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Original Article

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The effect of long-term opioid use on back-specific disability and health-related quality of life in patients with chronic low back pain

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Abstract

Context: Opioids are commonly utilized for the treatment of chronic pain. However, research regarding the long-term (≥12 months) outcomes of opioid therapy remains sparse.
Objectives: This study aims to evaluate the effects of long-term opioid therapy on measures of back-specific disability and health-related quality of life in patients with chronic low back pain.
Methods: In this retrospective cohort study, patients with chronic low back pain who reported consistent opioid use or abstinence for at least 12 months while enrolled in the Pain Registry for Epidemiological, Clinical, and Interventional Studies and Innovation Pain Research Registry were classified as long-term opioid users or nonusers, respectively. For comparison, intermediate-term and short-term opioid users and nonusers were also identified. Multiple linear regression analysis was performed to compare back-specific disability (Roland-Morris Disability Questionnaire [RMDQ]) and health-related quality of life (29-item Patient-Reported Outcomes Measurement Information System [PROMIS]) between opioid users and nonusers while controlling for pain intensity, depression, age, body mass index (BMI), and eight common comorbid conditions (herniated disc, sciatica, osteoporosis, osteoarthritis, heart disease, hypertension, diabetes, and asthma). Statistically significant findings were assessed for clinical relevance.
Results: There were 96 long-term opioid users and 204 long-term opioid nonusers. After controlling for potential confounders, long-term opioid use was a predictor of worse back-specific disability (adjusted mean difference=2.85, p<0.001), physical function (adjusted mean difference=−2.90, p=0.001), fatigue (adjusted mean difference=4.32, p=0.001), participation in social roles (adjusted mean difference=−4.10, p<0.001), and pain interference (adjusted mean difference=3.88, p<0.001) outcomes. Intermediate-term opioid use was a predictor of worse back-specific disability (adjusted mean difference=2.41, p<0.001), physical function (adjusted mean difference=−2.26, p=0.003), fatigue (adjusted mean difference=3.70, p=0.002), and sleep disturbance outcomes (adjusted mean difference=3.03, p=0.004), whereas short-term opioid use was a predictor of worse back-specific disability (adjusted mean difference=2.42, p<0.001) and physical function outcomes (adjusted mean difference=−1.90, p<0.001).
Conclusions: The findings of this study are largely consistent with existing literature regarding the outcomes of long-term opioid therapy. Taken in conjunction with the well-established risks of opioid medications, these findings draw into question the utility of long-term opioid therapy for chronic low back pain.

Keywords: chronic pain; disability; long-term opioid therapy; opioid; outcomes; quality of life.

Chronic pain affects approximately 50 million US adults, or 20.4% of the adult population [1] and incurs an economic burden greater than that of cancer and diabetes combined [2]. Pain is a complex and highly individual perceptual phenomenon [3]. In addition to physical discomfort, chronic pain can affect relationships, limit participation in social activities, and induce feelings of fear, demoralization, anxiety, and depression [3, 4]. Thus, the National Institutes of Health (NIH) Federal Pain Research Strategy recommends that pain intensity be measured in conjunction with non-pain outcomes such as physical function and health-related quality of life [3].

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This is consistent with the NIH Task Force on Research Standards for chronic low back pain, which endorses a biopsychosocial model of chronic pain [5].

Opioids are commonly utilized for the treatment of pain. Although systematic reviews have found a small beneficial effect of opioids on pain and function when utilized for short periods [6–9], research regarding long-term (≥12 months) outcomes of opioid therapy remains sparse [10]. The purpose of this retrospective cohort study was to evaluate the effects of long-term opioid therapy on self-reported measures of back-specific disability and health-related quality of life in patients with chronic low back pain.

Methods

The Pain Registry for Epidemiological, Clinical, and Interventional Studies and Innovation (PRECISION Pain Research Registry) was utilized to select patients for inclusion in this study. The registry received human subjects research approval from the North Texas Regional Institutional Review Board. All patients provided written informed consent prior to data collection. Consent and data collection were overseen by JCL and implemented by staff of the PRECISION Pain Research Registry. The registry began recruiting patients with low back pain in the Dallas-Fort Worth metroplex in April 2016 and expanded to recruit throughout the United States in January 2020. Patients enrolled in this registry provided quarterly self-reported data online regarding their low back pain and its management. Patients provided demographic information by self-report at the time of their enrollment in the registry. In 2020, data collection was terminated after 12 months of enrollment; prior to this date, patients provided quarterly data indefinitely (i.e., some patients provided data for longer than 12 months).

Inclusion criteria for this study consisted of being between 21 and 79 years of age at enrollment in the registry, self-reporting low back pain that meets the NIH case definition for chronic low back pain (low back pain for at least 3-6 months with a frequency of at least half the days in the past six months) [5], and having the ability to respond to data collection in English. The exclusion criteria consisted of being pregnant based on self-report or being institutionalized.

The patients who reported opioid use for 12 consecutive months while enrolled in the registry were classified as long-term opioid users, whereas the patients who denied opioid use for 12 consecutive months were classified as long-term opioid nonusers (Table 1). Although some patients had been enrolled in the registry for longer than 24 months at the time of this study, no patients met the criteria for being in both the long-term opioid user and long-term opioid nonuser groups during the time of their enrollment (i.e., no patients crossed over). If a patient met the criteria for their group at more than one encounter, data from the earliest encounter at which they met the criteria were utilized for analysis.

