

# Update on chronic musculoskeletal pain: narrative review

## Atualização sobre a dor crônica musculoesquelética: revisão narrativa

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<https://doi.org/10.5935/2595-0118.20240047-en>

### ABSTRACT

**BACKGROUND AND OBJECTIVES:** There are conditions in which chronic musculoskeletal pain is present without apparent tissue damage, such as fibromyalgia or non-specific low back pain. In these cases, understanding the disease and treatment are challenges for patients, professionals and health services. Therefore, the aim of this study was to carry out a narrative review on chronic musculoskeletal pain, discuss current definitions and classifications and present different management strategies in order to contribute to clinical practice.

**CONTENTS:** Chronic musculoskeletal pain, without apparent injury, is now considered a disease and has been updated in the International Code of Diseases 11 (ICD-11), being called primary chronic musculoskeletal pain. The main mechanism of this type of pain is nociplastic, in which there is no clear evidence of actual or potential tissue damage, causing the activation of

peripheral nociceptors or evidence of disease or injury to the somatosensory system that causes the pain.

**CONCLUSION:** Chronic musculoskeletal pain is now classified into subgroups: primary chronic pain, in which pain is understood as a disease; and secondary chronic pain, in which pain is a symptom that arises as part of a disease process. Emotional distress and functional disability are characteristic, but not exclusive, to primary chronic musculoskeletal pain, in which there are no tissue lesions or other diagnosis that explain the pain. Treatment strategies should be multimodal and multidisciplinary.

**Keywords:** Chronic pain, Models, Models biopsychosocial, Musculoskeletal pain.

### RESUMO

**JUSTIFICATIVA E OBJETIVOS:** Há condições nas quais a dor crônica musculoesquelética está presente sem lesão tecidual aparente, como nos casos de fibromialgia ou dor lombar inespecífica. Nestes casos, a compreensão da doença e o tratamento são desafios para os pacientes, profissionais e serviços de saúde. Assim, o objetivo deste estudo foi realizar uma revisão narrativa sobre a dor crônica musculoesquelética, discutir as definições e classificações atuais e apresentar diferentes estratégias de manejo de modo a contribuir na implementação destes conhecimentos na prática clínica.

**CONTEÚDO:** A dor crônica musculoesquelética, sem lesão aparente, passa a ser considerada uma doença e ganha uma atualização no Código Internacional de Doenças 11 (CID-11), sendo denominada dor crônica musculoesquelética primária. O principal mecanismo deste tipo de dor é o nociplástico, no qual não há evidência clara de dano tecidual real ou potencial, causando a ativação de nociceptores periféricos ou evidência de doença ou lesão do sistema somatossensorial que causa a dor.

**CONCLUSÃO:** A dor crônica musculoesquelética hoje é classificada em subgrupos: dor crônica primária, no qual a dor é entendida como uma doença; e dor crônica secundária, no qual a dor surge como parte de um processo de doença. O sofrimento emocional e incapacidade funcional são característicos, mas não exclusivos, da dor crônica musculoesquelética primária, na qual não há lesões teciduais ou outro diagnóstico que explique a dor. As estratégias de tratamento devem ser multimodais e multidisciplinares, além de incluir fatores biopsicossociais, e devem ser alinhadas com as preferências do paciente e atuar nos fatores modificáveis individuais.

**Descritores:** Dor crônica, Dor musculoesquelética. Modelos biopsicossocial.

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Submitted on February 02, 2024.

Accepted for publication on June 21, 2024.

Conflict of interests: none – Sponsoring sources: none.

### HIGHLIGHTS

- In the ICD-11, chronic musculoskeletal pain is now classified as primary and secondary chronic pain
- In addition to the nociceptive and neuropathic mechanisms of pain, the nociplastic mechanism is included
- The treatment of primary chronic musculoskeletal pain must include biopsychosocial factors in treatment strategies

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## INTRODUCTION

Chronic pain (CP) is a disabling condition and considered a public health problem that generates high costs for health services<sup>1-3</sup>. In Brazil, its prevalence is approximately 45% of the population, and it is more prevalent in adults and senior women, with a predominance in the low back area<sup>4,5</sup>. In recent decades, CP has gone from being a prevalent symptom of other diseases to a condition<sup>6,7</sup>, which has led to the need to update classifications, definitions and taxonomies<sup>8</sup>.

