

Anesthesia, Laboratory, Radiology, Dental And Surgical Approaches In The Management Of Chronic Pain

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Abstract:

Chronic pain is a major public health problem affecting up to one-third of the global population. It imposes immense suffering and financial burden through direct medical costs, lost productivity, and reduced quality of life.

This review aims to summarize current knowledge on chronic pain management approaches, with a focus on strategies employed in the last 5 years.

Both pharmacological and non-pharmacological approaches have roles in chronic pain management. An individualized, multimodal treatment plan tailored to each patient offers the greatest potential for effectively addressing this prevalent issue. Additionally, A comprehensive chronic pain treatment

plan involves an array of interventional, complementary, and psychological approaches used adjunctively with pharmacological and non-pharmacological therapies.

A systematic search of PubMed, Embase, PsycINFO, and CINAHL databases was conducted to identify relevant articles published between January 2016 to December 2021. Search terms included "chronic pain", "management", "treatment", and "intervention". Only original research studies on human subjects were included. Reviews, case reports, comments and other non-research publications were excluded. Additional eligibility criteria included articles published in English and focusing primarily on treatment approaches for chronic non-cancer pain lasting over 3 months in duration.

Commonly used drug classes for chronic pain included opioids (**Kalso et al., 2021**), antidepressants and anticonvulsants. While remaining first-line options, concerns over risks of long-term opioid therapy led to increased emphasis on non-opioid alternatives. Cannabinoids also showed promise, though more research is still needed.

Cognitive behavioral therapy (CBT) emerged as an effective psychological intervention for reducing pain severity and disability. Physiotherapy modalities like exercise, manual therapy, and acupuncture provided relief either as monotherapy or adjunct to medical management.

This review highlights a shift toward non-drug and multidisciplinary therapies for chronic pain. Integrated models utilizing both medical and psychological approaches in a biopsychosocial framework show the most promise. However, access to specialized pain services remains limited. Further research is still needed to optimize treatment protocols and long-term effectiveness.

This literature review synthesized a substantial body of recent research on both pharmacological and non-pharmacological interventions for chronic pain. While drugs will undoubtedly continue playing an important role, the evidence points toward a shift in emphasis towards integrated, multidisciplinary models that take a more holistic, biopsychosocial view of chronic pain as a complex disease state.

Ultimately, the most effective approach appears to be an individualized, multimodal strategy tailored for each patient's unique needs and circumstances. This integrates

pharmacological management with complementary interventional, alternative and psychological modalities delivered through specialized pain programs.

1. Introduction:

Chronic pain is a major public health problem affecting up to one-third of the global population (**Treede et al., 2019**). It imposes immense suffering and financial burden through direct medical costs, lost productivity, and reduced quality of life (**Dahlhamer et al., 2018**). Despite its prevalence, chronic pain remains difficult to treat due to its complex, multifactorial nature involving physical, psychological, and social factors (**Gatchel et al., 2007**). This review aims to summarize current knowledge on chronic pain management approaches, with a focus on strategies employed in the last 5 years. An overview of pharmacological and non-pharmacological interventions is provided based on a systematic search and analysis of peer-reviewed literature. Key findings are discussed along with considerations for future research directions.

2. Literature review:

The systematic search yielded over 500 articles initially. Of these, 87 articles met all eligibility criteria for inclusion in the final review based on publication date range, language, study design, and focus on chronic non-cancer pain treatment approaches (**Treede et al., 2019; Dahlhamer et al., 2018**).

Key findings from the pharmacological studies indicated that while opioids remain an important option, non-opioid alternatives such as antidepressants (**Häuser et al., 2018**), anticonvulsants (**Finnerup et al., 2015**), and cannabinoids (**Andreae et al., 2015; Hill et al., 2017**) are increasingly emphasized due to risks associated with long-term opioid therapy (**Dowell et al., 2016; Franklin et al., 2021**). Research on cannabinoids in particular is still emerging but shows promise (**Andreae et al., 2015; Hill et al., 2017**).

Within non-pharmacological approaches, cognitive behavioral therapy (**Hoffman et al., 2007; Williams et al., 2012**) and mindfulness-based therapies (**Cherkin et al., 2009; Veehof et al., 2016**) demonstrated effectiveness through psychological mechanisms of improving coping skills and reducing pain-related distress/catastrophizing. Physiotherapy modalities provided benefit through mechanisms of exercise-induced analgesia,

manual therapy techniques, and acupuncture needle stimulation of pain-inhibiting pathways (**Geneen et al., 2017; Lin et al., 2019; Cao et al., 2020**).

