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Medical cannabis and insomnia in older adults with chronic pain: a cross-sectional study

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ABSTRACT

Objectives Medical cannabis (MC) is increasingly being used for treatment of chronic pain symptoms. Among patients there is also a growing preference for the use of MC to manage sleep problems. The aim of the current study was to examine the associations between use of whole plant cannabis and sleep problems among chronic pain patients.

Methods A total of 128 individuals with chronic pain over the age of 50 years were recruited from the Rambam Institute for Pain Medicine in Haifa, Israel. Of them, 66 were MC users and 62 were non-users. Regression models tested the differences in sleep problems between the two groups. Furthermore, Pearson correlations between MC use measures (dose, length and frequency of use, number of strains used, tetrahydrocannabinol/cannabidiol levels) and sleep problems were assessed among MC users.

Results After adjustment for age, sex, pain level and use of sleep and anti-depressant medications, MC use was associated with less problems with waking up at night compared with non-MC use. No group differences were found for problems with falling asleep or waking up early without managing to fall back asleep. Frequent MC use was associated with more problems waking up at night and falling asleep.

Conclusions MC use may have an overall positive effect on maintaining sleep throughout the night in chronic pain patients. At the same time, tolerance towards potential sleep-inducing properties of MC may occur with frequent use. More research based on randomised control trials and other longitudinal designs is warranted.

INTRODUCTION

Chronic pain is a debilitating condition that affects an estimated 19%–37% of adults in developed countries[1] and is a leading cause of disability.[2] Individuals with chronic pain often suffer from comorbid insomnia[3] which includes difficulty initiating sleep, disrupted sleep and early morning awakenings.[4 5] While chronic pain and insomnia have independent detrimental effects for individuals, their combined impact in terms of suffering and lost productivity are likely magnified.

Medical cannabis (MC) policies are changing rapidly in various jurisdictions allowing increasingly more patients legal access to use MC to ease medical symptoms from various conditions. One of the most common areas of medicine in which MC has been integrated is chronic pain.[6] While there is relatively strong clinical evidence that MC is an efficacious pain reliever[7 8] effect sizes are small.[9 10] In addition to chronic pain, managing sleep problems has been widely reported as a motivation for cannabis use by MC patients.[11 12] Research has demonstrated that the endocannabinoid system has a role in the regulation of sleep, including the maintenance and promotion of sleep.[13–15] In recent years there has been a growth of randomised control trials (RCTs) that have examined the effects of cannabis on pain as a primary outcome, and sleep as secondary outcome. Despite many of these studies being of poor quality, most studies reported a significant and positive impact on sleep.[7 16] Preclinical studies have, however, also shown that chronic administration of tetrahydrocannabinol (THC) is related to tolerance to the sleep enhancing effects of cannabis.[5 13]

Most extant studies have examined the effects of MC in the context of orally administrated synthetic cannabinoids with a 1:1 THC/cannabidiol (CBD) ratio.[14] Yet, the vast majority of MC patients use the whole plant.[17 18] The cannabis flower differs from synthetic cannabis-based medicines in that the former consists of over 500 different compounds.[19] While THC and CBD are among the most well-known compounds, others are likely to

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have important effects as well.[20] It is possible that phytocannabinoids and various combinations of cannabinoids differ in their effects on sleep compared with THC and/or CBD alone. This process has been called the *entourage effect*[21] and suggests that findings from studies that administer THC/CBD extracted medicines are unreliable as indications of the effects of MC used by most chronic pain patients.

The present study was designed in order to examine the association between sleep problems and MC in middle age and older (50+ years of age) chronic pain patients. This relatively old age limit was chosen as both sleep and chronic pain problems have increased incidence in late-life[22 23] and the prevalence of the comorbid conditions is therefore expected to grow with the ageing population. The study builds on and complements findings from internally valid RCTs by employing a more ecologically valid, naturalistic approach. Specifically, the study examines the associations between use of whole plant cannabis and three main indicators of insomnia. We hypothesised that compared with chronic pain patients who do not use MC, MC chronic pain patients would report less sleep problems. In addition, among MC patients, we examine the association between sleep problems and different patterns of MC use. Due to the potential tolerance building effects of chronic MC administration noted in preclinical studies[5 13] we expected that length of MC treatment, frequency of use and higher dose and THC concentrations would be associated with more sleep problems.

