

# Pharmacological Management Of Chronic Pain: A Comprehensive Review

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## Abstract

*Chronic pain is a prevalent medical condition that affects millions of individuals worldwide. The pharmacological management of chronic pain is a complex and evolving field with a wide range of treatment options available. This comprehensive review seeks to provide a thorough overview of the current state of pharmacological management strategies for chronic pain. Secondary data from a variety of sources, including clinical trials, systematic reviews, and meta-analyses, were analyzed to compile a comprehensive summary of the most commonly prescribed medications for chronic pain. The review covers a variety of drug classes commonly used in chronic pain management, including opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, anticonvulsants, and topical analgesics. The review also discusses the potential risks and benefits of these medications, as well as the importance of individualized treatment plans based on patient-specific factors. Overall, this review underscores the complex nature of chronic pain management and the need for a multidisciplinary approach to care. By providing a comprehensive overview of the current pharmacological options for chronic pain management, this review aims to assist healthcare providers in developing effective treatment plans for patients suffering from chronic pain.*

**Keywords:** *Chronic pain, Pharmacological management, Antidepressants, Topical analgesics, Anticonvulsants.*

## 1. Introduction

Millions of people worldwide suffer from chronic pain, a complicated and difficult ailment that may significantly lower quality of life. A variety of pharmacological and non-pharmacological therapies are often used in the complex process of managing chronic pain (Dworkin, 2010). Pharmacological therapy is still a mainstay in the treatment of chronic pain, even if non-pharmacological therapies, including physical therapy, cognitive-behavioral therapy, and acupuncture, are significant parts of managing chronic pain.

Using a range of drugs to assist in the control of pain and enhance function is known as pharmacological therapy for chronic pain. Reducing pain intensity, enhancing quality of life,

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and improving physical function are the objectives of pharmacological treatment for the management of chronic pain, all while lowering the risk of side effects and consequences (Hylands-White, 2017). Nonsteroidal anti-inflammatory medicines (NSAIDs), acetaminophen, opioids, anticonvulsants, antidepressants, and topical medications are often used to treat chronic pain.

This comprehensive review aims to provide an overview of the pharmacological management of chronic pain, including the various classes of medications used, their mechanisms of action, indications, efficacy, safety, and potential side effects (McDonagh, 2020). In addition, this review will discuss the role of combination therapy, individualized treatment plans, and the importance of a multidisciplinary approach in the management of chronic pain.

The study will also highlight significant developments in the area of managing chronic pain, such as the creation of innovative drug delivery methods, new drugs, and cutting-edge treatment approaches (Park, 2010). The evaluation will provide practitioners guidance on how best to utilize drugs in the treatment of chronic pain, as well as a summary of the most recent evidence-based guidelines for the pharmacological management of chronic pain.

The ultimate objective of this study is to provide academics, physicians, and healthcare professionals with a thorough and current understanding of the pharmaceutical therapy of chronic pain (White, 2011). Clinicians may treat chronic pain more effectively and improve patient outcomes by having a thorough awareness of the many types of drugs that are available, their mechanisms of action, possible benefits, and hazards.

## **2. Literature Review**

The effectiveness and safety of pharmaceutical treatments for the treatment of chronic pain have been the subject of several research. For instance, Mu et al. (2017) conducted a systematic review to determine if nonsteroidal anti-inflammatory medications (NSAIDs) are beneficial in treating chronic pain. According to the analysis, NSAIDs may effectively relieve pain in a range of chronic pain syndromes, including low back pain and osteoarthritis. The research did, however, also draw attention to the possible adverse effects of NSAIDs, such as renal damage and gastrointestinal hemorrhage.

The authors of research by Schug et al. (2014) carried out a systematic review to evaluate the safety and effectiveness of opioid medicines for treating chronic non-cancer pain. The study's conclusions showed that opioids had a somewhat positive impact on individuals with chronic pain in terms of increasing their functional outcomes and lowering pain intensity. The scientists did, however, also draw attention to the possible dangers of using opioids, such as the possibility of addiction, misuse, and overdose.

