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a longitudinal study examining the relationship between sleep and pain outcomes

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Sleep disturbance in patients attending specialized chronic pain clinics in Denmark: a longitudinal study examining the relationship between sleep and pain outcomes

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Abstract

Objectives: Sleep disturbances are highly prevalent in patients with chronic pain. However, the majority of studies to date examining sleep disturbances in patients with chronic pain have been population-based cross-sectional studies. The aims of this study were to 1) examine the frequency of sleep disturbances in patients referred to two interdisciplinary chronic pain clinics in Denmark, 2) explore associations between sleep disturbances and pain intensity, disability and quality of life at baseline and follow-up, and 3) explore whether changes in sleep quality mediated the relationships between pain outcomes at baseline and pain outcomes at follow-up.

Methods: We carried out a longitudinal observational study, examining patients enrolled in two chronic pain clinics assessed at baseline (n=2,531) and post-treatment follow-up (n=657). Patients reported on their sleep disturbances using the sleep quality subscale of the Karolinska Sleep Questionnaire (KSQ), their pain intensity using 0–10 numerical rating scales, their pain-related disability using the Pain Disability Index (PDI), and quality of life using the EuroQol-VAS scale. The average time between baseline and follow-up was 207 days (SD=154).

Results: At baseline, the majority of patients reported frequent sleep disturbances. We found a significant association at baseline between self-reported sleep disturbances and pain intensity, pain-related disability, and quality of life, where greater sleep disturbance was associated with poorer outcomes. At follow-up, patients reported significant improvements across all pain and sleep outcomes. In two mediation models, we showed that changes in sleep disturbances from baseline to follow-up were significantly associated with (i) pain intensity at follow-up, and (ii) pain disability at follow-up. However, baseline pain intensity and disability scores were not associated with changes in sleep disturbances and, we did not find evidence for significant mediation of either pain outcome by changes in sleep disturbances.

Conclusions: Self-reported sleep disturbances were associated with pain outcomes at baseline and follow-up, with greater sleep disturbances associated with poorer pain outcomes. Changes in sleep quality did not mediate the relationships between baseline and follow-up scores for pain intensity and disability. These findings contribute to a growing body of evidence confirming an association between sleep and chronic pain experience, particularly suggestive of a sleep to pain link. Our data following patients after interdisciplinary treatment suggests that improved sleep is a marker for a better outcome after treatment.

Keywords: chronic pain; insomnia; pain treatment; sleep.

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Introduction

Sleep disturbances are prevalent in patients with chronic pain. In patients with chronic back pain for instance, between half and 78% experience clinically significant insomnia [1–3]. A Swedish registry study reported that 65% of patients with chronic pain met clinical criteria for insomnia [4]. In pain conditions such as fibromyalgia, more than 90% of patients report sleep disturbance (for review, see [5]). Furthermore, patients with chronic pain conditions

are significantly more likely to have insomnia compared to patients with other chronic health conditions [6]. The interaction between poor sleep and pain is important because pain can interfere with sleep, and sleep problems can cause or worsen pain, and have functional consequences for patients with pain conditions [7]. Pain and sleep disturbance are often assumed to be related in a reciprocal, bidirectional fashion [5]. However, there is now growing evidence suggesting that sleep impacts pain more than pain impacts sleep [8]. Longitudinal studies have also indicated that sleep disturbances are associated with the development of new-onset chronic pain, as well as worsening pain and disability in individuals with existing pain conditions [9].

Given the prevalence of sleep disturbance in chronic pain, a number of studies have examined whether treating sleep disorders can improve pain outcomes, with some promising findings. Several randomised controlled trials (RCTs) have used non-pharmacological interventions, typically based on cognitive behavioural therapy to treat insomnia (CBT-I) secondary to pain, which is first line treatment for insomnia. These have shown beneficial effects on sleep quality and efficiency, sleep latency and wakefulness after sleep onset, with improvements sustained for 3–12 months after the end of treatment [10, 11]. Improvements in pain-related outcomes have been observed in functional domains, such as pain interference and disability (e.g., [12]).

