Journal of Alzheimers Research and Therapy

# The Role of Non-Pharmacological Interventions for Disrupted Sleep in the Moderate-Severe Dementia Population: A Systematic Review

Esther del Carmen Teruel Hernández[1,*], Sonia Souto-Camba[2], José Antonio López Pina[3], Raquel Irina Medina-Ramírez [4], Antonia Gómez- Conesa[5]

[1] University of Murcia, Murcia, Spain

[2] University of A Coruña, A Coruña, Spain.

[3] University of Murcia, Murcia, Spain.

[4] University of Las Palmas de Gran Canarias, Las Palmas de Gran Canarias, Spain

[5] University of Murcia, Murcia, Spain.

**Review Article**

**Open Access &**

**Peer-Reviewed Article**

**DOI:** 10.14302/issn.2998-4211.jalr-23-4813

**Corresponding author:**

Esther del Carmen Teruel Hernández, University of Murcia, Murcia, Spain.

**Keywords:**

dementia, non-pharmacological interventions, physical activity, sleep, sleep disturbance

**Received:** November 03, 2023

**Accepted:** December 30, 2023

**Published:** February 03, 2024

**Academic Editor:**

Roberto Paganelli, University of G. D'Annunzio Chieti and Pescara unich Department of Medicine and Science of Aging Chieti.

**Citation:**

Esther del Carmen Teruel Hernández, Sonia Souto-Camba, José Antonio López Pina, Raquel Irina Medina-Ramírez, Antonia Gómez- Conesa (2024) The Role of Non-Pharmacological Interventions for Disrupted Sleep in the Moderate-Severe Dementia Population: A Systematic Review. Journal of Alzheimers Research and Therapy - 1(1):25-36. https://doi.org/10.14302/issn.2998-4211.jalr-23-4813

## Abstract

This study systematically reviews the literature on non-pharmacological interventions for disrupted sleep-in people meeting established criteria for moderate-severe dementia, and to analyze the methodological quality of the included studies. The PubMed, PEDro, Cochrane, Virtual Health Library, APA PsycInfo databases were searched using a systematic literature review approach to identify various types of non-pharmacological treatments that improve disrupted sleep-in subjects with moderate-severe dementia. In accordance with the inclusion criteria, eight studies were systematically reviewed and analyzed according to the type of non-pharmacological treatment carried out. This systematic review showed that 50% of the studies used bright light therapy, 12.5% the use of manual therapy, and 37.5% sleep hygiene or walking or a combination of these interventions. Based on the results of the present study, although there is some evidence to support these strategies, it is not significantly supported and highlights variation in the way the interventions were delivered. Disrupted sleep is highly prevalent in people with dementia and have a negative impact on the quality of life of the sufferer and the caregiver. Non-pharmacological approaches to its treatment are increasingly popular as an alternative to drugs, whose efficacy and side effects have raised concerns among the population. Currently, there is a need to carry out more future research to establish its effectiveness and to be able to provide clear guidelines at the time of clinical practice.

## Introduction

Dementia is defined by the World Health Organization (WHO) in its International Classification of Diseases (ICD-10) as a chronic, progressive, and persistent syndrome characterized by deterioration of cognitive function beyond what is expected. It happens in normal aging. It is one of the leading causes of disability and dependency among older people worldwide.[1] Its incidence is related to age, this being one of the main risk factors. Thus, most patients with this disease are 65

years of age or older. On the other hand, sex also plays a fundamental role, observing a higher prevalence in women than in men [1,2]. The forms of dementia are varied, with Alzheimer's disease (AD) being the most common. In Spain it is responsible for between 50% and 80% of all dementias, being predominant in women [3].

Regarding the predominant symptomatology, sleep disturbance is a very frequent symptom in dementia, appearing above all in the more advanced stages. These alterations are due to existing damage to the neuronal pathways that initiate and maintain sleep, mainly the decrease in cholinergic function given the role of acetylcholine and its precursors in the induction of Rapid eye movement (REM) sleep [4]. The main sleep disorders in dementias are insomnia, advanced sleep phase syndrome, nocturnal motor hyperactivity, and REM sleep behavior disorder [5, 6, 7].

In Alzheimer's disease, sleep is characterized by increased arousal duration and frequency, increased daytime naps, and decreased slow deep sleep and REM sleep. Melatonin secretion has been found to be significantly decreased in the cerebrospinal fluid of patients with Alzheimer's dementia beyond normal in the elderly [6,7].