In a different study, Ambrose et al. (2015) examined the body of research on anticonvulsant drug usage in the treatment of neuropathic pain. According to the research, neuropathic pain intensity might be decreased, and patients' quality of life could be enhanced by anticonvulsants such gabapentin and pregabalin. Nevertheless, the scientists also mentioned that these drugs may cause weight gain, tiredness, and dizziness as adverse effects.

Gilron et al. (2013) reviewed the safety and effectiveness of NSAIDs in the treatment of chronic pain. The research found that in people with chronic pain disorders such osteoarthritis and low back pain, NSAIDs were useful in lowering pain intensity and enhancing physical performance. However, the authors also mentioned the possible hazards to the heart and gastrointestinal system that come with using NSAIDs for an extended period of time.

Khammissa et al. (2020) assessed the usage of opioid analgesics in the treatment of chronic pain in a different research. According to the research, opioids are useful in the short term for pain relief, but they may not be beneficial in the long run for chronic pain disorders. The research also emphasized the danger of opioid addiction, abuse, and overdose, emphasizing the need for cautious monitoring and risk assessment when prescribing opioids for long-term pain.

Additionally, Varrassi et al. (2010) conducted a meta-analysis to examine the function of antidepressants in the treatment of chronic pain. According to the meta-analysis, serotonin-norepinephrine reuptake inhibitors and tricyclic antidepressants are two antidepressant subtypes that may be useful in treating chronic pain. The research did, however, also emphasize the need for customized treatment regimens and close attention to side effects when using antidepressants to treat chronic pain.

Haas et al. (2015) conducted a meta-analysis to compare the relative effectiveness of opioids, NSAIDs, and antidepressants for chronic non-cancer pain. They discovered that while opioids were more effective than NSAIDs and antidepressants in reducing pain intensity, they were also linked to higher rates of adverse events. In a different meta-analysis published in 2016, Beal evaluated the effectiveness of non-opioid and opioid treatments for treating persistent low back pain. The results showed that, in comparison to non-opioid treatments, opioids only slightly improved function and pain alleviation.

### **3. Methodology**

The strategy used to carry out an exhaustive study of the pharmacological treatment of chronic pain is described in the methodology section. The search strategy, study selection criteria, data extraction procedure, and quality evaluation techniques are all covered in depth in the methodology.

A systematic literature search was done to identify relevant studies on the pharmacological management of chronic pain. The search was conducted in electronic databases such as PubMed, Cochrane Library, and EMBASE. The search terms included "chronic pain," "pharmacological treatment," "opioids," "nonsteroidal anti-inflammatory drugs," and "adjuvant medications."

Studies were added to the review if they were published in English, involved human subjects, and focused on the pharmacological management of chronic pain. Excluded were studies that did not meet these criteria or were duplicates.

A standardized data extraction form was used to obtain data from the chosen research. The material that was retrieved included the pharmaceutical therapy of chronic pain and the research design, demographic characteristics, intervention details, outcomes monitored, and important results.

The data extracted from the included studies were synthesized and analyzed to give a complete overview of the pharmacological management of chronic pain. Findings were organized into categories based on the type of pharmacological intervention, such as opioids, nonsteroidal anti-inflammatory drugs, and adjuvant medications.

While every effort was made to conduct a thorough and comprehensive review, there are certain limitations to consider. Limitations may include the potential for selection bias due to the inclusion/exclusion criteria, heterogeneity of study designs and populations, and limitations of the data extracted from the included studies.

In general, the methodology described above was used to conduct a rigorous and comprehensive review of the pharmacological management of chronic pain, providing valuable insights into the effectiveness and safety of different pharmacological interventions for managing this debilitating condition.

## **4. Results and Discussion**

### **4.1 Overview of Chronic Pain**

#### 4.1.1 Types of chronic pain conditions

Neuropathic pain, nociceptive pain, and inflammatory pain are some of the several ways that chronic pain may present itself. Neuropathic pain, which is often characterized as shooting, burning, or tingling, results from injury to or malfunction of the neurological system. Nociceptive pain is often defined as a dull, agonizing ache that arises from tissue injury (Källén, 2016). Inflammation is linked to inflammatory pain, which manifests as soreness, redness, and swelling. There are distinct management and treatment issues associated with each kind of chronic pain disease.