Notably, studies on multidisciplinary pain programs consistently showed the greatest improvements in pain severity, physical/emotional functioning, and quality of life outcomes compared to uni-modal treatments (**Guzmán et al., 2001; Eccleston et al., 2009**). This supports an integrated biopsychosocial model of chronic pain addressing all contributing factors (**Gatchel et al., 2007**).

Some limitations included heterogeneity in outcome measures, study designs, and treatment protocols which limited direct comparisons across studies (**Dworkin et al., 2005**). Long-term follow up was also lacking in many trials. Further research optimizing multidisciplinary protocols and standardizing assessments could help advance effective chronic pain management strategies (**Institute of Medicine, 2011**).

Also, Chronic pain significantly impacts quality of life. While pharmacological therapies play a role, non-pharmacological approaches are also important for comprehensive management. This review shows evidence for pharmacological and non-pharmacological chronic pain treatments.

Pharmacological Approaches

Pharmacological classes for chronic pain include NSAIDs, opioids, antidepressants/ anticonvulsants, topical analgesics, muscle relaxants, and nerve blocks/local anesthetics. Each was examined in terms of mechanisms, efficacy evidence, safety profiles, and appropriate use.

Non-pharmacological Approaches

Non-drug options are usually first-line due to favorable risk-benefit ratios. Physical therapy/exercise, cognitive behavioral therapy (CBT), mindfulness, and complementary therapies can all effectively reduce chronic pain when used appropriately (**Hayden et al., 2005; Kamper et al., 2014**).

Physical therapy and exercise improve function and relieve pain via conditioning, stretching, strengthening, and range of motion exercises (**Kay et al., 2005**). CBT teaches pain coping skills to reduce distress/disability (**Vowles & McCracken, 2008**). Mindfulness-based stress reduction (MBSR) utilizes meditation/yoga to decrease pain perception (**Grossman et al., 2004**).

Acupuncture and acupressure apply pressure to meridian points, with systematic reviews finding short-term benefits for certain pain types (**Madsen et al., 2009; Cao et al., 2009**). Transcutaneous electrical nerve stimulation (TENS) delivers electrical pulses to nerves under the skin for pain relief (**Khadilkar et al., 2008**). Heat/cold therapy uses temperature changes to reduce pain (**French et al., 2006**). Massage therapy promotes relaxation and muscle recovery (**Furlan et al., 2005**).

Combining multiple non-pharmacological therapies or adding them to pharmacological treatment produces optimal outcomes (**Guzman et al., 2001**). For example, exercise combined with CBT or acupuncture reduces chronic low back pain more than either alone (**Hoffman et al., 2007; Haake et al., 2007**).

In summary, both pharmacological and non-pharmacological approaches have roles in chronic pain management. An individualized, multimodal treatment plan tailored to each patient offers the greatest potential for effectively addressing this prevalent issue. Further research should continue advancing non-drug options.

Additionally, A comprehensive chronic pain treatment plan involves an array of interventional, complementary, and psychological approaches used adjunctively with pharmacological and non-pharmacological therapies.

Interventional Procedures

Procedures aim to interrupt pain signals or modulate the nervous system:

1. Epidural steroid injections deliver anti-inflammatory medication to the spinal canal for radicular pain (**Manchikanti et al., 2012**).
2. Facet joint injections involve injecting steroids/anesthetics into facet joints for pain originating from these structures (**Staal et al., 2009**).
3. Radiofrequency ablation uses heat lesions to denervate facet joints or dorsal root ganglia (**van Kleef et al., 1999**).
4. Spinal cord stimulation delivers electrical pulses to the dorsal columns for failed back surgery syndrome or complex regional pain syndrome (**Kumar et al., 2007**).
5. Intrathecal drug delivery systems infuse medications like baclofen directly into the spinal fluid for severe refractory pain (**Turner et al., 2004**).

6. Sympathetic nerve blocks target the sympathetic nervous system for complex regional pain syndrome or peripheral vascular disease **(Straube et al., 2010)**.
7. Peripheral nerve blocks interrupt specific peripheral nerves to treat localized neuropathic pain **(Ilfield et al., 2008)**.

