american academy of pain management

Our Vision: No Life Limited by Pain

October 20, 2015

The Honorable Fred Upton
Chairman
House Energy and Commerce Committee
United States House of Representatives
Washington, DC

Dear Chairman Upton:

I am writing to you today on behalf of the American Academy of Pain Management (the Academy) to express our concerns about an effort underway by the US Centers for Disease Control and Prevention (CDC) to develop a guideline for prescribing of opioid analgesics to treat pain. While we have concerns about some of the content of the draft guideline that CDC has presented, the subject of this communication is the process that is being undertaken to develop that guideline. We are very concerned that this process is deeply flawed, and that any guideline developed as a result: 1) is in no way supported by current standards of chronic pain management; (2) will alter clinicians' decision processes relative to their most difficult pain control challenges; and (3) will certainly have negative impacts on patients. Following are some of the key points of concern, which we would like to bring to your attention.

Summary of the guideline development process

On January 15, 2015, CDC issued a request for applications, seeking assistance in developing an evidence-based guideline for prescribing of opioids to treat chronic pain. CDC then revealed no further information about this process publicly until June 16, 2015, when it invited a limited number of stakeholders to review an anticipated draft guideline. It should be noted that the draft guideline document, when eventually released, stated that the draft had been reviewed by a group of federal partner agencies, but the timing for that review is unknown to us.

CDC followed these emailed stakeholder invitations with an email to a larger group on August 25, 2015, announcing that it would hold a webinar for a limited number of interested participants on September 16, 2015. This emailed invitation noted that comments on the draft guidelines could be submitted orally over the telephone during the webinar, by writing in real-time via the webinar portal, and by email for 25 hours following the webinar. CDC later extended the deadline for email comments to 49 hours, and was forced to re-run the webinar on September 17 due a technical problem on September 16.

Participants in the webinar noted that there was no response from the CDC staff presenting the webinar to any comments that were made during the webinar, nor was there an attempt to answer any questions posed by webinar participants.

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In parallel with this, CDC released the draft guideline to the stakeholder review group on September 14, 2015, with a response deadline of October 1, 2015. Comments on the draft guideline were solicited in the form of a spreadsheet. CDC noted that it would compile comments from all sources, de-identify them in terms of their source, and post them on the CDC website on or around October 23, 2015. Stakeholders will be able to participate in a telephone review of this information on October 21, 2015.

Following compilation and consideration of the comments, a group of three physicians will advise CDC on revisions to the guideline. CDC anticipates issuing the final guideline in January, 2016.

An "evidence-based guideline" without an evidence base

On September 29 and 30, 2014, the National Institutes of Health held a *Pathways to Prevention* workshop on The Role of Opioids in the Treatment of Chronic Pain. Prior to this workshop, experts compiled the relevant available evidence through an exhaustive search of the literature. This compilation formed the basis for scholars who, at the workshop, reviewed the evidence of benefits and harms resulting from the use of opioid treatment for chronic pain. Following the workshop, an unbiased, independent panel developed a report summarizing the current state of affairs with respect to research into opioid treatment of chronic pain. Perhaps that report, released on October 2, 2015, is best summarized by this statement from its conclusion:

> "What was particularly striking to the panel was the realization that there is insufficient evidence for every clinical decision that a provider needs to make regarding the use of opioids for chronic pain, leaving the provider to rely on his or her own clinical experience."

Despite this statement from the panel's report, we were struck by the fact that, only three months later, CDC issued its request for applications to develop "an evidence-based guideline". We wonder how CDC could be calling for an "evidence-based guideline" when the National Institutes of Health, after a considerable investment of time and money, had just concluded that there was, in effect, no evidence. We also wish to note that a group of pain management experts, led by the Academy's current executive director, worked with CDC employees in 2012 and 2013 to review existing opioid treatment guidelines, and concluded that all of them were based on very sparse evidence—that they represented "consensus" guidelines, not "evidence-based" guidelines, because there was insufficient evidence on which to base a guideline.

In its draft guideline, CDC acknowledges just how weak the evidence is. The draft guideline provides twelve recommendations for prescribers, and rates the evidence base for these twelve guidelines as being of "low quality" in five cases and as being of "very low quality" in seven cases. Yet, in another puzzling twist, the draft guideline also rates eleven of the twelve recommendations as "strong" and only one as "weak". In our view, a recommendation based on "low" or "very low" quality evidence should hardly ever be a strong one, as it essentially represents an expert opinion, rather than a conclusion drawn from evidence.

