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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

Re: Draft Guideline for Prescribing Opioids for Chronic Pain, 2016 [CDC-2015-0112-0001]

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) Revised Draft Guideline for Prescribing Opioids for Chronic Pain, 2016.

We applaud CDC for opening up the guideline process for further public review and input. This guideline is likely to affect the way that individuals with cancer and survivors have their pain managed, and allowing robust review and input by all affected parties can only make the final product stronger. CDC has undertaken a significant amount of work in order to facilitate and evaluate the input from this public process, and we are grateful for CDC's recognition of the role that public discourse on this issue plays. ACS CAN was part of a select stakeholder review group that had an opportunity to review an earlier version of this guideline. As part of that review we expressed concern about the lack of evidence supporting the guideline, a lack of transparency in the development process, and CDC's failure to adhere to proper methodology in developing the guideline. Unfortunately, the revised recommendations issued for review still remain essentially unchanged from the earlier version we provided comments on in 2015, but we are hopeful that our further comments, along with others, will continue to inform constructive changes to the guideline.

We share the CDC's deep concern about the public health burden that exists today as a result of inappropriate use of opioids and the associated harms. As a nation, we must take steps to address the issue, and providing patient-centered and evidence-based guidance to improve the prescribing practices of general practitioners is one of many tools that can be employed. The issue of misuse must be addressed in a balanced way that recognizes the need to maintain access for individuals fighting pain from cancer that prevents them 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 reducing inappropriate use of opioids has paid very little attention to how these efforts may impede medically necessary access to these products for individuals affected by cancer.

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]. 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.

Guideline not based on solid evidence

Prescribing guidelines can be useful public policy tools to influence the practice of medicine; however, it is critical that any guideline be based on solid scientific evidence, be patient-centered, and adequately convey the individual nature of benefits and risks. Unfortunately the evidence needed to create a guideline for the use of opioids for chronic pain is weak or nonexistent. Last year a National Institute of Health workshop on the use of opioids for chronic pain concluded: *"…evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain."* [2] For example, no clinical studies have been conducted directly comparing the safety or efficacy of opioids versus non-opioids for chronic pain, which is the core question addressed by the CDC's proposed guideline.

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[1] Institute of Medicine. (2011). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research. National Academy of Sciences

[2] Reuben DB, Alvanzo AAH, Steffens DC, et al. National Instituted of Health pathways to prevention workshop: The role of opioids in the treatment of chronic pain. Ann Intern Med. 2015;162(4):295-300. doi: 10.7326/M14-2775

In the earlier version of the guideline seven of the twelve recommendations were based on "very low quality of evidence" and five of the twelve on "low quality of evidence." CDC has adopted slightly different nomenclature to describe the level of evidence in the current draft guideline, replacing the descriptive "low" and "very low" with numerical scores that have equivalent meanings. Despite the change in labeling, the evidence supporting the recommendations remains low to very low. In addition to changing the descriptors for the evidence, CDC also changed the categorization of the strength of each recommendation from the descriptive categories of "strong" and "weak" to essentially equivalent "A" and "B" ratings. The guideline describes these ratings as follows:

"Category A recommendations apply to all persons in a specified group and indicate that most patients should receive the recommended course of action. Category B recommendations indicate that there should be individual decision making; different choices will be appropriate for different patients, so providers must help patients arrive at a decision consistent with patient values and preferences, and specific clinical situations."

We note that based on the descriptions of "A" and "B," shared decision making between the patient and his or her physician is only promoted within category "B" recommendations. We believe strongly, however, that **every** therapeutic treatment decision should involve shared decision making between patients and their providers and that an "A" recommendation should not be a reason ignore patient goals and preferences in decision making about their care.

The change from descriptive categories to numerical and letter-based categories does not change the fact that strong recommendations for patient care are being made based on weak or incomplete evidence. This shortfall can only be resolved through the development of additional evidence or more closely correlating the strength of the recommendations to the strength of the evidence.

