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SCIENTIFIC INVESTIGATIONS

Daily associations between sleep and opioid use among adults with comorbid symptoms of insomnia and fibromyalgia

Mary Beth Miller, PhD[1]; Ashley F. Curtis, PhD[1,2]; Wai Sze Chan, PhD[3]; Chelsea B. Deroche, PhD[1]; Christina S. McCrae, PhD[1]

[1]Department of Psychiatry, University of Missouri School of Medicine, Columbia, Missouri; [2]Department of Psychological Sciences, University of Missouri, Columbia, Missouri; [3]Department of Psychology, The University of Hong Kong, Hong Kong

Study Objectives: Disturbed sleep and use of opioid pain medication are common among individuals with chronic pain. Anecdotally, opioids are thought to promote sleep by relieving pain. This study aimed to determine whether opioid use is associated with daily sleep parameters (and vice versa) in adults with comorbid symptoms of insomnia and fibromyalgia.

Methods: Individuals reporting symptoms of insomnia and opioid use for fibromyalgia (n = 65, 93% women, 79% White) wore wrist actigraphy and completed daily diaries for 14 days (910 observations). Analyses examined daily associations between opioid dose (measured in lowest recommended dosage units) and three sleep parameters (actigraphy/self-reported total wake time and self-reported sleep quality). Multilevel models were used to account for the clustering of daily sleep and opioid assessments (level 1) within individuals (level 2).

Results: Opioid use did not have a significant daily effect on total wake time or sleep quality, and sleep parameters did not significantly impact opioid use the next day; however, participants reported worse sleep quality and greater doses of opioids on evenings that they experienced greater pain.

Conclusions: Among adults reporting symptoms of insomnia and opioid use for fibromyalgia pain, opioid use is not reliably associated with wake time or sleep quality that night, and these sleep parameters are not significantly associated with opioid use the next day; however, evening pain has an adverse daily impact on both sleep quality and opioid use. Studies identifying strategies to prevent and manage fibromyalgia pain are needed, especially for individuals reporting comorbid insomnia and opioid use.

Keywords: sleep, insomnia, opioid, chronic pain, daily

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Previous studies examining the association between sleep and opioid use have done so primarily at the aggregate (between-person) level. This study aimed to examine dynamic, within-person associations between sleep and opioid use by individuals reporting comorbid symptoms of insomnia and fibromyalgia.

Study Impact: Findings suggest that opioid use has neither a beneficial nor a detrimental effect on sleep among individuals with comorbid symptoms of insomnia and fibromyalgia at the daily level; however, they also suggest that opioids are not alleviating the negative effects of pain on sleep. Providers are encouraged to screen for insomnia symptoms in individuals on opioid treatment for symptoms of fibromyalgia and recommend additional pain management strategies as appropriate.

INTRODUCTION

Sleep disturbance and opioid use are common among individuals with chronic pain. Up to 88% of individuals with chronic pain disorders report sleep disturbance.[1] In addition, up to 56% of individuals with chronic pain report use of opioids that is inconsistent with prescription instructions, and up to 23% meet criteria for opioid addiction.[2] Collectively, these conditions place a large economic burden on individuals living in the United States, with an estimated $635 billion spent on health care costs and lost productivity related to chronic pain,[3] another $100 billion on the treatment and management of sleep disorders,[4] and approximately $53 billion on the nonmedical use of prescription opioids.[5] Given the sleep-interfering effects of pain,[1] opioids may be prescribed in part to promote restful sleep by relieving acute symptoms of pain; however, a paucity of research has examined the impact of opioids on sleep, particularly on symptoms of insomnia.[6]

Research has documented both beneficial and detrimental effects of opioids on sleep duration and efficiency.[7] At least two drug trials have documented a beneficial opioid effect on sleep disturbance and problems among individuals with chronic low back pain.[8,9] In other studies, among patients with chronic noncancer pain, in multivariate models, opioid use did not predict concurrent sleep problems[10] or change in sleep quality from baseline to 2 months[11]; however, other research has linked opioid use to longer time to sleep onset and worse self-reported, objective, and physiological sleep among individuals with chronic pain.[12–14] Although numerous methodological differences may contribute to these inconsistencies in the literature,

all of these studies examined associations between opioid use and sleep outcomes at the aggregate (between-person) level. It is possible that opioid use has a more dynamic impact on sleep, in which case the impact of opioid use on sleep may be more evident when examined at the daily (within-person) level.