According to The Global Burden of Diseases study, chronic musculoskeletal pain (CMP) is the condition that causes the most life-year limitations and can evolve into disabilities<sup>9</sup>, however, its real impact may be underestimated due to the lack of standardized definitions and difficulties in collecting data worldwide, resulting in barriers for professionals, services and the health system as a whole<sup>10</sup>.

The lack of standardization in the use of definitions and concepts by the scientific community makes it difficult to understand the applicability of research in clinical practice. Therefore, the present narrative review aimed to discuss the new classifications of CP, especially CMP, and present current therapeutic proposals for its management.

## CONTENTS

This is a narrative literature review of publications in national and international journals. The study carried out a manual bibliographic search of published articles written in Portuguese and English in the LILACS, Pubmed and Scielo databases using the terms “chronic pain”, “chronic musculoskeletal pain” and “nociceptive pain”. Data was collected from September to December 2023. The eligibility criteria used the following confirmation steps: adherence of the article titles, which should contain the keywords searched, and text content in line with the review proposal. After identifying the articles, a qualitative analysis of the titles and abstracts was carried out in order to classify them according to relevance. In addition, some articles were consulted based on references in the articles searched in the databases.

### From symptom to disease - classification of pain and its characteristics

CP has gone from being a prevalent symptom in various diseases to becoming a condition in itself<sup>6,7</sup>. The update goes through the International Classification of Diseases (ICD) which, until its 10th edition, did not include CP in a systematic way, making it difficult to carry out a more precise epistemological analysis and to draw up public health policies<sup>11,12</sup>. New classification proposals were made and tested<sup>13</sup> and the World Health Organization (WHO) and the International Association for the Study of Pain (IASP) worked to update the ICD-11<sup>14,15</sup>, allowing for a better definition of the conditions that present CP<sup>16</sup>.

Thus, CP came to be understood as pain that lasts for more than three months, is influenced by biopsychosocial factors, and has a multifactorial aspect in nature<sup>17</sup>. CP comes in two subgroups: primary CP, in which the mechanism related to pain and the

consequent impacts are unclear; and secondary CP, in which pain, at least initially, can be understood as a symptom of some other disease<sup>11,18</sup>.

According to the ICD-11 definition, “Primary musculoskeletal CP presents one or more areas of pain that accompany significant emotional distress (anxiety, anger/frustration or depressive state) or functional disability (interference in activities of daily living with reduced social interaction). Primary CP is multifactorial and has factors that contribute to the pain syndrome: biological, psychological and social. The diagnosis is independent of biological or psychosocial influences, unless another diagnosis is appropriate for the symptoms demonstrated (authors’ translation)<sup>19</sup>. Examples of primary CP include generalized CP, complex regional pain type I, fibromyalgia, non-specific lumbar and cervical pain<sup>20</sup>.

This classification of primary CP is more comprehensive and makes it possible to emphasize the common aspects of the pain subtypes<sup>21</sup>. The new classification was also tested in low-, middle- and high-income countries to observe the accordance between evaluators from culturally diverse regions. The results showed high reliability between evaluators<sup>22</sup>.

Secondary CMP can be translated as “CP resulting from injuries to bone(s), joint(s), muscle(s), spine, tendon(s) or related soft tissue(s). It is a heterogeneous group of CP conditions originating from persistent nociception in joints, bones, muscles, spine, tendons and related soft tissues, with local and systemic etiologies, but also related to deep somatic lesions. Pain can be spontaneous or induced by movement<sup>19</sup>.

Although the ICD-11 officially came into effect globally on January 1, 2022, it is going to be active in Brazil starting in January 1, 2025. This is due to a transition period, in which translation, updating of information systems and training of health professionals is necessary<sup>23</sup>. However, the Brazilian Ministry of Health itself encourages the familiarization and training of professionals to take place before implementation and, to facilitate this process, ICD-11 training can be done in English<sup>24</sup>. Nonetheless, it is likely that few professionals will be able to complete this training, due to the need to have a good comprehension of the English language.

