




# Are Sleep Quality, Daytime Sleepiness, and Depression Associated with Knee Pain? A Cross-Sectional Study in Older Adults

Viviane Akemi Kakazu<sup>1</sup>  Rafael Z. Pinto<sup>2</sup> Vinicius Dokkedal-Silva<sup>1</sup> Guilherme Luiz Fernandes<sup>1</sup>  
Cynthia Gobbi Alves Araujo<sup>3</sup> Gabriel Natan Pires<sup>1</sup> Tayná A. Dias<sup>4</sup> Sergio Tufik<sup>1</sup> Monica L. Andersen<sup>1</sup>  
Priscila K. Morelhão<sup>1</sup>

<sup>1</sup> Departamento de Psicobiologia, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil

<sup>2</sup> Departamento de Fisioterapia, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil

<sup>3</sup> Departamento de Fisioterapia, Universidade Cesumar (UNICESUMAR), Maringá, PR, Brazil

Address for correspondence Priscila K Morelhão, PhD  
(e-mail: primorelhao@gmail.com).

<sup>4</sup> Departamento de Fisioterapia, Universidade Estadual Paulista Júlio de Mesquita Filho (UNESP), Presidente Prudente, SP, Brazil

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## Abstract

**Introduction** Osteoarthritis (OA) is common among older adults, and studies have suggested that it is commonly associated with sleep problems and depression. However, the results are inconsistent concerning overall sleep quality, daytime sleepiness, and depression in studies that consider OA knee pain specifically.

**Objectives** To examine the relationship between sleep quality, daytime sleepiness and depression, and OA knee pain in older adults.

**Methods** This was a cross-sectional study. Adults aged 60 and above with OA knee pain according to the National Institute for Health and Care Excellence (NICE) guidelines, and who had preserved cognitive function were recruited. Sleep quality, daytime sleepiness, and depression symptoms were assessed using the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale (ESS), and the Center for Epidemiologic Studies Depression Scale (CESD), respectively. The generalized linear model (GzLM) approach was used in the statistical analysis. A logistic regression model was performed to evaluate whether ESS, PSQI, and CESD symptoms were associated with knee pain.

**Results** The sample comprised 451 older adults. Sleep quality (OR = 1.22, 95% confidence interval [CI]: 1.07 to 1.40) and depressive symptoms (OR = 1.09, 95%CI: 1.01 to 1.17) were associated with knee pain, but there was no association with excessive daytime sleepiness (OR = 1.09, 95%CI: 0.90 to 1.20).

**Conclusions** Sleep quality and depression symptoms are associated with knee pain.

## Keywords

- sleep
- osteoarthritis
- pain
- older adults

## Introduction

Population aging has been observed globally, but it is projected to be more rapid in less developed countries, particularly those

in Asia and Latin America. In Brazil, it is estimated that the number of adults over 65 years old will triple between 2012 and 2050.<sup>1</sup> The main concern is that not all of these individuals will reach old age while maintaining good health, as many of

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the comorbidities associated with old age result in limitations, disabilities and a decline in the quality of life of older adults.<sup>1</sup>

One in three adults over 65 years suffer from osteoarthritis (OA). This disease is characterized by a loss of cartilage associated with inflammation at the site, resulting in joint pain and functional limitation. The most affected joints are those in the knees, hips, hands, and spine.<sup>2</sup> The pain generated by OA when performing daily living tasks limits mobility and range of motion,<sup>2</sup> and diseases with rheumatologic characteristics represent one of the main causes of disability in the world.<sup>3</sup>

A systematic review with meta-analysis showed that one-fifth of people with OA have symptoms of anxiety and depression and that the relative risk of depression in the OA group was 1.17 (95%CI 0.69 to 2.00, 3 studies,  $n = 941$ ).<sup>4</sup> It is possible that the pain caused by OA contributes to depression, but the relationship can be bidirectional, with one being a risk factor for the other.<sup>5</sup>

