



## CLINICAL REVIEW

# Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies



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## SUMMARY

Although sleep complaints are often reported in patients with fibromyalgia syndrome (FMS), there is no conclusive evidence that these complaints represent symptomatic disorders of sleep physiology. Thus, the question of the role of sleep disturbances as an etiological or maintenance factor in FMS remains open. This study identifies the subjective and objective characteristics of sleep disturbances in adult women diagnosed with FMS. We carried out a systematic review of publications since 1990, the publication year of the American College of Rheumatology criteria of FMS. We selected empirical studies comparing sleep characteristics of adult women with FMS and healthy women or women with rheumatic diseases. We identified 42 articles. Patients with FMS were more likely to exhibit sleep complaints and also a less efficient, lighter and fragmented sleep. The evidence of a FMS signature on objective measures of sleep is inconsistent, however, as the majority of studies lacks statistical power. Current evidence cannot confirm the role played by sleep physiology in the pathogenesis or maintenance of FMS symptoms; nonetheless, it is clear that sleep disturbances are present in this syndrome.

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## Introduction

Fibromyalgia syndrome (FMS) is characterized by chronic widespread musculoskeletal pain and multiple tender points [1,2]. The prevalence rate of FMS in the general population is high, ranging from 1.3% to 4.7%, and is more common among middle-aged and older women [3]. The syndrome has a severe impact on health systems due to the frequent health care utilization and treatment costs [4]. Recent estimates suggest that, only in the United States, the costs for managing care of patients with FMS have a combined value of up to \$10,000 per patient per year [5]. FMS also has a great impact on patients' and their relatives' quality of life as it is a significant source of suffering [6].

The new American College of Rheumatology (ACR) criteria for FMS [2] recognize the role of other non-specific pain-related symptoms in the severity of FMS. Thus, beyond pain, the diagnosis

for FMS is now based on a large number of symptoms and comorbidities [2], including sleep disturbances, fatigue, headache and migraine syndrome, neuropathic disorders, anxiety and/or depression disorders [4,7]. Among these, sleep disturbance is one of the most common and relevant symptoms in FMS [8]. Experimental and clinical studies on the complex relationship between sleep and pain have shown that pain can disrupt sleep and, at the same time, sleep deprivation can enhance pain sensitivity [9]. This so-called *vicious cycle* clearly explains this incapacitating condition: a day with intense pain is followed by a night of poor sleep quality and a poor night's sleep is followed by a reduction of pain perception threshold – i.e., an increase in pain intensity [10]. Moreover, a recent review of longitudinal studies suggests that sleep disturbances portend future pain better than pain portends future sleep disturbances [11]. It is also known that other symptoms of FMS (e.g., psychological distress, fatigue) are intrinsically related to sleep disturbances [12]. Thus, the early recognition and management of sleep disturbances in FMS patients might help to ameliorate morbidity in this syndrome [13], as suggested by several clinical trials using cognitive-behavioral therapy for insomnia [14,15]. Additionally, the study of sleep physiology and sleep behavior in these specific patients might improve the explanatory power of

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### List of abbreviations

|       |                                                                  |
|-------|------------------------------------------------------------------|
| ACR   | American College of Rheumatology                                 |
| AKT   | actigraphy                                                       |
| EEG   | electroencephalography                                           |
| EPHPP | effective public health practice project                         |
| FMS   | fibromyalgia syndrome                                            |
| NREM  | non-REM sleep                                                    |
| PICOS | participants, interventions; comparisons, outcomes, study design |
| PSG   | polysomnography                                                  |
| PSQI  | Pittsburgh sleep quality index                                   |
| REM   | rapid eye movement                                               |
| SWS   | slow wave sleep                                                  |
| VAS   | visual analogue scale                                            |

models that try to relate the etiology of FMS to sleep disturbance [16–19].

