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Thomas Frieden, MD, MPH
Director
Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30329-4027

Re: Docket No. CDC-2015-0112; Proposed 2016 Guideline for Prescribing Opioids for Chronic Pain

Dear Dr. Frieden:

On behalf of our physician and medical student members, the American Medical Association (AMA), the largest physician organization in the U.S., appreciates the opportunity to review and comment on the Centers for Disease Control and Prevention's (CDC) *Proposed Guideline for Prescribing Opioids for Chronic Pain*. We commend CDC's decision to open up a period of public comment to allow a broader group of important stakeholders the opportunity to provide their unique perspectives on the public health challenges related to the intersection of pain management, prescription opioid use, and opioid diversion, misuse, and unintentional overdose.

The AMA shares with CDC the goal of reducing the burden of harm from controlled substances, including opioid analgesics. The individual and family tragedies and societal costs attributable to opioid-related overdose, emergency department visits, deaths, and addiction are deeply concerning. To make meaningful progress towards ending this epidemic, a broad-based public health approach is required. This approach must balance patients' needs for comprehensive pain management services, including opioid analgesics when clinically appropriate, with efforts to promote appropriate prescribing, reduce diversion and misuse, promote an understanding that substance use disorders are chronic conditions that respond to treatment, and expand access to treatment for individuals with substance use disorders.

As it has done in addressing so many other serious epidemics, the AMA applauds CDC for treating the epidemic of opioid overdose deaths as a high priority. We continue to recommend that CDC's efforts in this area be aligned with those of other federal partners, including the White House and its Office of National Drug Control Policy, the Interagency Pain Research Coordinating Committee and its National Pain Strategy, the National Institute on Drug Abuse, the Substance Abuse and Mental Health Services Administration, the Department of Health and Human Services, and the U.S. Surgeon General. The White House initiative announced in October 2015 is designed to forge a collaborative effort involving multiple stakeholders in the medical community working towards a single set of measureable objectives. This collaborative effort includes commitments from the AMA, the American Dental Association, and the American Osteopathic Association, as well as other medical specialty societies and state medical associations. In a separate effort to engage the physician community more directly to implement solutions to opioid misuse and harm, the AMA formed a Task Force of national medical specialty society

and state medical association partners to promote appropriate pain care and reduce opioid-related harm by encouraging physicians to register for and consult their state's prescription drug monitoring program, access available high quality educational offerings intended to reduce opioid misuse and harm, expand the use of naloxone, and reduce the stigma commonly experienced by patients with chronic pain or substance use disorders (www.ama-assn.org/go/endopiodabuse).

GENERAL COMMENTS ON CDC METHODS AND RECOMMENDATIONS

While the discussion under several of the specific draft recommendations has been revised and/or amplified based on designated stakeholder input and provides additional clarity, the recommendations themselves are largely unchanged from the initial draft. Accordingly, while the AMA supports many of the recommendations, we continue to have serious concerns that some either contain a degree of specificity not supported by the existing evidence or conflict with official Food and Drug Administration (FDA)-approved product labeling for opioid analgesic products. It seems incongruous that virtually all of the specific guidelines carry a graded recommendation that CDC believes should "apply to all patients with chronic pain and that...most patients should receive the recommended course of action," given the limitations of the evidence, especially where CDC experts' opinions are the essential foundation for the recommendation.

States regulate the practice of medicine and many already have adopted opioid prescribing guidelines that were developed by a coalition of state-based stakeholders, including physicians and other health care professionals, public health officials, patients and patient advocates, and policy makers working together to ensure balance. The low or very low quality of evidence supporting the proposed CDC guidelines has the potential to create considerable confusion in the states. While CDC has acknowledged that the guidelines are advisory in nature and they do not intend for state legislators, professional licensing boards, hospitals, insurers, courts, or others to "officially" implement or follow specific elements of the guidelines, this is not a practical or realistic expectation given the national respect that comes with a guideline issued by CDC. Accordingly, concerns remain about potential unintended consequences for patients depending on how specific elements of the guidelines (as written) may be interpreted, implemented, or enforced. Some patients with chronic pain who have maintained functional improvement on stable opioid doses are already experiencing difficulties in keeping their current source of care and/or finding physicians who are willing to treat them.