### Pain mechanisms - from nociception to nociplasticity

The experience of pain classically arises from a noxious stimulus, which activates nociceptive receptors (transduction) and sends pain signals to the central nervous system (CNS) (transmission and modulation) to then be perceived and become conscious<sup>25</sup>. This is the nociceptive mechanism, which serves as an alarm system to maintain the body’s integrity<sup>26</sup>. Another mechanism is the neuropathic one, which, due to a lesion in the somatosensory system, mechanical trauma, metabolic disease, infection or tumor, usually has a worse prognosis and poorer quality of life<sup>27,28</sup>. Patients with CMP often don’t have a clear enough mechanism to explain their pain and dysfunction, as in the case of patients with fibromyalgia or non-specific low back pain<sup>29-31</sup>. These patients can be classified, according to the ICD-11, as having primary CMP. It is important to comprehend the mechanisms and origins of pain in order to indicate the best treatment for the

patients. Theories that help to understand the chronification of pain integrate neurophysiological concepts (such as Central Sensitization - CS) with cognitive ones (such as learning and the individual's perceptions)<sup>32</sup>.

The main process that helps to understand the experience of CP is CS<sup>33</sup>, since the pain is disproportionately more intense, continues beyond the time expected for recovery, with diffuse distribution, the presence of hyperalgesia (excessive response to a painful stimulus) and allodynia (sensation of abnormal pain from a stimulus that shouldn't cause pain), as well as increased sensitivity unrelated to the musculoskeletal system<sup>34,35</sup>.

CS can be defined as an amplification of a neuronal signal in the central nervous system that results in hypersensitivity<sup>36</sup>. By amplifying afferents from body systems, CS can induce maladaptive plasticity, resulting clinically in hyperalgesia and allodynia<sup>37-40</sup>. CS is driven by neuroinflammation in the Central Nervous System and Peripheral Nervous System, which reaches higher brain regions involved in the emotional and cognitive modulation of pain (for reviews)<sup>41,42</sup>.

Several musculoskeletal diseases and conditions present CS, such as osteoarthritis<sup>43</sup>, patellofemoral pain<sup>44</sup>, temporomandibular dysfunction<sup>45</sup>, shoulder pain<sup>46</sup>, tendinopathies<sup>47</sup>, fibromyalgia<sup>40</sup>, low back pain<sup>48</sup> and rheumatoid arthritis<sup>49</sup>. CS is influenced by neuroinflammation, so it becomes a common process in pain with nociceptive and neuropathic components<sup>50-53</sup>. Thus, CS can be considered an umbrella term for physiological adaptations (structural, functional and chemical), which can be maladaptive in the long term, and which favor unpleasant experiences related to pain<sup>54</sup>.

The terms "central sensitization pain", "central pain", "psychogenic pain" and "pain of psychosomatic origin" were used for indicating pain that could not be explained by nociception or neuropathic mechanisms<sup>55-57</sup>. Classifying the origin of pain as psychiatric due to a lack of understanding of the patient's physical symptoms favors misdiagnosis and inadequate treatment, which is why improving the nomenclature and diagnostic criteria is essential in order to increase the accuracy of the diagnosis and offer appropriate treatment<sup>58</sup>. These terminologies have been replaced by "nociceptive pain", which is more descriptive of the pain phenotype<sup>59</sup>. This term was proposed as a third descriptor<sup>60</sup> and is now recommended by the IASP.

According to the IASP, the current pain descriptors are:

- **Nociceptive pain:** pain that arises from an actual or potential lesion in a non-neural tissue as a result of nociceptive receptors.
- **Neuropathic pain:** pain caused by injury or disease associated with the somatosensory system. Neuropathic pain is considered a symptom and not a diagnosis in itself, and requires an injury or disease to establish it.
- **Nociplastic pain:** pain that arises from altered nociception, even though there is no evidence of disease, injury to the somatosensory system or clear suspicion or threat of actual tissue injury that causes activation of peripheral nociceptors, causing pain<sup>60,61</sup>. CS is present in the majority of nociplastic pain conditions<sup>60</sup>, especially in CMP and those that have the nervous system as a modulator, in addition to the locomotor system. However, it is possible for a patient to have pain with mixed mechanisms, with

associated nociceptive and nociplastic patterns, or neuropathic and nociplastic, and there may be a predominance of one mechanism over the other<sup>62</sup>. Nociplastic pain is a terminology that describes the mechanism of pain and is not a classification of the diagnosis itself, but it has the potential to bring health professionals closer to their patients, to reduce the stigmatization that "the pain is in the patient's head"<sup>63</sup>.

