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# UNDERSTANDING CHRONIC PAIN: TYPES, MECHANISMS, AND EMERGING MANAGEMENT STRATEGIES: A REVIEW

*Narrative Review*

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## ABSTRACT

**Background:** Chronic pain affects over 30% of the global population, imposing significant physical, psychological, and economic burdens. It is classified into nociceptive, neuropathic, and nociplastic pain, each with distinct mechanisms and management challenges. Despite advancements, the complexity of chronic pain necessitates a comprehensive understanding of its types, mechanisms, and emerging treatment strategies.

**Methods**: A narrative review was conducted using six electronic databases, including Medline, Embase, and PubMed. Studies examining the biological, psychological, socio-economic, and cultural factors influencing chronic pain were included without date or geographic restrictions. Systematic reviews and key research articles were prioritized.

**Results**: Nociceptive pain arises from tissue damage, as seen in arthritis and myofascial pain syndrome. Neuropathic pain originates from nerve injury or dysfunction, with examples like diabetic neuropathy and trigeminal neuralgia. Nociplastic pain, exemplified by fibromyalgia, involves altered central pain processing. Recent advancements in molecular and genetic research have uncovered potential therapeutic targets, while non-pharmacological interventions like physical therapy and mindfulness have demonstrated efficacy. However, diagnostic challenges and variability in treatment response highlight the need for individualized, multidisciplinary approaches.

**Conclusion**: This review underscores the importance of understanding chronic pain classifications and mechanisms to develop targeted and effective management strategies. Future directions should focus on integrating innovative diagnostic tools, enhancing patient education, and implementing personalized multimodal therapies to reduce the burden of chronic pain.

**Keywords**: Chronic Pain, Multidisciplinary Pain Management, Neuropathic Pain, Nociceptive Pain, Nociplastic Pain, Non-Pharmacological Interventions, Pain Management, Pain Mechanisms, Personalized Medicine, Therapeutics.

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## INTRODUCTION

Pain is characterized as an unpleasant emotional and sensory experience related with, or provoking, actual or potential tissue harm (1) Any discomfort that lasts longer than three months is considered chronic (1). More than 25% of American citizens have chronic discomfort. It is one of the most typical complaints that a patient brings to an outpatient clinic (2). Typically, chronic pain is characterized by recurrent pain that lasts for several months, and approximately 11–19% of adults experience this type of pain (3). Over 30% of individuals globally have chronic pain, which imposes a significant personal and financial burden, as per certain research (4).

In the realm of chronic pain, three distinct types emerge: Nociplastic, neuropathic, and nociceptive(1,4). These distinct types reflect different underlying mechanisms, from direct tissue damage to nerve dysfunction or altered pain processing in the central nervous system. By investigating these mechanisms and their interplay, the study seeks to highlight the importance of individualized and targeted interventions. The significance of addressing chronic pain extends beyond symptom management. It encompasses improving healthcare delivery, reducing economic costs, and alleviating the physical and emotional toll on patients and their families. Through this comprehensive review, the study aims to provide insights into effective strategies that can bridge gaps in current practices, ultimately enhancing the quality of life for individuals living with chronic pain. To better understand the complexity of chronic pain, Figure (1) provides an overview of its types, mechanisms, contributing factors, and management strategies. This framework sets the stage for the detailed discussions in this review, which aim to explore these dimensions comprehensively. By examining the interconnection of these elements, this study underscores the need for a multidisciplinary approach to improve outcomes for patients with chronic pain.