This study aimed to determine if opioid use impacts same-day sleep or sleep impacts next-day opioid use among adults who use opioids in the context of comorbid insomnia and fibromyalgia. Given the primarily negative impact of opioid use on sleep physiology and architecture,[15] we hypothesized that opioid use would be positively associated with same-night sleep disturbance, defined as longer total wake time (TWT) and worse self-reported sleep quality. These outcomes were chosen because they provide information on the aspects of sleep behavior that contribute to insomnia. Specifically, diagnostic criteria for insomnia include "a predominant complaint of dissatisfaction with sleep quantity or quality" that is associated with clinically significant daytime impairment and occurs despite adequate opportunity for sleep.[16] Because actigraphy (objective) and daily diary (self-reported) measures of sleep may assess unique dimensions of the sleep experience,[17] TWT was assessed using both objective and self-reported measures. To isolate the effect of opioid use from that of other predictors of sleep disturbance,[1,10,18] analyses controlled for evening pain and use of sleep medication.

METHODS

Participants and procedure

Data were collected from adults who participated in the baseline screening portion of a randomized, controlled trial examining the efficacy of Cognitive Behavioral Therapy for Insomnia among patients with comorbid insomnia and fibromyalgia (clinicaltrials.gov identifier NCT02001077).[19] Baseline eligibility included (1) either a clinical diagnosis of fibromyalgia or screening criteria for fibromyalgia (3+ months of widespread pain in all four quadrants of the body and no indication of another disorder that may cause chronic pain[20]); and (2) symptoms of insomnia, defined as > 30 minutes to fall asleep or > 30 minutes awake at night on 3 nights per week for the last 6 months.[21] Participants were excluded at screening if they reported a diagnosis of sleep apnea or use of a continuous positive airway pressure device for sleep apnea. Participants (n = 235) provided written informed consent and completed 2 weeks of daily assessment as part of the baseline screening protocol. Sixty-five participants reported use of opioids at least once across the 14 nights of baseline. These participants were included in the data analytic sample. Data were collected between 2009 and 2014, and all procedures were approved by the institutional review board. Sample demographics are presented in **Table 1**.

Measures

Sleep

Sleep parameters were assessed using daily sleep diaries and wrist actigraphy. Participants completed written sleep diaries for 14 days as part of the baseline assessment. Each morning, they estimated what time they got into bed, what time they tried to initiate sleep, how long it took them to fall asleep (sleep onset latency), how many times they woke up during the night, the total duration of those awakenings (wake after sleep onset), the time of their final awakening, and what time they got out of bed. Time elapsed between final awakening and getting out of bed was used to estimate early morning awakening. Sleep onset latency, wake after sleep onset, and early morning awakenings are key determinants of insomnia diagnosis[21] and can be summed to estimate the amount of time spent awake in bed or TWT. To reduce the number of statistical models conducted and the likelihood of type 1 error, analyses focused on the association between opioid use and TWT. Participants also rated their sleep quality on a scale from 1 (*very poor*) to 5 (*very good*).

Participants were also instructed to wear the Actiwatch 2 (Philips Respironics, Murrysville, Pennsylvania) continuously during the 14 days of baseline. The actigraph is a watchlike sensor that monitors body movement. It has been validated against polysomnography as a valid measure of sleep.[22,23] Data were analyzed using proprietary software in 30-second epochs. Actigraphy was also used to estimate sleep onset latency and wake after sleep onset, which again were summed to estimate TWT.

Opioid use

In daily sleep diaries, participants indicated (*yes/no*) whether they used an opioid pain medication each night and, if applicable, the milligrams of opioid pain medication consumed. Milligram values were converted to lowest recommended dosage (LRD) units for analysis (eg, for codeine, 15 mg = 1 and 30 mg = 2; for dextropropoxyphene (Darvocet), 750 mg = 1 and 1500 mg = 2; see *Results* for a complete list of opioids reported). If participants reported use of more than one type of opioid on a single day, lowest recommended dosage was summed for the two types (eg, 30 mg of codeine and 750 mg of Darvocet = 3.0 lowest recommended dosage units).

