



Physicians for Responsible Opioid Prescribing
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Rochelle P. Walensky, MD, MPH
Director, Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA 30329

Re: Docket No. CDC-2022-0024

Dear Dr. Walensky:

Physicians for Responsible Opioid Prescribing (PROP) appreciates the opportunity to submit a comment to Docket No. CDC-2022-0024. PROP's members include clinicians and researchers in the fields of Primary Care, Pain Medicine, Addiction Medicine, Anesthesiology, Physical Medicine and Rehabilitation, Emergency Medicine, Public Health, Internal Medicine, Neurology, Psychiatry, Rheumatology and other specialties.

PROP finds the CDC's draft guideline to be a valuable contribution. Whereas the 2016 guideline was based on the best available evidence at the time, the present guideline is updated to include what has become a vastly expanded evidence base consisting of many additional studies, often conducted to fill knowledge gaps existing in 2016. Updating the evidence review in the draft has been a formidable task achieved to the highest standards. The new guideline has also taken steps to minimize the risk that opioids will be abruptly discontinued in patients who are physiologically dependent on opioids.

The draft guideline includes new evidence on alternatives to opioids for the treatment of acute, subacute and chronic pain, and on opioid tapering for patients in whom harm is judged to exceed benefit. The new evidence and additional exploration of alternatives to opioids add considerable weight to the principles of the 2016 guideline, further supporting the recommendation that initiation of long-term opioids should be avoided whenever possible. New evidence also demonstrates significant risks of high dose opioids (>50 MME/day) and shows that alternatives to opioids often provide equal or superior benefit with a markedly better safety profile. These are important findings which PROP fully supports being widely disseminated to medical professionals and to the public.

PROP's suggested edits are limited to the Box 1 Guideline Recommendations. We believe that the content in the Box Recommendations is especially important because it may be the only portion of the guideline that will be widely disseminated and read. Our proposed changes would not alter the intended guidance, but would make the Box Recommendations far more useful by more clearly translating evidence and guidance contained elsewhere in the draft. Specifically, we suggest the following incremental changes to the Box 1 Guideline Recommendations:

Revisions pertaining to initiating opioid use:

1. **For Box Recommendation 1 (Acute Pain), incorporate key information discussed elsewhere in the draft.** The CDC's proposed language for the Box 1 Recommendation suggests that clinicians should weigh potential risks versus benefits when considering opioids for acute pain. We believe that most health care professionals already attempt to weigh risk and benefit when initiating treatments so simply making this suggestion, without including evidence on risks and benefits, is unlikely to improve practice.

Many prescribers are unaware that with daily use, physiological opioid dependence develops in as little as 3 days. We believe this important fact, discussed elsewhere in the draft, should be explicitly mentioned. Informing clinicians about the rapid development of dependence is necessary because dependence causes withdrawal symptoms when opioids are discontinued. These symptoms include worsening of pain that can lead to continued use, flu-like symptoms and severe anxiety. Including the important fact that dependence can develop rapidly would help clinicians better weigh risks versus benefits when considering opioids for acute pain.

2. **For Box Recommendation 1 (Acute Pain), include discussion with patients.** Whereas Recommendation 2 (Subacute and Chronic Pain) advises clinicians to discuss with patients "the known risks and realistic benefits of opioid therapy" this important suggestion was not included in Recommendation 1. We believe that Recommendation 1 should contain this same advice. Specifically, patients should be explicitly informed that 3 days or more of continued use can result in withdrawal symptoms with abrupt discontinuation and that continued use increases risk of opioid use disorder. This needs to be highlighted because many clinicians are unaware that physiological dependence can set in rapidly and that duration of use is a risk factor for OUD.
3. **For Box Recommendation 4, clarify what is meant by "dosage above levels likely to yield diminishing returns."** In the supporting materials, this is defined as 50 MME/day or higher. For clarity, we recommend adding "50 MME/day" in parentheses just as was done elsewhere in the draft. For example, the statement could read: "... dosage above levels likely to yield diminishing returns (i.e., 50 MME/day or higher)." This change would make this recommendation far more useful.