The majority of studies to date examining sleep disturbances in patients with chronic pain have been population-based cross-sectional studies. Experimental studies of pain and sleep, which have aimed to examine the directionality of effects, have been largely restricted to healthy adults (e.g., [13]). Studies addressing chronic pain and sleep disturbances are fewer in number, and frequently focus on prevalence or incidence rates or outcomes for specific pain-related condition (e.g. fibromyalgia, chronic low back pain or arthritis, [8, 14]. Far less work has examined patients who are undergoing specialist treatment for their pain, and this group is of interest because sleep disturbances can be assessed in relation to changes in pain that may come about.

Another outstanding question is whether treatment that targets chronic pain and general functioning, and not specifically sleeps disturbances, has an impact on patients' sleep. While a number of studies have implemented sleep interventions in patients with chronic pain [10, 12], there is little work examining the opposite direction: the effects of treatment for pain on sleep disturbances. Emerging evidence suggests that pain treatment may indeed positively impact sleep [15]. One feasibility trial examined the effects of different forms of physiotherapy compared to wait list on the sleep quality of patients with lower back pain, and reported positive intervention effects on sleep outcomes [15].

For the present analysis, we carried out a longitudinal observational study, examining the sleep disturbances of patients referred to two multidisciplinary chronic pain clinics in Denmark. First, we examined the association between patient-reported sleep disturbances and chronic pain intensity (and pain-related disability) in our patient sample prior to treatment. We hypothesised that sleep disturbances would be prevalent among the sample at baseline, and would be associated with pain intensity and disability. Second, we examined the association between sleep improvements and changes in pain intensity at a post-treatment measurement time point, using a mediation analysis.

Mediation analyses provide a statistical means to test a hypothetical model, where one variable (X) is associated with an outcome variable (Y), through an intermediate variable (M). While frequently applied to theoretical mechanisms, mediational analyses primarily yield the relationship of the mediator and outcome variables when partialling out the relationship between the predictor and mediator variables [16]. Given previous proposed mechanistic accounts of the pain/sleep relationship [17]. We hypothesised that baseline levels of pain (intensity and related disability) would predict follow-up levels of pain, and this relationship would be mediated by changes in sleep disturbance.

Materials and methods

Ethics

This study was conducted in accordance with the Declaration of Helsinki. Consistent with local legal guidelines in Denmark, there was no requirement for a formal ethical committee review because treatment was not affected by participation in the study [17]. Data for this study was obtained from a clinical and research pain registry PainData, an electronic system developed for online data capture and clinical reporting [18]. The system captures patient-specific information across multiple treatment-relevant domains of pain before the first consultation at the pain clinic as well as immediately after treatment. PainData is registered with the Danish Data Protection Agency (18/35221). Participants gave their informed consent for their data to be included in the 'PainData' registry and to be used for research purposes.

Participants

Patients in this study were referred for treatment by their general practitioner for chronic pain at one of two Danish public pain clinics, in two locations Odense and Silkeborg. The Odense Pain Clinic has an intake of about 1,200 patients a year, and a waiting list of around 42 weeks. The Silkeborg Pain Clinic has a smaller capacity, with about 300 patients per year. Referral to either clinic primarily required that

patients had non-malignant chronic pain, and an ambulant status (see Supplementary Materials for full referral criteria). As reported by previous studies, patients have a mean age of 50 years and 66% are women. Pain duration is eight to nine years, and a large proportion of patients report a high degree of pain-related disability, as well as psychological distress. Approximately 50% of patients use opioids and 35% report widespread pain [19–21]. Both clinics adopt a biopsychosocial model of pain, with multidisciplinary treatment broadly addressing the physical, psychological and social aspects of patients' pain. The treatment process begins with an initial consultation with a doctor and a nurse to discuss the patient's treatment concerns and expectations, which is then followed by a multidisciplinary conference with a psychologist, a social worker and a physiotherapist. Together, an individualised treatment plan is formulated, with the aim of improving the patient's daily functioning.