For comparison, intermediate-term and short-term opioid users and nonusers were also identified utilizing the PRECISION Pain Research Registry (Table 1). Patients who denied opioid use at one encounter and then consistently reported opioid use for at least three months but no more than six months were classified as intermediate-term opioid users. Patients who denied opioid use for 3–6 consecutive months were classified as intermediate-term opioid nonusers. If a patient met the criteria for an intermediate-term opioid user at any time, they were excluded from the intermediate-term opioid nonuser group. If a patient met the criteria for their group at multiple time-points, data from the earliest encounter at which they met the criteria were utilized for analysis. Similarly, patients who denied opioid use at one encounter and then reported opioid use in the subsequent encounter were classified as short-term opioid users. Patients who denied opioid use for one encounter were classified as short-term opioid nonusers. If a patient met the criteria for a short-term opioid user at any time, they were excluded from the short-term opioid nonuser group. If a patient met the criteria for their group at multiple time-points, data from the earliest encounter at which they met the criteria were utilized for analysis. An additional group of opioid users and nonusers for 6–12 consecutive months was not included; a preliminary identification of patients that met these criteria yielded a population size insufficient for meaningful statistical analysis.

The unadjusted means and 95% confidence intervals (CIs) of back-specific disability and health-related quality of life were calculated for both long-term opioid users and nonusers. These means were

Table 1: Identification of study groups utilizing the PRECISION Pain Research Registry.

Short-term opioid users	*Definition*: Patients who have used opioid medication for ≤3 months. *Inclusion criteria*: Patients who deny opioid use at one or more encounter(s), then report opioid use at the following encounter
Short-term opioid nonusers	*Definition*: Patients not using opioid medication at the time of encounter. *Inclusion criteria*: Patients who deny opioid use at one encounter.
Intermediate-term opioid users	*Definition*: Patients who have used opioid medication for greater than three months but no more than six months. *Inclusion criteria*: Patients who deny opioid use at one or more encounter(s), then report opioid use at the following two encounters
Intermediate-term opioid nonusers	*Definition*: Patients who have abstained from opioid medication for at least 3–6 months. *Inclusion criteria*: Patients who deny opioid use for two consecutive encounters
Long-term opioid users	*Definition*: Patients who have used opioid medication for ≥12 consecutive months. *Inclusion criteria*: Patients who report opioid use for at least five consecutive encounters
Long-term opioid nonusers	*Definition*: Patients who have abstained from opioid medication for ≥12 consecutive months. *Inclusion criteria*: Patients who deny opioid use for at least five consecutive encounters

Encounters are performed every three months. Opioid use is determined by self-report of currently using opioid medication at the time of encounter.

compared graphically. Multiple linear regression analyses of back-specific disability and health-related quality of life were then performed, comparing opioid users to opioid nonusers for each dataset (long-term, intermediate-term, and short-term). Potential confounders controlled for in this analysis included pain intensity, depression, age, body mass index (BMI), and eight common comorbid conditions (herniated disc, sciatica, osteoporosis, osteoarthritis, heart disease, hypertension, diabetes, and asthma). Because this study performed seven separate multiple linear regression analyses of each dataset, a Bonferroni correction was implemented for the determination of statistically significant findings. Thus, statistical significance for multiple linear regression analyses was set at a p-value of 0.007. Statistically significant findings were assessed for clinical relevance utilizing estimates of minimally important difference (MID) or magnitude of effect [11–16]. Statistical analysis was performed utilizing IBM SPSS Statistics version 26.

Back-specific disability was measured utilizing the Roland-Morris Disability Questionnaire (RMDQ) [17]. The RMDQ is considered a legacy measure by the NIH Task Force on Research Standards for chronic low back pain [5] and has demonstrated strong psychometric properties [18, 19]. The RMDQ scores range from 0 to 24, with higher scores indicating greater back-specific disability.

Health-related quality of life was measured utilizing six of the seven domains from the 29-item Patient-Reported Outcomes Measurement Information System (PROMIS-29), which has demonstrated reliability and construct validity [20]. These domains included sleep disturbance, pain interference with activities, anxiety, fatigue, physical function, and participation in social roles. The seventh PROMIS-29 domain, depression, was treated as a potential confounding variable instead of an outcome. Scores on the PROMIS-29 are standardized to the United States general population, with a mean score of 50 and a standard deviation of 10 [21]. Higher PROMIS scores more strongly reflect the scale descriptor (e.g., higher scores indicate better physical function but more anxiety) [20].

Pain intensity was measured utilizing an 11-point numerical rating scale (NRS) indicating the average low back pain intensity over the past seven days, ranging from 0 (no pain) to 10 (worst possible pain). The remaining variables controlled for in this analysis—age, BMI, and self-report of ever having received a diagnosis of herniated disc, sciatica, osteoporosis, osteoarthritis, heart disease, hypertension, diabetes, or asthma—utilize patient-reported data collected at the time of enrollment in the PRECISION Pain Research Registry. The comorbid conditions listed above were included in the multiple linear regression analyses as dichotomous variables.

Results

Figure 1 provides a flow diagram for the classification of patients as long-term opioid users and nonusers. Patient demographics and clinical characteristics for long-term, intermediate-term, and short-term opioid users and nonusers are presented in Table 2.