METHODS

Sample recruitment

Patients for this cross-sectional study were recruited from the Rambam Institute for Pain Medicine in Haifa, Israel in the period January–December 2018. In Israel, MC may be prescribed to patients suffering from chronic neuropathic pain of organic origin and who have been under treatment in a public pain relief clinic for over 1 year, after exhausting all other pain management modalities.[24] We therefore recruited patients (both MC license holders and non-MC license holders) with chronic neuropathical pain of organic origin. Exclusion criteria included age <50, a diagnosis of post-traumatic stress disorder, anxiety, clinical dementia, multiple sclerosis, Parkinson's disease, brain tumour, traumatic brain injury, stroke or serious mental illness, cancer patients who currently receive chemotherapy and individuals who do not understand Hebrew. Specific eligibility criteria for MC patients were that they had used MC for at least 1 year prior to data collection. A research assistant contacted eligible patients by phone and informed them that the study was observational, and no intervention would be applied.

According to sample size power calculation for a fixed effect model with one test variable and five covariates under the assumption of partial correlation=0.25 and nominal power=0.8, a total sample size of 120 was sufficient. A total of 128 eligible MC were contacted of whom 66 agreed to participate. Of those contacted but not included in the study, 20 did not answer the phone, 12 did not want to participate and 30 did not participate for other reasons. In terms of non-MC patients, 135 eligible patients were contacts, and 62 agreed to participate. Of those contacted but not included in the study, 19 did not answer the phone, 44 did not want to participate and 10 did not participate for other reasons.

Measures

Sleep variables

The three following indicators of insomnia were measured on a 7-point Likert scale (1=never–7=always): how often during the last month have you[1] had problems falling asleep,[2] woken up early in the morning without being able to fall back asleep,[3] woken up during sleep.

Independent variables

Basic sociodemographic information was collected (age, gender, years of study). Additionally, we recorded data on daily consumption of tobacco and alcohol use frequency (never, once a month, 2–4 times per month, 2–3 times per week, 4+ times per week). Average pain was measured on a Numerical Pain Rating Scale (NPRS) where patients were asked to give a number between 0 and 10 that best represented their pain intensity during the last 24 hours. Patients were instructed that 0 represented 'no pain at all' whereas the upper limit represented 'the worst pain possible'. NPRS has been shown to be valid assessment tools for pain in telephone interviews.[25] Use of any sleep aid medication during the last month was recorded (0=no use, 1=use). In addition, it is common practice to prescribe tricyclic antidepressants to chronic pain patients and these medications may have sedative hypnotic effects that promote sleep. We therefore collected data on anti-depressant medication use (0=no use, 1=use). As would be expected in a sample of chronic pain patients, all patients were taking analgesics medication (other than MC) during the course of the study.

All respondents were asked if they had ever used cannabis for recreational purposes (0=no use, 1=use). Furthermore, based on patients' MC license records, we recorded how many years the MC patients had used cannabis at the time of the interview and the monthly allowed dosage. MC patients were also asked how many different MC strains they were currently using. For each strain, we collected data on number of days used per week and number of times used on a typical use day. For each strain, these two frequency measures were multiplied to identify number of times each strain was used per week and then all the weekly strain frequency measures were added up to create an

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overall measure of number of times MC was used per week.

The THC and CBD level of MC strains used in Israel are objectively analysed by the Laboratory of Cancer Biology and Cannabinoid Research at the Israeli Institute of Technology (Technion). MC patients in our sample were asked to provide information about date of purchase, MC provider and MC strain. Based on these data the laboratory at the Technion provided accurate THC/CBD profiles of the MC consumed by the patients. The mean THC/CBD level was calculated across multiple strains used.

