

THERAPEUTIC APPROACHES IN CHRONIC PAIN TREATMENT: AN INTEGRATIVE REVIEW OF ADVANCES AND PERSPECTIVES

Andreson Assunção Vasconcelos

Universidade Ceuma (Uniceuma)

Imperatriz/MA

<https://lattes.cnpq.br/4788882102100562>

Renata de Oliveira Machado Amorim

Faculdade de Medicina de Olinda (FMO)

Recife / PE

<https://orcid.org/0009-0005-9726-4284>

Charles Couto Gomes Júnior

Universidade Ceuma (Uniceuma)

Imperatriz/MA

<http://lattes.cnpq.br/4195190238256883>

Sebastião Fiorot da Silva

Centro Universitário do Espírito Santo
(UNESC)

Colatina - ES

<http://lattes.cnpq.br/8142070536139216>

Gabriel Victor Motta Cruz

Universidade Ceuma (Uniceuma)

Imperatriz/MA

<http://lattes.cnpq.br/6552800093754763>

Andre Luiz Borges Camporez

Universidade Ceuma (Uniceuma)

Imperatriz/MA

<http://lattes.cnpq.br/7849046288163808>

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



Lara Formigoni Binda

Centro Universitário do Espírito Santo
(UNESC)
Colatina - ES
<https://orcid.org/0009-0007-0813-7924>

Jorge José da Conceição Júnior

Centro Universitário do Espírito Santo
(UNESC)
Colatina - ES
<https://orcid.org/0000-0003-4824-8825>

Beatriz Lopes Gonçalves

Centro Universitário do Espírito Santo
(UNESC)
Colatina - ES
<http://lattes.cnpq.br/7499015507735293>

Ana Beatriz Silva Sidronio

Centro Universitário do Espírito Santo
(UNESC)
Colatina - ES
<http://lattes.cnpq.br/5566794502853900>

Júlia Martins Oliveira

Universidade Nove de Julho
Cidade/estado: Bauru - SP
<https://lattes.cnpq.br/5492601156847765>

Carolline Damas de Andrade Oliveira

Centro Universitário do Planalto Central
Aparecido dos Santos - Uniceplac
Cidade/estado: Brasília - DF
<http://lattes.cnpq.br/2136375601822657>

Abstract: Chronic pain is a debilitating condition that affects millions of people around the world. Effective treatment of chronic pain is a significant challenge, and several therapeutic approaches have been explored to alleviate symptoms and improve patients' quality of life. In this integrative review, we sought to investigate the effectiveness of different therapeutic interventions in the treatment of chronic pain, based on a comprehensive analysis of the scientific literature. Nineteen relevant references were selected, including systematic studies, meta-analyses and systematic reviews. The therapeutic approaches investigated covered a wide range of modalities, including vitamin D supplementation, non-invasive non-pharmacological treatments, psychological interventions, specific diets, prolotherapy, virtual reality, physical exercises, conservative interventions, spinal cord stimulation, acupuncture, transcutaneous electrical nerve stimulation (TENS), functional neuroimaging and medicinal cannabinoids. The results of this integrative review indicated that several therapeutic approaches showed significant benefits in the treatment of chronic pain. Vitamin D supplementation has been shown to be effective in relieving fibromyalgia syndrome and chronic musculoskeletal pain. Non-pharmacological non-invasive treatments such as cognitive-behavioral therapy, physical therapy and chiropractic manipulation have also been shown to be effective. Psychological interventions such as acceptance and commitment therapy have been effective in managing chronic pain in children and adolescents. Additionally, specific diets such as intermittent fasting, calorie restriction, and the Mediterranean diet have demonstrated benefits in relieving chronic musculoskeletal pain. Other therapeutic approaches such as prolotherapy, virtual reality, physical exercise, spinal cord stimulation, and acupuncture

have also been associated with positive outcomes in the management of chronic pain. However, it is important to highlight that each therapeutic approach has its own limitations and specific considerations. Not all therapeutic interventions are equally effective for all patients, and the selection of the most appropriate treatment must be based on an individualized assessment, considering the clinical aspects and the patient's preferences. In conclusion, this integrative review highlights the diversity of therapeutic approaches available for the management of chronic pain. From the available evidence, it can be inferred that the combination of different therapeutic approaches, adapted to the individual needs of patients, can provide better results in the relief of chronic pain. However, more research is needed to deepen the understanding of these therapeutic approaches and their clinical applications, as well as to investigate emerging promising interventions.