Patient data was obtained from these two clinics between April 2016 and December 2018. During this period, 2,778 patients completed a set of baseline questionnaires and gave their informed consent for their data to be included in the 'PainData' registery and used for research purposes. The approximate response rate to the baseline questionnaire data was 80–85% [20]. During the period from which the data were extracted, 98% of patients in Silkeborg gave consent for their data to be used in research, and 93% in Odense. Two hundred and forty seven patients did not answer items related to sleep quality and pain intensity at baseline, and were therefore excluded from the analysis. The baseline sample comprises the remaining 2,531 patients. By December 2018, 1,665 of the patients had completed treatment at one of the clinics and were sent a post-treatment follow-up questionnaire and the response rate was 48%, a follow-up response rate similar to that previously reported [18]. An additional 135 patients (8%) were excluded for not completing the items related to sleep quality and pain intensity at follow-up, resulting in the follow-up sample of 657 patients.

Patient assessments

Baseline data collected included demographic information, substance use, pain-specific data, treatment status, psychological and physical functioning, as well as overall quality of life. Follow-up data collected included a shorter battery of questionnaires, re-assessing pain-specific measures and some aspects of psychological and physical functioning.

Sleep disturbance: Sleep disturbance was measured using the four items adapted from the Karolinska Sleep Questionnaire (KSQ) sleep quality subscale, assessing frequency of sleep disturbance, frequency of early awakenings, frequency of difficulties falling asleep and frequency of night time awakenings with difficulty returning to sleep [22, 23]. In the Danish version of the KSQ, participants respond using one of five categories (Every night or almost every night [score=1], Several times a week, Several times a month, Several times a year, Never, [score=5]). The questions and response options used in this study have previously been used to explore sleep difficulties in a large Danish study [24]. A Cronbach's alpha was calculated to assess the internal consistency between the four sleep disturbance items (α=0.80), which were then averaged to create a sleep disturbance score, with high scores indicating less sleep disturbance.

Pain intensity and duration: Patients rated their pain intensity using four items measuring pain intensity (i) at its worst in the last 24 h (ii) its least in the last 24 h (iii) averaged in the last 24 h (iv) and pain intensity when doing light physical activity. Response was recorded using a numeric rating scale (NRS) ranging from 0 (no pain) to 10 (worst imaginable pain) [25]. The four pain intensity items had a Cronbach's alpha level of 0.88, and were summed to create a total pain intensity score.

For pain duration, patients were asked to indicate the approximate date of pain onset as precisely as possible. The duration between completion of the questionnaire and the date of pain onset was used to calculate pain duration.

Pain-related disability: Pain-related disability was measured using five items from the Pain Disability Index (PDI). The PDI, which is a widely-used and validated to measure pain-related disability [26], and the five items included measured patients' disability related to family/home responsibilities, recreation, social activity, occupation, sexual behaviour (the PDI items related to self-care and life-support activities were excluded, as used in previous studies [27]. For each category, patients rated their typical level of disability due to pain on a 0–10 NRS, with 0 indicating no disability and 10 indicating maximum disability. Patients' responses to the five items were summed to create a total pain-related disability score.

Depression and anxiety symptoms: Depressive symptoms were measured using the Patient Health Questionnaire (PHQ-9) [28], a 9-item instrument for screening, diagnosing, monitoring and measuring the severity of depression. The PHQ-9 has good sensitivity (88%) and specificity (88%) for major depression and demonstrates concurrent validity with measures of functional impairment in patients with pain [28]. Scores of 5–9, 10–14, 15–19 and ≥20 have been validated to represent mild, moderate, moderately severe and severe depression respectively [28, 29]. Anxiety symptoms were measured using the Generalized Anxiety Disorder 7-item (GAD-7) scale [30]. The GAD-7 is widely-used in clinical practice as a brief measure of anxiety symptoms and severity, specifically linked to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM–IV) criteria [31]. Low scores reflect milder anxiety symptoms, and scores ≥15 represent severe anxiety [30].

Quality of life: Patients were asked to rate their current quality of life (QOL), using a visual analog scale (VAS) ranging from 0 (worst quality of life imaginable) to 100 (best quality of life imaginable) from the EuroQol 5-D questionnaire with 100 indicating the best QOL [32].