Poor sleep is also common in individuals with OA, with one study showing that symptoms of insomnia and apnea were present in 53% and 66%, respectively, of a sample of older adults with OA.<sup>6</sup> Moreover, a recent study demonstrated that poor sleep quality was related to increased pain in people with hip OA,<sup>7</sup> and another study reported findings that support this, with patients with knee or hip OA being found to have improved sleep quality after undergoing arthroplasty, with 74% of those who had poor sleep before the surgery reporting an improvement.<sup>8</sup>

Many studies have reported an association between pain/function and sleep parameters,<sup>9,10</sup> but little is known about how OA, particularly knee pain, can affect sleep. Given these findings discussed above, we hypothesized that OA knee pain would be associated with poor sleep quality, increased daytime sleepiness, and symptoms of depression. Thus, this study aimed to examine these possible associations in older adults diagnosed with OA knee pain according to the National Institute for Health and Care Excellence (NICE) guidelines.

## Materials and Methods

### Study Design

This was a secondary, cross-sectional study using data from a previous study,<sup>11</sup> approved by the Research Ethics Committee of the Universidade Estadual Paulista (UNESP), Presidente Prudente Campus, CAAE: 63835617.0.0000.5402.

### Sample Size Calculation

The method described by Peduzzi et al.,<sup>12</sup> which recommends using at least 10 participants for each variable explored in the study, was adopted. Our model included three variables, so at least 30 participants needed to be interviewed for this study. A sample loss of 20% was anticipated, therefore, at least 36 participants needed to be recruited.

### Sample Population and Recruitment

The recruitment process used was the same as that described in detail in the recent study by Morelhão et al.<sup>11</sup> Briefly, the participants were recruited from the municipality of Presidente Prudente, which is in the State of São Paulo, the most

populous state in Brazil. The municipality is culturally diverse as it is home to the descendants of immigrants from Asia, Europe, and Africa. The 2010 census conducted by the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística - IBGE*) reported that Presidente Prudente had 207,601 inhabitants, 13.5% of whom ( $N = 28,142$ ) were older adults.

For the study, the municipality was divided into five regions: north, south, east, west, and central. The postcodes for each region were randomized using an online tool ([www.random.org/lists](http://www.random.org/lists)) so that each street had an equal chance of being chosen. Alleys, rural areas, and districts were excluded from the study. The researchers went to the selected streets and asked in each house if there were individuals aged 60 years and over living there. If there were, the older adults were invited to participate in the research by completing the questionnaires and signing a written consent form giving their agreement to participate in the research. Approximately 100 older adults from each region were interviewed. The face-to-face interviews in the participants' homes took place in 2017.

### Study Procedure

Older adults who met the inclusion criteria were asked to complete questionnaires that gathered socio-demographic and anthropometric data, and information concerning comorbidities, sleep quality, excessive daytime sleepiness, depression, cognitive ability, and the history and/or presence of knee pain in the interview period. Each interview lasted approximately 45 minutes. The survey data was collected and managed using REDCap (Research Electronic Data Capture)<sup>13</sup> software. Data from this program were extracted into an Excel spreadsheet.

### Inclusion and Exclusion Criteria

Participants aged 60 years and over were invited to participate in the study. Participants who met the NICE criteria for OA were included in the knee pain group. Participants who did not meet any of the NICE criteria were included in the control group. Participants who had knee pain but did not meet the criteria for OA were excluded (this was necessary because their knee pain could be indicative of a condition other than OA).

### Data Collection

Any individuals with cognitive impairment identified through the Mini Mental State Examination (MMSE)<sup>14</sup> were excluded. The MMSE is a questionnaire that assesses cognitive status. It comprises 7 categories: time orientation, location orientation, 3-word recording, attention, and calculation, 3-word recall, language, and constructive visual ability. The overall score ranges from 0 to 30, but the cutoff scores are adjusted according to the respondent's educational level (illiterate:  $<14$ ; low and medium education:  $<18$ ; high education:  $<24$ ).<sup>14</sup> Participants who scored less than indicated for their educational level were classified as having a cognitive impairment and were excluded from the research.

Sociodemographic data, such as age, sex, marital status, education, smoking and drinking, and monthly income were

self-reported and used to characterize the sample. The other data were obtained as described below.

