjusted model, the average estimated change in pain per month over the year after discontinuation was $B = -0.20$ ($P = 0.14$), but this value did not significantly differ from zero. In other words, after controlling for patient demographic, clinical, and pain treatment utilization variables, average pain scores did not significantly change over the 12 months after LTOT discontinuation.

3.3. Examining within-patient variability in pain scores over time

In unadjusted and covariate-adjusted models that examined the change in pain over time, little variability about the slope was observed ($B = 0.02$, $P = 0.35$ for the unadjusted model; $B = 0.01$, $P = 0.15$ for the fully adjusted model). These data indicate that a fixed linear slope is an accurate estimate, on average, of the pain score trajectory for all patients in this sample. In addition, within-patient variability in pain scores over time was high. Figure 1 is a representation of the within-individual spread in pain scores for the 12 months before LTOT discontinuation and 12 months after LTOT discontinuation. One can readily observe that the average mean, minimum, and maximum reported pain scores in these 12-month intervals are very similar in the year before discontinuation when compared with the year after discontinuation, with an average spread of more than 4 points on the NRS in both the prediscontinuation and postdiscontinuation period. This indicates that not only do pain scores remain relatively stable over time, but the average within-patient variability remains relatively large and stable and is characterized by wide-ranging reports of pain by individual patients.

3.4. Mixture modeling to identify pain trajectory subgroups

Given wide variability in estimated pain scores between patients at the time of opioid discontinuation, we examined pain trajectory mixture models that estimated several multigroup solutions (1 through 6, as noted above; see online supplemental Table 1 for model fit statistics; available at <http://links.lww.com/PAIN/A600>). Using the BIC, we identified the 4-group model as the best fitting model on balance with clinical interpretability. As shown in Figure 2, the 4 groups were as follows: group 1: subclinical pain (30% of the sample; unadjusted average pain at discontinuation = 0.37); group 2: mild clinically significant pain (16%; unadjusted average pain = 3.90); group 3: moderate clinically significant pain (27%; unadjusted average pain = 6.33); and group 4: severe clinically significant pain (27%; unadjusted average pain = 8.23). Similar to the overall sample, pain trajectories in each of the 4 classes were characterized by slight reductions in pain over time, with patients in the mild and moderate pain trajectory categories experiencing the greatest pain reductions after discontinuation. Adjusted mean pain scores at

the time of discontinuation and associated slopes after controlling for prespecified covariates were similar (see Online Supplemental Table 2, available at <http://links.lww.com/PAIN/A600>).

3.5. Sensitivity analyses for pain at the time of discontinuation and pain trajectories

We conducted 3 sensitivity analyses. First, patients contributed varying numbers of pain scores to the data set, ranging from a single pain score to as many as 48 pain scores. In primary analyses, we used robust maximum-likelihood procedures to model the pain intercept and slope, including all available pain intensity score data for all patients in these models. We conducted a sensitivity analysis in which we only included patients with 2 or more valid pain scores (>99% of the sample) in the postdiscontinuation period, the minimum number of pain scores required to fit a linear slope for each patient. Unadjusted and covariate-adjusted models for the pain score intercept, single slope, and parallel slopes models were unchanged.

A second sensitivity analysis modeled patients' pain score trajectories over the entire 24-month evaluation period, including a "knot" at the point of discontinuation that resulted in two 12-month linear "splines" or segments: one for the prediscontinuation period and one for the postdiscontinuation period. This analysis allowed us to examine the possibility of sudden changes in pain scores after discontinuation, which would be characterized by an abrupt shift in (1) pain intensity immediately after discontinuation or (2) the slope of the pain trajectory in the postdiscontinuation period. In this piecewise model, pain scores increased slightly on a per month basis in the 12 months leading up to discontinuation ($B = 0.03$, $P = 0.02$) and decreased slightly over the 12 months after discontinuation ($B = -0.07$, $P < 0.01$). Notably, spikes or drops in patients' pain immediately after discontinuation or shifts in pain trajectories from the prediscontinuation period to the postdiscontinuation period were not observed. These data support findings from primary analyses and point to subtle, not drastic, changes in pain score trajectories after opioid discontinuation.