Demographics and covariates

Participants reported their age, sex, and race/ethnicity at baseline. Participants also reported (*yes/no*) if they used any other medications at bedtime. Although some of these medications (eg, benzodiazepines) could have been prescribed for other purposes, medications known to impact sleep were categorized as *sleep medications* (eg, hypnotic, antihistamine; see **Table 1** for list of medications). Participants also reported current pain intensity on each sleep diary using a visual analog scale from 0 (*no pain*) to 100 (*most intense pain imaginable*). These ratings were made at bedtime each night and are referred to henceforth as *evening pain*.

Data screening and analysis

Data were collected daily over the 14 days of baseline assessment. Given the daily clustering of sleep and opioid use variables within individuals, multilevel modeling was used to examine within- and between-person effects of opioid dose on sleep parameters and vice versa. Participants (n = 65) reported an average of 9.40 days of opioid use (standard deviation

Table 1—Descriptive statistics for the data analytic sample (n = 65).

	Mean (SD) or n (%)	Range
Age, y	52.91 (11.16)	25–74
Female sex	60 (92%)	—
Race/ethnicity	—	—
White	52 (80%)	—
Black	12 (19%)	—
Native Hawaiian/Pacific Islander	0 (0%)	—
Asian	0 (0%)	—
American Indian/Alaska native	1 (2%)	—
Bi/multiracial	0 (0%)	—
Hispanic/Latino	3 (5%)	—
Evening pain (0–100 scale)	58.25 (16.64)	17–95
Use of any sleep medication‡	37 (57%)	—
Days of sleep medication use over 14 days (n = 37)	8.24 (5.02)	1–14
Benzodiazepine (% of 37)	19 (51%)	—
Benzodiazepine-like hypnotic (% of 37)	6 (16%)	—
Antidepressant (% of 37)	17 (46%)	—
Antihistamine (% of 37)	12 (32%)	—
Use of any pain medication‡	65 (100%)	—
Days of pain medication use over 14 days (n = 65)	10.68 (4.02)	1–14
Over-the-counter pain medication (% of 65)	24 (37%)	—
Prescription pain medication (% of 65)	65 (100%)	—
NSAID pain medication (% of 65)	7 (11%)	—
Opioid pain medication (% of 65)	65 (100%)	—
Days of opioid use over 14 days (n = 65)	9.40 (4.88)	1–14
Avg LRD of opioid use per day (n = 65)	1.75 (0.73)	—
Also used benzodiazepines (% of 65)	24 (37%)	—
Duration of pain medication use (y)	6.98 (11.11)	0–43
Actigraphy sleep variables (min)	—	—
Sleep onset latency	59.23 (43.38)	5–201
Wake after sleep onset	58.40 (23.76)	10–107
Total wake time	150.22 (73.92)	40–351
Total sleep time	389.22 (76.94)	160–545
Self-reported sleep variables (in minutes)	—	—
Sleep quality (1–5 scale)	2.60 (0.64)	1–4
Sleep onset latency	60.81 (49.73)	3–230
Wake after sleep onset	46.41 (38.04)	2–231
Total wake time	137.98 (73.64)	26–361
Total sleep time	410.13 (75.90)	209–577

‡Groups are not mutually exclusive. LRD = lowest recommended dosage, NSAID = nonsteroidal anti-inflammatory drugs, SD = standard deviation. Frequency (days) and dose reported only for those who reported using each type of medication.

