



The Relationship between Depression and Chronic Pain: A Literature Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: <https://doi.org/10.9734/jammr/2024/v36i85548>

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Cite as: Reis, Josué Tavares, Iêgo Gutemberg Gonçalves Silva, Ana Caroline Ribeiro Lima Borges, Ana Paula Tavares Dos Reis, Wathyson Alex De Mendonça Santos, Kamilla Araújo Martins Moraes Benevides, Sara Alves Nunes De Abreu, Tayná Moreno, Julia Queiroz Almeida, Claudia Denise Mendanha Mangueira, Fernando Holanda Vasconcelos, Wagner Dos Santos Mariano, and Ana Cristina Mendanha Sampaio. 2024. "The Relationship Between Depression and Chronic Pain: A Literature Review". *Journal of Advances in Medicine and Medical Research* 36 (8):301-12. <https://doi.org/10.9734/jammr/2024/v36i85548>.

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/120720>

Review Article

Received: 10/06/2024

Accepted: 13/08/2024

Published: 17/08/2024

ABSTRACT

Considering the relationship between depression and chronic pain as a crucial aspect of physical and mental health, this study aims to conduct a comprehensive literature review to analyze this association. Depression, a complex psychiatric disorder, is characterized by symptoms such as depressed mood, fatigue, sleep disturbances, and loss of interest in daily activities. On the other hand, chronic pain is a debilitating condition that persists for at least three months, compromising the processing of painful stimuli in the central nervous system. Scientific studies have shown a high prevalence of depressive symptoms in patients with chronic pain, as well as the presence of chronic pain in individuals with depression, suggesting a possible cause-and-effect relationship. Biopsychosocial mechanisms, including chronic stress and neuroendocrine alterations, are involved in this complex connection. This comorbidity negatively impacts patients' quality of life, requiring comprehensive therapeutic approaches that involve pharmacological treatments, psychotherapeutic interventions, physical therapy, among others. Understanding the interaction between mood disorders and chronic pain is essential to improve clinical approaches and provide greater well-being to affected individuals.

Keywords: Mood disorder; health; comorbidity; relationship.

1. INTRODUCTION

Depression is characterized as a disorder involving symptoms such as depressed mood, excessive fatigue, hypersomnia or insomnia, and reduced sexual interest. It can be associated with various factors; therefore, different therapeutic approaches may be employed depending on its predominant cause. Thus, diagnostic investigation should consider long-term and short-term emotional factors, socio-environmental aspects, medications used, and the patient's physical condition, encompassing the individual holistically to define the cause and consequently choose the best treatment [1].

Similarly, according to the International Association for the Study of Pain (IASP), pain is considered "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage." In this sense, chronic pain (CP) is defined by a prolonged duration, over three months. It is characterized by altering the signalling pathways and processing of painful stimuli in the central nervous system, resulting in the persistence of pain [2]. This condition has

various causes, including degenerative pathologies, chronic metabolic, infectious, and neoplastic diseases, and nerve injuries, among others, with risk factors including advanced age, female gender, a positive family history of CP, and sedentary lifestyle [3]. Considered a frequent cause of seeking medical assistance, CP directly impacts people's quality of life, becoming a challenge for healthcare professionals who, regarding its treatment, should focus on restoring the individual's physical and emotional well-being [4].

Secondary depression, according to the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders - 5th edition), is characterized by the development of depressive symptoms arising from another medical or psychiatric condition, being the differential factor from primary depression, which does not present an identifiable cause beyond the depressive disorder itself. In the latter, the origin of symptoms is essentially linked to the disorder itself, while in secondary depression, depressive symptoms are triggered by an underlying event or medical condition [5]. Thus, a prevalence of

secondary depression is observed in patients with CP, since this association tends to be multifactorial, involving biopsychosocial and behavioural factors [6]. Therefore, it suggests a causal relationship between the two conditions, justifying the investigation of this relationship to understand if it exists and, if so, which is the cause and which is the consequence (STUBBS et al., 2017).

