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CLINICAL REVIEW

Prevalence of sleep disturbances in patients with chronic non-cancer pain: A systematic review and meta-analysis

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SUMMARY

In individuals with chronic pain, sleep disturbances have been suggested to increase suffering, perception of pain, and to negatively affect long-term prognosis. This systematic review and meta-analysis aims to determine the pooled prevalence of sleep disturbances in chronic non-cancer pain patients with no other sleep disorders, using the patient-rated questionnaires Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI). Multiple databases were searched for studies reporting the prevalence of sleep disturbances in chronic pain patients. The meta-analysis was conducted to examine the pooled prevalence of PSQI and ISI data using the inverse-variance random-effects model and to examine mean differences in PSQI scores. The systematic search resulted in 25,486 articles and 20 were included for analysis. In 12 studies using PSQI, the pooled prevalence of sleep disturbance was 75.3% among 3597 chronic pain patients. In eight studies using ISI, the pooled prevalence was 72.9% among 2578 chronic pain patients. The meta-analysis showed a significant mean difference of 2.75 ($p < 0.001$) in the global PSQI score between the chronic pain group versus the non-chronic pain group. The relatively high prevalence of sleep disturbances in chronic pain patients emphasizes the importance of further characterizing the relationship between sleep and chronic pain.

Introduction

In patients with chronic pain, sleep disturbances exacerbate suffering and disability, negatively impact the perception of pain, and worsen symptoms of depression [1,2]. Furthermore, individuals reporting greater levels of pain intensity clinically tend to experience more sleep impairments suggesting a bidirectional relationship between sleep and pain [3]. Pain is regarded as chronic when pain persists for greater than 3 months and is linked to significant emotional distress or functional disability or both [4]. In developed countries, it has been consistently shown that one out of five adults suffer from chronic pain of any type [5–7].

The prevalence of sleep disturbances in chronic pain populations has been investigated in recent years. The literature includes a number of articles examining sleep disturbances in various chronic pain populations [8–11]. Reviews have so far focused on a specific pain population such as back pain or fibromyalgia [12–14]. Recently, a meta-analysis was completed on the prevalence of diagnosed sleep disorders in chronic pain patients, specifically examining insomnia, restless legs syndrome, and obstructive sleep apnea [15].

There is no strict definition of sleep disturbance in the literature. Sleep disturbance encompasses disorders of initiating and maintaining sleep and abnormal events that may occur during sleep, like sleep apnea, restless legs syndrome, and insomnia. However, sleep

Abbreviations: CI, Confidence interval; ISI, Insomnia severity index; PSQI, Pittsburgh sleep quality index.

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Glossary of terms

Chronic pain	Pain that persists for greater than 3 months and is linked to significant emotional distress or functional disability or both
Insomnia severity index	Seven item self-rated questionnaire that measures a patient's perception of insomnia through their subjective nighttime symptoms and possible daytime consequences of insomnia. ISI cutoff of $\geq$8 was used to assess sleep disturbances
Pooled prevalence	Prevalence data combined from samples of multiple primary studies
Pittsburgh sleep quality index	Nineteen item self-rated questionnaire that measures patient's sleep quality and disturbances over a one month time period. PSQI cutoff of >5 was used to assess poor sleep quality
Sleep disturbance	Sleep abnormalities from poor sleep quality or insomnia, in the absence of other diagnosed comorbid sleep disorders
Sleep efficiency	The percentage of the total time spent asleep compared to the total time spent in bed (total sleep time/total time in bed $\times$ 100)
Sleep latency	The length of time to fall asleep, or the transition from full wakefulness to sleep.

disturbances can be better understood more broadly as abnormal sleep events that affect individuals not only immediately preceding and during the period of sleep, but also their normal functioning and mood during waking hours [16]. There is significant research in chronic pain and sleep disorders [2,15,17]. A systematic review and meta-analysis on the prevalence of sleep disturbance, more broadly than formally diagnosed sleep disorders, is an area lacking in the literature. In this systematic review and meta-analysis, we adopted the term sleep disturbance to capture the sleep abnormalities from poor sleep quality or insomnia, and to exclude comorbid sleep disorders.

In general, sleep disturbance can be examined by polysomnography, actigraphy, sleep diary, and patient-rated questionnaires. Polysomnography and actigraphy provide objective measures of sleep including quantity and quality whereas sleep diaries and patient-rated questionnaires provide a reliable estimate of the sleep disturbance and its severity [18,19]. Of those validated questionnaires, the Pittsburgh sleep quality index (PSQI) and Insomnia severity index (ISI) are commonly used for the evaluation of sleep disturbance in chronic pain populations [20,21].

Considering the high prevalence of chronic pain in the population, reliably estimating the prevalence of sleep disturbances in patients with chronic pain may guide future screening and treatment decisions. Using patient-rated questionnaires, the primary objective of this systematic review and meta-analysis is to determine the pooled prevalence of sleep disturbances in non-cancer chronic pain patients who have no comorbid sleep disorders. The secondary objectives include 1) performing a meta-analysis to determine the differences in sleep quality between chronic pain patients and a non-chronic pain group, 2) calculating the pooled prevalence in a few chronic pain conditions such as chronic back pain and fibromyalgia, and 3) explore potential confounders including measures of depression, anxiety, and use of sleep medication.

Methods

Study design and registration

The protocol of this study was registered in the International Prospective Register of Systematic Reviews (CRD42020194427). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [22].

