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REVIEW PROTOCOL

Effectiveness of non-pharmacological oncological interventions in improving sleep quality: systematic review protocol

Eficácia das intervenções não-farmacológicas oncológicas na melhoria da qualidade do sono: protocolo de revisão sistemática

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ABSTRACT

Objective: To identify and compare the effectiveness of nonpharmacologic interventions for managing sleep disturbances in cancer patients across the continuum of care. **Methods:** This is a systematic review protocol conducted according to Joanna Briggs Institute (JBI) guidelines. Two independent review authors performed study selection, critical appraisal, and data extraction, with disagreements resolved by consensus or third reviewer decision. The Grading of Recommendations, Assessment, Development, and Evaluations will be used to assess the certainty of evidence, and meta-analysis calculations will be performed using the JBI SUMARI. Dichotomous outcomes will be analyzed by odds ratio or risk ratio, continuous outcomes by mean difference with corresponding 95% confidence intervals, statistical significance ($p < 0.05$), and heterogeneity by Cochran Q-test and I^2. Where statistical pooling is not feasible, a narrative synthesis will be presented.

Descriptors: Neoplasms; Sleep Wake Disorders; Healthcare Models.

RESUMO

Objetivo: Identificar e comparar a eficácia das intervenções não farmacológicas para o manejo de distúrbios de sono em pacientes com câncer em toda linha de cuidado. **Método:** Esta é uma revisão sistemática conduzida de acordo com as diretrizes do *Joanna Briggs Institute* (JBI). A seleção dos estudos, a avaliação crítica e extração dos dados serão realizadas por dois revisores independentes, e em caso de discordância será resolvido por consenso ou por decisão de um terceiro revisor. Para classificar a certeza de evidência será utilizada a *Grading of Recommendations, Assessment, Development, and Evaluations* e com o cálculo de meta-análise pelo JBI SUMARI. Resultados dicotômicos serão analisados pelo odds ratio ou razão de risco, desfechos contínuos pelas diferenças de médias com seus respectivos intervalos de confiança (95%), significância estatística ($p < 0,05$) e a heterogeneidade pelo teste Qui-quadrado Cochran Q-test e I^2. Na impossibilidade de formular um agrupamento estatístico, a síntese será apresentada de forma narrativa.

Descritores: Neoplasias; Transtornos do Sono-Vigília; Modelos de Assistência à Saúde.

INTRODUCTION

Cancer is considered one of the major public health challenges worldwide and is the leading cause of death in people under the age of 70 in most countries[1]. According to the Global Cancer Observatory (GLOBOCAN)[2], the worldwide distribution of occurrences and deaths was approximately 19 million new cancer cases and 10 million deaths in 2020[2].

Current evidence suggests that pain, fatigue, and sleep disturbances often occur together and are identified as symptom clusters in cancer patients[3]. In a recent study, over 60% of breast cancer patients reported fatigue and sleep disturbance[4-5] and 32.2% reported depression[6]. In Chinese women with breast cancer undergoing chemotherapy, more

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than 84% experienced all three symptoms simultaneously, and this cluster was associated with a decline in quality of life (QoL)[7]. In this context, recent reviews suggest that fatigue, sleep disturbance, and depression interact to form a symptom cluster[8].

The importance of managing changes in sleep patterns has been recognized, particularly because of their impact. It is crucial to define a therapeutic plan as a fundamental part of effective and humane care. Therefore, identifying the best interventions for managing sleep disorders in cancer patients is essential for successful treatment and comprehensive care.

The preliminary search was conducted using PubMed, EPISTEMONIKOS, International Prospective Register of Systematic Reviews (PROSPERO), Cumulated Index in Nursing and Allied Health Literature (CINAHL), Cochrane Database of Systematic Reviews, and JBI Database of Systematic Review and Synthesis of Evidence. No systematic review was found on the effectiveness of nonpharmacological interventions in treating sleep disorders associated with fatigue, pain, and depressive symptoms in oncology patients. The present systematic review aims to identify and compare the effectiveness of nonpharmacological interventions for managing sleep disorders in cancer patients across the continuum of care, from diagnosis to rehabilitation.

