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Sleep disturbances and sleep disorders in adults living with chronic pain: A meta-analysis

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Abstract

Objectives: Chronic pain, with or without an identified diagnosis or cause, is widespread and commonly associated with sleep disturbances. However, research has often used poor quality measures of sleep and focused on specific pain conditions, thereby limiting its reliability and applicability to the wider CP population. This study meta-analysed the findings from studies that used objective polysomnographic measures of sleep or examined diagnosed sleep disorders in people with CP.

Methods: Three databases were searched (PubMed, PsychINFO, Embase; inception to June 2017) for case-controlled polysomnography studies and studies that reported the prevalence of diagnosed sleep disorders in adults with CP. Hedge's *g* effect sizes and prevalence rates were calculated using the data from 37 studies.

Results: Polysomnographic measures of sleep onset latency and efficiency, time awake after sleep onset and awakenings were all significantly worse in those with CP when compared to healthy controls (large effects). Total sleep time, light sleep duration (NREM 1), number of stage-shifts, respiratory-related events and periodic limb-movements were also worse for those with CP, albeit to a lesser extent (small to medium effects). The pooled prevalence of sleep disorders in CP was 44%, with insomnia (72%), restless legs syndrome (32%) and obstructive sleep apnea (32%) being the most common diagnoses.

Conclusions: Objective polysomnographic measures indicate that individuals with CP experience significant sleep disturbances, particularly with respect to sleep initiation and maintenance. Clinically diagnosed sleep disorders are also very prevalent. It is imperative that sleep disturbances and disorders be assessed and treated in conjunction with the CP.

Keywords:

Chronic pain, sleep disturbance, sleep disorders, polysomnography

1. Introduction

Chronic pain (CP), which is defined as pain that is present on most days for at least three months (International Association for the Study of Pain [IASP], [72], is experienced by 10% to 25% of adults (Currow et al., [35]; Goldberg & McGee [54]; Henderson et al., [63]). Some people have a clear medical cause for their CP, such as arthritis or cancer, but many do not (Blyth et al., [13]). Regardless of their diagnosis, a large number of people with CP also report experiencing poor sleep [74]. Although the relationship between CP and sleep is likely to be reciprocal (Finan et al., [51]; Fishbain et al., [55]; Lintzeris et al., 85]), there is evidence to suggest that sleep quality better predicts pain than pain does sleep (Bonvanie et al., [17]). Poor sleep may therefore play a vital role in the development and/or exacerbation of pain over time ([51], Odegard et al., [102]), highlighting the importance of accurate assessment and timely treatment of sleep problems to the outcomes of persons with CP (Bjurstrom & Irwin [10], Heffner et al., 62]).

The exact mechanisms underpinning the relationship between CP and disturbed sleep are unclear, but are likely to involve multiple contributors. For example, the physical discomfort associated with CP may disrupt sleep by increasing a person's level of internal arousal (Pascualy & Buchwald [106]; Roehrs [113]). Both CP and sleep disturbances are also associated with a variety of brain-based changes, including atypical levels of brain-wave activity (eg, increased limbic activity), structural (eg, hippocampal atrophy) and dopaminergic changes, and decreased neurotropic factors (which regulate neuronal survival and growth) (Boakye et al., [15]; Finan & Smith [52]). CP is additionally associated with alterations to the brain's inflammatory responses, which are critical for sleep-wake regulation (Zhang & An [149]). On a psychological level, depression (Harman et al., [60]), emotional responses to CP (Tang et al., [135]) and pain-related cognitions prior to sleeping (Smith et al., [128]) may contribute to sleep disturbances in those with pain. Moreover, various behaviours associated

with the CP itself, including decreased levels of activity and daytime napping, may also play a role (Smith & Haythornthwaite [127]).

The literature examining sleep disturbances in persons with CP is extensive (for reviews see Kelly et al., [56]; Menefee et al., [92]; Moldofsky, [95]), however, much of this research has used subjective assessments of sleep, such as sleep diaries, rating scales and questionnaires [92], which rely on retrospective accounts. Although commonly used, self-report measures are prone to inaccurate recall and memory biases, reducing their reliability (Spielman et al., [130]). More compelling evidence regarding the sleep disturbances experienced by people with CP comes from studies that have used either (1) polysomnography to objectively measure sleep quality and quantity, or (2) published diagnostic criteria to identify clinically-significant sleep disorders (eg, insomnia).

Polysomnography is generally regarded as the 'gold' standard measure of sleep and assesses multiple aspects, such as the duration of the different sleep stages and the number of awakenings, respiratory and cardiac events, and limb movements (Iber et al., [70]; Ryan, [118]). Thus far, most polysomnography studies of CP have focussed on fibromyalgia, with a recent meta-analysis reporting that this group experiences significantly less sleep, poorer sleep efficiency, longer awakenings after sleep-onset and more light sleep; all of which reflect clinically meaningful changes (Wu et al., [147]). Polysomnography has also been used with a number of other CP groups – including rheumatoid arthritis, osteoarthritis, chronic headache and temporomandibular pain (jaw/neck/shoulder pain) – although a recent systematic review failed to find a consistent pattern of sleep disturbance [10]. However, this review did not calculate effect sizes; instead relying on the statistical significance/non-significance reported by the original studies, which is affected by small sample sizes (48% of their studies had $N \leq 20$). There was also considerable heterogeneity in the data, potentially arising from differences in study design (eg, laboratory *vs* home setting; use of an adaptation night prior to data collection) and sample characteristics (eg, age, body mass index [BMI] and duration of CP; use of sleep-influencing medications/medication-washout period/exclusion of participants on medications;

whether pre-existing sleep/psychiatric disorders were excluded) [10, 147]. Again, these variables were not examined statistically.

Clinically-diagnosed sleep disorders, on the other hand, have been researched less frequently than self-reported sleep disturbances. Estimates of the prevalence of sleep disturbance in CP vary considerably, ranging from approximately 40% (Karaman et al., [81]) to 88% [128], depending on the specific sleep disturbance and CP group [92]. Once again, there are multiple sampling and methodological variables that may contribute to this heterogeneity, including differences in recruitment source (inpatient/outpatient/community; Civelek et al., [32]; Emery et al., [47]), CP severity (Aigner et al., [3]), psychiatric comorbidity [47], age and gender (Pampati & Manchikanti, [105]), and the methods used to diagnose sleep disorders (checklists *vs* clinical interviews) (Chen et al., [31]; Stehlik et al., 131]). Comparative data is also rarely available, with very few studies examining healthy controls [92]. Although the prevalence of sleep disorders in CP appears to be higher than the relevant base-rates for the general population ([3]; Aigner et al., [4]; Mogri et al., [93]; [131], the extent of these differences is unclear, as is their statistical and/or clinical significance.

Given the relationship between sleep and CP, pain management is likely to be more effective if sleep problems are evaluated and treated concurrently [10, 51]. However, a quantitative synthesis of high-quality data is first needed in order to understand the nature and extent of the sleep problems experienced by those with CP. The current meta-analysis therefore focused on research that has examined either sleep disturbances using polysomnography or clinically-diagnosed sleep disorders in adults with CP. Notably, we adapted a broad – rather than condition-specific – focus in order to explore the general CP experience, as a large proportion of people with CP either do not have an identified cause for their pain or they fail to meet the diagnostic criteria for a single/discrete pain condition (Burke et al., [22]). Thus, condition-specific findings are often not applicable to the experiences of many people with CP. Conditions known to have syndrome-specific sequelae (eg, cancer, spinal cord injury; North, [100]; Urbaniec et al., [140]) were excluded from this meta-analysis because these medical and psychological sequelae may have independently affected sleep,

necessitating their separate consideration. Only case-controlled polysomnography studies (CP *vs* healthy controls [HC]) were examined in order to determine whether the objectively measured sleep disturbances differed from those of their healthy peers. Diagnosed sleep disorders were additionally compared to published base-rates for the general community in order to determine the most common sleep disorders.