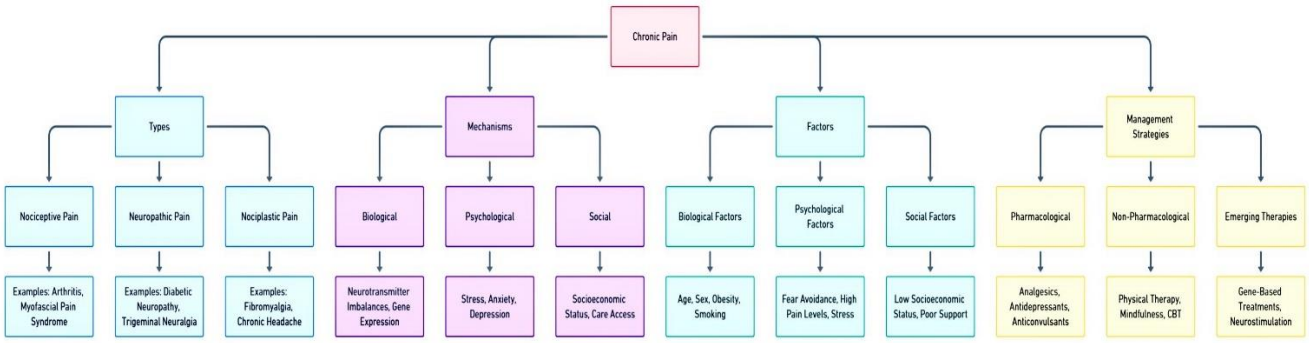


*Figure 1 Conceptual framework of chronic pain*

## METHODS

This narrative review was conducted to investigate the types, mechanisms, and management strategies associated with chronic pain. A comprehensive search strategy was employed to ensure the inclusion of relevant literature that examined the biological, psychological, socio-economic, and cultural factors influencing the onset, persistence, and management of chronic pain. To maintain the breadth of analysis, no restrictions were applied regarding the date of publication, country of origin, or study design. However, studies published in languages other than English and abstracts without access to the full text were excluded to ensure accessibility and validity of the data.

A systematic and thorough literature search was conducted across six major electronic databases, including Medline, Embase, the Cochrane Central Register of Controlled Trials, PubMed, the Cochrane Database of Systematic Reviews, and Web of Science. The search strategy utilized a combination of Medical Subject Headings (MeSH) and relevant keywords to retrieve the most pertinent studies. The primary search terms included “chronic pain” OR “persistent pain” in combination with “mechanisms,” “etiology,” “risk factors,” “management,” “treatment,” “interventions,” or “emerging strategies.” These keywords were structured to optimize search sensitivity and specificity, ensuring the inclusion of high-quality research. The databases were searched up to 2024 to incorporate the most recent advancements in chronic pain research.

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## Types of Chronic Pain and their Prevalent Conditions

### Nociceptive Pain

Occurs when nociceptors are activated as a result of recent or impending injury to non-neural tissues(1,4). Nociceptive pain results from tissue damage, which nociceptors then perceive as pain(1,4). This fundamental mechanism plays a crucial role in alerting the body to potential harm and initiating protective responses. The sensory experience of nociceptive pain serves as a warning signal, prompting individuals to take action to prevent further injury and promote healing (1,4). Understanding the intricate interplay between tissue damage and nociceptor activation is essential for unraveling the complexities of pain perception and developing targeted approaches for pain management. Although somatic pain is also regional, it can be regarded as dull, deep, and poorly localized, unlike nociceptive pain patterns, which are typically definite and exact like a pinprick. Generally speaking, well-defined pain triggers, including particular motions and activities, make it worse.(5). The most prevalent conditions of Nociceptive pain are as follow,

### Arthritis

From the Greek word "disease of the joints," arthritis is derived. It is described as either a sudden or persistent inflammation of the joints, frequently accompanied by discomfort and structural damage.(6) There are over a hundred varieties of arthritis that have been identified; the most prevalent variety is osteoarthritis, also known as degenerative arthritis, or non-inflammatory arthritis. There are various conditions that can lead to inflammatory arthritis, such as autoimmune diseases (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, etc.), infections (septic arthritis, Lyme's arthritis), or crystal deposition-induced diseases (gout, pseudogout, basic calcium phosphate disease). Other autoimmune connective tissue disorders such systemic lupus erythematosus, Sjogren syndrome, scleroderma, myositis, inflammatory bowel disease, celiac disease, etc., can also coexist with inflammatory arthritis.(6). Perceived pain is ultimately determined by the interaction between direct activation of peripheral nociceptors and central and peripheral modification of neuronal sensitivity along the nociceptive pathway.(7)

