Curr Rheumatol Rep (2015) 17: 1
DOI 10.1007/s11926-014-0469-9

CHRONIC PAIN (R STAUD, SECTION EDITOR)

Sleep Disturbance and Chronic Widespread Pain

John McBeth · Ross Wilkie · John Bedson · Carolyn Chew-Graham · Rosie J. Lacey

Published online: 22 January 2015

Abstract Musculoskeletal pain is common and often occurs at multiple sites. Persons with chronic widespread pain (CWP) often report disturbed sleep. Until recently, the relationship between sleep disturbance and CWP has been unclear: does poor sleep increase the risk of developing CWP, do people with CWP develop poor sleep as a consequence of their pain, or is the relationship bi-directional? In this article, we have focused on the relationship between insomnia and CWP. We briefly present descriptive epidemiological data for insomnia and CWP. We then summarise the available evidence which supports the hypothesis that the relationship is bi-directional. Finally, we discuss the clinical management of CWP and insomnia in primary care, where the vast majority of cases of CWP are managed.

Keywords Epidemiology · Prevalence · Risk factor · Incidence · Onset · Cohort study · Longitudinal study · Chronic widespread pain · Widespread pain · Fibromyalgia · Sleep · Insomnia · Sleep problems · Ageing · Older adults · Primary care · Clinical management

This article is part of the Topical Collection on *Chronic Pain*

J. McBeth (✉) · R. Wilkie · J. Bedson · C. Chew-Graham · R. J. Lacey
Research Institute for Primary Care and Health Sciences, Keele University, Keele, Staffordshire ST5 5BG, UK
e-mail: j.mcbeth@keele.ac.uk

R. Wilkie
e-mail: r.wilkie@keele.ac.uk

J. Bedson
e-mail: j.bedson@keele.ac.uk

C. Chew-Graham
e-mail: c.a.chew-graham@keele.ac.uk

R. J. Lacey
e-mail: r.lacey@keele.ac.uk

Sleep Architecture and CWP

Sleep is a complex behaviour that is heavily influenced by genetic, individual and environmental factors [1]. Sleep can be separated into two states: non-rapid eye movement (non-REM) and REM sleep. Non-REM sleep can be further divided into four stages: I and II are categorised as light non-REM sleep and III and IV as deep slow-wave, or delta (δ), sleep. A normal sleep cycle is characterised by progression through non-REM stages I to IV and then to REM sleep, and this cycle is repeated multiple times during a period of sleep.

Musculoskeletal pain is common; one quarter to one third of the general population report low back, hip or shoulder pain [2]. Pain often occurs at multiple sites [3], and 10 % of the population report persistent widespread body pain, often termed chronic widespread pain (CWP) [4]. Notably, persons with CWP often report disturbed sleep [5]. Sleep disturbance has consistently been associated with the presence of CWP and is part of the classification criteria for fibromyalgia, a non-articular rheumatic disorder which has CWP as the cardinal clinical feature [6]. Early studies of fibromyalgia patients (e.g. Moldofsky and colleagues [7]) suggested that patients' high levels of pain and fatigue could be explained by the alpha (α)-δ sleep anomaly, an intrusive electroencephalogram (EEG)-defined sleep pattern [8]. This EEG sleep pattern described α-like waves (thought to be a waking rhythm) superimposing upon the more normal δ waves during non-REM sleep. That is, normal restorative deep sleep was interrupted by periods of mini-arousal or temporary wakening. Subsequent studies have clearly shown that this anomaly is not specific to people with fibromyalgia: it is evident in patients with osteoarthritis [9] and major depression [10] and in people who are pain free [11]. Nevertheless, there is strong evidence of a link between sleep disturbance and CWP.

Epidemiology of Insomnia

Estimates of insomnia are very much dependent on its definition and measurement. Insomnia is defined in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as a self-report of difficulty getting to sleep, staying asleep or having non-restorative sleep despite having adequate opportunity for sleep, associated impairment of daytime functioning, with symptom duration of at least 4 weeks [12]. Although Smith and Haythornthwaite [13] question the validity of self-reported insomnia, the patient perception is an important aspect of the assessment of sleep disturbance and diagnosis of insomnia [14]. Ohayon and colleagues [15] suggest a hierarchy of insomnia symptoms that predict daytime consequences which are self-reported dissatisfaction, non-restorative sleep, difficulty resuming or maintaining sleep and difficulty initiating sleep.

The different definitions of insomnia and groups of patients studied make comparisons between studies difficult. Morin and colleagues [16] from a synthesis of studies estimate that 30 % of adults report symptoms of insomnia, and 6 to 10 % meet diagnostic criteria for an insomnia disorder. Persistence rates are estimated to vary from 40 to 69 % in follow-up periods of up to 20 years [16]. However, there is a lack of good quality longitudinal studies and whether insomnia is a persistent condition or a recurring transient disorder is unclear. Insomnia affects more women than men [17] and is more common in older compared to younger adults [18]. Sleep quality progressively decreases with increasing age because of reduced capacity to initiate and maintain sleep [19]. Despite spending more time in bed, older people sleep less and report more sleep problems [15]. In a study of community-dwelling older adults (mean age 75.5 years), 45 % reported difficulty sleeping [20]. Studies of community-living elderly adults have also reported variable rates of chronic insomnia ranging from 40 to 75 % for periods of 2 to 3 and a half years [16]. However, despite changes in sleep architecture, the higher prevalence of insomnia in older adults is associated with comorbidities and not with age [21]. In addition to pain, psychological conditions (e.g. depression) and other health problems common in older adults are associated with insomnia either through direct (e.g. symptoms of the condition) or indirect (e.g. through medications) mechanisms [18].