2. Method

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher et al., [94]) were followed throughout this meta-analysis.

2.1 Literature Search & inclusion/exclusion criteria

Three databases (PubMed, PsychInfo, and Embase) were searched under the guidance of an expert research librarian for studies, published prior to July 2017, that examined sleep disturbances using polysomnography and/or diagnosed sleep disorders in adults with CP (see Appendix A, on-line supplementary materials, for specific search strategies). The search terms included singular and plural forms of each term, as well as regional variations in spelling (eg, sleep apnea/apnoea), and both general and specific CP terms (eg, back, neck, musculoskeletal, fibromyalgia, arthritis, somatoform, chronic headache/migraine).

All studies in this meta-analysis met the following inclusion criteria: (1) the sample was aged ≥16 years (common age for access to adult pain services; [22]; (2) participants were experiencing CP (defined as pain on most days for ≥ 3 months; IASP, [76]); (3) the sample included $\underline{\geq}$ 10 participants (excludes case studies and very small samples); (4) the study investigated sleep disturbances using polysomnography or clinically-diagnosed sleep disorders; (5) the study reported data from which effect sizes could be calculated; and (6) the study was published in a journal in English.

Polysomnography studies were additionally required to meet the following criteria: (1) nocturnal sleep data (eg, non-rapid-eye movement [NREM], rapid-eye movement [REM], slow-wave sleep) were collected using standardised polysomnography in a laboratory or at home;

(2) a healthy control (HC) group was assessed using the same measures; (3) the CP sample was not known to include individuals who had any other neurological, psychiatric or medical disorder that could independently affect sleep; and (4) data that would enable the calculation of Hedge's *g* effect sizes were provided (mean and SD; or exact one-way F, *t* or *p*-value).

Studies of clinically-diagnosed sleep disorders had to meet the following additional criteria: (1) the sleep disorders were diagnosed using published criteria (eg, American Academy of Sleep Medicine, [6]; American Psychiatric Association, [7]; International Restless Legs Syndrome Study Group, [78]); and (2) the prevalence (*N* or %) of people with one or more clinically diagnosed sleep disorders was reported.

The current study focused on the general CP experience, therefore it excluded studies that examined specific medical, neurological or psychiatric CP conditions, which are known to be associated with syndrome-specific sequelae, namely: spinal cord injuries, stroke and traumatic brain injuries; cancer, cardiac and renal conditions; terminal/palliative conditions; and factitious disorder, psychosis, personality disorder and post-traumatic stress disorder. The sleep disorder, sleep bruxism (clenching/grinding of the teeth), was additionally excluded because it has been linked to a specific CP diagnosis (orofacial/temporomandibular pain; Camparis & Siqueira, [26]; Raphael et al., [109]). Headache-related pain was often examined according to its chronicity; commonly defined as episodic (symptoms on ≥8 days per month) or chronic (symptoms on ≥15 days per month for >3 months) (International Headache Society, [77]). Episodic headaches did not meet the standard definition of CP and were excluded, but chronic headaches were eligible. Lastly, studies that used actigraphy (a non-invasive method used for measuring rest and activity) were excluded because it is less reliable than polysomnography (McCall & McCall, [90]; Quante et al., [107]).

2.2 Search results & study selection

The literature search was deliberately kept broad, consequently it identified 7,597 records after duplicates were removed (see Figure 1). Initial screening of the titles and abstracts of these records revealed that many were not germane to the current study, reducing

the number of potentially relevant papers to 57. The full-text versions of these articles then underwent a detailed review (all screening completed MLC, ambiguous cases discussed with JLM and consensus decision reached). The corresponding authors of two studies were contacted during the study screening process: one author confirmed that their pain sample met the criteria for CP (Roehrs et al., [114]) and another provided additional demographic information for their chronic migraine sample [31]. All eligible studies were also examined to ensure they were independent of one another, with the data from non-independent studies being combined and treated as one study (see Figure 1 for details). In total, 37 independent studies met all of the inclusion/exclusion criteria; 22 of which were case-controlled polysomnography studies and 15 investigated the prevalence of sleep disorders in CP.

Insert Figure 1 here

2.3 Data extraction, preparation & analysis

The following information was extracted from each study: study and participant details (country, recruitment source, sample size, age, sex, relationship and employment status, education, ethnicity); pain-related details (CP diagnosis, duration and site), and sleep data (polysomnographic data, diagnosed sleep disorders). Where provided, data relating to variables that may have moderated the relationship between CP and sleep were also extracted for further analysis. These included variables related to the polysomnography (laboratory/home assessment; whether adaptation nights were used; whether medications were excluded or a washout period was), participant selection (whether CP group was screened for known sleep disorders), study design (whether the CP and HC groups were matched), and sample characteristics (body mass index [BMI]).

In total, 14 polysomnography variables were examined, which were grouped into three domains: sleep continuity (ability to initiate and maintain sleep during the night), sleep architecture (distribution of sleep stages) and indices of sleep fragmentation (number of stage-shifts, awakenings, and movement/respiratory disturbances). Table 1 lists these variables and their definitions. Arousals, respiratory events and periodic limb-movements of sleep (PLMS)

were measured as indices, defined by the mean number of events per hour of sleep. Slow-wave sleep was defined as NREM stage 3 sleep, according to the American Academy of Sleep Medicine guidelines (AASM) [70].

Insert Table 1 here

The prevalence of three different sleep disorders was examined by multiple studies, these being: insomnia (defined by problems with sleep onset/maintenance, waking too early, or non-restorative sleep), restless legs syndrome (RLS; a sleep-related movement disorder, characterised by a strong urge to move the legs, often accompanied by uncomfortable/painful sensations), and obstructive sleep apnea (OSA; a sleep-related breathing disorder characterised by upper-airway obstruction, increased respiratory effort, and decreased ventilation) (Thorpy [137]). Sleep disorders that were only examined by single studies were not considered further.

All data were analysed using the Comprehensive Meta-Analysis program (version 3.0; CMA; 2014, Biostat, Inc., Englewood, NJ, USA). Hedges *g* effect sizes were calculated for the polysomnographic data and prevalence rates were calculated for diagnosed sleep disorders. Forest plots were generated using GraphPad Prism Software (version 7) (GraphPad Software, [57]).

The polysomnographic variables were recorded as continuous data, with Hedges *g* being used to measure the standardised mean difference between the CP and HC groups. If studies used Rechtschaffen's and Kales' methodology to measure sleep Stages 3 and 4 separately, an average for these stages was computed in order to render the data more comparable to the more frequently reported NREM 3 (slow-wave sleep) measures [110]. Similarly, data were pooled when studies examined multiple CP groups. All Hedge's *g* effect sizes were calculated in such a way that a negative *g* indicated that the CP group had poorer sleep than the HC group (more disturbed sleep). Effect sizes were interpreted using Cohen's guidelines (0.2 = small, 0.5 = medium, and 0.8 = large effect) (Cohen, [33]).