Statistical procedure

To assess differences between MC patients and non-MC users χ^2 tests (for categorical variables) and independent t-tests (for continuous variables) were performed. Linear regression models were run on each of the three sleep variables separately to test whether there were differences between the MC and non-MC patients in these outcomes while controlling for any potential background differences in the two groups. The usual tests of regression model assumptions were conducted. There was homoscedasticity, as assessed by visual inspection of a plot of studentised residuals versus unstandardised predicted values. Variance inflation factors were consulted which showed that there was no multicollinearity. P-P plot were examined to confirm that the standardised residuals were normally distributed.

In separate analyses restricted to MC patients, we calculated Pearson correlations to test the association between MC use patterns (number of strains used, length of cannabis use, monthly dosage, frequency of use, THC and CBD concentrations) and sleep problems. There were no missing data on any of the variables included in the adjusted analyses. For THC/CBD data we only had information from 35 MC patients (missing n=31). Furthermore, only 54 individuals provided information about MC dose (missing n=12). All analyses were conducted in SPSS V.25.0.

RESULTS

The sample included a total of 129 participants (mean age=61±6 years; 49% males). The MC and non-MC patients (n=63 and 66, respectively) were similar except for age and gender. As shown in table 1, MC patients were on average 3 years younger than non-MC patients (mean age 60±6 vs 63±6 years, respectively, p=0.003) and slightly more likely to be male than non-MC patients (58% vs 40%, respectively, p=0.038). The two groups had similar education levels and alcohol and cigarette use patterns. The two groups also reported similar medication use and pain levels.

Table 1 Participant demographics, substance/medication use and sleep

	Non-medical cannabis patients	Medical cannabis patients	Total	P value*
	n=62	n=66	n=128	
Background variables				
Age, M (SD)	62.9 (6.10)	59.8 (5.78)	61.29 (6.10)	**0.003**
Education, M (SD)	13.82 (2.89)	13.44 (3.44)	13.65 (3.18)	0.497
Male, N (%)	25 (40.3)	38 (57.6)	63 (49.2)	**0.038**
Daily smoker, N (%)	12 (19.7)	18 (27.3)	30 (23.6)	0.213
Alcohol use frequency, M (SD)	1.79 (1.02)	2.12 (1.18)	1.96 (1.11)	0.094
Used non-medical cannabis, N (%)	7 (11.7)	14 (21.9)	21 (16.9)	0.101
Sleep medication, N (%)	25 (40.3)	26 (39.4)	51 (39.8)	0.529
Anti-depressants, N (%)	8 (12.9)	6 (9.1)	14 (10.9)	0.342
Average pain, M (SD)	7.21 (1.93)	6.82 (2.27)	7.02 (2.11)	0.296
Sleep measures				
Maintaining sleep, M (SD)	5.54 (1.84)	4.59 (2.11)	5.01 (2.02)	**0.018**
Initiating sleep, M (SD)	3.53 (2.34)	3.94 (2.33)	3.74 (2.32)	0.325
Early awakening, M (SD)	3.98 (2.32)	4.33 (2.36)	4.15 (2.33)	0.399
Medical cannabis use				
Years of medical cannabis use, M (SD)	NA	3.93 (2.51)		
Monthly dosage, M (SD)	NA	31.20 (12.17)		
No. of strains, M (SD)	NA	1.80 (0.10)		
No. of times use per week, M (SD)	NA	32.91 (23.90)		
% THC, M (SD)†	NA	15.6 (6.47)		
% CBD, M (SD)†	NA	2.84 (4.06)		

*Differences in categorical variables were measured using χ^2 tests, and independent t-tests were performed for continuous variables.
†Based on 35 respondents who provided data on strains.
CBD, cannabidiol; THC, tetrahydrocannabinol.

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Table 2 Regression models testing associations between sleep problems and medical cannabis use (n=128)

	Wake up at night			Waking up early			Problems falling asleep		
	Beta	SE	P value	Beta	SE	P value	Beta	SE	P value
Age	−0.13	0.03	0.160	−0.18	0.04	0.062	−0.08	0.04	0.398
Male	0.11	0.37	0.240	0.08	0.43	0.403	0.01	0.43	0.950
Average pain	0.12	0.08	0.164	0.14	0.10	0.114	0.17	0.10	0.062
Sleep medication	−0.09	0.38	0.362	0.10	0.45	0.278	0.04	0.45	0.711
Anti-depressants	−0.003	0.60	0.971	−0.02	0.70	0.872	0.06	0.71	0.560
Medical cannabis use	**−0.25**	**0.37**	**0.008**	0.03	0.44	0.761	0.09	0.44	0.372

Of the total sample of 129 subjects, 24.1% reported always waking up early and not falling back asleep, 20.2% reported always having difficulties falling asleep, and 27.2% reported always waking up during the night. Table 1 shows that MC patients were less likely to wake up at night (M=4.59 vs M=5.54, p=0.018) whereas there were no differences between the two groups in terms of the other sleep measures.