While the summary and introductory discussion acknowledge that "the guideline does not focus broadly on pain management," and "it is important that patients receive appropriate pain treatment," the guideline otherwise lacks a patient-centric view, other than to note that for patients who are already maintained on "high opioid dosages," "providers should empathetically review benefits and risks of continued high dose opioid therapy and should offer to work with the patient to taper opioids to safer dosages." Although the guideline is expressly focused on prescribing opioids for chronic pain, by crafting the first recommendation as "nonpharmacologic and nonopioid pharmacologic therapies are preferred for chronic pain," CDC cannot disavow an obligation to frame the pain management discussion in a balanced fashion. The AMA, therefore, asks that CDC include patient advocates in its formal review of these and other comments to ensure that patient needs are adequately addressed.

Although population-level data may be relied on to help construct clinical guidance, pain is an intensely personal and conscious experience influenced by emotion, cognition, memory, interpersonal and social

context, and other factors. Patient-reported intensity of pain may not correlate with the magnitude or identifiable source of injury. Because objective tests for pain intensity (or even the presence or absence of pain) are still at a rudimentary stage of development, the best clinical approach in most circumstances is to assume that the patient is reporting a true experience. Accepting a patient's complaint of pain as valid does not require clinical identification of a physical cause, or demand the initiation of a specific treatment. It does, however, provide a foundation for assessment and the basis for developing an effective patient-physician dialogue and an approach to individualized, patient-centered treatment. Meaningful and appropriate treatments are best achieved via shared decision-making. Health disparities in pain management and legitimate access to opioid analgesics for acute pain remain evident, and clinically relevant differences in pain expression and responsiveness based on sex, race/ethnicity, and genetic constitution also exist. Based on feedback from patient groups, patients suffering from chronic pain increasingly view themselves as collateral damage in efforts to restrict opioid prescribing decisions via state-based regulations and legislative mandates, and are fearful of the potential effect these guidelines may have on access for patients with legitimate medical needs. It is important that this not be an unintended consequence of this process. Accordingly, the proposed guideline could be substantially improved by incorporating some fundamental acknowledgements that many patients experience persistent pain that is not well controlled, substantially impairs their quality of life and/or functional status, stigmatizes them, and could be managed with more compassionate patient care. The National Pain Strategy has acknowledged that clinician biases and negative attitudes towards pain negatively affect the care and services they provide to patients.

The AMA has great respect for the core mission and activities of CDC that are designed to protect the health of the public. Individuals from a variety of disciplines and settings with specific expertise were chosen for the expert panel, a reflection of the challenges faced in trying to address this complex public health issue in a balanced fashion. The expert panel was charged with the most significant assignment in this process. It appears, however, that only a limited number of clinicians who are actively managing chronic pain patients were included. While it is necessary to integrate various disciplines because of the complex nature of prescription drug misuse and addiction, the process moving forward would benefit from a balanced Advisory Committee that includes patient advocates, as well as clinicians from various medical specialty and practice settings representing a diverse set of views and experiences in treating chronic pain and opioid use disorder, and limiting participation of individuals aligned with public policies that may have a predictable effect on the recommendations. This type of approach is even more important when the evidence-base is limited, thereby requiring a consensus-type approach and the use of "expert opinion." The AMA asks, therefore, that before commencing with the formal review and consideration of revisions submitted by stakeholders, CDC broaden the Advisory Committee by inviting patient advocates and clinicians, including physicians, pharmacists, and dentists, who treat a broad base of patients with pain. The AMA would be pleased to recommend physicians from member organizations of the AMA Task Force to Reduce Opioid Abuse to help accomplish this.

Finally, the change in terminology from "low quality" or "very low quality" evidence to category 3 or 4 evidence is not helpful to the reader and primarily serves to camouflage the criticism derived from issuing "strong" recommendations based on low quality evidence. Because the guidelines may eventually be used by a broad range of stakeholders as described earlier, the AMA recommends that CDC clearly identify the quality of the evidence used by returning to the easily understandable and common sense language used in the original draft.

SPECIFIC COMMENTS ON CDC RECOMMENDATIONS

Recommendation #1

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 to the patient (recommendation category A, evidence type 3).