Study selection criteria

Inclusion criteria: 1) Studies must have primarily adult patients $\geq$18 y with chronic non-cancer pain, often defined as experiencing pain for greater than 3 months and linked to significant emotional distress or functional disability or both. 2) Randomized controlled trials, prospective and retrospective cohort studies, cross-sectional studies, and case-control studies. 3) A sample size $\geq$100. 4) Prevalence data on sleep disturbances was recorded.

Exclusion criteria: 1) Comorbid sleep disorders such as sleep disordered breathing and restless leg syndrome. 2) As this review is focused on general chronic pain experiences, studies with specific focus on the following types of pain conditions were excluded: cancer, spinal cord injuries, traumatic brain injuries, palliative conditions, dysmenorrhea, irritable bowel syndrome, and episodic headache.

Search strategy

With the help of an information specialist (ME), a comprehensive literature search was conducted in the following electronic databases: Medline (Ovid), Medline In-Process/ePubs (Ovid), Embase (Ovid), Cochrane Database of Systematic Reviews (Ovid), Cochrane CENTRAL (Ovid), ClinicalTrials.gov, and WHO International Clinical Trials Registry Platform. The searches were conducted on May 1, 2020. Studies were restricted to only the English language and no limit was specified on date of publication. The reference lists of eligible studies and review articles were handsearched to capture articles potentially missed from the original search [12–15]. Search terms captured different chronic pain conditions and sleep disturbances using combinations of terms such as “chronic pain”, “chronic noncancer pain”, “back pain”, “fibromyalgia”, “arthritis”, “sleep”, “sleep depriv*”, “insomnia”, “sleep qualit*”, and “sleep disturbance”. The full list of search terms is attached in the supplementary section (S1).

Study selection and data extraction

The PRISMA (Preferred reporting items for systematic reviews and meta-analyses) flow diagram of the search and selection process is illustrated in Fig. 1. The systematic search resulted in 25,486 articles, and an additional 13 articles were identified through

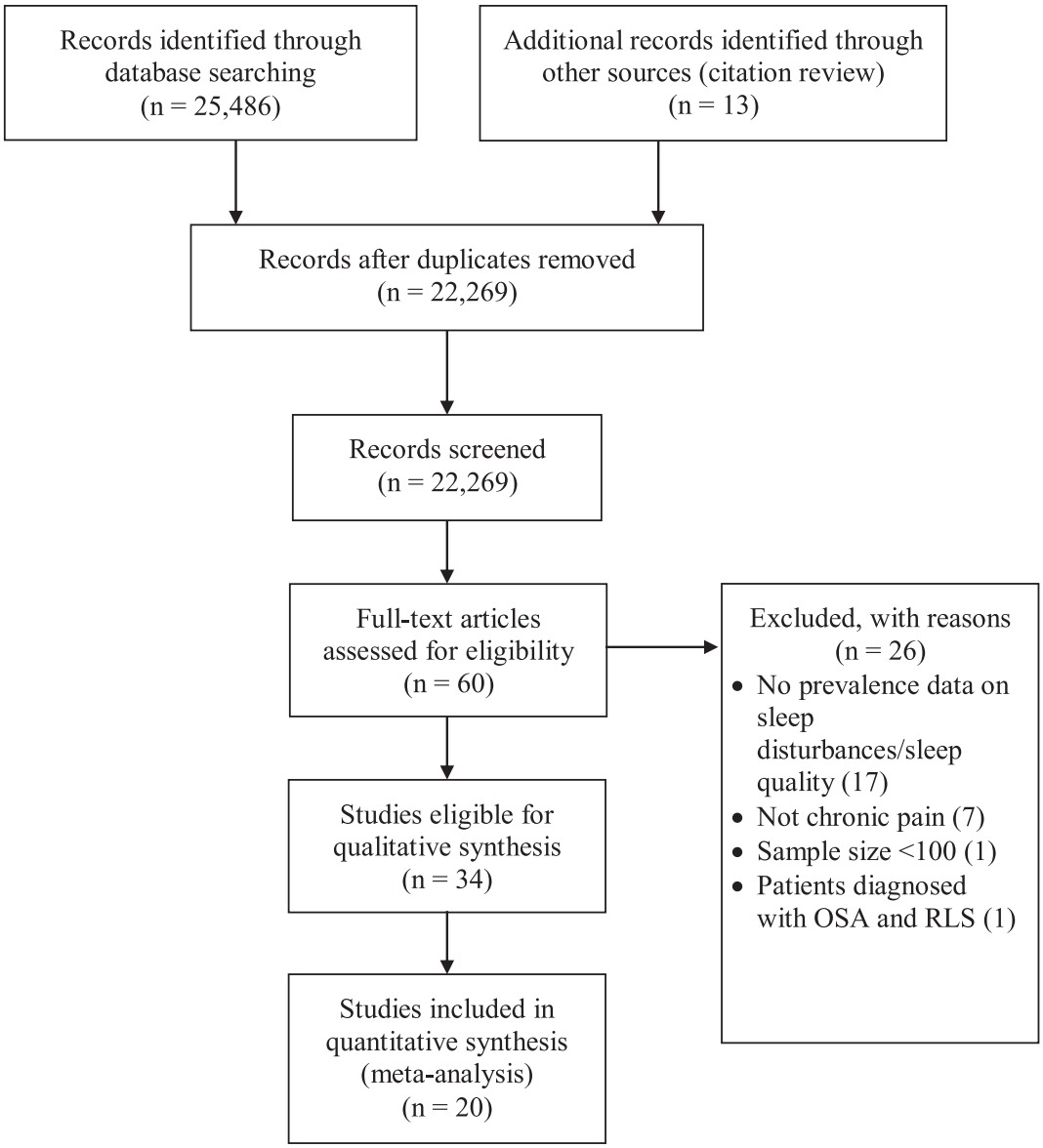

Fig. 1. PRISMA Diagram. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) diagram of study selection process. Abbreviations: N, number of articles; OSA, obstructive sleep apnea; RLS, restless legs syndrome.