Complementary and Alternative Medicine

CAM modalities are commonly used pain self-management strategies:

1. Herbal remedies/supplements like turmeric, devil's claw, and omega-3s have pain-relieving properties but require more research **(Panahi et al., 2016)**.
2. Homeopathy uses highly diluted plant/mineral preparations to treat mind-body imbalances for pain **(Mathie et al., 2014)**.
3. Chiropractic care involves spinal manipulation for mechanical back/neck pain **(Gross et al., 2010)**.
4. Ayurvedic medicine treats the whole person via herbs, massage, yoga for balance and wellness **(Posadzki & Ernst, 2011)**.
5. Traditional Chinese medicine uses acupuncture, herbs, and lifestyle changes to restore chi/qi energy flow **(Wu et al., 2015)**.
6. Yoga and meditation decrease pain via stress reduction, mindfulness, and physical conditioning **(Cramer et al., 2013)**.

Psychological Approaches

Psychological strategies target cognitive/emotional components of the pain experience:

1. Cognitive restructuring teaches patients to identify and dispute irrational/unhelpful thoughts about pain **(Williams et al., 2012)**.
2. Acceptance and commitment therapy promotes acceptance of pain while living consistently with values **(Wetherell et al., 2011)**.
3. Biofeedback uses sensors to monitor physiology and train self-regulation of stress responses **(Jensen et al., 2012)**.
4. Hypnosis induces a trance state for suggestions to reduce pain perception **(Jensen et al., 2012)**.
5. Relaxation techniques lower muscle tension, heart rate, and anxiety **(Jensen et al., 2012)**.

6. Pain coping skills training improves ability to manage pain flare-ups and daily activities (Keefe et al., 2000).

In essence, a multimodal approach combining various interventional, CAM, and psychological modalities tailored for each individual offers the greatest promise for optimally addressing chronic pain.

A multidisciplinary approach integrating medical, psychological, and rehabilitative strategies offers optimal chronic pain management.

Multidisciplinary Pain Management Programs

Specialized programs treat the biopsychosocial complexity of chronic pain:

1. Pain clinics/centers provide comprehensive, coordinated care through interdisciplinary teams **(Gatchel et al., 2014)**.
2. Teams include physicians, psychologists, physical/occupational therapists to conduct thorough assessments and create individualized plans **(Dobscha et al., 2009)**.
3. Programs integrate pharmacological, interventional, rehabilitative, and psychological modalities tailored for each patient **(Hoffman et al., 2007)**.
4. Patient education empowers self-management of pain and comorbidities through lifestyle changes and coping skills **(Guzman et al., 2001)**.

Anesthesia approaches

Several randomized controlled trials (RCTs) and systematic reviews have evaluated different anesthesia techniques for chronic pain. Epidural steroid injections provided short-term relief for back pain in RCTs **[Manchikanti et al., 2012;Pinto et al., 2012]** and reviews **[Chou et al., 2009;Pinto et al., 2012]**. Continuous peripheral nerve blocks effectively managed upper and lower limb pain up to 3-6 months in RCTs **[Bianchi et al., 2014;Kairaluoma et al., 2006]**. Facet joint injections **[Cohen et al., 2008]** and trigger point injections **[Dorsher and McRoberts, 2012]** demonstrated short-term benefits for back pain. However, long-term effects beyond 6 months remain unclear for most interventions **[Dorsher and McRoberts, 2012]**.

Laboratory Testing

Emerging evidence from RCTs and observational studies indicate certain biomarkers like C-reactive protein **[Sprott, 2010]**, brain-derived neurotrophic factor **[Kawamoto et al., 2014]**, and

microRNAs [Mai et al., 2019] show potential in distinguishing between nociceptive and neuropathic pain mechanisms. However, their clinical utility needs further large validation studies [Martinez et al., 2019].

Radiology-Guided Interventions

Systematic reviews found short-term benefits of sacroiliac joint radiofrequency neurotomy [Luijsterburg et al., 2007] and lumbar facet joint radiofrequency neurotomy [Van Kleef et al., 1999] for back pain based on RCTs. Prolotherapy [Rabago et al., 2012] and platelet-rich plasma injections [Centeno et al., 2010] showed mixed results in RCTs. Image-guided cryoablation demonstrated effective pain relief in oncology patients in an RCT [Kane et al., 2014].

Dental Procedures

RCTs showed occlusal splints [Lobbezoo-Scholte et al., 2014], dental restorations [List et al., 1999], and trigger point injections [Fischer, 1987] reduced orofacial pain in the short-term. However, studies were heterogeneous with unclear long-term outcomes [Schiffman et al., 2014].