Expansion of the discussion on various non-opioid pharmacologic therapies is a helpful revision. Clearly, the use of acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) for musculoskeletal pain, and certain antiepileptic or antidepressant drugs for neuropathic pain are well established treatments. While it is true that NSAIDs can be helpful for mild-moderate musculoskeletal pain, the risks associated with both the acute and chronic use of these drugs should not be minimized. Much attention has been devoted to limiting the use of NSAIDs to the lowest dose for the shortest duration of time (Alliance for Rational Use of NSAIDs; <http://nsaidalliance.com>).

The evidence review concludes that “several non-pharmacologic and non-opioid pharmacological treatments have been shown to be effective in managing chronic pain.” The evidence presented for the effectiveness of non-pharmacologic approaches focuses on cognitive behavioral therapy (CBT), exercise therapy, and integrative multimodal therapies. While some modest short-term effects are apparent, none of these studies are sufficient to conclude that such approaches can be widely implemented and are effective for long-term use. Broad-based, effective implementation would require large scale changes in the public and private payer communities and better evidence to inform the most effective non-pharmacologic approach for various chronic pain conditions.

Furthermore, access to non-pharmacologic and non-opioid pharmacological treatments and reimbursement for them are often inadequate, especially for multidisciplinary care (<http://www.painmed.org/files/minimum-insurance-benefits-for-patients-with-chronic-pain.pdf>). The National Pain Strategy specifically identifies that a pressing need exists to assess insurer practices such as prior authorization, step therapy, fail-first protocols, specialty tier payment structures, and other limits on reimbursement for multidisciplinary care treatments that act as barriers to effective care. Moreover, it is not clear how many primary care clinicians (the target audience of these guidelines) are proficient in offering important non-pharmacologic approaches, including mindfulness, focused imagery, biofeedback, relaxation, or CBT, which at its most comprehensive implementation requires a multidisciplinary approach performed by various experts. This recommendation may be interpreted as requiring a “fail-first” approach of all available treatments for chronic pain before opioids should even be considered. We ask that CDC clarify that it does not support fail-first protocols or other policies meant to inhibit access to care, especially for serious illnesses and conditions such as chronic pain.

We also reiterate our concerns about the evidence base used to inform the guidelines. It is not clear from the discussion whether the standard for the non-pharmacologic and non-opioid pharmacological treatments also required randomized trials with study duration of one year to be included in the efficacy analysis. The methodology description notes that evidence for the guideline built on systematic reviews conducted in 2009 and 2014, with an update of the 2014 review. However, the inclusion criteria for opioid efficacy studies were changed from a best evidence approach in 2009 to a one-year, randomized

trial requirement. The same standard was not applied to the measurement of harms, nor apparently to the non-opioid based therapies. The same standard should be applied to all treatments that are being evaluated for efficacy for chronic pain and for which the guidelines state or conclude they are effective, and the analysis and discussion should be revised to reflect that approach.

Therefore, we recommend the following revisions to Recommendation #1. This recommendation is not implementable without the corresponding responsibilities of payers being addressed.

Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain. Providers should only consider adding using opioid therapy if expected benefits for both pain and/or function are anticipated to outweigh risks. In order to achieve this goal, public and private payer policies must be fundamentally altered and aligned to support payment for non-pharmacologic treatments and multimodal care. In addition, more evidence must be developed to inform clinical decision-making on the use of non-pharmacologic approaches, and more clinicians need to be trained in their effective use.

Recommendation #2

Before starting long-term opioid therapy, providers should establish treatment goals with all patients, including realistic goals for pain and function. Providers should not initiate opioid therapy without consideration of how therapy will be discontinued. Providers should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (recommendation category: A, evidence type: 4).

While we generally support this recommendation, some situations exist where patients may have intractable pain and sufficient disability such that functional improvement is not possible, and relief of pain and suffering is a supportable primary goal. This is noted in the revised discussion. In an analogous fashion, some patients may demonstrate functional improvement, with limited changes in pain scores. We find the discussion about the nuances of acute pain, chronic pain, prescription length, and corresponding evidence disconnected. Prescribers are advised to make decisions regarding the appropriateness of opioid therapy based on common definitions of chronic pain (>3 months or beyond the time of normal tissue healing, which could be significantly shorter than 3 months) and potential uncertainty in the transition from acute to chronic pain, but the evidence review disregards any opioid-based studies (albeit low or very low quality evidence) less than one year in duration. Because both pain and function may not improve in responsive patients, and “treatment goals” are the grounding element, we recommend the following revisions to Recommendation #2.