The MC patients had used MC for 4 years on average and they used 31 g per month on average. Mode of use was not mutually exclusive as MC patients used different strains through different modes. The main modes of administration were by smoking (68.6%), oil extracts (21.4%) and vaporisation (20.0%). MC patients used 1.8 stains on average, the average THC level was 15.6% and the average CBD level was 2.84%.

The adjusted regression models showed that MC patients were less likely to report waking up at night whereas there were no significant group differences in terms of sleep latency and early awakenings. These models controlled for age and gender because these factors were shown to differ between the two patient groups. We also adjusted for average pain and use of sleep aid and anti-depressants to calculate the association between MC use and the sleep measures net of these factors (table 2).

In the final analyses with the subsample of MC patients only, Pearson correlations showed that only frequency of MC use was associated with sleep problems. Specifically, more frequent use was associated with more problems related to waking up at night and problems falling asleep (see table 3).

DISCUSSION

Given the large scale of sleep problems in the general population and among chronic pain patients in particular, along with rapid developments in the field of MC, it is surprising how few studies have focused on the sleep-inducing effects of MC treatment in chronic pain patients. There are currently three classes of medications that are prescribed for sleep disorders: benzodiazepines, barbiturates and non-benzodiazepine hypnotic medications. All of these have serious adverse side effects including, but not limited to, dependence and withdrawal.[26] It is possible that MC may help with sleep problems with more limited adverse side effects. The current observational study was designed as an exploratory study that could lead the way to a better understanding of the relation between different sleep parameters and MC use among individuals with chronic pain.

Waking up at night was the most commonly reported sleep problem in this population which echoes previous findings showing that staying asleep is the most commonly reported sleep problem among chronic pain patients.[27] It is also in line with research

Table 3 Pearson correlation table of relations between sleep problems and medical cannabis (MC) use patterns in MC patient subsample

	Wake up at night	Waking up early	Problems falling asleep	Years since cannabis treatment onset	No. of strains	No. of times use per week	Dose	THC
Waking up early	0.272*	1						
Problems falling asleep	0.367**	0.265*	1					
Years since cannabis treatment onset	0.166	0.218	0.032	1				
No. of strains	0.005	−0.022	0.108	−0.123	1			
No. of times use per week	0.258*	0.061	**0.308***	−0.020	0.301	1		
Dose	0.057	0.033	0.211	−0.681	0.358***	0.279*	1	
THC	0.126	−0.0454	−0.038	−0.351**	−0.044	0.289*	0.289	1
CBD	0.022	−0.026	0.004	0.150	0.027	−0.279	−0.257	−0.756

*p<0.05; **p<0.01; ***p<0.001.
CBD, cannabidiol; THC, tetrahydrocannabinol.

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showing that night-time awakenings and difficulty staying asleep are particularly characteristic of sleep problems in older adults.[28] Our findings showed that MC patients were less likely to report problems with staying asleep compared with non-MC patients, independently of potential confounders. No differences between medical and non-MC patients were found for the other sleep measures (ie, falling asleep and waking up early). This suggests that MC may have a sleep-promoting characteristic in terms of minimising awakenings during the night, but not in terms of other types of sleep problems. Future studies are needed to confirm whether cannabis may have specific effects on particular sleep problems and if so, what the mechanisms of action are.