Statistical analysis

Descriptive data variables are reported as proportions or means and SDs. A series of linear regression models were used to examine the associations between patients' sleep disturbance and reports of pain-related experiences (pain intensity, pain-related disability) at baseline controlling for demographic, psychological and treatment-related variables. Diagnostic plots of the outcome variable data (e.g., pain intensity) were inspected with regards to the assumptions of multiple regressions including linearity, homoscedasticity and normally distributed residuals, and no serious violations were detected. Changes in patient outcomes from baseline to follow-up were assessed using paired samples t-tests. Linear regression models were used to examine baseline sleep quality, and key baseline variables, and their association with pain-related outcomes at follow-up.

For the follow-up analyses, regression-based mediation analyses, estimating the indirect effects using a bootstrapping approach with 5,000 samples, were used to examine changes in sleep disturbance as a mediator (*M*) of changes in pain and pain-related disability from baseline (*X*) to follow-up (*Y*) (Figure 2). For mediation analyses, the total effect (c path) of the *X* variable (baseline pain measure) on the outcome variable (*Y*, post treatment pain measure) is decomposed into a direct (path c') and an indirect effect (ab, in verbal form, path a multiplied by path b). The indirect effect goes through a mediator variable, sleep disturbance (*M*) (paths *a* and *b*, in Figure 2) and the remaining effect reflects the direct effect (c' path).These mediation models can be considered as testing atemporal associations, rather than temporal associations [16], because changes in sleep disturbance (the *M* variable) were measured concurrently with the outcome variable (*Y*). All statistical analyses were performed in SPSS version 26 (IBM Corporation, Armonk, NY). $p<0.05$ was considered significant.

Results

The demographic characteristics of the baseline sample of patients are presented in Table 1. The age range was from 14 to 98 years, and over two thirds of the patients were women. The proportion of participants with university (or similar tertiary education) as the highest education level was approximately one third. Over half of the participants had lived with chronic pain for nearly seven years (median: 6.8 years). The majority of patients (86.5%) reported analgesic use at baseline. Nearly one-third of patients had PHQ-9 scores indicating moderate depression and 14% had GAD-7 scores indicating moderate anxiety. Pain-related disability was substantial, with a mean patient score of 36.7 out of a maximum of 50.

Table 1: Baseline sample demographics and self-reported pain and health-related factors (n=2,531).

Demographic variable, missing data %	n	%	M	SD
Age: years, range 14–98 years			48.7	14.2
Female	1730	68.4		
Treatment location: Odense	1994	78.8		
Reporting analgesic use	2,189	86.5		
Marital status (2.8%)				
Married/cohabiting	1712	67.6		
Single	748	29.6		
Highest level of education, (1.6%)				
Primary school (9th/10th grade)	492	19.4		
Secondary education	139	5.5		
Vocational secondary education	795	31.4		
Short-cycle tertiary education	257	10.2		
Medium-cycle tertiary education	538	21.3		
Long-cycle tertiary education	118	4.7		
Other education	151	6.0		
BMI (4.2%)			27.7	5.9
Years with pain (2.5%)			10.1	10.0
Sleep quality score, scale 1[worst] – 5 [best].			2.1	1.0
Pain intensity score, scale: 0 [best] – 40 [worst].			26.2	7.0
PHQ-9, scale: 0–27 (5.2%)			10.2	5.6
PDI-5			34.9	9.7
Quality of life (3%)			42.55	22.04

Sleep disturbance and pain at baseline

The majority of patients (81%) reported experiencing 'restless or disturbed sleep' at least several times per week (see Figure 1). For the remaining three sleep quality items (difficulties falling asleep, early awakenings, difficulties falling back asleep), more than two-thirds of patients reported difficulties at least several times per week. The mean averaged score for sleep quality was 2.1 (SD=1), where one represented the worse possible sleep quality score, and five the best score. The majority of patients reported considerable levels of pain in the previous 24 h: 70% of patients rated their average pain experience in the last 24 h as 6 or above out of 10 (worst imaginable pain). For pain while doing light physical activity, 32% of patients reported a score of 9 or 10. The overall mean pain intensity score was 26.2 (SD=7). For all three outcomes, patients' sleep quality scores were significantly associated with patients' pain intensity, pain-related disability and quality of life (Table 2). Greater sleep disturbance was associated with poorer outcomes in each instance. This association held after adjusting for demographic variables (age, gender, and education level), use of analgesics and psychological functioning (depression and anxiety symptoms).