Comprehending phenotypes is important in order to guide the best treatment for the patient. It must be noted that nociplastic pain is not a phenotypic mechanism that excludes other types of pain (nociceptive or neuropathic pain) and presents specific conditions for its classification. The clinical criteria for classifying nociplastic musculoskeletal pain (or primary CMP) are:

- Pain lasting more than three months;
- Pain with a local rather than discrete distribution;
- Pain that cannot be completely explained by neuropathic or nociceptive mechanisms;
- Clinical presence of signs of pain hypersensitivity (i.e. evoked pain hypersensitivity phenomena, such as static or dynamic allodynia mechanisms, cold- or heat-induced allodynia, and/or pain sensation after the hypersensitivity assessment mentioned) in the location of pain<sup>64</sup>.

When the four criteria above mentioned are identified, patients are classified as having "possible nociplastic pain", and when patients have all four criteria, plus a history of hypersensitivity in the region of pain (sensitivity to touch, movement, pressure or heat/cold), and at least one comorbidity (cognitive problems; fatigue; altered sleep with an increase in the number of times waking up at night; increased sensitivity to sound, light or odors), the pain can be classified as a "probable nociplastic mechanism"<sup>64</sup>.

It is important to highlight that nociplastic pain is a terminology used for various conditions that present the same neurophysiological mechanism, validating previously unexplained pain complaints, and which can occur concomitantly with other clinical diseases<sup>65</sup>. For example, patients with low back pain with a nociplastic component have concomitant comorbidities such as depression, anxiety and catastrophizing, as well as a poorer response to rehabilitation, especially pain control<sup>66</sup>.

Recently, a partnership was established between clinicians and researchers from thirteen countries to develop recommendations that will make it possible to identify the predominant pain mechanism in patients with low back pain and propose treatment strategies according to the predominant mechanism<sup>67</sup>.

Primary CMP has a predominantly nociplastic mechanism, while secondary CMP has a predominantly nociceptive mechanism<sup>68,69</sup>. Table 1 explains the differences between the classifications.

CMP has also been observed in patients with post-COVID syndrome, characterized by the worsening of pre-existing pain, when influenced by the clinical impacts of infection, drug use, treatment interruption, physical inactivity or the onset of new pain<sup>70-72</sup>. The mechanism of CMP after COVID can be nociceptive, neuropathic, nociplastic or of mixed presentation, but the nociplastic pain mechanism seems to be the primary cause presented by patients<sup>73,74</sup>. In two meta-analyses, it was pointed out

**Table 1.** Characterization of primary and secondary chronic pain. Adaptation<sup>82,83</sup>.

Clinical feature	Secondary musculoskeletal chronic pain (predominantly nociceptive)	Primary musculoskeletal chronic pain (predominantly nociplastic)
Etiology	Actual or potential tissue damage	Dysfunctional processing of pain or other sensory stimuli without tissue damage
Descriptors	Throbbing, beating, pressuring pain	Acute, stabbing, lacerating, burning, bruising pain
Sensory deficit	Rare	Common, with diffuse distribution
Motor deficits	Possible presence of pain-induced muscle weakness	Generalized fatigue is common and physical deconditioning may be related to weakness
Hypersensitivity	Uncommon, except in the affected location	Common, may be diffuse, with hyperalgesia and sensitivity to mechanical stimuli being more common than allodynia
Pattern of pain	Irradiated pain is uncommon. Referred pain can occur in nearby structures	More diffuse and variable, not following an anatomical reference pattern (does not follow a nerve or dermatome path)
Factors (relieving or triggering) that influence pain	Exacerbation of pain is less common and usually associated some activity	Common, usually associated with psychosocial stressors
Autonomic signs	Uncommon	Possible presence of signs of autonomic dysfunction
Change in quality of life	Worsening quality of life is usually less than in neuropathic conditions	Decreased quality of life is usually equal to or greater than in neuropathic conditions
Comorbidities	Usually there are fewer associated psychopathologies, may be accompanied by cardiovascular diseases, hypertension, insomnia, obesity and cognitive dysfunctions	Greater presence of psychopathologies, cognitive dysfunctions and pain comorbidities than in other predominantly nociceptive and neuropathic pains
Examples of diseases according to previous classification	Pain as a symptom of inflammatory, infectious, metabolic or autoimmune etiology, such as osteoarthritis and rheumatoid arthritis	Pain as a disease of undefined etiology, such as fibromyalgia and non-specific low back pain