### Myofascial Pain Syndrome

A common condition among people with musculoskeletal pain issues is myofascial pain syndrome (MPS). MPS is a type of pain that starts in the surrounding fascia and muscles. Patients typically arrive with referred pain of different patterns or localized pain in a small location.(8). Nociceptive pain is the standard classification for myofascial pain. In the current research, findings supporting the nociceptive, nociplastic, or mixed-type phenotype subgrouping of individuals with myofascial TrP pain are summarized.(5)

### Visceral Pain

Visceral pain is characterized by its diffuse nature, is usually related to nonvisceral tissues, and is not always linked to organ damage. Every organ is innervated by a pair of nerves that have distinct roles and some overlap. Visceral nociceptors are among the several stimulation modes that sensory endings in viscera are frequently sensitive to. Disease and inflammation can sensitize both visceral nociceptors and low-threshold, non-nociceptor mechanosensors.(9)

### Musculoskeletal Pain conditions

Arthritic, musculoskeletal, postsurgical, and metastatic bone pain are a few instances of somatic nociceptive pain (10). Patients reporting pain related to their musculoskeletal system frequently report nociceptive and neuropathic pain. Neuropathic-like symptoms can appear in certain musculoskeletal pain diseases that are classed as nociceptive pain, such as impingement syndrome of the shoulder, rotator cuff tears, and osteoarthritis of the knee. While there is a trade-off between a number of pain features that indicate whether a patient has nociceptive pain or neuropathic-like symptoms, prior research indicated that individuals with neuropathic-like symptoms did not fare well.(11)

### Neuropathic Pain

Resulting from pathology or injury to the somatosensory nerve system; usually accompanied by anomalies in sensory perception, including numbness and allodynia(4). Unlike nociceptive pain, which is triggered by damage to non-neural tissues, neuropathic pain originates from malfunctions or injuries affecting the nerves themselves. The IASP states that pain is classified as neuropathic when one of the following three conditions is met: 1. the pain is restricted to a "neuroanatomically plausible" distribution of the system; 2. the pain is supported by clinical examination, laboratory findings, and/or imaging results; and 3. the pain is caused by a lesion or disease of the somatosensory nervous system (i.e., central or peripheral nervous system)(5). The physiologic reaction to nociceptor activation is known

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as nociceptive pain, and it has a valuable purpose since it promotes defensive responses. Neuropathic pain is defined as pain that is not associated with nociceptor activation. It is most likely not helpful and arises from sensitization and autonomous ectopic activity of several pro-nociceptive entities, primarily sodium and calcium channels. Neuropathic pain is intense in contrast to nociceptive pain, which is dull. Although not all neuropathic pain is chronic, there is overlap between neuropathic and chronic pain (12). Examples of Neuropathic pain conditions are as,

**Complex Regional Pain Syndrome (CRPS)**

A neuropathic pain condition known as Complex Regional Pain Syndrome (CRPS) is characterized by persistent pain that is out of proportion to the extent of tissue damage and lasts longer than is typically anticipated for tissue repair. Abnormalities related to the senses, muscles, and nervous system accompany pain (13). Allodynia, hyperalgesia, abnormalities in sudomotor and vasomotor function, and trophic alterations are among the distinctive clinical symptoms that characterize complex regional pain syndrome (CRPS), a neuropathic pain disease (13). It is a kind II chronic neuropathic pain that develops after soft-tissue, bone, or nerve injury. The pain is more severe and lasts longer than one may anticipate given the initial tissue damage. Additional symptoms include trophic (such as skin or bone shrinkage, hair loss, joint contractures), autonomic (such as sweating, vasomotor irregularities), and motor (such as weakness, dystonia) disturbances.(14)

**Trigeminal Neuralgia**

Tic douloureux is a well-known case of neuropathic pain. This devastating illness, also known as trigeminal neuralgia, causes excruciating pain attacks in the face when left untreated.(15). The neuropathic nature of this pain condition involves abnormal signaling in the nervous system, leading to heightened and inappropriate pain responses.