Makeup of groups advising CDC on guideline development

Although CDC has not been
transparent about the members of the Core Expert Group that helped it develop the initial recommendations, the Stakeholder Review Group, or the three experts who will assist it in developing a final draft, we are privy to this information because we are one of the stakeholder groups invited to review the draft. We find the makeup of these groups both puzzling and concerning. To wit:

Core Expert Group: This group of 17 individuals contains one person who is a *bona fide* pain management expert—Dr. Jane Ballantyne, a retired physician most recently from the University of Washington. The remaining members include five non-physicians and eleven physicians from a variety of medical specialties. For instance, one is a retired cardiologist who works for a state health department, while another is an emergency physician and medical toxicologist who, by virtue of his specialty, treats primarily acute pain and overdoses, rather than chronic pain. Another is a neurologist who is best known for his nationwide advocacy of efforts to markedly curtail opioid prescribing. In sum, this is a panel filled with individuals who are on the record as opposing the use of opioids to treat chronic pain in nearly all circumstances. By virtue of their work, they focus on the potential harms of opioid treatment without focusing on the potential benefits—which is not surprising, given that they come from backgrounds that do not expose them to people with pain who are successfully treated with opioids.

Stakeholder Review Group: Eighteen groups are identified as stakeholders, and each of those stakeholders has identified a point person. Here, the representation of pain management organizations is somewhat better: six of the 18 groups are specifically pain management provider organizations. Another nine groups represent various medical specialties in which pain is prevalent; two represent people who have chronic pain; and one is an organization that has been prominent in efforts to curb opioid prescribing across all patient groups.

Final Review Group: This group consists of three physicians, one of whom is a pain management specialist. The remaining two members are an expert in outcomes research and healthcare communication, and an emergency medicine specialist and medical toxicologist who has published extensively with the toxicologist previously identified as a member of the Core Expert Group. Interestingly, this individual's website lists her research expertise as, "Evaluating methods to limit initiation of new opioid users and modify opioid misuse through interventions in the ED, regionally and nationally." We are struck by two facts here: this has very limited applicability to the treatment of chronic pain, which is the supposed subject of the guideline; and that this is a public statement that the primary goal of her research is to reduce the total number of opioid prescriptions written, a fact that is inconsistent with the effort to develop a guideline addressing the prescription of opioids to manage chronic pain.

These groups, charged with developing a guideline on how best to use opioids to treat chronic pain, are overwhelmingly dominated by individuals with no apparent expertise in the subject, nearly devoid of groups representing and advocating for people with pain, and studded with a number of individuals who are publicly on record as opposing the use of opioids to treat most types of chronic pain. This leads us to our next source of concern.

<u>Potential sources of bias in expert groups</u>

In its draft guideline document,
CDC describes at length the steps it took to seat an unbiased panel, stating that it considered not only bias associated with employment as a consultant by pharmaceutical manufacturers, but also public statements made by experts, and a number of additional sources of bias. CDC asserts that it has succeeded in identifying an unbiased panel.

Yet, in the disclosures found in the CDC document, it is noted that Dr. Ballantyne, the only pain management expert in the Core Expert Group, has served as a paid consultant to a law firm that has aggressively shopped, to various levels of government, lawsuits against opioid manufacturers, alleging that those manufacturers are responsible for substantial harms to those government entities, resulting from adverse effects of opioid treatment that, in turn, resulted from illegal and/or inappropriate marketing practices by those manufacturers. If the CDC was going to such great lengths to seat an unbiased panel, they should have easily identified that this law firm would undoubtedly be aided in litigating its cases by the establishment of a CDC clinical practice guideline recommending severe restrictions on the use of opioids.

Two members of the Core Expert Group, two designated reviewers in the Stakeholder Group, and one of the three experts assisting with the final draft of the guideline, all are members of the board of directors of an anti-opioid lobbying organization named Physicians for Responsible Opioid Prescribing. This group has been extremely active in attempts to limit opioid use, including a Citizen Petition effort to convince the US Food and Drug Administration (FDA) to change the label indications for extended release and long-acting opioids so as to limit their approved use to no more than 90 consecutive days and to doses at or below the equivalent of 100 mg of oral morphine daily, for all persons with non-cancer pain. It should be noted that FDA denied this Citizen Petition on the basis of its review of the scientific evidence, opting instead to make minor, but still significant, changes to those label indications. Specifically, FDA found no evidence supporting either a duration or dose limit on these medications. (A copy of FDA's decision and its explanation is attached.) One of the recommendations contained in the draft guideline is that opioid doses above the equivalent of 90 mg of morphine daily be avoided.

It also should be noted that a long-time employee of the CDC's National Center for Injury Prevention and Control, the home agency for this guideline, is a former member of the board of directors for Physicians for Responsible Opioid Prescribing; his name appeared on the letterhead used to submit the Citizen Petition to FDA. The extent to which this individual participated in the guideline development process is unknown.

It is our contention that, if CDC intended to exclude experts who may have displayed a bias through their public statements and professional activities, it failed. Several members of all three expert groups have written and spoken extensively and inaccurately about a supposed lack of utility for opioids in treating chronic pain, and several also have consulted with government agencies, non-governmental organizations engaged in addressing prescription drug abuse, and others, suggesting ways in which to limit opioid use. It is not known to us if any of these individuals might also have consulted with for-profit entities such as workers' compensation insurance companies.

