January 13, 2015

Debra Houry, MD, MPH
Director, National Center for Injury Prevention and Control
Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30329-4027

RE: Docket No. CDC-2015-0112

Dear Dr. Houry,

On behalf of the American Society of Addiction Medicine (ASAM), a national medical specialty society representing more than 3,800 physicians and other clinicians who specialize in the treatment of addiction, I am pleased to offer the following comments on the Draft CDC Guideline for Prescribing Opioids for Chronic Pain (Draft Guideline) as well as ASAM's support and gratitude for CDC's leadership in developing the Draft Guideline.

While opioids offer relief to many patients with pain and should remain an available and acceptable option for pain management when medically indicated, it is clear from prescribing data and related addiction treatment admission and overdose death data that the medical community has over-relied on opioids to treat pain. Indeed, between 1999 and 2008, sales of opioid pain relievers increased fourfold, while opioid-related substance use treatment admissions increased nearly six-fold and opioid-related overdose deaths nearly quadrupled.[1] Despite the increase in opioid prescriptions, evidence indicates that 40 to 70% of people with chronic pain are not receiving proper medical treatment. An NIH panel recently concluded that, "Together, the prevalence of chronic pain and the increasing use of opioids have created a 'silent epidemic' of distress, disability, and danger to a large percentage of Americans."[2]

Meanwhile, the latest epidemiological data on drug-poisoning deaths involving opioid analgesics and heroin released by the National Center for Health Statistics show that our nation's epidemic of opioid misuse and related overdose deaths is worsening.[3] Drug-poisoning deaths involving opioid analgesics increased 16% between 2013 and 2014, and overdose deaths related to heroin increased 28% during the same period. Clearly, we are not only failing to treat chronic pain well, but we are failing to prevent the devastating consequences of opioid misuse.

ASAM has long supported increased education of all health professionals licensed to prescribe controlled substances as a key part of a comprehensive strategy to reduce opioid misuse, addiction and overdose deaths.[4] Evidence-based clinical guidelines for prescribing opioids in primary care, such as CDC's Draft Guideline, can support such increased education and potentially lead to a more informed health care workforce and more judicious opioid prescribing.

4601 N. Park Avenue, Upper Arcade #101, Chevy Chase, MD 20815
Phone: 301.656.3920 | Fax: 301.656.3815
www.ASAM.org

ASAM commends CDC for developing such a guideline which encourages careful and thoughtful opioid prescribing by primary care practitioners who are treating patients with chronic, non-malignant and non-terminal pain. Indeed, ASAM believes the CDC Draft Guideline is an important step forward in advancing the two ethical principles identified by the NIH panel: beneficence and doing no harm, specifically between the clinically indicated prescribing of opioids and the need to prevent opioid misuse and related harms.

ASAM encourages CDC to release the final guidelines as expeditiously as possible. This guidance is urgently needed by primary care practitioners. Guidance related to recommended dosing and duration of opioid therapy is especially critical, as we know that opioids are frequently prescribed in dosages and for durations that exceed what would generally suffice to alleviate pain and allow for healing of acute injuries. ASAM commends CDC for including recommendations in the Draft Guideline that direct providers to prescribe the lowest possible effective dosage and prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids.

With that commendation, ASAM would like to offer the following general comments and recommendations, which we feel will strengthen the Draft Guideline. Additional and specific comments submitted by members of ASAM's Quality Improvement Council are also included as an appendix to this letter.

1. **Consider expanding the Draft Guideline's target audience beyond primary care providers.** Dentists, pain management specialists, and surgical specialties are also heavy prescribers of opioids. Although the rationale may be that they prescribe primarily for acute pain conditions, that is not always the case. Consider broadening the scope of the Draft Guideline to include any prescriber of opioids for chronic, non-end-of-life pain.

2. **Emphasize functional improvement as a primary goal of pain management.** Effective pain management – with or without opioid pharmacotherapy – improves function with some diminution in pain scale ratings. While the document, even from the beginning, mentions reduction in pain as an outcome of opioids, there is little mention of functional improvement as the primary goal. This should be emphasized as patients and providers often focus on pain ratings with less attention paid to functional improvements. This is an opportunity to broaden patients and providers' understanding of the goals of pain management and correct the misperception that reduced pain is the only or primary end point of treatment.

3. **Consider including high-quality observational studies and research on effectiveness.** While randomized controlled trials (RCTs) are the gold standard for medication efficacy studies, well-done, observational studies can provide needed longitudinal data in this area. The document seems to apply the GRADE approach to say that observational studies just by their methodology are low-quality studies, potentially not discriminating between methodologically robust longitudinal studies and those that clearly are of low quality. Given that much of the research on lung cancer and smoking was observational, consideration should be given to the potential of including some observational studies, especially in the absence of RCTs. Further, the criteria for inclusion of low-quality and high-quality studies seem inconsistently applied across the five different clinical questions as it reports no studies being included for the question on effectiveness while observational and uncontrolled studies are included in the question on harms.