- **Knee pain:** OA was evaluated according to the NICE criteria.<sup>15</sup> The criteria involve the following questions: "1) Are you over 45 years old?". As all recruited participants were over 60 years of age, the answer "yes" was unanimous, therefore no one was excluded following this question, and all were indicated to answer the second question: "2) Do you have activity-related joint pain?". Those who answered "no" were allocated to the CG and those who answered "yes" answered the third question. "3) Do you have morning stiffness in your joints?". Participants who answered "no" were identified as people with OA and included in the knee pain group. Those who answered "yes" to question 3 were asked to answer one last question. "4) Does this stiffness last longer than 30 minutes?" All those who answered "yes" to this question were also screened as people with OA and included in the knee pain group. All those who answered "no" were excluded by the criterion of having knee pain not related to OA.
- **Sleep quality:** The Pittsburgh Sleep Quality Index (PSQI) is used to measure sleep quality over the last month in different populations<sup>16</sup>. It comprises seven domains: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disorders, use of sleeping medications, and daytime dysfunction. The total score ranges from 0 to 21 points. Higher scores indicate worse sleep quality.
- **Excessive daytime sleepiness:** The Brazilian version of the Epworth Sleepiness Scale (ESS)<sup>17</sup> was used to assess daytime sleepiness. The ESS has eight questions regarding the probability of napping in different situations. The score ranges from 0 to 24.
- **Depressive symptoms:** The Center For Epidemiologic Studies Depression scale (CES-D)<sup>18</sup> was used to assess the frequency of depression symptoms in the previous 7 days. The CES-D comprises 20 items, and for each item, the score ranges from 0 to 3 points: rarely or never (without a score) a few times (1 point), sometimes (2 points), and almost always or always (3 points). The closer the total score to 60, the greater the tendency towards depression. The analysis was performed using continuous data.
- **Body Mass Index (BMI):** Participants self-reported their weight and height. The BMI calculation was performed as weight divided by height squared and the result was given in kg/m<sup>2</sup><sup>19</sup>.
- **Comorbidities:** The Self-Administered Comorbidity Questionnaire<sup>20</sup> was used to investigate the presence of common comorbidities in the sample. Participants were asked if they had any of the following diseases: heart disease, hypertension, lung disease, diabetes, stomach ulcer or disease, kidney disease, liver disease, anemia or other blood disease, cancer, depression, arthritis, or back pain. The score was given by the sum of the number of comorbidities and was used to categorize the sample into 3 groups: without comorbidity, 1 to 4 comorbidities, and 5 or more comorbidities. Any comorbidity found that was not on the list was added to it.

## Statistical Analysis

Continuous variables were expressed as mean and standard deviation, and to check whether the data were statistically significant in the comparison between having or not having knee pain with the predictors, an ANOVA was performed. Categorical variables were expressed as percentages, and to check whether the data were statistically significant, the chi-square test was performed. The generalized linear model (GzLM) approach was used in the statistical analysis. A logistic regression model was performed to evaluate whether excessive daytime sleepiness, sleep quality, and depressive symptoms were associated with knee pain. Next, an interaction analysis between the predictors (excessive daytime sleepiness, sleep quality, and depressive symptoms) and outcome (knee pain) was undertaken. P-values lower than 0.05 were considered statistically significant.