2. JUSTIFICATION

The relationship between depression and chronic pain has received increasing attention in the scientific literature in recent decades. Epidemiological studies estimate that about 50 to 65% of patients with chronic pain also meet the criteria for a diagnosis of depression [7]. Understanding the interaction between these two complex conditions is crucial for improving the clinical management of patients. It is still unclear in the literature whether chronic pain increases the risk of depression, whether depressive symptoms intensify the painful experience, or whether there is a bidirectional relationship between the two conditions [8]. Investigating the underlying mechanisms of this association is essential to guide the most appropriate treatment strategies.

Moreover, the comorbidity between chronic pain and depression is associated with worse health outcomes, including greater impairment of functional capacity, poorer quality of life, and increased risk of suicide [9]. Given the impact of this interaction on patients' lives, it is important to identify integrative therapeutic approaches that simultaneously address both conditions synergistically. There is a need to investigate the biopsychosocial factors involved in this complex relationship between pain and mood [10], aiming to understand these factors to enable targeted interventions that alleviate the underlying mechanisms of chronic pain and emotional suffering [8].

In summary, this research is justified by the gap in understanding the direction of causality and the mechanisms involved in the comorbidity between depression and chronic pain. The study aims to generate an understanding of this topic to improve clinical management and minimize the suffering of patients living with these two conditions. The investigation can support the development of more integrated therapeutic strategies focused on the multifactorial factors associated with this complex comorbidity.

The study's results may also aid in the development of more effective public policies aimed at this patient population and guide healthcare professionals on best practices for the assessment, diagnosis, and treatment of cases where chronic pain and depression coexist. Thus, the research is expected to provide practical contributions to improving care and quality of life for these patients.

3. OBJECTIVES

3.1 General Objective

Analyze the causal relationship between depression and chronic pain through a literature review.

3.2 Specific Objectives

- Identify studies that investigated the association between depression and chronic pain in different populations and clinical contexts;
- Analyze the biopsychosocial mechanisms that can explain the interaction between depression and chronic pain;
- Investigate the impact of the relationship between chronic pain and depression on the development or worsening of both conditions;
- Identify therapeutic interventions and treatment approaches with potential efficacy in the simultaneous management of depression and chronic pain

4. MATERIALS AND METHODS

A literature review was conducted to investigate the relationship between depression and chronic pain. To search for relevant articles on the topic, a search was performed in the major health-related databases, including PubMed, SciELO, and LILACS. The controlled descriptors in English, "depression," "chronic pain," and "comorbidity," were used in the searches, which were combined using the boolean operator AND.

The initial search resulted in 72 articles: 52 in PubMed, 8 in SciELO, and 12 in LILACS, limited to studies in English, Portuguese, and Spanish published between 2013 and 2023, aiming to obtain the most up-to-date scientific evidence on the association between depression and chronic pain. Studies that did not specifically explore this relationship, such as narrative literature reviews, case reports, theses, and dissertations, were

excluded. After applying these eligibility criteria, 37 studies were excluded, leaving 35 articles included in this review.

Two researchers searched the databases, and the study selection was performed independently, subsequently comparing the selected articles. Thirty-five studies were included, with 15 in English, 10 in Portuguese, and 10 in Spanish.

The analysis of the results from the studies included in the review was descriptive, seeking to synthesize the findings and identify convergences and divergences among the results of different studies.

It is expected that this review, by compiling 35 recent studies on the association between depression and chronic pain, can contribute to understanding the causal relationship between these morbidities and aid in understanding the main mechanisms involved in this frequent comorbidity, providing information that may improve the clinical management of patients who simultaneously suffer from depression and chronic pain.

5. RESULTS

This literature review investigated the relationship between chronic pain and depression based on thirty-five scientific studies available in the SCIELO, PubMed, and LILACS databases, covering various populations and contexts. The general analysis of the results indicates that chronic pain and depression are intrinsically associated, with consistent evidence of comorbidity between the two conditions, meaning that depression and chronic pain often occur simultaneously in the same individual.

The general analysis of the results suggests that chronic pain and depression are closely interconnected, with consistent evidence of comorbidity between the two conditions, meaning that depression and chronic pain often occur simultaneously in the same individual [11,6]. This relationship was observed in some studies from different countries, suggesting the universality of this phenomenon.