Before starting long-term opioid therapy, providers should establish treatment goals with all patients, including realistic goals for pain and function. Providers should not initiate long-term opioid therapy without consideration of how therapy will be discontinued if benefits do not exceed risks. Providers should continue opioid therapy only if there is clinically meaningful improvement in treatment goals pain and function that outweighs risks to patient safety.

Recommendation #3

Before starting and periodically during opioid therapy, providers should discuss with patients known risks and realistic benefits of opioid therapy and patient and provider responsibilities for managing therapy (recommendation category: A, evidence type: 3).

We generally support this recommendation, although it introduces a modifying term for benefits (realistic) that does not appear elsewhere. The additional considerations regarding use in patients who are cognitively impaired and directions to secure safe storage are helpful additions. With respect to discussion about “fatal overdose,” it may be helpful to better explain that the real concern is respiratory depression to perhaps facilitate better recognition of its occurrence. Taken one by one, the points of emphasis have varying levels of merit, but taken together they must be implemented in a patient-centered way, on an individual basis, and in a manner that does not promote stigma or adversely affect the patient-physician relationship. This list, moreover, is an example of the type of list that will likely be relied upon by others in creating new requirements for physicians who treat patients with pain.

The AMA also asks, therefore, that specific language preceding the list be revised to read as follows: Providers are encouraged to have open and honest discussions with their patients so as to avoid stigmatizing the decision to start, continue, or discontinue opioids or non-opioid therapy. Providers should do the following. Considerations for providers include the following:

Recommendation #4

When starting opioid therapy, providers should prescribe short-acting opioids instead of extended release/long-acting (ER/LA) opioids.

We generally support this recommendation. We also note that this section raises considerable concern about the use of methadone and transdermal fentanyl. This may be an opportunity for CDC to work with the FDA and others to help promote education for clinicians on the appropriate use of these two long-acting, extended release products. The AMA stands ready to promote such education. Overall, the AMA is pleased that CDC relies on the FDA-approved labeling of ER/LA opioids for guidance under this recommendation. While it is true that abuse deterrent formulations do not prevent opioid misuse through oral intake or unintentional overdose through this route, they are less subject to product manipulation. Interestingly, the expert panel was unable to affirm any value in the clinical use of these formulations, despite the fact that virtually all product approvals in this category will have this expectation moving forward.

Recommendation #5

When opioids are started, providers should prescribe the lowest possible effective dosage. Providers should use caution when prescribing opioids at any dosage, should implement additional precautions when increasing dosage to > 50 morphine milligram equivalents (MME)/day and should generally avoid increasing dosages to > 90 MME/day.

We agree with the recommendation to prescribe the lowest effective dose. This recommendation is not unique to clinical decisions on pain management, but is a general tenet of designing a dosage regimen and

treatment plan. However, in contrast to the discussion of the clinical role of ER/LA opioids, this recommendation is in direct conflict with approved product labeling for the clinical use of opioid analgesics and the findings of the recent review by the FDA regarding clinical decision algorithms based on daily MME. A variety of prescriber behaviors, patient/user behaviors and characteristics, and environmental and systemic determinants exist that contribute to opioid overdose mortality. These factors may operate independently but interact in complex ways according to geography and population (King NB et al. *Am J Public Health*. 2014 Aug; 104(8):e32-42). Accordingly, preventing additional opioid-related mortality will require interventions that address multiple determinants that are tailored to specific locations and populations. In addition, the language of this recommendation is vague and open to wide interpretation. What constitutes “caution” when using any dose? What additional precautions should be taken when increasing a daily dose above 50 MME?