**Diabetic Peripheral Neuropathy**

Extensive epidemiological research examined the frequency of NP in individuals with diabetes. 20.3% of 766 diabetes individuals in a cross-sectional survey reported having persistent pain with neuropathic features (16). This finding underscores the significant prevalence of neuropathic pain in the diabetic population, highlighting the need for targeted interventions and management strategies to address this specific aspect of diabetic complications. This finding underscores the significant prevalence of neuropathic pain in the diabetic population, highlighting the need for targeted interventions and management strategies to address this specific aspect of diabetic complications.

**Peripheral Nerve Injury**

Peripheral nerve injury refers to damage or trauma that affects the nerves outside the brain and spinal cord. The most recent classification indicates that "chronic NP after peripheral nerve injury" is a third-level diagnosis within the "chronic NP" category. It can also be derived from "chronic posttraumatic pain," another parent diagnosis.(17)

**Chronic Postsurgical Pain Disorders**

Following surgery, persistent postsurgical pain may arise. The following conditions are associated with this particular form of pain: persistent pain following amputation, persistent pain following spinal surgery, persistent pain following thoracotomy, persistent pain following breast surgery, persistent pain following herniotomy, persistent pain following hysterectomy, and persistent pain following arthroplasty.(17)

## Advancements in Neuropathic Pain Research

Recent advancements in neuropathic pain research, as highlighted in the article (18), include the identification of specific gene expression profiles in injured dorsal root ganglia (DRG) after peripheral nerve injury. Utilizing single-cell RNA sequencing, the study reveals dynamic changes in DRG neuron types, potential analgesic targets, and insights into gene regulatory networks during the development of neuropathic pain. The (19) article uses single-cell RNA sequencing to examine mouse DRG cells after sparing nerve injury (SNI), which advances our understanding of neuropathic pain. It reveals gene regulatory networks, three SNI-induced neuronal clusters, and their genesis, providing insight into the complex molecular pathways and possible therapeutic targets in the development of neuropathic pain. According to Article (20), neuropathic pain research has advanced significantly. Novel therapeutic approaches and

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a better comprehension of molecular pathways are examples of recent advancements that open the door to more focused and efficient neuropathic pain management techniques.

**Nociplastic Pain**

Occurs when there is altered processing of pain signals without obvious signs of somatosensory system dysfunction or impairment (4). In contrast to the well-established nociceptive and neuropathic pain, the term Nociplastic pain (NcplP) was first proposed and discussed in 2016 (21). The phrase "neuroplastic pain" is wide and probably refers to a variety of CNS pathways that cause either lower suppression of pain or increased processing of pain signals, or both (22). NcplP is a sort of pain in which there is no other indication of a sensorimotor illness or tissue damage that could trigger nociceptors (21). It manifests in long-term pain disorders as fibromyalgia, headaches, and low back pain (LBP)(21). As such, a new term for disorders resulting from altered nociception in the absence of obvious evidence of actual or imminent tissue damage is Nociplastic pain (NP), which encompasses a range of conditions related to CP. By attempting to describe diseases that were previously classified as functional pain syndromes or unexplained pain, this new descriptor hopes to relieve patients of the potential stigma associated with making "all in my head" excuses.(23). The most prevalent condition of Nociceptive pain is Fibromyalgia as following,