that among individuals who had COVID, 10%-22% had CMP at some point in the first year after infection<sup>75,76</sup>.

Comorbidities such as anxiety, depression, cognitive changes, sleep disorders, fatigue, sarcopenia, osteopenia and dyspnea have also been reported in patients with post-COVID syndrome or long-term COVID and contribute to CMP<sup>77-81</sup>. Despite the heterogeneity of the studies, these data reinforce the importance of including screening for previous COVID infections and other possible symptoms common in post-COVID syndrome in the assessment of patients with CMP.

In Brazil, patients with CMP during and after COVID infection were twice as likely to need health services<sup>82</sup>. More time spent in physical activities during the pandemic was positively associated with a higher level of self-efficacy in patients with CMP<sup>83</sup>. These data indicate the need to develop public policies that encourage a higher level of physical activity and seek to prepare health professionals and services for the care of patients with CMP after COVID<sup>70,82</sup>.

### Evaluation of the different pain mechanisms

Pain assessment is an important phase in developing an appropriate therapeutic strategy and should include multiple domains such as intensity, perceptual qualities, body distribution, temporal aspects, psychological and emotional domains, dysfunction and movement restrictions<sup>84,85</sup>. Possible barriers that hinder patient adherence to rehabilitation should also be investigated<sup>86</sup>.

CS, present in different chronic pain mechanisms, can be investigated with the Sensory Quantification Test (SQT), which refers to an umbrella term for different tests that assess the sensory

threshold with a controlled stimulus, these being mechanical, electrical, thermal and vibratory<sup>87,88</sup>, and allows for the identification of allodynia and hypersensitivity.

The SQT can be used to investigate peripheral and central mechanisms that contribute to pain, showing good neural sensitivity for CMP<sup>89,90</sup>. Another form of assessment is through patient self-report and completion of questionnaires such as the Central Sensitization Inventory (CSI). The CSI aims to identify patients with symptoms or a high risk of CS<sup>91,92</sup> and, in the Brazilian population, has a specificity of over 90% when its score reaches 35/100<sup>93</sup>.

Psychological factors such as depression, anxiety, catastrophizing and kinesiophobia can increase the perception of pain and influence the process of its chronification<sup>94-98</sup>. These factors interfere with a patient's daily activities and functionality<sup>99</sup>. These psychological factors can be assessed in clinical practice and in research using specific scales validated for Portuguese that evaluate depression<sup>100</sup>, anxiety<sup>101</sup>, catastrophizing<sup>102</sup> and kinesiophobia<sup>103</sup>. Other self-administered instruments can be used to assess aspects such as quality of life<sup>104,105</sup>, sleep quality<sup>106</sup>, catastrophic thinking<sup>102</sup>, attitudes towards CP<sup>107</sup>, the profile of CP<sup>108</sup> and the McGill pain questionnaire<sup>109</sup>.

### Treatment strategies

Ideally, treatment for CP should include multimodal and multidisciplinary strategies aligned with the patient's preferences, beliefs and expectations<sup>69,110-112</sup>. It is necessary to understand the patient's context (social, economic and cultural) and environment and what resources are available to treat them as a whole<sup>113</sup>. The management of CP should focus on long-term strategies



with the objective of reducing suffering and improving the patients' quality of life and functionality<sup>114,115</sup>.