In terms of MC use patterns, more frequent use was associated with problems staying asleep during the night and more problems falling asleep. This may signal the development of tolerance after chronic administration of MC akin to what has been found in preclinical studies.[5 13] It is, however, also plausible that patients who use more frequently suffer more from pain or other comorbidities (eg, depression/anxiety) which may in turn be associated with more sleep problems. No relationship was found for years of use. However, it needs to be noted that all patients included in the sample had used MC for at least 1 year which may limit the possibility of detecting any development of tolerance related to length of use if this mainly occurs shortly after onset of use. Furthermore, while research has suggested that dose modulates the effect of cannabis on sleep,[14] our results did not show a relationship between MC dose or potency and sleep. It needs, however, to be kept in mind that we only had a very rough measure of dose (monthly dose) and a more sensitive measure of exact dose per use session would be more informative in terms of reaching a better understanding of the association between different MC dosages and sleep problems. Furthermore, we only have THC/CBD concentrations and dose measures for a subgroup of MC patients which also limits the ability to detect significant associations.

Limitations

It is important to note the limitations of the study. Although Rambam Health Care Campus is the main chronic pain centre of northern Israel, this study was limited to data collection in a single chronic pain treatment centre, possibly limiting the generalisability of results. Due to its cross-sectional and observational design no causal inferences can be made in terms of the effects of MC on sleep. Furthermore, we do not have exact data on specific timing of MC administration. This may have limited the ability to detect associations between MC and sleep as the study participants likely varied in terms of timing of MC administration and one may expect a stronger association between MC use and sleep when MC is used before bedtime. MC patients also use different strains which may have differential effects on sleep. Future research is needed to examine this variability in more detail.

In this study we were interested in the association between different characteristics of sleep problems and we thereby used single-item questions as opposed to creating a composite score. Overall, single-item questions may be less reliable than scales.[29] Nevertheless, research has found that sleep indexes composed of multiple related questions are no better than single-item questions.[30] Finally, subjective sleep measures such as the ones used in the current study may be less reliable than objective sleep measures. Research has found that patients tend to overestimate sleep onset latency and underestimate the number of awakenings they experienced each night.[31] Yet, we have no reason to believe that this potential bias will be different across the two patient groups included in the sample, thus, if there is misclassification, such bias can only result in an underestimation of the true associations.

CONCLUSION

This study is among the first to test the link between whole plant MC use and sleep quality. In our sample of older (50+ years) chronic pain patients we found that MC may be related to fewer awakenings at night. Yet patients may also develop tolerance to the sleep-aid characteristics of MC. These findings may have large public health impacts considering the ageing of the population, the relatively high prevalence of sleep problems in this population along with increasing use of MC. Yet, considering the limitations of this study, one may wish to consider the results reported here as preliminary. Certainly, much more research using animal and human models and with longitudinal and randomised control designs is needed in order to better understand the potential acute and long-term effects of different strains/doses and modes of administration of MC on different sleep parameters.

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Competing interests None declared.

Patient consent for publication On agreement to participate, the patients gave oral consent and a time was scheduled to conduct a phone or face-to-face interview.

Ethics approval The study protocol was approved by the institutional ethics committee.

