REVIEW ARTICLE

# Diagnosis and Pharmacological Management of Chronic Low Back Pain - A Review

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## Abstract

Chronic low back pain (cLBP) causes significant social, economic, and professional consequences and is a foremost public health and workplace concern. One of the main reasons for disability/incapacity is painful lumbar spine disorders. Most global guidelines for diagnosis place a strong emphasis on recognizing red, blue, yellow, and black flags to assess the risk of chronic pain or long-term disability/incapacity. Lower back discomfort and functional impairments have been successfully managed using different pharmacological treatments. A comprehensive understanding of available drugs and the mechanisms underlying LBP is necessary to select the appropriate pharmacological therapy. In this review, we have addressed alert flags for cLBP pain, along with pharmacological therapy modalities such as acetaminophen, NSAIDs, opioids, skeletal muscle relaxants, anticonvulsants, Tricyclic antidepressants (TCA), serotonin–norepinephrine reuptake inhibitors (SNRI), and topical treatments for persistent lower back pain.

**Keywords:** *Chronic back pain, low back pain, alert flags, diagnosis, pharmacological management.*

## INTRODUCTION

Chronic low back pain (cLBP) is defined in various ways, with some sources such as the French Agency for Healthcare Evaluation (Agence Nationale d'Évaluation en Santé, ANAES) describing it as persistent lumbar pain lasting more than three months. In contrast, others define it as pain that persists for at least 6 months (the American Society of Interventional Pain Physicians, ASIPP) [1]. The term "nonspecific low back pain" originated in a 1966 study that found that, in a general practice setting, the precise cause of chronic low back pain could not be determined in 79% of men and 89% of women [2]. The World Health Organization conducted a global Survey to estimate the cross-country mean proportion of the population with pain in the past 30 days, reporting 27.5% [3]. There are reports of 4% cLBP prevalence in individuals aged 24 to 39 years, with a linear increase to approximately 20% in the 6$^{th}$ decade of life [4].

The usefulness of clinical examination and imaging in diagnosing cLBP remains a topic of ongoing debate. When it comes to treatment, most international recommendations emphasize non-pharmacological approaches such as exercises, regular physical activity, physical therapy, and patient education. In some instances, multidisciplinary rehabilitation is considered the primary treatment for individuals with non-specific cLBP. The use of various medications is also debated and may be appropriate for carefully selected patients with well-defined characteristics. Diagnostic accuracy for cLBP can be limited. Nonetheless, all major guidelines advocate for a multimodal treatment strategy. In everyday clinical settings, managing non-specific cLBP typically involves a combination of non-drug and drug-based interventions. Future studies should further personalize these treatment plans [5].

LBP may be classified as neuropathic, nociceptive, or nociplastic, the latter referring to pain resulting from altered nociception without apparent signs of tissue damage or nerve injury [6]. A recent grouping system for cLBP classifies patients into three pain categories based on likely underlying mechanisms and the presence or absence of degenerative changes. Non-degenerative cLBP includes pain stemming from identifiable conditions like trauma, tumors, spondylolysis, infections or inflammatory diseases. In such cases, cLBP may indicate a potentially grave medical condition that warrants thorough diagnostic evaluation or referral to a specialist [7]. Chronic low back pain (cLBP) of unknown origin refers to pain that does not appear to be linked to any identifiable anatomical abnormalities. In such cases, assessment tools such as the Fear Avoidance Beliefs Questionnaire and similar scales can be helpful. The term "degenerative cLBP" has now largely replaced "nonspecific low back pain" to define pain associated with degenerative changes in the intervertebral discs, facet joints, and/or ligaments, which may occur with or without localized or overall changes in spinal alignment [8]. Taking a thorough medical history is crucial in narrowing down the differential diagnosis, guiding the physical examination, and tailoring treatment plans to the individual patient. This section begins by addressing the key components of history-taking specific to

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Received: July 07, 2025; Revised: November 12, 2025; Accepted: November 18, 2025
DOI: https://doi.org/10.37184/jlnh.2959-1805.4.12

  

low back pain, including the identification of "Red" and "Yellow" flags. It also touches on other relevant historical factors that may contribute to the development of cLBP, influence treatment choices, affect recovery outcomes, or point to conditions that could mimic cLBP. While not exhaustive, the discussion emphasizes the most pertinent elements of medical history necessary for effectively evaluating cases with cLBP [9].