4. **Clearly distinguish dependence and tolerance from addiction.** The development of physical dependence and tolerance should not be included as consequences of opioid therapy to be avoided. They are predictable phenomena that also occur with other medications that primary care and other physicians expect and manage. Opioids are no exception in this. So while note of these phenomena should be made, they are qualitatively different from addiction and should be clearly distinguished as such.

5. **Expand Recommendation 12 to incorporate more thoroughly extended-release injectable naltrexone as an effective treatment option for patients with addiction involving opioid use.** ASAM applauds CDC for including a recommendation for providers to offer or arrange evidence-based treatment for patients with opioid use disorder and is grateful that the recommendation includes a reference to the recently released ASAM National Practice Guideline on the Use of Medications for the Treatment of Addiction Involving Opioid Use. However, the recommendation focuses almost exclusively on the use of agonist (methadone) and partial agonist (buprenorphine) treatment options and neglects to provide sufficient detail related to oral and extended-release injectable naltrexone as alternative treatment options. For example, the recommendation includes information on how physicians can become waivered to prescribe buprenorphine in their office settings, but does not mention that physicians need no such waiver to offer naltrexone as part of their daily practice. Providers offering naltrexone should also be included in the list of specialists to whom primary care physicians should consider referring patients in need of treatment for addiction involving opioid use. Such an expansion of this recommendation would present a more complete picture of the treatment options available and reinforce the principle that treatment should be individualized to meet each patient's particular needs and circumstances.

Thank you again for the opportunity to comment on this important Draft Guideline, and thank you especially for CDC's leadership in developing it. ASAM believes the guideline will be an important tool to inform safer and more judicious prescribing of opioid analgesics, which can help prevent further growth of the current epidemic of opioid misuse and related overdose deaths.

Sincerely,

R. Jeffrey Goldsmith, MD, DLFAPA, DFASAM
President, American Society of Addiction Medicine

Appendix: Detailed Comments from ASAM's Quality Improvement Council

Section or Recommendation #	Page # and Paragraph #	Comment
General	28	The Summary Recommendation grid should be moved to the front of the document. The document is too long for busy physicians and prescribers to read so the most impact will be from the summary recommendations table.
General	1	What is the rationale for focusing the guideline only on primary care providers? Dentists, pain management specialists, and surgical specialties are also heavy prescribers of opioids and although the rationale may be that they prescribe primarily for acute pain conditions, that is not always the case. Consider broadening the scope to any prescriber of opioids for chronic, non-end-of-life pain.
General	Page 1 and paragraph 2	The statistic of 20% of patients receiving an opioid prescription refers to patients presenting with "pain symptoms or diagnoses" --- for clarity, would qualify "diagnoses" -- is it "related diagnoses" or only "pain-defined diagnoses"?
General	Page 1 and paragraph 2	"The average opioid rate of growth" is very awkward phrasing. Consider rewording.
General	Page 1 and paragraph 3	Appropriate pain treatment also rests on careful assessment of the pain complaint, the specific type of pain, and history and physical examination including what treatments have been tried in the past with resulting response. That needs to be better clarified here as these are important considerations in determining treatment options.
General	Page 2, paragraph 2	DSM 5 terminology for opioid use disorder is very much appreciated. There is a mention of 2013 data for 1.9 million persons "abused or were dependent on….". Given the consistent use of DSM 5 terminology elsewhere in the document, I would suggest specifying that this statistic was estimated using DSM-IV language.

General	p. 2 prg 4	The development of physical dependence and tolerance should not be included as consequences of opioid therapy to be avoided -- they are predictable phenomenon that also occurs with other medications that primary care and other physicians expect and manage. Opioids are no exception in this. So while note of these phenomena should be made, they are qualitatively different from addiction. Putting these 3 concepts together in one sentence does not sufficiently or effectively make that distinction.
General	p.2 prg 4	There is a statement that overprescribing of opioid medications will "decrease the effectiveness of the medication in relieving pain." This association is unclear and while there is a reference for this, further clarification is warranted.
General		Effective pain management whether with an opioid or non-opioid containing regimen, improves function with some diminution in pain scale ratings. While the document, even from the beginning, mentions reduction in pain as an outcome of opioids, there is little mention of functional improvement as the primary goal. This should be emphasized as patients and providers often focus on pain ratings with less attention paid to functional improvements. This is an opportunity to correct that misperception.
General	p.3 scope and audience	The scope of the targeted patient population is described as including those with current or past cancer diagnoses. Given that the focus of the guideline is to primary care providers, there seems to be a disconnect between target patient and provider populations. Patients with current cancer diagnoses typically do not receive prescription opioids from PCPs, so why does the guideline not extend to oncologists, surgeons, or pain management specialists? In addition, with overly broad diagnostic targets there is a significant risk that the disparities in adequate pain treatment that was well documented in the 1980's and early 1990's may recur. Finally, given that the pathology related to most cancer-associated pain is different from that of chronic non-cancer pain, it seems that