The prevalence of diagnosed sleep disorders in CP was calculated for: (A) diagnosed sleep disorders of any type, and (B) the specific diagnoses of insomnia, RLS and OSA. Insomnia was diagnosed using published diagnostic criteria (DSM or ICSD, which include nocturnal and daytime symptoms), which do not require any objective assessments of sleep. RLS was diagnosed using subjective criteria [78], including an urge to move the legs, which begins or worsens during times of inactivity and/or in the evening or night. Lastly, OSA was diagnosed on the basis of a combination of objective (PSG: ≥ 5 apneas/hour of sleep) and subjective features (eg, unrefreshing sleep, daytime fatigue, or waking with a dry mouth). Unfortunately, only two prevalence studies examined a HC group, therefore population base-rates were obtained from large-scale epidemiological studies and then compared to the data from the current study using Fischer's exact tests.

All effect sizes from individual studies were weighted using their inverse-variance prior to calculating mean effect sizes. This weighting takes into account differences in the precision of the effects calculated from individual studies (larger studies show less variability/greater precision and assigned higher weights) (Borenstein et al., [19]). Probability (*p*-values) were calculated to assess the statistical significance of Hedge's *g* effect sizes.

Heterogeneity was assessed using the *Q*-statistic, with significant values indicating variability in the effect sizes reported by different studies [19]. I^2 was used to measure the proportion of variance in the individual/study effect sizes that was not attributable to sampling error, with I^2 values 25%, 50%, and 75% suggesting low, moderate, and high levels of heterogeneity (Higgins et al., 65]). Heterogeneity was expected, given the range of CP conditions and measures, and was therefore additionally addressed by using a random-effects model, which takes into account both within-study variance (sampling error) and between-study variance caused by methodological differences. Data permitting, heterogeneity was then examined using subgroup analyses, which examined whether the effect sizes obtained from different studies varied according to a number of methodological and sampling variables (eg, polysomnography methodology, participant screening). Notably, *Q* and I^2 analyses may have been underpowered when number of studies or sample size was small, thus subgroup

analyses were only performed when there was sufficient statistical power (ie, $N_{studies}$ >20 or $N_{participants}$ > 80) (Huedo-Medina et al., [69]).

Duval and Tweedie's [43] trim-and-fill procedure was used to assess publication bias, based on a random-effects model. This procedure estimates the number of missing/unpublished studies that may exist and calculates the likely impact of any such studies on the current findings (Sutton et al., [132]). Lastly, Orwin's fail-safe *N* (N_{fs}) was additionally calculated to provide an estimate of the number of unpublished studies that would be required to reduce a study finding to a small/trivial effect [19]. A small effect was defined as 0.2 (or -0.2) for Hedge's *g* [33] and 10% (any type of sleep disorder) or 5% (insomnia, RLS, or OSA) for the prevalence rates. The latter criterion values were based on the estimated prevalence of sleep disorders in the general community (Ohayon, [103]; Ohayon & Roth, [104]; Sleep Health Foundation, [126]; Young et al., [148]). If the N_{fs} was greater than the number of studies contributing to an effect size, publication bias was thought unlikely to affect the study conclusions.

CP was considered to be associated with greater sleep disturbances when: (1) Hedges' *g* (polysomnography studies) was negative and moderate or larger in size ($g \leq -.5$), statistically significant ($p < .05$), and the N_{fs} statistic was greater than the number of studies examining that variable; and (2) the prevalence rates of specific diagnosed sleep diagnoses differed significantly from the base-rates reported in large-scale epidemiological studies.

3. Results

3.1 Study characteristics

Summary participant and study details for both the polysomnography and prevalence studies are provided in Table 2 (see on-line supplementary materials, Appendix B for details of individual studies). Twenty-three studies indicated that their sample had been diagnosed with CP, 11 reported a pain diagnosis together with a duration that qualified as CP (mean minus 1*SD* ≥ 3 months), and three labelled their sample as CP.

The 22 polysomnography studies provided data for a total of 674 adults (mostly females) who had been experiencing CP for a mean of nine years. On average, the CP group fell within the normal to obese BMI categories, whereas HCs fell in the normal to overweight range (World Health Organisation, [146]). As seen in Table 2, very few studies reported marital or employment status, educational level or ethnicity. Most polysomnography studies originated in America or Europe and examined fibromyalgia, arthritis, facial and mixed CP groups. Typically, participants were recruited from treatment settings (CP) and the general community (HCs), with polysomnography mostly conducted in sleep laboratories/clinics and just over half using an adaptation night. Moreover, approximately 77% ($N_{studies}$= 17) dealt with medication effects, either by excluding participants who were taking sleep-influencing medications ($N_{studies}$ = 5) or by having a medication-washout period prior to polysomnography $N_{studies}$ = 12). Of 12 studies that used a washout period, one ceased all pain medications 24-hours prior to the PSG, two ceased pain medications and sleep-altering medications 1-week prior to the PSG and the remaining nine ceased analgesics and medications that were known to affect sleep and/or psychotropic medications 2-weeks prior to PSG. Approximately 54% (n = 12) of studies included age-matched CP and HC samples (with some also matching by gender and/or BMI).

Insert Table 2 here

The 15 prevalence studies examined diagnosed sleep disorders in a total of 5,769, predominantly female, adults with CP (see Table 2). Although reported by less than 50% of studies, the average pain duration was 10.5 years and BMI scores largely fell within the normal to obese range [146]. As above, very few studies reported marital or employment status, educational level or ethnicity. Most of the research was conducted in Europe or America and examined a range of CP conditions, with participants primarily recruited through treatment centres, including specialist pain clinics and rehabilitation centres (see Table 2).

3.2 Polysomnography findings

The polysomnography case-controlled studies ($N_{studies}$= 22) provided data for 14 sleep outcomes (see Table 3), but most Q and I^2 statistics indicated high levels of heterogeneity (also

visible in the 95% CIs), suggesting that the findings from individual studies varied considerably. With the exception of REM latency, there were medium to large and significant group differences with very good N_{fs} statistics in all of the sleep continuity outcomes: total sleep time, sleep onset latency, sleep efficiency and time awake after sleep onset (see Table 3). This indicates that patients with CP had less sleep time, took longer to get to sleep, and spent more time awake, compared to HCs.

Insert Table 3 here

In terms of sleep architecture, only NREM 1 showed a moderate and significant difference, with the CP group spending more time in the first stage of sleep, compared to HCs (see Table 3). The N_{fs} statistic suggests that this was a relatively robust finding. In contrast, there were no significant differences between the CP and HC groups in the percentage of time spent in all other stages of sleep (NREM 2, NREM 3 and REM).

Lastly, there was some evidence that those with CP experienced more fragmented sleep (Table 3). In particular, there were large and significant differences in the number of awakenings, with the CP group transitioning from sleep to wakefulness more frequently. A significant medium effect was also observed for the PLMS index, such that the CP group experienced more periodic limb movements per hour of sleep than HCs. Although smaller significant effects were found for the total number of stage shifts (CP group had more shifts between sleep stages) and the apnea-hypopnea index (CP group experienced more respiratory events per/hour of sleep), these findings fell below the criteria for moderate or larger effects ($g \leq -.5$) and the latter finding had a low N_{fs}.

When Duval and Tweedie's trim-and-fill procedure was used to assess the potential impact of publication bias on the polysomnography findings (overall measure), it was found that five studies were likely to be missing, all with larger negative effects, and after adjusting for these studies the overall Hedge's *g* went from -0.59 to -0.75 (see Figure 2a) [43]. The current findings therefore appear to provide a conservative estimate of the impact of CP on polysomnography.

Insert Figure 2 here

3.3 Prevalence of diagnosed sleep disorders

Fifteen studies used published diagnostic criteria to examine the prevalence of sleep disorders in CP samples (see Table 4). As with the analysis of the polysomnography studies, the *Q* and I^2 statistics generally indicated considerable heterogeneity between the prevalence rates reported by individual studies.

