**Draft CDC Clinical Practice Guideline for Prescribing Opioids – United States, 2022:**

# Board of Scientific Counselors of the National Center for Injury Prevention and Control's Opioid Workgroup Report and CDC Response

## Overview

On Dec. 4, 2019, the Board of Scientific Counselors of the National Center for Injury Prevention and Control (BSC/NCIPC) established the Opioid Workgroup (OWG) at CDC's request. The OWG reported to the BSC/NCIPC, a federal advisory committee.

The primary purpose of the OWG was to review the updated draft Guideline for opioid prescribing (as prepared by CDC) and to develop a report that provided the workgroup's findings and observations about the draft Guideline to the BSC/NCIPC, providing independent, broad, external, transparent input on the diverse and complex issues involved in this effort.

The OWG consisted of 23 members. In accordance with federal advisory committee policy that at least two BSC/NCIPC members must serve on the OWG, and one of the two members must serve as the workgroup chair, the OWG included a total of three BSC/NCIPC members, with one BSC/NCIPC member serving as the OWG chair. A NCIPC subject matter expert served as the OWG's Designated Federal Officer (DFO). OWG members included patients with pain, caregivers, and family members of patients with pain. The OWG also comprised clinicians and subject matter experts, with the following perspectives represented: primary care, pain medicine, public health, behavioral health, pharmacy, emergency medicine, medical toxicology, obstetrics/gynecology, bioethics, orthopedic surgery, plastic surgery, dentistry, sickle cell disease, substance use disorder treatment, and research. Diversity in perspectives was also represented in regard to sex, race/ethnicity, and geographic region. Federal partners served as ex-officio members of the OWG. More information about the OWG is available on the BSC/NCIPC website.

The OWG had a total of 11 virtual meetings from October 2020 through June 2021. Prior to receiving the draft of the Guideline update, the OWG met to review the processes used for community engagement and also received an overview of GRADE or Grading of Recommendations, Assessment, Development and Evaluations. This is the framework used by CDC to rate the quality of evidence. CDC sent the draft of the Guideline update to the OWG in March 2021. The OWG had a series of 7 meetings from April through June 2021 to review the draft and develop their report of findings and observations. The OWG report was presented to the BSC/NCIPC at a public meeting on July 16, 2021. The BSC/NCIPC voted unanimously that CDC adopt the OWG report, while considering ideas and suggestions raised by the BSC/NCIPC and the public during the meeting, and that the OWG's work be considered complete.

The OWG report is included in this document in its entirety. Beginning on page 15 of this document, CDC's responses to each report section are described in a table. CDC carefully reviewed each comment and considered modifications to the guideline document in response. This document includes examples of how CDC incorporated OWG observations and comments in the revised draft Guideline. CDC thanks the OWG members for providing invaluable insights in their report to help update the *CDC Guideline for Prescribing Opioids* with the best scientific evidence available and a keen understanding of the myriad factors that play a role in the lives of individuals living with pain.

**Observations of the Opioid Workgroup of the Board of Scientific Counselors of the National Center for Injury Prevention and Control on the Updated CDC Guideline for Prescribing Opioids**

Submitted by:

Chinazo Cunningham, MD, MS, Opioid Workgroup Chair

On behalf of the:

**Opioid Workgroup Members**

Anne Burns, RPh

Wilson Compton, MD, MPE

Beth Darnall, PhD

Frank Floyd, MD, FACP

Neeraj Gandotra, MD

Christine Goertz, DC, PhD

Elizabeth Habermann, PhD, MPH

Joseph Hsu, MD

Marjorie Meyer, MD

Paul Moore, DMD, PhD, MPH

Aimee Moulin, MD, MAS

Mallika Mundkur, MD, MPH

Kate Nicholson, JD

Ted Park, MD, MSc

Jeanmarie Perrone, MD

Travis Rieder, PhD, MA

Stephen Rudd, MD, FAAFP, CPPS

Roberto Salinas, MD, CAQ, (G, HPM)

Doreleena Sammons-Hackett, SM, CPM

Wally Smith, MD

Jennifer Waljee, MD, MPH, MS

Mark Wallace, MD

**Designated Federal Officer:**

CDR Melanie R. Ross, MPH, MCHES

**Observations on CDC Guideline for Prescribing Opioids – United States, 2022**

This document outlines the observations of the Opioid Workgroup on the updated CDC Guideline for Prescribing Opioids. CDC recommendations for prescribing opioids for outpatients with pain outside of sickle cell disease-related pain management, cancer pain treatment, palliative care, and end-of-life care. The observations presented here follow the ordering of the draft Guideline.