		combining approaches to all of these is mixing apples and oranges.
General	Guideline development and results of review	While clearly RCTs are the gold standard for medication efficacy studies, well-done, observational studies can provide needed longitudinal data in this area. The document seems to apply the GRADE approach to say that observational studies just by their methodology are low quality studies, potentially not discriminating between methodologically robust longitudinal studies and those that clearly are of low quality. Given that much of the research on lung cancer and smoking was observational, consideration should be given to the potential of including some observational studies, especially in the absence of RCTs. The criteria for inclusion of low quality and high quality studies seem inconsistently applied across the 5 different clinical questions as p. 7 reports 0 studies being included for the question on effectiveness while observational and uncontrolled studies are included in the question on harms.
General	p.4 pg 2	There is mention of "overdose, addiction, abuse, and misuse" in this paragraph. The rest of the document clearly uses overdose, misuse, and addiction as appropriate DSM-5 driven and medically consistent terminology. It is therefore unclear why "abuse" is included in this list and what different scenario it would indicate. It probably should be removed.
General	p.6 clinical question 2 and 3	There is mention of "abuse, addiction, overdose, and other harms…." The rest of the document clearly uses overdose, misuse, and addiction as appropriate DSM-5 driven and medically consistent terminology. It is therefore unclear why "abuse" is included in this list and what different scenario it would indicate. The term "abuse" should be removed.

General	P. 6 clinical question 4	This question should clarify that the treatment strategies being compared for those with addictions refers to chronic pain treatment strategies and not addiction treatment as the latter is outside the scope of this guideline.
Recommendation 2	14	The importance of setting short term potentially more easily obtainable functional goals and long term goals
Recommendation 2	14	Continually monitoring objective goals of improved hours of sleep, increased mobility, e.g. walking distance, etc.
Recommendation 3	15	Consider review of family history of substance use problems and opioid use/efficacy history
Recommendation 4	16	Reasoning that SAO should not be added to ER-LA opiates as needed due to increase in development of tolerance.
Recommendation 4	16	Individual patient response due to polymorphism variability to opioid types
Recommendation 5	17	Consider clear recommendations surrounding the availability of naloxone in the home at higher MME/day
Recommendation 7	19	Question the tapering of opioids during pregnancy, endpoint?, Are the AE dose related?, only taper during the second trimester, greater risk to developing fetus the withdrawal effect more so than the opioid.
Recommendation 8	21	Though the sensitivity and specificity of the tools listed do not reach a level of validity I think for clinicians to be aware of these tools, including the DIRE, are important. Aspects of the tools, e.g. history of sexual abuse, nicotine dependence (easily assessed) and reliability are important aspects of an assessment particularly outside of the ED where more long-term management is taking place.
Recommendation 8	21	Offering naloxone can result in at least an important discussion if not resulting in a life-saving medication being available.
Recommendation 10	23	Agree with the routine UDT resulting in decrease stigma. No other area of medicine would we risk patient safety by overlooking as important a screening tool as the UDT. At the same time providers using these medication should be adequately educated in the interpretation of UDT. The

		ASAM white paper is a consensus tool available for review.
Recommendation 10	p. 23	The recommended frequency of at least annual urine testing seems very low compared to the intensity of many of the other recommendations especially given that urine drug testing is one of the only objective measures (aside from PDMP perhaps) of adherence to the medication being prescribed or risk for other use. Consider increasing the recommended frequency of testing to something more along the lines of frequency of visits.
Recommendation 11	25	Rebound anxiety should be listed as being "associated with" abrupt withdrawal.
Other general comments		The recommendations are fine and supported by the reviewers, but the research is lacking. Specifically, there is a lack of inclusion of any studies on effectiveness. While there may not be high quality evidence, this absence did not prevent the inclusion of low quality studies in addressing the other clinical questions.
		It would also be helpful to have background or epidemiologic data on the scope of chronic pain in the US and the issue of inadequately treated pain. The latter is a particularly pertinent issue for people with opioid use disorder as poorly treated pain is often a trigger for relapse and there was good documentation in the 1980's and 1990's of health disparities related to appropriate pain management. It would seem appropriate and beneficial context to include data and information on the scope of chronic pain and the balance that the CDC and others are trying to achieve between effective and appropriate pain management using all the available tools while minimizing harms and risk as they have outlined in the current version of the guideline.

[1] Paulozzi LJ, Jones CM, Mack KA, Rudd RA. Vital Signs: Overdoses of Prescription Opioid Pain Relievers — United States, 1999–2008. *MMWR.* 2011;50(43):1487-1492.

[2] NIH. Pathways to Prevention Workshop: The Role of Opioids in the Treatment of Chronic Pain Final Report. Available at: https://prevention.nih.gov/docs/programs/p2p/ODPPainPanelStatementFinal_10-02-14.pdf Accessed December 14, 2015.

[3] CDC/NCHS, National Vital Statistics System, Mortality File. Available at: http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Heroin_US_2000-2014.pdf Accessed December 14, 2015.

[4] ASAM. Public Policy Statement on Measures to Counteract Prescription Drug Diversion, Misuse and Addiction. January 25, 2012. Available at: http://www.asam.org/advocacy/find-a-policy-statement/view-policy-statement/public-policy-statements/2012/01/26/measures-to-counteract-prescription-drug-diversion-misuse-and-addiction Accessed December 14, 2015.