## Results

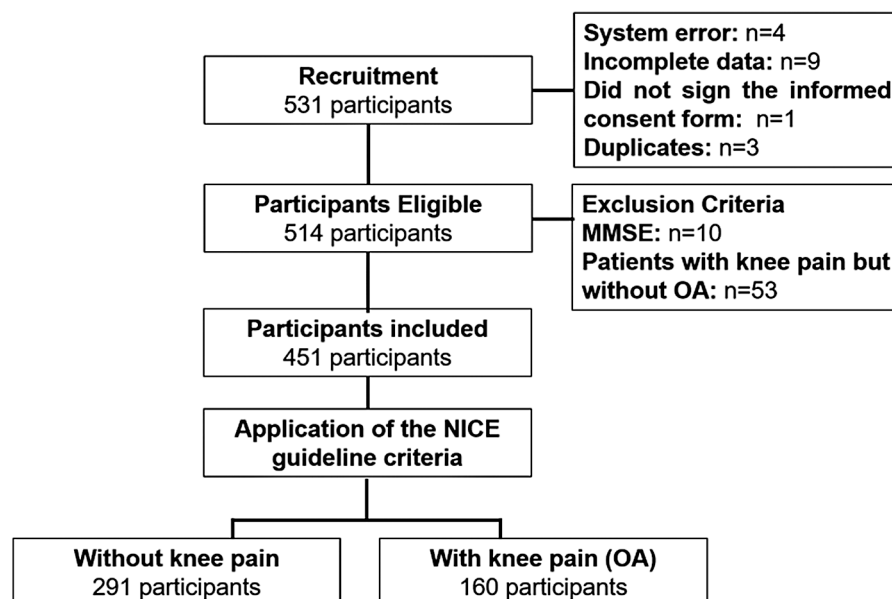
The initial sample study comprised 531 older adults, of these 80 were excluded because they were duplicates ( $n = 3$ ), due to system error/incomplete data ( $n = 13$ ), failure to sign the consent ( $n = 1$ ), because they met the exclusion criteria ( $n = 10$ ), or by reporting OA pain but not meeting the NICE guideline criteria ( $n = 53$ ). Therefore, the final sample was composed of 451 final participants. The final model represents 2 groups: 1 group without knee pain, and another with OA knee pain. The participant flowchart is illustrated in ►Fig. 1.

Women comprised 67.8% of the total sample. They corresponded to 60.01% of the group without knee pain and 81.9% of the group with pain. The mean age of the participants was 71.8 ( $\pm 7.89$ ) years for the general sample, 70.95 ( $\pm 7.83$ ) for those with knee pain, and 72.27 ( $\pm 7.09$ ) for those without pain. The mean BMI was 26.9 kg/m<sup>2</sup> ( $\pm 4.59$ ) for the general sample, 28.32 ( $\pm 5.25$ ) for those with pain, and 26.12 ( $\pm 3.99$ ) for those without pain.

The prevalence of participants with 1 to 4 comorbidities was 59%. It was 10.6% in the group with pain, and 35.4% in the group without pain. The prevalence of older people with more than 5 comorbidities was 33.7% and was 87.5% in the group with pain, and 54.6% in the group without pain. The mean score for the CESD questionnaire was 11.46 ( $\pm 11.10$ ), among participants with pain it was 14.61 ( $\pm 11.73$ ), and among those without pain, it was 9.73 ( $\pm 10.36$ ).

In respect of sleep, the overall PSQI score was 8.48 ( $\pm 3.29$ ). Participants with pain scored 9.49 ( $\pm 3.49$ ), and those without pain, 7.92 ( $\pm 3.03$ ). The overall ESS score was 4.68 ( $\pm 3.65$ ), 5.32 ( $\pm 3.39$ ) for patients with pain, and 4.33 ( $\pm 3.42$ ) for those without pain. The sample characteristics are detailed in ►Table 1.

The results expressed in ►Table 2 show that there was an association between depression (OR= 1.09, 95%CI: 1.01 to 1.17) and knee pain. A relationship was also found between sleep quality (OR= 1.22, 95%CI: 1.07 to 1.40) and knee pain. However, we found no association between excessive daytime sleepiness (OR= 1.09, 95%CI: 0.90 to 1.20) and knee