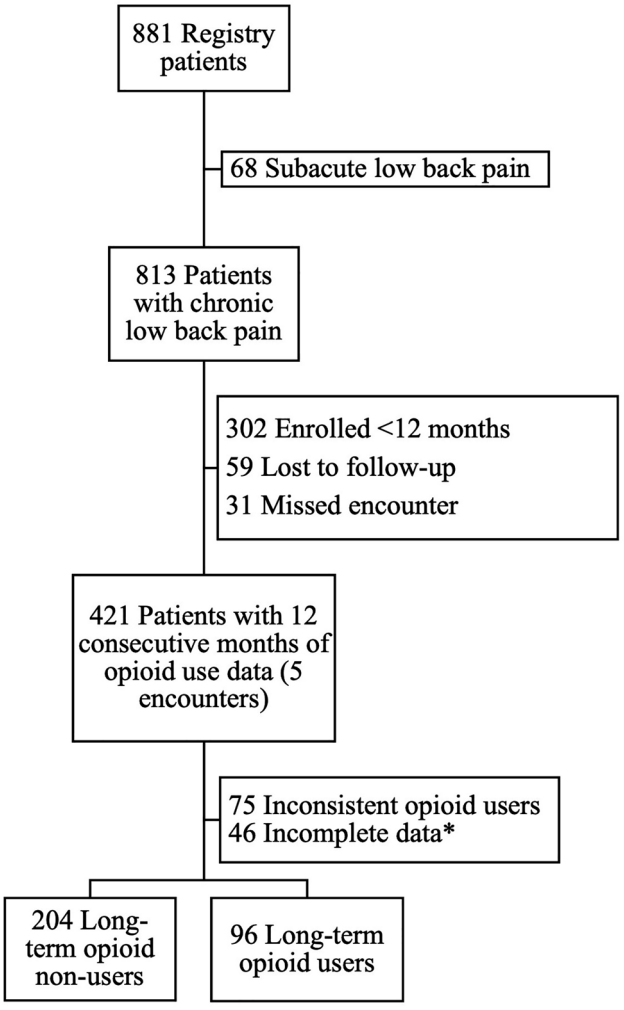

Figure 1: Flow diagram for the classification of patients as long-term opioid users and nonusers.
*Patients had incomplete data if they could only be classified as a long-term opioid user or nonuser at an encounter in which data required for analysis (e.g., PROMIS-29) were not collected.

Long-term groups

There were 96 long-term opioid users and 204 long-term opioid nonusers. Compared to long-term opioid nonusers, long-term opioid users were older and reported greater pain intensity, depression, and BMI. A greater proportion of long-term opioid users reported a history of herniated disc, sciatica, osteoporosis, osteoarthritis, hypertension, and diabetes.

Table 2: Demographic and clinical characteristics of opioid users and nonusers.

Characteristics	Long-term		Intermediate-term		Short-term	
	Opioid users (n=96)	Opioid nonusers (n=204)	Opioid users (n=70)	Opioid nonusers (n=401)	Opioid users (n=167)	Opioid nonusers (n=423)
Mean age, years (SD, range)	56.4 (10.6, 27–77)[d]	53.0 (12.9, 23–77)	53.1 (12.0, 28–76)	52.5 (13.4, 21–79)	51.9 (12.0, 21–76)	52.2 (13.7, 21–79)
Female, n (%)	69 (71.9)	146 (71.6)	50 (71.4)	288 (71.8)	120 (71.9)	299 (70.7)
Male, n (%)	27 (28.1)	58 (28.4)	20 (28.6)	113 (28.2)	47 (28.1)	124 (29.3)
Mean BMI, kg/m^2 (SD, range)	33.9 (8.2, 16.6–66.7)[d]	31.8 (7.3, 17.0–55.5)	34.3 (9.3, 20.6–63.4)	32.4 (7.8, 17.0–61.9)	34.2 (8.6, 18.4–63.4)[d]	32.1 (7.8, 15.4–61.9)
Mean pain intensity, (SD, range)[a,b]	6.7 (2.0, 2–8)[d]	5.0 (2.2.0–10)	6.5 (1.9, 2–10)[d]	5.5 (2.1, 0–10)	6.5 (2.1, 0–10)[d]	5.8 (1.9, 1–10)
Mean depression (SD, range)[a,c]	54.4 (9.6, 41.0–79.4)[d]	49.6 (9.3.41.0–79.4)	54.8 (10.2, 41.0–79.4)[d]	51.3 (9.4, 41.0–79.4)	53.1 (9.6, 41.0–79.4)	52.6 (9.5, 41.0–79.4)
Herniated disc, n (%)	46 (47.9)[d]	54 (26.5)	31 (44.3)[d]	115 (28.7)	65 (38.9)	134 (31.7)
Sciatica, n (%)	49 (51.0)[d]	51 (25.0)	24 (34.3)	153 (38.2)	53 (31.7)[d]	184 (43.5)
Osteoporosis, n (%)	20 (20.8)[d]	15 (7.4)	8 (11.4)	43 (10.7)	15 (9.0)	52 (12.3)
Osteoarthritis, n (%)	45 (46.9)[d]	54 (26.5)	19 (27.1)	137 (34.2)	49 (29.3)[d]	164 (38.8)
Heart disease, n (%)	14 (14.6)[d]	15 (7.4)	3 (4.3)	44 (11.0)	15 (9.0)	43 (10.2)
Hypertension, n (%)	52 (54.2)[d]	70 (34.3)	28 (40.0)	156 (38.9)	71 (42.5)	163 (38.5)
Diabetes, n (%)	29 (30.2)[d]	29 (14.2)	22 (31.4)[d]	63 (15.7)	50 (29.9)[d]	63 (14.9)
Asthma, n (%)	32 (33.3)	55 (27.0)	16 (22.9)	107 (26.7)	40 (24.0)	116 (27.4)

[a]Data collected at time of inclusion in the study. All others collected at time of enrollment in the registry. [b]Pain intensity measured utilizing an 11-point numerical rating scale indicating average low back pain intensity over the past seven days, ranging from 0 (no pain) to 10 (worst pain imaginable). [c]Depression measured utilizing PROMIS-29 Depression domain, with a mean score of 50 and a standard deviation of 10 in the US general population. [d]Significant between-group difference ($p<0.05$) utilizing independent samples t-test for numerical variables and Pearson chi-square test for categorical variables. BMI, body mass index; SD, standard deviation.