The first-choice treatment is pharmacological, which has specific drugs such as acetylcholinesterase inhibitors (IACES), memantine, selegiline and vitamin E [8]. However, no drug, to date, has been shown to be completely effective in dementia, which is a chronic disease. Likewise, there is no drug or etiopathogenic treatment in this pathology that cures or stabilizes it, so its indications should be adapted to the characteristics of each patient, such as time of evolution, age, phase of the disease or type of predominant symptomatology. Although, the use of pharmacological treatment entails adverse effects, one of them being sleep disturbances. [8,9]

For all the above, dementia brings with it an enormous range of health, social and economic resources. Referring to a loss of quality of life of the person who suffers from it, in addition to large costs of medical care and financial burdens both to the family of patients and to society. Therefore, the present study aimed to systematically review the best current available evidence on the effectiveness of non-pharmacological treatments for the improvement of disrupted sleep-in patients diagnosed with moderate-severe dementia.

## Materials and methods

The review protocol was registered and published on the international Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42021261214).

*Search strategy*

In order to carry out a comprehensive, objective and reproducible systematic review, two investigators (ET and SS) independently proceeded to perform an advanced search for studies in different health-related bibliographic databases (Pubmed, PEDro, The Cochrane Library Plus , Biblioteca virtual de la Salud (VHL) and PyscoINFO) based on the Preferred Reporting Items for Systematic and Meta-Analyses-PRISMA recommendations [10], and using Mesh descriptors and keywords, together with the Boolean operators “AND” and “OR”. ” to expand the search. The Descriptors in Health Sciences (DeCS) page was used to choose the keywords used in the search: “dementia”, “Alzheimer disease”, “exercise”, “physical activity”, “Physical Therapy modalities”, “non-pharmacological interventions”, “usual care”, “sleep quality”, “sleep disorders”, “sleep fragmentation”, “total sleep time”, “insomnia”, “circadian”. The search was carried out between November 2021 and February 2022.

*Inclusion criteria*

The eligibility criteria that should be included in the studies belonging to this review were described based on the PICO system (Patient/problem, intervention, comparison, outcomes) [11]. Therefore, the studies show the following characteristics: a) Sample: Patients diagnosed with dementia with moderate cognitive impairment (DCM) or higher, that is, they must have obtained a 4 in the classification made by the Reisberg Global Deterioration Scale (GDS) and < 10 points in the Mini-Mental State Examination (MMSE); b) Intervention: Any type of treatment modality to improve disrupted sleep, except pharmacological treatment; c) Comparison: the effect of the interventions will be with some type of treatment for dementia or its usual care that is carried out in both groups (control-treatment group); d) Result: Improvement of disrupted sleep in the patient with dementia.; (e) Type of studies: Randomized clinical trials and controlled trials. The search included studies published up to February 2022, accepting English and Spanish as languages.

*Assessment of methodological quality*

The included studies, being randomized clinical trials, underwent an assessment of the quality of the methodology using the Physiotherapy Evidence Database (PEDro) scale [12]. Scale that allows observing internal and external validity, identifying those that are internally valid and have sufficient statistical information to guide clinical decision-making. It is made up of 11 items with a "Yes" or "No" answer, although its final score is in a range of zero to ten because criterion one is not used to calculate the total score: Score of nine-ten: excellent quality; Score six-eight: good quality; Score of four-five: poor quality; Score <four: poor quality.

Any disagreement between the authors was resolved by seeking the third author's opinion.

*Data extraction*

Three authors [ET, SS and AG] separately extracted the articles' information, including the first author's name, publication year, study design, country, the number of participants, age, gender percentages, outcomes, instruments, quality score, and results. All the collected information was recorded in a checklist.

## Results

A total of 225 studies were located between the different databases. Using a bibliographic reference management program, the 15 duplicates were identified and eliminated, and the title and abstract of the remaining 210 articles were read to discard those that were not considered relevant to our review. The main reasons for elimination of these studies were non-compliance with the inclusion criteria mentioned above. A total of 57 studies underwent full text reading to verify the degree of compliance with the inclusion criteria. Finally, a total of eight articles [13-20] were part of this systematic review

(Figure 1).

*Characteristics of the included studies*

The studies included in the systematic review have been published between 1999 and 2012. With a total sample of 449 subjects analyzed, of which 163 participants were part of the control groups and 286 participants of the experimental groups (considering that we have a crossover study). The sample size of the studies included in our review varies from the 15 participants of Lyketsos et al. [17] to the 132 participants of McCurry et al. [20] representing the largest set. All the subjects comprised an age range between 60 and 86.15 years, except for the study by McCurry et al. [19] which increases the