Insert Table 4 here

Overall, 44% of CP patients met the diagnostic criteria for a sleep disorder of some type (95% CI = 29% to 60%) (see Table 4). The most prevalent sleep disorder examined by these studies was insomnia ($N_{studies}$= 4), with 72% (95% CI = 48.0% to 88.0%) of people diagnosed with insomnia on the basis of a clinical criteria. This was followed by RLS and OSA, both with prevalence rates of 32% (RLS: $N_{studies}$= 8; 95% CIs = 19%-48%; OSA: $N_{studies}$= 5; 95% CIs = 15%-54%).

An examination of the potential impact of publication bias on the overall prevalence of sleep disorders (any type), using Duval and Tweedies' trim-and-fill procedure, indicated that no studies were likely to be missing (see Figure 2b) [43]. Thus, the estimated 44% of people with CP who had a sleep disorder of some type is unlikely to be affected by publication bias.

In the absence of control groups, base-rate data was sourced from large American and European (the main origins for the CP studies) epidemiological studies in order to evaluate the prevalence data. Specifically, the base-rate for insomnia (DSM-IV criteria) came from a large French study [[103]; RLS came from a very large study of five European countries that used DSM-IV and ICSD diagnostic criteria [104]; and OSA came from a large-scale community sample of adult women ([148]; Note: CP studies of OSA predominantly included females). As seen in Table 4, all three community base-rates were very low (≤ 5.6%) and, when compared to the rates for the CP sample, it was apparent that CP groups experienced significantly higher rates of insomnia, RLS, and OSA than the general community. Indeed, individuals with CP

were almost 13 times more likely to be diagnosed with insomnia, nearly six times more likely to have RLS, and 16 times more likely to have OSA.

3.4 Subgroup analyses

Given the aforementioned heterogeneity in the findings of the individual polysomnography studies, subgroup analyses were carried out to examine the extent to which specific variables may have contributed to this heterogeneity. Subgroup analyses were planned for the polysomnogaphy measures that showed moderate to large and significant differences between the CP and HC groups, and significant heterogeneity (ie, total sleep time, sleep onset latency, sleep efficiency, wake after sleep, awakenings and PLMS). The grouping variables were chosen a-priori, based on reviews by Bjurstom et al., [11] and Wu et al., [147]. Those variables for which there were adequate data were: the study setting (laboratory/home), use of adaption night (yes/no), participant selection (exclusion of individuals with known sleep disorders), and medication status (controlled: wash-out period used or participants taking medications excluded *vs* not controlled: participants on medications/not specified).

Subgroup analyses revealed that Total sleep time was the only variable that differed according to study setting (Q = 11.6, p = 0.001), with larger effects (less total sleep time in the CP group) observed in the laboratory than at-home (see Table 5). However, significant heterogeneity remained for studies conducted in the laboratory, suggesting that other factors were contributing to the findings. Similarly, the use of an adaptation night was only related to the PLMS index (see Table 5), with significantly larger effects (more PLMS in the CP group) seen in those studies that did not use an adaptation night (Q = 5.85, p = 0.02), although significant heterogeneity remained. When studies were grouped according to whether the CP samples excluded those with known sleep disorders versus those whose status was unknown, the number of awakenings differed between these subgroups (Q = 5.40, p = 0.02) (see Table 5). Specifically, the CP group was found to have many more awakenings when they were not screened for sleep problems that pre-dated the CP. Significant heterogeneity remained even when studies excluded known sleep disorders. Lastly, when comparing the findings from studies whose participants were not taking medications at the time their PSG with studies

whose participants were taking medications, it was found that total sleep time and number of awakenings differed (Q = 5.84, p = 0.016): those who were not taking medications had less sleep time and more awakenings (see Table 5). Significant heterogeneity remained in the total sleep time findings for those studies that either used a medication washout period prior to PSG or excluded participants who were taking medications.

Insert Table 5 here

4. Discussion

Estimates of the prevalence of sleep disturbances in people suffering from CP have proven to be quite variable, but are often based on subjective or poor quality measures of sleep, which limits the clinical utility of the data. The current meta-analysis consolidated the findings from studies that used either polysomnography to obtain objective measures of sleep disturbances or *formal* diagnostic criteria to identify clinically recognised sleep disorders, in order to improve our understanding of the extent to which poor sleep is impacting on those with CP. It also extended the literature in two notable ways. First, CP was examined from a broad, rather than condition-specific, perspective in order to capture the lived experience of the large numbers of people with CP who are diagnosed either with multiple comorbidities or idiopathic/non-specific CP [13]. Second, it used case-controlled and epidemiological data to evaluate the clinical significance of the sleep disturbances and disorders experienced by those with CP.

4.1 Sleep disturbances

The data from 22 case-controlled polysomnography studies revealed that nine of the fourteen measures of sleep were significantly poorer in those with CP than in healthy persons; seven of these were at least moderately worse. Consistent with a previous meta-analysis that examined fibromyalgia [147] and a systematic review of mixed CP groups [10], sleep continuity was most affected. Specifically, CP was associated with less time spent asleep, a greater delay in sleep onset, poorer sleep efficiency (% of time asleep, relative to time spent in bed) and more time awake after initially falling asleep.

Sleep architecture appeared to be less affected by CP, with only NREM 1 duration being longer in those with CP. NREM 1 sleep is a transition stage between wakefulness and sleep and between the different stages of sleep (Shrivastava et al., [124]). As the lightest stage of sleep, with a low arousal threshold, it is more prone to awakenings due to external and internal stimuli (Carskadon & Dement, [28]), including CP. Notably, NREM 3 sleep (slow-wave sleep), which has a restorative function (Drewes et al., [42]), was not significantly shorter in those with CP, although it did approach significance (p = .06). Previous evidence for changes to NREM 3 sleep in those with CP has been mixed, with fibromyalgia reportedly being associated with reduced NREM 3 sleep [147] and rheumatoid arthritis associated with increased amounts, possibly as a reparative response to inflammation [42].

Lastly, those with CP experienced greater sleep fragmentation, such that they had significantly more awakenings and movement-related disruptions to sleep (apnea/hypopnea, PLMS) than their healthy peers. They also experienced significantly more stage shifts (transitions between light and deep sleep) and respiratory-related disruptions, although these differences were smaller (low-moderate effects). It is possible that the increased sleep fragmentation found in the CP sample was associated with the fact that they also spent comparatively more time in Stage 1 sleep, which is when conscious awareness of CP sensations would be greatest. However, it is also possible that the movement- and respiratory-related findings were related to other sleep disorders or medication use. Chronic opioid-use, for example, is known to suppress the respiratory system and increase the likelihood of sleep-disordered breathing during NREM sleep (Guilleminault et al., [58]). Indeed, the largest effect size came from a study that assessed persons who regularly used long-acting opioids (Rose et al., [115]). Unfortunately, neither explanation could be assessed because less than half of the studies screened for known sleep disorders. Moreover, most studies (N = 17) used a medication washout period or excluded those who were taking medications, severely limiting the data relating to medication use (eg, dose, type).

