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Effect of Melatonin on Sleep Quality in an Older Adult Population With Insomnia: A Systematic Review

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ADMINISTRATIVE INFORMATION

Support - Proyecto PAPIIT IN307326.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 May 2026 and was last updated on 10 May 2026.

INTRODUCTION

Review question / Objective The objective of this systematic review is to critically evaluate the effectiveness of melatonin, including immediate-release and prolonged-release formulations, compared with placebo or benzodiazepine treatment, in improving sleep quality among older adults with insomnia. The review question was formulated according to the PICO framework: Population (older adults aged 60 years and older with insomnia), Intervention (melatonin treatment), Comparison (placebo or benzodiazepine treatment), and Outcomes (sleep quality, treatment adherence, and adverse events). The guiding research question is: What is the effect of melatonin on improving sleep quality in older adults with insomnia?

Rationale Insomnia is one of the most prevalent sleep disorders among older adults and represents a significant public health concern due to its high prevalence and its impact on functionality, well-being, daytime fatigue, cognitive impairment, increased risk of falls, institutionalization, and reduced quality of life in this population. [1,2] These sleep disturbances are partially explained by physiological changes associated with aging, the presence of chronic noncommunicable diseases, and psychosocial factors such as anxiety, depression, and polypharmacy, all of which contribute to reduced deep sleep, circadian rhythm alterations, sleep fragmentation, and other primary sleep disorders.[3]

Despite the clinical relevance and impact of insomnia in older adults, treatment approaches are not always comprehensive, as most interventions rely primarily on pharmacological therapies, particularly benzodiazepines.[4] In geriatric settings, this issue is especially concerning because polypharmacy increases the risk of adverse drug reactions, drug interactions, dependency, falls, and cognitive decline. Consequently, there is a need to identify safer and more effective therapeutic alternatives capable of improving sleep quality without compromising patient safety.[5,6]

Melatonin, a hormone involved in the regulation of the sleep–wake cycle whose secretion declines with age, has been proposed as a potentially useful intervention for insomnia treatment in older adults. Exogenous melatonin administration aims to improve sleep quality by restoring circadian synchronization, reducing sleep latency, increasing total sleep duration, and improving subjective sleep quality.[7] Evidence from systematic reviews and meta-analyses suggests that melatonin produces statistically significant yet clinically modest improvements. Nevertheless, its favorable safety profile makes it a relevant therapeutic option in geriatric care, particularly when compared with hypnotic medications. However, its effectiveness may vary according to individual factors (age and comorbidities) and methodological factors (dosage, treatment duration, and study design). [8,9]

Existing systematic reviews present important limitations, including heterogeneous populations, variability in insomnia diagnostic criteria, and differences in melatonin dosage regimens, which generate uncertainty regarding the interpretation and applicability of findings in older adults. Therefore, conducting a systematic review exclusively focused on this population is justified to rigorously synthesize the available evidence concerning the effects of melatonin on sleep quality. The findings may contribute to improving clinical decision-making, optimizing geriatric prescribing practices, and promoting the efficient use of healthcare resources.[10].

Condition being studied This review focuses on insomnia, defined as a sleep disorder characterized by difficulty initiating or maintaining sleep, as well as the presence of non-restorative sleep. In older adults, insomnia not only affects sleep quality but also negatively impacts functionality, cognitive status, emotional balance, and quality of life, increasing the risk of falls and dependency. [11,12] These alterations are common in this population and present a multifactorial etiology, including physiological changes associated with aging, chronic comorbidities, circadian rhythm disturbances, and decreased melatonin secretion. [13,14] Within this context, insomnia management represents both a clinical and caregiving challenge, thereby justifying the exploration of safe and effective therapeutic interventions such as melatonin. Melatonin has been proposed as a practical and safe therapeutic intervention for improving sleep quality, reducing sleep latency, increasing sleep duration, regulating the sleep–wake cycle, and optimizing sleep parameters. However, evidence regarding its effectiveness and safety in older adults remains heterogeneous. [15,16]

METHODS

Search strategy A literature search was conducted following the PRISMA guidelines through April 27, 2026, in scientific databases including PubMed, Web of Science, SCOPUS, SciELO, and LILACS. The search terms used were: melatonin, sleep quality, sleep disorders, insomnia, aged, and older adults, in both English and Spanish. In addition, the Boolean operators AND and OR were applied. The following search strategy was developed: (Aged) OR ("Older adults") OR (elderly) AND (Melatonin) AND (sleep) OR (sleep disorder) OR (insomnia). This strategy was adapted for each database, using primarily English and Spanish terms. Furthermore, a search of the gray literature was conducted in order to identify unpublished studies that could be relevant and useful for this systematic review.

Participant or population Studies evaluating older adults aged ≥60 years diagnosed with insomnia will be included, regardless of sex or comorbidities.

Intervention Melatonin administration in any dosage, duration, or formulation.

Comparator Placebo or benzodiazepine treatment.

Study designs to be included Primary experimental and observational studies evaluating the effects of melatonin on sleep outcomes will be included, particularly randomized controlled trials (RCTs) and quasi-experimental studies involving melatonin (at any dose) versus placebo or benzodiazepine treatment. If evidence is limited, analytical observational studies such as cohort studies and case-control studies will also be considered to broaden understanding of the phenomenon in real-world contexts.