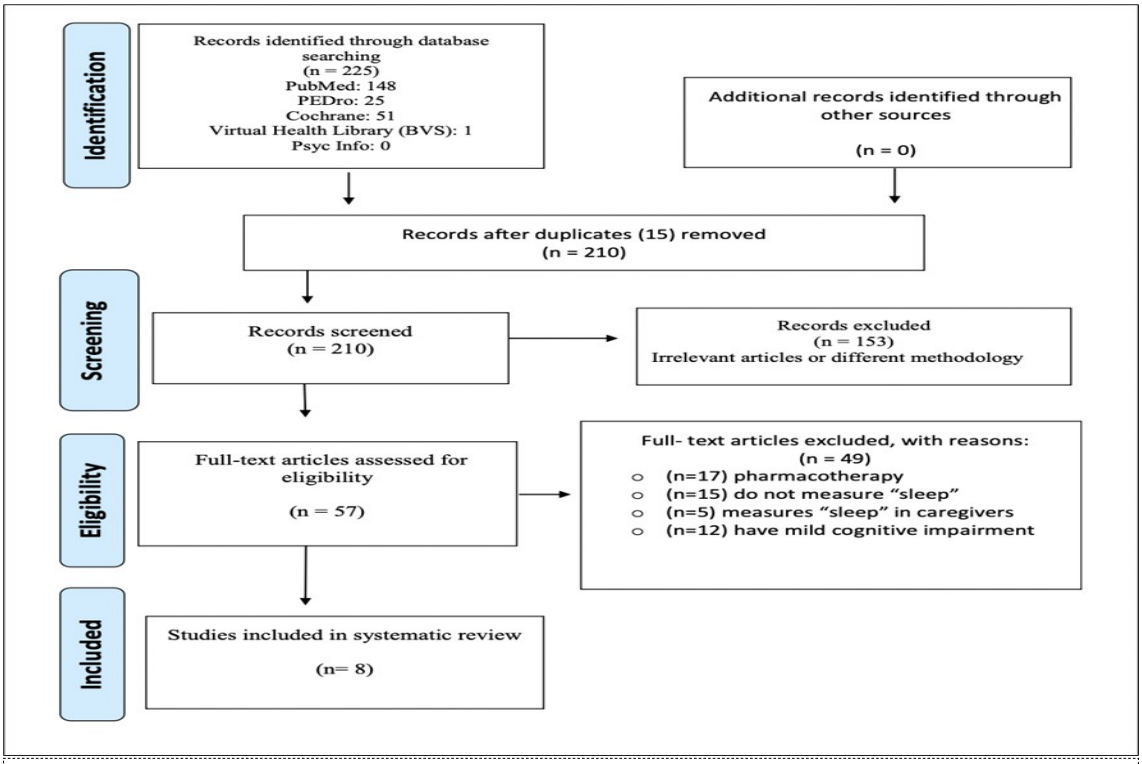


Figure 1. PRISMA Flow diagram.

range to 101 years. The mean of the range of all ages is 82 years.

The methodological quality of the eight randomized clinical trials studied using the Physiotherapy Evidence Database (PEDro) scale is between six-seven points out of 10, except for the study by Harris et al. 12, which scores three/ten. In none of the studies were the subjects blinded or blinded. (Table 1)

Table 1. Assessment of the methodological quality of the studies using the PEDro scale.

| | Methodological quality criteria | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| References | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | Punctuation |
| Burns A et al (2009)[13] | Yes | Yes | No | Yes | No | No | Yes | Yes | Yes | Yes | Yes | 7/10 |
| Dowling GA et al (2005)[14] | Yes | Yes | No | Yes | No | No | No | Yes | Yes | Yes | Yes | 6/10 |
| Dowling GA et al (2005)[15] | Yes | Yes | No | Yes | No | No | No | Yes | Yes | Yes | Yes | 6/10 |
| Harris M et al (2012)[16] | Yes | Yes | No | No | No | No | No | Yes | No | SI | No | 3/10 |
| Lyketsos CG et al (1999)[17] | Yes | Yes | No | Yes | No | No | Yes | No | Yes | Yes | Yes | 6/10 |
| McCurry SM et al (2005)[18] | Yes | Yes | No | Yes | No | No | Yes | Yes | Yes | Yes | Yes | 7/10 |
| McCurry SM et al (2012)[19] | Yes | Yes | No | Yes | No | No | No | Yes | Yes | Yes | Yes | 6/10 |
| McCurry SM et al (2011)[20] | Yes | Yes | Yes | Yes | No | No | Yes | Yes | Yes | Yes | Yes | 8/10 |

1.Eligibility criteria were specified;2. Subjects were randomly allocated to groups;3.Allocation was concealed; 4. The groups were similar at baseline regarding the most important prognostic indicators; 5. There was blinding of all subjects; 6. There was blinding of all therapists who administered the therapy; 7. There was blinding of all assessors who measured at least one key outcome; 8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; 9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one kye outcome was analyzed "intention to treat"; 10. The results of between-group statistical comparisons are reported for at least one key outcome; 11. The study provides both point measures and measures of variability for at least one key outcome.