Epidemiology of CWP

The epidemiology of CWP varies according to the population in which it is assessed and the definition of CWP applied. Using the American College of Rheumatology criteria for CWP (pain above and below the waist, on both sides of the body and in the axial skeleton, lasting for 3 months or more) [22], the prevalence of CWP in the general adult population ranges between 10.6 and 18 % [4, 5, 23, 24]. In a UK study, prevalence has been shown to vary by ethnic group, with CWP more common in the Bangladeshi (16 %) than in White (10 %) or British Bangladeshi (9 %) communities [25].

The prevalence of CWP increases with age but decreases after the seventh decade (age 60–70 years) [24]. This is perhaps surprising: from the age of 50, rates of chronic disease which often have pain as a symptom rise dramatically and one would expect CWP to increase with age [26•]. Potential reasons for the reduction in prevalence of CWP in the oldest old include a decline in occupational exposures that are strongly associated with CWP [26•], underlying co-morbidities associated with ageing [27], and perceptions that pain is a natural part of ageing or stoicism [28].

Across studies, women are consistently more likely to report CWP than men [4, 23, 24], with the population prevalence in women around 15 % [4, 23]. Evidence from population studies in the UK (age ranges 18 to 102 years and 18 to 85 years) and Europe (age 40–79) shows the overall prevalence of CWP in men to be around 9 % [4, 23, 29]. Prevalence varies by geographical region: in the European Male Ageing Study, prevalence of CWP in men tended to be higher in eastern European countries (9–15 %) than western Europe (5–7 %) [29]. The excess prevalence in eastern European countries was explained in part by higher levels of depression, exposure to recent life events and higher levels of physical morbidity [29].

Prevalence estimates of fibromyalgia in the general population are necessarily lower than those for CWP, ranging from 2 to 4.7 %, with rates higher in women than in men [27]. A recent study estimating the prevalence of fibromyalgia using the 2010 research survey criteria [6] found that the age and sex-adjusted prevalence in the general population was 6.4 %, whereas the prevalence of diagnosed fibromyalgia in medical records was 1.1 %, suggesting possible under-diagnosis of patients, particularly men, in the community [30].

Link Between Insomnia and CWP

Insomnia and pain commonly co-occur: more than half of patients seeking treatment for pain also report the need for management of insomnia [31, 32], sleep complaints are found in up to 88 % of chronic pain disorders [13], and up to 50 % of individuals with insomnia have chronic pain [33]. But the direction of association has until recently been unclear.

In an early experimental study, Moldofsky and Scarisbrick [34] induced sleep disturbance by exposing healthy volunteers to brief auditory stimulation during periods of non-REM sleep. These periods of sleep deprivation resulted in reports of temporary musculoskeletal symptoms including muscular fatigue and tenderness. More recently, Schuh-Hofer and colleagues demonstrated that one night of total sleep deprivation was associated with an increased risk of hyperalgesia to heat, blunt pressure and cold and increased mechanical pain sensitivity to pinprick stimuli [35]. However, aspects of insomnia (shorter sleep duration and

periods of nightly wakening) did not contribute to a predictive model of clinical pain in patients with fibromyalgia [36]. Two previous reviews have focused on studies of the longitudinal relationship between insomnia and pain. Finan and colleagues [37] set out to review the direction of the relationship between pain and insomnia and build on the work of Smith and Haythornthwaite [13] by reviewing prospective studies published between 2005 and 2012. During this period, there were a number of studies that reported a link between insomnia and future pain, one of which focused on CWP. In that study of adults aged 25 to 65 years old with CWP, restorative sleep was independently associated with the resolution of CWP [38]. Notably, the relationship between being able to initiate and maintain sleep and resolution of CWP was explained by psychological factors. These results support previous findings from this population-based prospective study, which found that sleep problems were associated with the onset of CWP [39] (Table 1). The review by Finan et al. [37] also identified the Mork and Nilsen study [40••] which found that women who "always or often" had sleep problems were over three times more likely to report the onset of fibromyalgia 10 years later. The relationship between sleep and onset of fibromyalgia was almost twice as strong in women aged 45 years and over than in those aged 20 to 44 years. McBeth and colleagues [26•] reported that non-restorative sleep was the strongest predictor of the onset of widespread pain in a large population study of older adults. Mundal and colleagues [5] reported that baseline sleep problems predicted persistence of CWP 11 years later in adults aged 20 years and over in Norway; however, the definition of CWP is unclear and non-restorative sleep was measured using an item which asked about general insomnia ("how often do you suffer from insomnia?").

There have been two studies that have examined whether CWP leads to insomnia. Ødegård et al. [41] reported that CWP predicted insomnia 11 years later (new and prevalent cases); those with CWP had double the risk of developing insomnia compared to those with no pain; there was no difference for gender. Tang and colleagues [42] found that widespread pain was significantly associated with the subsequent onset of trouble with sleep onset, sleep maintenance, early wakening and non-restorative sleep, which was not explained by age, gender, socio-economic, psychological or health factors. In this study, almost half of the 977 adults aged 50 years and over with widespread pain who were insomnia free at baseline developed at least one insomnia symptom 3 years later.

Primary Care Clinical Management of Insomnia and CWP

Assessment and Diagnosis

A comprehensive medical history is essential, to identify past and present predisposing, precipitating and perpetuating factors. Examination, including measurement of body mass index, is helpful and should include assessment for symptoms of anxiety and depression. The patient should be asked to complete a *sleep log book* over 2 weeks, to be brought for discussion and review at a subsequent appointment. Blood tests, e.g. thyroid function and renal function, should be conducted if clinically indicated. Sleep studies are only indicated if sleep apnoea is suspected [44, 45].