citation search. Search results were imported into Endnote and duplicates removed. After removing 3230 duplicate records, 22,269 articles were screened. Four reviewers (YS, AS, IL, CP) participated in the screening process using Rayyan database, a web-tool designed to help researchers collaborate on screening and selecting studies for systematic reviews. Articles were independently selected by two of the four reviewers who screened the titles and abstracts according to the inclusion and exclusion criteria. Sixty full text articles were retrieved for further examination by two reviewers (YS, IL). Disagreements were resolved by consultation with the senior author (FC).

Following full text screening, 26 articles were excluded, with the majority due to lack of prevalence data or chronic pain study population. The full list of exclusion criteria are listed in Fig. 1. Another 14 articles were not eligible for data extraction due to the heterogeneity of their sleep measures. The articles used different subjective sleep measures ranging from one-to four-item questionnaires to clinical interviews; only one article used a validated sleep questionnaire, the Mini Sleep Questionnaire.

The 20 remaining articles, containing prevalence data either from the PSQI or ISI, met the eligibility criteria, and data was extracted into an Excel database. Extracted data consisted of: study design, study setting, chronic pain condition studied, demographics, measures of sleep disturbance, and prevalence of sleep disturbances. Potential confounders including measures of depression, anxiety, and sleep medication use were extracted in the articles that reported them. Outcome data were extracted and calculated in the systematic review and meta-analysis.

Quality assessment of studies - Newcastle-Ottawa quality assessment scale

Two reviewers (YS, IL) independently critically appraised each included study by using the Newcastle-Ottawa quality assessment scale for case-control studies and cohort studies as well as the modified version for cross-sectional studies [23,24]. Disagreements were resolved in discussion with the two team members. The scale

assessed the case-control and cohort studies for three components (selection, comparability, exposure/outcome) with eight question items. The modified scale for cross-sectional studies assessed for the same three components with seven question items: representativeness of the sample, sample size, non-respondents, ascertainment of exposure, risk factors, assessment of outcome, statistical test.

Measures of sleep disturbances - Pittsburgh sleep quality index and Insomnia severity index

Polysomnography and actigraphy are two objective measures of sleep, but were not included in this review as all the articles using these two objective measures did not meet the inclusion criteria for sample size. The PSQI is a self-rated questionnaire that measures sleep quality and disturbances over a one month time period. It contains 19 question items and measures seven components of sleep quality: subjective sleep quality, sleep latency, sleep efficiency, sleep duration, sleep disturbances, use of sleep medication, and daytime dysfunction. The global PSQI score is the sum of the seven components and is scored from 0 to 21. A global PSQI score >5 can be used as a cutoff to indicate poor sleep quality, with a diagnostic sensitivity of 89.6% and specificity of 86.5% [20].

The ISI is a seven item self-rated questionnaire that measures a patient's perception of insomnia through their subjective nighttime symptoms and possible daytime consequences of insomnia. Each item is scored from 0 to 4 and the total score ranges from 0 to 28, with the following interpretation: 0–7: no clinically significant insomnia; 8–14: subthreshold insomnia; 15–21: clinical insomnia (moderate severity), 22–28: clinical insomnia (severe). An ISI score ≥ 8 can indicate the patient is experiencing symptoms of subthreshold to clinical insomnia, with a diagnostic sensitivity of 95.8% and specificity of 78.3% when detecting cases of insomnia in the community [21].

Data analysis

Meta-analyses were performed with a random-effects model to examine the concordance of sleep disturbance prevalence in chronic pain by comparing mean differences. Studies using the PSQI and ISI were analyzed separately. The prevalence of sleep disturbances were extracted from studies using a PSQI cutoff of >5 and ISI cutoff of ≥8. In interventional studies, only baseline data values were used. In studies with multiple groups, chronic pain patients were pooled together [25]. The pooled prevalence was calculated using the inverse-variance random-effects model. The 95% confidence interval (CI) was calculated using the normal approximation calculation [26]. Regression analysis was performed to determine if the prevalence data was influenced by mean age or gender of chronic pain participants, both variables separately as well as age and gender together. Analyses were performed with Stata 15.1, Review Manager 5.4, Microsoft Office Excel, and GraphPad Prism 8.

Results

Study characteristics

The study characteristics of the 20 studies included in the systematic review with subjective sleep prevalence data from the PSQI and ISI are listed in Table 1 [8–11,27–42]. The included studies were from 12 different countries: United States (4), Turkey (3), United Kingdom (3), Taiwan (2), Australia (1), Denmark (1), India (1), Mexico (1), Morocco (1), Pakistan (1), South Korea (1), and Sweden (1). Eighteen studies were retrospective cross-sectional studies, one was a prospective cohort study, and one was a case-control study.

The studies containing PSQI data had a pooled total of 3597 chronic pain patients and studies with ISI data had a pooled total of 2578 chronic pain patients. The studies recruited chronic pain patients from various settings including pain clinics, rehabilitation programs, specialist clinics, a family medicine unit, and a population register. In all studies, the reported mean age was greater than 40 y old and 16 studies had more female participants than male. In studies using the PSQI, the chronic pain patients had a mean age of 53 ± 12 y and 74.4% were female. In studies using the ISI, the mean age was 63 ± 12 y and 56.7% were female.