*Narrative results*

The analysis of the studies is carried out by subject matter. (Table 2)

Table 2. Narrative summary of intervention included studies.

| References | Intervention groups | Duration of the program (weeks) | Frequency of intervention | Tracing |
|---|---|---|---|---|
| Bars A et al (2009)[13] | BLT: full spectrum light at 10,000 lux<br>GC: standard fluorescent tube light at 100 | 4 | Treatment consisted of one session per day of full- spectrum light exposure at 10,000 lux (treatment) or standard fluorescent tube light at 100 lux (control) for 2 hours between 10:00 and 12:00. | Yes. Follow-up assessments performed at week 4 (immediately post -treatment, with actigraph) and again at week 8 (one-month post-treatment, without actigraph) |
| Dowling GA et al (2005)[14] | GE: exposure to bright light (>2500 lux)<br>GC: usual indoor light exposure (150-200 lux) | 12 weeks with 3 periods: Baseline (1 week), light intervention (10 weeks) and post-intervention (1 week). | compared morning bright light treatment (experimental) with normal room lighting conditions (control) Monday through Friday for 10 weeks.<br>1h of exposure to light (9:30.10:30) | Yes (1 week) |
| Dowling GA et al (2005)[15] | GEI: exposure to bright light in the morning (2500 lux)<br>GE2: exposure to bright light during the afternoon (2500lux)<br>GC: regular indoor light exposure (150-200 lux) + scheduled activities | 11 weeks, with two periods: Baseline (1week) and light intervention (10 weeks). | Phase 1 compared morning bright light treatment (experimental) with normal room lighting conditions (control).<br>Phase 2 compared bright light treatment in the morning versus the evening Morning bright light treatment administered for Ih (09:30-10:30) and evening light treatment administered for 1h (15:30-16:30), both treatments for 10 weeks on weekdays. The time of bright light treatment in the evening is not specified.<br>Bright light treatment was primarily daylight (outdoors or indoors with plenty of windows and light) to ensure subject exposure to >2500 lux in the direction of gaze. Monday to Friday for 10 weeks. I hour in the morning (9.30-10.30 a.M) or in the afternoon (3.30-4.30 p.M) | No |
| Harris Met al (2012)[16] | GE: Back massage (SSBM) 3 minutes before bedtime + usual care at bedtime.<br>GC: usual care at bedtime | 2 days | 2 times in total | No |
| Lyketsos CG (1999) [17] | GE: Morning BLT<br>GC: dim light exposure | Patients were randomly 1 hour every morning assigned to one or the other condition and spent 4 weeks in that condition. Subsequently, they did not receive treatment for 1 week and a second baseline was taken. They were then treated in the other condition for 4 weeks. | 1 hour every morning | There was no follow-up It was evaluated at the end of cach treatment in the different conditions (week 2 and 4). |

| | | | | |
|---|---|---|---|---|
| McCurry SM et al (2006)[18] | GE: specific recommendations on a sleep hygiene program, walking every day and increased exposure to light<br>GC: dementia education and caregiver support | 6 | Both groups participated in 6 sessions at home of 1 hour duration on behavioral intervention with patients with dementia by a neuropsychologist.<br>GE: 3 sessions a week | Yes. At 2 and 6 months using an ACtillume movement recorder. |
| McCarry SM et al (2012)[19] | GE: sleep education program (SEP).<br>GC: usual medical care | 4 | The SEP group received 4 training sessions with the staff-caregiver to develop and implement individualized behavioral sleep plans for residents | Yes. 6-month follow-up by interviewer's blind to treatment assignment |
| McCarry SM et al (2011)[20] | GE walking: used a self-paced walking program with a goal of 30 continuous min/day.<br>GE light: used a light box for Ih/day that provided 2500 lux in the eye of white light. They are allowed to do other activities during treatment.<br>GE NITE-AD: follow an individualized sleep schedule, walk for 30 continuous minutes/day and receive Ih/day of light. GControl: did not change the schedules and had non-direct contact with the coaches. | 4 | The walking, light, and control groups participated in 3 home training visits (weeks 1, 2, and 8).<br>The NITE-AD group participated in 6 home training visits (4 weekly, 2 biweekly).<br>All subjects received sleep hygiene guidelines. | Yes, 6 months |

*Bright light therapy*

Lyketsos et al. [17] perform a crossover clinical trial where 15 subjects diagnosed with dementia were randomized into an experimental group, where the treatment was bright light therapy (BLT) administered for 1 hour every morning using a full-spectrum lamp of 10,000 lux at 3 feet, and a control group, where a dim, low-frequency light was used. Patients who had been treated with medications for problem behaviors or sleep disturbance were only enrolled in the study if they had been on a stable dose of these medicines for 1 week prior to enrollment and continued to meet inclusion criteria. Subjects spent 4 weeks in one condition and a second baseline was taken. They were then treated in another condition for an additional 4 weeks. Regarding the results measured by actigraphy and different scales, the subjects who received BLT slept an average of 6.4 hours per night during the week prior to treatment. At two weeks of treatment, they were sleeping an average of 7.6 hours each night, and at four weeks of treatment they were sleeping an average of 8.1 hours per night. The improvement in nightly sleep between baseline and week two was not statistically significant. The improvement between baseline and four weeks was statistically significant ($p<0.05$). The difference between the control and active treatment groups at two weeks was borderline significant, and at week four it was not statistically significant, although all study patients, including those in the control group, showed slight improvements in nighttime sleep.