**Fibromyalgia**

Fibromyalgia syndrome, or FMS, is a prevalent disorder marked by widespread, persistent pain that also causes intrusive tiredness, sleep disturbances, poor cognitive and physical function, and psychological anguish.(24) Millions of individuals worldwide (between 0.2 and 6.6% of the total population), particularly women over 50, suffer with the illness known as fibromyalgia (FM).(25) Many attempts have been made to identify a "neurophysiological/neuroimaging signature" of FM patients as FM is now understood to be a neuroplastic pain disorder. Research has shown that FM alters brain morphometry and that individuals with FM may have a distinct retinal imprint.(26) Abnormalities in the processing of pain include an excess of excitatory neurotransmitters, such as glutamate and substance P (which are found in the cerebrospinal fluid at levels that are two to three times higher), low levels of inhibitor neurotransmitters, such as serotonin and norepinephrine in the descending spinal antinociceptive pathways, and changes in endogenous opioids in certain brain regions involved in dopamine deregulation and pain modulation.(27)

### Recent Findings related to Fibromyalgia and Implications for its diagnosis and treatment

Recent fibromyalgia studies, including "Centralized Nociplastic Pain Causing Fibromyalgia (28)," emphasize understanding central pain for accurate diagnosis. The "Fibromyalgia Position Paper (29), advocates a multidisciplinary diagnostic approach, recognizing the complexity of fibromyalgia. "The Diagnosis of Fibromyalgia Syndrome (24)" addresses diagnostic challenges, shedding light on difficulties and proposing potential strategies. "Physical Therapy Modalities for Treating Fibromyalgia (25), explores non-pharmacological treatments like aerobic exercises and aquatic therapy. Lastly, "Fibromyalgia: One Year in Review 2023 (26)" consolidates recent advancements, guiding future avenues for diagnosis and treatment.

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**Table 1: Key research findings and implications for fibromyalgia management**

| S.no | Source | Key findings related to Fibromyalgia | Implications for diagnosis and treatment |
|---|---|---|---|
| 1. | Centralized nociplastic pain causing fibromyalgia: an emperor with no clothes? (28) | • Centralized nociplastic pain is the core of fibromyalgia, encompassing diverse symptoms. OMERACT identifies key symptoms. Individualized treatment based on clinimetric measures (FIQ, FAS) aids in assessing severity. Set realistic goals for tailored therapy.<br>• Self-administered questionnaires (FIQ, FAS, PHQ15) quantify fibromyalgia. Evolving diagnostic criteria offer nuanced severity assessment. Categorization based on optimal cut-off values aids individualized treatment goals. Multimodal therapy includes education, fitness, pharmacological (antidepressants, anticonvulsants), and non-pharmacological (exercise, cognitive therapy) approaches. | • Recognizing diverse symptoms is crucial for diagnosis. Clinimetric measures (FIQ, FAS) provide insights into daily functioning. Set realistic treatment goals based on severity categories.<br>• Individualized treatment and realistic goals are emphasized. A multidisciplinary approach, including both pharmacological and non-pharmacological strategies, is recommended. |
| 2. | Fibromyalgia position paper (29) | • Fibromyalgia (FM) is a complex syndrome with no objective signs or biomarkers, diagnosed based on patient-reported symptoms. Patient-reported outcomes (PROs) aid in identifying individual symptoms for tailored therapy. Various self-administered questionnaires (FIQ, FIQR, FAS, FSC, PHQ15) quantify symptoms and assist in categorizing severity.<br>• Multi-dimensional, disease-specific measures (FIQR, FIQ, FAS, PDS) assess FM severity. Individualized, patient-centered treatment is crucial. Three pillars of FM treatment include patient education and fitness, pharmacological (antidepressants, anticonvulsants), and psychotherapy. Non-pharmacological strategies such as balneotherapy, Tai Chi, acupuncture, and mindfulness interventions show promise. | • Diagnosis and follow-up rely on patients' symptoms. PROs help identify crucial symptoms, guiding tailored therapy. Severity categorization aids in individualized treatment.<br>• Severity scores guide treatment. A multidisciplinary approach, including both pharmacological and non-pharmacological interventions, is recommended. Mindfulness-based therapies and certain alternative treatments may benefit FM patients. |
| 3. | The Diagnosis of Fibromyalgia Syndrome (24) | • Fibromyalgia (FMS) is a widespread primary pain condition with a prevalence of 2%–4%. Recent research highlights changes in the central and peripheral nervous systems and immunological activity.<br>• Features indicating the need for FMS assessment include widespread pain, intrusive fatigue, hypersensitivities, symptoms lasting over 3 months, ineffective prior treatments, and feeling overwhelmed.<br>• FMS may coexist with other conditions, and clinicians should consider differentials. Diagnostic uncertainty may require a 'watchful waiting' strategy, and a shared plan for chronic pain management is essential. | • Diagnosis is challenging due to the absence of clinical laboratory tests. Symptoms vary, making alignment with established categories difficult. Early and accurate diagnosis is crucial.<br>• Diagnosing FMS involves assessing widespread pain index (WPI) and symptom severity scale (SSS) scores. Referral to a specialist is recommended in uncertain cases.<br>• Clinical management involves addressing pain through information, rehabilitation, and support groups. Perioperative care considerations are vital for surgical cases with FMS. |
| 4. | Physical therapy modalities for treating fibromyalgia (25) | • Fibromyalgia is characterized by chronic musculoskeletal pain, hyperalgesia, and psychosomatic symptoms (fatigue, sleep disturbances, anxiety, depression, cognitive dysfunction, headache, gastrointestinal disorders)<br>• FM is prevalent, affecting millions worldwide, especially women<br>• Non-pharmacological therapies, particularly physical therapy, gaining importance | • Explore physical therapy as an alternative with fewer side effects<br>• Assess patient response to TENS and electroacupuncture; Consider individualized treatment protocols |