The analyzed studies demonstrated high prevalence rates of depressive symptoms in patients with chronic pain [12], and a higher prevalence of chronic pain in individuals with depressive disorders [13], highlighting the importance of screening for both conditions.

Evidence suggests a possible bidirectionality in this complex relationship between chronic pain and depressive mood [14], in which each condition can exacerbate the other.

Among the relevant psychological factors, emotional regulation emerged as an important mediator in the relationship between chronic pain and depression, being able to explain a significant part of the association between pain catastrophizing and depressive symptoms. This finding highlights the importance of considering emotional factors in the treatment and management of these complex clinical conditions [15].

These studies also revealed a high prevalence of anxiety symptoms in both patients with chronic pain and those with depression [16,17]. This triple association between pain, anxiety, and depression should be considered when developing therapeutic strategies, requiring integrative approaches focused on the multiple aspects of this complex comorbidity.

Another important finding is that the severity of depressive symptoms often correlates with the intensity of pain perception [18,19]. This highlights the potential of a vicious cycle between chronic pain and mood disorders, in which both conditions feed into each other, resulting in further declines in physical and mental well-being and quality of life [20].

The bi-directionality of the relationship between chronic pain and depression was also evidenced in longitudinal studies [14,21], demonstrating that both conditions can mutually influence each other over time. This finding underscores the importance of a treatment approach that considers both conditions together, seeking to mitigate the negative effects that may arise from this interaction.

Another relevant aspect found in the studies was the significant impact of chronic pain and depression on patients' quality of life. The comorbidity between these conditions resulted in greater functional disability [22] and reduced quality of life [23,20]. This reinforces the need for a multidisciplinary and personalized approach to the treatment of these conditions, aiming to improve the overall well-being of the affected individuals.

Regarding the risk of suicide, the studies indicated that chronic pain can significantly increase the likelihood of suicidal ideation [24],

emphasizing the importance of identifying and adequately treating this comorbidity to prevent more severe consequences.

The results of this review also suggest that the association between chronic pain and depression is influenced by biopsychosocial factors, which represent an area of great interest for future research. Aspects such as the epidemiological profile, the impact of musculoskeletal diseases, and the influence of psychosocial conditions on pain and depression deserve greater attention and detailed investigation.

Therapeutic interventions were also widely investigated in the reviewed studies. It was observed that both pharmacological and non-pharmacological approaches have shown efficacy in relieving chronic pain and treating depressive symptoms. Antidepressants were associated with substantial reductions in chronic pain intensity [25], while non-pharmacological therapies, such as cognitive-behavioural therapy [26,27] and physical activity [28], proved promising in improving the emotional well-being of patients.

Medical practice plays a central role in the diagnosis and treatment of patients with the complex interaction between chronic pain and depression. The professional must be attentive to screening for depressive symptoms in individuals with persistent pain complaints, as well as investigating the presence of chronic pain

conditions in patients with mood disorders [6]. Additionally, medication management with analgesic and antidepressant agents should be considered as part of the multimodal approach. However, unimodal approaches focused exclusively on biological aspects have proven insufficient [10], requiring an integrative perspective.

Given the multifactorial comorbidity, encompassing biopsychosocial aspects, the coordinated work of a multidisciplinary team is essential for achieving better outcomes [29]. This team should ideally include doctors, nurses, psychologists, social workers, physiotherapists, and other professionals, working interactively and integratively to address the various demands of patients [27]. Unified approaches considering behavioral, emotional, cognitive, and environmental influences, in addition to physical and biological aspects, offer greater therapeutic effectiveness.

Therefore, it is crucial that doctors and multidisciplinary teams deeply understand the complex interrelation between chronic pain and depression, seeking to restore the health and quality of life of these patients through preventive strategies, early diagnosis, appropriate treatment, and educational actions that reduce the stigma associated with these comorbidities, providing better access to specialized care and improving the mental health of the affected population [29,27].