Some interventions for pain management and prevention should focus on modifiable factors such as: improving sleep quality and hygiene, diet, physical exercise, psychotherapy and interventions related to the mind-body binomial that promote relaxation, with physical exercise being the intervention with most evidence in the literature, especially when conducted by movement professionals, physical educators and physiotherapists (for reviews)<sup>116-121</sup>.

Low to moderate intensity global physical exercise is also an appropriate treatment resource when it comes to the nociplastic pain mechanism in patients with primary CMP<sup>122</sup>. Kinesiophobia and catastrophizing can make it difficult to adhere to active pain management strategies. In these cases, gradual exposure based on the individual's tolerance and the development of coping strategies together with the patient are recommended<sup>123,124</sup>. Some coping strategies for CP patients are also related to religious practices and social support<sup>125,126</sup>.

Modifiable factors mentioned above are related to individual strategies that are related to a change in lifestyle. These changes should be built together with the patient to facilitate their motivation and long-term adherence to pain management<sup>86</sup>. More global treatment and prevention strategies depend on the implementation of public policies. Improved income distribution and access to education are likely factors for a more positive prognosis for CP<sup>121</sup>. In addition, the implementation of multidisciplinary teams to care for patients in the public health system, in primary care, is something that is feasible and can reduce the burden on secondary care and save a good amount of public money<sup>127,128</sup>.

In Brazil, the guidelines recommendation for the *Protocolos Clínicos e Diretrizes Terapêuticas* (PCDT - Clinical Protocols and Therapeutic guidelines recommendation Report) for CD was updated in October 2022, and presents a survey of drugs and doses indicated for the different types of pain according to the *Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde* (National Commission for the Incorporation of Technologies into the Public Health System), which incorporates, excludes or alters drugs, products and procedures<sup>129</sup>. It is strongly suggested that you familiarize yourself with this document, as a pharmacological review is beyond the scope of this review. However, it is important to mention that, considering the mechanism of nociplastic pain, as in the case of primary CMP, pharmacological treatment does not seem to be beneficial, and it is necessary to use it in association with other therapies<sup>21,114,130</sup>, such as physical exercise and psychotherapy<sup>110,131</sup>.

Other treatment modalities may include different types of electrical brain stimulation; however, the evidence is of low quality and the variability of protocols and application times still need to be researched<sup>132,133</sup>. As a tendency for the future, the identification of possible biomarkers as predictors of clinical evolution is being studied<sup>134,135</sup>, as well as the neuronal profile of each patient<sup>136</sup>, which could increase the possibility of individualized treatment.

Comprehending the prognosis associated with CMP and the psychological, social and environmental factors that influence the maintenance of pain are aspects that health professionals

should consider when designing pain prevention and management strategies<sup>131,137,138</sup>. The incidence of CMP and the burden associated with it will continue to rise, especially in low- and middle-income countries such as Brazil, as factors such as the aging of the population, increased obesity and sedentary lifestyle influence the incidence of CMP<sup>10,139,140</sup>.

## CONCLUSION

CMP is a disabling condition that has been classified by the ICD-11 into subgroups: primary CP, in which pain is understood as a disease; and secondary CP, in which pain is a symptom. CMP will be included as a disease in the *Sistema Único de Saúde* (Brazilian public health system) from 2025 on, but professionals must familiarize themselves with the new classification and, above all, treatment strategies. Emotional suffering and functional incapacity are features of primary CMP, but not exclusive. Therefore, assessment and treatment strategies should be multimodal and multidisciplinary, aligned with patient preferences, acting on individual modifiable factors, and encouraging long-term changes.

The main mechanism of primary CMP is nociplastic, driven by CS. The classic pain mechanisms (nociceptive and neuropathic) can occur simultaneously with the nociplastic one, so chronic musculoskeletal pain can have mixed characteristics. Patients with pain with a predominantly nociplastic mechanism do not seem to respond as well to rehabilitation and pharmacotherapy. It is important to emphasize that the nociplastic mechanism has specific clinical criteria and treatment strategies should include biopsychosocial factors and physical exercise.

## AUTHORS' CONTRIBUTIONS

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