Subgroup analyses revealed that four aspects of the polysomnography methodology (laboratory/home assessment; adaptation night used/ not used; individuals screened/not

screened for prior sleep disorders; medication controlled/not controlled) had a significant impact on a number of the findings. In particular, the CP sample had less total sleep time when assessed in a laboratory compared to their home, which was not unexpected, given healthy individuals also experience sleep disturbance when assessed in a laboratory (Iber et al., [71]). They also experienced less sleep time if they were not taking pain or sleep medications. Those with CP had significantly more PLMS than healthy persons when adaptation nights were not used prior to undertaking the polysomnography. Adaptation nights are designed to reduce the problem of people sleeping more poorly during the first night of a sleep study (due to the equipment or new environment) (Herbst et al., [64]). PLMS are known to vary from night-to-night in healthy adults, but do not appear to be prone to 'first night' effects (Homyak et al., [67]; Sforza & Haba-Rubio, [122]); leaving the reason for this finding unclear and in need of further investigation. In addition, studies that did not state that they had excluded persons with known sleep disorders reported significantly more awakenings than those that did. It is well recognised that certain sleep disorders (eg, restless legs, periodic limb-movements, and apneas/hypopneas) lead to increased arousals and awakenings, independently of CP (Epstein et al., [48]; [67]; Schutte-Rodin, [121]). Thus, the failure to screen for known sleep disorders may have artificially inflated the prevalence of sleep disturbances that are attributable to the CP. Unsurprisingly, people with CP experienced more awakenings if they were not taking their pain and/or sleep medications at the time of their PSG, compared to those who continued to take these medications.

4.2 Diagnosed sleep disorders

The prevalence rates of diagnosed sleep disorders found in the CP sample was compelling. Overall, 44% of individuals with CP had some type of diagnosed sleep disorder, which is much higher than the equivalent rate of 10% for people who are living in the general community (Ram et al., [108]; [126]). The pooled prevalence for insomnia was particularly high (72%) and significantly higher than that of the general population (5.6%) [103]. However, the number of studies was small ($N_{studies}$ = 4) and there was a high prevalence (up to 55%) of comorbid affective disorders (especially depression) in the three studies that reported the

highest rates of insomnia ([3, 47]; Sancisi et al., [119]), rasing the possibility that insomnia may be secondary to depression and/or CP. Regardless of the cause, the results indicated that individuals with CP were thirteen times more likely to be diagnosed with insomnia than their healthy peers. RLS, on the other hand, had a prevalence rate of 32%, which was significantly higher than the general community (5.5%) [104]. Notably, RLS was diagnosed using a number of different methods, which may have inflated the prevalence.

Finally, 32% of those with CP met the diagnostic criteria for OSA, making it 16 times more likely that someone with CP would be diagnosed with this disorder than their healthy peers (prevalence 2%; [148]). The prevalence rates for OSA varied significantly between studies, possibly reflecting differences in how OSA was diagnosed. Whereas, some studies used the apnea-hypopnea index to diagnose OSA (>5 events per/hour) (Evers et al., [49]; [93]; Smith et al., [129]), others examined OSA-syndrome (Mutoh et al., [98]; [105]), which additionally requires excessive daytime sleepiness and has a lower prevalence in the general community [126]. OSA may also be more common in persons with high BMIs and/or those using opioids for pain management [93, 98, 105]. Unfortunately, BMI and opioid-use were not consistently reported, although two studies [93, 105] included people who were chronic opioid users. These studies reported quite different prevalence rates (14% and 36%, respectively), with the lowest coming from a very large sample (n =4,036).

4.3 Strengths, limitations and future research

The main strengths of this meta-analysis were that it focused on high-quality measures of sleep in those with chronic pain (≥3 months), viewed from a general perspective, with the findings being compared to those of the general community and effect sizes calculated to make the findings more clinically meaningful. Sub-group analyses were additionally performed to examine potential sources of variability in the findings from different studies. Balanced against this were a number of limitations. Specifically, the prevalence studies did not report the duration of the sleep disorders or when they were diagnosed in relation to the CP, therefore the data may overestimate the number of people who developed sleep disorders as a direct

consequence of their CP. Although some sleep disorders may have pre-dated the CP, it does not diminish the importance of these findings because sleep disorders have the potential to undermine treatments for CP, regardless of when they develop (prior to or secondary to the CP) (McCrae & Lichstein, [91]). In the absence of case-control studies examining diagnosed sleep disorders, the prevalence data were compared to that of large-scale epidemiological studies, which examined community base-rates for sleep disorders using comparable diagnostic criteria. Without this comparative data, it would not have been possible to determine whether, and to what extent, the prevalence of sleep problems in persons with CP exceeded that of their healthy peers. These analyses arguably provide important information but are limited by the fact that the data were collected in separate studies.

In addition, the data needed to complete some of the planned subgroup analyses were not provided by a sufficient number of studies, thus it was not possible to examine whether CP duration/severity, BMI and psychiatric comorbidity were impacting on the findings. The fact that significant heterogeneity remained even after considering specific moderators (study setting: total sleep time; adaption night: PLMS index; exclusion of known sleep disorders: number of awakenings; medication washout: total sleep time), suggest that these other sources of variability need to be investigated, as does their combined effect. In addition, this study examined CP from a general perspective in order to provide clinically relevant data for the many people who suffer from CP, but either do not have a diagnosis identifying the cause of their pain and/or experience multiple comorbidities. Although applicable to those with 'undifferentiated CP', 'idiopathic pain', 'chronic primary pain' (Lipowski, [86]; Treede, et al., [138]) or multiple diagnosed co-morbidities, the findings may be less useful for those who have a single specific diagnosis.

This meta-analysis also confined itself to research that was published in English journals, which meant that it may have overlooked studies in other languages or that appeared in the 'grey' literature. The grey literature includes unpublished studies that may differ from published studies because they were poorer quality or they found non-significant findings. Instead, the potential impact of publication bias was assessed using Duval and Tweedie's trim-

and-fill method and by calculating Fail-safe Ns [43]. Finally, the study was not registered with PROSPERO, which is increasingly being used to avoid duplication and to improve transparency.

With the aforementioned limitations in mind, research now needs to focus on refining our understanding of the relationship between sleep and CP by focussing on the variables that moderate this relationship. This will help build a better understanding of the relationship between sleep and CP and, in turn, assist us to identify those individuals with CP who are most at risk of comorbid sleep disturbances. Left undiagnosed and untreated, comorbid sleep disturbances have the potential to undermine any treatment that a person receives for their CP. Researchers should ensure that they use high-quality measures of sleep and more consistently report information relating to variables that have the potential to explain some of the variability in the findings (eg, CP duration/severity, BMI, psychiatric history and comorbidity, medication-use); all with the view to improving the quality of the evidence that is informing clinical practice.

4.4 Conclusions

The current findings confirm that persons with CP suffer from poorer sleep than their peers and highlight that this is, in fact, a clinically meaningful difference. In particular, polysomnography studies indicate that persons with CP experience problems with sleep continuity (sleep time, onset and efficiency, staying asleep), sleep architecture (increased NREM 1/lighter sleep), and sleep fragmentation (more awakenings and movement-related disturbances and, to a lesser extent, more stage shifts and respiratory-related events). The prevalence of common sleep disorders, including insomnia, RLS and OSA, was also significantly higher for those with CP than for the general population. Indeed, persons with CP are between six and 16 times more likely to have a clinically-diagnosed sleep disorder than their healthy peers, highlighting the clinical importance of these findings. Given that the prevalence of self-reported sleep problems is much higher than these figures [103, 126], it is highly likely that the current data underestimates the number of people with CP who are experiencing distress as a consequence of poor sleep.

Although sleep has long been recommended as a routine inclusion in pain assessment, (Dworkin et al., [44]), the degree to which it is actively addressed in treatment varies considerably. The current findings highlight the importance of routinely assessing the extent to which those with CP suffer from sleep problems and, where there is a suspicion of a comorbid sleep disorder, referring the patient for a specialist assessment. They also provide valuable targets to guide interventions designed to improve sleep. For example, cognitive-behavioural therapy – a therapeutic approach that is commonly used in the treatment of CP – could also be used to improve sleep onset, sleep efficiency and sleep time, and reduce the frequency and duration of awakenings [91, 121]. Given the range of measureable sleep disturbances and high rates of diagnosed sleep disorders, there is a definite need to design and implement interventions that address both the symptoms of CP and sleep disturbance simultaneously (Davin et al., [37]; Tang, [133]).