Third, we defined an opioid discontinuation index date as the date patients filled their last VA opioid prescription. The majority of patients were prescribed 28- or 30-day supplies of opioids, with remaining patients being prescribed fewer than 28 days of opioids for their final prescription. In this final sensitivity analysis, we modeled 11 months of postdiscontinuation pain intensity, starting 30 days after the index date (ie, the point at which patients in this sample would have run out of VA-prescribed opioids). Unadjusted models for the pain score intercept, single slope, and parallel slopes models were unchanged. Two differences in covariate-adjusted models of the single-slope pain trajectory sensitivity analysis were observed: prediscontinuation average pain intensity was not associated with postdiscontinuation pain ($B = -0.02$, $P = 0.07$) and having a psychotic disorder diagnosis was associated with less improvement in pain overtime ($B = -0.15$, $P = 0.05$). See Online Supplement 3 for covariate-adjusted models of the pain score intercept, single slope, and parallel slopes models for this sensitivity analysis (available at <http://links.lww.com/PAIN/A600>).

4. Discussion

In the current investigation of potential changes in pain intensity after discontinuation of LTOT, we found that although patients differed in the intensity of pain they experienced after discontinuation, as a whole, they evidenced relatively stable average pain levels over 12 months after discontinuation. However, pain intensity differed between patients, with some experiencing subclinical levels of pain and others experiencing mild, moderate, or severe pain warranting clinical attention. Notably, postdiscontinuation pain intensity varied widely within patients, ranging, on average, more than 4 points on the NRS pain intensity measure. The wide range of pain scores reported by patients in the postdiscontinuation period was similar to the range of scores reported by patients in the prediscontinuation period. These findings are consistent with previous research studies characterizing pain intensity in patients with various chronic musculoskeletal pain conditions.^{4,9,14,17,29} Study results suggest that patients may experience fluctuations in pain intensity after discontinuation of LTOT, similar to what they experience while on opioids, but on the whole, average pain intensity does not significantly worsen in the 12 months after discontinuation, and for some patients may in fact improve. This finding complements results from a randomized controlled trial of 240 veterans with chronic back pain or hip or knee osteoarthritis pain that found patients randomized to receive opioid therapy fared no better than patients randomized to receive nonopioid analgesic pharmacotherapy in pain-related function at 12-month follow-up and had worse pain intensity and more adverse medication-related side effects,¹⁶ further suggesting that the benefit of LTOT for chronic pain may be limited.

Average pain intensity before opioid discontinuation predicted pain intensity immediately after discontinuation and change in pain over time. This held true when controlling for a variety of prespecified covariates, including demographic characteristics, comorbid medical diagnoses, and pain treatment utilization. Specifically, higher pain before discontinuation suggests that patients will experience few, if any, changes in pain intensity after discontinuation of opioid therapy. These patients may require more comprehensive interdisciplinary pain rehabilitation programs that emphasize improvements in function and overall quality of life, rather than emphasizing reductions in pain intensity as a primary objective.¹¹

Pain intensity NRS scores in the current study were collected as part of routine clinical care, unlike the preponderance of studies that have examined longitudinal pain scores collected as part of research activities.^{4,9,17,29} Although previous research studies have shown moderate correlations between pain intensity scores collected in clinical settings and those collected as part of research,^{12,15,19} with correlations ranging from 0.56 to 0.63, these by no means represent perfect or even near-perfect associations. Indeed, some research has found that pain intensity NRS scores collected in clinical practice are systematically lower than pain assessed through more comprehensive measures of pain intensity and interference such as the Brief Pain Inventory.¹² Despite limitations of the NRS pain intensity measure, it continues to be the most common assessment of pain in routine clinical care across many large health care systems such as the VA.

Our findings also have significant clinical implications for the ways in which opioid discontinuation processes and conversations take place between patients and clinicians. Current opioid treatment guidelines for chronic noncancer pain discourage initiation of opioid therapy and suggest limits to its duration when used to treat chronic pain.^{7,28} Our data suggest that patients who discontinue opioid therapy will not experience worse pain; rather, their pain will remain similar or slightly improve, on average, relative to their levels of pain before discontinuation, and they will experience wide variability to their pain, similar to their experience while on prescription opioids. In addition, previous studies indicate that pain intensity may further improve when patients receive multidisciplinary pain care as part of the opioid taper and discontinuation process.¹⁰ These data can aid clinicians during discussions about opioid discontinuation with patients.

It is important to note that pain intensity is but one important patient outcome that should be considered when evaluating the impact of opioid discontinuation. We did not evaluate pain interference or quality of life in this study, both of which have been identified as important outcomes when evaluating patients' well-being in the context of opioid therapy.¹⁰ In addition, some patients may experience onset or exacerbation of mental health and SUD symptoms after opioid discontinuation. Recent empirical findings associate increased rates of heroin overdose with trends to reduce opioid prescription, suggesting that some patients with opioid use disorder may be substituting a "street drug" for prescription opioid medications.³ Others have described high rates of suicidal ideation and suicide attempts after discontinuation of prescription opioid therapy,⁵ whereas still others note that up to 20% of patients receiving care within a single health care system disengage from medical services once discontinued from opioids.²⁰ Unintended negative consequences of opioid discontinuation should not be underestimated, and clinicians must carefully weigh risks and benefits to individual patients when considering an opioid taper.