## OWG Overall Observations

### Overarching Themes

- Overall, many workgroup members felt that much of the supporting text of the guideline was not balanced and was missing key studies. Many workgroup members felt that the guideline focused heavily on the risks or potential harms of opioids, while less attention was focused on the potential benefits of opioids, or the risk of not taking opioids or undertreating pain. In addition, some workgroup members felt that the language of the recommendation statements or supporting text conveyed more certainty or was more absolute than warranted by the evidence.
- Much of the discussion of the recommendations centered around the concern for misapplication of the guideline. Because of the consequences of misapplication of the 2016 guideline, many workgroup members were concerned about how the recommendation could be misapplied, leading to potential harm to patients. The workgroup discussion thus focused on how best to mitigate against this valid concern while preserving the benefits of the guideline. However, some were concerned that the workgroup may have been over-correcting and so much concern about future misapplication could potentially be detrimental to the greater good.
- Many workgroup members felt the guideline paid too little attention and had minimal discussion about racial/ethnic disparities and inequities in how pain is perceived, valued, and managed, and the potential implications of these disparities on implementation of the guideline, including disparities in access to recommended treatments, along with how the guideline could impact disparities.
- Many workgroup members noted how the guideline has a constant tension between public health benefits versus patient benefits. This issue is minimally addressed in the guideline and comes very late. Workgroup members felt it is important to directly address this tension between risks and benefits to public health versus individual patients, and to contextualize how individual providers should use this guideline in caring for their patients versus considering potential public health consequences. In addition, several workgroup members felt that overall, the guideline was not sufficiently patient-centered.
- Many workgroup members were cautious about including specific opioid dose thresholds in the recommendations. Workgroup members acknowledged the importance of having benchmarks, but many felt that specific opioid doses would be misapplied as absolute cutoffs or thresholds for policies or practices. Many workgroup members felt the specific opioid dose thresholds belonged in the supporting text where the discussion could be more nuanced. In addition, there is no single standard formula for calculating MMEs.
- Many workgroup members noted a sense of exceptionalism throughout the guideline. Specifically, certain conditions were named in the text, while others were not. Naming of specific conditions may lead to interpretation regarding whether pain is “real” or “worthy” of certain types of treatment. In addition, while the guideline states it does not apply to sickle cell disease, cancer, palliative care, or end-of-life care, palliative care is not clearly defined.
- Many workgroup members felt that the recommendation category A was overutilized (11 of the 12 statements had recommendation category A). Members felt that this type of grading likely contributed to the misapplication of the 2016 guideline.
- Many members of the workgroup developed a document that described the workgroup’s guiding principles when

providing observations on the guideline. Guiding principles include: minimize bias, ensure scientific integrity, enhance inclusivity, establish patient- and clinician-centered guidance, and mitigate harms from unintended consequences. The document is included as Appendix A.

**Determining Whether or Not to Initiate Opioids for Pain**

***Recommendation #1:*** *Nonopioid therapies are preferred for many common types of acute pain. Clinicians should only consider opioid therapy for acute pain only if benefits are anticipated to outweigh risks to the patient. (Recommendation Category: A; Evidence Type: 3)*

**OWG Observations:**

- Several workgroup members recommended changing the wording of Recommendation #1—remove the second "only", consider changing "preferred" to "effective".
- Several workgroup members were concerned about the large and unclear category of acute pain, and felt further clarification is needed. For example, should post-surgical pain be in this category of acute pain? Several workgroup members felt the statement was an oversimplification and there were situations or conditions that should be exceptions. Workgroup members also felt that categorizing pain should be based on pathophysiology or severity, rather than time. Several members noted that it is often unclear when acute pain transitions to subacute pain, and when subacute pain transitions to chronic pain. In addition, there is little attention to acute-on-chronic pain.
- Some workgroup members felt the recommendation does not consider shared decision-making.
- Several workgroup members were concerned that the recommendation could be misinterpreted and translated into bad policy. There was particular concern about limited access to non-opioid pain management modalities, in part due to lack of availability or lack of coverage by payers. Improving access to non-opioid pain management modalities should be a priority.
- Recommendation Category: Most, though not all, workgroup members felt this statement should be graded category B.