## METHODOLOGY

The literature was searched electronically on PubMed and Google Scholar. Systematic keywords used were: Chronic low back pain, management of chronic low back pain, and diagnosis and management of chronic low back pain. The following filters were applied: Free full text, Review, English, Humans, and adults. We have selected 76 articles in total. All references were moved to EndNote X9. A total of 71 articles were included in the final review based on their provision of comprehensive information on the clinical presentation of chronic low back pain, alert flags, and its management. 5 articles were excluded for reporting data with repetitions and for relevance to specific interventional approaches, such as Yoga, transcutaneous electrical nerve stimulation, acupuncture, virtual reality exposure therapy, and laser therapy.

## CHARACTERISTICS FOR CHRONIC LOW BACK PAIN EVALUATION

A detailed pain history is essential for identifying key characteristics of chronic low back pain (cLBP), guiding targeted questioning and physical examination, and uncovering any co-existing conditions that may impact treatment decisions.

***Pain Onset:*** It includes information on LBP for patients. The onset should note whether a specific triggering event occurred, *e.g*., pain beginning after an accident or a fall, *versus* pain that initiated without any trauma or identifiable cause [9].

***Progression:*** Pain progression should be noted. Pain that has existed for years but has worsened over the past month may raise diagnostic or therapeutic concerns [9].

***Location:*** Pain location should be correctly identified (*i.e*., paraspinal for facets, *etc*). Sometimes, patients describe pain as diffuse and widespread [9].

***Characteristic:*** The descriptions usually vary, *e.g*., dull, sharp, stabbing, crampy, and/or burning, *etc*. A precise description may be helpful to elucidate a probable systemic connection (*e.g.*, morning stiffness for more than 30 minutes may suggest inflammatory back pain *versus* degenerative cLBP) [9].

***Severity:*** Patients rate the pain from zero to ten out of ten (0-10/10) using a numeric rating scale (NRS) or a visual Analog scale (VAS), *i.e*., 3/10 pain during resting that rises to 6/10 pain with lumbar extension [9].

***Provoking and Relieving Elements:*** Provoking elements include factors that worsen the patients' back pain. Positions (sitting/standing), activities (flexion/extension, walking, *etc*.), or timing (morning/evening) can be targeted when pain intensifies. Relieving elements can be identified, *i.e*., the position in which pain is reduced. The patients may respond to treatment options after questioning, *i.e*., relief in pain with ice or after taking medication [9].

***Symptoms Radiation:*** The patients may report radiation of symptoms, *e.g*., outside the lumbar spine area and preceding the gluteal folds; the pain with a dermatomal or radicular pattern towards the entire lower extremity is suspected to have a neural origin [9].

***Other Related Symptoms:*** Other symptoms may suggest other processes distinct from spinal degenerative changes, *e.g*., weight loss, numbness, weakness, fever, pain that worsens at night, or abdominal pain [9].

***Responses to Medical Therapies***: Responses to various treatments, including physical therapy, medications/injectables, and a comprehensive surgical history, should be gathered. Other modalities include acupuncture, yoga, massage, traction, heat/ice packs, *etc.*, with variable levels of evidence and recommendations; if yoga was beneficial specifically for a patient's myofascial pain for a couple of years, then the patient should return to yoga [9].

### Warning Signs (Alert Flags) and Associated Features of Chronic Low Back Pain

#### *Red Flags*

"Red flags" refer to specific historical details and signs/symptoms that may indicate a more serious underlying condition as the cause of LBP. First introduced in the 1980s [10], the concept has since evolved, but there remains no universal consensus on which indicators should be classified as red flags. A comprehensive 2016 review published in the European Spine Journal analyzed 21 guidelines issued by different countries and organizations, ultimately including 16 in the comparison. The most frequently associated conditions identified by red flags were malignancy, fractures, infections, and cauda equina syndrome (CES), with additional references to ankylosing spondylitis, aortic aneurysms, and myelopathy [11]. Severe underlying conditions indicated by red flags in cases of low back pain are

uncommon [12]. However, clinicians should remain vigilant by thoroughly reviewing the patient's history and consistently monitoring for any new or worsening symptoms during follow-up visits. The following four are the most common pathological states detailed in the review red flag guidelines:

- ***Malignancy:*** Fourteen red flags associated with malignancy were recognized, with a history of carcinoma being the only one consistently mentioned across all guidelines, with a small contribution of about 0.7%. The second-most-cited indicator was unintentional weight loss. Additional red flags encompassed pain occurring at rest or during the night, increased ESR levels, decreased appetite, persistent fatigue, fever, paraparesis, progressively worsening symptoms, and a solid clinical doubt of malignancy [13].
- ***Fracture:*** Eleven red flags have been identified as potential indicators of spinal fracture. The most frequently reported is significant trauma, followed by long-term steroid use or immunosuppression. Other commonly noted factors include older age (typically between 50 and 70 years), female sex, a history of former fractures, low body weight, pronounced thoracic kyphosis, structural deformities, and even slight trauma. Fractures account for approximately 4% of red flags for chronic low back pain [13].
- ***Infection:*** The most frequently cited indicators of possible infection include fever, corticosteroid use, immunosuppression, intravenous drug use, pain occurring at night or while at rest, and localized bone tenderness over the spinous processes. Infections are usually a red flag at 0.01% for chronic low back pain [13].
- ***Cauda Equina Syndrome (CES):*** In total, nine red flags were identified as indicators of potential cauda equina syndrome (CES), with the most reported being new-onset saddle anesthesia (numbness in the perineal area) and bladder dysfunction [11]. Variability in CES prevalence has been observed, with reports of annual prevalence ranging from 0.34 to 7 per 100,000 individuals [14].

### *Yellow Flags*

The notion of "yellow flags" was first introduced by Kendall and colleagues in 1997, following a joint initiative in New Zealand involving the National Health Committee and the Accident Rehabilitation Compensation Insurance Corporation (ACC). This project highlighted psychosocial risk elements that contribute to long-term incapacity and work-associated absence due to LBP [15, 16]. Ever since, growing attention has been given to the role of psychosocial and occupational aspects in the progression of cLBP. The North American Spine Society (NASS), in its evidence-based review, issued a Grade A recommendation, the utmost evidence level for assessing these factors, recognizing their significant impact on the development of disability associated with cLBP [17]. The European Guidelines for Chronic Low Back Pain define yellow flags as psychosocial risk aspects that may contribute to the persistence of pain and disability. These include:

1. Misconceptions and unhelpful beliefs about back pain, such as viewing it as harmful or inevitably incapacitating, or having unrealistic anticipations that passive management will be more effective than active ones.
2. Maladaptive pain actions, like fear-avoidance and decreased physical activity due to fear of pain aggravation.
3. Work-related or compensation concerns.
4. Emotional issues, including stress, anxiety, depression, and social exclusion.

When yellow flags are identified through patient history or screening tools, healthcare providers should consider incorporating cognitive and behavioral strategies into the treatment plan to support recovery [18].

### *Blue Flags*

These are prognostic factors that reflect how a worker views their job and work environment. They include:

- Physically demanding increased workload
- High job demands paired with limited control over work tasks
- Disability to amend or adjust work duties
- Insufficient social support in the workplace
- Stress to meet tight deadlines
- Low overall job satisfaction
- Work-related stress
- A sense of hopelessness about returning to work
- Fearing a recurrence of symptoms [19]

### *Black Flags*

"Black flags" are prognostic factors linked to organizational, healthcare, and insurance system issues. These include:

- Workplace policies that hinder a gradual return to work or restrict job modifications

- Financial instability
- Compensation system rules and eligibility criteria
- Financial incentives that may discourage returning to work
- Poor communication between the employee and the workplace
- Sick leave duration [19]

## MANAGEMENT OF CLBP

The management of LBP usually varies across different countries. Despite the limited clinical value of imaging in most cases, its use remains high, reported at 54% in the United States [20] and 56% in Italy [21]. Even though exercise is widely regarded as the most effective management for cLBP, many physiotherapists still rely primarily on passive therapies [22]. Likewise, many physicians tend to focus on medication-based approaches [23]. To improve patient outcomes and prevent progression to cLBP, it is essential to implement effective care strategies. The development and adoption of clinical guidelines have the potential to enhance the management of LBP [24]. In recent years, several countries, including the United States, Denmark, England, and Belgium, have published such guidelines to standardize and optimize treatment approaches [25-28]. The latest international guidelines [27], which include literature up to March 2016, aim to provide updated scientific evidence on LBP, with or without radiculalgia. The most recent guidelines were published in 2000 in France and are now outdated. To address this, the French National Authority for Health (FNAH), in response to a request from the National Health Insurance Fund, revised and updated the national guidelines on low back pain, including cases with associated radiculopathy [19].

### Interventional Care Approaches

There are several interventional strategies for cLBP, including exercise therapy and physical activity [19, 29], strongly endorsed by the American College of Occupational and Environmental Medicine (ACOEM). Exercises such as Pilates, yoga, and Tai Chi are often recommended to manage cLBP [17]. Physiotherapy is considered a primary treatment option for cLBP [19], such as the use of massage and soft tissue mobilization. Other procedures, such as transcutaneous electrical nerve stimulation (TENS), manual therapy, and the McKenzie method, are occasionally mentioned [17]. Cognitive behavioral therapy (CBT) is suggested alongside physical therapy to help reduce pain intensities and to enhance functional outcomes [30]. Interventions that address fear-avoidant behaviors, when combined with physical therapy within the first 6 months, may also be beneficial.

