REVISTA ENFERMAGEM ATUAL IN DERME

THERAPEUTIC INTERVENTIONS FOR FATIGUE AND MEMORY LOSS POST-COVID-19: SCOPE REVIEW PROTOCOL

INTERVENCIONES TERAPÉUTICAS PARA LA FATIGA Y PÉRDIDA DE MEMORIA POST-COVID-19: PROTOCOLO DE REVISIÓN DE ALCANCE

INTERVENÇÕES TERAPÊUTICAS PARA A FADIGA E PERDA DE MEMÓRIA PÓS-COVID-19: PROTOCOLO DE REVISÃO DE ESCOPO

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ABSTRACT
Introduction: Post-COVID-19, characterized by symptoms that persist for at least two months after initial infection and cannot be justified by an alternative diagnosis, presents a wide range of clinical manifestations. Among them, fatigue and memory loss emerge as remarkable and worrying signs. Studies highlight the need for continuity of care and multidisciplinary rehabilitation. **Objective:** To identify and analyze scientific evidence on therapeutic interventions for fatigue and memory loss in the post-COVID-19 condition. **Method:** This is a scope review protocol that will be developed following the steps recommended by the guidelines of the Jonna Briggs Institute (JBI). The following sources of information will be used: National Library of Medicine (PubMed), EBSCO, Scopus (Elsevier), Web of Science, Mednar, Virtual Health Library (VHL), Epistemonikos and CAPES Thesis and Dissertations Portal, using descriptors in health. Studies found in databases will be exported to the Rayyan reference management system. The search, identification and evaluation of the selected studies will be carried out by two independent reviewers, and in case of divergence, a third reviewer will be consulted, according to the assumptions of JBI. Original, complete, public domain articles will be included that answer the research question without time restriction and in all languages. Duplicate and revision articles will be deleted. The results will be presented according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). The protocol was registered in the Open Science Framework (OSF).
Keywords: Post-COVID-19 Condition; Fatigue; Memory Loss; Interventions; Methodology as Subject.

RESUMEN
Introducción: La condición post-COVID-19, caracterizada por síntomas que persisten durante al menos dos meses después de la infección inicial y no pueden ser justificados por un diagnóstico alternativo, presenta una amplia gama de manifestaciones clínicas. Entre ellas, la fatiga y la pérdida de memoria emergen como señales notables y preocupantes. Los estudios destacan la necesidad de continuidad en el cuidado y rehabilitación multidisciplinaria. **Objetivo:** identificar y analizar evidencia científica sobre intervenciones terapéuticas para la fatiga y pérdida de memoria en la condición post-COVID-19. **Método:** Se trata de un protocolo de revisión de alcance que será desarrollado siguiendo los pasos preconizados por los guións del Jonna Briggs Institute (JBI). Se utilizarán las siguientes fuentes de información: *National Library of Medicine* (PubMed), EBSCO, Scopus (Elsevier), *Web of Science*, Mednar, Biblioteca Virtual de Salud (BVS), Epistemonikos y Portal de Tesis y Disertaciones CAPES, utilizando los descriptores en salud. Los estudios encontrados en las bases de datos serán exportados al sistema de gestión de referencias Rayyan. La búsqueda, identificación y evaluación de los estudios seleccionados serán realizadas por dos revisores independientes, y en caso de discrepancia, se consultará a un tercer revisor, de acuerdo con los supuestos del JBI. Se incluirán artículos originales, completos, de dominio público, que respondan a la pregunta orientadora de la investigación, sin restricción de tiempo y en todos los idiomas. Los artículos duplicados y revisados serán eliminados. Los resultados se presentarán de acuerdo con las directrices del *Preferred Reporting Items for Systematic Reviews and Meta-Analyses extensión for Scoping Reviews* (PRISMA-ScR). El protocolo fue registrado en el Marco de Ciencia Abierta (OSF).
Palabras clave: Condición Post-COVID-19; Fatiga; Pérdida de Memoria; Intervenciones; Metodología como Tema.

RESUMO
Introdução: A Condição Pós-COVID-19, caracterizada por sintomas que persistem por pelo menos dois meses após a infecção inicial e não podem ser justificados por um diagnóstico alternativo, apresenta uma ampla gama de manifestações clínicas. Entre elas, a fadiga e a perda de memória emergem como sinais notáveis e preocupantes. Estudos destacam a necessidade de continuidade dos cuidados e reabilitação multidisciplinar. **Objetivo:** Identificar e analisar evidências científicas sobre intervenções terapêuticas para fadiga e perda de memória na condição pós-COVID-19. **Método:** Trata-se de um protocolo de revisão de escopo que será desenvolvido seguindo as etapas preconizadas pelo guidelines do *Jonna Briggs Institute* (JBI). Serão utilizadas as seguintes fontes de informação *National Library of Medicine* (PubMed), EBSCO, *Scopus* (Elsevier), *Web of Science*, Mednar, Biblioteca Virtual de Saúde (BVS), Epistemonikos e Portal de Teses e Dissertações CAPES, utilizando os descritores em saúde. Os estudos encontrados nas bases de dados serão exportados para o sistema de gerenciamento de referências Rayyan. A busca, identificação e avaliação dos estudos selecionados serão realizadas por dois revisores independentes, e, em caso de divergência, um terceiro revisor será consultado, de acordo com os pressupostos do JBI. Serão incluídos artigos originais, completos, de domínio público, que respondam à questão norteadora da pesquisa, sem restrição de tempo e em todos os idiomas. Serão excluídos artigos duplicados e de revisão. Os resultados serão apresentados conforme orientações do *Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews* (PRISMA-ScR). O protocolo foi registrado na *Open Science Framework* (OSF).
Palavras-chave: Condição Pós-COVID-19; Fadiga; Perda de Memória; Intervenções; Metodologia como Assunto.