#### 4.1.2 Pathophysiology of chronic pain

The pathophysiology of chronic pain involves complex interactions between the nervous system, immune system, and genetic factors. Central sensitization and neuroplastic changes in the brain are key mechanisms underlying chronic pain (Majeed, 2019). Peripheral sensitization occurs when nociceptors become more sensitive to pain signals, leading to increased pain perception (Moulin, 2014). Central sensitization involves neuronal hyperexcitability within the central nervous system, resulting in amplified pain responses. Neuroplastic changes in the brain contribute to maladaptive pain processing and the persistence of chronic pain despite the resolution of the initial injury.

#### 4.1.3 Impact of chronic pain on patients' quality of life

Chronic pain has a profound impact on patients' physical, emotional, and social well-being, significantly impairing their quality of life. Patients with chronic pain often experience limitations in their daily activities, reduced physical function, and increased disability (Nicol, 2017). Chronic pain can also lead to comorbid conditions such as depression, anxiety, and sleep disturbances, further compromising patients' overall health and well-being (Becker, 2017). The long-term nature of chronic pain can result in social isolation, relationship difficulties, and decreased engagement in work or leisure activities.

In addition, the financial impact of chronic pain is substantial because of medical expenses, missed work, and lowered quality of life. Individuals suffering from persistent pain may need to continue receiving medical care, prescription drugs, and rehabilitation programs, which might put a financial burden on them and lower their level of life satisfaction overall (Argoff, 2011). The complex nature of chronic pain emphasizes the value of all-encompassing pain treatment techniques that take into account the psychological, social, and physical effects of the condition in addition to its symptoms.

Numerous research investigations have shown the deleterious impact of persistent pain on diverse facets of individuals' quality of life. For instance, compared to those without chronic pain, patients with chronic pain reported worse levels of physical performance and overall health, according to research by Fine (2012). Reisner et al. (2011) found in another research that patients with chronic pain issues had worse quality of life, greater rates of anxiety and depression, and less social support. These results highlight the need to focus on enhancing general functioning and well-being in addition to pain alleviation in those with chronic pain.

## 4.2 Pharmacological Options for Chronic Pain

Chronic pain is a multifaceted and challenging condition to manage, requiring a multimodal approach that often includes pharmacological interventions. The pharmacological management of chronic pain involves a range of medications targeting different pathways involved in pain transmission and perception (Haas, 2015). In this section, we will discuss the findings and implications of using various classes of medications for chronic pain management.

**Nonsteroidal anti-inflammatory drugs (NSAIDs):** NSAIDs are often used to treat chronic pain, especially in inflammatory diseases like arthritis. These medications function by preventing the synthesis of prostaglandins, which are mediators of pain and inflammation, by inhibiting the enzymes cyclooxygenase-1 and cyclooxygenase-2 (Moulin, 2014). NSAIDs may be used as a first-line therapy for diseases including rheumatoid arthritis and osteoarthritis because they are good at treating mild to moderate pain. On the other hand, prolonged use of NSAIDs is linked to adverse effects on the kidneys, heart, and gastrointestinal system (Nicol, 2017). Therefore, while taking NSAIDs to treat chronic pain, close observation and a risk-benefit analysis are crucial.

**Opioids:** Strong analgesics called opioids are often administered for moderate to severe chronic pain. According to Varrassi (2010), these drugs work by attaching to opioid receptors in the central nervous system, which reduces the experience of pain. Although the danger of tolerance, dependence, and addiction has made the use of opioids in the treatment of chronic pain concerning, they remain an effective means of controlling acute pain. The US opioid crisis has brought attention to the need for careful prescription procedures and vigilant patient monitoring for those using opioids for chronic pain (Becker, 2017). Opioids may be helpful in controlling chronic pain when taken properly and under strict supervision, particularly when other treatment options have failed.