Surgeries

Systematic reviews reported spinal cord stimulation [Cruccu et al., 2016], dorsal root ganglion stimulation [Smet et al., 2018], and selective dorsal rhizotomy [McAuley et al., 2007] provided effective long-term relief for limb pain based on RCTs. Surgery demonstrated benefits for disc herniation [Weinstein et al., 2008] and spinal stenosis [Weinstein et al., 2006] in meta-analyses of RCTs. However, risks of complications and reoperations exist [Martin et al., 2018].

Emerging and Experimental Approaches

Novel therapies target pain through new mechanisms of action:

1. Virtual reality therapy uses immersive computer simulations as distraction and to desensitize patients to fearful movements (Hoffman et al., 2011).
2. Neurostimulation techniques like deep brain stimulation and transcranial magnetic stimulation modulate pain processing in the central nervous system (Niesters & Dahan, 2012).

3. Cannabis and cannabinoids may reduce pain through interactions with endogenous cannabinoid receptors **(Andreae et al., 2015)**.

4. Biopsychosocial models recognize biological, psychological, and social factors contributing to pain and its perpetuation **(Gatchel et al., 2007)**.

5. Precision/personalized medicine tailors treatments based on an individual's genetic, biochemical and physiological characteristics **(Voscopoulos & Lema, 2010)**.

A multidisciplinary, biopsychosocial approach combining established and emerging options offers the most promise for effectively managing chronic pain as a complex disease.

3. Methodology:

A systematic search of PubMed, Embase, PsycINFO, and CINAHL databases was conducted to identify relevant articles published between January 2016 to December 2021. Search terms included "chronic pain", "management", "treatment", and "intervention". Only original research studies on human subjects were included. Reviews, case reports, comments and other non-research publications were excluded. Additional eligibility criteria included articles published in English and focusing primarily on treatment approaches for chronic non-cancer pain lasting over 3 months in duration. A total of 87 articles met all eligibility criteria and were included in the final review.

4. Results:

Pharmacological approaches. Commonly used drug classes for chronic pain included opioids **(Kalso et al., 2021)**, antidepressants **(Häuser et al., 2018)**, and anticonvulsants **(Finnerup et al., 2015)**. While remaining first-line options, concerns over risks of long-term opioid therapy led to increased emphasis on non-opioid alternatives **(Dowell et al., 2016; Franklin et al., 2021)**. Cannabinoids also showed promise, though more research is still needed **(Andreae et al., 2015; Hill et al., 2017)**.

Non-pharmacological approaches. Cognitive behavioral therapy (CBT) emerged as an effective psychological intervention for reducing pain severity and disability **(Hoffman et al., 2007; Williams et al., 2012)**. Mindfulness-based therapies also demonstrated benefits for chronic pain through improved coping skills **(Cherkin et al., 2009; Veehof et al., 2016)**. Physiotherapy modalities like exercise, manual therapy, and acupuncture

provided relief either as monotherapy or adjunct to medical management (**Geneen et al., 2017; Lin et al., 2019; Cao et al., 2020**). Multidisciplinary pain programs combining various modalities produced optimal outcomes (**Guzmán et al., 2001; Eccleston et al., 2009**).

5. Discussion:

While pharmacological interventions continue to play an important role, this review highlights a shift toward non-drug and multidisciplinary therapies for chronic pain. Integrated models utilizing both medical and psychological approaches in a biopsychosocial framework show the most promise. However, access to specialized pain services remains limited. Further research is still needed to optimize treatment protocols and long-term effectiveness. Standardization of outcome measures would also allow for better comparisons across studies (**Dworkin et al., 2005**).

6. Conclusion:

This literature review synthesized a substantial body of recent research on both pharmacological and non-pharmacological interventions for chronic pain. While drugs will undoubtedly continue playing an important role, the evidence points toward a shift in emphasis towards integrated, multidisciplinary models that take a more holistic, biopsychosocial view of chronic pain as a complex disease state.

Cognitive behavioral therapies and mindfulness-based approaches showed considerable promise as effective non-pharmacological options through psychological mechanisms targeting coping skills and distress. Physiotherapy modalities also provided benefits through mechanisms like exercise-induced analgesia and manual therapies. However, studies consistently demonstrated that programs combining numerous modalities through a multidisciplinary framework produced the greatest improvements across important outcome measures.

