

**Letters to the Editor**



## Comments on the Efficacy and Safety of Opioid Analgesics for the Management of Chronic Low Back Pain

### TO THE EDITOR:

With great interest we have read the article written by Boya et al (1). This was a systematic review and network meta-analysis in which opioids were ranked on efficacy and safety for the treatment of chronic low back pain (CLBP). The authors concluded that oxymorphone is the most effective opioid, and hydromorphone is the safest. However, as mentioned by the authors, oxymorphone recently had its United States (U.S.) Food and Drug Administration (FDA)-approval withdrawn because of its misuse. This points to the reason why we are writing this letter. We are currently in the midst of a global opioid crisis driven by misuse of prescription opioids. In 2019, 70% of the drug-related overdose deaths in the U.S. were opioid-related (2). During the COVID-19 pandemic, the number of overdose-related deaths are continuing to rise, with some states in the U.S. experiencing increases as high as 50% from March 2019 to March 2020 (3). Opioids increase the risk of mortality and can potentially lead to addiction, dependence, and other serious side effects (4). Recent guidelines for CLBP discourage the use of opioids (5). The effects on pain relief by opioids in persons with CLBP are small and not clinically relevant, even at high doses (6). Thus, current guidelines for CLBP recommend weak opioids only as a third step treatment for a short-term period (5). Considering this evidence and our quest as health professionals to decrease opioid prescriptions, we found the research question out of context.

In addition to the lack of efficacy, we questioned whether the safety outcome as defined by Boya et al (1) truly recognizes the harms done by opioids through dependence and addiction. Boya et al (1) defined safety as study withdrawal due to any reason. The authors reported that the reason for withdrawal was assumed to be negative side effects of drug use. However, considering opioids are potentially addictive, we believe the relationship between group assignment and withdrawal is complicated and does not necessarily reflect this. Reasons for withdrawal could include negative

side effects from opioids, but it could also include lack of efficacy. On the other hand, participants might stay in a study for reasons other than pain control (i.e., because of the very effects that lead to addiction). Another problem in measuring safety, that the authors did agree on, is that most included studies used a short follow-up period. However, adverse events such as addiction, dependence, and opioid overdose typically emerge after longer-term use (7). Respectfully, in our opinion, opioid safety should not be defined based on withdrawal alone.

Finally, we are concerned that ranking the probability of effectiveness in pain reduction without reporting actual efficacy (or lack thereof) can lead to misinterpretation of these results. At this moment it remains unknown for the reader whether oxymorphone, the most effective opioid according to this study, has a clinically relevant effect on CLBP. In fact, a recent systematic review reported that oxymorphone likely does not confer a clinically relevant benefit in CLBP (4). Moreover, considering opioids are not the only treatment and certainly not the safest treatment for CLBP, we think including a ranking of nonopioid treatment strategies, based on current guidelines (5) would have been favorable. Other forms of treatment include exercise therapy (5) or different medications such as antidepressants (8).

Considering these observations, we are concerned about the recommendations on pain treatment for CLBP as put forth by this study. In our opinion, the conclusions of Boya et al (1) could give the wrong message that clinicians should be prescribing oxymorphone or other highly ranked opioids and that some opioids are safe, when in fact other safer and more effective treatments are both available and recommended (5).

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