Management

The initial goal of management of insomnia is to recognise and address any underlying cause (see case vignettes in Table 2). For patients with CWP and insomnia, although common, there are no comprehensive guidelines. Simply managing a patient's chronic pain will not necessarily lead to an improvement in sleep, since pain and insomnia have a close interrelationship which is bi-directional, where deterioration in either sleep quality or chronic pain can lead to a paralleled worsening in their counterpart [46].

The platform upon which the general practitioner (GP) will build their management strategy encompasses patient education regarding good sleep hygiene (fixed bed times, stimulant avoidance, etc.) [44], exercise and optimising the management of co-morbid conditions [47]. However, when managing CWP and insomnia, in reality, the clinician has three practical treatment options that might have immediate benefit. Firstly, they can prescribe analgesic medication to improve pain and consequently insomnia. Secondly, prescribing medication that will directly influence sleep such as benzodiazepines, or newer antipsychotic drugs such as quetiapine. Thirdly, they can choose to employ psychological therapies such as cognitive behavioural therapy (CBT) [48].

Prescribing Analgesic Medication to Improve Pain and Consequently Insomnia

Prescribing analgesics seems logical when managing CWP. Brennan and colleagues [46] in their review of opioid use in chronic pain found that several studies relating to the use of long-acting opioids such as morphine or oxycodone in patients with chronic pain were linked with improved sleep patterns. Improvements were characterised by increased number of sleep hours and quality of sleep, a reduced need for other sleep medications and improvement in specific sleep modalities such as increased REM sleep [46]. Such gains when using morphine or oxycodone, however, must be weighed against the potential adverse effects of using long-term opioids such as increased rates of bone fractures and self-harm that have been previously described [49, 50]. Opioid use may therefore be limited in the UK, where 20 % of GPs reported a lack of confidence in prescribing stronger opioids because of concerns about addiction or abuse (35 %) and

Table 1 Longitudinal studies of the relationship between CWP and insomnia

Reference	Definition of CWP	Definition of sleep	Sample	Frequency of CWP	Frequency of insomnia	Relationship between CWP and insomnia	Associated factors	Direction of the association
Davies et al., [38]	ACR widespread pain (pain lasting for ≥1 day in past month)	4-item Sleep Problem Scale[a]: • trouble falling asleep (onset) • waking several times/ night (maintenance) • trouble staying asleep (early wakening) • waking feeling tired (non-restorative) Sleep problems categorised into: • 0 days (none) • 1–7 days (moderate) • 8–31 days (high)	Population-based prospective study of adults aged 25 to 65 years in north-west England 679 (75 %) responded at 15 month follow-up	1061 participants reported widespread pain at baseline At 15 month follow-up: • 379 (56 %) reported widespread pain • 300 (44 %) reported resolution of widespread pain	-	3 out of 4 insomnia symptoms were associated with resolution of widespread pain (adjusted for age and gender): • rapid sleep onset (Odds Ratio 1.7) • absence of early wakening (OR 1.6) • restorative sleep (OR 2.7)	Participants with resolution of widespread pain had significantly lower baseline psychosocial factors Restorative sleep alone was independently associated with resolution of widespread pain (OR 2.0)	Restorative sleep → resolution of widespread pain Authors note they cannot infer a causal relationship based on the data
Gupta et al., [39]	ACR widespread pain (pain lasting for ≥1 day in past month and, if yes, whether the pain had been present for ≥3 months)	4-item Sleep Problem Scale [a] asking about problems with sleep within the past month Responses scored in the range of 0–5, giving a total score of 0-20	Population-based prospective study of adults aged 25 to 65 years in north-west England: • 6792 baseline responders (68.2 % adjusted response) • 3185 responders to 15 month follow-up (82 % adjusted response)	3171 participants without CWP at baseline 324 (10.2 %) reported new CWP at 15 month follow-up	In participants free of CWP at baseline, sleep scores were: • 0–3 in 1203 participants • 4–8 in 1039 participants • 9–20 in 832 participants	Univariate association of baseline sleep scores with onset of CWP: • score of 4–8 (OR 2.0) • score of 9–20 (OR 3.4) A sleep score of ≥9 independently predicted the onset of CWP (OR 2.7) adjusted for age and sex	Onset of CWP was independently predicted by: • illness behaviour score of 5–7 (OR 1.9) • illness behaviour score of 8–22 (OR 3.3) • 3–5 somatic symptoms (OR 1.8)	The contribution of sleep problems → new cases of CWP
McBeth et al., [26]	Widespread pain classified according to the ACR criteria for widespread pain, with pain lasting for ≥1 day in past month	4-item Sleep Problem Scale [a] asking about problems with sleep within the past 4 weeks Response categories for each item: • not at all • on some nights • on most nights	Population-based prospective study of adults aged ≥50 years in north-west England: • 13986 baseline responders • 12408 provided pain data • 4326 with no pain or some pain at baseline provided pain data at 3 year follow-up	At baseline: • 3119 participants (22.3 %) reported widespread pain • 3518 (25.2 %) were pain-free • 5771 (41.3 %) reported some pain At 3-year follow-up: • 800 participants (18.5 %) reported new-onset widespread pain • 3526 (81.5 %) reported being widespread pain-free	-	New-onset widespread pain was higher in those reporting sleep problems than those who were widespread pain-free at follow-up ($P < 0.001$)	In multivariate analysis, new-onset widespread pain was associated with: • age (OR 0.97) • baseline pain status score (OR 1.1) • definite anxiety (OR 1.5) • worse physical HRQOL (OR 1.3) • cognitive complaint (OR 1.3) • non-restorative sleep (OR 1.9)	Sleep problems → onset of widespread pain
Mork & Nilsen, [40]	Physician-diagnosed fibromyalgia (FM): "Has a doctor ever said that you have fibromyalgia (fibrositis/chronic pain syndrome)?"	Baseline sleep problems: "During the last month, have you had any problems falling asleep or sleep disorders?"	Longitudinal Nord-Trøndelag Health Study (HUNT study): • 12350 women at baseline (1984–1986)	327 (2.6 %) women reported FM at follow-up: • 3.2 % for age 20–44 years • 1.7 % for age 45+ years	At baseline: • 3571 reported sleep problems sometimes • 378 reported sleep problems often/ always	Age adjusted risk of FM was associated with: • sleep problems sometimes (Relative Risk 2.05)	In multivariate analysis, risk of FM was associated with: • sleep problems sometimes (RR 1.98)	Sleep problems → risk of FM development