We remain concerned that the biases of expert consultants have not been fully disclosed, and that some members of these groups perhaps should have been excluded.

Unnecessary secrecy and extremely limited opportunities to provide comments

We acknowledge that, because the document in question is a guideline, and not a proposed rule, the ordinary standards for obtaining and considering feedback from anyone who wishes to comment do not apply. We also note that members of the Senate Health, Education, Labor, and Pensions Committee have very recently expressed concern about government agencies using a guideline development process as a means of circumventing the standard requirements for transparency and public comment (http://www.help.senate.gov/chair/newsroom/press/senators-challenge-department-of-labor-regulatory-actions). That said, we are at a loss to explain the extraordinary secrecy and extremely limited opportunities for comment attached to this guideline development process.

Within both the medical and regulatory fields, it is axiomatic that transparency and vigorous debate considering a wide variety of viewpoints produces the best results. To that end, when most government regulatory bodies propose new policies, they fully disclose the expert consultants advising them, and they accept comments from a wide array of sources, allowing at least 30, and more often 90, days to receive those comments. This allows all stakeholders concerned by the content of the proposed policy to a) be aware of the proposal so they can ensure that their concerns are communicated; and b) have time to carefully consider and discuss the proposals so that they can offer well-reasoned comments and suggestions for approval. Due to the strict secrecy and limited participation in the development process established by CDC in this case, neither of those was possible, except as it concerns the expert groups.

Consider:

- To this date, CDC has not publicly identified the members of any of the three expert groups
- Every communication we receive as a stakeholder group reminds us to maintain confidentiality with respect to the content of the draft guideline
- The comment period provided to webinar participants was extraordinarily limited, to such an extent that it was challenging even for experts in this arena to construct well-reasoned comments in time to submit them
- There will be no further review by stakeholders after the next draft of the guideline is written
- Comments received by CDC will be stripped of information identifying their source, and may also have their content edited so as to allow presentation of a summary of the comments, rather than the actual comments. This contrasts sharply with the practice of regulatory agencies that post all comments, with attribution, on their websites.

In the end, this guideline doesn't give us anything we don't already have

As our prior work with CDC demonstrated, there is no shortage of clinical practice guidelines, issued by a variety of professional organizations and regulatory bodies, with a variety of patient populations in mind. All of them are consensus guidelines, reflecting primarily the opinions of experienced clinicians because of the paucity of evidence regarding long-term use of opioids to treat chronic pain. The recommendations contained in the existing guidelines vary to some degree, but most of them are consistent with the recommendations in CDC's draft guideline. So what have we accomplished, if CDC issues another such guideline? In one sense, we will have achieved nothing, because it won't

contribute something new to the
discussion. In another sense, though, the potential for unintended negative consequences for people with pain is substantial. Experience with similar clinical practice guidelines has shown that many clinicians treat them as rules, not as guidelines, and that a substantial portion of primary care providers (the stated targets of this guideline) will simply opt to stop prescribing opioids to their patients with chronic pain. What will these people do to address their pain?

Our request

In light of the concerns we have detailed here, we respectfully request that your committee look into CDC's actions with respect to this guideline development process. We think that questions need to be asked and answered, with respect to: the poor-quality evidence underlying these "strongly recommended" "evidence-based" guidelines; the process of selecting experts to participate in the various groups involved in developing these guidelines; potential sources of undisclosed bias from a variety of sources; the implications of CDC issuing a clinical practice guideline developed without the benefit of appropriate peer review, that could limit access to pain medications for people who benefit from them; and the reasoning behind the lack of transparency and opportunity for comment from the public found in this process. Unless these questions are adequately addressed, the organizations with clinicians who strive to treat chronic pain, and in fact do so with opioids, will not support them but will, by necessity, be forced to actively oppose them, ensuring that clinicians understand why.

As we mentioned above, we believe that this is a situation in which transparency and robust academic debate will produce the best outcome. We urge you to strongly encourage CDC to withdraw this draft guideline and, should they decide to start over, to engage in a process that is more transparent and inclusive of the needs and views of all clinicians and patients—both those with pain and those who misuse opioid pain relievers.

Robert Twillman, PhD Sincerely,

Robert Twillman, Ph.D., FAPM
Executive Director
American Academy of Pain Management

cc: The Honorable Frank Pallone, Jr.
Ranking Member
House Energy and Commerce Committee

The Honorable Joseph R. Pitts
Chair, Health Subcommittee
House Energy and Commerce Committee

The Honorable Tim Murphy, Ph.D.
Chair, Oversight and Investigations Subcommittee
House Energy and Commerce Committee