Keywords: chronic pain, treatment, opioids, exercise, diet, acupuncture, cannabis, prolotherapy, functional neuroimaging, virtual reality, non-pharmacological interventions.

INTRODUCTION

Chronic pain is a complex and debilitating condition that affects millions of people around the world. It is characterized by a persistent experience of pain that extends over an extended period of time, usually resulting from injury, illness, or disorders of the nervous system. Proper management of chronic pain is essential to improve patients' quality of life and reduce the negative impact that constant pain can have on their physical and psychological well-being.

In recent decades, several therapeutic approaches have been explored for the treatment of chronic pain, with the aim of alleviating pain, improving physical function

and promoting the general well-being of patients. In this integrative review, we sought to examine and summarize the current scientific literature on different therapeutic approaches in the treatment of chronic pain.

One of the therapeutic approaches considered is vitamin D supplementation, which has been studied in relation to its effectiveness in the treatment of fibromyalgia syndrome and chronic musculoskeletal pain Lombardo et al. (2022). Furthermore, non-invasive and non-pharmacological approaches have been explored, as evidenced by a systematic review that updated knowledge on non-pharmacological treatment of chronic pain Skelly et al. (2020).

The reduction of long-term opioid use in the management of non-cancer chronic pain is also an area of interest, and a systematic review and meta-analysis was performed to assess the effectiveness of interventions in this context Avery et al. (2022). In the pediatric context, psychological therapies have been investigated for the management of chronic pain in children and adolescents Fisher et al. (2018).

In addition, diet-related interventions have been explored, such as intermittent fasting, calorie restriction, and diets such as ketogenic and Mediterranean, which are considered part of the treatment plan to improve health and chronic musculoskeletal pain Cuevas-Cervera et al. (2022) and Dragan et al. (2020).

Other therapeutic approaches evaluated in this review include prolotherapy for patients with chronic musculoskeletal pain Bae et al.(2021), the use of virtual reality as an analgesic for acute and chronic pain in adults Mallari et al. (2019), spinal cord stimulation for the treatment of chronic pain Baranidharan et al. (2021), physical exercise as a chronic pain relief strategy Polaski et al. (2019), acupuncture for chronic low back pain Baroncini et al. (2022) and Witt et al. (2019),

transcutaneous electrical nerve stimulation (TENS) as a non-pharmacological treatment option for chronic pain Castellini et al. (2022) and Gibson et al. (2019) and the effects of chronic pain treatment on the functional and metabolic activities of the brain Kim et al. (2021).

Furthermore, the use of cannabinoids to treat chronic pain has been the subject of systematic reviews and meta-analyses Johal et al. (2020), Okusanya et al. (2020) and Lang-Illievich et al. (2023) and botulinum toxin as adjuvant therapy for chronic musculoskeletal pain Battista et al. (2021). Considerations about the best treatment options for adult and elderly patients with chronic musculoskeletal pain are also included in the review by Koechlin et al. (2019).

When reviewing the available evidence on therapeutic approaches in the management of chronic pain, it is important to consider the efficacy and safety of each intervention, as well as its clinical applicability and potential side effects. Understanding these therapeutic approaches can help guide healthcare professionals in choosing the best treatment options for their patients with chronic pain.

In this integrative review, we gathered a series of studies that address different therapeutic approaches in the treatment of chronic pain. The analysis of these studies will allow a more comprehensive understanding of the available options, providing valuable information for clinical decision making and improvement of care for patients with chronic pain.

By the end of this review, we hope to provide an updated overview of the scientific evidence on therapeutic approaches in the management of chronic pain, allowing for a better understanding of their efficacy, safety and potential clinical benefit. This can help guide clinical practice and provide useful information for effective management of

chronic pain, improving patients' quality of life.

METHODOLOGY

The methodology used in this integrative review consisted of a systematic search and careful selection of relevant studies on therapeutic approaches in the treatment of chronic pain based on a selection of 21 studies published between 2018 and 2023.

The following inclusion criteria were used: meta-analysis studies and systematic review of literature in English, in English, with free access to the full text. The review addresses a variety of therapeutic interventions and their effects in the management of chronic pain.

Among the therapeutic interventions studied, vitamin D supplementation stands out, which demonstrated efficacy in the treatment of fibromyalgia syndrome and chronic musculoskeletal pain. Other non-pharmacological approaches such as acupuncture, psychological therapies, transcutaneous electrical nerve stimulation (TENS) and prolotherapy have also been investigated and have shown promise for chronic pain relief.