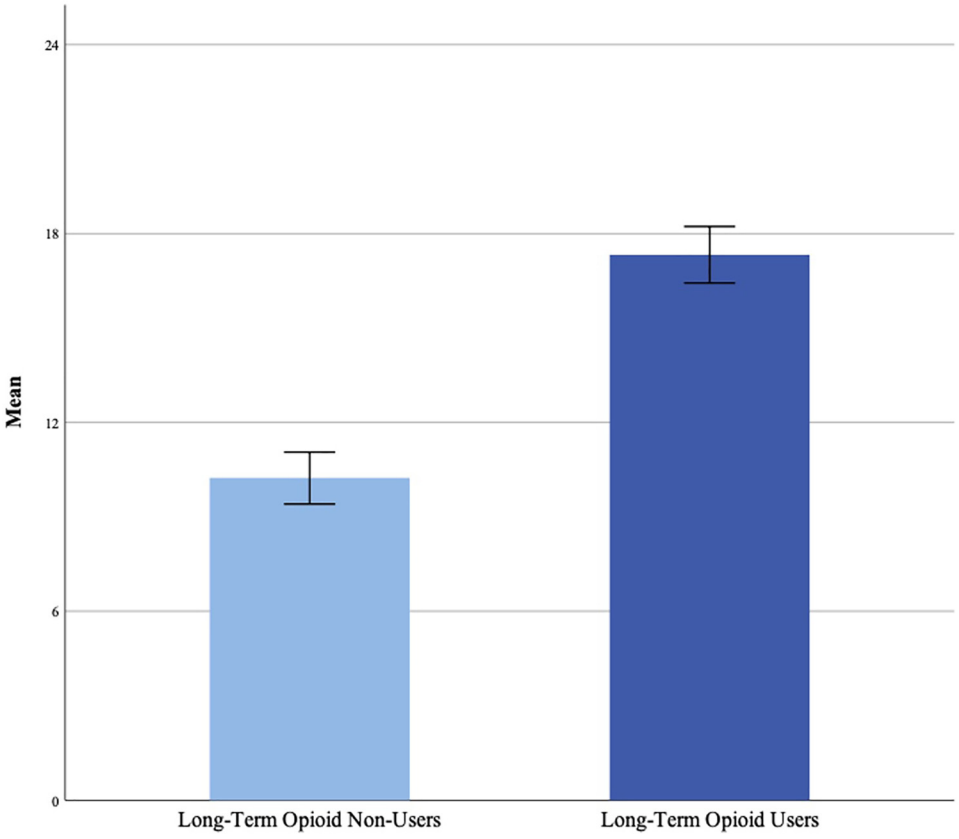

Figure 2: Measures of back-related disability (Roland-Morris Disability Questionnaire, RMDQ) for long-term opioid users and nonusers. RMDQ scores range from 0 to 24, with higher scores indicating greater back-specific disability. Error bars represent 95% confidence interval.

Intermediate-term groups

There were 70 intermediate-term opioid users and 401 intermediate-term opioid nonusers. Compared to the intermediate-term opioid nonusers, intermediate-term opioid users reported greater pain intensity and depression. In addition, a greater proportion of intermediate term opioid users reported a history of herniated disc and diabetes.

Short-term groups

There were 167 short-term opioid users and 423 short-term opioid nonusers. Compared to the short-term opioid nonusers, the short-term opioid users reported greater pain intensity and BMI. A greater proportion of short-term opioid users reported a history of diabetes, whereas a greater proportion of short-term opioid nonusers reported a history of sciatica and osteoarthritis.

Back-specific disability

The mean RMDQ score was 17.67 (95% CI=16.76–18.57) for long-term opioid users and 10.69 (95% CI=9.76–11.62) for long-term opioid nonusers (Figure 2). Upon multiple linear regression analysis (Table 3), long-term opioid use was a predictor of greater back-specific disability, with an adjusted mean difference of 2.85 ($p<0.001$). Thus, if the effects of the potential confounders accounted for in this study are held constant, a patient with chronic low back pain receiving ≥12 months of opioid therapy would be expected to report a RMDQ score 2.85 points greater than a patient who refrained from opioid therapy for at least 12 months. Intermediate- and short-term opioid use were also predictors of greater disability, with adjusted mean differences of 2.41 ($p<0.001$) and 2.42 ($p<0.001$), respectively [11]. The adjusted mean difference for long-term, intermediate-term, and short-term groups all constitute a moderate effect according to clinical practice guidelines from the American College of Physicians [11].

Table 3: Multiple linear regression analyses of back-specific disability and health-related quality of life comparing opioid users to opioid nonusers.

	Adjusted mean difference (95% CI)	Std. error	t-score	p-Value	Magnitude of effect or mid
Back-specific disability (RMDQ)					
Short-term	2.42 (1.54 to 3.30)	0.45	5.40	<0.001	Moderate effect [11]
Intermediate-term	2.41 (1.13 to 3.69)	0.65	3.70	<0.001	Moderate effect [11]
Long-term	2.85 (1.49 to 4.20)	0.69	4.13	<0.001	Moderate effect [11]
Physical function (PROMIS physical function)					
Short-term	−1.90 (−2.91 to −0.89)	0.51	−3.68	<0.001	Meets MID [12]
Intermediate-term	−2.26 (−3.73 to −0.79)	0.75	−3.01	0.003	Exceeds MID [12]
Long-term	−2.90 (−4.54 to −1.25)	0.84	−3.47	0.001	Exceeds MID [12]
Anxiety (PROMIS anxiety)					
Short-term	1.51 (0.24 to 2.77)	0.64	2.34	0.019	Does not meet MID [13]
Intermediate-term	0.47 (−1.28 to 2.22)	0.89	0.53	0.597	N/A
Long-term	−0.44 (−2.23 to 1.35)	0.91	−0.48	0.632	N/A
Fatigue (PROMIS fatigue)					
Short-term	0.72 (−0.84 to 2.28)	0.79	0.91	0.363	N/A
Intermediate-term	3.70 (1.34 to 6.07)	1.20	3.07	0.002	Meets MID [13]
Long-term	4.32 (1.81 to 6.83)	1.28	3.39	0.001	Exceeds MID [13]
Sleep disturbance (PROMIS sleep disturbance)					
Short-term	0.27 (−1.12 to 1.65)	0.70	0.38	0.707	N/A
Intermediate-term	3.03 (0.99 to 5.07)	1.04	2.92	0.004	Meets MID [13]
Long-term	2.80 (0.56 to 5.05)	1.14	2.46	0.015	Meets MID [13]
Participation in social roles (PROMIS participation in social roles)					
Short-term	−0.73 (−2.01 to 0.55)	0.65	−1.12	0.264	N/A
Intermediate-term	−2.31 (−4.20 to −0.41)	0.96	−2.40	0.017	Meets MID [13]
Long-term	−4.10 (−6.32 to −1.88)	1.13	−3.63	<0.001	Exceeds MID [13]
Pain interference with activities (PROMIS pain interference)					
Short-term	0.89 (−0.23 to 2.00)	0.57	1.56	0.119	N/A
Intermediate-term	1.92 (0.30 to 3.53)	0.82	2.33	0.020	Does not meet MID [14]
Long-term	3.88 (2.17 to 5.58)	0.87	4.47	<0.001	Exceeds MID [14]