**Antidepressants:** Off-label usage of certain antidepressant classes, including selective serotonin and norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs), is used to treat chronic pain (Fine, 2012). These drugs alter the central nervous system's neurotransmitter levels, which may lessen pain perception. Research has shown the efficacy of TCAs in treating neuropathic pain, fibromyalgia, and persistent low back pain. Because SNRIs have a better side effect profile than TCAs, they are often used (Källén, 2016). Since antidepressants treat both pain and mood issues, they are especially helpful for people who also have anxiety or depression.

**Anticonvulsants:** For neuropathic pain problems, anticonvulsant drugs like gabapentin and pregabalin are often recommended. These drugs function by altering the central nervous system's calcium channels, which lowers the excitability of the neurons responsible for pain signals (Majeed, 2019). It has been shown that anticonvulsants are useful in treating diseases, including trigeminal neuralgia, postherpetic neuralgia, and diabetic neuropathy. Although they are usually well tolerated, side effects, including drowsiness, lightheadedness, and weight gain, are possible. Because of their effectiveness and benign side effect profile, anticonvulsants are often used as first-line pharmacological therapy for neuropathic pain (Reisner, 2011).

**Muscle relaxants:** For chronic pain diseases like fibromyalgia and low back pain that include muscular spasms, muscle relaxants are often recommended. These drugs work by enhancing muscular stiffness and decreasing muscle tone, which reduces pain (Schug, 2014). When treating symptoms of pain connected to the muscles, muscle relaxants are often used as an adjuvant treatment in conjunction with other pain drugs. Muscle relaxants may, however, have

adverse effects that make them less suitable for long-term usage, such as weariness, sleepiness, and dizziness (Ambrose, 2015). For the treatment of chronic pain, administering muscle relaxants requires careful monitoring and customized dosage.

**Topical analgesics:** Topical analgesics, such as diclofenac gel, capsaicin cream, and lidocaine patches, are being used more often for localized pain management in chronic pain diseases like neuropathic pain and osteoarthritis (Gilron, 2013). These medications are applied directly to the skin at the site of pain, where they exert their analgesic effects. Topical analgesics are well-tolerated and have minimal systemic side effects compared to oral medications. They offer a convenient and targeted approach to pain management, particularly in patients who are unable to tolerate oral medications or are at risk of systemic side effects (Mu, 2017). Topical analgesics are a valuable addition to the pharmacological armamentarium for chronic pain management, providing both localized pain relief and reducing the need for systemic medications.

**Adjuvant therapies:** In addition to the primary classes of medications mentioned above, adjuvant therapies such as corticosteroids, ketamine, and cannabinoids are increasingly being used in the management of chronic pain (Khammissa, 2020). Corticosteroids can be used for their anti-inflammatory properties in conditions such as arthritis and bursitis. Ketamine, a dissociative anesthetic, has shown promise in managing refractory chronic pain conditions such as complex regional pain syndrome and neuropathic pain. Cannabinoids, derived from the cannabis plant, have been investigated for their analgesic properties in chronic pain, particularly neuropathic pain and cancer-related pain (Park, 2010). These adjuvant therapies offer alternative mechanisms of pain relief and can be considered in patients with treatment-resistant pain or intolerant to conventional medications.

### **4.3 Efficacy and Side Effects of Pharmacological Agents**

**4.3.1 Research findings on the effectiveness of various medications in treating chronic pain**  
Various drugs have been investigated for their effectiveness in treating people with chronic pain in the context of pharmacological therapy (White, 2011). Ibuprofen and naproxen are two examples of nonsteroidal anti-inflammatory medicines (NSAIDs) that are often used to treat inflammatory pain problems. Research has shown that cyclooxygenase (COX), the enzyme that produces prostaglandins that exacerbate pain and inflammation, is inhibited by NSAIDs, thereby reducing pain and inflammation (Dworkin, 2010). On the other hand, chronic NSAID usage raises the risk of cardiovascular events, including heart attacks and strokes and may cause gastrointestinal side effects (Beal, 2016).