Quality assessment of studies

Quality assessment of the included studies using the Newcastle-Ottawa scales are presented in Table S1. The scores ranged from 5 to 9 out of 10 for the cross-sectional studies, 7 out of 9 for the cohort study, and 9 out of 9 for the case-control study. The domains where the studies scored best on were appropriately ascertaining the exposure, accounting for risk factors, assessing for outcomes, and performing relevant statistical tests. Many of the studies did not provide justification for their sample sizes and information on non-respondents or response rate.

Prevalence of sleep disturbances in chronic pain patients

In the 12 studies using the PSQI, ten used a cutoff of PSQI global score >5 for categorizing chronic pain patients as having poor sleep quality, with two using different cutoffs of greater than 4 and 8 [28,35]. The prevalence of poor sleep quality ranged from 41% to 96% (Table 2). In 3597 patients with chronic pain, the pooled prevalence for poor sleep quality was 75.3% (95% CI 62.8%, 87.8%) (Table 3, Fig. 2A). Furthermore, seven of the 12 studies had data on the average score for each PSQI component (Table S2). Two of the studies using PSQI had non-chronic pain comparison groups, and the pooled prevalence of sleep disturbances was 23.2% (95% CI 20.8%, 25.6%) in 1182 non-chronic pain participants [32,34].

In the eight studies using the ISI, seven contained data of patients with ISI score ≥ 8, and the prevalence data were subdivided into the categories of subthreshold insomnia (ISI score: 8–14) and moderate or severe clinical insomnia (ISI score: 15–28). Roberts et al. contained only prevalence data using the cutoff of ISI score ≥ 10 [40]. The prevalence of at least subthreshold insomnia ranged from 59% to 95% (Table 2). In 2578 patients with chronic pain, the pooled prevalence for insomnia symptoms was 72.9% (95% CI 62.5%, 83.4%) (Table 3, Fig. 2B).

Regression analysis found that gender and mean age of chronic pain participants, both variables individually and together, were not significantly associated with prevalence of sleep disturbances ($p > 0.05$). When examining the pooled prevalence based on the location of the chronic pain participants, no country or continental region had a statistically significant difference from the total PSQI and ISI pooled prevalence ($p > 0.05$).

Pooled prevalence of sleep disturbances in chronic pain conditions

In studies using the PSQI, the pooled prevalence data was determined for the different chronic pain conditions (Table 3, Fig. S1). In studies with general chronic pain, the pooled prevalence for poor sleep quality was 77.2%. In rheumatoid arthritis, chronic back pain and osteoarthritis, the pooled prevalence were similar; 65.4%, 72.1% and 70.3% respectively. In fibromyalgia, the pooled prevalence was high at 95.5%.

Table 1
Demographic data of chronic pain patients in included studies.

Study author, year (location)	Study Type	Study Population	N	Age (years) mean ± SD	Gender (%F)
Studies using Pittsburgh sleep quality index					
Naughton et al., 2007 (UK) [27]	RC	Chronic pain	155	53 ± 13	69
Bigatti et al., 2008 (USA) [28]	PC	Fibromyalgia	600	54 ± 11	95
Luyster et al., 2011 (USA) [29]	RC	RA	162	58 ± 10	76
Covarrubias-Gomez and Mendoza-Reyes, 2013 (Mexico) [30]	RC	Chronic pain	311	62 ± 13	81
Chen et al., 2014 (Taiwan) [31]	RC	OA	192	68	72
Karaman et al., 2014 (Turkey) [32]	RC	Chronic pain	1014	48 ± 15	66
Loppenthin et al., 2015 (Denmark) [33]	RC	RA	384	NR	80
Sezgin et al., 2015 (Turkey) [34]	RCC	CBP	200	50 ± 14	50
Harrison et al., 2016 (UK) [35]	RC	Chronic pain	221	51 ± 15	59
Katz et al., 2016 (USA) [36]	RC	RA	158	59 ± 11	85
Srivastava et al., 2018 (India) [8]	RC	CBP > 12 wk	100	51 ± 14	64
Turkoglu and Selvi, 2020 (Turkey) [9]	RC	Fibromyalgia	100	42 ± 9	79
Studies using Insomnia severity index					
Bahouq et al., 2013 (Morocco) [37]	RC	CBP	100	43 ± 8	50
Purushothaman et al., 2013 (UK) [38]	RC	CBP	120	55	52
Asih et al., 2014 (USA) [39]	RC	Chronic MSK pain	326	46 ± 11	32
Roberts and Drummond, 2016 (Australia) [40]	RC	Chronic pain	101	59 ± 15	56
Wang et al., 2016 (Taiwan) [41]	RC	CBP	225	41 ± 11	46
Dragioti et al., 2017 (Sweden) [10]	RC	Chronic pain	1154	76[a]	66
Majid et al., 2017 (Pakistan) [42]	RC	CBP	358	NR	60
Yun et al., 2017 (South Korea) [11]	RC	FBSS	194	65 ± 12	58

Abbreviations: CBP, chronic back pain; F, female; FBSS, failed back surgery syndrome; ISI, Insomnia severity index; M, male; MSK, musculoskeletal; N, number of chronic pain patients; NR, not reported; OA, osteoarthritis; PC, prospective cohort; PSQI, Pittsburgh sleep quality index; RA, rheumatoid arthritis; RC, retrospective cross-sectional; RCC, retrospective case–control; SD, standard deviation.
Chronic pain is defined as non-cancer pain greater than 3 mo and is linked to significant emotional distress or functional disability or both unless otherwise stated.
[a] Mean was estimated from median and interquartile range [60].