Sleep disturbance and pain outcomes at follow-up

The mean duration of treatment for the sample available at follow-up was 207 days (range 1–756 days, SD=154, some patients had just one consultation). As presented in Table 3, there was significant improvement across all patient outcomes, including sleep quality and pain scores, with Cohen's d suggesting small effect sizes overall. There was a significant reduction in the numbers of patients reporting analgesic use at follow-up (87.2% at baseline, 79.6% at follow-up, Chi Square test=13.6, $p<0.001$).

We examined whether patients' baseline sleep quality scores predicted pain outcomes at follow-up using two linear regression models (Table 4 presents all baseline variables included in the models). Baseline sleep quality

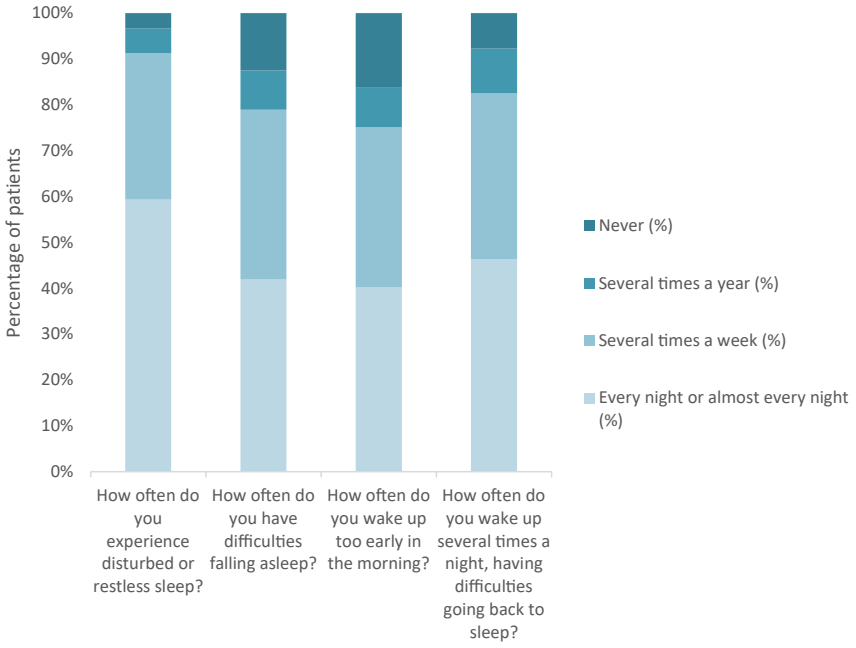

Figure 1: Patients' baseline responses (n=2,531) to the four sleep disturbance items.

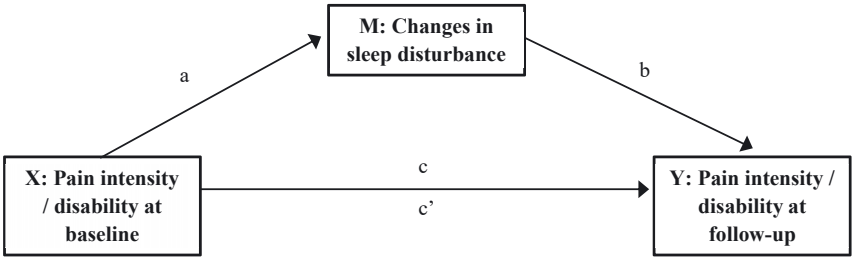

Figure 2: Mediation model with changes in sleep as a hypothesis mediator of changes in pain intensity/disability from baseline to follow-up.

was a significant predictor of pain intensity, but not pain-related disability (PDI). For PDI scores, both patients' anxiety scores, and their baseline PDI scores, were significant predictors. Adding treatment duration (days) to the models did not change the results for either outcome variable. At follow-up, changes in patients' sleep quality score (baseline to follow-up) were significantly correlated with both changes in pain intensity (n=618, r=–0.27, p<0.0001) and changes in pain-related disability (n=608, r=–0.21, p<0.0001), controlling for treatment duration, duration of patients' pain, age, gender, education level, use of analgesics and affective symptoms at baseline.