### The present review

Although subjective poor sleep quality is a consistent and relevant finding among patients with FMS [20], the presence of specific polysomnographic sleep patterns in FMS is not yet clear. In fact, more than two decades of sleep research in FMS have not yielded robust findings about a FMS signature on objective assessments of sleep parameters. Polysomnography (PSG), as the gold standard sleep measure, still has not revealed a unique and consistent FMS pattern in sleep architecture among patients. The conflicting findings across studies make integrative conclusions on the basis of PSG difficult. Several studies have found low sleep efficiency [21–23], long wake time after sleep onset [21,24,25], and high percentage of light sleep [21,23,26,27] to be common in FMS sleep patterns. Furthermore, some studies have suggested micro-structure abnormalities in FMS patients, mainly an electroencephalography (EEG) non-REM sleep anomaly [19] characterized by high alpha frequency band power (7.5–11 Hz) ( $\alpha$ -EEG sleep) [28]. Contrarily, several studies have reported minimal differences [25,29,30] or no abnormalities at all between FMS patients and controls [31], suggesting that sleep complaints in FMS only reflect sleep misperception (e.g., [32]). These discrepancies in results might be due to the heterogeneity that characterizes the clinical profiles of FMS patients [33] and to inconsistencies in the studies' methods and recording tools [9]. Thus, a systematic review of the methodology and overall quality of sleep studies in FMS, which has not been performed as of yet, could reconcile the contradictory results of these studies. Here, we reviewed observational studies that assessed objective and/or subjective sleep parameters in FMS patients compared with healthy controls and/or rheumatologic patients (sleep disturbances might be associated to various rheumatologic disorders, and not only to FMS [34]).

## Methods

### Study eligibility criteria

We followed specific inclusion criteria to select the articles analyzed in this review following the “PICOS” approach [35] (see Table 1): 1) participants: adult women diagnosed with FMS according the ACR 1990 classification criteria [1]; 2) study design: observational designs (*ex post facto* studies); 3) comparisons:

healthy women or women patients with other chronic rheumatic diseases; 4) reported outcomes: subjective and objective sleep parameters.

### Search methods

We conducted a comprehensive search of the relevant peer reviewed articles by using four electronic bibliographic databases: SCOPUS, PsycINFO, Medline, and Lilacs/Ibecs. We included English and non-English (Spanish, Portuguese, and Italian) scientific literature published between 1990, the year that the ACR criteria for the classification of FMS was published [1], to May 15th, 2014. Search terms were: “fibromyalgia”, “sleep\*”, “polysomnography”, “PSG”, “actigraphy”, “AKT”. The complete search algorithm with the keywords for each database is available upon request from the authors. To identify additional studies not found in the electronic search we also conducted a manual search of the bibliographies of each retrieved article. Additionally, we examined relevant grey literature (doctoral theses and reports) by using two online databases: OpenGrey and OALster.

### Data collection and analysis

#### Selection of studies

Initially, two independent reviewers screened titles and abstracts of the retrieved articles for relevance. Articles included by either reviewer were considered potentially relevant and eligible for full text screening. A discussion about the inclusion criteria for each article followed. This process continued until both reviewers reached a consensus. Finally, a third sleep researcher examined all the articles included from each database to ensure that the selected works fulfilled the study and report eligibility criteria. For those citations fulfilling the inclusion criteria, or for which inclusion or exclusion could not be ascertained, two researchers independently reviewed the full texts. Fig. 1 shows the detailed outline of the study selection process.

#### Data extraction and management

We assessed the selected articles using a standardized form, which included data regarding authors, date of publication, objective(s), research design, participants, instruments, outcomes, and results. The document with data extraction results is available upon request from the authors.

Outcomes of interest are described in Table 2. Subjective and objective sleep measures were reported as means and standard deviations. Effect sizes (Cohen's *d*) were calculated for each difference. If, in a given study, the information was not provided for an outcome, when possible we calculated the expected outcomes (i.e., combining means and standard deviations when outcomes were reported separated). Post-hoc power analyses were performed for each test using G\*Power 3.1.3 (available at <http://www.gpower.hhu.de/>). Sample sizes for each group, computed effect sizes, and  $\alpha = .05$  were introduced to obtain the power to detect a difference between means in outcomes of interest.

#### Quality assessment and strength of evidence

We assessed the methodological quality of the studies by using an adaptation of the Effective Public Health Practice Project's (EPHPP) tool [36]. This tool includes the following items: selection of participants and allocation bias, blinding, confounders, data collection methods, withdrawals and dropouts. The adaptations consisted of minor changes in several item descriptions regarding the *confounders* (ethnic group, sex, marital status/family, age, socioeconomic status, education, health status, medication intake, body mass index, physical activity levels, menopausal status) so

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