***Recommendation #2:*** *Nonopioid therapies are preferred for subacute and chronic pain. Clinicians should only consider initiating opioid therapy if expected benefits for pain and function are anticipated to outweigh risks to the patient. Before starting opioid therapy for subacute or chronic pain, clinicians should discuss with patients known risks and realistic benefits of opioid therapy, should establish treatment goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. If opioids are used, they should be combined with other therapies as appropriate. (Recommendation Category: A, Evidence Type: 3)*

**OWG Observations:**

- Several workgroup members voiced appreciation for this statement because of the attempt to be inclusive and comprehensive, take into account pain and function, and be realistic upfront with patients. In addition, the attention to de-prescribing and exit strategies is appreciated.
- Some workgroup members felt shared decision-making should be emphasized here and in other recommendations.
- Several workgroup members noted that certain conditions for which this guideline does not apply feels like exceptionalism in terms of what's serious pain versus what's not and may reflect what types of pain conditions receive research funding or other attention.
- Some workgroup members felt the language in this recommendation is somewhat too strong, given problems with some of the cited evidence. Words like "are preferred" might be softened to "may be preferred" or "may be

effective". Although the harms of opioids are very well-defined, the benefits (especially long-term) are not well understood and difficult to study.

- Recommendation Category: Some workgroup members felt the recommendation category should be B.

**Opioid Selection and Dosage**

***Recommendation #3****: When starting opioid therapy for acute, subacute, or chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids. (Recommendation Category: A and Evidence Type: 3)*

**OWG Observations:**

- Most workgroup members overall agreed with the statement. Some felt the need to define "starting" and opioid-naïve more clearly, particularly given patients' historical context of prior pain management strategies.
- Several workgroup members appreciated the support text discussion regarding abuse-deterrent formulations.
- Recommendation Category: Most workgroup members agreed with the recommendation category A.

***Recommendation #4:*** *When opioids are started for opioid-naïve patients with acute, subacute, or chronic pain, clinicians should prescribe the lowest effective dosage. If opioids are continued for subacute or chronic pain, clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to >90 MME/day. (Recommendation Category: A and Evidence Type: 3)*

**OWG Observations:**

- Many workgroup members voiced concern about the dose thresholds written into the recommendation. Many were concerned that this recommendation would lead to forced tapers or other potentially harmful consequences. Though workgroup members recognized the need to have thresholds as benchmarks, many felt that including these thresholds in the supporting text could serve to de-emphasize them as absolute thresholds, and thus recommended removing the specific MME range from the recommendation. In addition, these thresholds are felt to be arbitrary to some degree and could be calculated differently based on different conversion formulas, but when they appear in the statement, they appear to be authoritative.
- Several workgroup members appreciated the split of recommendations #4 and #5, which differentiated those who were starting opioids from those who were already receiving higher doses of opioids.
- Some workgroup members noted that the term "justify" was concerning, as it reflects legal language. To whom should providers be justifying their management decisions? Terms like "evaluating" benefits seemed more appropriate to the treatment context. In addition, some were concerned about the term "avoid" being too strong as well.
- Recommendation Category: Several workgroup members felt the grading should be a B, but if the specific dose thresholds were removed from the text, then the grade should be an A.

***Recommendation #5:*** *For patients already receiving higher opioid dosages (e.g., >90 MME/day), clinicians should carefully weigh benefits and risks and exercise care when reducing or continuing opioid dosage. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids. (Recommendation Category: A and Evidence Type: 4)*