Additionally, dietary interventions such as intermittent fasting, calorie restriction, and ketogenic and Mediterranean diets have been considered as part of an effective treatment plan to improve overall health and reduce chronic musculoskeletal pain.

Other therapeutic approaches have included the use of virtual reality as an analgesic for acute and chronic pain in adults, physical exercises to induce hypoalgesia and reduce chronic pain, spinal cord stimulation, acupuncture, medical cannabis use, and functional neuroimaging analyzes to understand changes in the brain resulting from chronic pain treatment.

The descriptors used to search for articles were chronic pain, treatment, opioids, exercise,

diet, acupuncture, cannabis, prolotherapy, functional neuroimaging, virtual reality, non-pharmacological interventions.

The review concludes that there are several effective therapeutic approaches in the treatment of chronic pain, but it is important to consider the individual characteristics of patients and select the most appropriate approach for each case. These approaches may offer alternatives to conventional treatments, such as the use of opioids, and provide personalized and effective options for managing chronic pain.

RESULTS

Chronic pain is a debilitating condition that affects millions of people around the world. Understanding effective therapeutic approaches for treating chronic pain is extremely important to improve patients' quality of life. In this integrative review, we explore several therapeutic interventions that have been studied in relation to the treatment of chronic pain.

One of the therapeutic approaches that has been investigated is vitamin D supplementation. A study carried out by Lombardo et al. (2022) investigated the effectiveness of vitamin D supplementation in the treatment of fibromyalgia syndrome and chronic musculoskeletal pain. The results showed significant benefits in reducing pain and improving the quality of life of patients.

Another therapeutic approach that has been widely studied is the use of non-pharmacological interventions. Skelly et al. (2020) conducted an updated systematic review on non-invasive and non-pharmacological treatment of chronic pain. They found evidence that various interventions such as physical therapy, acupuncture, transcutaneous electrical nerve stimulation (TENS) and virtual reality can be effective in relieving chronic pain.

The use of opioids for the treatment of chronic pain has been common practice, but it has also been associated with significant risks. Avery et al. (2022) performed a systematic review and meta-analysis to assess the effectiveness of interventions to reduce long-term opioid use in the management of chronic non-cancer pain. The results indicated that some interventions, such as cognitive-behavioral therapies and physical exercises, can be effective in reducing opioid use and managing chronic pain.

In the context of chronic pain treatment in children and adolescents, Fisher et al. (2018) conducted a systematic review of psychological therapies used in the management of chronic pain in this population. The authors found evidence that cognitive-behavioral therapies, biofeedback therapy and relaxation therapy can be effective in relieving chronic pain in children and adolescents.

Furthermore, some dietary interventions have been investigated in the treatment of chronic pain. Cuevas-Cervera et al. (2022) performed a systematic review to assess the effectiveness of intermittent fasting, calorie restriction, the ketogenic diet, and the Mediterranean diet in the management of chronic musculoskeletal pain. The results indicated that these interventions may have beneficial effects in relieving chronic pain.

Other therapeutic approaches studied include prolotherapy Bae et al. (2021), spinal cord stimulation Baranidharan et al. (2021), acupuncture Baroncini et al. (2022), virtual reality Mallari et al. (2019), physical exercise Polaski et al. (2019), conservative interventions Castellini et al. (2022), and medical cannabis use Okusanya et al. (2020) and Johal et al. (2020).

In summary, this integrative review highlighted several therapeutic approaches that have been studied in the management of chronic pain. Although there are a variety

of interventions available, it is important to consider the individual characteristics of patients and the multidisciplinary approach to achieve better results in the management of chronic pain.

DISCUSSION

Chronic pain is a debilitating condition that affects millions of people worldwide, presenting significant challenges for healthcare professionals in effectively managing it. In this integrative review, several therapeutic approaches were explored in the context of chronic pain management.

One of the studied therapeutic approaches is vitamin D supplementation. Lombardo et al. (2022) investigated the effectiveness of vitamin D supplementation in the treatment of fibromyalgia syndrome and chronic musculoskeletal pain. The results indicated significant benefits in reducing pain and improving the quality of life of patients. However, further studies are needed to confirm these results and establish adequate supplementation protocols.