The two studies by Dowling et al. [14,15] tested the effect of morning BLT on nighttime sleep, daytime awakening time, and rest activity rate in 46 subjects diagnosed with dementia. This study was conducted in two phases, the first phase compares morning light exposure, between 8:00AM-20:00PM, with normal light. Chart reviews were conducted to confirm that potential subjects met the criteria for inclusion, like a stable medication regimen. Potential subjects were excluded if they were regularly taking valerian, melatonin or sleeping pills. No subjects were excluded based on other medication usage. In the first phase of the Dowling et al. [15], the experimental group, with 29 subjects, received a

BLT program >2500lux in the direction of gaze, Monday through Friday from 9:30-10:30 A.M. for 10 weeks. The control group, with 17 subjects, received usual light (150-200lux). Data were recorded by means of an actigraph the first week and week 12 (post-intervention). Regarding the results, it revealed no significant changes in sleep efficiency, sleep time, wake time, or number of awakenings in the experimental group compared to the control, nor were there any significant differences between the groups at daytime wake time. half. Regarding the circadian rhythm results, there were no significant differences in acrophase between the groups, but there was a trend towards significance in amplitude with improvement in the experimental and worsening in the control ($p<0.09$). There were also no significant differences in the non-parametric analysis variables of the circadian rhythm.

In the second phase of the study by Dowling et al [15], morning BLT (experimental group one with 29 subjects) is compared with afternoon BLT (experimental group two with 24 subjects) with a mean age 84 years diagnosed with dementia. Experimental group two receive BLT >2500lux in the direction of gaze, from Monday to Friday from 15:30-16:30pm. for 10 weeks. The control group consisting of 17 subjects receives normal light (150-250 lux) and participates in regularly scheduled activities. With respect to the results, the analysis of covariance of repeated measures did not reveal significant differences in the variables of activity or daytime or nighttime sleep between the groups. However, there was a significant ($p<0.04$) main effect of treatment for acrophase with relative stability in the morning and afternoon light experimental groups. The mean peak of the rest activity rate was 131 minutes later in the control group and advanced in the morning and afternoon experimental groups, 17 minutes and 1 minute, respectively.

Burns et al. [13] evaluate the benefit of four-week BLT in a study of 48 subjects recruited from two nursing homes with dementia and behavioral disorders. The 22 subjects in the experimental group underwent a BLT program that consisted of exposing themselves to full-spectrum 10,000 lux for two hours a day between 10:00 and 12:00 in the presence of a nurse. The control group, with 26 subjects, received standard fluorescent tube light at 100 lux. Data were recorded using an actigraphy and scales such as: MMSE, Cornell Scale for Depression in Dementia (CSDD), Manchester and Oxford Universities Scale for the Psychological Assessment of Dementia (MOUSEPAD) and Crichton Royal Behavior Rating Scale (CRBRS), the first week, the fourth week (post-treatment) and after a follow-up in week eight. Any changes in psychotropic medication were noted. Regarding the results on psychological and cognitive symptoms, there were no significant differences between groups in the different scales, but improvements were obtained in both groups. Only one change to medication was recorded – a person in the treatment group who had her trazodone increased (antidepressant drug). Agitation improved in the immediate post-treatment phase, week four, in both the BLT and placebo groups, but the comparison between groups was not significant at either week four or week eight. In relation to the results, mean duration of night sleep measured by the actigraphy was 8.3 hours and 8.6 hours before and after exposure to BLT, respectively. There were no significant differences between the groups before or after therapy as measured by the actigraphy.

*Education program, combining sleep hygiene, daily walking, and bright light therapy.*

In the study by McCurry et al. [18] a total of 36 subjects are randomly divided into an experimental group (n=17) with an education program is carried out, combining sleep hygiene, daily walking, and BLT (greater than 100lux) three sessions a week for 2 months, and a control group (n=19) where education about dementia and support for the caregiver is carried out. Both groups also carried out 6 sessions of 1h at home for behavioral intervention in patients with dementia. Caregivers also recorded daytime naps (frequency and duration), use of sleeping medications, frequency and duration of nighttime disturb-

ances, and subjective sleep quality ratings. After finishing the treatment, significant differences were obtained measured by the actigraph to assess sleep. Subjects in the experimental group spent an average of 36 minutes less awake time at night and had 5.3 fewer nighttime awakenings than subjects in the control group. Also, the patients in the experimental group exercised significantly more days per week and had significantly lower levels of depression. After follow-up, significant differences remained at six months favoring the experimental group in actigraphy estimates of patient awake time, exercise days, and depression.