**OWG Observations:**

- Many opioid workgroup members appreciated the language that acknowledged the complexity of the situation.
- Similar to the observations noted for recommendation #4, many workgroup members felt that the threshold dose should be removed from the statement and included in the supporting text.
- Several workgroup members noted that the framing of this recommendation is not balanced – that it does not include the risk/benefit calculation of continuing opioids. For example, a more balanced approach is to have one sentence about continuing opioids and one sentence about tapering opioids in terms of risk/benefit analyses. Also, not fully acknowledged is that continuing opioids and not tapering opioids avoids risks of poor analgesia, worsening functioning, and suffering, and potentially illicit opioid use.
- Some workgroup members felt more discussion is needed regarding working with patients or obtaining consent from patients when prior to initiating and prior to tapering opioids, and limiting involuntary tapering. Others felt that consent should occur prior to initiating opioids, and that it may not be feasible to obtain consent at each point in which clinical management is changed.
- Some workgroup members noted that the supporting text for recommendation #5 and other areas of the guideline document flips back and forth between "harm" and "risk". Some felt that the document should use "risk", as assessing risk is one of the biggest challenges providers face.
- Several workgroup members felt an explicit and fuller discussion regarding benefits to society versus individual patients was warranted with this recommendation.
- Many workgroup members appreciated the supporting text. However, there were some specific issues that were noted as concerning by some members, these included: never going back up in dosage during opioid tapering; lack of inclusion of observational studies showing potential dangers of tapering; minimal discussion about risk of tapering; role of patient-centeredness approach; representing the role of buprenorphine as established rather than emerging; an explicit discussion of goals of tapers is needed, particularly related to public health versus individual patient outcomes; there seems to be an underlying assumption that the goal is to get to zero MME, but perhaps it should be to get to a safer dose or better symptoms or function; a section on iatrogenic harms of tapering may be warranted.
- Some workgroup members were concerned that much of the discussion was about over-correcting for possible misapplication of the guideline, which could lead to the detriment of the greater good.
- Recommendation Category: Many workgroup members felt that grade B is more appropriate. In addition, several noted that there is a bit of a mismatch in grading. For example, when there are several caveats and individualization in the language in the statement, how can it be recommended for all people?

**Opioid Duration and Follow-Up**

**Recommendation #6:** *When opioids are used for acute pain, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. One to three days or less will often be sufficient; more than seven days will rarely be needed. (Recommendation Category: A and Evidence Type: 4)*

**OWG Observations:**

- Several workgroup members were concerned about the potential application of this recommendation. Some felt that removing the last sentence would reduce risk of misapplication and questioned the evidence supporting the statement (evidence type = 4). The challenges of defining acute pain were noted again (see observations for statement #1 - e.g., it is not a diagnosis, it does not reflect pathophysiology), and some workgroup members felt many potential exceptions may require more than 3 days of opioids (and that "rarely" doesn't seem accurate). However, others felt differently, and did not want to water down this statement so much that it doesn't help improve excess opioid prescribing that exists.

- Some workgroup members wanted clarification and discussion in the text about the goal of this statement—whether it is about patients versus public health outcomes.
- Some workgroup members discussed how implementation of this guideline can have differential outcomes on patients based on their sociodemographic characteristics. For example, some patients will navigate the health care system to get refills as needed, while for others it will be impossible, thereby leading to potential different consequences.
- Several workgroup members recommended moving the last sentence into the supporting text rather than the recommendation (e.g., not including 3-7 days in the statement), or adding qualifiers like "most patients" or "many patients" or "initial prescription", and felt that doing so would allow for more flexibility and patient centeredness.
- Recommendation Category: Several workgroup members felt that the first sentence was category A, but not the second sentence. And that category A for the second sentence was out of step with the evidence type 4, and the qualifiers that are necessary to describe the exceptions.

***Recommendation #7:*** *Clinicians should continue opioid therapy for subacute or chronic pain only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for subacute or chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. (Recommendation Category: A, Evidence Type: 4)*

**OWG Observations:**

- Overall, many workgroup members felt ok with the statement in general and the recommendation category. They noted that there is little evidence to support it, particularly the specific time frames of 1-4 weeks and 3 months; however, it was reasonable and reflects common practice.
- As mentioned in overall themes, several group members observed that the use of "risks" and "harms" in this recommendation is inconsistent and recommend more careful and consistent consideration of these terms. Several members felt that using the term risk would be more appropriate than harms, as harms are typically not currently present.
- In the supporting text, there is discussion about 50 MME, while in other places the threshold is 90 MME. 50 MME as a threshold to increase the frequency of visits is a bit arbitrary.
- As mentioned in overall themes, many workgroup members noted that the issue of health disparities and health equity should be more central in the supporting text for this recommendation. These issues, including social determinants of health, are important and have real consequences when recommending frequent visits. For example, the duration of prescriptions or the frequency of visits may need to be guided more by social determinants of health or payer issues (e.g., co-pays) than by opioid dose.

**Assessing Risk and Addressing Harms of Opioid Use**

***Recommendation Statement #8:*** *Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk for opioid-related harms and discuss with patients. Clinicians should incorporate into the management plan strategies to mitigate risk, including offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present. (Recommendation Category: A, Evidence Type: 4)*

**OWG Observations:**

- Several workgroup members noted concern about naming specific conditions that increase risk; it suggests a parity among them. There is concern that listing these conditions implies that they carry equal risk, and that other conditions that are not listed carry less risk. In addition, specifying the 50 MME dose threshold is concerning, and

conveys similar risk as the other conditions. The dose threshold is arbitrary and inconsistent with other sections of the guideline (50 vs. 90 MME). As noted in overarching themes, many members recommended that these specific conditions be removed from the recommendation.