Another therapeutic approach addressed in this review is the use of non-pharmacological interventions. Skelly et al. (2020) performed a systematic review that highlighted the effectiveness of non-invasive and non-pharmacological interventions such as physical therapy, acupuncture, transcutaneous electrical nerve stimulation (TENS) and virtual reality in relieving chronic pain. These interventions offer safe and effective treatment options, reducing dependence on medications and their potential side effects.

Reducing long-term opioid use has been an important concern in the management of chronic pain. Avery et al. (2022) performed a meta-analysis that evaluated the effectiveness of interventions to reduce opioid use in the treatment of chronic non-cancer pain. The results suggest that cognitive-behavioral

therapies and physical exercises can be effective alternatives to reduce opioid dependence and improve chronic pain management.

In addition to psychological and pharmacological interventions, dietary interventions have also been investigated in the treatment of chronic pain. Cuevas-Cervera et al. (2022) conducted a systematic review that analyzed the effect of different dietary approaches, such as intermittent fasting, caloric restriction, ketogenic diet, and Mediterranean diet, in the management of chronic musculoskeletal pain. The results suggest that these interventions may have beneficial effects in relieving chronic pain, although more research is needed to confirm these findings.

Other therapeutic approaches addressed in this review include prolotherapy Bae et al. (2021), spinal cord stimulation Baranidharan et al. (2021), acupuncture Baroncini et al. (2022), virtual reality Mallari et al. (2019), physical exercise Polaski et al. (2019), conservative interventions Castellini et al. (2022) and medical cannabis use Okusanya et al. (2020); Johal et al. (2020). These approaches have shown promising results in the management of chronic pain, but it is important to consider the individuality of patients and carefully select interventions based on each individual's specific needs.

In summary, this integrative review highlighted several therapeutic approaches in the management of chronic pain. The use of non-pharmacological interventions, cognitive-behavioral therapies, physical exercises and dietary approaches can provide effective and safe options for managing chronic pain. However, an individualized approach is essential, considering patient characteristics, pain severity and the presence of comorbidities, in order to optimize treatment results. Collaboration between different healthcare professionals

in a multidisciplinary approach is critical to ensure a comprehensive and personalized approach to chronic pain management.

FINAL CONSIDERATIONS

This integrative review highlights the importance of multifaceted therapeutic approaches in the management of chronic pain. From the comprehensive review of selected references, it is evident that there is no single approach that is universally effective for all patients. Instead, a personalized and individualized approach is needed to address the specific needs of each person living with chronic pain.

Non-pharmacological interventions such as physical therapy, acupuncture, TENS and virtual reality have been shown to be effective in relieving chronic pain, providing safe and effective options for those wishing to avoid or reduce medication use. In addition, cognitive-behavioral and psychological therapies play a key role in the management of chronic pain in children, adolescents and adults, helping to improve emotional well-being and quality of life.

Dietary approaches such as intermittent fasting, caloric restriction and the Mediterranean diet have shown benefits in managing chronic pain and can be considered as part of a comprehensive treatment plan.

Additionally, complementary therapies such as prolotherapy, spinal cord stimulation, and the use of medical cannabis have all shown promising results, although more research is needed to fully understand their long-term benefits and effects.

Importantly, chronic pain is a complex condition that may require a multimodal approach, involving a combination of therapeutic interventions. Each individual may respond differently to different approaches, and consultation with qualified healthcare professionals is critical to develop an individualized treatment plan.

As an ever-evolving field, chronic pain management continues to benefit from additional research and well-designed clinical trials. More research is needed to identify innovative therapeutic approaches, better understand mechanisms underlying chronic pain, and improve available treatment options.

In summary, non-pharmacological therapeutic approaches, cognitive-behavioral therapies, dietary interventions and complementary therapies play a crucial role in the management of chronic pain. With a personalized, multidisciplinary approach, it is possible to improve patients' quality of life and offer hope to those living with this challenging condition.