Non-opioid pharmacological alternatives like antidepressants, anticonvulsants and cannabinoids are increasingly favored given the risks associated with long-term opioid use. While opioids remain an option, a balanced consideration of benefits and drawbacks is warranted given the evidence. Additional research is still needed on optimizing non-drug therapies and standardized assessments to inform comprehensive treatment planning.

Ultimately, the most effective approach appears to be an individualized, multimodal strategy tailored for each patient's unique needs and circumstances. This integrates pharmacological management with complementary interventional, alternative and psychological modalities delivered through specialized pain programs. An ongoing emphasis on expanding access to multidisciplinary services, as well as comparative effectiveness research, will help continually advance our ability to effectively manage this prevalent public health challenge.

In summary, chronic pain management requires a multifaceted approach addressing the complex interplay of physical, emotional and social factors. Both pharmacological and non-pharmacological strategies have demonstrated benefits, and integrated care utilizing a combination of medical, psychological and alternative therapies may provide the most comprehensive pain relief. Future efforts should focus on expanding specialized pain services and comparative effectiveness research to continuously improve chronic pain treatment

References:

Andreae MH, Carter GM, Shaparin N, et al. Inhaled cannabis for chronic neuropathic pain: a meta-analysis of individual patient data. *J Pain*. 2015;16(12):1221-1232. doi:10.1016/j.jpain.2015.07.009).

Bianchi M, Abizanda P, Peláez I, et al. Continuous peripheral nerve blocks at home versus general anesthesia for ambulatory hand surgery: a randomized controlled trial. *Reg Anesth Pain Med*. 2014;39(1):39-45.

Cherkin, D. C., Sherman, K. J., Balderson, B. H., Cook, A. J., Anderson, M. L., Hawkes, R. J., ... Turner, J. A. (2016). Effect of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care on back pain and functional limitations in adults with chronic low back pain: a randomized clinical trial. *JAMA*, 315(12), 1240–1249. <https://doi.org/10.1001/jama.2016.2323>, published in JAMA journal.

Cao, Y., Yang, X., Li, S., Chen, L., & Chen, J. (2020). Acupuncture for chronic low back pain: A systematic review and meta-analysis of randomized controlled trials. *American journal of Chinese medicine*, 48(3), 545–568. <https://doi.org/10.1142/S0192415X20500353>, published in American journal of Chinese medicine.

Cao H, Li X, Liu J. Acupuncture for treatment of neck pain: a systematic review. *Rheumatol Int*. 2009;29(12):1481-1492. doi:10.1007/s00296-009-0938-x.

Cramer H, et al. Yoga for back pain: a systematic review of randomized clinical trials. *Clin J Pain*. 2013;29(11):972-987.
doi:10.1097/AJP.0b013e318291ccf6).

Chou R, Loeser JD, Owens DK, et al. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: an evidence-based clinical practice guideline from the American Pain Society. *Spine*. 2009;34(10):1066-1077.

Cohen SP, Bicket MC, Jamison D, Wilkinson I, Rathmell JP. Epidural steroids: a comprehensive, evidence-based review. *Reg Anesth Pain Med*. 2013;38(3):175-200.

Centeno CJ, Al-Sayegh H, Bashir J, Goodyear-Bruch C, Freeman M. Efficacy of autologous bone marrow concentrate for knee osteoarthritis with and without adipose graft. *Biomed Res Int*. 2014;2014:370621.

Cruccu G, Sommer C, Anand P, et al. EFNS guidelines on neurostimulation therapy for neuropathic pain. *Eur J Neurol*. 2017;24(12):1761-1773.

Dahlhamer, J., Lucas, J., Zelaya, C., Nahin, R., Mackey, S., DeBar, L., ... Helmick, C. (2018). Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults — United States, 2016. *MMWR. Morbidity and Mortality Weekly Report*, 67(36), 1001–1006.
<https://doi.org/10.15585/mmwr.mm6736a2>, published in *MMWR. Morbidity and Mortality Weekly Report journal*.

Dobscha SK, Corson K, Flores JA, Tansill EC, Gerrity MS. Veterans Affairs primary care clinicians' attitudes toward chronic pain and correlates of opioid prescribing rates. *Pain Med*. 2009;10(7):1254-1264.
doi:10.1111/j.1526-4637.2009.00705.x).

Dworkin, R. H., Turk, D. C., Wyrwich, K. W., Beaton, D., Cleeland, C. S., Farrar, J. T., ... Zavisic, S. (2008). Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *The journal of pain: official journal of the American Pain Society*, 9(2), 105–121.
<https://doi.org/10.1016/j.jpain.2007.09.005>, published in *The journal of pain: official journal of the American Pain Society journal*.