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Conflicts of interest

None to declare

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***** Denotes a study that provided data for the meta-analysis (including epidemiological studies for base-rate comparisons of sleep disorder prevalence)

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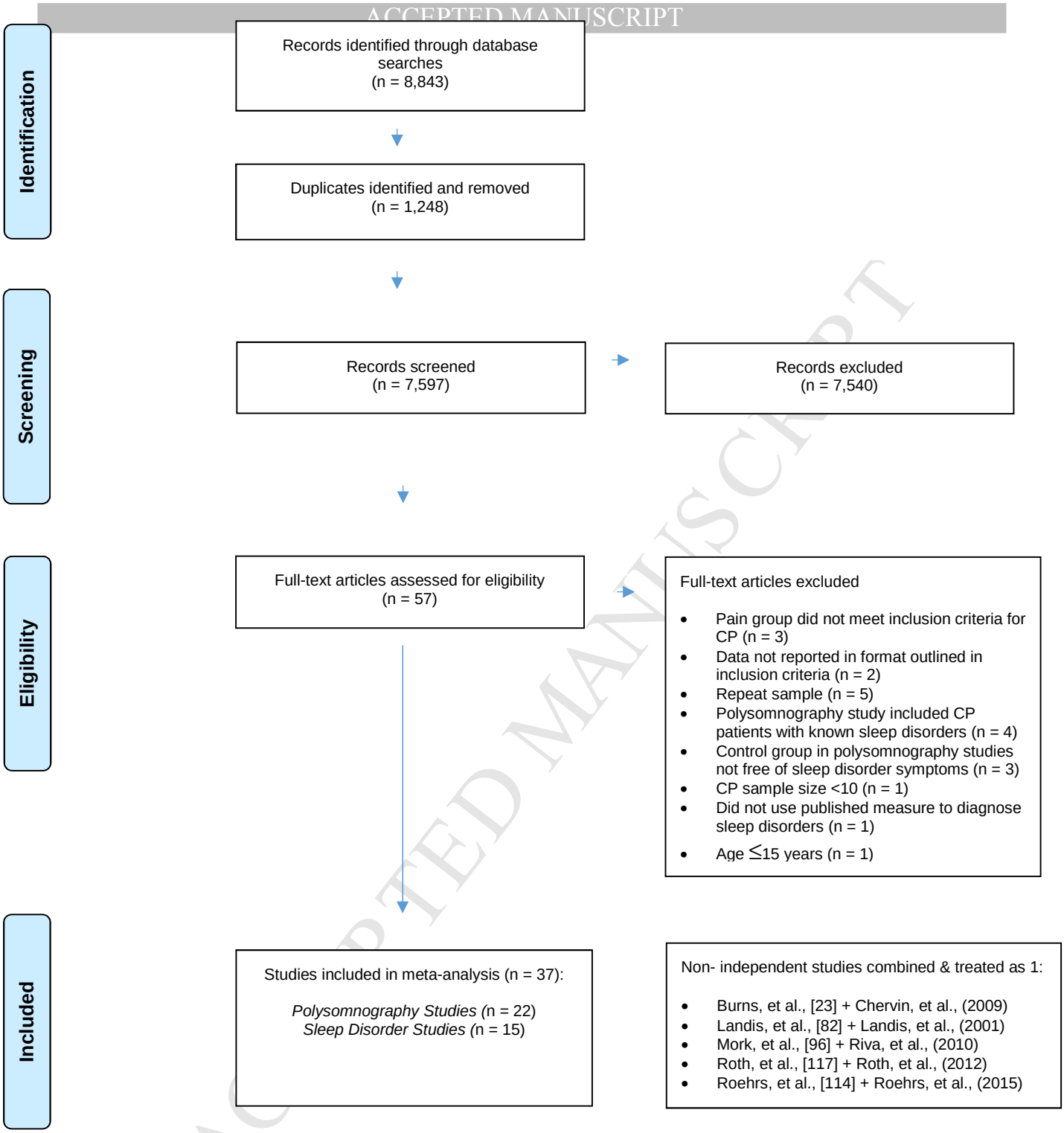


Figure 1

PRISMA flow diagram showing the study search and selection process

Table 1

Summary of the polysomnography variables

Variable	Definition
Sleep continuity	
Total sleep time (mins)	Total amount of sleep (sleep onset to the final awakening)
Sleep onset latency (mins)	Time between lights out & first epoch (30-second interval recordings) of NREM sleep
REM latency (mins)	Duration between sleep onset & first epoch of REM
Sleep efficiency (%)	% of total sleep time, relative to time spent in bed (total sleep time/time in bed x 100)
Wake after sleep onset (mins)	Total time spent awake after the first epoch of sleep
Sleep architecture	
Time in each sleep stage (%)	Proportion of total time spent in each sleep stage: o NREM Stage 1 (N1) o NREM Stage 2 (N2) o NREM Stage 3 (N3) * o REM
Sleep fragmentation	
Awakenings (no.)	Total number of epochs scored as wakefulness
Stage shifts (no.)	Total number of shifts from sleep to wakefulness or to another sleep stage, per hour of sleep
Arousals (no.)	Abrupt transient shift in brain wave frequency during sleep of ≥3 seconds.
Arousal index (no.)	Average number of arousals per hour of sleep
Apnea (no. episodes)	Complete cessation of airflow lasting ≥10 seconds.
Obstructive apnea (no. episodes)	Cessation of airflow associated with inspiratory effort
Hypopnea	Reduction in airflow lasting ≥ 10 seconds, associated with oxygen desaturation or arousal
Apnea-hypopnea index (no. episodes)	Average number of apneas & hypopneas per hour of sleep
Periodic limb movements of sleep (PLMS) (no. episodes)	Repetitive stereotyped leg movement, lasting .5 to 10 seconds PLMS series: consists of ≥4 leg movements, 5 to 90 seconds apart
Periodic limb movements of sleep (PLMS) Index (no. episodes)	Average number of PLMS series per hour of sleep

Abbreviations: NREM = non-rapid-eye-movement; REM = rapid eye movement; PLMS = periodic limb movements of sleep.
*NREM Stage 3 (N3) was formerly referred to as slow-wave sleep Stages 3 and 4 (Rechtschaffen & Kales, [110])
Note: Terminology is based on the American Academy of Sleep Medicine (2007) (Iber et al., [70]). Rules for scoring apneas and hypopneas vary depending on the scoring manual and edition used by polysomnography technicians. The general definitions of sleep-related respiratory events are listed above