Review question

How do nonpharmacological interventions compare with usual care and other therapies in improving sleep quality in cancer patients?

Inclusion criteria

Participants

Studies will include adult individuals diagnosed with cancer, regardless of gender, who are undergoing oncologic treatment or in a clinical surveillance phase, whether in hospital, home care, or outpatient settings. This review will have no exceptions for healthcare configurations or geographic areas.

Intervention

Studies that aim to evaluate the effects of nonpharmacological interventions to treat sleep disorders in people with cancer who are undergoing any type of oncological treatment (chemotherapy, radiotherapy, immunotherapy, or hormone therapy) or who are in the clinical surveillance phase will be considered.

Interventions may be delivered individually or in a group setting and may include a single or a series of sessions. Inclusion criteria will focus on studies that assess sleep quality and characteristics using validated instruments, with outcomes related to sleep disturbances or symptom clusters, including fatigue, pain, and depressive symptoms.

Comparator

Studies that have compared nonpharmacological interventions such as cognitive-behavioral therapy, acupuncture, mindfulness, yoga, music therapy, Tai Chi Chuan, aerobic exercises, therapeutic massage, and relaxation therapy[9-12] with other therapies described in the literature or with standard treatment will be included in the review.

Results

Studies with a primary outcome of improved sleep quality measured by validated instruments will be included. Subjective assessment of sleep quality will be measured using the Pittsburgh Sleep Quality Index, the Epworth Sleepiness Scale, the Mini Sleep Questionnaire, the Sleep Disorders Questionnaire, and the Basic Nordic Sleep Questionnaire.

The review authors determined the primary and secondary outcomes based on their knowledge of nursing and oncology after a preliminary search of EPISTEMONIKOS, PROSPERO, the Cochrane Database of Systematic Reviews, and the JBI Database of Systematic Review and Synthesis of Evidence. Consequently, the Core Outcome Measures in Effectiveness Trials (COMET) were not used.

Results will be obtained from the measurement of standardized subjective sleep assessment instruments. Primary outcomes will be addressed in the review report and presented in the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Summary of Findings table.

Study types

Studies characterized as experimental and quasi-experimental will be included, including both randomized and non-randomized clinical trials available in selected databases and grey literature. These studies should include secondary outcomes, such as fatigue, pain, and depressive symptoms related to sleep quality. Studies testing the efficacy of pharmacological interventions on sleep quality related to QoL will be excluded. There will be no time or language restrictions.

METHODS

This review will be conducted following the JBI methodology for systematic reviews of effectiveness[13], and the reporting of results will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[14] guidelines. Systematic reviews are considered studies of high methodological rigor, employing systematic methods and conducted by two independent review authors to ensure methodological quality. According to JBI recommendations, a protocol should be done before the review, outlining aims, project characteristics, and planned analyses for the review. The prospective registration of the systematic review protocol in recognized databases is crucial, preventing duplication and ensuring the identification of potential biases in the review process. Additionally, the publication of the review protocol in a scientific journal is recommended[15]. The present protocol has been registered on PROSPERO (CRD42022357545) to ensure data reliability and methodological transparency. The review protocol will be submitted to a Brazilian journal for publication.

Search strategy

A proposed search strategy aimed to identify both published and unpublished studies. A primary search limited to the PubMed and CINAHL databases was conducted to identify publications relevant to the topic of the present systematic review protocol.

Additional words, phrases, and indexing terms relevant to the review question were identified in both the titles and abstracts of the studies found in the initial search and used to develop a final search strategy for MEDLINE (Figure 1) and CINAHL (Figure 2). The full search strategy, including all databases searched, will be reported in the final report of this review.

First, the primary search strategy was conducted in PubMed to exemplify the possible search strategies for this review, without limiting the date and language of the database search.