Table 2
Prevalence of poor sleep quality in chronic pain patients in studies using Pittsburgh sleep quality index and Insomnia severity index.

Study (author, year)	Study Population	N	PSQI > 5 (N)	Calculated Prevalence % (95% CI)
Naughton, 2007 [27]	Chronic pain	155	144	92.9 (88.9, 97.0)
Bigatti, 2008 [28]	Fibromyalgia	600	576[a]	96.0 (94.4, 97.6)
Luyster, 2011 [29]	RA	162	99	61.1 (53.6, 68.6)
Covarrubias-Gomez, 2013 [30]	Chronic pain	311	276	88.8 (85.2, 92.2)
Chen, 2014 [31]	OA	192	135	70.3 (63.9, 76.8)
Karaman, 2014 [32]	Chronic pain	1014	413	40.7 (37.7, 43.8)
Loppenthin, 2015 [33]	RA	384	233	60.7 (55.8, 65.6)
Sezgin, 2015 [34]	CBP	200	131	65.5 (58.9, 72.1)
Harrison, 2016 [35]	Chronic pain	221	191[b]	86.4 (81.9, 90.9)
Katz, 2016 [36]	RA	158	118	74.7 (67.9, 81.5)
Srivastava, 2018 [8]	CBP > 12 wk	100	81	81.0 (73.3, 88.7)
Turkoglu, 2020 [9]	Fibromyalgia	100	85	85.0 (78.0, 92.0)

Study (author, year)	Study Population	N	ISI ≥ 8 (N)	Calculated Prevalence % (95% CI)	Subthreshold insomnia % (N) ISI 8–14	Moderate/severe clinical insomnia % (N) ISI 15–28
Bahouq, 2013 [37]	CBP	100	78	78.0 (69.9, 86.1)	34.0 (34)	44.0 (44)
Purushothaman, 2013 [38]	CBP	120	95	79.2 (71.9, 86.4)	32.5 (39)	46.7 (56)
Asih, 2014 [39]	Chronic MSK pain	326	308	94.5 (92.0, 97.0)	21.2 (69)	73.3 (239)
Roberts, 2016 [40]	Chronic pain	101	76[c]	75.3 (66.8, 83.7)	NR	NR
Wang, 2016 [41]	CBP	225	137	60.9 (54.5, 67.3)	35.1 (79)	25.8 (58)
Dragioti, 2017 [10]	Chronic pain	1154	845	73.2 (70.7, 75.8)	48.6 (561)	24.6 (284)
Majid, 2017 [42]	CBP	358	210	58.7 (53.6, 63.8)	36.0 (129)	21.0 (75)
Yun, 2017 [11]	FBSS	194	123	63.4 (56.6, 70.2)	37.1 (72)	26.3 (51)

Abbreviations: CBP, chronic back pain; CI, confidence interval; FBSS, failed back surgery syndrome; ISI, Insomnia severity index; MSK, musculoskeletal; N, number of patients; NR, not reported; OA, osteoarthritis; PSQI, Pittsburgh sleep quality index; RA, rheumatoid arthritis.
Chronic pain is defined as non-cancer pain greater than 3 months and is linked to significant emotional distress or functional disability or both unless otherwise stated. The PSQI is scored from 0 to 21, with scores greater than 5 indicating poor sleep quality [20]. The ISI is scored from 0 to 28, with the following score categories: 0–7: no clinically significant insomnia; 8–14: subthreshold insomnia; 15–21: clinical insomnia (moderate severity), 22–28: clinical insomnia (severe) [21]. 95% confidence intervals calculated using the normal approximation calculation [26].
[a] Biggatti et al. used a cutoff of PSQI >4.
[b] Harrison et al. used a cutoff PSQI >8.
[c] Roberts et al. used a cutoff of ISI score ≥10.

In studies using the ISI, the pooled prevalence data in the chronic pain conditions are as follows: chronic back pain: 68.9% and general chronic pain: 73.4%. In chronic musculoskeletal pain, the prevalence of insomnia symptoms was 94.5% and in failed back surgery syndrome, the prevalence was 63.4%.

Depression, anxiety, and use of sleep medication

Fourteen of the 20 studies contained data on depression. Depression was collected by six different scales based on symptoms of depression in addition to clinical diagnoses based on the

Table 3
Pooled prevalence data for PSQI studies and ISI studies categorized by chronic pain conditions.