Higher RMDQ scores indicate greater back-specific disability. Higher PROMIS scores more strongly reflect the scale descriptor (e.g., higher scores indicate better physical function but more anxiety). Statistical significance for multiple linear regression analyses was set at a p-value of 0.007. Multiple linear regression analyses performed while controlling for pain intensity, depression, body mass index, age, and history of herniated disc, sciatica, osteoporosis, osteoarthritis, heart disease, hypertension, and asthma. CI, confidence interval; MID, minimally important difference; PROMIS, patient-reported outcomes measurement information system; RMDQ, Roland-Morris disability questionnaire.

Physical function

The unadjusted mean PROMIS Physical Function score was 33.76 (95% CI=32.77–34.74) for long-term opioid users and 40.73 (95% CI=39.68–41.79) for long-term opioid nonusers (Figure 3). Upon multiple linear regression analysis (Table 3), long-term opioid use was a predictor of poorer physical function, with an adjusted mean difference of −2.90 (p=0.001). Intermediate-term and short-term opioid use were also predictors of poorer physical function, with adjusted mean difference values of −2.26 (p=0.003) and −1.90 (p<0.001), respectively. The adjusted mean difference values for long-term and intermediate-term opioid use exceed the minimally important difference (MID) of 1.9–2.2 previously estimated for the PROMIS Physical Function domain in a group of patients with osteoarthritis [12], whereas the adjusted mean difference for short-term opioid use falls within this MID.

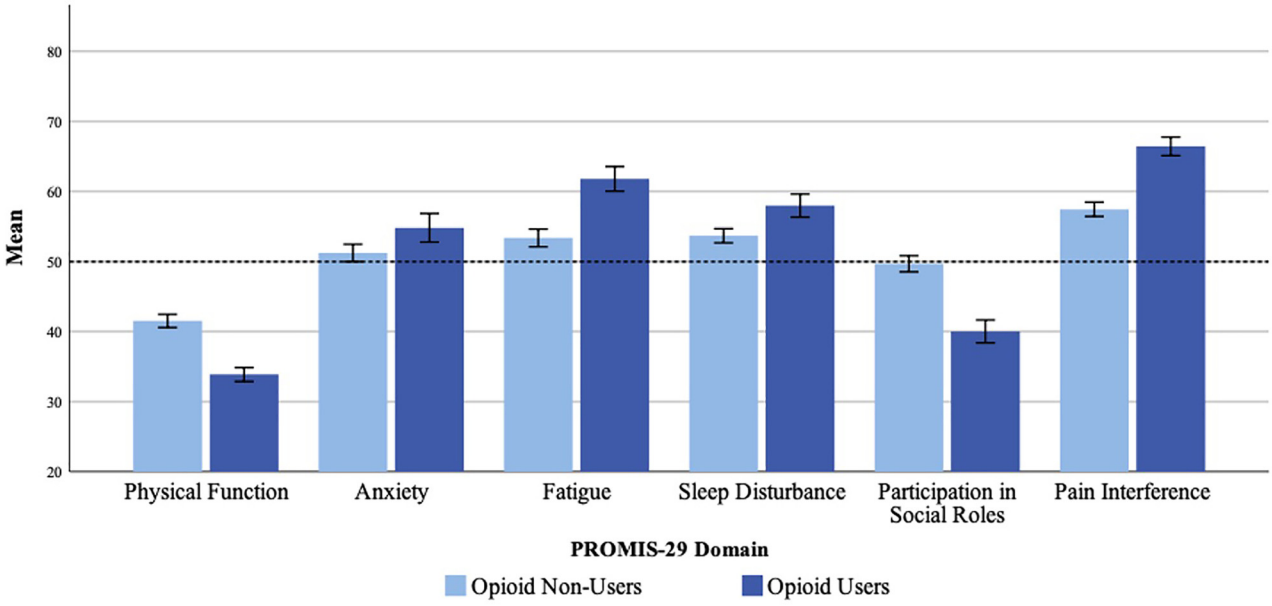

Figure 3: Measures of health-related quality of life (29-Item Patient-Reported Outcomes Measurement Information System, PROMIS-29) for long-term opioid users and nonusers. PROMIS scores are standardized to the US general population, with a mean of 50 and a standard deviation of 10. Higher PROMIS scores more strongly reflect the scale descriptor (e.g., higher scores indicate better physical function but more anxiety). Error bars represent a 95% confidence interval.

Anxiety

The unadjusted mean PROMIS Anxiety score was 54.94 (95% CI=52.90–56.99) for long-term opioid users and 51.57 (95% CI=50.18–52.96) for long-term opioid nonusers (Figure 3). Upon multiple linear regression analysis (Table 3), long-term, intermediate-term, and short-term opioid use were not predictors of anxiety when utilizing a p-value of 0.007.

Fatigue

The unadjusted mean PROMIS Fatigue score was 61.82 (95% CI=60.08–63.56) for long-term opioid users and 53.86 (95% CI=52.44–55.28) for long-term opioid nonusers (Figure 3). Upon multiple linear regression analysis (Table 3), long-term opioid use was a predictor of greater fatigue, with an adjusted mean difference of 4.32 (p=0.001). Intermediate-term opioid use was also a predictor of greater fatigue, with an adjusted mean difference of 3.70 (p=0.002), whereas short-term opioid use was not a significant predictor of fatigue. There are no published MID estimates specific to the PROMIS Fatigue domain in a noncancer population. However, based on MID estimates for other PROMIS domains, an MID of 2–4 points has previously been utilized for this domain in chronic pain patients [13]. Utilizing these values, the adjusted mean difference for long-term opioid use exceeds the MID, whereas the adjusted mean difference for intermediate-term opioid use falls within the MID estimate [13].