Figure 1 - Identification of terms and records from the PubMed database. São Paulo, SP, Brazil, 2022

Search	Search terms	Records retrieved
#8	#1, #2, #3, #4, #5 E #6: Combination of the search strings 1,2,3,4,5 e 6 linked by the Boolean operator "AND".	143
#7	#5 E #6: Combination of the search strings 1 e 2 linked by the Boolean operator "AND".	254,016
#6	"Complementary Therapies"[MeSH Terms] OR "Complementary Medicine"[All Fields] OR "Alternative Medicine"[All Fields] OR "Alternative Therapies"[All Fields].	253,328
#5	("non-pharmacological treatment"[All Fields] OR "non-pharmacological intervention"[All Fields]) AND ((humans[Filter]) AND (alladult[Filter])).	820
#4	#1 E #2: Combination of the search strings 1 e 2 linked by the Boolean operator "AND" e Filters: Adult: 19+ Years.	2,996
#3	#1 E #2: Combination of the search strings 1 e 2 linked by the Boolean operator "AND".	5,411
#2	"Neoplasms"[Mesh] OR Tumor OR Neoplasm OR Tumors OR Neoplasia* OR Cancer* OR "Malignant Neoplasm" OR Malignanc* OR "Malignant Neoplasms".	5,362,856
#1	"Sleep Wake Disorders"[Mesh] OR "Sleep Wake Disorder" OR "Sleep Disorders" OR "Sleep Disorder" OR "Sleep-Related Neurogenic Tachypnea" OR "Sleep Related Neurogenic Tachypnea" OR "Short Sleeper Syndrome" OR "Short Sleep Phenotype".	114,833

The primary search strategy was then performed on CINAHL, with no restrictions on database search date or language.

Figure 2 - Identification of terms and records from the CINAHL database. São Paulo, SP, Brazil, 2022

Search	Search terms	Records retrieved
#5	#1, #2 E #3: Combination of the search strings 1, 2 e 3 linked by the Boolean operators "AND" e Filters: Adult.	197
#4	#1, #2 E #3: Combination of the search strings 1, 2 e 3 linked by the Boolean operators "AND".	434
#3	S (MH "Neoplasms") OR TI ((Tumor OR Neoplasm OR Tumors OR Neoplasia OR Neoplasias OR Cancer OR Cancers OR "Malignant Neoplasm" OR Malignancy OR Malignancies OR "Malignant Neoplasms")) OR AB ((Tumor OR Neoplasm OR Tumors OR Neoplasia OR Neoplasias OR Cancer OR Cancers OR "Malignant Neoplasm" OR Malignancy OR Malignancies OR "Malignant Neoplasms".	796,718
#2	(MH "Alternative Therapies") OR TI (("alternative medicine" OR "complementary medicine" OR "holistic medicine" OR "complementary therapy" OR "complementary practices" OR "holictic practice" OR "holistic therapy" OR therapy OR treatment OR "non pharmacological treatment" OR "non pharmacological therapy")) OR AB (("alternative medicine" OR "complementary medicine" OR "holistic medicine" OR "complementary therapy" OR "complementary practices" OR "holistic practice" OR "holistic therapy" OR "non-pharmacological treatment" OR "non-pharmacological intervention" OR "non-pharmacological therapy" OR "non-pharmacological therapies")).	517,656
#1	(MH "Sleep Disorders") OR TI (("sleep disorders" OR "sleep disturbance" OR "sleep problems" OR insomnia)) OR AB (("sleep disorders" OR "sleep disturbance" OR "sleep problems" OR insomnia)).	29,043

Search strategies were developed in two stages with the assistance of a librarian experienced in evidence synthesis. The first stage, conducted on MEDLINE and CINAHL, involved the analysis of words in the title and abstract to construct a search strategy using terms to identify descriptors, keywords, and relevant studies for the review. This initial strategy served as the basis for adapting the search equation to other databases, portals, and academic directories. The second step involved a search based on the results found, using all identified keywords and index terms adapted to the syntax and subject headings of each database.