**Fig. 1** Entry and exit flowchart of study participants.

**Table 1** Baseline characteristics and outcomes measures

Characteristics	Older Adults (n = 451)	Without Knee Pain (n = 291)	With Knee Pain (n = 160)	p(value)
Age, mean ( $\pm$ SD, years)	71.8 ( $\pm$ 7.89)	72.27 ( $\pm$ 7.90)	70.95 $\pm$ 7.83	0.090
BMI, mean ( $\pm$ SD, kg/m <sup>2</sup> )	26.9 ( $\pm$ 4.59)	26.12 ( $\pm$ 3.99)	28.32 $\pm$ 5.25	0.000
CESD, mean ( $\pm$ SD, points)	11.46 ( $\pm$ 11.10)	9.73 ( $\pm$ 10.36)	14.61 $\pm$ 11.73	0.000
PSQI, mean ( $\pm$ SD, points)	8.48 ( $\pm$ 3.29)	7.92 ( $\pm$ 3.03)	9.49 $\pm$ 3.49	0.000
ESS, mean ( $\pm$ SD, points)	4.68 ( $\pm$ 3.65)	4.33 ( $\pm$ 3.42)	5.32 $\pm$ 3.39	0.006
Women, n (%)	306 (67.8)	175 (60.1)	131 (81.9)	0.000
Comorbidities (categories), n (%)				0.000
Without comorbidities	33 (7.3)	29 (10)	3 (1.9)	
1 to 4 comorbidities	266 (59.0)	103 (35.4)	17 (10.6)	
5 or more comorbidities	152 (33.7)	159 (54.6)	140 (87.5)	

Abbreviation: CESD, Center for Epidemiologic Studies Depression Scale; CI, Confidence Interval; ESS, Epworth Sleepiness Scale; OR, Odds Ratio; PSQI, Pittsburgh Sleep Quality Index; SD, Standard Deviation.

NOTES: Data are mean  $\pm$  standard deviation and frequency (proportion).

pain. Interactions between depressive symptoms and sleep quality; sleep quality and excessive daytime sleepiness; and excessive daytime sleepiness and depressive symptoms were analyzed, as were the three variables together. None of these interactions had a statistically significant association with knee pain in the sample.

## Discussion

The study aimed to investigate whether sleep quality, daytime sleepiness, and depression symptoms were associated with OA knee pain in older adults. Of the 451 participants who were interviewed, the prevalence of knee pain was 35.48%. Depressive symptoms (OR = 1.09, 95%CI: 1.01 to 1.17) and sleep quality (OR = 1.22, 95%CI: 1.07 to 1.40)

were associated with knee pain in older adults, but excessive daytime sleepiness was not (OR = 1.09, 95%CI: 0.90 to 1.20).

Riley Martinez et al.<sup>21</sup> used the American College of Rheumatology (ACR) criteria and radiography to diagnose hip OA, the PSQI to classify sleep quality, and the Visual Analogue Scale to measure pain. Participants with the most pain reported worse sleep quality. According to the findings of Skou et al.<sup>22</sup> the ACR identifies only half of the cases of hip OA, with or without radiography, while the NICE criteria identify the majority. The present study used only the NICE criteria for the diagnosis of knee OA but, as in the study on hip OA, reached the same conclusion regarding sleep quality. Despite the use of different tools, both studies agree that chronic pain in large joints can generate sleep disturbances. Another cross-sectional study reported a strong linear

**Table 2** Logistic regressions estimating the association between predictors and knee pain

Variables	Knee pain (OR 95%CI)	p(value)
CESD	1.09 (1.01 to 1.17)	0.027
PSQI	1.22 (1.07 to 1.40)	0.002
ESS	1.09 (0.90 to 1.20)	0.537
Interaction		
PSQI*ESS	0.99 (0.97 to 1.01)	0.456
ESS*CESD	0.99 (0.98 to 1.006)	0.547
PSQI*CESD	0.94 (0.98 to 1.001)	0.109
PSQI*ESS*CESD	1.00 (0.99 to 1.001)	0.478

Legend: CESD, Center for Epidemiologic Studies Depression Scale; CI, Confidence Interval; ESS, Epworth Sleepiness Scale; OR, Odds Ratio; PSQI, Pittsburgh Sleep Quality Index.

association between the frequency of restless sleep and knee OA pain -  $\beta = 1.82$ , (95%CI: 1.20 to 2.450), stiffness -  $\beta = 0.55$  (95% CI: 0.25 to 0.84), and physical function -  $\beta = 5.49$  (95%CI: 3.49 to 7.49), with similar trends observed for men and women.<sup>23</sup> According to a mediation study, pain catastrophizing and arthritis self-efficacy partially mediated the relationship between sleep disturbance and the severity of OA symptoms.<sup>24</sup> The results of our study point in the same direction as these previous studies. Although the methodologies used in these studies are not the same, they indicate that poor sleep quality is an important variable for people who suffer from knee pain.