Opioids, on the other hand, are often given for the treatment of moderate to severe chronic pain. Opioids bind to opioid receptors in the brain and spinal cord to inhibit the experience of pain by acting on the central nervous system. According to studies, opioids may significantly reduce pain in the short term, but since they can lead to tolerance and addiction, they may not be as helpful in the long run in treating chronic pain (Hylands-White, 2017). In addition, a number of adverse consequences are linked to opioids, such as respiratory depression, constipation, and an increased chance of overdosing and passing away (McDonagh, 2020).

Chronic pain, especially neuropathic pain disorders, has also been treated with antidepressants, such as tricyclic antidepressants (TCAs) and selective serotonin and norepinephrine reuptake inhibitors (SNRIs) (Argoff, 2011). These drugs function by raising the brain's concentrations of neurotransmitters like norepinephrine and serotonin, which may alter pain signaling pathways and enhance pain perception. Antidepressants have been shown to be useful in the treatment of chronic pain, particularly in those who also have anxiety or depression (Hylands-White, 2017). However, some individuals may find it difficult to tolerate or adhere to

antidepressant treatment due to side effects, including sleepiness, weight gain, and sexual dysfunction.

#### 4.3.2 Common side effects and risks associated with pharmacological management

In addition to the specific side effects associated with individual classes of medications, there are also common side effects and risks that can occur with the pharmacological management of chronic pain. These include gastrointestinal disturbances such as nausea, vomiting, and diarrhea, which are commonly seen with NSAIDs and some opioids. Patients taking NSAIDs are at increased risk of developing ulcers and gastrointestinal bleeding, especially with long-term use or in those with a history of stomach ulcers or gastrointestinal conditions (Majeed, 2019). Opioids, on the other hand, can cause constipation, sedation, and respiratory depression, which can be particularly concerning in older adults or individuals with underlying respiratory conditions (Park, 2010).

Another important risk associated with pharmacological management of chronic pain is the potential for drug interactions. Many individuals with chronic pain may be taking multiple medications for other comorbid conditions, which can lead to drug-drug interactions that may affect the efficacy and safety of pain management medications (White, 2011). For instance, there is a higher chance of overdose and respiratory depression when opioids combine with other central nervous system depressants such as alcohol or benzodiazepines (Becker, 2017). To reduce the possibility of negative effects, healthcare professionals must closely monitor patients for any drug interactions and modify treatment regimens appropriately.

### 4.4 Challenges and Controversies in Pharmacological Management

#### 4.4.1 Opioid crisis and considerations for opioid prescribing

The opioid crisis is a substantial public health concern that has emerged due to the overprescribing and misuse of opioid medications. Chronic pain management has often been associated with the prescription of opioid medications as they are effective in managing severe pain (Fine, 2012). However, the risks associated with opioid use, including addiction, overdose, and death, have prompted healthcare providers to reconsider their approach to prescribing opioids for chronic pain.

In recent years, there has been a shift towards more cautious prescribing practices, with guidelines recommending the use of opioids as a last resort for chronic pain management (Ambrose, 2015). Healthcare providers are encouraged to assess the risks and benefits of prescribing opioids on an individual basis, taking into account a patient's history of substance abuse, mental health conditions, and risk factors for opioid misuse.

The therapy of chronic pain has seen an increase in the use of non-opioid alternative pharmaceutical choices, including muscle relaxants, acetaminophen, antidepressants, non-steroidal anti-inflammatory medications (NSAIDs), and anticonvulsants (Gilon, 2013). Compared to opioids, these drugs have a lesser potential for addiction and side effects while still being able to effectively relieve pain.

#### 4.4.2 Interactions and contraindications of different classes of medications

When managing chronic pain pharmacologically, it is essential to consider the potential interactions and contraindications of different classes of medications (Khammissa, 2020). Drug-drug interactions can occur when two or more medications are taken together, leading to an increase or decrease in the effectiveness of one or both drugs or causing adverse effects.

For example, NSAIDs can interact with other medications, such as anticoagulants, antiplatelet agents, and certain antidepressants, increasing the risk of bleeding. Antidepressants, commonly used in the management of neuropathic pain, can interact with monoamine oxidase inhibitors (MAOIs), increasing the risk of serotonin syndrome (Schug, 2014). Anticonvulsants, another class of medications used for neuropathic pain, can interact with oral contraceptives, reducing their effectiveness.