Our first mediation model (Table 5) indicated that pain intensity at baseline was significantly associated with pain intensity at follow-up (path c'), but we did not find evidence for mediation by changes in sleep quality. Baseline pain intensity was not significantly associated with changes in sleep (path a). However, changes in sleep quality were significantly associated with pain intensity at follow-up (path b) and the total indirect effect was not significant.

Our second mediation model (Table 5) indicated that pain-related disability at baseline was significantly associated with pain-related disability at follow-up (path c'), but again, we did not find evidence for significant mediation by changes in sleep (indirect effect). Baseline pain-related disability was not significantly associated with changes in sleep (path a). However, changes in sleep disturbance were significantly associated with pain-related disability at follow-up (path b).

Participants lost to follow-up

In total, 1,008 participants (61%) were either lost to follow-up or had incomplete data on sleep quality and/or pain intensity items at follow-up. Participants not included in the follow-up sample were, on average, significantly younger (mean difference of two years, p<0.004), more likely to be single (p<0.003), reported lower levels of education (p<0.001) and had higher pain intensity (mean difference of 1 point, p<0.004) and anxiety scores (mean

Table 2: Linear regression models examining the effects of patients' self-reported sleep quality score at baseline on (a) baseline pain intensity scores (b) baseline pain-related disability and (c) baseline quality of life, adjusting for age, gender, depression and anxiety symptoms, education level and analgesic use. Gender code=0 is women. B=unstandardized coefficients, and Beta=standardized coefficients.

	B	SE	Beta	Sig.		95% CI
(a) Pain intensity (n=2,346)						
Total sleep quality score	−1.61	0.15	−0.23	<0.001	−1.90	−1.33
Gender (0, 1)	0.14	0.29	0.01	0.62	−0.42	0.71
Age	0.07	0.01	0.15	<0.001	0.06	0.09
Education level	−0.26	0.07	−0.07	<0.001	−0.39	−0.12
Analgesics use (0, 1)	0.39	0.39	0.02	0.32	−0.38	1.16
PHQ-9	0.18	0.04	0.15	<0.001	0.11	0.25
GAD-7	0.10	0.04	0.07	0.01	0.02	0.17
(b) Pain-related disability (n=2,326)						
Total sleep quality score	−1.53	0.20	−0.16	<0.001	−1.91	−1.14
Gender (0, 1)	0.31	0.39	0.02	0.42	−0.45	1.07
Age	0.05	0.01	0.07	<0.001	0.02	0.07
Education level	−0.05	0.09	−0.01	0.63	−0.23	0.14
Analgesics use (0, 1)	2.56	0.53	0.09	<0.001	1.53	3.59
PHQ-9	0.68	0.05	0.40	<0.001	0.59	0.77
GAD-7	−0.11	0.05	−0.06	0.03	−0.21	−0.01
(c) Quality of Life (n=2,316)						
Total sleep quality score	1.79	0.45	0.08	<0.001	0.90	2.68
Gender (0, 1)	−3.48	0.89	−0.07	<0.001	−5.23	−1.74
Age	−0.26	0.03	−0.16	<0.001	−0.32	−0.20
Education level	0.29	0.22	0.03	0.18	−0.13	0.72
Analgesics use (0, 1)	−1.50	1.21	−0.02	0.22	−3.88	0.88
PHQ-9	−1.30	0.11	−0.33	<0.001	−1.52	−1.09
GAD-7	−0.33	0.12	−0.07	0.01	−0.56	−0.10

Table 3: Analysis of changes in outcome from baseline to follow-up.