In the present study, excessive daytime sleepiness was not associated with knee pain in older adults. A possible explanation for this is due to the score achieved in the ESS, which has a mean of 4.33 points. This value is well below what the questionnaire considers as the cutoff point for daytime sleepiness (values greater than or equal to 10 points). This does not mean that drowsiness should not be considered during a health assessment of older adults, as a recent study using ESS reported that older adults with greater daytime sleepiness were three times more likely to be afraid of falling.<sup>25</sup> Another issue that may have affected our results is that although the ESS is widely used in studies to assess sleepiness due to its reliability, it does not have good reproducibility in clinical practice.<sup>26</sup> Many health professionals are not trained in the use of tools to assess sleep<sup>27</sup>. This is an area that needs to be addressed because both falls and pain may be reduced by interventions designed to improve sleep quality<sup>25</sup>. Professionals trained in sleep medicine may be able to offer more appropriate interventions<sup>28</sup>. For example, interventions based on increased physical activity have been shown to improve sleep quality<sup>29</sup> and reduce pain in older adults.<sup>29</sup>

A cross-sectional study by Cho Y et al.<sup>30</sup> used radiographs to identify the presence or absence of OA and sleep self-report to assess whether sleep time was related to having or not having OA in a group of older Koreans, and found that insufficient sleep time was associated with the presence of OA. In the present study, the association between pain

(one of the most obvious symptoms of OA), rather than a diagnosis of OA, and sleep quality was evaluated; however, the results of the study were similar to those of Cho et al.<sup>30</sup>

Data from a systematic review<sup>31</sup> suggested that pain and depression are intertwined and may harm physical and mental functioning. A Chinese longitudinal study<sup>32</sup> evaluated the relationship between chronic illness and depression (using the CESD) in 17,707 adults  $\geq 45$  years. All 12 chronic diseases analyzed were associated with depressive symptoms, with arthritis having a prevalence of 55.25%. The prevalence of depression was higher in adults over 65 years of age and in those with a greater number of chronic diseases. The present cross-sectional design study used the CESD to identify depressive symptoms in older participants, and 59% of this sample had 1 to 4 comorbidities. Based on the results of the Chinese study,<sup>32</sup> the advanced age and the number of comorbidities of our participants were probably aggregating factors for the positive association between knee pain and depressive symptoms. These results of this study are in line with ours, as 87.5% of participants with knee pain had more than five comorbidities. Furthermore, significant results between depressive symptoms and knee pain were found.

One of the strengths of this study was the use of a random sampling method to recruit a large sample of older adults. However, this research has some limitations, such as the cross-sectional nature of the study, which precludes making any conclusions about causality in the findings. Another point that needs to be mentioned is the use of subjective evaluation methods. Although the use of questionnaires is widespread in studies due to their ease of use and low cost, they are always subject to recall bias. However, as it was not possible to acquire data on sleep using objective tests such as polysomnography and actigraphy in this study because it would have been prohibitively expensive in such a large sample, it was necessary to use self-reported measures. For similar reasons, we did not have confirmation of knee OA by radiological findings but used the standard NICE criteria instead, which are widely recognized as being reliable. A further potential limitation is that the use of either hypnotic or analgesic medication was not evaluated. It is possible that hypnotic medication impacts pain sensitivity and that analgesics affect sleep.

## Conclusions

Sleep quality and depressive symptoms were associated with knee pain, but no association was found in respect of excessive daytime sleepiness. Longitudinal studies should investigate the clinical course of sleep in older adults with knee pain. Understanding such associations can enable health professionals, especially physical therapists, to use this information to guide their clinical practice. The patient's pathological condition may be linked to modifiable factors that are increasingly discussed in the literature, such as sleep quality.

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#### Interest of Conflict

All authors have seen and approved the manuscript and report no conflicts of interest.

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