As a result, this recommendation as currently stated has the potential to cause confusion, uncertainty, and conflicting institutional or state policies that may have unintended consequences. One likely consequence is that most insurers and other payers will use this recommendation to deny or impose new hurdles to coverage of any dose that exceeds the threshold. Another likely consequence is that patients experiencing pain who require a daily dose above 50 MME will face additional prejudice and stigma. While several states have enacted laws or regulations designed to modify clinical decision-making based on MMEs, analysis of the actual efficacy of these approaches and their effect on reducing overdose and pain management is lacking, including whether they may have unintended consequences (Ziegler SJ. *Pain Medicine*, 2015). In states that have adopted MME thresholds, prescribers appear to modify behavior to avoid specific sanctions and/or the need for additional action steps. The effects on patients have not been quantified. New data from Ohio, which has an 80 mg MME threshold, demonstrate that fewer high dose prescriptions were issued and the number of prescriptions was reduced overall, but death rates due to opioids, and in particular heroin, continued to rise. The reliance on expert opinion throughout this section, the existing multitude of state MME thresholds, and the absence of MME thresholds from the current product labeling for opioid analgesics coupled with a high degree of variability in patient responsiveness to opioids and uncertainty in morphine equivalent calculators, argue against establishing a bright line for clinical decision-making based solely on this variable.

The AMA asks, therefore, that this recommendation either be reconsidered in its entirety, or that the focus be redirected to encouraging use of the lowest possible effective dose, with any dose escalation based on clinical response and the existence of continued improvement in pain and function. This could be accomplished by revising recommendation #2 to read as follows:

Before starting long-term opioid therapy, providers should establish treatment goals with all patients, including realistic goals for pain and function. Providers should initiate opioid therapy with the lowest effective dose. Continued opioid therapy and/or dose escalation should occur only if there is clinically meaningful improvement in treatment goals pain and function that outweighs risks to patient safety.

Recommendation #6

Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, providers should prescribe the lowest effective dose of short-acting opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to

require opioids. Three or fewer days will usually be sufficient for non-traumatic pain not related to major surgery (recommendation category: A, evidence type 4).

The three-day limit imposed by this recommendation in the outpatient setting is arbitrary and the surrounding circumstances are clinically vague. If this recommendation is targeting post-surgical prescriptions (which would deviate from the stated goal of the guidelines to apply to primary care), then an effort should be made to provide the supporting evidence base. What is the definition of “major surgery”? The referenced clinical practice guidelines from emergency department protocols or “bridge” prescriptions for a three-day limit are prudent and widely supported, but are not applicable in a broad-based fashion to all scenarios of acute pain. States that have supported limits on opioid analgesics prescribed in the emergency department have largely done so to allow the patient sufficient time to follow-up with their primary care provider or other physician managing the patient’s chronic pain, and not as a clinical recommendation based on anticipated healing time or duration of pain sufficient to require an opioid analgesic. Nevertheless, we strongly support messaging about the need to conservatively tailor the number of pills per prescription for acute pain. We believe this can be accomplished by modifying this recommendation to read as follows (with the various clinical guidance of three to 14 days appearing in the supporting narrative discussion):

Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, providers should prescribe the lowest effective dose of short-acting opioids and should prescribe no greater in a quantity than-needed only for the expected duration of pain severe enough to require opioids, and not based on prescriber or patient convenience. Three or fewer days will usually be sufficient for non-traumatic pain not related to major surgery.

Recommendation #7

Providers should evaluate patients within 1 to 4 weeks of starting long-term opioid therapy or of dose escalation to assess benefits and harms of continued opioid therapy. Providers should evaluate patients receiving long-term opioid therapy every 3 months or more frequently for benefits and harms of continued opioid therapy. If benefits do not outweigh harms of continued opioid therapy, providers should work with patients to reduce opioid dosage and to discontinue opioids when possible (recommendation category: A, evidence type: 4).

We agree with the need to appropriately monitor patients during the onset of long-term therapy or after dosage escalation, but recommend that CDC pay close attention to comments received from various medical specialty societies, including those in the stakeholder review panel, to address the specific timeframes that might comprise this recommendation. While it may be somewhat nuanced, the last sentence in this recommendation does not accommodate a clinical situation where reducing the opioid dose may restore an appropriate risk/benefit ratio. **The AMA asks, therefore, that the last sentence should be revised to read as follows:**

If benefits do not outweigh harms of continued opioid therapy, providers should work with patients to reduce opioid dosage and, if necessary, to discontinue opioids to prevent harm when possible.