Table 2
Summary demographic information for the meta-analyzed studies

	Polysomnography ($N_{studies}$ = 22)						Diagnosed sleep disorders ($N_{studies}$ = 15)		
	Chronic pain			Healthy controls			Chronic pain		
	$N_{studies}$	$N_{participants}$ (%)	*M (SD)*	$N_{studies}$	$N_{participants}$ (%)	*M (SD)*	$N_{studies}$	$N_{participants}$ (%)	*M (SD)*
N (total sample)	22	674	30.6 (25.3)	22	536	24.4 (14.3)	15	5,769	384.6 (1014.7)
Age	22		47.6 (10.1)	22		45.1 (11.3)	12		49.4 (9.9)
Pain duration (years)	7		9.0 (3.5)	0			7		10.5 (5.4)
Body Mass Index	10		27.9 (2.7)	10		25.6 (0.90)	5		27.4 (4.5)
	$N_{studies}$	$N_{participants}$		$N_{studies}$	$N_{participants}$		$N_{studies}$	$N_{participants}$	
Gender									
Male	22	108 (16%)		21	105 (20%)		12	1,941 (35%)	
Female	22	566 (84%)		21	412 (80%)		12	3,612 (65%)	
Relationship status									
Married/partnered	5	91 (59%)		5	65 (37%)		3	178 (55%)	
Single/separated/ Widowed	5	62 (41%)		5	113 (63%)		3	147 (45%)	
Employment status									
Employed	5	82 (49%)		4	73 (44%)		3	110 (35%)	
Not employed	5	85 (51%)		4	92 (56%)		3	205 (65%)	
Highest education level									
Secondary	3	19 (33%)		3	15 (23%)		2	65 (53%)	
Tertiary	3	38 (67%)		3	49 (77%)		2	58 (47%)	
Ethnicity									
White	7	269 (83%)		6	157 (56%)		2	3,693 (93%)	
Not white	7	56 (17%)		6	121 (44%)		2	296 (7%)	
Country									
Australia	1	24 (6%)		1	20 (5%)		-	-	
America	6	157 (37%)		6	186 (50%)		5	4,419 (79%)	
Europe	8	226 (53%)		8	158 (42%)		6	670 (12%)	
Asia	-	-		-	-		2	476 (9%)	
Africa	1	20 (4%)		1	10 (3%)		-	-	
Pain type									
Fibromyalgia	12	406 (65%)		12	286 (59%)		3	519 (9%)	
Arthritis	5	135 (22%)		5	125 (25%)		2	119 (2%)	
Musculoskeletal	-	-		-	-		1	98 (2%)	
Headache/migraine	-	-		-	-		4	637 (11%)	
Facial	2	51 (8%)		2	70 (14%)		1	53 (1%)	
Somatoform	-	-		-	-		2	247 (4%)	
Mixed	1	34 (5%)		1	16 (3%)		2	4,096 (71%)	
Recruitment source									
Treatment-seeking	9	252 (54%)		-	-		13	5,535 (96%)	
Community-based	4	69 (15%)		10	232 (96%)		-	-	
Primary care	-	-		-	-		-	-	
Inpatient	-	-		-	-		1	62 (1%)	
Multiple sources	5	145 (31%)		-	-		1	172 (3%)	
Professional staff	-	-		1	9 (4%)		-	-	
Sleep diagnoses investigated									
Multiple/mixed sleep disorders							2	158 (2%)	
Insomnia							2	207 (4%)	
Restless legs syndrome							7	1,192 (21%)	
Obstructive sleep apnea							4	4,212 (73%)	

Polysomnography setting				
Laboratory	14	467	14	373
At-home	7	196	7	152
Polysomnography Adaptation night	12	427	12	350
Polysomnography Medication washout^	17	529	17	403
Matched Healthy Controls	12	286	12	239

$N_{participants}$ (%): combined total number of participants; $N_{studies}$: number of total studies included in the analysis; $N_{studies}$(%): number of studies/expressed as a percentage
^Studies that employed medication washout or excluded participants who were taking medications known to affect sleep
If subtotals in the $N_{studies}$ columns do not equal the total number of studies, it was because the data were not provided by some studies

Table 3
Summary of the differences in polysomnography-measured sleep variables between CP and HCs

	Sleep Variable	$N_{studies}$	$N_{participants}$ CP	$N_{participants}$ HC	Hedges *g*	*p*	N_{fs}	Heterogeneity Q	Heterogeneity I^2	Study References
Sleep continuity	Total Sleep Time (mins)	19	629	503	**-0.69**	0.01	47	284.58*	93.67	4-8, 11-13, 16-20, 23, 28-30, 32, 34
	Sleep Onset Latency (mins)	14	476	365	**-0.79**	0.001	41	118.65*	89.04	1, 4-5, 7-8, 11, 16-19, 23, 29, 31-32
	REM Latency (mins)	8	204	179	-0.07	0.51	0	4.99	0.00	1, 4, 7, 13, 17-18, 23, 21
	Sleep Efficiency (%)	18	557	433	**-1.24**	<0.001	94	224.63*	92.43	1, 4-7, 11-13, 17-20, 23, 28, 31-32, 34-35
	Wake After Sleep Onset (mins)	11	400	312	**-1.08**	<0.001	48	115.38*	91.33	4, 6-7, 11-12, 16-18, 23, 29, 32
Sleep architecture	NREM 1 (%)	18	495	435	-0.47	0.01	24	97.18*	82.51	1, 4-8, 11, 13, 16-18, 20, 23, 28-29, 31, 34-35
	NREM 2 (%)	18	495	435	0.07	0.65	0	81.84*	79.23	1, 4-8, 11, 13, 16-18, 20, 23, 28-29, 31, 34-35
	NREM 3 (%)	19	519	455	-0.38	0.06	17	150.11*	88.01	1, 4-8, 11, 13, 16-18, 20, 23, 28-31, 34-35
	REM (%)	18	508	444	0.06	0.60	0	49.51*	65.66	1, 4-8, 11, 13, 16-18, 20, 23, 28-31, 34
Sleep fragmentation	Stage Shifts (total)	4	79	59	-0.43	0.01	5	2.34	0.00	6, 12-13, 35
	Awakenings (total)	6	284	194	**-0.96**	<0.001	23	17.55*	71.51	4-5, 11, 17-18, 32
	Arousal Index	9	239	186	-0.74	0.06	24	110.27*	92.75	1, 5, 7, 13, 23, 28, 30-31, 34
	Apnea-Hypopnea Index	9	241	207	-0.34	0.01	6	13.93	42.59	1, 5-7, 13, 16-17, 30, 34
	Periodic Limb Movement Index	7	208	177	**-0.51**	0.03	11	26.86*	77.66	1, 5, 7, 13, 16-17, 23

-2 -1.5 -1 0 1 -1.5 -2

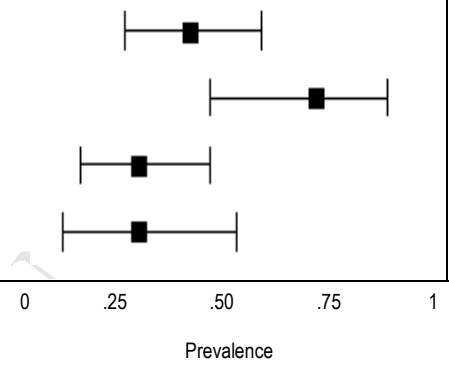
CP outcomes worse CP outcomes better

*p<0.05 – indicates significant heterogeneity; data in bold indicates significant Hedges' *g* result
$N_{studies}$: number of studies included in the analysis; $N_{participants}$: total number of participants included in the analysis (chronic pain and control groups combined)
N_{fs}: Orwin's fail-safe *N;* REM: rapid eye movement; NREM: non-rapid eye movement

Table 4

Prevalence of sleep disorders

	CP sample								Published community base-rates			
Sleep disorder	$N_{studies}$	$N_{participants}$	Prevalence	N_{fs}	Study references	Heterogeneity Q	I^2	Proportion	$N_{participants}$	Prevalence	p	Study reference
Any type	15	5,769	0.44	129	2,3,9,10,14,15,21, 22,24,27,33,36-39	810.90*	98.27					
Insomnia	4	365	0.72	66	2,14,33,36	47.15*	93.64		5622	0.056	<0.001	25
RLS	8	1,245	0.32	82	3,9,10,21,36-39	177.03*	96.05		18,980	0.055	<0.001	26
OSA	5	4,249	0.32	27	15,22,24,27,36	107.34*	96.27		250	0.02	<0.001	40