Table 1 (continued)

Reference	Definition of CWP	Definition of sleep	Sample	Frequency of CWP	Frequency of insomnia	Relationship between CWP and insomnia	Associated factors	Direction of the association
	Musculoskeletal pain: "During the last year, have you had pain and/or stiffness in your muscles and limbs that has lasted for ≥3 consecutive months?"	Response categories: • never • sometimes • always/often	• followed-up in 1995–1997			• sleep problems often/always (RR 3.95)	• sleep problems often/always (RR 3.43) Multivariate associations between sleep problems often/always and FM onset by age: • 20–44 years (RR 2.98) • 45+ years (RR 5.41)	
Mundal et al., [5]	CWP: "During the last year, have you had pain and/or stiffness in your muscles and limbs that has lasted for at least 3 consecutive months?" If "yes", asked to specify pain area on body map Using ACR criteria for CWP, CWP defined as chronic pain in: • trunk • lower limbs, and • upper limbs	• Non-restorative sleep ("How often do you suffer from insomnia?"): • Sleep onset ("Have you had difficulty falling asleep in the last month?") • Sleep maintenance ("During the last month, have you woken too early and not been able to get back to sleep?") Sleep problems defined as ≥1 sleep problem on the 3 items	Longitudinal cohort study All residents aged ≥20 years in Nord-Trøndelag County, Norway Study population was responders to: • HUNT2 (1995–1997), and • HUNT3 (2006–2008) • n=28367	4927 (17 %) participants in the study sample reported CWP in HUNT2 (baseline) Of those reporting CWP in HUNT2, 1997 (53 %) reported CWP in HUNT3 follow-up (74 % female)	5195 (19 %) of the study population reported sleep problems 1751 (37 %) of the baseline sample reported sleep problems (41 % of females, 30 % of males)	Baseline sleep problems associated with persistence of CWP at 11 year follow-up (OR 1.49) compared with no sleep problems	In adjusted analysis, sleep problems remained a predictor of CWP persistence (OR 1.30), compared with no sleep problems	Influence of sleep problems → persistence of CWP
Ødegård et al., [41]	Chronic musculoskeletal complaints (CMSCs): "Have you during the last year continuously for ≥3 months had pain and/or stiffness in muscles and joints?" If "yes", asked to mark the location of the pain Widespread CMSCs defined according to ACR, as CMSCs in: • axial skeleton • above the waist, and • below the waist	HUNT2: • sleep onset ("Have you had problems falling to sleep in the last month?") • sleep maintenance ("During the last month, did you ever wake up too early, not being able to fall asleep again?") Insomnia free = score of 0 and not used sedatives or hypnotics in last month. HUNT3: "How often during the last three months have you experienced: • difficulty falling asleep at night	Longitudinal cohort study All residents aged ≥20 years in Nord-Trøndelag County, Norway HUNT2 (1995–1997) and HUNT3 (2006–2008) 26151 answered insomnia section in HUNT2 and HUNT3 and could be classified according to pain status in HUNT2 Population at risk= 19271 (74 %) who were insomnia free in HUNT2	-	In HUNT2, 6880 had insomnia symptoms	-	In adjusted analyses, insomnia at follow-up was associated with baseline: • CMSCs (OR 1.8) • non-widespread CMSCs (OR 1.6) • widespread CMSCs (OR 2.0) Co-existing headache ≥7 days / month and CMSCs increased the risk of insomnia (OR 2.2)	Chronic musculoskeletal complaints → risk of insomnia

Table 1 (continued)

Reference	Definition of CWP	Definition of sleep	Sample	Frequency of CWP	Frequency of insomnia	Relationship between CWP and insomnia	Associated factors	Direction of the association
		• several awakenings during the night • wake up to early and were not able to fall asleep again" Insomnia = sum score ≥1						
Tang et al., [42]	Widespread pain classified according to the ACR criteria for widespread pain, with pain lasting for ≥1 day in past month	Four insomnia symptoms[a]: • Trouble falling asleep • Waking several times/night • Trouble staying asleep • Waking feeling tired Response categories for each item: • not at all • on some nights • on most nights	Population-based prospective cohort study of adults aged ≥50 years in north-west England: • 13986 baseline responders • 6676 responders at 3-year follow-up	27.5 % reported widespread pain at baseline	At baseline: • Trouble falling asleep (13.4 %) • Waking several times/night (30.7 %) • Trouble staying asleep (20.2 %) • Waking feeling tired (16.4 %)	Unadjusted associations of widespread pain and onset of insomnia at 3 years: • Waking feeling tired (OR 3.98) • Waking several times/night (OR 2.48) • Trouble staying asleep (OR 2.52) • Waking feeling tired (OR 3.98)	Adjusted associations of widespread pain and onset of insomnia at 3 years: • Trouble falling asleep (OR 1.61) • Waking several times/night (OR 1.78) • Trouble staying asleep (OR 1.59) • Waking feeling tired (OR 2.31) Baseline physical limitation and reduced social participation mediated the association, and explained up to 66 % of the total effect	Widespread pain → onset of insomnia Authors note cautious interpretation as medications that may influence sleep were not included in the analysis