[SD] = 4.88; 910 data points, 608 of which involved an opioid dose ≥ 1). Sleep and opioid variables were missing on 8.4% and 1.2% of data points, respectively. All available data were used. No imputation procedures were used because imputation does not improve the accuracy of multilevel modeling estimates.[24] Multilevel-model fixed effect and standard error estimates are also robust to violations of normality.[25]

Analyses were conducted in IBM SPSS Statistics 25 (Armonk, New York). Unconditional, multilevel models were conducted to determine the intraclass correlation coefficient for each outcome. Intraclass correlation coefficients indicated that 71% of the variance in opioid dose, 35% of variance in self-reported TWT, 46% of variance in actigraphy TWT, and 30% of variance in sleep quality occurred between individuals

(level 2). Remaining variance occurred within individuals over time (level 1). This evidence of both between- and within-person variability in outcomes justifies use of multilevel modeling.[26]

Full models, including level 1 (within-person) and level 2 (between-person) variables, were then specified. All models controlled for within-person (daily) variability in the use of sleep medication (*yes/no*) and evening pain, as well as between-person (baseline) variability in age, days of sleep medication use, and evening pain.[1] Models examining opioid dose as a predictor of sleep parameters also controlled for within- and between-person variability in use of other pain medications, either over-the-counter or nonsteroidal anti-inflammatory drugs (NSAIDs). In models examining the impact of opioid dose on sleep parameters, opioid dose was assumed to precede sleep. In models examining the impact of sleep parameters on opioid dose, opioid dose was lagged so that sleep parameters would predict opioid dose the following day. Continuous within-person predictors were person-mean centered, and between-person predictors were grand-mean centered.[27] Model specifications were determined using an iterative procedure, first specifying an autoregressive covariance structure (assuming smaller correlations with increased distance in time) for repeated effects and random intercepts (to allow for individual differences in each outcome at baseline); however, because it provided better fit in all models, a compound symmetry covariance structure (assuming equal correlation among all time points) was retained in final models. Similarly, inclusion of the random intercept produced intercept covariance parameters that approximated zero, indicating that the amount of variation within individuals did not differ meaningfully across individuals; therefore, random intercepts were removed. Bonferroni correction ($P = .05/6 = .008$) was used to control for inflation in type 1 error. In the case of significant effects, a pseudo-R^2 value was calculated using formulas provided in Lorah (2018).[28]

RESULTS

Participant demographics and medication use characteristics are detailed in **Table 1**. All participants reported use of an opioid pain medication at least once over the 14 days of daily diaries ($M = 9.40$ days of opioid use, SD = 4.88). One in three participants (37%) also reported the use of over-the-counter pain medication, 11% reported use of NSAIDs, and 29% reported use of benzodiazepines. At baseline, participants reported taking pain medication for an average of 6.9 years (SD = 11.1; range, 1 month to 42 years).

Participants reported using the following opioid medications: codeine (n = 1), Darvocet (n = 8), Darvon (propoxyphene, n = 1), Demerol (meperidine, n = 1), Fioricet (acetaminophen butalbital, and caffeine; n = 3), hydrocodone (n = 21), Lortab (hydrocodone bitartrate and acetaminophen, n = 7), methadone (n = 4), morphine (n = 7), Nucynta (tapentadol; n = 2), oxycodone (n = 16), oxycontin (n = 4), Percocet (n = 6), Roxicet (oxycodone and acetaminophen; n = 1), Roxicodone (oxycodone hydrochloride; n = 2), and tramadol (n = 17). Most participants reported use of only one type of opioid over the 14 days of baseline (n = 37, 57%); however, 21 participants (32%) reported use of two types, 6 (9%) reported use of three types, and 1 reported use of four types of opioids over the 14 days (codeine, hydrocodone, Lortab, and Darvocet).

Fixed effects of opioid dose on same-day sleep parameters

Bivariate correlations among study variables are presented in **Table 2**, and the fixed effects of opioid dose on sleep outcomes are presented in **Table 3**. There were no significant between- or within-person predictors of self-reported or actigraphy TWT. Between- and within-person evening pain and within-person use of sleep medication were the only significant predictors of self-reported sleep quality (see **Table 3**). Based on R^2 estimations, the full model accounted for 32.4% of variance in sleep quality. Participants reporting above-average evening pain reported worse sleep quality than other participants in the study. Similarly, on evenings when participants' pain was greater than their within-person average, participants reported worse sleep quality than they did on other nights. Conversely, they reported better sleep quality on nights that they used sleep medications. Age and dose of pain medication (over-the-counter, NSAIDs, or opioid) were not significantly associated with any of the sleep parameters assessed.