Implementation/applicability guidance should be included in the guideline material

We remain concerned about the potential for misapplication of the proposed guideline by providers, insurers, health systems and oversight bodies. CDC has indicated that the guideline "is intended for primary care providers," and that CDC will create implementation materials at a later time. We strongly believe that implementation guidance and materials should be part of the guideline when it is released in a final form. Because of the potential for misapplication in the field, the guideline should include case studies to illustrate which providers, patients, and

settings it is intended for and where it does not apply. For example, how would CDC anticipate the application of projected dosing limits to stable cancer patients or long-term survivors already on a dose exceeding the recommended dosage, and to patients seeing providers other than primary care practitioners for whom the guideline is intended (e.g. pain specialists, oncologists, surgeons, etc.)?

The guideline proposes three explicit exemptions: for individuals in active cancer treatment, at the end of life, or receiving palliative care. We greatly appreciate that CDC has recognized the important role that pain management plays in caring for patients in these groups, and the need to preserve all options for dealing with that pain. Cancer patients often begin experiencing pain during active treatment due to the cancer itself or the treatments, including chemotherapy or surgery. For cancer patients who are cured or enter remission, often their pain does not stop with the end of treatment, but rather can continue for a significant period of time or even indefinitely. As an example, research has concluded that about one-quarter of women who have had breast cancer surgery have significant and persistent breast pain six months after the procedure[3], which under this guideline would qualify as chronic pain. Similarly, chemotherapy-induced neuropathy can persist beyond treatment and become chronic. Individuals with these types of pain are neither in active treatment nor are they at end of life, but they do require active pain management. The guideline indicates that cancer patients under treatment are exempt from the guideline, while those who have completed treatment are not. From the standpoint of a patient and his or her provider, the existence of pain does not abruptly change on the final day of treatment, and neither should the management of that patient's pain. The guideline's distinction between active cancer treatment and surveillance is arbitrary and seems to fail to recognize the pain experienced by cancer survivors.

Another area in need of clarification is how CDC defines "palliative care." Patients receiving palliative care are rightfully exempted from the guideline, but understanding this intended exemption is critical to effective implementation. The guideline references the Institute of Medicine (IOM) definition of palliative care, (see below) which explicitly lists pain management as a critical component of palliative care and further clarifies that palliative care is not synonymous with end-of-life care. The fact is, the provision of palliative care is appropriate from the point of diagnosis of serious illness, through treatment and, if needed, through

[3] 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.

survivorship. Palliative care is appropriately given at any stage of the disease trajectory. When treating cancer, this means that palliative care could continue after the completion of active treatment if pain or other symptoms of treatment persist. The "Scope" section of the guideline, however, indicates that once active cancer treatment has ended, this guideline would apply to survivors, which is in contradiction to the exemption accorded to palliative care. As a result, the guideline is confusing and cancer patients and their providers need clarity on this point to assure access to needed opioids if they are still in pain after active cancer treatment has ended.

Conversely, CDC should explicitly clarify under which conditions pain management for cancer survivors is not considered palliative in nature and therefore subject to this guideline.

> *IOM Definition of Palliative Care:*
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> *"The committee defined palliative care for this report as care that provides relief from pain and other symptoms, that supports quality of life, and that is focused on patients with serious advanced illness and their families. Hospice is an important approach to addressing the palliative care needs of patients with limited life expectancy and their families. For people with a terminal illness or at high risk of dying in the near future, hospice is a comprehensive, socially supportive, pain-reducing, and comforting alternative to technologically elaborate, medically centered interventions. It therefore has many features in common with palliative care.* ***Palliative care can begin early in the course of treatment for any serious illness that requires excellent management of pain or other distressing symptoms, such as difficulty breathing or swallowing, and for patients of any age. It can be provided in conjunction with treatments for cancer, heart disease, or congenital disorders, for example. Palliative care is provided in settings throughout the continuum of care."*** [emphasis added]
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> *-- Institute of Medicine: "Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life"*