REFERENCES

1. LOMBARDO M, FERACO A, OTTAVIANI M, RIZZO G, CAMAJANI E, CAPRIO M, ARMANI A. **The Efficacy of Vitamin D Supplementation in the Treatment of Fibromyalgia Syndrome and Chronic Musculoskeletal Pain.** *Nutrients.* 2022 Jul 22;14(15):3010. doi: 10.3390/nu14153010. PMID: 35893864; PMCID: PMC9330000.
2. SKELLY AC, CHOU R, DETTORI JR, TURNER JA, FRIEDLY JL, RUNDELL SD, FU R, BRODT ED, WASSON N, KANTNER S, FERGUON AJR. **Noninvasive Nonpharmacological Treatment for Chronic Pain: A Systematic Review Update** [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2020 Apr. Report No.: 20-EHC009. PMID: 32338846.
3. AVERY N, MCNEILAGE AG, STANAWAY F, ASHTON-JAMES CE, BLYTH FM, MARTIN R, GHOLAMREZAEI A, GLARE P. **Efficacy of interventions to reduce long term opioid treatment for chronic non-cancer pain: systematic review and meta-analysis.** *BMJ.* 2022 Apr 4;377:e066375. doi: 10.1136/bmj-2021-066375. PMID: 35379650; PMCID: PMC8977989.

4. FISHERE, LAW E, DUDENEY J, PALERMO TM, STEWART G, ECCLESTON C. **Psychological therapies for the management of chronic and recurrent pain in children and adolescents.** *Cochrane Database Syst Rev.* 2018 Sep 29;9(9):CD003968. doi: 10.1002/14651858.CD003968.pub5. PMID: 30270423; PMCID: PMC6257251.
5. CUEVAS-CERVERA M, PEREZ-MONTILLA JJ, GONZALEZ-MUÑOZ A, GARCIA-RIOS MC, NAVARRO-LEDESMA S. **The Effectiveness of Intermittent Fasting, Time Restricted Feeding, Caloric Restriction, a Ketogenic Diet and the Mediterranean Diet as Part of the Treatment Plan to Improve Health and Chronic Musculoskeletal Pain: A Systematic Review.** *Int J Environ Res Public Health.* 2022 May 30;19(11):6698. doi: 10.3390/ijerph19116698. PMID: 35682282; PMCID: PMC9180920.
6. DRAGAN S, ȘERBAN MC, DAMIAN G, BULEU F, VALCOVICI M, CHRISTODORESCU R. **Dietary Patterns and Interventions to Alleviate Chronic Pain.** *Nutrients.* 2020 Aug 19;12(9):2510. doi: 10.3390/nu12092510. PMID: 32825189; PMCID: PMC7551034.
7. BAE G, KIM S, LEE S, LEE WY, LIM Y. **Prolotherapy for the patients with chronic musculoskeletal pain: systematic review and meta-analysis.** *Anesth Pain Med (Seoul).* 2021 Jan;16(1):81-95. doi: 10.17085/apm.20078. Epub 2020 Dec 16. PMID: 33348947; PMCID: PMC7861898.
8. MALLARI B, SPAETH EK, GOH H, BOYD BS. **Virtual reality as an analgesic for acute and chronic pain in adults: a systematic review and meta-analysis.** *J Pain Res.* 2019 Jul 3;12:2053-2085. doi: 10.2147/JPR.S200498. PMID: 31308733; PMCID: PMC6613199.
9. POLASKI AM, PHELPS AL, KOSTEK MC, SZUCS KA, KOLBER BJ. **Exercise-induced hypoalgesia: A meta-analysis of exercise dosing for the treatment of chronic pain.** *PLoS One.* 2019 Jan 9;14(1):e0210418. doi: 10.1371/journal.pone.0210418. PMID: 30625201; PMCID: PMC6326521.
10. CASTELLINI G, PILLASTRINI P, VANTI C, BARGERI S, GIAGIO S, BORDIGNON E, FASCIANI F, MARZIONI F, INNOCENTI T, CHIAROTTO A, GIANOLA S, BERTOZZI L. **Some conservative interventions are more effective than others for people with chronic non-specific neck pain: a systematic review and network meta-analysis.** *J Physiother.* 2022 Oct;68(4):244-254. doi: 10.1016/j.jphys.2022.09.007. Epub 2022 Oct 17. PMID: 36266185.
11. BARANIDHARAN G, EDGAR D, BRETHERTON B, CROWTHER T, LALKHEN AG, FRITZ AK, VAJRAMANI G. **Efficacy and Safety of 10 kHz Spinal Cord Stimulation for the Treatment of Chronic Pain: A Systematic Review and Narrative Synthesis of Real-World Retrospective Studies.** *Biomedicines.* 2021 Feb 11;9(2):180. doi: 10.3390/biomedicines9020180. PMID: 33670252; PMCID: PMC7918133.
12. BARONCINI A, MAFFULLI N, ESCHWEILER J, MOLSBERGER F, KLIMUCH A, MIGLIORINI F. **Acupuncture in chronic specific low back pain: a Bayesian network meta-analysis.** *J Orthop Surg Res.* 2022 Jun 20;17(1):319. doi: 10.1186/s13018-022-03212-3. PMID: 35725480; PMCID: PMC9208133.
13. GIBSON W, WAND BM, MEADS C, CATLEY MJ, O'CONNELL NE. **Transcutaneous electrical nerve stimulation (TENS) for chronic pain - an overview of Cochrane Reviews.** *Cochrane Database Syst Rev.* 2019 Apr 3;4(4):CD011890. doi: 10.1002/14651858.CD011890.pub3. PMID: 30941745; PMCID: PMC6446021.
14. KIM D, CHAE Y, PARK HJ, LEE IS. **Effects of Chronic Pain Treatment on Altered Functional and Metabolic Activities in the Brain: A Systematic Review and Meta-Analysis of Functional Neuroimaging Studies.** *Front Neurosci.* 2021 Jul 5;15:684926. doi: 10.3389/fnins.2021.684926. PMID: 34290582; PMCID: PMC8287208.
15. JOHAL H, DEVJI T, CHANG Y, SIMONE J, VANNABOUATHONG C, BHANDARI M. **Cannabinoids in Chronic Non-Cancer Pain: A Systematic Review and Meta-Analysis.** *Clin Med Insights Arthritis Musculoskelet Disord.* 2020 Feb 19;13:1179544120906461. doi: 10.1177/1179544120906461. PMID: 32127750; PMCID: PMC7031792.
16. KOECHLIN H, WHALLEY B, WELTON NJ, LOCHER C. **The best treatment option(s) for adult and elderly patients with chronic primary musculoskeletal pain: a protocol for a systematic review and network meta-analysis.** *Syst Rev.* 2019 Nov 9;8(1):269. doi: 10.1186/s13643-019-1174-6. PMID: 31706330; PMCID: PMC6842192.
17. OKUSANYA BO, ASAOLU IO, EHIRI JE, KIMARU LJ, OKECHUKWU A, ROSALES C. **Medical cannabis for the reduction of opioid dosage in the treatment of non-cancer chronic pain: a systematic review.** *Syst Rev.* 2020 Jul 28;9(1):167. doi: 10.1186/s13643-020-01425-3. PMID: 32723354; PMCID: PMC7388229.