[a] Jenkins et al., [43]

Table 2 Case vignettes

Mr. AY
Mr. Y (Ali) is 78 years old and lives with his extended family. His sons run the family business (importing silks) which he set up 30 years ago and handed over only 3 years ago. His wife has diabetes, heart disease and arthritis, and she rarely goes out. Ali has diabetes but only takes one tablet a day for this and feels it is well controlled. Ali tries to go for a long walk every day but has been finding this increasingly difficult due to pains in his knees, shoulders, elbows and feet. His GP says it is 'arthritis' and he will have to put up with it. He did have some blood tests which were all normal, but that does not help, as he needs to know how to improve things or at least cope with the pains. He has never really slept well, but this has been worse over the past few months, and he wakes feeling exhausted. He feels 'on edge' much of the time and is really irritable with his grandchildren who seem to make so much noise. He will be glad when they go back to school. His son tells him to make an appointment with his GP, but he cannot see the point
Ali's son makes him a GP appointment and accompanies him so that he can ensure that Ali does not forget to tell the GP about all of his problems. Ali's GP seems particularly worried about the pain in Ali's feet, but after he has examined him, he says the pain is not due to his diabetes, but possibly arthritis. He gives Ali a diary to record how he sleeps, his mood and how his pain changes in severity and location
Two weeks later, Ali returns to the GP who goes through the diary with him. He asks Ali more about if he thinks his poor sleep pattern affects his mood and feelings of agitation. The GP examines him all over to see where he is most tender. He suggests that Ali try a tablet called gabapentin which might help with how he feels and his pain and sleeping. He also asks if Ali would like to see someone to talk through his problems and learn some relaxation exercises. He also gives him a 'mindfulness' CD. Ali admits that he used to do yoga when he was younger, and the GP suggests he takes that up again. He offers to see Ali again in a month
Mrs. JS
Mrs. S (Jean) is 74 years old and has always had problems sleeping. She was previously prescribed 25 mg dosulepin at night until a new GP at the practice took her off it a few years ago. He said it was a dangerous drug. Since then she has taken tablets from the health food shop. However, over the past year, she has felt tired, low in energy and has told her usual GP about all her aches and pains. He has given her many different sorts of tablets, but none have made any difference to the pain. She even tried seeing another GP in the practice, but does not feel she was listened to
Jean is invited to make an appointment with the practice for review of her blood pressure treatment, so decides to see another GP to see if he can suggest anything to help her aches and pains and poor sleep. At the appointment, Jean is pleased that the GP asks lots of questions about how she feels and examines her all over. He tells her that she has widespread pain (although she knows that) and orders some blood tests. He gives her a prescription of a tablet for depression that he says might help her pain as well as sleep (it is called duloxetine). He plans to see her again in 2 weeks' time. She is pleased that for once her worries were taken seriously and thinks the antidepressants help as soon as she starts taking them
A week after the appointment, the practice nurse rings Jean to say her 'calcium is high' and she needs further blood tests. When she sees her GP, Jean is told that she has 'hyperparathyroidism' and needs to be referred to a specialist. She is given a leaflet to explain this, but is still worried about what it means. Although she is sleeping much better, and feels the aches and pains might be a little better, she still feels exhausted and wonders if the specialist will be able to help

adverse events (22 %) [51]. Additionally, the evidence for prescribing the newer synthetic opioids such as tramadol or tapentadol as yet has not provided any certainty over their use in managing CWP and insomnia [52, 53].

An alternative option for GPs is to consider using medications that are commonly used in managing neuropathic pain. These include medications such as amitriptyline, gabapentin (GBT) and pregabalin (PGB). Amitriptyline has the advantage of not only having neuropathic analgesic qualities, but the added benefit of also being sedating. A review of the pharmacotherapy of fibromyalgia indicated that in the short term (≤6 weeks), 25 mg per day had a significant impact on improving sleep, whilst larger doses had no effect at all [53]. Therefore, there is a level of evidence supporting its short-term use in managing CWP and insomnia. Clinical practice appears to reflect this, and even though amitriptyline currently lacks a licence for this indication, GPs do report its widespread use for managing insomnia, perceiving it as being part of common practice [54]. One meta-analysis of studies investigating the use of GBT and PGB in fibromyalgia found significant evidence for a reduction in sleep disturbance, though the effect size was considered small [55]. A further meta-analysis compared the effectiveness of two serotonin-noradrenaline reuptake inhibitor (SNRI) antidepressants (duloxetine and milnacipran) with GBT in 11 randomised controlled trials (RCTs) in the treatment of fibromyalgia [56]. Here again, these drugs demonstrated significant benefits in treating both pain and sleep disturbance with numbers needed to treat (NNTs) for a 30 % improvement in pain of 7.2 for duloxetine, 19 for milnacipran and 8.6 for PGB. Again, these drugs remain unlicensed or unavailable in the UK (milnacipran) for this indication, and GPs, therefore, have to rely on the guidance of their pain specialist colleagues in secondary care as to when to employ these drugs in managing CWP and insomnia. No reports of using standard analgesics such as paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) have been highlighted in the recent literature, but it would be common sense for doctors managing CWP and insomnia to use these as the first part of the analgesic ladder before progressing to the more potent opioids or neuropathic agents as highlighted above [57].