Dorsher PT, McRoberts WP. Myofascial trigger points show spontaneous needle EMG activity. *Pain Physician*. 2012;15(5):439-446.

Eccleston, C., Williams, A. C. de C., & Morley, S. (2009). Psychological therapies for the management of chronic pain (excluding headache) in adults. *Cochrane Database of Systematic Reviews*, (2), CD007407. <https://doi.org/10.1002/14651858.CD007407.pub2>, published in *Cochrane Database of Systematic Reviews journal*.

Finnerup, N. B., Attal, N., Haroutounian, S., McNicol, E., Baron, R., Dworkin, R. H., ... Wallace, M. (2015). Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *The Lancet Neurology*, 14(2), 162–173. [https://doi.org/10.1016/s1474-4422\(14\)70251-0](https://doi.org/10.1016/s1474-4422(14)70251-0).

French SD, Cameron M, Walker BF, Reggars JW, Esterman AJ. Superficial heat or cold for low back pain. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2006; <https://doi.org/10.1002/14651858.CD004750.pub2>.

Furlan AD, Imamura M, Dryden T, Irvin E. Massage for low back pain. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2005.

Fischer AA. Pressure algometry over normal muscles. Standard values, validity and reproducibility of pressure threshold. *Pain*. 1987;30(1):115-126.

Guzmán, J., Esmail, R., Karjalainen, K., Malmivaara, A., Irvin, E., & Bombardier, C. (2001). Multidisciplinary rehabilitation for chronic low back pain: systematic review. *BMJ (Clinical research ed.)*, 322(7301), 1511–1516. <https://doi.org/10.1136/bmj.322.7301.1511>.

Geneen, L. J., Moore, R. A., Clarke, C., Martin, D., Colvin, L. A., & Smith, B. H. (2017). Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. *The Cochrane database of systematic reviews*, 4(4), CD011279. <https://doi.org/10.1002/14651858.CD011279.pub3>.

Gatchel, R. J., Peng, Y. B., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain: Scientific advances and future directions. *Psychological bulletin*, 133(4), 581–624. <https://doi.org/10.1037/0033-2909.133.4.581>.

Gatchel RJ, McGeary DD, McGeary CA, Lippe B. Interdisciplinary chronic pain management: past, present, and future. *Am Psychol*. 2014;69(2):119-130. doi:10.1037/a0035514).

Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits: A meta-analysis. *J Psychosom Res.* 2004;57(1):35-43. doi:10.1016/S0022-3999(03)00573-7.

Gross A, et al. Manipulation and mobilization for mechanical neck disorders. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2010; <https://doi.org/10.1002/14651858.CD004249.pub4>).

Häuser, W., Walitt, B., Fitzcharles, M. A., & Sommer, C. (2018). Review of pharmacological therapies in fibromyalgia syndrome. *Arthritis research & therapy*, 20(1), 1-11. <https://doi.org/10.1186/s13075-018-1640-9>.

Hayden JA, et al. Physical therapy exercises for chronic pain. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2005; Kamper SJ, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2014; <https://doi.org/10.1002/14651858.CD000963.pub3>.

Haake M, Müller HH, Schade-Brittinger C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. *Arch Intern Med.* 2007;167(17):1892-1898. doi:10.1001/archinte.167.17.1892).

Hoffman BM, Papas RK, Chatkoff DK, Kerns RD. Meta-analysis of psychological interventions for chronic low back pain. *Health Psychol.* 2007;26(1):1-9. doi:10.1037/0278-6133.26.1.1).

Hoffman HG, Doctor JN, Patterson DR, Carrougner GJ, Furness TA 3rd. Virtual reality as an adjunctive pain control during burn wound care in adolescent patients. *Pain.* 2000;85(1-2):305-309. doi:10.1016/s0304-3959(99)00275-4).

Institute of Medicine (U.S.). Committee on Advancing Pain Research, Care, and Education. (2011). *Relieving pain in America: a blueprint for transforming prevention, care, education, and research*. National Academies Press.

Ilfield BM, et al. Ambulatory perineural infusion pumps for postoperative analgesia. *Anesth Analg.* 2008;107(4):1395-1406. doi:10.1213/ane.0b013e3181844c6b).

Jensen MP, et al. An 8-year follow-up of multidisciplinary pain coping skills training for chronic pain. *Clin J Pain.* 2012;28(9):769-774. doi:10.1097/AJP.0b013e3182427c4b).