	Baseline M, SD	Follow-up M, SD	Change (95 % CI)	Cohen's d
Sleep quality score (n=657)	2.16 (1.00)	2.42 (1.07)	0.26 (0.20, 0.32)*	0.25
Pain intensity (n=657)	25.89 (6.93)	23.34 (7.99)	−2.55 (−3.08, −2.03)*	0.34
PDI-5 (n=645)	34.84 (9.51)	32.09 (10.40)	−2.75 (−3.39, −2.10)*	0.27
#PHQ-9 (n=307)	9.83 (5.37)	8.79 (5.42)	−1.05 (−1.64, −0.46)*	0.19
Quality of life (n=636)	42.06 (21.24)	50.34 (24.15)	8.28 (6.44, 10.12)*	0.36

*p<0.0001, paired t-tests, #PHQ-9 was added to the PainData questionnaire battery later in data collection.

Table 4: Linear regression models examining baseline predictors of patients' (a) pain intensity scores and (b) PDI at follow-up. Gender code=0 is women. B=unstandardized coefficients, and Beta=standardized coefficients.

	B	SE	Beta	Sig.		95% CI
(a) Pain intensity at FU (n=618)						
Δ sleep quality score	−0.59	0.3	−0.07	0.05	−1.19	0
Pain intensity (baseline)	0.64	0.04	0.55	<0.001	0.56	0.72
Gender (0, 1)	−0.28	0.57	−0.02	0.62	−1.41	0.84
Age	−0.03	0.02	−0.05	0.18	−0.07	0.01
Education level	−0.08	0.15	−0.02	0.61	−0.38	0.22
Analgesics use (0, 1)	0.23	0.79	0.01	0.77	−1.33	1.79
PHQ-9	0.12	0.07	0.08	0.1	−0.02	0.27
GAD-7	−0.1	0.08	−0.06	0.21	−0.25	0.06
Duration of pain (years, baseline)	0.01	0.03	0.01	0.77	−0.04	0.06

Table 4: (continued)

	B	SE	Beta	Sig.	95% CI	
(b) PDI at FU (n=608)						
Δ sleep quality score	−0.23	0.35	−0.02	0.52	−0.92	0.46
PDI (baseline)	0.72	0.04	0.65	<0.001	0.65	0.8
Gender (0, 1)	−0.8	0.68	−0.04	0.24	−2.14	0.55
Age	0.05	0.02	0.06	0.05	0	0.1
Education level	−0.11	0.18	−0.02	0.53	−0.47	0.24
Analgesics use (0, 1)	1.82	0.95	0.06	0.06	−0.05	3.69
PHQ-9	0.15	0.09	0.08	0.1	−0.03	0.33
GAD-7	−0.28	0.09	−0.13	<0.001	−0.46	−0.09
Duration of pain (years, baseline)	−0.07	0.03	−0.07	0.03	−0.13	−0.01

Table 5: Results of two mediation analyses, using a bootstrapping estimation approach to estimate indirect effects, examining follow-up pain intensity scores/follow up disability scores (*Y*) and changes in sleep quality (M), with (a) baseline pain intensity scores and (b) pain-related disability at baseline (*X*).

	Path a		Path b		Direct effect c'		Total effect c		Indirect effect
	Beta (95% CI)	p-Value	Beta (95% CI)	p-Value	Beta (95% CI)	p-Value	Beta (95% CI)	p-Value	Bootstrap [95 % CI]
(a) Pain intensity (n=657)	−0.003 (−0.01, 0.01)	0.54	2.03 (1.46, 2.61)	<0.001	0.66 (0.6, 0.74)	<0.001	0.67 (0.60, 0.74)	<0.001	−0.006 (−0.03, 0.01)
(b) Pain-related disability (n=677)	−0.002 (−0.01, 0.005)	0.55	2.18 (1.47, 2.89)	<0.001	0.7 (0.65, 0.78)	<0.001	0.7 (0.65, 0.78)	<0.001	−0.004 (−0.02, 0.01)

difference of 0.6 of a point, p<0.02; see Supplementary Table 1 for a full comparison).