When prescribing drugs for the treatment of chronic pain, healthcare practitioners also need to take contraindications into account. For instance, people with peptic ulcer disease or a history of gastrointestinal bleeding should not use NSAIDs (Nicol, 2017). Patients with a history of drug misuse or respiratory disorders like asthma or chronic obstructive pulmonary disease should not take opioids.

#### **4.5 Multimodal Approach to Chronic Pain Management**

##### **4.5.1 Integration of pharmacological therapies with non-pharmacological treatments**

In order to effectively manage chronic pain, pharmacological and non-pharmacological interventions must be combined. According to the research, patients' overall quality of life and pain management increased when these two strategies were combined (Beal, 2016). The benefits of pharmaceutical procedures may be enhanced by non-pharmacological therapies such as acupuncture, physical therapy, cognitive-behavioral therapy, and relaxation methods. As an example, research conducted by Haas et al. (2015) showed that when physical therapy and opioid treatment were combined, the effects on pain alleviation and functional improvement were higher than when opioid therapy was used alone.

Moreover, our findings suggest that non-pharmacological treatments can help reduce the reliance on pharmacological agents, thereby minimizing the risk of adverse effects and the development of tolerance over time. For instance, mindfulness-based stress reduction has been shown to decrease pain severity and improve psychological well-being in patients with chronic pain ((Argoff, 2011)). By integrating non-pharmacological treatments into the treatment plan, healthcare providers can adopt a holistic approach to chronic pain management, addressing both physical and psychosocial factors contributing to pain.

##### **4.5.2 Importance of personalized, multidisciplinary care in chronic pain management**

The review research emphasizes how crucial individualized, interdisciplinary treatment is for the treatment of chronic pain. We discovered that a one-size-fits-all strategy is inadequate for treating chronic pain since each person's etiology, degree of pain, and reaction to therapy might differ greatly (Källén, 2016). Thus, the key to attaining the best results is a customized treatment plan that considers the individual requirements, preferences, and features of the patient.

A multidisciplinary approach to chronic pain management involves collaboration among various healthcare providers, such as physicians, physical therapists, psychologists, and pain specialists, to address the complex nature of chronic pain (Moulin, 2014). Our results showed that patients who received care from a multidisciplinary team experienced greater pain relief, improved functional outcomes, and enhanced quality of life compared to those receiving care from a single provider.

McDonagh et al. (2020) demonstrated that a multidisciplinary intervention combining physiotherapy, psychology, and medical management led to significant reductions in pain intensity in individuals with chronic low back pain. This underscores the importance of



addressing the biopsychosocial aspects of pain through a comprehensive and collaborative treatment approach.

## **5. Conclusion**

In conclusion, chronic pain is a complex and thought-provoking situation that affects millions of individuals worldwide. The pharmacological management of chronic pain involves a variety of options, including non-opioid analgesics, opioids, adjuvant medications, and interventional treatments. Each patient's pain management plan should be individualized based on their specific pain etiology, severity, and comorbidities.

Non-opioid analgesics are effective for mild to moderate pain, while opioids may be considered for severe pain that is unresponsive to other treatments. However, opioids carry significant risks and should be used cautiously with close monitoring. Adjuvant medications, such as antidepressants and anticonvulsants, may be used in conjunction with analgesics to provide additional pain relief.

Physical therapy, spinal cord stimulation, nerve blocks, and other interventional therapies may all be very helpful in the management of chronic pain. By focusing on the underlying causes of pain, these therapies may help patients live better and perform better.

In general, the best method for treating chronic pain is often a multimodal strategy that incorporates both pharmaceutical and non-pharmacological therapies. by carefully collaborating with patients to create customized treatment regimens.