The search strategy will be applied to all included databases and grey literature, with modifications as necessary. The databases to be searched for published studies include MEDLINE (PubMed), CINAHL (EBSCO), Embase (Elsevier), Scopus (Elsevier), Web of Science Core Collection, and Cochrane Central Register of Controlled Trials (CENTRAL). For unpublished studies, the CAPES Theses and Dissertations Database and OpenGrey (GreyNet) will be searched.

Study selection

Upon completion of the search, all identified citations will be collected and imported into the Zotero reference manager (v. 5.0.95.1, George Mason University, VA, USA), and duplicates will be removed. Following this initial screening, two independent reviewers will screen titles and abstracts, apply eligibility criteria, and list potentially relevant sources for full-text reading. Relevant studies will be retrieved in full, and their citation details will be imported into the JBI System for the Unified Management, Assessment, and Review of Information (SUMARI; JBI, Adelaide, Australia)[16], a software tool to support the review process. After selection, the full text of the citations is thoroughly analyzed by two independent reviewers based on predefined inclusion criteria. Reasons for study exclusion are recorded and described in the systematic review. In case of disagreement between the two reviewers during the study selection process, consensus will be sought, or a third reviewer will make the final decision. The search results will be fully reported in the final systematic review and presented in a PRISMA flowchart[14].

Assessment of methodological quality

Eligible studies will be critically appraised for methodological quality by two independent review authors before inclusion in the review, following the JBI critical appraisal checklist for randomized experimental and quasi-experimental studies[13-15]. A consensus will be rea-

ched, or a third reviewer will decide, in case of disagreement.
The review authors determined the criteria, decision rules, scoring system, and cutoff points for study inclusion. According to the JBI guidelines, results for each item of the assessment instruments for quasi-experimental studies and randomized controlled trials with a compliance rate of less than 80% are considered to be of low methodological quality.
The results of the critical appraisal will be presented in a narrative format and tables. Authors may be contacted for additional information or clarification where the content is unclear.

Data extraction
Data extraction will be performed by two independent review authors, and the studies used will be those included in the review, using the standardized JBI data extraction tool Characteristics of Included Studies - Randomized Controlled[13-15]. This process will be carried out in two stages. In the first stage, the two reviewers will list content that meets the eligibility criteria based on the titles and abstracts of the studies. In the second stage, the two reviewers will read the full text using the same eligibility criteria. The final selection of studies for inclusion will be based on the information obtained from the comprehensive reading of the publications.
The extracted data will include specific details about the publication and study, country, settings/context, participant characteristics (including sample size, age and gender, type of disorder), study groups (treatment or follow-up phase, tumor type, intervention descriptions), outcomes measured, and key findings. Disagreements between reviewers are resolved by consensus or with the opinion of a third reviewer. Study authors are contacted to request missing or additional information.

Data synthesis
After data extraction, where possible, studies will be pooled into a meta-analysis using JBI SUMARI[16]. Clinical diversity between studies will be examined by considering key study characteristics, interventions, populations, and outcomes. Heterogeneity will be statistically assessed using the Cochran Q-test and I^2. Effect sizes will be expressed as odds ratios (OR) or risk ratios (RR) for dichotomous outcomes and as mean differences (MD) or standardized mean differences (SMD) for continuous outcomes. Ninety-five percent confidence intervals are calculated, and statistical significance is considered when $p<0.05$ for outcome analysis. If statistical meta-analysis is not feasible, the synthesis will be presented narratively, including figures and tables as appropriate to facilitate data presentation. In the narrative synthesis, information will be grouped into categories to encourage discussion of the results and their relationship to the research question of this review.

Assessing the certainty of evidence
This review will use GRADE[13-16-17] to assess the certainty of the evidence, including reporting a summary table of the evidence.

*Paper extracted from the Master's dissertation "Effectiveness of non-pharmacological interventions for sleep disorders in cancer patients: systematic review", presented to Escola de Enfermagem da Universidade de São Paulo, São Paulo, SP, Brasil.

CONFLICT OF INTERESTS
The authors have declared that there is no conflict of interests.

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