This study has several limitations. First, the sample included VA patients with an SUD and matched controls, and the results may not generalize to the broader population of VA or non-VA patients who discontinue opioid therapy. Second, we were unable to ascertain the extent to which patients may have been prescribed opioids, opioid agonist treatments (ie, methadone maintenance or buprenorphine), or used other nonopioid treatments outside the VA in the preopioid discontinuation or postopioid discontinuation periods, although all patients did remain enrolled in VA care for the full year after discontinuation of LTOT. Third, the available data did not permit us to treat nonpharmacologic pain treatment encounters as time-varying covariates in statistical models because we did not possess the exact date of postdiscontinuation pain treatment encounters. We instead included prediscontinuation pain treatment utilization to ensure that pain treatments preceded postdiscontinuation pain scores that were the focus of the primary analyses. Future research should identify specific nonopioid pain treatments that are of greatest benefit to patients who discontinue LTOT. Fourth, we did not obtain VA data on nonopioid analgesic pharmacotherapy in the prediscontinuation period and were thus unable to control for this form of pain treatment in statistical models. Finally, functioning and quality of life are not systematically assessed in VA administrative databases and thus are not available for analysis. These are important patient outcomes and future studies should longitudinally assess these constructs in the context of opioid discontinuation.

In conclusion, this study provides some of the first empirical evidence that pain intensity remains largely unchanged after discontinuation from LTOT under usual care. Clinicians should consider these findings when discussing with patients the risks of opioid therapy, as well as potential outcomes of opioid tapering. As the medical culture shifts away from prescribing opioid therapy for chronic noncancer pain, a growing number of patients currently prescribed LTOT will experience opioid discontinuation. It is recommended that clinical care teams provide patients who discontinue opioid therapy with appropriate education and nonopioid pain treatment options that incorporate multidisciplinary team approaches to ensure that patients' pain and psychosocial needs are adequately managed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Prediscontinuation *Postdiscontinuation*

0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8 8.5 9 9.5 10
0-10 Numeric Rating Scale Pain Intensity Score

Figure 1.

Average within-individual pain intensity numeric rating scale score medians, minimums, maximums, and interquartile ranges during the prediscontinuation and postdiscontinuation periods.

Figure 2.

Class-specific unadjusted pain score intercepts and slopes during the 12 months.

Table 1

Patient characteristics documented in the preopioid discontinuation period (N = 551).

Baseline characteristics	M (SD); % (N)
Age [*]	54.63 (10.96)
Male sex	94.74% (522)
Race	
White, non-Hispanic	71.14% (392)
Black, non-Hispanic	15.61% (86)
Hispanic	2.54% (14)
Other/unknown	10.71% (59)
Diagnoses, comorbidities, and other clinical variables	
VA service-connected disability	57.35% (316)
Elixhauser Comorbidity Index [†]	1.00 (1.00)
No. of pain diagnoses [*]	1.04 (0.54)
Average pain score before discontinuation [†]	4.80 (3.53)
Average morphine-equivalent daily dose of opioids, mg [*]	75.76 (88.40)
Any substance use disorder diagnosis	51.00% (281)
Depressive disorder diagnosis	24.68% (136)
Bipolar disorder diagnosis	7.26% (40)
Posttraumatic stress disorder diagnosis	31.94% (176)
Other anxiety disorder diagnosis	25.41% (140)
Psychotic disorder diagnosis	7.62% (42)
Pain treatment utilization	
Any specialty pain clinic visits	16.70% (92)
Any rehabilitation medicine visits	6.7% (37)
Any occupational therapy visits	4.5% (25)
Reasons for discontinuation of opioid therapy	
Patient-initiated discontinuation	15.43% (85)

Demographic characteristics, clinical diagnoses, medical comorbidities, and prescription information were obtained for the year before discontinuation of opioid therapy.

^{*} Mean (SD).

[†] Median (interquartile range).

Table 2

Correlates of estimated pain score at the time of long-term opioid therapy discontinuation.