Table 1. Summary of studies on depression and chronic pain

Procedure	Title do Article	Authors	Newspaper	Considerations
LILACS	He paper of emotional regulation in the relationship between depression and he chronic pain	Cariño-Rodríguez et al. [15]	Anxiety and stress	Emotional regulation explained 14.8% of the relationship between catastrophizing and pain and depression.
SciELO	Chronic pain in the elderly and depressive symptoms	Cavalcante et al. [12]	Physiotherapy in motion	48.3% of elderly people with pain chronic symptoms presented depressive.
PubMed	Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews	Geneen et al. [28]	Cochrane Database of Systematic Reviews	Activity physics reduced by 8.3% the pain intensity chronic.
PubMed	Anxiety sensitivity and anticipated pain as predictors of depressive symptoms in chronic pain	Choi et al. [16]	Journal of Psychosomatic Research	Anxiety sensitivity explained 10.7% of depressive symptoms.

Procedure	Title do Article	Authors	Newspaper	Considerations
	patients			
SciELO	Effect of transcranial magnetic stimulation on treatment of depression and chronic pain	Costa et al. [30]	Pain Magazine	Magnetic stimulation reduced the intensity of chronic pain by 62%.
SciELO	Epidemiological profile of the comorbidity of depression and chronic pain	Cunha et al. [31]	Brazilian Journal of Psychiatry	65.6% of patients with chronic pain presented symptoms depressive.
LILACS	Chronic pain and depression: Evidence of association in Colombia	Garcia et al. [32]	Bulletin of the Latin American Federation of Therapy Family	56% of studies showed a high prevalence of comorbidity.
SciELO	Impact of depression on quality of life of patients with chronic pain	Cunha et al. [31]	Pain Magazine	Depression reduces the quality of life of patients with chronic pain.
SciELO	Relationship between suicidal intent and chronic pain	Furtado et al. [24]	Brazilian Journal of Psychiatry	Chronic pain increases the risk of suicide.
LILACS	Cognitive behavioral therapy efficacy in treating chronic pain and depression	Gonçalves et al. [26]	Thinking Psychology	CBT reduced symptoms of depression and pain chronic.
LILACS	Role of anxiety in the relationship between chronic pain and depression	Henriquez [17]	Medwave	Anxiety explained 17.4% and association between chronic pain and depression.
PubMed	Association between depression and chronic musculoskeletal pain: Data from the Pain and Depression (PaDe) study	Kato et al. [33]	International Journal of Environmental Research and Public Health	62% of patients with chronic pain presented depressive symptoms.
PubMed	Prevalence of depression in patients with chronic pain attending a pain clinic: A systematic review and meta-analysis	Lee et al. [34]	Psychiatry Research	52.89% of patients with chronic pain were diagnosed with depression.
LILACS	Pharmacological management of chronic pain and depression	Lopes et al. [35]	Occupational Medicine Magazine	Antidepressants reduced pain intensity by 57% chronic.
SciELO	Degree of disability in patients with chronic pain and depressive symptoms	Mattos Junior et al. [22]	Brazilian Journal of Psychiatry	Depressed patients had 98% more disability due to pain chronic.
SciELO	Prevalence of depression in patients with chronic low back pain	Menezes et al. [36]	Physiotherapy and Research	67.7% of patients with chronic low back pain had depression.
SciELO	Influence of symptoms of anxiety and depression in chronic pain and	Moura et al. [37]	BrJP	Anxiety and depression increased pain intensity by 82%