Sleep disturbance

The unadjusted mean PROMIS Sleep Disturbance score was 58.07 (95% CI=56.40–59.74) for long-term opioid users and 53.92 (95% CI=52.80–55.04) for long-term opioid nonusers (Figure 3). Upon multiple linear regression analysis (Table 3), long-term opioid use was a not predictor of greater sleep disturbance when utilizing a p-value of 0.007. Intermediate-term opioid use a predictor of greater sleep disturbance, with an adjusted mean difference of 3.03 (p=0.002), while short-term opioid use was not a significant predictor of sleep disturbance. There are no published MID estimates specific to the PROMIS Sleep Disturbance domain. However, based on MID estimates for other PROMIS domains, an MID of 2–4 points has previously been utilized for this domain [13]. Utilizing these values, the adjusted mean difference for intermediate-term opioid use falls within the MID estimate [13].

Participation in social roles

The unadjusted mean PROMIS Participation in Social Roles score was 39.93 (95% CI=38.27–41.60) for long-term opioid users and 48.69 (95% CI=47.40–49.98) for long-term opioid nonusers (Figure 3). Upon multiple linear regression analysis (Table 3), long-term opioid use was a predictor of less participation in social roles, with an adjusted mean difference of –4.10 ($p<0.001$). Intermediate-term and short-term opioid use were not significant predictors of participation in social roles when utilizing a p-value of 0.007. There are no published MID estimates specific to the PROMIS Participation in Social Roles domain. However, based on MID estimates for other PROMIS domains, an MID of 2–4 points has previously been utilized for this domain [13]. Utilizing these values, the adjusted mean difference for long-term opioid use exceeds the MID.

Pain interference with activities

The unadjusted mean PROMIS Pain Interference score was 66.65 (95% CI=65.40–67.91) for long-term opioid users and 58.09 (95% CI=56.96–59.23) for long-term opioid nonusers (Figure 3). Upon multiple linear regression analysis (Table 3), long-term opioid use was a predictor of greater pain interference with activities, with an adjusted mean difference of 3.88 ($p<0.001$). Intermediate-term and short-term opioid use were not significant predictors of greater pain interference with activities when utilizing a p-value of 0.007. The adjusted mean difference for long-term opioid use exceeds the MCID of 2–3 that was previously established in a group of patients with chronic pain [14].

Discussion

The adverse effects of long-term opioid therapy are well known, including the risk of abuse and overdose [22–24]. However, evidence regarding the potential therapeutic benefit of long-term opioid therapy for chronic pain remains sparse [10]. In this study, after controlling for potential confounders, long-term opioid use among patients with chronic low back pain was a predictor of worse back-specific disability, physical function, fatigue, participation in social roles, and pain interference outcomes. Intermediate-term opioid use was a predictor of worse back-specific disability, physical function, fatigue, and sleep disturbance outcomes. Short-term opioid use was a predictor of worse back-specific disability and physical function outcomes. We hypothesize that the adverse sequelae demonstrated by long-term and intermediate-term opioid users can be attributed to prolonged opioid use, whereas the adverse sequelae demonstrated by short-term opioid users may be the result of an acute worsening in their clinical course.

Two other studies have compared the effects of opioid use vs. nonuse for ≥12 months in patients with chronic pain. The Strategies for Prescribing Analgesics Comparative Effectiveness (SPACE) trial [25] was a pragmatic, 12-month randomized controlled trial that evaluated the effects of opioid vs. nonopioid therapy on pain-related function (Brief Pain Inventory [BPI] interference scale) and pain intensity (BPI severity scale) in 240 Veterans Affairs clinic patients with moderate to severe chronic back pain or hip or knee osteoarthritis. The secondary outcomes measured in this study included the RMDQ and PROMIS Sleep Disturbance scale, as well as measures of physical health, mental health, depression, fatigue, sexual function, and headache disability. There were 117 patients in each group that completed the trial. Although both groups demonstrated improvement in pain-related function, there was no significant between-group difference over 12 months (overall p=0.58). The mean BPI interference score at 12 months was 3.4 (SD=2.5) in the opioid group and 3.3 (SD=2.6) in the nonopioid group. Both groups also demonstrated improvement in pain intensity; however, pain intensity was significantly better in the nonopioid group over 12 months (overall p=0.03). The mean BPI severity score at 12 months was 4.0 (SD=2.0) in the opioid group and 3.5 (SD=1.9) in the nonopioid group. For secondary outcomes, the only significant between-group difference was anxiety (7-item Generalized Anxiety Disorder Questionnaire), with opioid users reporting a greater improvement in anxiety symptoms over 12 months (overall p=0.02).

The Middle-Aged/Seniors Chronic Opioid Therapy (MASCOT) study was a cohort study of 1,477 patients initiating opioid therapy for chronic noncancer pain [26]. Analysis of patients with 12-month follow-up data (n=1,157) found that patients who utilized opioids minimally or not at all (n=573) had better activity interference outcomes, measured by their response to the question, “In the past month, how much has pain interfered with your daily activities?” utilizing a 0–10 scale where 0 is “no interference” and 10 is “unable to carry on any activities.” The estimated effect of opioid use on activity interference was 0.84 points (95% CI=0.51–1.17) for intermittent/lower-dose opioid users (n=284) and 1.08 points (95% CI=0.75–1.40) for regular/higher-dose opioid users (n=300). Patients who utilized opioids minimally or not at all had also better pain intensity at 12 months (Graded Chronic Pain Scale). On a

scale of 0–10, with higher scores indicating greater pain intensity, the estimated effect of opioid use at 12 months was 0.80 (95% CI=0.59–1.10) for intermittent/lower-dose opioid users and 0.81 (95% CI=0.61–1.02) for regular/higher-dose opioid users.