Study Population	Number of Studies	Pooled Chronic Pain Patients (N)	Pooled Prevalence % (95% CI)
Studies using Pittsburgh sleep quality index			
General Chronic Pain	4	1701	77.2 (50.1, 100.0)
Rheumatoid Arthritis	3	704	65.4 (56.5, 74.3)
Fibromyalgia	2	700	95.5 (93.9, 97.0)
Chronic Back Pain	2	300	72.1 (67.1, 77.1)
Osteoarthritis[a]	1	192	70.3 (63.3, 76.7)
Total	12	3597	75.3 (62.8, 87.8)
Studies using Insomnia severity index			
Chronic Back Pain	4	803	68.9 (58.3, 79.6)
General Chronic Pain	2	1255	73.4 (70.9, 75.8)
Chronic MSK Pain[a]	1	326	94.5 (91.4, 96.7)
Failed Back Surgery Syndrome[a]	1	194	63.4 (56.6, 70.2)
Total	8	2578	72.9 (62.5, 83.4)

Abbreviations: CI, confidence interval; N, number of patients.
Chronic pain is defined as non-cancer pain greater than three months unless otherwise stated in Table 1. The PSQI is scored from 0 to 21, with scores greater than 5 indicating poor sleep [20]. The ISI is scored from 0 to 28, with the following score categories: 0–7: no clinically significant insomnia; 8–14: subthreshold insomnia; 15–21: clinical insomnia (moderate severity), 22–28: clinical insomnia (severe) [21]. Pooled prevalence was calculated using the inverse-variance random-effects model and 95% confidence interval was calculated using the normal approximation calculation [26].
[a] Prevalence was not pooled because there was only one study for the chronic pain condition.

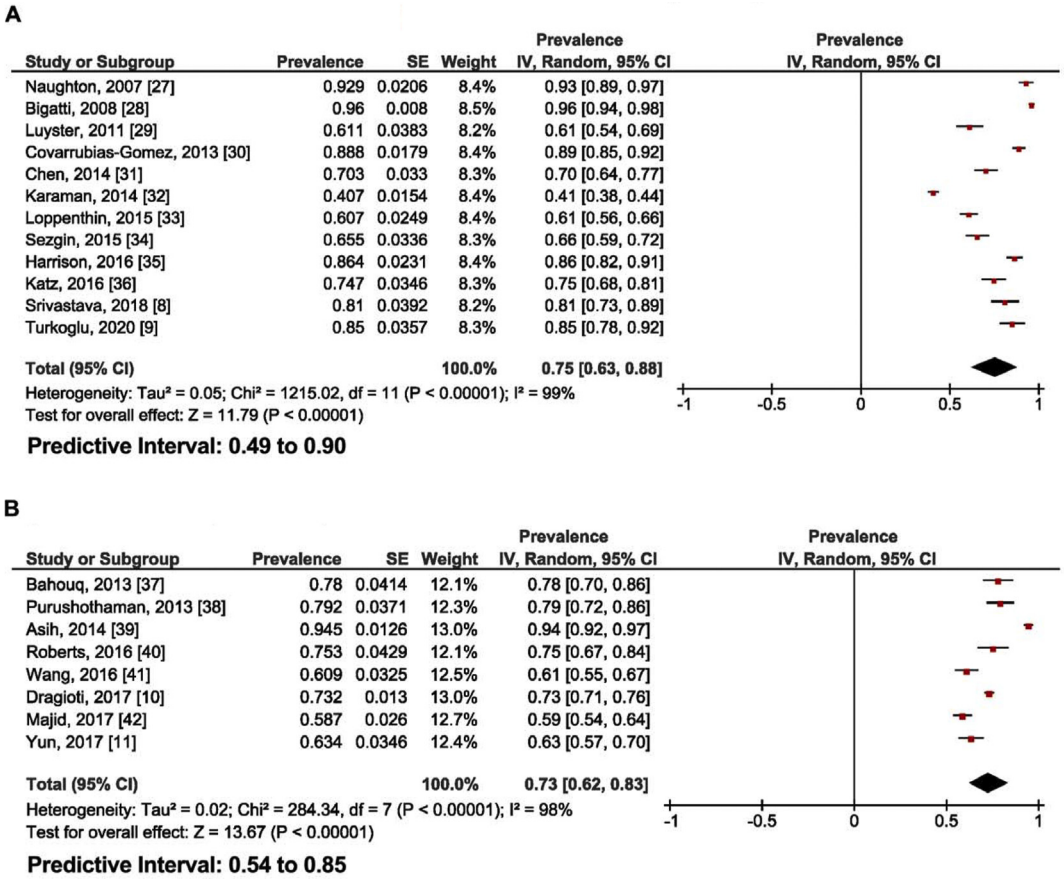

Fig. 2. Prevalence data of chronic pain patients with poor sleep quality (Pittsburgh sleep quality index > 5) and chronic pain patients with insomnia symptoms (Insomnia severity index ≥ 8). Prevalence data of A) chronic pain patients with a Pittsburgh sleep quality index (PSQI) global score > 5 indicating poor sleep quality in studies using the PSQI and B) chronic pain patients with an Insomnia severity index (ISI) score ≥ 8 indicating insomnia symptoms in studies using the ISI. The PSQI is scored from 0 to 21, with scores greater than 5 indicating poor sleep quality [20]. The ISI is scored from 0 to 28, with the following score categories: 0–7: no clinically significant insomnia; 8–14: subthreshold insomnia; 15–21: clinical insomnia (moderate severity), 22–28: clinical insomnia (severe) [21]. Pooled prevalence was calculated using the inverse-variance random-effects model and 95% confidence interval was calculated using the normal approximation calculation [26]. Bigatti et al. used a cutoff of PSQI >4, Harrison et al. used a cutoff PSQI >8, and Roberts et al. used a cutoff of ISI score ≥10.

Diagnostic and Statistical Manual of Mental Disorders. Eleven studies contained prevalence data on depression in their samples of chronic pain patients, which ranged from 0% to 74%. Eight studies, as measured by PSQI, and four studies, as measured by ISI, found an association between sleep disturbances and depression in their samples of chronic pain patients. Only four studies had prevalence

data on sleeping medication use, which ranged from 18% to 57%, and two studies contained anxiety prevalence data, 23% and 28%, for their samples of chronic pain patients (Table S3).