Procedure	Title do Article	Authors	Newspaper	Considerations
	inability			chronic.
LILACS	Bidirectional association between depression and chronic pain: a systematic review and meta-analysis in adult population	Muñoz-Navarro et al. [14]	Clinical Medicine	Depression increased the risk of chronic pain by 29%, and vice versa.
LILACS	Prevalence of depression in patients with pain chronic no oncological	Pereira-Morales et al. [38]	medicine Family	37.7% of patients with chronic pain had symptoms depressive.
SciELO	Chronic pain as a risk factor for depression	Pereira et al. [21]	Brazilian Journal of Psychiatry	Chronic pain increases the risk of depression.
LILACS	Depression and chronic pain	Pepper and Cross	Journal of Rheumatology	Factors biopsychosocial factors explain 69% of the relationship between chronic pain and depression.
SciELO	Influence of depression and anxiety on the components of chronic pain: cross-sectional study	Ribeiro et al. [18]	BrJP	Depression and anxiety increased pain intensity by 53%.
SciELO	Efficacy of antidepressants in relieving chronic pain	Rodrigues et al. [25]	Brazilian Journal of Psychiatry	Antidepressants reduced pain intensity by 62% chronic.
SciELO	Hippotherapy in treatment of fibromyalgia: benefits in controlling chronic pain and symptoms of depression	Rose et al. [39]	Physiotherapy and Search	Hippotherapy reduced me 78% a pain intensity in fibromyalgia.
LILACS	Effects of physical therapy on depression in patients with chronic pain lumbar	Ruiz-Vicente et al. [40]	Physiotherapy	Physiotherapy reduced depressive symptoms in pain patients by 52% low back.
LILACS	Evaluation of quality of life in patients with chronic pain and depression	Salazar et al. [20]	Sinergia Medical Magazine	Depression reduced the quality of life of patients with chronic pain.
LILACS	Prevalence of chronic pain in patients with major depression	Santos et al. [13]	Journal of Research in Psychology	63.1% of patients with major depression had pain chronic.
LILACS	Psychological interventions for managing chronic pain and depressive symptoms	Segura- Ortí [27]	Thinking Psychology	Psychological interventions reduced the intensity of chronic pain and symptoms by 58% depressive.
Ssky	Multimodal approach to the management of chronic pain and depression	Silva et al. [29]	Brazilian Journal of Psychiatry	Multimodal approach reduced chronic pain intensity by 81% and depression.
PubMed	The relationship between chronic pain	Wang et al. [19]	Journal of Pain Research	Greater pain intensity increased

Procedure	Title do Article	Authors	Newspaper	Considerations
	and depressive symptoms in stroke survivors: A national cross-sectional survey in China			post-stroke depressive symptoms by 47%.
PubMed	Depression in patients with chronic pain attending a specialised pain treatment centre: prevalence and impact on health care costs	Rayner et al. [6]	Pain	46% of chronic pain patients had depression, which was associated with higher healthcare costs.
PubMed	Frequency of painful physical symptoms with major depressive disorder in Asia: relationship with disease severity and quality of life	Lee et al. [34]	Journal of Clinical Psychiatry	65.4% of patients with major depression had chronic pain; depression severity associated with higher and worse pain scores quality of life.
PubMed	Chronic opioid use in fibromyalgia syndrome: a clinical review	Painter & Crofford [41]	Journal of Clinical Rheumatology	Evidence of high prevalence of depression and anxiety in chronic opioid users with fibromyalgia; recommended non-opioid therapies such as first line.
PubMed	Depression and pain comorbidity: a literature review	Bair et al. [42]	Archives of Internal Medicine	Review on prevalence, impact and proposed mechanisms for comorbidity between depression and conditions painful; highlighted the necessity of more research.
PubMed	Neuroinflammation and Comorbidity of Pain and Depression	Walker et al. [43]	Pharmacological Reviews	Systemic inflammation may be in the base of comorbidity between conditions dlt is chronic pain It is depression; highlighted the potential of agents anti-inflammatories.

Source: Authors, 2024

6. DISCUSSION

This review highlighted a prevalence of comorbidity between depression and chronic pain of 50-65% [24], converging with findings from many of the analyzed studies [31,11]. Such magnitude emphasizes how frequent this association is, likely

underdiagnosed in clinical practice. Preventive interventions and enhanced professional training are needed given this high rate.

The bidirectionality of the relationship, widely demonstrated in systematic reviews [9], was also observed here. Longitudinal studies show that

both conditions can exacerbate each other over time [14,21], creating a vicious cycle—chronic pain increases the risk of depression, and depressive symptoms worsen the pain experience. Results also suggest a correlation between pain intensity and severity of depressive symptoms [18,19].

Thus, therapeutic strategies focused solely on one of these conditions are generally ineffective. This complex interaction results in greater functional limitations and worsened quality of life. Unimodal therapeutic approaches often prove insufficient. A multidisciplinary perspective is recommended, with integrated pharmacological and non-pharmacological interventions addressing both physical and psychological aspects [25,27].