18. WITT CM, VERTOSICK EA, FOSTER NE, LEWITH G, LINDE K, MACPHERSON H, SHERMAN KJ, VICKERS AJ; **Acupuncture Trialists' Collaboration. The Effect of Patient Characteristics on Acupuncture Treatment Outcomes: An Individual Patient Data Meta-Analysis of 20,827 Chronic Pain Patients in Randomized Controlled Trials.** Clin J Pain. 2019 May;35(5):428-434. doi: 10.1097/AJP.0000000000000691. PMID: 30908336; PMCID: PMC6450709.
19. BATTISTA S, BUZZATTI L, GANDOLFI M, FINOCCHI C, FALSIROLI ML, VICECONTI A, GIARDULLI B, TESTA M. **The Use of Botulinum Toxin A as an Adjunctive Therapy in the Management of Chronic Musculoskeletal Pain: A Systematic Review with Meta-Analysis.** Toxins (Basel). 2021 Sep 10;13(9):640. doi: 10.3390/toxins13090640. PMID: 34564644; PMCID: PMC8473399.
20. GIBSON W, WAND BM, MEADS C, CATLEY MJ, O'CONNELL NE. **Transcutaneous electrical nerve stimulation (TENS) for chronic pain - an overview of Cochrane Reviews.** Cochrane Database Syst Rev. 2019 Feb 19;2(2):CD011890. doi: 10.1002/14651858.CD011890.pub2. Update in: Cochrane Database Syst Rev. 2019 Apr 03;4:CD011890. PMID: 30776855; PMCID: PMC6379178.
21. LANG-LLIEVICH K, KLIVINYI C, LASSER C, BRENNAN CTA, SZILAGYI IS, BORNEMANN-CIMENTI H. **Palmitoylethanolamide in the Treatment of Chronic Pain: A Systematic Review and Meta-Analysis of Double-Blind Randomized Controlled Trials.** Nutrients. 2023 Mar 10;15(6):1350. doi: 10.3390/nu15061350. PMID: 36986081; PMCID: PMC10053226.