Additionally, mindfulness-based stress reduction techniques can be included in the treatment plan [13]. Patient education emphasizes the importance of encouraging maximum activity levels and supporting an early return to work or regular daily routines [29]. Multidisciplinary rehabilitation programs incorporate at least one physical element, typically exercise and activity, as well as at least one component addressing psychological, social, or occupational factors, in line with the biopsychosocial model. These include CBT, strategies for developing pain-handling abilities, and mindfulness-based stress decline methods [30]. Complementary therapies, including acupuncture and manual therapy, are the most widely endorsed [31].

### Pharmacological Treatments

There are various pharmacological options available for managing pain, particularly during acute flare-ups. For the majority of the individuals experiencing LBP—regardless of how long the symptoms have persisted—paracetamol (acetaminophen) and non-steroidal anti-inflammatory drugs (NSAIDs) are typically recommended as the first options for pain management. Although opioids provide more substantial pain relief, they are generally avoided as initial therapy because of their potential for dependence and misuse. In cases of acute LBP, skeletal muscle relaxants and benzodiazepines may be prescribed as supplementary treatments, though they often cause significant drowsiness. For chronic cases, tricyclic antidepressants and anticonvulsants may be considered, but their effectiveness in reducing pain remains limited or uncertain. It is also essential to recognize that depression frequently coexists with low back pain and should be managed appropriately [32].

#### *Acetaminophen and NSAIDs*

There is broad agreement on utilizing oral NSAIDs as a first-line therapy for LBP, provided they are used with caution, considering potential toxicity and individual risk factors. The standard guideline is to use the lowest effective dose for the shortest duration necessary. When NSAIDs are contraindicated, not well-tolerated, or ineffective, weak opioids, either alone or combined with acetaminophen, are typically recommended as a second-line option. However, there is no apparent unanimity in using acetaminophen alone. Additionally, the use of opioids, antidepressants, anticonvulsants, and muscle relaxants remains controversial and varies across guidelines [33, 34]. Acetaminophen is a commonly used pain-relieving and anti-inflammatory drug, though

its exact mechanism of action remains unclear. It is frequently chosen as an initial treatment for patients with low back pain (LBP), likely due to its ease of access, over-the-counter availability, and generally safe profile. However, individuals with liver impairment or those who consume large amounts of alcohol are at greater risk of adverse effects.

Additionally, prolonged use of acetaminophen may lead to potential cardiovascular, respiratory, or kidney-related complications [35]. Non-steroidal anti-inflammatory drugs (NSAIDs) provide pain relief and reduce inflammation by blocking the activity of cyclooxygenase (COX) enzymes. They are widely used in the treatment of low back pain (LBP), with several types such as ibuprofen, diclofenac, naproxen, meloxicam, and celecoxib available over the counter. Most clinical guidelines recommend NSAIDs as first- or second-line therapies for managing LBP [26]. Moderate-quality evidence indicates that NSAIDs provide a modest decrease in low back pain intensity and some improvement in functional ability [36]. Nevertheless, the possible side effects of NSAIDs on the gastrointestinal, liver, heart, and kidney systems particularly in older adults should be carefully considered. Clinical guidelines advise combining NSAIDs with gastroprotective therapy and using the minimum effective dose for the shortest necessary duration [26].

### *Skeletal Muscle Relaxants*

Muscle relaxants are commonly prescribed for LBP thought to originate from myofascial causes, and some formulations are combined with acetaminophen. This drug class comprises various agents with different chemical structures that act on multiple receptor types. Examples include tizanidine (an alpha-2 agonist), orphenadrine (a muscarinic cholinergic antagonist and antihistamine), carisoprodol (which acts through GABAergic pathways), cyclobenzaprine (a 5-HT2 receptor antagonist), baclofen (a GABA-B agonist), and benzodiazepines. According to a systematic review, muscle relaxants excluding benzodiazepines offer only short-term pain relief in patients with LBP [37]. Research on the use of benzodiazepines for LBP is limited, with slightly more substantial support for their use in acute cases compared to chronic ones. In the management of neuropathic pain overall, there is little evidence backing the effectiveness of muscle relaxants, except possibly for baclofen, which, however, has not been evaluated explicitly for radiculopathy [38]. Muscle relaxants carry risks such as drowsiness, dependence, and potential misuse. Overall, there is no evidence supporting their long-term effectiveness in managing LBP. Therefore, their use should be limited to short durations and reserved for patients experiencing significant or recurrent muscle spasms associated with LBP [39].