Meta-analysis of mean differences in PSQI scores

Two studies reported data on mean global PSQI scores and mean PSQI component scores in both their chronic pain group (n = 1214) and non-chronic pain group (n = 1182) [32,34]. A meta-analysis showed a significant mean difference of 2.75 (95% CI 1.36, 4.14; $p < 0.001$) in the global PSQI scores between the chronic pain group and the non-chronic pain group (Fig. 3).

Four of the seven PSQI component scores showed a significant mean difference between the chronic pain group and the non-chronic pain group ($p < 0.05$) (Fig. S2). The components were: sleep latency with a mean difference of 0.58 (95% CI 0.16, 1.00); sleep efficiency with a mean difference of 0.29 (95% CI 0.10, 0.49); sleep duration with a mean difference of 0.38 (95% CI 0.19, 0.58); and sleep disturbances with a mean difference of 0.45 (95% CI 0.37, 0.53). Meta-analysis of mean differences in ISI scores was not performed as none of the included ISI studies had a non-chronic pain comparison group.

Discussion

Prevalence of sleep disturbances

This review aimed to determine the prevalence of sleep disturbances in patients with chronic pain. In our review, the PSQI and ISI were the most frequently used measures in studies collecting prevalence data. In chronic pain patients, the pooled prevalence of sleep disturbances as measured by PSQI (75.3%) and ISI (72.9%) studies did not differ significantly and was much higher than the pooled prevalence of sleep disturbances in non-chronic pain patients (23.2%). We found that the pooled prevalence of sleep disturbances was lowest at 65.4% in rheumatoid arthritis patients and highest in fibromyalgia patients at 95.5%. This is consistent with unrefreshed sleep being used as a part of the somatic symptoms scale for the 2010 diagnostic criteria for fibromyalgia [43]. Though it has been shown in the literature that female gender and age are significantly associated with poor quality of sleep [44], neither demographic variable seemed to significantly impact the prevalence data reported.

In the general population, the prevalence of poor sleep quality is usually lower. In a Spanish study of 2144 participants, a 38.2% prevalence was found for poor sleep quality based on PSQI [44]. In a Canadian study of 2000 participants, a 40.2% prevalence for insomnia symptoms was reported [45]. The prevalence of sleep disturbances is higher than the reported prevalence of sleep disorders in chronic pain populations. A systematic review of 5769 chronic pain participants reported a 44% prevalence of any type of sleep disorder, with the top three being insomnia, restless legs syndrome, and obstructive sleep apnea [15].

The relatively high prevalence of sleep disturbances in chronic pain patients, in the absence of a comorbid sleep disorder, emphasizes the importance of characterizing the relationship between sleep and chronic pain. Management of sleep disturbances in chronic pain patients has been shown to decrease pain severity and improve pain-related outcomes [3,46]. Since chronic pain places such a high burden on patient quality of life, it highlights the need for early screening of sleep disturbances in chronic pain patients so that management can be initiated early, and especially true for chronic pain conditions such as fibromyalgia.

Early screening and management of sleep disturbances in chronic pain patients will require education of both health care professionals and patients. The current literature on pharmacologic management of sleep disturbances in chronic pain patients has mixed data on the efficacy and adverse effects of sedative-hypnotics and opioids [1]. For example, chronic opioid and sedative use may be associated with sleep disordered breathing [47,48]. However, newer hypnotic agents and antidepressants can help improve sleep in chronic pain patients [1]. For non-pharmacologic management, promising interventions include cognitive-behavioral therapy for insomnia and physical exercise intervention. Both have been shown in randomized controlled trials to improve sleep disturbances in patients with chronic pain [49,50].

Comparing PSQI and ISI data

Interestingly, despite the PSQI assessing for poor sleep quality and ISI assessing for insomnia symptoms, the pooled prevalence of sleep disturbances in chronic pain patients was not significantly different between the two questionnaires. In fact, in the same chronic pain conditions, such as chronic back pain, similar prevalence rates of sleep disturbances were observed across PSQI and ISI studies (Table 3). This consistency suggests that the PSQI and ISI may have similar sensitivities to sleep disturbances and the measured prevalence in chronic pain patients may be reproducible with either questionnaire.

A 2016 meta-analysis found that for insomnia screening specifically, PSQI and ISI yield comparable diagnostic capabilities [51]. Even with the differences in the purpose of the tools (PSQI assessing for poor quality sleep and ISI screening for insomnia symptoms), both have similar question items. For example, both have question items concerning difficulties falling asleep, difficulties staying asleep, and impact on daytime functioning. Given their similarities, the PSQI and ISI may be comparable enough to detect similar subjective experiences of sleep disturbances in chronic pain patients.

Impact of depression

Depression may be a key confounding factor in detecting sleep disturbances using subjective questionnaires such as PSQI and ISI.