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| S.no | Source | Key findings related to Fibromyalgia | Implications for diagnosis and treatment |
|---|---|---|---|
| | | • Aerobic exercises, resistance exercises, and stretching effective in FM treatment and Aquatic therapy, Massage therapy (myofascial release), and Electrical analgesic currents (TENS, electroacupuncture) shows moderate to strong evidence for pain reduction and quality of life improvement | |
| 5. | Fibromyalgia: one year in review 2023 (26) | • Depression and Dissociative Disorders<br>• Small Nerve Fibre Neuropathy<br>• Provides a comprehensive overview of recent advancements in fibromyalgia research. | • High prevalence of depression (40%-80%). Potential link with dissociative experiences, trauma, and victimization. Antidepressants may influence dissociative symptoms.<br>• Associated with pain in fibromyalgia. Lower sensitivity and pain thresholds observed. Correlation with serum brain-derived neurotrophic factor. |

These studies collectively contribute to a nuanced understanding of fibromyalgia and underscore the importance of personalized and multidisciplinary approaches in its diagnosis and treatment.

**Factors associated with chronic pain**

Chronic pain develops due to a combination of biological, psychological, and social factors. Biologically, age, sex, obesity, and smoking increase the risk of chronic pain. Psychologically, factors such as fear avoidance, high initial pain levels, sleep disturbances, and stressful life events are linked to chronicity. Socially, lower socioeconomic status and poor support networks contribute to the development of chronic pain. Understanding these factors is vital for creating effective prevention and treatment strategies for managing chronic pain. Below is a (table 2) summarizing key factors associated with the development of chronic pain.

**Table 2: Key biological, psychological, and social factors influencing chronic pain**

| S.no | Category | Factors |
|---|---|---|
| 1. | **Biological** | - Age: Increasing age is associated with higher risk.<br>- Sex: Females are more likely to develop chronic pain.<br>- Obesity: Higher body mass index (>30) increases risk.<br>- Smoking: Associated with higher risk of chronic musculoskeletal pain. |
| 2. | **Psychological** | - Fear Avoidance: Avoiding activities due to fear of pain.<br>- High Initial Pain Levels: Severe pain at onset linked to chronicity.<br>- Sleep Disturbances: Poor sleep quality increases risk.<br>- Stressful Life Events: Contribute to chronic pain development. |
| 3. | Social | - Lower Socioeconomic Status: Linked to higher chronic pain risk.<br>- Poor Support Networks: Lack of social support increases risk. |