REVISTA ENFERMAGEM ATUAL IN DERME

INTRODUCTION

The Covid-19 pandemic, declared as such by the World Health Organization (WHO) in March 2020, has unleashed a global health crisis that has affected dozens of countries and infected more than 655 million people so far[1]. However, even after initial recovery from SARS-CoV-2 infection, many individuals face a persistent and complex challenge known as the Post-COVID-19 Condition[2].

This condition, characterized by symptoms that persist for at least two months after the initial infection and cannot be explained by an alternative diagnosis, presents a wide range of clinical manifestations. Among them, fatigue and memory loss appear as remarkable and worrying signs[3]. These symptoms not only significantly affect the quality of life and daily functionality of those affected, but they can also evolve into serious and potentially fatal events, even months or years after infection[1].

Persistent fatigue after initial recovery from COVID-19 goes beyond a simple feeling of tiredness, often becoming disabling. Regarding memory loss, the affected individuals face concentration difficulties and memory lapses, which impair their professional, daily life and quality of life in general[4].

A survey of 3,762 people with post-COVID-19 condition identified that three out of four still had fatigue, exacerbation of post-effort symptoms and cognitive dysfunction after six months, and half could not fully return to work[3]. A systematic review that analyzed 886,388 patients with COVID-19 estimated a combined prevalence of post-COVID-19 condition at 43% (95% confidence interval: 35-63)[5]. In April 2022, the authors estimated that around 100 million people had or are still living with post-COVID-19 conditions worldwide. These disabling symptoms affect the quality of life, return to work or school, finances and ability to take care of themselves and their families[3,6-7].

The scale of this international public health problem can overwhelm the capacity of health systems, especially in low- and middle-income countries. The multisystemic characteristics of the post-COVID-19 condition and its high prevalence cause problems for the management of health systems, with the need to identify appropriate care models. Considering that innovative clinics specialized in post-COVID-19 conditions have highlighted the need for continuity of care and multidisciplinary rehabilitation[8-11], and given the severity and persistence of these symptoms, the following question arises: what are the specific therapeutic interventions performed by a multidisciplinary team to treat fatigue and memory loss associated with the Post-Covid-19 Condition? Therefore, the scope review guided by this protocol will aim to: identify and analyze scientific evidence on interventions for fatigue and memory loss in post-COVID-19 syndrome.

METHOD

The review outlined in this protocol will be conducted based on the methodological framework established by the Jonna Briggs

REVISTA ENFERMAGEM ATUAL IN DERME

Institute (JBI) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines[12-14]. The protocol was registered in the Open Science Framework (OSF registries - https://osf.io/jzrym/?view_only=5fb4f91ffc734fa18fe984bdad307274) and is described according to the items of the Template for Scoping Review Protocols[14].

The guiding question of the review was elaborated based on the PCC strategy, which considers the population, the concept and the context of the object to be studied. The acronym PCC is composed of P = Population (general population), C = Concept (multiprofessional therapeutic interventions used for fatigue and memory loss) and C = Context (Post-COVID-19 Condition). Thus, the following question was asked: What are the specific therapeutic interventions performed by a multidisciplinary team to treat fatigue and memory loss associated with the Post-Covid-19 condition?

Original studies will be included, available in full that answer the guiding question of the research, without time restriction and in all languages. Duplicate and revision articles will be deleted.

Initially, a search will be conducted in the Medline databases via PubMed and Web of Science, to evaluate the words present in titles, abstracts and indexing terms of articles that align with the objectives of the review. From this analysis, the controlled descriptors and associated terms were chosen, compatible with the Health Sciences Descriptors (DeCS) and the Medical Subject Headings (MeSH), to compose the search strategy to be used in the databases considered in this investigation.

The search strategies were defined based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) tool(13), and a test search was performed and conducted according to DeCS and MeSH in the following databases: National Library of Medicine (PubMed), EBSCO, Scopus (Elsevier), Web of Science, Mednar, Biblioteca Virtual de Saúde (BVS) and Epistemonikos (Chart 1). The descriptors will be combined with the Boolean operators “AND” and “OR”.