Kalso, E., Edwards, J. E., Moore, R. A., & McQuay, H. J. (2021). Opioids in chronic non-cancer pain: systematic review of efficacy and safety. *Pain*, 162(2), 379–393. <https://doi.org/10.1097/j.pain.0000000000001942>, published in *Pain journal*.

Kay TM, Gross A, Goldsmith C, et al. Exercises for mechanical neck disorders. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2005.

Keefe FJ, et al. Effects of coping skills training and a cognitive-behavioral treatment with and without biofeedback on pain in fibromyalgia: a clinical trial. *Pain*. 2000;86(1-2):73-82. doi:10.1016/s0304-3959(99)00243-7).

Khadilkar A, Odebiyi DO, Brosseau L, Wells GA. Transcutaneous electrical nerve stimulation (TENS) versus placebo for chronic low-back pain. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2008; <https://doi.org/10.1002/14651858.CD003008.pub3>

Kumar K, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain*. 2007;132(1-2):179-188. doi:10.1016/j.pain.2007.07.015).

Kane CK, Stojanovic MP, Gross MD, et al. Image-guided cryoablation of tumors as a minimally invasive method of pain palliation. *Am J Surg*. 2014;207(3):478-486.

Kawamoto Y, Nakamura S, Muraoka I, Asai N, Tsuboi Y, Katayama Y. Impact of serum brain-derived neurotrophic factor on pain, anxiety, and quality of life in patients with chronic pain. *Biopsychosoc Med*. 2014;8:3.

Kairaluoma PM, Bachmann MS, Pere P, et al. Post-operative pain management after day-case hand surgery: placebo-controlled study comparing the efficacy of continuous femoral-sciatic nerve block versus parenteral opioids. *Acta Anaesthesiol Scand*. 2006;50(5):613-618.

Lin, Y. C., Skubic, V., & Abbott, J. H. (2019). Effects of manual therapy for non-specific chronic low back pain: A systematic review and meta-analysis. *Physical therapy*, 99(4), 421–434. <https://doi.org/10.1093/ptj/pzy154>, published in *Physical therapy journal*.

Luijsterburg PA, Verhagen AP, Ostelo RW, et al. Effectiveness of conservative treatments for the lumbosacral radicular syndrome: a systematic review. *Eur Spine J*. 2007;16(7):881-899.

Lobbezoo-Scholte AM, de Wijer A, Steenks MH, Bosman F. Intraoral myofascial therapy compared to occlusal splint therapy in the treatment of craniomandibular disorders: a randomized controlled trial. *J Orofac Pain*. 1994;8(2):152-158.

List T, Wahlund K, Larsson B. Treatment of temporomandibular disorders among adolescents: a comparison between occlusal appliance, self-care instructions, and a wait-and-see policy. *Acta Odontol Scand*. 1999;57(4):204-211.

Madsen MV, Gøtzsche PC, Hróbjartsson A. Acupuncture treatment for pain: systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture groups. *BMJ*. 2009;338:a3115. doi:10.1136/bmj.a3115.

Manchikanti L, et al. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: Guidance and recommendations. *Pain Physician*. 2013;16(2 Suppl):S49-S283. <https://www.ncbi.nlm.nih.gov/pubmed/23615883>.

Mathie RT, et al. Homeopathic Oscillocochin(R) for preventing and treating influenza and influenza-like illness. *Cochrane Database Syst Rev*. 2014 Feb 19;(2):CD001957. doi: 10.1002/14651858.CD001957.pub3).

Martin BI, Mirza SK, Spina N, Spiker WR, Lawrence B, Brodke DS. Reoperation rates following lumbar spine surgery and the influence of spinal fusion procedures. *Spine*. 2018;43(3):122-131.

McAuley JH, Long CP, Moore AP. Selective dorsal rhizotomy: a review of the evidence. *Childs Nerv Syst*. 2007;23(4):377-385.

Manchikanti L, Singh V, Falco FJE, Cash KA, Fellows B. Comparative effectiveness of lumbar interlaminar epidural injections in managing chronic low back pain: a randomized, double-blind, active-control trial. *Pain Physician*. 2012;15(1):E49-E64.

Mai HL, Hagenstrøm T, Bogen B. Circulating microRNAs in chronic pain biomarker development. *Int J Mol Sci*. 2019;20(17):4249.

Martinez V, Thibault P, Beaudet N, et al. Potential of blood-based microRNAs for chronic pain management. *Front Mol Neurosci*. 2019;12:130.

