
Appendix 2. Papers reviewed

Review articles (n = 11)

1. Bolton M, Hodkinson A, Boda S, et al. Serious adverse events reported in placebo randomised controlled trials of oral naltrexone: A systematic review and meta-analysis. *BMC Med* 2019;17(1):10. doi: 10.1186/s12916-018-1242-0.
2. Bostick KM, McCarter AG, Nykamp D. The use of low-dose naltrexone for chronic pain. *Sr Care Pharm* 2019;34(1):43–46. doi: 10.4140/TCP.n.2019.43.
3. Cheng CW, Wong CS, Hui GK, Chung EK, Wong SH. Fibromyalgia: Is it a neuropathic pain? *Pain Manag* 2018;8(5):377–88. doi: 10.2217/pmt-2018-0024.
4. Hatfield E, Phillips K, Swidan S, Ashman L. Use of low-dose naltrexone in the management of chronic pain conditions: A systematic review. *J Am Dent Assoc* 2020;151(12):891–902 e1. doi: 10.1016/j.adaj.2020.08.019.
5. Kim PS, Fishman MA. Low-dose naltrexone for chronic pain: Update and systemic review. *Curr Pain Headache Rep* 2020;24(10):64. doi: 10.1007/s11916-020-00898-0.
6. Lawson K. Potential drug therapies for the treatment of fibromyalgia. *Expert Opin Investig Drugs* 2016;25(9):1071–81. doi: 10.1080/13543784.2016.1197906.
7. Littlejohn G. Neurogenic neuroinflammation in fibromyalgia and complex regional pain syndrome. *Nat Rev Rheumatol* 2015;11(11):639–48. doi: 10.1038/nrrheum.2015.100.
8. Patten DK, Schultz BG, Berlau DJ. The safety and efficacy of low-dose naltrexone in the management of chronic pain and inflammation in multiple sclerosis, fibromyalgia, Crohn's disease, and other chronic pain disorders. *Pharmacotherapy* 2018;38(3):382–89. doi: 10.1002/phar.2086.
9. Toljan K, Vrooman B. Low-dose naltrexone (LDN)-review of therapeutic utilization. *Med Sci (Basel)* 2018;6(4):82. doi: 10.3390/medsci6040082.
10. Trofimovitch D, Baumrucker SJ. Pharmacology update: Low-dose naltrexone as a possible nonopioid modality for some chronic, nonmalignant pain syndromes. *Am J Hosp Palliat Care* 2019;36(10):907–12. doi: 10.1177/1049909119838974.
11. Younger J, Parkitny L, McLain D. The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain. *Clin Rheumatol* 2014;33(4):451–59. doi: 10.1007/s10067-014-2517-2.

Clinical studies (n = 5)

12. Bruun-Plesner K, Blichfeldt-Eckhardt MR, Vaegter HB, Lauridsen JT, Amris K, Toft P. Low-dose naltrexone for the treatment of fibromyalgia: Investigation of dose-response relationships. *Pain Med* 2020;21(10):2253–61. doi: 10.1093/pm/pnaa001.
13. Jackson D, Singh S, Zhang-James Y, Faraone S, Johnson B. The effects of low dose naltrexone on opioid induced hyperalgesia and fibromyalgia. *Front Psychiatry* 2021;12:593842. doi: 10.3389/fpsy.2021.593842.
14. Parkitny L, Younger J. Reduced pro-inflammatory cytokines after eight weeks of low-dose naltrexone for fibromyalgia. *Biomedicines* 2017;5(2): 16. doi: 10.3390/biomedicines5020016.
15. Younger J, Mackey S. Fibromyalgia symptoms are reduced by low-dose naltrexone: A pilot study. *Pain Med* 2009;10(4):663–72. doi: 10.1111/j.1526-4637.2009.00613.x.
16. Younger J, Noor N, McCue R, Mackey S. Low-dose naltrexone for the treatment of fibromyalgia: Findings of a small, randomized, double-blind, placebo-controlled, counterbalanced, crossover trial assessing daily pain levels. *Arthritis Rheum* 2013;65(2):529–38. doi: 10.1002/art.37734.

Case reports (n = 2)

17. Bolton MJ, Chapman BP, Van Marwijk H. Low-dose naltrexone as a treatment for chronic fatigue syndrome. *BMJ Case Rep* 2020;13(1):e232502. doi: 10.1136/bcr-2019-232502.
18. Ramanathan S, Panksepp J, Johnson B. Is fibromyalgia an endocrine/endorphin deficit disorder? Is low dose naltrexone a new treatment option? *Psychosomatics* 2012;53(6):591–94. doi: 10.1016/j.psym.2011.11.006.

Protocol papers (n = 2)

19. Bruun KD, Amris K, Vaegter HB, et al. Low-dose naltrexone for the treatment of fibromyalgia: Protocol for a double-blind, randomized, placebo-controlled trial. *Trials* 2021;22(1):804. doi: 10.1186/s13063-021-05776-7.
20. Colomer-Carbonell A, Sanabria-Mazo JP, Hernandez-Negrin H, et al. Study protocol for a randomised, double-blinded, placebo-controlled phase III trial examining the add-on efficacy, cost-utility and neurobiological effects of low-dose naltrexone (LDN) in patients with fibromyalgia (INNOVA study). *BMJ Open* 2022;12(1):e055351. doi: 10.1136/bmjopen-2021-055351.

Primary biomedical research (n = 1)

21. Kučić N, Rački V, Šverko R, Vidović T, Grahovac I, Mršić-Pelčić J. Immunometabolic modulatory role of naltrexone in BV-2 microglia cells. *Int J Mol Sci* 2021;22(16):8429. doi: 10.3390/ijms22168429.
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