

Cochrane in CORR®: Interventions for the Reduction of Prescribed Opioid Use in Chronic Non-cancer Pain

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A note from the Editor-in-Chief: We are pleased to publish the next installment of Cochrane in CORR®, our partnership between CORR®, The Cochrane Collaboration®, and McMaster University's Evidence-Based Orthopaedics Group. In this column, researchers from McMaster University and other institutions will provide expert perspective on an abstract originally published in The Cochrane Library that we think is especially important.

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Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and The Cochrane Library (<http://www.thecochranelibrary.com>) should be consulted for the most recent version of the review.

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Importance of the Topic

Opioid use and its associated harms have become a major area of concern for patients, healthcare professionals, and the public. Adverse effects of opioid use can include death, addiction/dependence, hyperalgesia, sedation, impaired cognition, and fractures, among others [1, 7]. Additionally, there is little evidence that opioids are effective for pain management long-term [6]. Orthopaedic surgeons rank third among physicians—behind family practitioners and internists—in terms of the amount of opioids prescribed [9]. With increased attention on the risks of opioid use, several groups have developed evidence-based guidelines for responsible opioid prescription including the CDC [3], and a McMaster University-led Canadian guidelines group [2]. Both guidelines recommend maximizing nonopioid therapy before opioid therapy for chronic noncancer pain, using the minimum effective dose of opioids if they are needed, and for patients who are using greater than 90 mg morphine equivalents daily, to attempt tapering to the lowest effective dose. Because many patients with chronic noncancer pain have been on high doses of opioids for a long time, it can be challenging or

impossible to reduce their opioid dosage without serious increases in pain, decreases in function, and withdrawal symptoms. Guidelines strongly recommend that these patients receive formal medical assistance to reduce opioid use, but they do not explore which strategies are most effective [2, 3].

Upon Closer Inspection

This recently updated systematic review of five trials (278 patients) found that the evidence for interventions to reduce prescribed opioid use are mixed [4]. The results varied, with some interventions showing promise in the short-term but not longer-term, and others showing either no difference or a small reduction across groups. The authors planned to pool results and report relative risks, number needed to treat, and number needed to harm, but they ultimately decided against pooling data because they judged the studies as too heterogeneous. The Cochrane Handbook [5] defines heterogeneity as differences across studies. This can mean differences in populations, interventions, or outcomes (clinical heterogeneity), differences in key study design elements (methodological heterogeneity), or differences in intervention effects above and beyond chance (statistical heterogeneity). The Cochrane Handbook [5] suggests a number of different methods of dealing with heterogeneity, each with their own strengths and weaknesses:

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- **Exclude heterogeneous studies.** This is typically not the best choice unless there is a good prespecified reason to do so. Excluding studies without a prespecified reason can lead to bias, and is analogous to excluding patients in a trial after they have been randomized.
- **Ignore heterogeneity by using fixed-effects models.** This is not ideal, since this analytic approach can lead to overly narrow confidence intervals, minimizing the differences among studies and making the data seem more uniform than they actually are.
- **Include heterogeneity by using random-effects models.** This method should be used for unexplained heterogeneity only because a better alternative is to explore reasons for heterogeneity. The heterogeneity in the Cochrane review likely can be explained by the different interventions and other clinical characteristics.
- **Explore heterogeneity with subgroup analyses or meta-regression.** These analyses should be specified in advance otherwise they can be misleading. Posthoc subgroup analyses are often “dredged” from the data rather than based on previous evidence and clinical rationale [8]. The Cochrane review authors prespecified subgroup analyses, but there were not enough studies to proceed with this method.
- **Do not pool data.** Systematic review authors usually make every attempt to pool data because it condenses a large amount of information from many studies into one statistic. However, pooling data is not always possible or appropriate because the studies are too heterogeneous to provide a meaningful summary estimate.

This Cochrane review included five studies evaluating four different interventions (cognitive behavioral therapy [CBT], mindfulness, interactive voice response therapy, and electroacupuncture), which is likely a major cause of heterogeneity [4]. Ideally, with more studies evaluating each type of intervention, the Cochrane authors could have pooled results and analyzed subgroup effects. Although the decision not to pool the data in this Cochrane review results in a summary that is not as quantitative as it might be, choosing not to pool the studies likely was the best option because the heterogeneity of the included studies would lead to misleading results.

Take-home Messages

Based on only one or two studies per intervention, interactive voice response therapy, and mindfulness seem more promising than electroacupuncture and CBT. Interactive voice response therapy was significantly better than CBT for pain reduction, opioid use, and physical and psychological function. Mindfulness was better than a typical support group for pain reduction and physical functioning but not opioid use or psychological functioning outcomes. CBT and electroacupuncture did not significantly differ from control groups on any outcome. However, this Cochrane review was ultimately inconclusive because of insufficient high-quality data [4]. Opioid reduction is an important issue that deserves more attention to minimize harm and maximize benefits for patients. The Cochrane review authors prespecified the methods that they would use in case of heterogeneity, which is a great strength of this review. Further high-quality research is needed so that future systematic reviews can

pool data appropriately. There are two slightly larger ongoing trials that are expected to have results by 2021 (NCT02602535, NCT02935621) and may be able to contribute to future systematic reviews on this topic.

References

1. Baldini A, Von Korff M, Lin EH. A review of potential adverse effects of long-term opioid therapy: A practitioner's guide. *Prim Care Companion CNS Disord.* 2012; 14(3).
2. Busse JW, Craigie S, Juurlink DN, Buckley DN, Wang L, Couban RJ, Agoritsas T, Akl EA, Carrasco-Labra A, Cooper L, Cull C, da Costa BR, Frank JW, Grant G, Iorio A, Persaud N, Stern S, Tugwell P, Vandvik PO, Guyatt GH. Guideline for opioid therapy and chronic noncancer pain. *CMAJ.* 2017;189:E659–666.
3. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA.* 2016;315:1624–1645.
4. Eccleston C, Fisher E, Thomas KH, Hearn L, Derry S, Stannard C, Knaggs R, Moore RA. Interventions for the reduction of prescribed opioid use in chronic non-cancer pain. *Cochrane Database Syst Rev.* 2017;11:CD010323.
5. JPTHiggins JPT, SGreen S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*. London, United Kingdom: The Cochrane Collaboration; 2011.
6. Manchikanti L, Vallejo R, Manchikanti KN, Benyamin RM, Datta S, Christo PJ. Effectiveness of long-term opioid therapy for chronic non-cancer pain. *Pain Physician.* 2011;14:E133–156.
7. Miller M, Stürmer T, Azrael D, Levin R, Solomon DH. Opioid analgesics and the risk of fractures in older adults with arthritis. *J Am Geriatr Soc.* 2011;59:430–438.
8. SPRINT Investigators, Sun X, Heels-Ansdell D, Walter SD, Guyatt G, Sprague S, Bhandari M, Sanders D, Schemitsch E, Tometta P 3rd, Swiontkowski M. Is a subgroup claim believable? A user's guide to subgroup analyses in the surgical literature. *J Bone Joint Surg Am.* 2011;93:e8.
9. Volkow ND, McLellan TA, Cotto JH, Karithanom M, Weiss SR. Characteristics of opioid prescriptions in 2009. *JAMA.* 2011;305:1299–1301.