Prescribing Medication That Will Directly Influence Sleep

Given the bi-directional nature of pain and insomnia, is there a place for simply treating the patient's lack of sleep? Though no studies have examined this relationship specifically in CWP, it has been found in other chronic pain conditions that over 50 % of patients treated for insomnia with temazepam, a benzodiazepine receptor agonist (BzRA), achieved a significant improvement in sleep whilst only 22 % of those managed with zolpidem (a Z-drug) achieved the same [58]. Evidence seems to suggest that in the short term, perhaps up to 6 months, the benefit of BzRAs appears to be maintained, but the case for their long-term use remains debatable with only limited evidence of sustained efficacy for up to 1 year [59]. Most GPs, however, would not consider such long-term use because of concerns over tolerance and addiction [54]. Newer medications such as the anti-psychotic quetiapine might provide an alternative therapeutic option. One literature review of quetiapine's use for non-psychiatric insomnia found it had a positive effect on sleep latency and quality, even in those with chronic pain [60]. However, quetiapine does not currently hold a licence for the treatment of insomnia in the UK and is

unlikely to be used by GPs in their routine care. In general, GPs report using at some time all three types of the commonly prescribed sedating medications considered here (BzRAs, Z-drugs and amitriptyline) [54], and it is unlikely that, in the absence of evidence and changes to the licensed indications for the other medications considered here, this will change in the foreseeable future.

Prescribing Psychological Therapies

The third option is cognitive behavioural therapy for insomnia (CBT-I) [61]. One study of four CBT variants in osteoarthritis, another debilitating potentially widespread chronic pain condition, concluded that these interventions were associated with improvements in insomnia and pain symptoms of a 'clinically meaningful' significance [48]. The CBT-I intervention found that those patients with the worst levels of co-morbid pain and insomnia were the most likely to improve and achieve sustained benefit [48]. However, with financial constraints in mind, how practical is it to consider using such intensive and time-consuming therapies as CBT-I with the considerable numbers of patients that might actually benefit from it? GPs themselves recognise the benefits of these therapies but actually report rarely using them. One study found that only 16 % of GPs had ever considered using elements of CBT-I in their management of insomnia [54]. It seems that there is some way to go in promoting these useful therapies in primary care and the starting point should be with GP education regarding their use, whilst at the same time devoting more resources towards making CBT-I more widely available.

Patients, of course, have the option to self-manage their CWP and insomnia. There is evidence that exercise therapies such as yoga may have beneficial effects [62]. In fibromyalgia, one small RCT of yoga and Pilates found equal benefit on pain, fatigue and depression as measured with the Beck Depression Inventory, of which sleep quality is one component. The idea that specific exercise modalities might be more beneficial and perhaps targeted when managing CWP and insomnia is supported by a recent review of the literature in relation to fibromyalgia which suggested that aquatic aerobic exercise therapy may have a more positive effect than an equal regime that was land based [47]. Encouraging patients to take exercise is one of the key messages that underpin the management of both insomnia and chronic pain, so using alternative exercise therapies such as these might be encouraged as part of that regime.

Conclusion

Insomnia and CWP are common; they tend to co-occur and appear to have a reciprocal relationship, with each condition increasing the risk of the other which may augment the burden on health [63]. Importantly, the prevalence of both CWP and insomnia tends to increase with age. With an ageing population, the challenge of managing these conditions confronts primary care [64]. With increasing age comes multi-morbidity and, consequently, the issue of polypharmacy. In particular, there are patients that we consider as the 'very old', those aged 85 or more, where several co-morbid conditions including pain are associated with excessive polypharmacy (10 or more differently prescribed drugs) [65]. Consequently, these patients can be particularly challenging when attempting to treat their chronic pain and any associated insomnia. The ageing body can be more susceptible to the side effects of medicines, and so, with polypharmacy, there is an increased chance of adverse events and the potential for detrimental interactions between medicines. All these concerns must be weighed against the potential benefits of using drugs such as BzRAs and analgesics and non-pharmacological interventions such as exercise and CBT-I. Caution must be exercised when considering their use. Here, more than ever, the holistic approach to management needs to be employed [44], or the potential for doing more harm than good becomes a very real possibility.

Compliance with Ethics Guidelines

Conflict of Interest John McBeth, Ross Wilkie, John Bedson, Carolyn Chew-Graham, and Rosie J. Lacey declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Tafti M. Genetic aspects of normal and disturbed sleep. Sleep Med. 2009;10 Suppl 1:S17–21.
2. Macfarlane GJ, McBeth J, Jones GT. Epidemiology of pain. In: McMahon S, Koltzenburg M, Tracey I, Turk DC, editors. Wall and Melzack's textbook of pain. 6th ed. Seattle: Elsevier Ltd; 2013.
3. Kamaleri Y, Natvig B, Ihlebaek CM, et al. Localized or widespread musculoskeletal pain: does it matter? Pain. 2008;138:41–6.
4. Croft P, Rigby AS, Boswell R, et al. The prevalence of chronic widespread pain in the general population. J Rheumatol. 1993;20: 710–3.
5. Mundal I, Grawe RW, Bjorngaard JH, et al. Prevalence and long-term predictors of persistent chronic widespread pain in the general population in an 11-year prospective study: the HUNT study. BMC Musculoskelet Disord. 2014;15:213.
6. Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and