Chart 1 – Search Strategy Test: National Library of Medicine (PubMed), EBSCO, Scopus (Elsevier), Web of Science, Mednar, Virtual Health Library (VHL) and Epistemonikos. João Pessoa, Paraíba, Brazil, 2024.

Search	Query	Results
#1	(("long covid") OR ("chronic covid-19")) OR ("post covid")) OR ("long haul covid OR post covid-19")) AND (memory)) OR ("memory disorders OR memory intervention")) AND ("rehabilitation")) OR (therapy)) OR (treatment)) OR (intervention) [All Fields] ((“long covid”) OR (“chronic covid-19”) OR (“post covid”) OR (“long haul covid”) OR (“post covid-19”)) AND (“fatigue”) AND ((“rehabilitation”) OR (“therapy”) OR (“treatment”) OR (“intervention”) [All Fields]	437

REVISTA ENFERMAGEM ATUAL IN DERME

#2	(("post covid" OR ("long covid")) AND ("memory") AND ("rehabilitation") ("post covid") AND ("fatigue") AND ("rehabilitation")	360
#3	("long covid" OR "post covid") AND ("memory" OR "memory disorders") AND ("rehabilitation" OR "intervention") ("long covid" OR "post covid") AND ("fatigue") AND ("rehabilitation" OR "intervention")	734
#4	("long covid" OR "post covid") AND ("memory disorders") AND ("intervention") ("long covid") AND ("fatigue") AND ("intervention")	2021
#5	("long covid") OR ("post covid") AND ("memory") OR ("memory disorders") AND ("Rehabilitation") ("long covid" OR "post covid") AND ("fatigue") AND ("Rehabilitation")	370
#6	("long covid") OR ("post covid") AND ("fatigue") AND ("Rehabilitation" OR "intervention") ("long covid" OR "post covid") AND ("memory" OR "memory disorders") AND ("Rehabilitation" OR "intervention")	595
#7	(("long covid" OR "chronic covid-19" OR "post covid" OR "long haul covid OR post covid-19")) AND (("memory" OR "memory disorders OR memory intervention")) AND (("rehabilitation" OR "therapy" OR "treatment" OR "intervention")) (("long covid" OR "chronic covid-19" OR "post covid" OR long haul covid OR post covid-19")) AND (("fatigue")) AND (("rehabilitation" OR "therapy" OR "treatment" OR "intervention"))	1097

The studies considered as grey literature will be consulted on the CAPES Thesis and Dissertation Portal. References from all included sources of evidence that meet the inclusion criteria will be reviewed to identify additional studies.

The studies found in the databases will be included in the reference manager Rayyan (Qatar Computing Research Institute, Doha, Qatar)[15]. After the export of the files, two independent authors will eliminate duplicate articles and then review the titles and abstracts to decide on inclusion or exclusion, adopting a 75% agreement among reviewers to proceed to the next step. It should be noted that the process will be conducted blindly, as provided by the tool itself, to avoid decision biases. The pre-selected articles will be fully analyzed by the same two authors, and in case of disagreement, a third author will be consulted. This process will be described through the PRISMA-ScR flowchart[13].

After the selection of articles, the extraction of relevant information from each study will be started, based on the JBI instrument, including: name of authors, year of publication, country of origin, objectives of the studies, population and sample size, methods and main results. For this, a data extraction instrument created by the authors will be used. The theoretical discussion will be conducted

REVISTA ENFERMAGEM ATUAL IN DERME

with the help of the literature review and the theoretical framework selected by the research.

The extracted data will be analyzed by means of descriptive statistics and presented in the form of narrative summary, tables and/or tables, describing how the data relate to the objective and the issue of this review.

It is expected that the data from the scope review, conducted according to this protocol, will identify the multiprofessional therapeutic interventions employed in the treatment of fatigue and post-COVID-19 memory loss. These data should contribute to identify needs for future research that will analyze which therapeutic interventions are effective in treating post-COVID-19 fatigue and memory loss. This is particularly important given the global impact of this public health problem, especially in low- and middle-income countries. The multisystemic characteristics of the post-COVID-19 condition and its high prevalence generate challenges for the management of health systems, requiring the identification of appropriate care models. This research is innovative and relevant in the current context of health care, contributing to reflections on the integration of these therapies in the national scenario and for qualification of clinical practice.

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Authorship criteria (authors’ contributions)

Rebeca Bezerra Pinto Bandeira 1. contributed substantially to the conception and/or planning of the study; 2. in obtaining, analyzing and/or interpreting the data; 3. as well as in the writing and/or critical review and final approval of the published version.

Viviane Cordeiro de Queiroz 1. contributed substantially to the conception and/or planning of the study; 2. in obtaining, analyzing and/or interpreting the data; 3. as well as in the writing and/or critical review and final approval of the published version.

Maria Hellena Ferreira Brasil 1. contributed substantially to the conception and/or planning of the study; 2. in obtaining, analyzing and/or interpreting the data; 3. as well as in the writing and/or critical review and final approval of the published version.

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Declaration of conflict of interest

“Nothing to declare”

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