Fixed effects of sleep parameters on next-day opioid dose

The fixed effects of sleep parameters on next-day opioid dose are depicted in **Table 4**. Within-person variability in evening pain was the only significant predictor of opioid dose across all models. Overall, models accounted for 71% to 73% of variance in opioid dose. On nights their evening pain was greater than their own within-person average, participants reported using larger doses of opioids. Age, use of sleep medication, and sleep parameters were not associated with next-day opioid dose.

DISCUSSION

Both sleep disturbance and opioid use are common in individuals with chronic pain conditions such as fibromyalgia.[1,2] This study extends previous research by documenting the effects of opioid use on sleep parameters (and vice versa) at the daily level. Although previous research has found between-group differences in self-reported, objective, and physiological sleep among opioid users and nonusers,[12–14] this study found no evidence of an association between opioid use and sleep parameters at the daily level. Rather, among adults with insomnia who already use opioids for fibromyalgia pain, day-to-day variation in opioid use did not have a significant impact on objective or self-reported total wake time or sleep quality, and day-to-day variation in those sleep parameters did not have a significant impact on opioid use. Findings suggest that opioid use has neither a beneficial nor detrimental sustained effect on daily sleep in individuals with insomnia who use opioids for fibromyalgia pain.

In contrast to the lack of association between sleep and opioid dose, evening pain had an adverse daily impact on either sleep

Table 2—Bivariate correlations among primary study variables (n = 910 observations of 65 participants).

	2	3	4	5	6	7	8	9	10
1. L2 evening pain	−0.08*	0.04	0.01	−0.38*	0.76*	−0.08*	0.03	0.02	−0.22*
2. L2 LRD opioid	–	0.03	−0.02	0.09*	−0.06	0.85*	0.02	−0.01	0.06
3. L2 TWT		—	0.42*	−0.26*	0.03	0.03	0.63*	0.33*	-0.15*
4. L2 actigraphy TWT			—	−0.04	0.01	−0.004	0.27*	0.70*	−0.02
5. L2 sleep quality				—	−0.29*	0.08*	−0.16*	-0.05	0.59*
6. L1 evening pain					—	−0.01	0.04	0.03	−0.23*
7. L1 opioid LRD						—	0.03	0.02	0.04
8. L1 TWT							—	0.34*	−0.37*
9. L1 actigraphy TWT								—	−0.10*
10. L1 sleep quality									—

*$P < .05$. L1 = level 1 (daily within-person variables), L2 = level 2 (between-person variables), LRD = lowest recommended dosage, TWT = total wake time, Y/N = yes/no.

and opioid use within this population. Within persons, participants reported worse sleep quality and greater opioid use on evenings that they experienced above-average levels of pain. Because pain and opioid dose were assessed on the same day, it is unclear which of these variables occurred first; however, it seems logical that greater pain might lead to increased opioid use. The finding that evening pain was associated with worse self-reported sleep quality that same night—but not self-reported or objectively measured total wake time—is also consistent with evidence that perceptions of sleep may not correspond with objective sleep measures.[17] That is, although participants perceived worse sleep after nights of greater pain, those perceptions may or may not correspond with behavioral (actigraphy) or physiological (polysomnography) measures of sleep; however, multiple polysomnographic studies have found higher rates of sleep discontinuity among individuals with chronic nonmalignant pain relative to control participants.[29] Pain has also been found to moderate the association between opioid use and both self-reported and physiologically measured sleep parameters at the between-person level.[14,30] Thus, the impact of pain on sleep may vary based on the level of analysis (between vs within persons) and the way the sleep parameter is being assessed (self-reported, behavioral, or physiological).

The impact of pain on sleep may also depend on the population, as data from this study contrast findings among chronic pain patients with insomnia who do not use opioids. Specifically, Tang and colleagues (2012)[31] found presleep cognitive arousal to be associated with subsequent sleep quality that night, but presleep pain was not.[31] The most obvious difference between these two studies is the population (ie, individuals who did and did not use opioids). Because we did not assess cognitive arousal at the daily level, however, future studies may examine the moderating or potentially mediating role of cognitive arousal in the association between pain and sleep in this population. Tang and colleagues[31] also used a slightly different measure of pain (how much pain, as opposed to pain intensity), which may or may not have contributed to variability in outcomes.