The findings of this study provide additional insight into the effects of long-term opioid therapy in several meaningful ways. First, this study is intended to investigate the effects of long-term opioid therapy on the outcomes of back-related disability and health-related quality of life, rather than pain intensity. By controlling for pain intensity in addition to depression, age, BMI, and eight common comorbid conditions (herniated disc, sciatica, osteoporosis, osteoarthritis, heart disease, hypertension, diabetes, and asthma), this study was designed to identify such effects independent of other factors that could reasonably contribute to one's disability or health-related quality of life. Such nonpain outcomes are perhaps more important than pain intensity outcomes, because the NIH Federal Pain Research Strategy states that improvement in pain without concomitant improvement in other domains may not constitute a clinically meaningful outcome [3].

In comparison to the single-item measure of activity interference utilized by the MASCOT study [26], our analysis of the individual domains of the PROMIS-29 provides a more validated, detailed, and holistic analysis of health-related quality of life. Although the SPACE trial [25] appears to have collected sufficient data to evaluate health-related quality of life, the authors utilized a variety of different questionnaires, each with different scoring methods and interpretation guidelines. In contrast, the different components of health-related quality of life in our study are measured utilizing one questionnaire with consistent scoring methods and interpretation guidelines. Such a design makes it easier to compare the effects of opioid therapy across different components of health-related quality of life.

As a noninterventional, registry-based study, the findings of this study depict the outcomes of opioid therapy compared to nonopioid therapy in the community, outside the constraints of controlled trials. The relative lack of control in such a study design lends itself to potential weaknesses. Disparities in quality of care may exist between opioid users and nonusers, which may have a confounding effect on our findings. In addition, while every attempt was made to control for potential confounding variables, the possibility that unidentified confounders contributed to our findings cannot be ruled out.

In our study, long-term opioid therapy was defined as consistent opioid use for ≥12 months. This definition is consistent with the Centers for Disease Control and Prevention (CDC) guideline for prescribing opioids for chronic pain [27] and other studies investigating the effects of long-term opioid therapy [25, 26]. However, a number of other studies define long-term opioid therapy or other synonymous concepts (e.g., "persistent," "chronic," etc.) differently [28–38]. A review of the evolving definitions of chronic opioid therapy found an increasing proportion of studies defining chronic opioid therapy as ">90 days' supply." [39] This definition is consistent with the intermediate-term opioid group in this study. Compared to opioid nonusers, the intermediate-term opioid users in this study demonstrated worse back-related disability and health-related quality of life, which can likely be attributed to prolonged opioid use. However, long-term (≥12-month) opioid users reported greater disability and poorer health-related quality of life compared to intermediate-term opioid users. Although these differences appear to be marginal and a less specific definition of long-term opioid therapy may be acceptable, a standard definition of long-term opioid therapy would be useful to establish consistency going forward.

Conclusions

After controlling for pain intensity, depression, age, BMI, and eight common comorbid conditions (herniated disc, sciatica, osteoporosis, osteoarthritis, heart disease, hypertension, diabetes, and asthma), long-term term opioid use among patients with chronic low back pain was a predictor of worse back-specific disability, physical function, fatigue, participation in social roles, and pain interference outcomes. Intermediate-term opioid use was a predictor of worse back-specific disability, physical function, fatigue, and sleep disturbance outcomes, while short-term opioid use was a predictor of worse back-specific disability and physical function outcomes. These findings, in conjunction with the well-established risks of long-term opioid use, draw into question the utility of long-term opioid therapy for chronic low back pain.