Recommendation #8

Before starting and periodically during continuation of opioid therapy, providers should evaluate risk factors for opioid-related harms. Providers should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, or higher opioid dosages (≥ 50 MME), are present (recommendation category: A, evidence type: 4).

We agree with the language presented in recommendation #8 as a prudent clinical approach, as well as the guidance offered on expanding the use of naloxone. However, this recommendation is somewhat redundant with others, such as #1, #2, #3, and #7 that also urge a consideration of benefits versus risks. Because the evidence review concludes that primary care physicians are not well equipped to assign risk profiles, commonly recommended screening instruments do not work, and physicians already have heightened concerns and misgivings about managing patients with chronic pain and prescribing opioid analgesics, additional clarity about CDC's intent for this recommendation is needed.

The supporting text concerning risk factors identifies patients with sleep-disordered breathing, women of reproductive age, pregnant women, and patients with renal or hepatic insufficiency, patients aged over 65 years, patients with mental health conditions and those receiving benzodiazepines, and patients with substance use disorder. Otherwise, providers are: 1) directed to ask patients about drug and alcohol use, use Prescription Drug Monitoring Programs (PDMP) data and drug testing as appropriate to assess for concurrent substance use that might place patients at higher risk for opioid use disorder and/or overdose; 2) advised to counsel patients on increased risks of overdose when opioids are combined with other drugs or alcohol; and, 3) directed to ensure that patients receive effective treatment for substance use disorders when needed. The AMA is concerned with aspects of this section that may cause additional stigma to a patient who benefits from opioid therapy. The reactions of state legislatures to neonatal abstinence syndrome demonstrate the significant challenges in crafting hardline policies that would apply to every patient. In no case should a pregnant woman be treated as a criminal if she and her physician determine that opioids are needed, but that is how some policymakers have approached this clinical determination. In addition, a woman in pain deserves to have her pain treated; if the benefits of opioids outweigh the risks of harm, then that decision should be respected. CDC's discussion needs to more fully reflect this delicate balance. Furthermore, significant knowledge gaps exist regarding the use and interpretation of urine testing, as well as payment barriers. It may be helpful to identify specific questions (or line of questioning) in the supporting discussion that would comprise adequate history taking for alcohol and drug use.

Recommendation #9

Providers should review the patient's history of controlled substance prescriptions using state PDMP data to determine whether the patient is receiving excessive opioid dosages or dangerous combinations that put him/her at high risk for overdose. Providers should review PDMP data when starting opioid therapy and periodically during long-term opioid therapy, ranging from every prescription to every 3 months (recommendation category: A, evidence type: 4).

We strongly agree with the need for physicians and other prescribers to register for and access their state-based PDMP when clinically appropriate. This is a primary goal of the AMA Task Force. We appreciate

that CDC recognizes the sometimes significant barriers to PDMPs being more widely used by physicians. The AMA has long advocated for reauthorization and full funding of National All Schedules Prescription Electronic Reporting Act, and we work regularly with state medical associations to advocate for stable funding streams for state PDMPs. Furthermore, we are pleased to see that CDC also recognizes that some patients may suffer unintended consequences by being discharged from the practice. Specifically, the AMA notes that CDC and several states have publicized decreases in the incidence of individuals who would qualify as “doctor shoppers.” Data are lacking about the characteristics of these individuals, and uncertainties remain about what happens to them after they are identified. For example, some may be receiving multiple controlled substances from multiple providers because of fragmented care in need of coordination (e.g., Medicare Part D beneficiaries). Some are in need of treatment for an opioid use disorder, and some may be promptly discharged from the practice and be at risk for seeking illicit substances. While PDMPs can help identify patients receiving multiple prescriptions from multiple prescribers or dispensers, and this behavior is a risk factor for unintentional overdose, we believe the steps to be taken after identifying such individuals are much more complex and require further research and attention. While it is an important variable to quantify, one should not be satisfied with concluding that PDMP data were used to reduce doctor shopping; further examination of what happens to these individuals is warranted. We defer to the medical specialty society stakeholders to comment on the appropriate triggers for how often a PDMP should be consulted, and in the absence of consensus, the AMA recommends the following revisions to Recommendation #9. As with Recommendation #3, consider using the term “respiratory depression” rather than overdose.