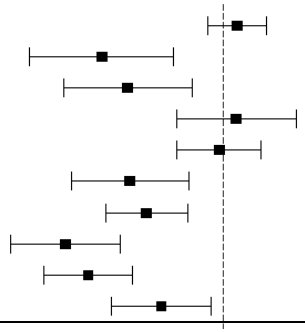


*p<0.05 – indicates significant heterogeneity
$N_{participants}$: total number of participants included in the analysis; $N_{fs:}$ Orwin's fail-safe N; p: Fischer's exact probability statistic (two-sided); RLS: restless legs syndrome; OSA: obstructive sleep apnea

Table 5

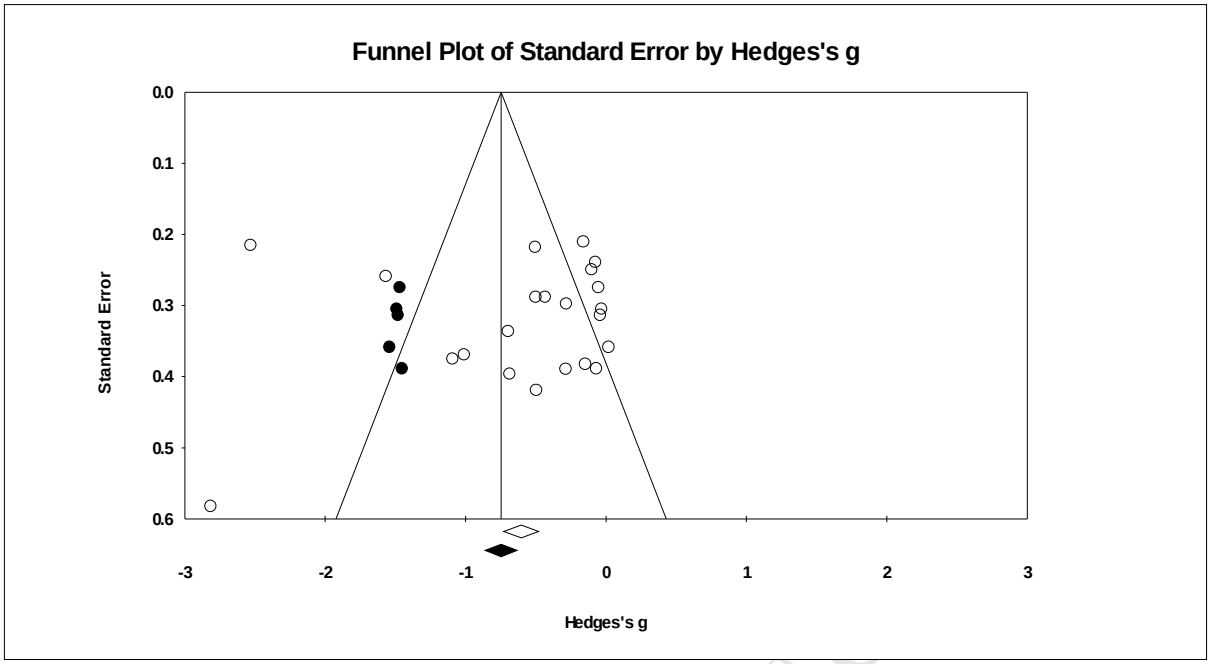
Subgroup analyses for polysomnography measures

Sleep outcome		Subgroup	$N_{studies}$	$N_{participants}$	Hedges' *g*	Heterogeneity *Q*	Heterogeneity I^2	Hedges' *g*
Total sleep time	study setting	at-home	7	388	0.13	10.04	40.26	
		laboratory	12	784	-1.17	191.31*	94.25	
	medication	controlled	15	884	-0.92	230.08*	93.92	
		not controlled	4	248	0.12	14.50*	79.32	
PLMS index	adaptation night	included	3	198	-0.04	3.72	46.23	
		not included	4	187	-0.90	9.87*	69.59	
Awakenings	sleep disorders	excluded	4	428	-0.74	9.03*	66.79	
		unknown	2	90	-1.52	1.25	20.26	
	medication	controlled	3	274	-1.30	3.70	46.00	
		not controlled	3	204	-0.60	5.35	62.64	



*$p<0.05$ – indicates significant heterogeneity
$N_{participants}$: total number of participants included in analysis; *p*: probability statistic;
PLMS Index: periodic limb movements of sleep index

(a) Polysomnography studies (sleep disturbances)



(b) Prevalence studies (sleep disorders)

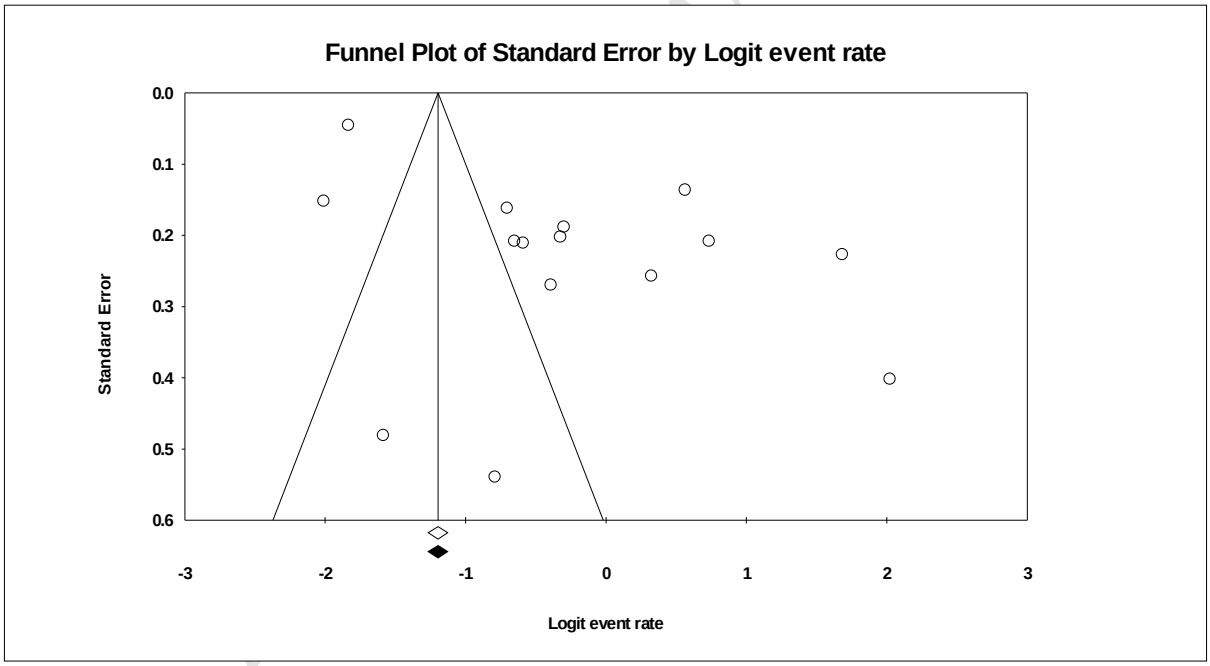


Figure 2

Results of Duval and Tweedie's [43] trim-and-fill for (a) the polysomnography studies (mean overall Hedge's *g*) and (b) the prevalence studies (sleep disorders, any type)

Sleep disturbances and sleep disorders in adults living with chronic pain: A meta-analysis

Mathias, J L, Cant, M L, & Burke, A L J

Highlights

- Sleep initiation and maintenance are most affected in those with CP
- Clinically diagnosed sleep disorders are very prevalent in persons with CP
- Sleep problems should always be assessed and then treated in conjunction with CP