Potential impact of CDC guidelines

ACS CAN shares your goal of encouraging appropriate use of opioids through a variety of policy, educational, and scientific efforts. A prescribing guideline officially sanctioned by the CDC is likely to have significantly greater impact than guidelines promulgated by other organizations. In fact, the CDC imprimatur makes it more likely that these recommendations become de facto

requirements through adoption by state health departments, professional licensing bodies and insurers. This is already taking place within both the federal government and certain states. For example, a pending bill in the U.S. House of Representatives (H.R. 4063) would mandate the adoption of the CDC guideline by the Veteran's Administration (VA). The recently enacted omnibus spending bill (Public Law 114-113) included report language directing the VA to adopt CDC's prescribing guideline. Further, many state legislatures will look to the CDC guideline for creation of state legislation. A bill introduced by the governor of Massachusetts (MA HB 3817) limits first-time opioid prescriptions to 72 hours unless a medical emergency exists, with no exception for cancer patients, palliative care, or the end of life, and no limitation to general practitioners. The CDC guideline proposes this same 72-hour limit.

CDC indicates that adherence to the prescribing guideline is not mandatory, but as the examples above illustrate, others are interpreting the proposal not only as mandatory, but also expanding the scope and audience for guidance beyond the intended primary care audience which is likely to affect cancer patients. The fact that these legislative efforts are being influenced by the content of the proposed guideline just reinforces our view that there needs to be a stronger evidence base and greater effort to provide implementation guidance. Given its influence, the guideline should be clear about intent, strength of evidence and applicability.

Coordination with other agencies

We encourage CDC's Center for Injury Prevention and Control to coordinate and seek guidance from others with expertise within the Department of Health and Human Services including experts in the Food and Drug Administration (FDA), the Agency for Healthcare Research and Quality (AHRQ), and the National Institutes of Health (NIH). Individuals within these agencies have expertise in the issues at hand, and may have broader perspectives about the various tools needed to resolve the opioid abuse problem in such areas as prescription monitoring programs, public education strategies, research into alternative clinical and non-clinical alternatives to opioids in pain relief, and evidence about appropriate dose levels. FDA, for example, is responsible for reviewing safety and efficacy of drugs, including opioids, and their extensive analysis should be incorporated into the guideline process. It is notable that after review of a recent citizen petition requesting that opioid labeling be revised to limit dosages to 100 MME per day or less, FDA found that the evidence did not support this change, yet CDC has recommended a 90 MME per day dosing ceiling in the proposed guideline.

Evaluation, evidence and balance

CDC acknowledges that additional efforts must be made by others outside of the agency's control if the nation is going to make a serious and comprehensive effort to both end opioid abuse and to provide patients reasonable alternatives to opioids.

"In addition, policy initiatives that address barriers to implementation of the guidelines, such as accessibility of PDMP data, availability of providers of medication-assisted treatment for opioid use disorder, insurance coverage for nonpharmacologic treatments and appropriate urine drug testing, and reimbursable time for patient counseling might likewise be effective in enhancing implementation of the recommended practices."

These are key tools and tactics that need to be enhanced in any national and comprehensive public health strategy to combat opioid addiction and abuse. It is not enough for CDC to acknowledge these known barriers to feasible implementation of the guideline and then to make no commitment as to how they should be addressed. As the nation's public health agency there is much more that CDC can do, including committing to:

- more research to provide an evidence base for the use of opioids for chronic pain
- fully analyzing the prevalence of chronic pain in the U.S. and its impact on public health
- collecting more data on the barriers patients face to effective pain relief
- monitoring the effect of implementing the proposed guideline on
    - patient access to appropriate pain treatment
    - overall prevalence of chronic pain and disability due to pain
    - shifts to illicit drugs

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 cancer survivors. We are concerned that the draft document does not reflect the weakness of the evidence on which it was created, does not emphasize patient-centeredness, and will remain challenging to implement in a way that does not adversely impact cancer patients and survivors. We also stress that guidelines are but one of many policy tools available to combat the harms caused by inappropriate opioid use, and we call on CDC to commit to ensuring that the necessary policy steps and infrastructure are in place to make any new guideline possible to implement, including generating additional data to inform future guidelines as well as ongoing educational efforts on harm and abuse prevention.

Thank you for the opportunity to comment on the proposed guideline. We stand ready to work with you to improve the 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