Providers should review the patient’s history of controlled substance prescriptions using state PDMP data to determine whether the patient is receiving excessive opioid dosages or dangerous combinations that put him/her at high risk for overdose. Providers should review PDMP data when starting opioid therapy and periodically during long-term opioid therapy, ranging from every prescription to every 3 months.

Recommendation #10

When prescribing opioids for chronic pain, providers should use urine drug testing before starting opioids therapy and consider urine drug testing at least annually for all patients on long-term opioid therapy to assess for prescribed medications as well as other controlled substances and illicit drugs (recommendation: B, evidence type: 4).

We note that the evidence review relied on by CDC does not support the conclusion that urine drug testing improves outcomes in patients receiving opioids for chronic pain. Nevertheless, it is one objective measure that can be used as part of a broader risk mitigation strategy when designing treatment and monitoring strategies for individual patients on chronic opioid therapy. The decision on how and when to use urine drug testing for individual patients should be left up to the treating physician. This recommendation offers another example of where the AMA agrees with CDC’s intent, but the practical implications need to be more adequately addressed. Significant knowledge gaps exist regarding the use of interpretation of urine drug tests in primary care and different monitoring frequencies may be required based on individual patient variables. Furthermore, the wide variability in insurance coverage is not insignificant, with implications for physician reimbursement for interpretation, to the potential costs for both private and public payer systems. Of equal, if not more significance, is the fact that many patients currently have to pay for urine testing out of pocket, which may impact their ability to comply with a pain

care agreement. Because consensus is lacking on this issue, the AMA recommends the following revisions to Recommendation #10:

When prescribing opioids for chronic pain, providers should use urine drug testing before starting chronic opioids therapy and consider urine drug testing periodically at least annually for all patients on long-term opioid therapy to assess for prescribed medications as well as other controlled substances and illicit drugs.

Recommendation #11

Providers should avoid prescribing of opioid pain medication and benzodiazepines concurrently whenever possible (recommendation category: A, evidence type: 3).

Benzodiazepines are a co-occurring substance in a substantial minority of patients who suffer an opioid-related overdose, just as they are commonly used by other individuals as a pattern of polysubstance abuse. Therefore, we prefer that the language be framed in a way that recognizes the clinical-decision making authority of the treating physician, to read as follows:

Providers should avoid prescribing of opioid medication and benzodiazepines concurrently whenever possible, unless it is clinically indicated and required for optimal patient management.

Recommendation #12

Providers should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 3).

We support this recommendation. While the recommendation focuses on opioid agonist treatment in combination with behavioral therapies, patients also may respond to naltrexone (as noted in the discussion) and some may respond to abstinence-based approaches; perhaps the latter also can be noted in the narrative. However, the ability of primary care physicians to “ensure that patients get treatment for opioid use disorder when needed” is severely constrained by a lack of access to treatment and numerous public and private payer policies that are based on a lack of understanding that addiction is a chronic brain disease. Accordingly, we urge that this recommendation be revised to read as follows:

Providers should offer or arrange evidence-based treatment (usually opioid agonist treatment in combination with behavioral therapies) for patients with opioid use disorder. In order to achieve this goal, more physicians need to be trained in providing direct patient care for individuals with opioid use disorder, and government funding, as well as public and private payer policies, must be fundamentally altered and aligned in support of expanded access to treatment. In addition, efforts should be directed at reducing the stigma associated with substance use disorders and raising awareness that addiction is a chronic brain disease.

The AMA appreciates the opportunity to review and comment on this important issue. We sincerely hope that CDC will seize the opportunity to align itself with other ongoing efforts designed to foster a balanced, public health-based approach to improving pain management practices while minimizing the

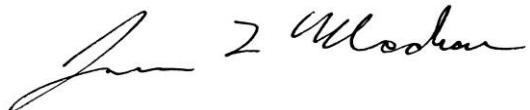
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diversion of controlled substances, reducing unintentional overdoses and deaths from opioid analgesics, and supporting improved access to treatment for patients with substance use disorders.

Sincerely,

A handwritten signature in black ink, appearing to read "James L. Madara". The signature is fluid and cursive, with "James" on the left and "L. Madara" on the right.

James L. Madara, MD

cc: Deborah Dowell, MD, MPH