American Cancer Society
Cancer Action Network
555 11th Street, NW
Suite 300
Washington, DC 20004
202.661.5700
www.acscan.org

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Tom Frieden, M.D., M.P.H.
Director, Centers for Disease Control and Prevention

Debra Houry, M.D., M.P.H.
Director, National Center for Injury Prevention and Control

United States Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, Georgia 30329-4027

Dear Drs. Frieden and Houry,

The American Cancer Society Cancer Action Network (ACS CAN) is pleased to offer comments on the Centers for Disease Control and Prevention's (CDC's) Draft Guideline for Prescribing Opioids for Chronic Pain, 2016.

Like you, we are deeply concerned about the public health emergency that exists today as a result of inappropriate use of opioids and the harms associated with such use. As a nation, we must take steps to address the issue. But we must do so in a balanced way that recognizes the need to maintain access for individuals fighting pain from cancer and other diseases and conditions that disable thousands of Americans from working, living independently and enjoying a productive quality of life. There is very little scientific understanding of the basic biologic causes of pain, and today there are even fewer ways of treating debilitating pain. We are concerned that the emphasis on how to reduce inappropriate use of opioids has paid very little attention to how these efforts may impede medically necessary access to these products.

With respect to the CDC's current effort, we believe the proposed guidelines have the potential to significantly limit cancer patient access to needed pain medicines. We have concerns about the lack of evidence on which the guidelines were based, the methodology used to develop the guidelines, and the transparency of the entire process. Our concerns are so serious that we cannot endorse the proposed guidelines in any way and suggest suspending the process until the methodological flaws are corrected and more evidence is available to support prescribing recommendations.

Pain is one of the most feared symptoms for cancer patients and survivors, with nearly 60 percent of patients in active treatment and 30 percent of patients who have completed treatment experiencing pain [1]. For example, research has concluded that about one-quarter of women who've had breast cancer surgery have significant and persistent breast pain six months after the procedure [2]. Integrative pain care that includes non-drug therapies along with medications is encouraged to keep patient pain under control. While not the only tool, opioid medications are recognized as a mainstay of treatment for moderate to severe cancer pain and can be a beneficial treatment for managing serious, persistent pain.

Potential Impact of CDC Guidelines

ACS CAN shares your goal of encouraging appropriate use of opioids. It is critical, however, that any public policies crafted to define appropriateness be based on solid scientific evidence. Unfortunately the guidelines drafted by CDC, by its own admission, are based on weak or nonexistent evidence. Guidelines officially sanctioned by the CDC are likely to have significantly greater impact than guidelines promulgated by other organizations. In fact, the CDC imprimatur makes it more likely that these guidelines become de facto requirements through adoption by state health departments, professional licensing bodies or insurers. CDC even acknowledges that this is one of the goals of this process.

> *"Clinical guidelines represent one strategy to improve prescribing practices and health outcomes. Efforts are required to disseminate the guideline and achieve widespread adoption and implementation of the recommendations in clinical settings. CDC is dedicated to translating this guideline into user-friendly materials for distribution and use by health systems, medical professional societies, insurers, public health departments, health information technology developers, and providers, and engaging in dissemination efforts."*

Guidelines not based on solid evidence

CDC purported to follow a widely used framework for producing evidence-based recommendations known as GRADE (Grading of Recommendations, Assessment, Development and Evaluation) to create the proposed guidelines. In reality, however, CDC appears to have deviated significantly from the established methodology, calling into question the integrity and validity of the ensuing recommendations. Seven of the 12 recommendations were based on "very low quality of evidence" and five of the 12 on "low quality of evidence," yet six of the

seven recommendations with evidence rated "very low" and all of the recommendations with "low" evidence ratings were designated as "strong" recommendations. The GRADE process ordinarily permits this discordance only in exceptional circumstances, and this stark departure from GRADE methodology was done without associated justification. The rationale statements appeared to rely heavily on expert opinion, but this was not explicitly acknowledged.