Clinical implications

Although it is promising that opioids do not seem to have an adverse daily effect on sleep in this population, findings also counter the assumption that opioids may promote sleep by relieving pain. In contrast, opioids were not associated with same-day sleep parameters, and evening pain impaired self-reported sleep even in the presence of opioids. Collectively, these data suggest that opioids are not alleviating the negative effects of pain on sleep among patients with fibromyalgia. This is particularly notable in the context of chronic pain, as poor sleep quality is associated with worse pain upon awakening and in the first half of the day.[31] Indeed, low-quality sleep is known to increase perceptions of pain[32] and other pain-related symptoms, such as fatigue.[33] Thus, opioids do not seem to be breaking this negative bidirectional association between sleep and pain. Although opioids are commonly prescribed for chronic pain,[34] data from this study are consistent with standard of care recommendations, which discourage the use of strong opioids as a treatment for fibromyalgia.[35]

The pattern of medication use reported in this sample is also somewhat concerning, as one in three participants reported use of both opioids and benzodiazepines. The combination of opioid use and some sleep medications—particularly benzodiazepines—increases the risk of opioid overdose and death.[36] For this reason, concurrent prescription of opioids and benzodiazepines is discouraged.[34] Beyond the physiological risks associated with concurrent use of sleep and pain medication, behavioral treatment of insomnia may be preferable to sleep medication in those at risk for substance use disorder because it does not reinforce the mindset that substances (in this case, sleep medication) are needed to manage distress.[37] Research documenting the prevalence and predictors of the course of opioids and other substances, especially among high-risk individuals, such as those with sleep disturbance and chronic pain, is encouraged.

Limitations

This study is among the first to examine daily associations between opioid use and sleep in individuals with comorbid

Table 3—Estimated fixed effects of opioid dose on same-day sleep parameters (n = 65).

Predictors	Outcome: Self-Reported TWT				
	Estimate	SE	*P*	95% CI	
Intercept	144.39	10.27	<.001	123.96	164.81
L2 age (gmc)	−0.60	0.87	.50	−2.35	1.16
L2 evening pain (gmc)	0.40	0.58	.50	−0.76	1.55
L2 sleep med days (gmc)	3.05	1.98	.13	−0.88	6.99
L2 over-the-counter LRD (gmc)	−1.22	15.11	.94	−31.48	29.04
L2 NSAID LRD (gmc)	−1.09	0.60	.07	−2.29	0.10
L2 opioid LRD (gmc)	2.55	10.46	.81	−18.39	23.49
L1 evening pain (pmc)	0.17	0.23	.45	−0.28	0.62
L1 use of sleep meds (Y/N)	−18.55	12.55	.14	−43.18	6.09
L1 over-the-counter LRD (pmc)	2.51	5.49	.65	−8.26	13.29
L1 NSAID LRD (pmc)	−2.52	18.38	.89	−38.60	33.56
L1 opioid LRD (pmc)	7.46	5.54	.18	−3.41	18.33
Predictors	**Outcome: Actigraphy TWT**				
	Estimate	**SE**	***P***	**95% CI**	
Intercept	144.15	10.23	<.001	123.75	164.56
L2 age (gmc)	−1.06	0.90	.25	−2.86	0.75
L2 evening pain (gmc)	0.15	0.58	.80	−1.02	1.32
L2 sleep med days (gmc)	−1.81	1.95	.36	−5.70	2.07
L2 over-the-counter LRD (gmc)	−11.58	15.45	.46	−42.53	19.36
L2 NSAID LRD (gmc)	−0.15	0.61	.80	−1.37	1.06
L2 opioid LRD (gmc)	−0.10	10.64	.99	−21.42	21.22
L1 evening pain (pmc)	0.18	0.20	.37	−0.21	0.56
L1 use of sleep meds (Y/N)	15.88	10.72	.14	-5.18	36.94
L1 over-the-counter LRD (pmc)	6.29	4.71	.18	−2.96	15.54
L1 NSAID LRD (pmc)	−15.43	15.66	.33	−46.18	15.32
L1 opioid LRD (pmc)	3.46	4.59	.45	−5.55	12.46
Predictors	**Outcome: Self-Reported Sleep Quality**				
	Estimate	**SE**	***P***	**95% CI**	
Intercept	2.49	0.09	<.001	2.32	2.66
L2 age (gmc)	−0.005	0.01	.49	−0.02	0.01
L2 evening pain (gmc)	−0.01	0.005	.002*	−0.02	−0.01
L2 sleep med days (gmc)	−0.02	0.02	.19	−0.05	0.01
L2 over-the-counter LRD (gmc)	−0.09	0.12	.48	−0.33	0.16
L2 NSAID LRD (gmc)	0.01	0.005	.27	−0.004	0.01
L2 opioid LRD (gmc)	0.03	0.08	.72	−0.14	0.20
L1 evening pain (pmc)	−0.01	0.002	<.001*	−0.01	−0.003
L1 use of sleep meds (Y/N)	0.32	0.12	.008*	0.08	0.55
L1 over-the-counter LRD (pmc)	−0.10	0.05	.05	−0.20	−0.001
L1 NSAID LRD (pmc)	−0.04	0.17	.81	−0.37	0.29
L1 opioid LRD (pmc)	–0.05	0.05	.30	−0.16	0.05