Revisions pertaining to patients already using opioids long-term:

4. **Separate the recommendations concerning patients already using opioids long-term [Box Recommendations 5 and 12] from recommendations concerning patients initiating opioid use (all other recommendations).** By clearly distinguishing clinical issues pertaining to patients already using opioids long-term from those initiating opioid use, the distinctly different clinical considerations will be clarified.
5. **For Box Recommendation 5, clarify what is meant by “For patients already receiving higher opioid doses”.** In the supporting evidence review, this is defined as 50 mg morphine equivalent dose (MME)/day or higher. We recommend revising Box Recommendation 5 to say, “For patients already receiving higher opioids doses (i.e. 50 MME/day or greater).” By clarifying what the term “higher opioid doses” means the guidance in this recommendation will be far more useful.
6. **For Box Recommendation 5, highlight the importance of avoiding abrupt opioid discontinuation or rapid dose reduction.** We believe this important recommendation should be made more prominent by separating the first and second parts of Recommendation 5, and by highlighting (in bold or italics font) the caution to avoid abrupt discontinuation or rapid tapering. In addition, we recommend that a sentence be added stressing the utility of buprenorphine as an adjunct or alternative to tapering for patients having difficulty tapering with or without diagnosed Opioid Use Disorder.
7. **For Box Recommendation 12, expand the treatment with medications to include opioid dependent patients doing poorly on opioids but unable to taper off, as well as patients with Opioid Use Disorder.** We believe it is essential that Recommendations 5 and 12 be placed together, so that needs of patients already using opioids long-term are highlighted and considered separately. Also important to clarify the kinds of medications that are effective (e.g. “...or arrange treatment with medication (i.e., buprenorphine or other opioid agonist with lower overdose risk”).

Revision pertaining to duration and follow up:

8. **For Recommendation 6, incorporate key information in the Box Recommendation.** The draft guideline discusses the problem of opioid overprescribing for acute pain, which places patients at risk for dependence and OUD and increases opportunities for misuse. Evidence discussed in the draft shows that clinicians often overestimate the quantity of opioids needed. If clinicians routinely overestimate the quantity of opioid pills needed, then explicit guidance is necessary to reduce harm to patients and to limit excess opioids in the community. Unfortunately, Box Recommendation 6, as written, fails to offer practical guidance on the quantity and/or duration

of opioids that are typically needed. The evidence review included a finding that after common surgical procedures, the median number of opioid pills consumed was equal to three pills or less (K. A. Robinson et al., 2020). Evidence cited in the report, as well as international comparisons, suggest that the quantity of opioids prescribed for acute pain could be significantly reduced without a negative impact on treatment of pain. For example, a recently published international comparison of post-operative opioid use found that 91% of U.S. patients were prescribed opioids after surgery with a median of 20 pills, compared to 5% of non-U.S. patients receiving opioids. (HMA Kaafarani et al., 2020).

Revision pertaining to all recommendations:

- 9. Clarify the difficulties in weighing evidence for benefits versus risks of opioids for Recommendations 1, 2, 4, 5, 7, and 8.** The evidence review finds that opioid risk assessment tools are of unproven value. It also finds that, on average, benefits of opioids are modest for acute pain, while benefits for chronic pain have not been established, with a recent trial finding somewhat more intense pain for patients receiving opioids relative to those receiving non-opioid medications. In contrast, potential harms of opioids are now well established, including overdose and opioid use disorder, as well as physical and psychological adverse effects. It is especially difficult for clinicians and patients to weigh the risks and benefits of a controlled substance like opioids because opioid tolerance and dependence change the balance of benefit versus risk as well as the perception of benefit over time. Experienced clinicians report difficulty predicting benefits and risks of opioid use, other than the potential for prolonged use. These observations suggest that opioids are often a poor choice.

To clarify difficulties of weighing benefits and risks, we recommend adding a sixth guiding principle that states: “Assessment of benefits and risks for opioid use is complex and difficult due to the development of opioid tolerance and dependence. Available evidence indicates modest benefits of opioids for acute pain relative to placebo, while benefits for chronic pain have not been shown. Opioid risks have been well established, including drug overdose, opioid use disorder and physical and psychological adverse effects, and these harms affect a significant proportion of patients using opioids long-term.”

Sincerely,

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