### *Anticonvulsants*

Most clinical guidelines recommend gabapentin and pregabalin as first-line medications for the management of neuropathic pain [40]. Gabapentinoids produce pain-relieving effects by binding to the α-2-δ subunit of voltage-gated calcium channels on presynaptic terminals of afferent neurons. Since neuropathic mechanisms are believed to play a role in the development and continuation of lumbosacral radicular pain and neurogenic claudication, these medications are frequently prescribed for such conditions. However, systematic reviews of clinical trials have found that gabapentinoids offer no significant improvement over placebo or other analgesics in chronic low back pain, with or without radiculopathy. Additionally, patients using gabapentinoids commonly experience side effects such as dizziness, confusion, tiredness, and vision problems [41]. Concerns have also been raised regarding the potential for misuse, diversion, and dependence associated with prolonged use of these drugs. It is therefore advisable to conduct a trial period of up to four weeks at therapeutic doses and discontinue treatment if no meaningful improvement is observed [42].

### *Tricyclic Antidepressants (TCAs) and Serotonin–Norepinephrine Reuptake Inhibitors (SNRIs)*

Antidepressants are frequently prescribed to patients with LBP to help manage pain as well as associated symptoms such as depression, anxiety, and sleep disturbances. However, research findings on their effectiveness remain inconsistent. A recent systematic review on LBP pharmacotherapy found that tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) did not show significant pain relief compared to placebo, and the evidence regarding their side effects was inconclusive. In contrast, duloxetine demonstrated both pain reduction and improved function compared with placebo, though it was associated with a higher risk of discontinuation due to adverse effects. Similar to the approach with gabapentinoids, patients with LBP exhibiting strong neuropathic features may be considered for a short trial (two to four weeks) of a TCA or serotonin-norepinephrine reuptake inhibitor (SNRI), discontinuing the medication if adequate pain relief is not achieved [36].

### *Opioids*

Opioids are the most frequently prescribed medications for managing chronic LBP, with many patients relying on them for long-term pain control [43]. As with other pain-relieving drugs, there is little controlled trial evidence supporting the effectiveness of opioids for use beyond four months. Prolonged opioid therapy is also linked to a higher risk of dependence and overdose. A systematic review of 15 studies involving patients with LBP lasting three months or more, who used opioids for at least one month, showed short-term benefits, with moderate improvement in pain and minor improvement in function compared to placebo [44]. Two recent systematic reviews examining the short-term use of opioids for low back pain reported moderate-quality evidence supporting their effectiveness in reducing pain [45].

### *Topical Treatments*

Topical capsicum is an effective short-term treatment for LBP [46]. Two herbal-based topical remedies, Capsicum frutescens (commonly known as cayenne or capsaicin) and a blend of Gaultheria procumbens (wintergreen oil) with Mentha piperita (peppermint oil), are considered viable alternatives to NSAIDs and COX-2 inhibitors, potentially offering a more favorable benefit-to-risk profile. Capsaicin acts as a potent local stimulant that, with repetitive use, leads to sustained pain desensitization [47]. In clinical settings, topical capsaicin is frequently used to manage cLBP. Its effectiveness is supported by three randomized, placebo-controlled trials: one on acute mechanical back pain and two on chronic nonspecific back pain [48], all of which demonstrated significant reductions in pain compared with placebo. A later review [49] of two of these trials found that capsaicin achieved a statistically substantial 60% decline in pain. Adverse effects are generally mild, with about one-third of patients experiencing localized skin reactions [47].

## CONCLUSION

Identifying the underlying causes of cLBP remains a substantial challenge in both clinical research and practice, given its multifactorial nature, which involves both anatomical and psychosocial components. Yet, contemporary advances in clinical assessment techniques, imaging, and a better understanding of spinal biomechanics have provided new insights into cLBP. This has led to increased interest in the concept of patient phenotyping, which is developing more accurate, individualized diagnoses and personalized, effective treatment strategies. While all major guidelines emphasize a multimodal treatment approach, the integration of both pharmacological and non-pharmacological therapies should be individualized. Future research must prioritize the development of more tailored and personalized treatment pathways for managing cLBP.

## FUNDING

None.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ACKNOWLEDGEMENTS

Declared none.

## AUTHORS' CONTRIBUTION

MS: Conceptualization, literature search, critical review, and editing.

AK: Literature search, Drafting of the initial manuscript.

## GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work the author(s) limitedly used ChatGPT (GPT-4, OpenAI) to get language suggestions and do minor proofreading in some parts of the manuscript. After using this tool/ service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

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