Chronic pain is influenced by a combination of biological, psychological, and social factors, each contributing to its development and persistence. Biological factors include increasing age, with older individuals having a higher prevalence of chronic pain, and sex differences, where females are more likely to experience chronic pain compared to males. Additionally, obesity (BMI >30) has been linked to an increased risk of chronic pain, while smoking is associated with a higher likelihood of developing musculoskeletal pain

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disorders (30–33). Psychological factors such as fear avoidance, where individuals restrict activity due to pain-related fear, and high initial pain levels have been found to correlate with pain chronicity. Moreover, poor sleep quality and stressful life events significantly contribute to prolonged pain experiences (32,34,35). Social factors also play a crucial role, with lower socioeconomic status and inadequate support networks increasing vulnerability to chronic pain conditions (32). These findings highlight the necessity of a multidimensional approach to chronic pain management, integrating targeted interventions addressing biological, psychological, and social determinants to improve patient outcomes.

### Limitations & Future Directions

This review has several limitations. First, it is a narrative review, and while comprehensive, it does not provide a systematic or meta-analytic assessment of the literature. Second, the studies included in this review may differ in their methodologies, definitions of chronic pain, and populations studied, which could introduce variability in the findings. Third, the search strategy may not have captured all relevant studies, particularly those published in languages other than English or studies with limited accessibility. Lastly, as chronic pain is influenced by complex interactions between biological, psychological, and social factors, this review might not fully address all the intricacies of these relationships.

Future directions should focus on integrating novel diagnostic tools, enhancing patient education, and implementing personalized multimodal therapies to address the diverse spectrum of chronic pain syndromes. These efforts aim to reduce the personal and societal burden of chronic pain, fostering a holistic approach to care that prioritizes both symptom management and patient well-being.

## CONCLUSION

Chronic pain syndromes, encompassing nociceptive, neuropathic, and nociplastic pain, represent a complex interplay of biological, neurological, and psychosocial factors. Nociceptive pain arises from tissue damage, neuropathic pain results from somatosensory system dysfunction, and nociplastic pain involves altered pain processing mechanisms. Each type exhibits distinct clinical manifestations and requires tailored diagnostic and therapeutic approaches. Emerging research in chronic pain highlights the role of molecular, genetic, and neurophysiological factors in understanding and managing pain syndromes. Neuropathic pain advancements include single-cell RNA sequencing to uncover gene expression changes, while studies on nociplastic pain, particularly fibromyalgia, underscore the importance of a multidisciplinary, patient-centered approach. Innovations in physical therapy, non-pharmacological interventions, and personalized treatments have demonstrated promise in improving the quality of life for individuals with chronic pain.

**Author Contribution**

| Author | Contribution |
|---|---|
| Aisha Ijlal* | Substantial Contribution to study design, analysis, acquisition of Data<br>Manuscript Writing<br>Has given Final Approval of the version to be published |
| Salman Jawed | Substantial Contribution to study design, acquisition and interpretation of Data<br>Critical Review and Manuscript Writing<br>Has given Final Approval of the version to be published |
| Nimarta Fulwani | Substantial Contribution to acquisition and interpretation of Data<br>Has given Final Approval of the version to be published |
| Anzalna Irfan | Contributed to Data Collection and Analysis<br>Has given Final Approval of the version to be published |
| Aqsa Mahdi | Contributed to Data Collection and Analysis<br>Has given Final Approval of the version to be published |
| Muhammad Yasir Saeed | Substantial Contribution to study design and Data Analysis<br>Has given Final Approval of the version to be published |
| Syeda Afreen Fatima | Contributed to study concept and Data collection<br>Has given Final Approval of the version to be published |
| Aisha Sattar Khan | Writing - Review & Editing, Assistance with Data Curation |

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