As noted by Cunha [23] and Mattos Junior et al. [22], and confirmed throughout this review, this comorbidity significantly associated with worse functional limitations and health-related quality of life [12,20]. This underscores the need for multimodal approaches to reverse this trend, aiming at rehabilitation and greater well-being.

The aetiology of this comorbidity involves a complex network of biological, psychological, and social factors. Proposed mechanisms include neuroendocrine, inflammatory, neuroplastic changes, and pain modulation systems [10]. Other significant mediators include anxiety [17,16], psychosocial stress [10], low self-efficacy [8], maladaptive coping strategies [15], and secure attachment [43].

Understanding these multifactorial mechanisms behind the comorbidity of depression and chronic pain is crucial for developing personalized and effective therapeutic strategies [15]. Non-pharmacological techniques such as cognitive-behavioural therapy, mindfulness, physical exercises, and complementary therapies have shown promising results [28,26,39].

In summary, this is a highly prevalent and debilitating comorbidity that requires integrated management of physical and emotional aspects. Advances in elucidating the pathophysiological mechanisms and in multimodal treatments are essential to improve care and quality of life for patients with this condition.

Therefore, both physicians and multidisciplinary teams play a crucial role in managing the comorbidity between chronic pain and

depression, requiring a comprehensive understanding of the multiple facets that compose this complex relationship between body and mind, aiming for health restoration and improved quality of life for these patients [29,26].

Finally, the importance of preventive strategies and mental health promotion in dealing with chronic pain and depression is emphasized. Early diagnosis and proper treatment can help reduce the incidence and severity of these conditions, providing a better quality of life for affected patients [7,6]. Moreover, educating the public about the relationship between chronic pain and depression can help reduce the stigma associated with these conditions and improve access to mental health services and specialized care [9,41].

7. CONCLUSION

Given the extensive literature review conducted on the causative relationship between depression and chronic pain, it was possible to observe that these two conditions are intrinsically interconnected, with consistent evidence of comorbidity between them [6,11]. The analyzed studies demonstrated that depression and chronic pain often coexist, amplifying their negative effects on the lives of affected individuals [10,22]. Furthermore, the investigation revealed that emotional regulation has emerged as a significant mediator in this relationship, emphasizing the relevance of emotional stability for the well-being of patients [15,1].

The findings of this review highlight that secondary depression is a common condition in patients with chronic pain, triggered by biopsychosocial and behavioral factors [43,2]. Chronic pain, in turn, can lead to the development or exacerbation of depression, creating a vicious cycle that requires timely and appropriate intervention [14,41]. Understanding the nature of this relationship is crucial for healthcare professionals treating patients with these conditions, enabling more comprehensive and effective therapeutic approaches [8,4].

From the analysis of the biopsychosocial mechanisms involved in the interaction between depression and chronic pain, the importance of a holistic approach in the treatment of these patients becomes evident [10,3]. Therapeutic interventions that consider both the physical and emotional aspects of the conditions can lead to more promising results [27,26]. In this regard,

cognitive-behavioral therapy (CBT) and physical activity have proven effective in the simultaneous management of depression and chronic pain, providing significant improvements in patients' quality of life [26,28].

Additionally, it is crucial to recognize that the association between depression and chronic pain has implications not only for individual health but also for the healthcare system as a whole. The high prevalence of comorbidity between these conditions increases the demand for medical assistance and can result in significant costs to society [6,13]. Therefore, the adoption of public policies aimed at preventing and adequately treating both conditions is fundamental to reduce the negative impact on the population [33,4].

In medicine, understanding the complex relationship between depression and chronic pain is essential for addressing the overall well-being of these patients. Just as with any other health condition, it is necessary to consider the organism as an integrated whole, seeking complete homeostatic balance to achieve a healthy and prosperous life. In this context, this literature review provided a broad and comprehensive view of the intersection between depression and chronic pain, pointing to the importance of an integrated and multidisciplinary approach to dealing with these conditions [27,29]. Understanding these issues is essential for providing more effective and comprehensive care, offering a healthier and more resilient future for those facing the challenge of this intersection between depression and chronic pain [44,45].

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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