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References

1. Dahlhamer J, Lucas J, Zelaya C, Nahin R, Mackey S, DeBar L, et al. Prevalence of chronic pain and high-impact chronic pain among adults – United States, 2016. MMWR Morb Mortal Wkly Rep 2018; 67:1001–6.
2. Institute of Medicine. Relieving pain in America: a blueprint for transforming prevention, care, education, and research. Washington, DC: The National Academies Press; 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK91497/.
3. NIH Interagency Pain Research Coordinating Committee. Federal pain research strategy; 2018. Available from: https://www.iprcc.nih.gov/sites/default/files/documents/FPRS_Research_Recommendations_Final_508C.pdf.
4. Reuben DB, Alvanzo AAH, Ashikaga T, Bogat GA, Callahan CM, Ruffing V, et al. National institutes of health pathways to prevention workshop: the role of opioids in the treatment of chronic pain. Ann Intern Med 2015;162:295–303.
5. Deyo RA, Dworkin SF, Amtmann D, Andersson G, Borenstein D, Carragee E, et al. Report of the NIH Task Force on research standards for chronic low back pain. J Pain 2014;15:569–85.
6. Chaparro LE, Furlan AD, Deshpande A, Mailis-Gagnon A, Atlas S, Turk DC. Opioids compared to placebo or other treatments for chronic low-back pain. Cochrane Database Syst Rev 2013;1–77. https://doi.org/10.1002/14651858.CD004959.pub4.
7. Abdel Shaheed C, Maher CG, Williams KA, Day R, McLachlan AJ. Efficacy, tolerability, and dose-dependent effects of opioid analgesics for low back pain: a systematic review and meta-analysis. JAMA Intern Med 2016;176:958–68.
8. Chou R, Deyo R, Friedly J, Skelly A, Weimer M, Fu R, et al. Systemic pharmacologic therapies for low back pain: a systematic review for an American College of Physicians clinical practice guideline. Ann Intern Med 2017;166:480–92.
9. Megale RZ, Deveza LA, Blyth FM, Naganathan V, Ferreira PH, McLachlan AJ, et al. Efficacy and safety of oral and transdermal opioid analgesics for musculoskeletal pain in older adults: a systematic review of randomized, placebo-controlled trials. J Pain 2018;19:475.e1–24.
10. Chou R, Turner JA, Devine EB, Hansen RN, Sullivan SD, Blazina I, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a national institutes of health pathways to prevention workshop. Ann Intern Med 2015; 162:276–86.
11. Qaseem A, Wilt TJ, McLean RM, Forciea MA. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2017;166:514–30.
12. Lee AC, Driban JB, Price LL, Harvey WF, Rodday AM, Wang C. Responsiveness and minimally important differences for 4 patient-reported outcomes measurement information system short forms: physical function, pain interference, depression, and anxiety in knee osteoarthritis. J Pain 2017;18:1096–110.
13. Kroenke K, Talib TL, Stump TE, Kean J, Haggstrom DA, DeChant P, et al. Incorporating PROMIS symptom measures into primary care practice-a randomized clinical trial. J Gen Intern Med 2018;33: 1245–52.
14. Chen CX, Kroenke K, Stump TE, Kean J, Carpenter JS, Krebs EE, et al. Estimating minimally important differences for the PROMIS pain interference scales: results from 3 randomized clinical trials. Pain 2018;159:775–82.
15. Amtmann D, Kim J, Chung H, Askew RL, Park R, Cook KF. Minimally important differences for patient reported outcomes measurement information system pain interference for individuals with back pain. J Pain Res 2016;9:251–5.
16. Yost KJ, Eton DT, Garcia SF, Cella D. Minimally important differences were estimated for six patient-reported outcomes measurement information system-cancer scales in advanced-stage cancer patients. J Clin Epidemiol 2011;64:507–16.
17. Roland M, Morris R. A study of the natural history of back pain. Part I: development of a reliable and sensitive measure of disability in low-back pain. Spine (Phila Pa 1976) 1983;8: 141–4.
18. Davies CC, Nitz AJ. Psychometric properties of the roland-morris disability questionnaire compared to the oswestry disability index: a systematic review. Phys Ther Rev 2009;14:399–408.
19. Ramasamy A, Martin ML, Blum SI, Liedgens H, Argoff C, Freynhagen R, et al. Assessment of patient-reported outcome instruments to assess chronic low back pain. Pain Med 2017;18: 1098–110.
20. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The patient-reported outcomes measurement information system (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. J Clin Epidemiol 2010;63:1179–94.
21. Liu H, Cella D, Gershon R, Shen J, Morales LS, Riley W, et al. Representativeness of the patient-reported outcomes measurement information system internet panel. J Clin Epidemiol 2010;63:1169–78.
22. Bell TJ, Panchal SJ, Miaskowski C, Bolge SC, Milanova T, Williamson R. The prevalence, severity, and impact of opioid-induced bowel dysfunction: results of a US and European patient survey (PROBE 1). Pain Med 2009;10:35–42.
23. Lembke A, Humphreys K, Newmark J. Weighing the risks and benefits of chronic opioid therapy. Am Fam Physician 2016;93: 982–90.
24. Webster LR, Choi Y, Desai H, Webster L, Grant BJ. Sleep-disordered breathing and chronic opioid therapy. Pain Med 2008;9:425–32.
25. Krebs EE, Gravely A, Nugent S, Jensen AC, DeRonne B, Goldsmith ES, et al. Effect of opioid vs. nonopioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain: the SPACE randomized clinical trial. JAMA 2018;319:872–82.

26. Turner JA, Shortreed SM, Saunders KW, Leresche L, Von Korff M. Association of levels of opioid use with pain and activity interference among patients initiating chronic opioid therapy. Pain 2016;157:849–57.
27. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain–United States, 2016. JAMA 2016;315: 1624–45.
28. Elsesser K, Cegla T. Long-term treatment in chronic noncancer pain: results of an observational study comparing opioid and nonopioid therapy. Scand J Pain 2017;17:87–98.
29. Thornton JD, Goyat R, Dwibedi N, Kelley GA. Health-related quality of life in patients receiving long-term opioid therapy: a systematic review with meta-analysis. Qual Life Res 2017;26:1955–67.
30. Morasco BJ, Yarborough BJ, Smith NX, Dobscha SK, Deyo RA, Perrin NA, et al. Higher prescription opioid dose is associated with worse patient-reported pain outcomes and more health care utilization. J Pain 2017;18:437–45.
31. Ferrari R, Zanolin ME, Duse G, Visentin M. Effectiveness of opioid analgesics in chronic noncancer pain. Pain Pract 2015;15:272–8.
32. Adams MH, Dobscha SK, Smith NX, Yarborough BJ, Deyo RA, Morasco BJ. Prevalence and correlates of low pain interference among patients with high pain intensity who are prescribed long-term opioid therapy. J Pain 2018;19:1074–81.
33. Boudreau D, Von Korff M, Rutter CM, Saunders K, Ray GT, Sullivan MD, et al. Trends in long-term opioid therapy for chronic non-cancer pain. Pharmacoepidemiol Drug Saf 2009;18:1166–75.
34. Frank JW, Lovejoy TI, Becker WC, Morasco BJ, Koenig CJ, Hoffecker L, et al. Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: a systematic review. Ann Intern Med 2017;167:181–91.
35. Lozier CC, Nugent SM, Smith NX, Yarborough BJ, Dobscha SK, Deyo RA, et al. Correlates of use and perceived effectiveness of non-pharmacologic strategies for chronic pain among patients prescribed long-term opioid therapy. J Gen Intern Med 2018;33: 46–53.
36. Shah D, Zhao X, Wei W, Gandhi K, Dwibedi N, Webster L, et al. A longitudinal study of the association of opioid use with change in pain interference and functional limitations in a nationally representative cohort of adults with osteoarthritis in the United States. Adv Ther 2020;37:819–32.
37. Strick V. Management of severe chronic pain with tapentadol prolonged release – long-term data from pain specialists. Curr Med Res Opin 2014;30:2085–92.
38. Zgierska AE, Burzinski CA, Cox J, Kloke J, Singles J, Mirgain S, et al. Mindfulness meditation-based intervention is feasible, acceptable, and safe for chronic low back pain requiring long-term daily opioid therapy. J Alternative Compl Med 2016;22: 610–20.
39. Shen Y, Bhagwandass H, Branchcomb T, Galvez SA, Grande I, Lessing J, et al. Chronic opioid therapy: a scoping literature review on evolving clinical and scientific definitions. J Pain 2021; 22:246–62.