In one example, the draft recommendation document states:

> *"For KQ1 [KeyQuestion #1], no study of opioid therapy versus placebo, no opioid therapy, or non-opioid therapy for chronic pain evaluated long-term (>1 year) outcomes related to pain, function, or quality of life."*

In other words, despite the fact that no scientific study could be located comparing the effectiveness of long-term opioid use relative to other options, CDC nonetheless issued a strong recommendation that non-opioid therapy was the preferred treatment.

> *"Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain. Providers should only consider adding opioid therapy if expected benefits for both pain and function are anticipated to outweigh risks (strong recommendation, low quality of evidence)."*

Use of cost in guideline development process

We take strong exception to the use of cost data as an input to the guidelines. The costs highlighted in the document deal with non-medical use, abuse and overdose of opioids, but no mention is made of the costs due to chronic pain. Further, while costs may be a valid consideration in the context of GRADE methodology, it is wholly inappropriate for the government to use cost, rather than efficacy, to suggest restricting access to treatments that patients pay for themselves through copays and insurance premiums.

Role, composition and influence of the Core Expert Group

The distinct roles of CDC staff members and the Core Expert Group have not been made clear. According to the draft recommendation document, the Core Expert Group was not actually involved in writing the draft guideline; rather it was CDC staff who authored the draft. The Core Expert Group commented on the CDC-drafted recommendations, and no information was

provided about whether and how the Core Expert Group's input resulted in changes to the recommendations.

> *"Based on a review of the clinical and contextual evidence (review methods described in more detail below), CDC drafted recommendation statements focusing on determining when to initiate or continue opioids for chronic pain outside of end-of-life care; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use. CDC then solicited expert opinion in the form of individual ratings, discussions, and written comment to inform a refinement of the recommendations."*

Given the limited and low-quality evidence on which the guidelines were based, the individual opinions of the Core Expert Group have the potential to significantly impact the nature of the guidelines. Broad stakeholder representation and robust conflict of interest protection, in theory, could mitigate biases in this group, or at the very least make them transparent. CDC indicates that it undertook an effort to discern conflicts of interest, but it is not clear that CDC fully accounted for intellectual and professional activities and relationships or developed an explicit strategy to mitigate biases.

Lack of transparency and opportunity for public input

We have concerns that the attempts to solicit public input on the draft guidelines were cursory and did not allow adequate opportunity for thoughtful responses. While a public webinar was held to discuss the recommended guidelines, it was not well advertised and many interested parties were denied access because the webinar lacked sufficient capacity. Further, only a brief summary of each of the recommendations was shared, with no supporting documentation to provide evidence, context, or insight into the process. The public had 48 hours to comment, a rather abbreviated time period when compared to typical 30-90 day comment periods for similarly impactful proposed policies by the administration. By legal definition the guideline is not a proposed regulation subject to the Administrative Procedures Act, but clearly the intent of CDC is that the guideline be distributed to and adopted by state public health entities and certifying organizations as if it had the legal authority of a regulation. Given the potential public impact of the proposed guidelines, CDC should provide more complete information to the public regarding their draft guidelines and provide commensurate opportunity for input.

Conclusion

We share the goal of reducing inappropriate use and adverse events related to opioids, but we also have grave concerns about unduly restricting access to appropriate and effective pain management for individuals with cancer and other chronic conditions. We are concerned that the draft document does not reflect the appropriate weighing of benefits and harms at the individual and population levels, a fundamental element of rigorous guideline development. The process that the CDC followed departed from reliance upon evidence and methodological rigor, as well as accepted standards of transparency. We strongly suggest that CDC withdraw its draft guideline and instead focus on generating additional data to inform future guidelines as well as ongoing educational efforts on harm and abuse prevention.

On behalf of ACS CAN I thank you for the opportunity to comment on the proposed guidelines. If you have any questions, please feel free to contact me or have your staff contact Mark Fleury (mark.fleury@cancer.org).

Sincerely,

Christopher W. Hansen
President
American Cancer Society Cancer Action Network

1. Institute of Medicine. (2011). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research. National Academy of Sciences.
2. Miaskowski C, Cooper B, Paul SM, et al. (2012). Identification of Patient Subgroups and Risk Factors for Persistent Breast Pain Following Breast Cancer Surgery. J Pain; 13(12) pp 1172-1187.