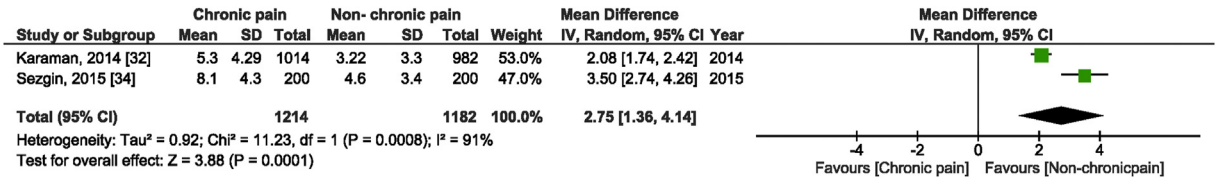

Fig. 3. Meta-analysis of mean differences in global PSQI score in chronic pain patients compared to control group. Meta-analysis and forest plot showing the mean differences in the global Pittsburgh sleep quality index (PSQI) scores in chronic pain patients compared to the control group. The PSQI is scored from 0 to 21, with higher scores indicating worse sleep quality [20]. It includes seven components (subjective sleep quality, sleep latency, sleep efficiency, sleep duration, sleep disturbances, use of sleep medication, daytime dysfunction), each with a score from 0 to 3.

In patients with chronic pain, we found that 12 of the 20 studies had an association between sleep disturbances and depression. In fact, there is strong evidence showing an association between chronic pain and depression, suggesting that all three conditions: chronic pain, sleep disturbance, and depression, may be interdependent [52,53]. Furthermore, many of the scales used to measure depression were based on depressive symptoms. However, whether the depressive symptoms are attributed to sleep disturbances or a comorbid depression is difficult to discern. For example in the literature, depressive symptoms may be common in patients with various sleep disturbances, further complicating the relationship between sleep disturbances and depression as a confounding variable [54,55].

Both the PSQI and ISI have been described in the literature as having significant correlations with measures of depression. For example, PSQI global scores were found to be correlated with depression as measured with the Center for Epidemiological Studies Depression scale and ISI was correlated with depression as measured with the Beck Depression Index [56,57]. However, subjective measures of sleep like the PSQI and ISI may be better able to account for the important cognitive component of sleep disturbances, including pain-related beliefs and the tendency to catastrophize [58].

The literature on the impact of depression on sleep and pain have shown that depression can mediate the relationship between sleep and chronic pain, for example the psychological adaptation to chronic pain and the dysfunctional sleep beliefs that can perpetuate insomnia [3,59]. Thus, screening for depression is valuable during assessment for sleep disturbances in chronic pain patients. As well, PSQI and ISI scores may be impacted differently by comorbid conditions such as depression along with pharmacological and non-pharmacological interventions for sleep and pain. Further research in characterizing this relationship between depression and sleep disturbances is needed.

Meta-analysis of mean differences

Compared to the general population, patients with chronic pain have a higher prevalence of sleep disturbances and also report worse sleep quality. Our meta-analysis of the mean differences in global PSQI scores suggests that the overall sleep quality is significantly worse in patients with chronic pain compared to non-chronic pain patients. Our findings in chronic pain patients is consistent with a meta-analysis of seven studies with 501 fibromyalgia patients showing worse sleep quality, as assessed by PSQI scores versus healthy controls [14].

In addition, our meta-analysis found significant differences in PSQI components sleep latency, sleep efficiency, sleep duration, and sleep disturbances in chronic pain patients versus non-chronic pain patients. Wu et al. also found significant differences using PSQI in sleep latency and sleep efficiency in fibromyalgia patients compared to healthy controls [14]. However, they did not find a significant difference in the PSQI component for sleep duration, and they did not assess the other PSQI components. Our findings are also consistent with a meta-analysis of polysomnography case-controlled studies, where significant effect sizes were found between chronic pain patients and controls in sleep onset latency, sleep efficiency, and sleep duration [15]. Further research may be needed to better understand how PSQI component scores may be impacted in chronic pain patients compared to non-chronic pain patients, especially in different chronic pain conditions.

Limitations

There are several limitations in this review. First, the studies were heterogeneous with different clinical settings, patient populations, and varying study personnel and procedures. Second, retrospective studies may have differences in baseline characteristics. Third, the included studies were cross-sectional, cohort, and case control studies and their associated lack of randomization potentially introduced selection bias. Fourth, studies were limited to English. Finally, prevalence data using objective measures of sleep, such as polysomnography and actigraphy, were not included due to their small sample sizes. Nonetheless, this review identified the important pooled prevalence data on sleep disturbances in 6175 chronic pain patients and it highlights the necessity of early screening and further characterization of the relationship between chronic pain and sleep.

Conclusion

This systematic review and meta-analysis demonstrated that the prevalence of sleep disturbances, as measured by PSQI (75%) and ISI (73%) studies, is very high in chronic pain patients. Depression may be a key confounding variable in detecting sleep disturbances when using the PSQI and ISI. Further work is needed to identify the types of sleep disturbances that are present, which can be impactful on improving outcomes in chronic pain patients.

Practice points

1) The focus of previous systematic reviews and meta-analyses of sleep disturbances was on specific subgroups of chronic pain patients and diagnosed sleep disorders.
2) This systematic review and meta-analysis demonstrated that the prevalence of sleep disturbances, as measured by PSQI (75%) and ISI (73%) studies, is very high in chronic pain patients.
3) Compared to the general population, patients with chronic pain report worse sleep quality, sleep latency, sleep efficiency, sleep duration, and sleep disturbances.
4) The large number of chronic pain patents that report poor sleep quality warrants early screening for sleep disturbances in this subgroup.
5) Depression may be a key confounding variable in detecting sleep disturbances when using the PSQI and ISI.

Research agenda

1) Larger sample prevalence studies on sleep disturbances in chronic pain patients using objective measures of sleep are needed.
2) Further work is needed to identify the types of sleep disturbances that are present, which can be impactful on improving outcomes in chronic pain patients.

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Conflicts of interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smrv.2021.101467.

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