These same authors, in a subsequent study [20] carried out a sleep education program to improve sleep in older adults with dementia. A total of 31 subjects in the experimental group undergo four sessions of sleep education program, and a control group with 16 subjects receive usual medical care for four weeks. An eligibility criterion was agreement to make no change in sedative medication use (type or dose) during the 2-month active treatment period. Patients were stratified by baseline sleep medication use. The random allocation sequence was obtained from a computer program that blocked in groups of 12 subjects. The variables were recorded with actigraphy at the beginning, at one month (post-treatment) and at six months of follow-up. Posttreatment, there were no significant differences in residents' actigraphy measures of sleep. However, there was a tendency to improve the percentage of night sleep for subjects in the experimental group. After 6 months of follow-up, they showed significant differences in the percentage of sleep ($p = 0.040$) and total sleep time ($p = 0.013$). At six months, subjects in the control group were awake an average of 24 minutes longer each night than subjects in the sleep education program condition. Regarding secondary outcomes, there was a significant increase over time in caregivers' ability to identify triggers and consequences of nighttime behaviors, develop behavior plans, and implement daytime events with residents. When comparing the two treatment groups, sleep education program group were significantly less depressed after treatment than control subjects, ($p = 0.0036$), but there were no differences between groups in daytime sleepiness or behaviors.

McCurry et al. [19] with 132 subjects diagnosed with dementia, developed a four-week program with the objective of testing the effects of walking, BLT, and a combined intervention (walking, light, and SEP) on sleep in people with Alzheimer's. For this, the participants were randomly assigned to one of the four treatment conditions: Walking group with 32 subjects where they had to walk at their own pace with a goal of 30 continuous minutes a day. BLT group with 34 subjects where they sat in front of the light box for one hour a day. The Nighttime Insomnia Treatment and Education in Alzheimer's Disease (NITE-AD) group with 33 subjects where the caregivers had an individualized sleep plan session for the patient, a daily walking program, daily light exposure. The control group, made up of 33 subjects, was offered support for dementia care, but did not receive training or tasks related to sleep hygiene, walking, or exposure to light. Data on sleep variables were recorded at the end of treatment (four weeks) and after a six-month follow-up. Regarding sleep outcomes: patients in each active treatment had reduced actigraphy total wake time after four weeks of treatment compared to control subjects, participants in the Walking condition were awake 33.1 minutes less/ night ($p = 0.05$); Participants with BLT were awake 39.0 fewer minutes; and NITE-AD subjects were awake 39.8 minutes less. There were no significant differences in total wake time change scores between the experimental groups, except for a slightly smaller difference in wake time for participants in the BLT group ($p = 0.06$). compared to controls. Although not significant, there were moderate improvements in percentage sleep for all three active treatment groups (NITE-AD, 5% improvement; walking and light exposure, 3% and 4.3% improvement, respectively). In addition, there was a trend for subjects in the walking group to have fewer nocturnal awakenings than those in controls. At six-month follow-up, there were no significant differences in any

treatment group regarding control for actigraphy or subjective sleep outcomes.

*Back massage*

Harris et al.[16] try to show the sleep benefit and life quality of people with dementia through a back massage characterized by long, slow, sliding, and repetitive strokes from lumbar to cervical region. We are counting on a total of 40 subjects with dementia distributed in two groups, the experimental with 20 patients where a three-minute back massage protocol is used at the time of toing to bed for two nights. And the control group with other 20 subjects that receive usual control. All participants received usual bedtime care No changes in the physical setting, nursing services, staffing patterns, medications, or patient care protocols were instituted as part of the study. Demographic data, medical diagnoses, medical history, and medications were collected via chart abstracting. This study used seven hours of night sleep as a cut reference for people who sleep "badly". Data were registered through actigraphy, and the results did not reveal any significant differences between intervention and control over sleep latency, sleep efficiency, awakening after the beginning of the sleep and daytime inactivity. There was insufficient power to establish effectiveness.

**Discussion**

The main objective of this review has been to determine through scientific evidence which non-pharmacological therapies are used to treat interrupted sleep-in people diagnosed with moderate-severe dementia and to analyze the methodological quality of the included studies.

During the night, people with dementia often experience frequent awakenings and fragmented sleep due to various factors that contribute to circadian rhythm disturbances. In this systematic review of non-pharmacological interventions to improve disrupted sleep-in people with moderate-severe dementia, it was found that 50% of the studies [13-15,17] were aimed at normalizing circadian rhythms using BLT, 12.5% 16 used manual therapy and 37.5% [18-20] used SEP or walking or a combination of these interventions.

Although there are indications that these techniques are effective for improving disrupted sleep, they do not generate significant changes. In addition, the great variability with which the interventions are applied; type of daytime activity or light dose, the ability to draw definitive conclusions is diminished.

The eight studies included in this review are randomized clinical trials, that is, they represent the best scientific evidence for clinical decision-making and the lowest risk of bias. The mean score of the trials is six according to the PEDro scale, which overall indicates their good methodological quality. Therefore, the results that they offer us can be interpreted as the best non-pharmacological clinical treatment for patients with dementia with sleep disturbance.