*Significant predictors ($P \leq .008$). CI = confidence interval, gmc = grand-mean centered, L1 = level 1 (daily within-person variables), L2 = level 2 (between-person variables), LRD = lowest recommended dosage, NSAID = nonsteroidal anti-inflammatory drugs, pmc = person-mean centered, TWT = total wake time, Y/N = yes/no (coded 1/0).

symptoms of insomnia and a chronic pain condition (in this case, fibromyalgia). It builds on the rigor of previous studies, which primarily used aggregated data; however, limitations should be considered when interpreting results. First, women constituted 93% of this sample. Whereas rates of insomnia[38] and chronic pain[39] are higher among women, research is needed to determine

Table 4—Estimated fixed effects of sleep parameters on next-day opioid dose (n = 65).

Predictors	Outcome: Next-Day Opioid LRD				
	Estimate	SE	*P*	95% CI	
Intercept	1.23	0.12	<.001	0.98	1.48
L2 age (gmc)	0.02	0.01	.15	−0.01	0.04
L2 sleep med days (gmc)	0.01	0.02	.57	−0.03	0.06
L2 evening pain (gmc)	−0.004	0.01	.55	−0.02	0.01
L2 TWT (gmc)	0.0005	0.002	.77	−0.003	0.004
L1 use of sleep meds (Y/N)	0.07	0.08	.42	−0.10	0.23
L1 next-day evening pain (pmc)	0.01	0.002	<.001*	0.004	0.01
L1 self-report TWT (pmc)	−0.0001	0.0002	.54	−0.001	0.0003
Predictors	**Estimate**	**SE**	***P***	**95% CI**	
Intercept	1.24	0.13	<.001	0.99	1.50
L2 age (gmc)	0.01	0.01	.22	−0.01	0.04
L2 sleep med days (gmc)	0.01	0.02	.69	−0.04	0.06
L2 evening pain (gmc)	−0.005	0.01	.52	−0.02	0.01
L2 TWT (gmc)	0.001	0.002	.75	−0.003	0.004
L1 use of sleep meds (Y/N)	0.11	0.09	.25	−0.08	0.29
L1 next-day evening pain (pmc)	0.01	0.002	<.001*	0.004	0.01
L1 actigraphy TWT (pmc)	<0.001	0.0003	.98	−0.001	0.001
Predictors	**Estimate**	**SE**	***P***	**95% CI**	
Intercept	1.25	0.13	<.001	1.00	1.50
L2 age (gmc)	0.02	0.01	.17	−0.01	0.04
L2 sleep med days (gmc)	0.01	0.02	.57	−0.03	0.06
L2 evening pain (gmc)	−0.002	0.01	.77	−0.02	0.01
L2 sleep quality (gmc)	0.12	0.21	.56	−0.29	0.54
L1 use of sleep meds (Y/N)	0.07	0.08	.44	−0.10	0.23
L1 next-day evening pain (pmc)	0.01	0.002	<.001*	0.004	0.01
L1 self-report sleep quality (pmc)	0.03	0.03	.19	-0.02	0.08

