

add support to the notion that “clinicians should consider tapering opioid dosage among long-term opioid therapy users in accordance with clinical practice guidelines.” While this is a reasonable statement on its own, the study design and results of this study do not support this conclusion.

Primary care clinicians face 2 distinct questions surrounding LTOT for chronic pain. The first question is whether starting opioid-naïve individuals with chronic pain syndromes on LTOT will result in benefit compared with nonopioid therapies. The authors note the small but growing body of literature that suggests only modest, if any, benefit of this approach over the long-term for pain control and functioning.<sup>2,3</sup>

A second, separate question is whether tapering or stopping LTOT in opioid-dependent individuals will result in benefit. To our knowledge, there are no randomized trials assessing this question. Observation data from multiple studies find associations of increased harms with tapering.<sup>4,5</sup> These studies have notable limitations and should not stop clinicians from discussing with patients the issue of tapering LTOT, as there remain risks associated with LTOT continuation.<sup>6</sup> Neither should they dissuade considerations to transition from full agonists to buprenorphine, an approach that is likely to reduce risks associated with continuation or tapering of full agonists.<sup>7</sup> This question is not addressed by the study design in Licciardone et al, yet the authors conclude that their findings indicate that clinicians should consider tapering opioid dosage among long-term opioid therapy users in accordance with clinical practice guidelines. This statement risks adding unmerited confidence to a clinical scenario that remains nuanced.

Whether to initiate LTOT in opioid-naïve individuals with chronic pain seems increasingly clear: the limited benefits with noted risks make this pathway one that should be rarely taken, and when done so, guidelines suggest buprenorphine as the safest opioid.<sup>8</sup> The data presented by Licciardone et al do not offer signals to suggest otherwise. Yet the questions of whether and when to recommend tapering LTOT or transitioning full agonist LTOT to buprenorphine are not addressed in Licciardone et al, are ones in need of more evidence, and for now, should be approached with careful nuance and individualization by primary care clinicians.

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## Response: Re: Effectiveness of Long-Term Opioid Therapy for Chronic Low Back Pain

*To the Editor:* In a letter regarding our publication,<sup>1</sup> Waters and Simon contend that our study design and results did not support the conclusion that clinicians should consider tapering opioid dosage among long-term opioid therapy (LTOT) users in accordance with clinical practice guidelines.<sup>2</sup> Our study was conducted to address the scant evidence from randomized controlled trials on the long-term effects of opioid therapy.<sup>3</sup> Given that there are known harms with opioid therapy, the performance of long-term trials is limited both by methodological issues and ethical concerns. When randomized controlled trials are not feasible, cohort studies are generally considered the best alternative for deriving evidence to drive clinical decision making. Beyond conducting long-term follow-up, our cohort study used propensity score matching of treatment groups to control for potential confounders. This matching included several variables not often measured in clinical trials involving low back pain, such as pain catastrophizing, pain self-efficacy, widespread pain, health-related quality of life, wage replacement benefits, and litigation.<sup>3</sup>

Our results consistently demonstrated that LTOT was not associated with any benefits pertaining to pain intensity, back-related disability, or pain impact, including in analyses that also considered the duration of opioid therapy, dose response, and complete treatment adherence over 12 months (analogous to per-protocol treatment in a clinical trial). Thus, it is unclear why Waters and Simon believe that these cohort study results do not further support Recommendation 5 of the Centers for Disease Control and Prevention (CDC) Guideline for

Prescribing Opioids for Pain.<sup>4</sup> Therein, with respect to patients already using LTOT, it states that “If benefits do not outweigh risks of continued opioid therapy, clinicians should optimize other therapies and work closely with patients to gradually taper to lower dosages or, if warranted based on the individual circumstances of the patient, appropriately taper and discontinue opioids.”

Waters and Simon also raise the question of whether tapering or discontinuing LTOT is beneficial. Their cited studies on the associations of rapid opioid tapering with drug overdose and mental health crisis (depression, anxiety, suicide attempt),<sup>5</sup> and of opioid discontinuation with overdose death,<sup>6</sup> have been widely recognized. Consequently, the updated 2022 CDC guideline<sup>4</sup> incorporated this new evidence on opioid tapering and discontinuation to help mitigate misapplication of its prior 2016 guideline for prescribing opioids for chronic pain.<sup>7</sup> However, the current guideline continues to recommend opioid tapering or discontinuation among patients using LTOT for chronic pain if the benefits of opioid therapy do not outweigh its risks.

Finally, although beyond the scope of our study, Waters and Simon advocate for greater consideration of buprenorphine as an alternative to continued opioid use or tapering. Indeed, the current CDC guideline states that “Emerging evidence suggests that patients for whom risks of continued high-dose opioid use outweigh benefits but who are unable to taper and who do not meet criteria for opioid use disorder might benefit from transition to buprenorphine.”<sup>4</sup> Buprenorphine is a partial agonist opioid that may be used to treat pain and opioid use disorder while less often causing respiratory depression and lowering overdose risk compared with full agonist opioids. Nevertheless, transitioning patients to buprenorphine is not a simple matter because it requires specific timing of the initial buprenorphine dose depending on factors such as whether patients are using short- or long-acting full agonist opioids, and whether low-dose initiation of buprenorphine may be used for patients not yet in opioid withdrawal. Consequently, to address such issues, the current CDC

guideline promotes the Providers Clinical Support System (<https://pcssnow.org/>) that offers training, technical assistance, and mentors to assist clinicians who are unfamiliar with initiation of buprenorphine.<sup>4</sup>

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