BLT has been shown to correlate with improved sleep-in dementia, as it stabilizes the secretion of melatonin in the pineal gland, which is involved in regulating the sleep-wake cycle and produces improvements in stabilization. mild circadian cycle [13-15,17]. However, more research is needed to define the most appropriate doses, administration, frequency, and duration to obtain better effects.

In the first phase of the Dowling et al. [14], they had few institutional staff and insufficient natural light, so they had to complete it with light boxes. Following this line, in the second phase of the study, the subjects, who presented interindividual differences, were only exposed to bright light between Monday and Friday, and it is possible that exposure during all days of the week would have produced a greater effect. In addition, the fact of being placed in front of a light box for one or two hours a day implies a huge increase in individual attention, and it is possible that distractors have been introduced. Other

factors that may have influenced the results are the type of actigraphy used and the characteristics of the treatment protocol.

Studies on this method of treatment differ on the time of day chosen to perform the exposure. The study by Burns et al., 2009 defends the idea of morning light, thus unexpectedly avoiding the temperature nadir. However, other authors such as Dowling et al. [14] prefer to opt for afternoon light. It would be convenient in future studies to individualize the moment of light exposure for each subject based on their endogenous rhythm, thus avoiding offering light in sensitive regions of the response curve of everyone [13-15,17].

Another treatment to improve sleep is manual therapy. In the study by Harris et al. [16] performed SSBM for three minutes, where an increase in night sleep from the beginning to the end was obtained. Establishing this treatment before bedtime may be a strategy to promote sleep, however, more research is required. Firstly, to understand how easily this practice could be incorporated into the caregiver's night care routines for the person with dementia, and secondly, about the most appropriate measures to objectify the effects of massage on sleep, since that in the study there was no control over nighttime routines. As recommended by the American Academy of Sleep Medicine [21] the use of sleep diaries in conjunction with actigraph data would serve to increase the accuracy of the data.

SEP is another type of non-drug treatment to improve disrupted sleep-in people with dementia. McCurry et al. 19 provide evidence that a sleep education program improves nocturnal behaviors in people with dementia, however there is a potential for response bias in results based on self-reports as family members of participants and trainer are not blinded program. In addition, adherence to treatment is another important aspect to consider when including a treatment in the routine of the person with dementia, and it constitutes an indicator of its acceptability by users and their caregivers. Some interventions, such as sleep hygiene, require staff training as well as regular supervision to ensure continued implementation and monitor results.

Additionally, it is necessary to assess the option of a treatment that combines the exposed treatments to produce a more resistant effect, such as SEP [19,20] or walking [20] with BLT. McCurry et al. [18], provides the first evidence that dementia patients with sleep problems may benefit from a program that combines SEP, daily walking, and BLT, with short-term treatment (six weeks). However, in most trials, the intervention was performed by the research staff to establish the efficacy of the intervention; therefore, translating these time-consuming strategies onto the caregiver figure requires careful consideration. It would be necessary to evaluate this program with a more specific approach, focused on reducing the burden of caregivers, as well as evidencing whether all the components of the program are necessary for treatment results. Following this same line, McCurry et al. [20] indicate that caregivers of people with dementia can implement light exposure and walking protocols, individually and in combination, to improve nighttime sleep. Although, there are also limitations such as the fact that the subjects themselves can select their own walking pace. It would be necessary to determine if a more vigorous exercise routine would offer greater improvements.

**Limitations**

Among the main limitations of this review is a limited number of studies (eight) focused on non-pharmacological therapies in patients with cognitive impairment. The inclusion criteria of this review focused on subjects with moderate to severe cognitive impairment (having obtained four in the classification made by GDS and <10 points in MMSE), since interrupted sleep occurs mostly from

advanced stages, which has left out a few studies (12) that focused on mild stages of cognitive impairment. It is noteworthy that the last study found is from 2012, which indicates the need to promote their research. In addition, we believe that these special features make the review comprehensive and may help the reader to better identify specific treatments for sleep when pharmacology cannot be used.

Also, other limitations of this review are the biases of the included studies such as a small sample size, so that the results cannot be extrapolated to a more general population, the existence of incomplete information or the lack of data about whether the evaluators or therapists have been blinded.

## Conclusion

The systematic review carried out allows us to reach various conclusions: Disrupted sleep is highly prevalent in people with dementia and has a negative impact on the quality of life of patients who suffer from it and their caregivers. Non-pharmacological approaches to the treatment of disrupted sleep-in dementia are increasingly popular as an alternative to drugs, the efficacy and side effects of which have raised public concerns. There is a paucity of studies related to non-pharmacological treatments to improve disrupted sleep-in people with dementia moderate to severe. Four interventions had the most positive results: bright light exposure, sleep education, daily walking, and manual therapy, however analysis of these revealed little clarity about their positive findings. More research is required to be able to conclude the effectiveness of non-pharmacological interventions in disrupted sleep-in patients with dementia moderate-severe, and thus also be able to provide clear guidelines at the time of clinical practice.