Intercept covariates	Model 1, B (SE)	Model 2, B (SE)	Model 3, B (SE)	Model 4, B (SE)
Age	-0.026 (0.015)	-0.010 (0.014)	-0.012 (0.014)	-0.016 (0.014)
Sex	0.160 (0.641)	-0.359 (0.564)	-0.403 (0.564)	-0.320 (0.558)
Race	-0.136 (0.155)	-0.072 (0.134)	-0.062 (0.134)	-0.038 (0.133)
Diagnoses, comorbidities, and other clinical variables				
VA service-connected disability		-0.405 (0.304)	-0.384 (0.303)	-0.311 (0.301)
Elixhauser Comorbidity Index		-0.101 (0.111)	-0.091 (0.111)	-0.107 (0.110)
No. of pain diagnoses		-0.091 (0.269)	-0.014 (0.271)	-0.050 (0.270)
Average pain score before discontinuation		0.610(0.063) *	0.610 (0.063) *	0.604 (0.062) *
Average morphine-equivalent daily dose of opioids, mg		0.001 (0.002)	0.002 (0.002)	0.001 (0.002)
Any substance use disorder diagnosis		0.2325 (0.288)	0.363 (0.287)	0.340 (0.285)
Depressive disorder diagnosis		-0.548 (0.317)	-0.573 (0.3116)	-0.531 (0.313)
Bipolar disorder diagnosis		0.290 (0.496)	0.389 (0.500)	0.320 (0.495)
Post-traumatic stress disorder diagnosis		0.287 (0.326)	0.339 (0.326)	0.331 (0.322)
Other anxiety disorder diagnosis		-0.349 (0.307)	-0.377 (0.305)	-0.390 (0.302)
Psychotic disorder diagnosis		-0.126 (0.509)	-0.097 (0.506)	-0.157 (0.501)
Pain treatment utilization				
No. of specialty pain clinic visits			-0.026 (0.019)	-0.027 (0.019)
No. of rehabilitation medicine visits			-0.088 (0.065)	-0.090 (0.065)
No. of occupational therapy visits			-0.006 (0.015)	-0.007 (0.015)
Reasons for discontinuation of opioid therapy				
Patient-initiated discontinuation [†]				-1.154 (0.361) *

Demographic characteristics, clinical diagnoses, medical comorbidities, and prescription information were obtained for the year before discontinuation of opioid therapy.

* $P < 0.05$.[†] Reason for discontinuation of opioid therapy compares patient- to clinician-initiated discontinuation.

Table 3

Correlates of 12-month pain score trajectories after discontinuation of long-term opioid therapy.

Linear slope covariates	Model 1, B (SE)	Model 2, B (SE)	Model 3, B (SE)	Model 4, B (SE)
Age	0.002 (0.002)	0.001 (0.002)	0.001 (0.002)	0.001 (0.002)
Sex	0.065 (0.075)	0.100(0.073)	0.105(0.073)	0.106(0.073)
Race	0.007(0.019)	0.006(0.018)	0.005(0.018)	0.004(0.018)
Diagnoses, comorbidities, and other clinical variables				
VA service-connected disability		0.016(0.040)	0.011 (0.040)	0.010(0.040)
Elixhauser comorbidity index		0.008(0.014)	0.006(0.014)	-0.007(0.014)
No. of pain diagnosis		-0.008 (0.035)	-0.016 (0.035)	-0.020 (0.035)
Average pain score before discontinuation		-0.019(0.008)*	-0.019 (0.008)*	-0.018(0.008)*
Average morphine-equivalent daily dose of opioids, mg		0.000 (0.000)	0.000 (0.000)	0.000 (0.000)
Any substance use disorder diagnosis		-0.014(0.039)	-0.017 (0.039)	-0.015(0.038)
Depressive disorder diagnosis		0.077 (0.041)	0.079(0.041)	0.079 (0.041)
Bipolar disorder diagnosis		0.046 (0.071)	0.035 (0.072)	0.041 (0.072)
Post-traumatic stress disorder diagnosis		-0.047 (0.043)	-0.047 (0.043)	-0.048 (0.043)
Other anxiety disorder diagnosis		0.030 (0.040)	0.033 (0.040)	0.036 (0.040)
Psychotic disorder diagnosis		-0.056 (0.067)	-0.055 (0.067)	-0.049 (0.067)
Pain treatment utilization				
No. of specialty pain clinic visits			0.002 (0.002)	0.002 (0.002)
No. of rehabilitation medicine visits			0.011 (0.008)	0.011 (0.008)
No. of occupational therapy visits			-0.001 (0.002)	-0.001 (0.002)
Reasons for discontinuation of opioid therapy				
Patient-initiated discontinuation [†]				0.042 (0.049)

Demographic characteristics, clinical diagnoses, medical comorbidities, and prescription information were obtained for the year before discontinuation of opioid therapy.

* $P < 0.05$.

[†] Reason for discontinuation of opioid therapy compares patient- to clinician-initiated discontinuation.