Eligibility criteria Eligibility criteria will be established according to the PICO framework in order to ensure rigorous study selection. Studies conducted in older adults aged ≥60 years with sleep quality disturbances will be included, regardless of sex or comorbidities. Studies evaluating the administration of melatonin at any dosage, formulation, frequency, or duration, compared with placebo or benzodiazepine use, will be considered. Studies reporting the primary outcome of sleep quality assessed through validated instruments, such as the Pittsburgh

Sleep Quality Index (PSQI) or other standardized scales (e.g., the Insomnia Severity Index), will be included. Secondary outcomes will include treatment adherence to melatonin therapy, while the third outcome will consist of adverse events associated with the intervention. Regarding study design, randomized controlled trials will be prioritized; however, non-randomized trials and analytical observational studies (cohort and case-control studies) will also be considered in the event of limited evidence. No restrictions regarding language, publication period, country, or setting will be applied, with the aim of minimizing bias and avoiding arbitrary limitations.

Information sources The literature search was conducted in international electronic health science databases, including PubMed, Web of Science, SCOPUS, SciELO, and LILACS, using the predefined search strategy. In addition, a complementary search of the gray literature was performed, primarily through TESIUNAM and Google Scholar, to minimize potential bias. Furthermore, manual searches were carried out in the reference lists of the included studies, relevant reviews, and other non-indexed sources whenever considered appropriate. These strategies are intended to identify additional evidence that may not have been retrieved through the electronic database searches.

Main outcome(s) The primary outcome of this review will be sleep quality in older adults, assessed using validated instruments such as the Pittsburgh Sleep Quality Index (PSQI) or other standardized scales, including the Insomnia Severity Index (ISI). This outcome was selected because of its direct clinical relevance to the well-being and functional status of older adults. Outcome measurements reported in each study will be considered, with priority given to short- and medium-term assessments following the intervention. These evaluations will also contribute to identifying the secondary outcome, namely treatment adherence to melatonin therapy, which will be measured and reported as continuous or categorical scores according to the scale used in each study. Finally, adverse events associated with melatonin use will also be considered as outcomes in order to provide a comprehensive assessment of the potential benefits and risks of the intervention.

Additional outcome(s) Additional outcomes will include quality of life, daytime sleepiness, and sleep satisfaction, provided that these variables are assessed using validated instruments. These outcomes will contribute to a more comprehensive interpretation of the effects of melatonin from a well-being perspective in older adults. Furthermore, adverse events associated with the intervention will also be included in order to evaluate the safety profile of melatonin use in this population.

Data management Data management will be conducted through a systematic and standardized process that will include the selection, organization, and extraction of relevant information from the included studies. Study selection will initially involve the screening of titles and abstracts, followed by full-text assessment according to the established eligibility criteria. Any discrepancies arising during the selection process will be resolved through consultation with a second reviewer. The identified records will be managed using spreadsheet software (Excel), which will facilitate study organization, duplicate removal, and data extraction. Data extraction will be independently supported by a second reviewer using a data collection form currently under development, which will include information regarding study characteristics, population, intervention, comparators, and outcomes. For data analysis, appropriate statistical software, such as RevMan, will be used according to the type of analysis required.

Quality assessment / Risk of bias analysis The methodological quality of the included studies will be assessed independently by two reviewers using validated tools according to the study design. For randomized controlled trials, the RoB 2 (Risk of Bias 2) tool will be employed, whereas ROBINS-I will be used for non-randomized studies. In the case of observational studies, appropriate instruments such as the Newcastle–Ottawa Scale will be considered. Domains including selection bias, performance bias, detection bias, attrition bias, and reporting bias will be evaluated in order to identify potential sources of bias. Any discrepancies between reviewers will be resolved through consensus or, when necessary, through consultation with a third reviewer.

Strategy of data synthesis Data synthesis will be conducted using both qualitative and quantitative approaches. Initially, a narrative synthesis of the characteristics and findings of the included studies will be performed. If sufficient clinical and methodological homogeneity is identified, a meta-analysis will subsequently be conducted. For continuous outcomes, such as sleep quality, mean differences and confidence intervals will be calculated. For dichotomous outcomes, relative risks or odds ratios will be used, and analyses will be performed using the inverse variance method.

In the presence of heterogeneity among studies, inferential statistical analyses, primarily chi-square tests, may be applied. All analyses will be conducted using specialized software, such as RevMan version 5.4.1. If a meta-analysis is not feasible, the findings will be presented in a descriptive and structured manner.

Subgroup analysis Pre-specified subgroup analyses will be conducted to explore potential sources of heterogeneity in the effects of melatonin on sleep outcomes in older adults. The factors to be considered may include the type of melatonin formulation (immediate-release vs. prolonged-release), administered dosage, and treatment duration (short-term vs. long-term), as these variables may influence the intervention outcomes. However, if insufficient information is available or substantial heterogeneity is identified, subgroup analyses will not be performed.

Sensitivity analysis Sensitivity analyses will be conducted to evaluate the robustness and stability of the results in relation to methodological decisions. These analyses will include the exclusion of studies with a high risk of bias, studies with small sample sizes, and studies with incomplete data. Additionally, the use of different statistical models will be explored when considered appropriate. These procedures are intended to strengthen the validity of the findings. In the event that substantial variations are identified, they will be critically described and interpreted.

Language restriction No language restrictions will be applied; studies in any language with accessible full texts will be included to minimize bias and ensure comprehensive evidence collection.

Country(ies) involved The present systematic review will be conducted in Mexico.

Keywords Older adults, melatonin, sleep, insomnia; Randomized controlled trials; Systematic review; Meta-analysis.

Dissemination plans The findings of this systematic review will be disseminated through publication in a high-impact, peer-reviewed scientific journal and through presentations at national and international academic conferences. Furthermore, the results may be shared with healthcare professionals and the academic community in order to strengthen evidence-based practice in the management of sleep disorders among older adults.

Contributions of each author

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