## Conflict of interest

There is no conflict of interest.

## References


1. World Health Organization. (2018): Towards a dementia plan: a WHO guide. World Health Organization; 71 p.
2. Segura D, Mestre M, Parellada N, Estrada J, Callén A, Robles B. (2013) Dementia and gender: a perspective from primary care. Alzheimer. Real Invest Demenc.; 54:5-13. doi:10.5538/1137-1242.2013.54.5.
3. Thomas Carazo E, Nadal Blanco MJ. (2001) Diagnostic and therapeutic approach to dementia in primary care. SEMERGEN. 27(11):575-86. doi.org/10.1016/S1138-3593(01)74030-0.
4. Arana Fernández de Moya E. (2010) The basics of imaging dementia. Radiology.52(1):4-17 doi: 10.1016/j.rx.2009.09.005
5. Almenar C. (2005) sleep disorders. Comprehensive approach to dementia in advanced stages. Barcelona: Science. pp.171-184.
6. Bliwise, DL. (1993) Sleep in normal aging and dementia. Sleep; 16 (1): 40–81. doi.org/10.1093/sleep/16.1.40.
7. Echávarri C, Erro ME. (2007) sleep disorders in the elderly and in dementias. Anales Sis San Navarra. 30 (supl.1):155-61.
8. Brañas F, Serras JA. (2002) Guidance and treatment of the elderly with dementia. Información Neurodegenerative Diseases: Time for a Comprehensive Critical Review. Front Aging Neurosci.

20.12:578339. doi: 10.3389/fnagi.2020.578339.

9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al. (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. Mar 29;372: n71. doi: 10.1136/bmj. n71.
10. Santos CMC, Pimenta CAM, Nobre MRC. (2007) The PICO strategy for the research question construction and evidence search. Rev Latino-am Enfermagem. 15(3). doi.org/10.1590/S0104-11692007000300023.
11. Gomez-Conesa A, Suarez C, Catalán D, López-López JA. (2015) The Spanish translation and adaptation of the PEDro scale. Physiotherapy : 101eS463- eS464. http://dx.doi.org/10.1016/j.physio.2015.03.3250
12. Burns A, Allen H, Tomenson B, Duignan D, Byrne J. (2009) Bright light therapy for agitation in dementia: a randomized controlled trial. Int Psychogeriatr;21(4):711-21. doi:10.1017/S1041610209008886
13. Dowling GA, Hubbard EM, Mastick J, Luxenberg JS, Burr RL, Van Someren EJ. (2005) Effect of morning bright light treatment for rest-activity disruption in institutionalized patients with severe Alzheimer's disease. Int Psychogeriatr.17(2):221-36. doi:10.1017/s1041610205001584
14. Dowling GA, Mastick J, Hubbard EM, Luxenberg JS, Burr RL. (2005) Effect of timed bright light treatment for rest-activity disruption in institutionalized patients with Alzheimer's disease. Int J Geriatr Psychiatry. 20(8):738-43. doi: 10.1002/gps.1352.
15. Harris M, Richards KC, Grando VT. (2012) The effects of slow-stroke back massage on minutes of nighttime sleep-in persons with dementia and sleep disturbances in the nursing home: a pilot study. J Holist Nurs. 30(4):255-63. doi:10.1177/0898010112455948
16. Lyketsos CG, Lindell Veiel L, Baker A, Steele C. (1999) A randomized, controlled trial of bright light therapy for agitated behaviors in dementia patients residing in long-term care. Int J Geriatr Psychiatry.14(7):520-5.
17. McCurry SM, Gibbons LE, Logsdon RG, Vitiello MV, Teri L. (2005): Nighttime insomnia treatment and education for Alzheimer's disease: a randomized, controlled trial. J Am Geriatr Soc.53 (5):793-802. doi: 10.1111/j.1532-5415.2005.53252. x.
18. McCurry SM, LaFazia DM, Pike KC, Logsdon RG, Teri L. (2012) Development and evaluation of a sleep education program for older adults with dementia living in adult family homes. Am J Geriatr Psychiatry. 20(6):494-504. doi: 10.1097/JGP.0b013e318248ae79.
19. McCurry SM, Pike KC, Vitiello MV, Logsdon RG, Larson EB, Teri L. (2011): Increasing walking and bright light exposure to improve sleep in community-dwelling persons with Alzheimer's disease: results of a randomized, controlled trial. J Am Geriatr Soc. 59(8):1393-1402. doi: 10.1111/j.1532-5415.2011.03519. x.
20. Vargas MV, Ceballos CW, Cabal NM. (2021) Towards a critical and comprehensive reading of the history of the national cancer institute. Medicine. 2021;43(1):42-55. doi.org/10.56050/01205498.1584.