*Significant predictors ($P \leq .008$). CI = confidence interval, gmc = grand mean centered, L1 = level 1 (daily within-person variables), L2 = level 2 (between-person variables), LRD = lowest recommended dosage, Meds = medications, pmc = person-mean centered, SQ = sleep quality, TWT = total wake time, Y/N = yes/no (coded 1/0). [†]Models were also conducted including and excluding each participant's apnea-hypopnea index, periodic limb movement arousal index, symptoms of depression (measured using the Beck Depression Inventory II), and symptoms of anxiety (measured using the State Trait Anxiety Inventory) at baseline as level 2 (between-person) covariates. None of these variables was significantly associated with outcomes, and they did not change the overall pattern of results. Therefore, they were not included as covariates in final models.

the extent to which findings may generalize to men and other diverse samples. The impact of opioids on sleep may also vary as a function of drug tolerance.[15] Because most participants in this study had been taking pain medications for extended periods, research examining the within-person association between opioid use and sleep among naïve opioid users may be warranted. Similarly, although we did not exclude participants for comorbid chronic pain conditions, the focal chronic pain condition for this study was fibromyalgia; thus, it is unclear to what extent findings may generalize to adults with other chronic pain conditions. It is possible that results may generalize to other chronic pain conditions with similar underlying pathophysiology (eg, central sensitization), but this is speculative without additional research. Finally, although level 2 sample sizes of 30 or more tend to have minimal impact on estimated fixed effects and standard errors at level 1 in multilevel models,[40] we reported data for a relatively small number of participants, in which case it is important to replicate these findings in larger samples. Results should be extrapolated only to individuals with chronic insomnia and fibromyalgia.

Beyond generalizability to various populations, there were a few methodological limitations that readers should keep in mind. First, although multilevel models are a valuable tool for determining temporal associations among variables, they do not reflect causal associations. Second, although participants were instructed to complete daily diaries each morning, sleep diaries were completed via pen-and-paper forms that were collected once a week; therefore, the timeliness of reports may have varied. Future investigators are encouraged to use methods that allow reports to be time-stamped (eg, electronic diaries). Sleep parameters assessed in this study were also limited to self-report and actigraphy measures. There is some evidence linking opioid use to sleep-disordered breathing (both central and obstructive sleep apnea)[41,42] and other

physiological sleep parameters,[14] which we did not assess at the daily level. Therefore, future studies examining daily associations between opioid use and physiological sleep outcomes may be warranted. It is also noteworthy that our models left ~70% of variance in sleep parameters and ~30% of variance in opioid use unexplained, suggesting the presence of other influences on sleep and opioid use at the daily level. Cannabis is being used increasingly for sleep disturbance and chronic pain, despite the persistence of sleep disturbance in those who use cannabis for chronic pain.[43,44] Among adult women, long-term opioid use (≥ 90 days) is also associated with increased risk of menopause,[45] and changes in hormone levels (such as those experienced during menopause) may increase risk of both insomnia[46] and pain.[47] Thus, cannabis and menopause are two confounding variables that may impact these associations over time.

CONCLUSIONS

Insomnia and opioid use are common in individuals with chronic pain and create a burden on the health care system. In this study, no significant association was found between day-to-day variation in opioid use and sleep parameters assessed using self-report or actigraphy; however, evening pain had an adverse impact on both sleep and opioid use at the daily level, such that participants reported worse sleep quality and greater opioid doses on evenings that they experienced above-average levels of pain. Whereas the findings suggest that opioid use has neither a beneficial nor detrimental sustained effect on daily sleep among individuals with insomnia and fibromyalgia, they also suggest that opioids are not alleviating the negative effects of pain on sleep. Studies identifying effective strategies to prevent and manage fibromyalgia pain are needed, especially for individuals reporting comorbid symptoms of insomnia and opioid use.

ABBREVIATION

TWT, total wake time

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Address correspondence to: Christina S. McCrae, PhD, One Hospital Drive DC067.00, Columbia, MO 65211; Tel: (573) 882-0982; Fax: (573) 884-1070; Email: mccraec@health.missouri.edu

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