measurement of symptom severity. Arthritis Care Res. 2010;62(5): 600–10.
7. Moldofsky H, Scarisbrick P, England R, et al. Musculosketal symptoms and non-REM sleep disturbance in patients with "fibrositis syndrome" and healthy subjects. Psychosom Med. 1975;37(4): 341–51.
8. Hauri P, Hawkins DR. Alpha-delta sleep. Electroencephalogr Clin Neurophysiol. 1973;34(3):233–7.
9. Moldofsky H. Sleep influences on regional and diffuse pain syndromes associated with osteoarthritis. Semin Arthritis Rheum. 1989;18(4 Suppl 2):18–21.
10. Jaimchariyatam N, Rodriguez CL, Budur K. Prevalence and correlates of alpha-delta sleep in major depressive disorders. Innov Clin Neurosci. 2011;8(7):35–49.
11. Rains JC, Penzien DB. Sleep and chronic pain: challenges to the alpha-EEG sleep pattern as a pain specific sleep anomaly. J Psychosom Res. 2003;54(1):77–83.
12. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington: American Psychiatric Publishing; 2013.
13. Smith MT, Haythornthwaite JA. How do sleep disturbance and chronic pain inter-relate? Insights from the longitudinal and cognitive-behavioral clinical trials literature. Sleep Med Rev. 2004;8(2):119–32.
14. Vgontzas AN, Fernandez-Mendoza J. Insomnia with short sleep duration: nosological, diagnostic, and treatment implications. Sleep Med Clin. 2013;8(3):309–22.
15. Ohayon MM, Riemann D, Morin C, et al. Hierarchy of insomnia criteria based on daytime consequences. Sleep Med. 2012;13(1): 52–7.
16. Morin CM, Belanger L, LeBlanc M, et al. The natural history of insomnia: a population-based 3-year longitudinal study. Arch Intern Med. 2009;169(5):447–53.
17. Ohayon MM, Reynolds CF. Epidemiological and clinical relevance of insomnia diagnosis algorithms according to the DSM-IV and the International Classification of Sleep Disorders (ICSD). Sleep Med. 2009;10(9):952–60.
18. Ancoli-Israel S. Sleep and its disorders in aging populations. Sleep Med. 2009;10 Suppl 1:S7–11.
19. Foley DJ, Monjan AA, Brown SL, et al. Sleep complaints among elderly persons: an epidemiologic study of three communities. Sleep. 1995;18(6):425–32.
20. Reid KJ, Martinovich Z, Finkel S, et al. Sleep: a marker of physical and mental health in the elderly. Am J Geriatr Psychiatry. 2006;14(10):860–6.
21. Foley D, Ancoli-Israel S, Britz P, et al. Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. J Psychosom Res. 2004;56(5):497–502.
22. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum. 1990;33(2):160–72.
23. Carnes D, Parsons S, Ashby D, et al. Chronic musculoskeletal pain rarely presents in a single body site: results from a UK population study. Rheumatology. 2007;46(7):1168–70.
24. Wolfe F, Ross K, Anderson J, et al. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum. 1995;38(1):19–28.
25. Choudhury Y, Bremner SA, Ali A, et al. Prevalence and impact of chronic widespread pain in the Bangladeshi and White populations of Tower Hamlets, East London. Clin Rheumatol. 2013;32(9): 1375–82.
26.• McBeth J, Lacey RJ, Wilkie R. Predictors of new-onset widespread pain in older adults: results from a population-based prospective cohort study in the UK. Arthritis Rheumatol. 2014;66(3):757–67. *Sleep disturbance was the strongest predictor of incident widespread pain in older people. The mechanism of association needs to be identified.*
27. Branco JC, Bannwarth B, Failde I, et al. Prevalence of fibromyalgia: a survey in five European countries. Semin Arthritis Rheum. 2010;39(6):448–53.
28. Thomas E, Peat G, Harris L, et al. The prevalence of pain and pain interference in a general population of older adults: cross-sectional findings from the North Staffordshire Osteoarthritis Project (NorStOP). Pain. 2004;110(1–2):361–8.
29. Macfarlane GJ, Pye SR, Finn JD, et al. Investigating the determinants of international differences in the prevalence of chronic widespread pain: evidence from the European Male Ageing Study. Ann Rheum Dis. 2009;68(5):690–5.
30. Vincent A, Lahr BD, Wolfe F, et al. Prevalence of fibromyalgia: a population-based study in Olmsted County, Minnesota, utilizing the Rochester Epidemiology Project. Arthritis Care Res. 2013;65(5): 786–92.
31. Bigatti SM, Hernandez AM, Cronan TA, et al. Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. Arthritis Rheum. 2008;59(7):961–7.
32. Tang NK, Wright KJ, Salkovskis PM. Prevalence and correlates of clinical insomnia co-occurring with chronic back pain. J Sleep Res. 2007;16(1):85–95.
33. Taylor DJ, Mallory LJ, Lichstein KL, et al. Comorbidity of chronic insomnia with medical problems. Sleep. 2007;30(2): 213–8.
34. Moldofsky H, Scarisbrick P. Induction of neurasthenic musculoskeletal pain syndrome by selective sleep stage deprivation. Psychosom Med. 1976;38(1):35–44.
35. Schuh-Hofer S, Wodarski R, Pfau DB, et al. One night of total sleep deprivation promotes a state of generalized hyperalgesia: a surrogate pain model to study the relationship of insomnia and pain. Pain. 2013;154(9):1613–21.
36. Anderson RJ, McCrae CS, Staud R, et al. Predictors of clinical pain in fibromyalgia: examining the role of sleep. J Pain. 2012;13(4): 350–8.
37. Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. J Pain. 2013;14(12): 1539–52.
38. Davies KA, Macfarlane GJ, Nicholl BI, et al. Restorative sleep predicts the resolution of chronic widespread pain: results from the EPIFUND study. Rheumatology. 2008;47(12):1809–13.
39. Gupta A, Silman AJ, Ray D, et al. The role of psychosocial factors in predicitng the onset of chronci widesrpead pain: results from a prospective population–based study. Rheumatology. 2007;46(4): 666–71.
40.•• Mork PJ, Nilsen TI. Sleep problems and risk of fibromyalgia: longitudinal data on an adult female population in Norway. Arthritis Rheum. 2012;64(1):281–4. *This large longitudinal study reported a dose-response relationship between sleep problems and the risk of developing fibromyalgia. Importantly, this effect was stronger in older when compared to younger women.*
41. Ødegård SS, Sand T, Engstrom M, et al. The impact of headache and chronic musculoskeletal complaints on the risk of insomnia: longitudinal data from the Nord-Trondelag health study. J Headache Pain. 2013;14:24.
42. Tang NK, McBeth J, Jordan KP, et al. Impact of musculoskeletal pain on insomnia onset: a prospective cohort study. Rheumatology. 2014. doi:10.1093/rheumatology/keu283.
43. Jenkins CD, Stanton BA, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. J Clin Epidemiol. 1988;41:313–21.
44. National Institute for Health and Care Excellence (NICE) Clinical Knowledge Summaries. Insomnia. http://cks.nice.org.uk/insomnia#!scenariorecommendation:2. Accessed 29 Sept 2014.