Discussion

In this study, we assessed a large sample of treatment-seeking patients with chronic pain before and after they received multidisciplinary treatment at one of two specialised pain clinics. At baseline, the majority of patients reported frequent sleep disturbances, which were significantly associated with their pain intensity, pain-related disability, and quality of life. At follow-up post treatment, there were small, but significant improvements in patients' sleep quality and pain outcomes.

Improvements in pain outcomes are of similar magnitude as recently reported by multidisciplinary pain centers in Canada [33] and in a large meta-analysis [34]. Improvements in sleep quality after treatment are also in line with the effects observed after physiotherapy [15] and a 12-week multidisciplinary digital program [35], although the questionnaires used to assess outcomes were different.

Patients' sleep quality scores at baseline were a significant predictor of their pain intensity at follow-up, but not their pain-related disability (PDI). Our mediation analysis indicated that improvements in patients' sleep from baseline to follow-up were associated with improvements in pain outcomes (path b). We suggest that sleep improvements might therefore reflect a general positive response to treatment, although we cannot determine the temporal relationship between changes in sleep quality and pain.

Although the association between poor-quality sleep and pain is well-established [8], it is often assumed that sleep disturbance is the result of the severe pain that characterises chronic pain conditions. Mounting evidence suggests that sleep disturbance plays at least as strong a role in the onset and maintenance of pain than the opposite [8]. While we cannot establish a causal role for sleep disturbance in the treatment improvements in the current study, the association between improved sleep and improved outcomes is, nonetheless, of interest. Our findings demonstrate that an association exists between improved sleep and better pain-related outcomes, consistent with other work in the field [36], and plausible from a mechanistic perspective [5]. We also suggest that if initial sleep disturbance is indeed an important predictor of pain-intensity outcomes, this strengthens the argument for targeting sleep disturbances when treating patients with chronic pain.

We examined sleep in patients who were treated with the aim of improving their management of pain, and their quality of life. The treatment process at both clinics is broad and does not focus on delivering a targeted, evidenced-based treatment for insomnia, such as CBT-I [37]. Our main novel finding is that baseline pain intensity was not associated with sleep quality improvements, but sleep quality improvements were associated with treatment improvements. This suggests that baseline pain impairment is not a strong predictor of sleep-related changes, although it did predict overall outcome.

Strengths and limitations

We note a number of strengths and limitations to the present work. We tested a large sample of patients, both prior to treatment and at a follow-up time point with a sample size that is comparable to that typically included in previous longitudinal assessments of the relationship between pain and sleep [8]. Our sample comprised a naturalistic patient population, with the majority of patients accessing treatment at the clinics responding to the baseline assessments. We examined sleep disturbances in patients who were treated with the aim of improving their management of pain, and their quality of life. The treatment process at both clinics is broad and neither clinic delivers a targeted treatment for insomnia, such as CBT-I [37].

Given the heterogeneous nature of the treatment patients received, we cannot make any conclusions about how treatment and treatment-related changes (like a reduction in analgesic use) impacted sleep quality. Furthermore, we did not have an 'untreated' control group, and we did not measure sleep quality mid-treatment, which would have allowed us to test if sleep quality changes temporally mediated pain changes [16]. Of note, there was significant non-response at follow-up, with less than 50% completion rates. Given the lengthy average duration of treatment, and the resultant long-follow-up period, this is perhaps unsurprising. Our analyses suggested that attrition was non-random: participants lost to follow up were slightly younger than those included in the follow-up sample (around two years), more likely to be single, with lower levels of education, and higher scores on pain intensity and anxiety measures. It is possible that non-responders at follow-up had worse pain-related treatment outcomes, and also sleep quality outcomes, than responders. We caveat our mediation analysis findings with this non-response rate in mind. The lack of information on type of chronic pain conditions as well as the use of a selection of questions from validated questionnaires are limitations.

Conclusions

Self-reported sleep disturbances were associated with pain outcomes at baseline and follow-up with greater sleep disturbances associated with poorer pain outcomes. However, changes in sleep quality did not mediate the relationships between baseline and follow-up scores for (i) pain intensity and (ii) pain disability. As improved sleep may be related to better outcomes after treatment, sleep disturbances may constitute an important target within treatment plans for chronic pain.

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