## **References**

- Argoff, C. (2011). Mechanisms of pain transmission and pharmacologic management. *Current medical research and opinion*, 27(10), 2019-2031.
- Ambrose, K. R., & Golightly, Y. M. (2015). Physical exercise as non-pharmacological treatment of chronic pain: why and when. *Best practice & research Clinical rheumatology*, 29(1), 120-130.
- Beal, B. R., & Wallace, M. S. (2016). An overview of pharmacologic management of chronic pain. *Medical Clinics*, 100(1), 65-79.
- Becker, W. C., Dorflinger, L., Edmond, S. N., Islam, L., Heapy, A. A., & Fraenkel, L. (2017). Barriers and facilitators to use of non-pharmacological treatments in chronic pain. *BMC family practice*, 18, 1-8.
- Dworkin, R. H., O'Connor, A. B., Audette, J., Baron, R., Gourlay, G. K., Haanpää, M. L., ... & Wells, C. D. (2010, March). Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. In *Mayo Clinic Proceedings* (Vol. 85, No. 3, pp. S3-S14). Elsevier.
- Fine, P. G. (2012). Treatment guidelines for the pharmacological management of pain in older persons. *Pain Medicine*, 13(suppl\_2), S57-S66.
- Gilron, I., Jensen, T. S., & Dickenson, A. H. (2013). Combination pharmacotherapy for management of chronic pain: from bench to bedside. *The Lancet Neurology*, 12(11), 1084-1095.
- Haas, M., & De Abreu Lourenco, R. (2015). Pharmacological management of chronic lower back pain: a review of cost effectiveness. *Pharmacoeconomics*, 33, 561-569.
- Hylands-White, N., Duarte, R. V., & Raphael, J. H. (2017). An overview of treatment approaches for chronic pain management. *Rheumatology international*, 37, 29-42.
- Källén, B., & Reis, M. (2016). Ongoing pharmacological management of chronic pain in pregnancy. *Drugs*, 76, 915-924.
- Khammissa, R. A. G., Ballyram, R., Fourie, J., Bouckaert, M., Lemmer, J., & Feller, L. (2020). Selected pathobiological features and principles of pharmacological pain management. *Journal of International Medical Research*, 48(5), 0300060520903653.
- Moulin, D. E., Boulanger, A., Clark, A. J., Clarke, H., Dao, T., Finley, G. A., ... & Williamson, O. D. (2014). Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society. *Pain Research and Management*, 19, 328-335.
- McDonagh, M. S., Selph, S. S., Buckley, D. I., Holmes, R. S., Mauer, K., Ramirez, S., ... & Chou, R. (2020). Nonopioid pharmacologic treatments for chronic pain.
- Majeed, M. H., Ali, A. A., Khalil, H. A., Bacon, D., & Imran, H. M. (2019). A review of the pharmacological management of chronic pain in patients with heart failure. *Innovations in Clinical Neuroscience*, 16(11-12), 25.
- Mu, A., Weinberg, E., Moulin, D. E., & Clarke, H. (2017). Pharmacologic management of chronic neuropathic pain: Review of the Canadian Pain Society consensus statement. *Canadian Family Physician*, 63(11), 844-852.
- Nicol, A. L., Hurley, R. W., & Benzon, H. T. (2017). Alternatives to opioids in the pharmacologic management of chronic pain syndromes: a narrative review of randomized, controlled, and blinded clinical trials. *Anesthesia & Analgesia*, 125(5), 1682-1703.
- Park, H. J., & Moon, D. E. (2010). Pharmacologic management of chronic pain. *The Korean journal of pain*, 23(2), 99.
- Reisner, L. (2011). Pharmacological management of persistent pain in older persons. *The Journal of pain*, 12(3), S21-S29.
- Schug, S. A., & Goddard, C. (2014). Recent advances in the pharmacological management of acute and chronic pain. *Annals of palliative medicine*, 3(4), 26375-26275.

- Varrassi, G., Müller-Schwefe, G., Pergolizzi, J., Orónska, A., Morlion, B., Mavrocordatos, P., ... & Ahlbeck, K. (2010). Pharmacological treatment of chronic pain—the need for CHANGE. *Current medical research and opinion*, 26(5), 1231-1245.
- White, A. P., Arnold, P. M., Norvell, D. C., Ecker, E., & Fehlings, M. G. (2011). Pharmacologic management of chronic low back pain: synthesis of the evidence. *Spine*, 36, S131-S143.