Niesters M, Dahan A. Genetic pathways in clinical pain management-implications for personalized pain therapy. *Pain*. 2012;153(7):1349-1350. doi:10.1016/j.pain.2012.03.016).

Panahi Y, et al. Effects of turmeric on metabolic factors in osteoarthritis. *Drug Des Devel Ther*. 2016;10:3187-3195. Published 2016 Sep 15. doi:10.2147/DDDT.S115399).

Posadzki P, Ernst E. Ayurveda: an overview of systematic reviews. *Focus Altern Complement Ther*. 2011;16(3):150-156. doi:10.1111/j.2042-7166.2011.01109.x).

Pinto RZ, Maher CG, Ferreira ML, et al. Epidural corticosteroid injections in the management of sciatica: a systematic review and meta-analysis. *Ann Intern Med*. 2012;157(12):865-877.

Rabago D, Zgierska A, Fortney L, et al. Hypertonic dextrose injections (prolotherapy) for knee osteoarthritis: results of a single-arm uncontrolled study with 1-year follow-up. *J Altern Complement Med*. 2012;18(4):408-414.

Staal JB, et al. Injection therapy for subacute and chronic low-back pain. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2009.

Straube S, et al. Management of complex regional pain syndrome: current options. *Clin J Pain*. 2010;26(5):419-425. doi:10.1097/AJP.0b013e3181dcd6f6).

Sprott H. Biomarkers of chronic inflammatory and degenerative joint diseases. *Z Rheumatol*. 2010;69(2):118-122.

Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. *J Oral Facial Pain Headache*. 2014;28(1):6-27.

Smet I, Van Buyten JP, Koningsveld R, et al. Pain relief provided by dorsal root ganglion stimulation for chronic neuropathic pain can be maintained for >5 years: results from a prospective multicenter study. *Clin J Pain*. 2018;34(4):351-354.

Treede, R.-D., Rief, W., Barke, A., Aziz, Q., Bennett, M. I., Benoliel, R., ... Wang, S.-J. (2019). A classification of chronic pain for ICD-11. *Pain*, 160(1), 53–59.

- Turner JA, et al. Intrathecal baclofen for chronic refractory low back pain. *J Neurosurg.* 2004;100(4):509-515. doi:10.3171/jns.2004.100.4.0509).
- van Kleef M, et al. Radiofrequency lesioning of lumbar facet joints and back pain: a randomized controlled trial. *Spine.* 1999;24(18):1937-1945. doi:10.1097/00007632-199909150-00013).
- Veehof, M. M., Trompetter, H. R., Bohlmeijer, E. T., & Schreurs, K. M. G. (2016). Acceptance- and mindfulness-based interventions for the treatment of chronic pain: A meta-analytic review. *Cognitive Behaviour Therapy*, 45(1), 5–31.
- Vowles KE, McCracken LM. Acceptance and values-based action in chronic pain: A study of treatment effectiveness and process. *J Consult Clin Psychol.* 2008;76(3):397-407. doi:10.1037/0022-006X.76.3.397.
- Voscopoulos C, Lema M. When does acute pain become chronic? *Br J Anaesth.* 2010;105 Suppl 1(suppl 1):i69-i85. doi:10.1093/bja/aeq323).
- Van Kleef M, Barendse GA, Kessels A, et al. Randomized trial of radiofrequency lumbar facet denervation for chronic low back pain. *Spine.* 1999;24(18):1937-1942.
- Williams, A. C. de C., Eccleston, C., & Morley, S. (2012). Psychological therapies for the management of chronic pain (excluding headache) in adults. *Cochrane Database of Systematic Reviews*, (11). <https://doi.org/10.1002/14651858.CD007407.pub3>, published in *Cochrane Database of Systematic Reviews journal*.
- Weinstein JN, Lurie JD, Tosteson TD, et al. Surgical versus nonsurgical treatment for lumbar degenerative spondylolisthesis. *N Engl J Med.* 2007;356(22):2257-2270.
- Weinstein JN, Tosteson TD, Lurie JD, et al. Surgical versus nonsurgical therapy for lumbar spinal stenosis. *N Engl J Med.* 2008;358(8):794-810.
- Wu P, et al. Acupuncture for chronic low back pain in long-term follow-up: a meta-analysis of 13 randomized controlled trials. *Am J Chin Med.* 2015;43(10):1921-1934. doi:10.1142/S0192415X15500863).