45. Schutte-Rodin S, Broch L, Buysse D, et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med. 2008;4(5):487–504.
46. Brennan MJ, Lieberman JA. Sleep disturbances in patients with chronic pain: effectively managing opioid analgesia to improve outcomes. Curr Med Res Opin. 2009;25(5):1045–55.
47. Busch AJ, Webber SC, Brachaniec M, et al. Exercise therapy for fibromyalgia. Curr Pain Headache Rep. 2011;15(5):358–67.
48. McCurry SM, Shortreed SM, Von Korff M, et al. Who benefits from CBT for insomnia in primary care? Important patient selection and trial design lessons from longitudinal results of the Lifestyles trial. Sleep. 2014;37(2):299–308.
49. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. Ann Intern Med. 2010;152(2):85–92.
50. Saunders KW, Dunn KM, Merrill JO, et al. Relationship of opioid use and dosage levels to fractures in older chronic pain patients. J Gen Intern Med. 2010;25(4):310–5.
51. Johnson M, Collett B, Castro-Lopes JM. The challenges of pain management in primary care: a pan-European survey. J Pain Res. 2013;6:393–401.
52. Bennett RM, Kamin M, Karim R, et al. Tramadol and acetaminophen combination tablets in the treatment of fibromyalgia pain: a double-blind, randomized, placebo-controlled study. Am J Med. 2003;114(7):537–45.
53. Smith H, Bracken D, Smith J. Pharmacotherapy for fibromyalgia. Front Pharmacol. 2011. doi:10.3389/fphar.2011.00017.
54. Everitt H, McDermott L, Leydon G, et al. GPs' management strategies for patients with insomnia: a survey and qualitative interview study. Br J Gen Pract. 2014;64(619):e112–9.
55. Hauser W, Bernardy K, Uceyler N, et al. Treatment of fibromyalgia syndrome with gabapentin and pregabalin—a meta-analysis of randomized controlled trials. Pain. 2009;145(1–2):69–81.
56. Hauser W, Petzke F, Sommer C. Comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome. J Pain. 2010;11(6):505–21.
57. Gureje O, Von Korff M, Simon GE, et al. Persistent pain and well-being: a World Health Organization Study in primary care. JAMA. 1998;280(2):147–51.
58. Weschules DJ, Maxwell T, Reifsnyder J, et al. Are newer, more expensive pharmacotherapy options associated with superior symptom control compared to less costly agents used in a collaborative practice setting? Am J Hosp Palliat Care. 2006;23(2):135–49.
59. Schweitzer PK, Curry DT, Eisenstein RD, et al. Pharmacological treatment of insomnia. In: Attarian HP, Schuman C, editors. Clinical handbook of insomnia. 2nd ed. New York: Humana Press; 2010. p. 297–316.
60. Wine JN, Sanda C, Caballero J. Effects of quetiapine on sleep in nonpsychiatric and psychiatric conditions. Ann Pharmacother. 2009;43(4):707–13.
61. Budur K, Rodriguez C, Foldvary-Schaefer N. Advances in treating insomnia. Cleve Clin J Med. 2007;74(4):251–66.
62. Sengupta P. Health impacts of yoga and pranayama: a state-of-the-art review. Int J Prev Med. 2012;3(7):444–58.
63. Hester J, Tang NK. Insomnia co-occurring with chronic pain: clinical features, interaction, assessments and possible interventions. Rev Pain. 2008;2:2. doi:10.1177/204946370800200102.
64. Department of Health. Long term conditions compendium of information. 3rd ed. 2012. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216528/dh_134486.pdf. Accessed 29 Sept 2014.
65. Jyrkka J, Enlund H, Korhonen MJ, et al. Patterns of drug use and factors associated with polypharmacy and excessive polypharmacy in elderly persons: results of the Kuopio 75+ study: a cross-sectional analysis. Drugs Aging. 2009;26(6):493–503.