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REFERENCES

1 Breivik H, Collett B, Ventafridda V, *et al*. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain* 2006;10.
2 IHME. *Findings from the global burden of disease study 2017*. Seattle, WA: Institute for Health Metrics and Evaluation, 2018.
3 Boakye PA, Olechowski C, Rashiq S, *et al*. A critical review of neurobiological factors involved in the interactions between chronic pain, depression, and sleep disruption. *Clin J Pain* 2016;32:327–36.
4 American Academy of Sleep Medicine. *The International classification of sleep disorders*. Rochester, MN: Allen Press, 1997.
5 Menefee LA, Cohen MJ, Anderson WR, *et al*. Sleep disturbance and nonmalignant chronic pain: a comprehensive review of the literature. *Pain Med* 2000;1:156–72.
6 Boehnke KF, Gangopadhyay S, Clauw DJ, *et al*. Qualifying conditions of medical cannabis license holders in the United States. *Health Aff* 2019;38:295–302.
7 Abrams DI. The therapeutic effects of cannabis and cannabinoids: an update from the National academies of sciences, engineering and medicine report. *Eur J Intern Med* 2018;49:7–11.
8 Boychuk DG, Goddard G, Mauro G, *et al*. The effectiveness of cannabinoids in the management of chronic nonmalignant neuropathic pain: a systematic review. *J Oral Facial Pain Headache* 2015;29:7–14.
9 Häuser W, Finnerup NB, Moore RA. Systematic reviews with meta-analysis on cannabis-based medicines for chronic pain: a methodological and political minefield. *Pain* 2018;159:1906–7.
10 Stockings E, Campbell G, Hall WD, *et al*. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. *Pain* 2018;159:1932–54.
11 Bonn-Miller MO, Babson KA, Vandrey R. Using cannabis to help you sleep: heightened frequency of medical cannabis use among those with PTSD. *Drug Alcohol Depend* 2014;136:162–5.
12 Belendiuk KA, Babson KA, Vandrey R, *et al*. Cannabis species and cannabinoid concentration preference among sleep-disturbed medicinal cannabis users. *Addict Behav* 2015;50:178–81.
13 Vaughn LK, Denning G, Stuhr KL, *et al*. Endocannabinoid signalling: has it got rhythm? *Br J Pharmacol* 2010;160:530–43.
14 Babson KA, Sottile J, Morabito D. Cannabis, cannabinoids, and sleep: a review of the literature. *Curr Psychiatry Rep* 2017;19:23.
15 Prospéro-García O, Amancio-Belmont O, Becerril Meléndez AL, *et al*. Endocannabinoids and sleep. *Neurosci Biobehav Rev* 2016;71:671–9.
16 Gates PJ, Albertella L, Copeland J. The effects of cannabinoid administration on sleep: a systematic review of human studies. *Sleep Med Rev* 2014;18:477–87.
17 Ware MA, Doyle CR, Woods R, *et al*. Cannabis use for chronic non-cancer pain: results of a prospective survey. *Pain* 2003;102:211–6.
18 Clark AJ, Ware MA, Yazer E, *et al*. Patterns of cannabis use among patients with multiple sclerosis. *Neurology* 2004;62:2098–100.
19 Elsohly MA, Slade D. Chemical constituents of marijuana: the complex mixture of natural cannabinoids. *Life Sci* 2005;78:539–48.
20 Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol* 2011;163:1344–64.
21 De Petrocellis L, Ligresti A, Moriello AS, *et al*. Effects of cannabinoids and cannabinoid-enriched *Cannabis* extracts on TRP channels and endocannabinoid metabolic enzymes. *Br J Pharmacol* 2011;163:1479–94.
22 Fayaz A, Croft P, Langford RM, *et al*. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. *BMJ Open* 2016;6:e010364.
23 Klink ME, Quan SF, Kaltenborn WT, *et al*. Risk factors associated with complaints of insomnia in a general adult population. Influence of previous complaints of insomnia. *Arch Intern Med* 1992;152:1634–7.
24 MOH. Medical Cannabis Licensing Procedure - Procedure no. 1062013; 2014.
25 Von Korff M, Jensen MP, Karoly P. Assessing global pain severity by self-report in clinical and health services research. *Spine* 2000;25:3140–51.
26 Asnis G, Thomas M, Henderson M. Pharmacotherapy treatment options for insomnia: a primer for clinicians. *Int J Mol Sci* 2015;17:50.
27 Asih S, Neblett R, Mayer TG, *et al*. Insomnia in a chronic musculoskeletal pain with disability population is independent of pain and depression. *The Spine Journal* 2014;14:2000–7.
28 Åkerstedt T, Schwarz J, Gruber G, *et al*. The relation between polysomnography and subjective sleep and its dependence on age - poor sleep may become good sleep. *J Sleep Res* 2016;25:565–70.
29 Nunnally JO, Bernstein IH. *Psychometric theory*. New York: McGraw-Hill, 1994.
30 Croy I, Smith MG, Gidlöf-Gunnarsson A, *et al*. Optimal questions for sleep in epidemiological studies: comparisons of subjective and objective measures in laboratory and field studies. *Behav Sleep Med* 2017;15:466–82.
31 Wilson KG, Watson ST, Currie SR. Daily diary and ambulatory activity monitoring of sleep in patients with insomnia associated with chronic musculoskeletal pain. *Pain* 1998;75:75–84.

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