- A few members noted concerns with potential downstream effects of offering naloxone for patients of limited means, with concerns specifically about the cost of purchasing naloxone (e.g., in some areas, patients were required to fill and pay for naloxone).
- Some members noted specific conditions that were concerning:
    - Pregnancy seems to be missing as a risk factor, though there is a different framework for pregnant women with OUD. There is concern about the framing that benefits outweigh risks for pregnant patients receiving MOUD, but not those with pain, despite the fact that not prescribing opioids could lead to withdrawal. In addition, pregnancy statements were overgeneralized, and there was concern that with the supporting text, pregnant women undergoing procedures could be at risk of not receiving adequate treatment.
    - Because buprenorphine has a very high MME, it's not clear what the implications would be.
- Many workgroup members noted that the supporting text was not balanced, and a full discussion of risks and benefits are needed – that address risk/benefits of prescribing opioids and of not prescribing or limiting opioids. For example, the discussion about older adults focuses on risks of opioids, but there is no discussion about risks of untreated or undertreated pain in this population (e.g., potential worsening of blood pressure, mood, cognition). A similar point was made regarding individuals with psychiatric conditions, and the possibility of destabilization with untreated or undertreated pain. Likewise, the discussion about people with substance use disorders was unbalanced, with little discussion regarding the challenges of pain management (and buprenorphine's analgesic effect was missing). This issue of an unbalanced discussion in the supporting text is noted as an overall theme throughout the guideline.
- Some workgroup members noted that there is little consideration about the problem of lack of access to alternative pain treatments.
- While many workgroup members noted that naloxone should remain in the recommendation, some felt that taking a more comprehensive risk mitigation approach is warranted.
- Recommendation Category: Several workgroup members noted that evidence category A was appropriate if the list of conditions were removed. However, if the list of conditions remains in the recommendation statement, then the recommendation category should be B. Some workgroup members disagreed and felt the evidence category should remain A regardless of the list of conditions.

***Recommendation #9****: Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for acute or chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months. (Recommendation Category: A, Evidence Type: 4)*

**OWG Observations:**

- Several workgroup members felt that the word "dangerous" may be too strong and too binary. Some felt "high-risk" may be more appropriate, noting that there are nuances to deciding whether specific combinations of medications put individuals at risk. In addition, some workgroup members noted that it would be important to check the PDMP for risks that are broader than overdose.
- There were conflicting opinions regarding checking the PDMP for acute pain. Some workgroup members felt that prior to prescribing opioids for a small number of days, checking the PDMP may not be warranted or feasible, and

therefore, the word “acute” should be removed or a qualifying term like “when possible” should be added. Others disagreed and felt acute pain should remain in the recommendation statement.

- Some workgroup members expressed caution regarding potential harms of the PDMP, particularly when algorithms are used to create risk scores that lack evidence without qualifications. Some mentioned the cost to the patient-provider relationship; however, others discussed that when protocols are standardized, there is less risk to negatively impacting the patient-provider relationship and less risk of bias.
- Some workgroup members appreciated the recommendation that patients are not dismissed due to PDMP information. Perhaps this declaration should be more prominent, given this real risk to patients.
- Some workgroup members felt the supporting text needs to be re-worked, especially regarding acute pain.
- Recommendation Category: The workgroup was split regarding the recommendation category. Some felt that category A is appropriate. Others felt category A is appropriate only if acute pain were removed and/or if there were qualifying language like “when possible” or “when available”. As with several other recommendation statements, several members of the workgroup felt it was difficult to assign a recommendation category to the statement while recommending changes to the statement. It becomes unclear if the category would/should be applied to a modified statement or the existing statement.

***Recommendation #10:*** *When prescribing opioids for chronic pain, clinicians should use drug testing before starting opioid therapy and consider drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs. (Recommendation Category: B, Evidence Type: 4).*

**OWG Observations:**

- Illicit drugs are not defined, which is particularly problematic for cannabis. The issues around cannabis create challenges for providers, which vary by state. Perhaps cannabis should be approached similarly to alcohol, which is not routinely tested among individuals taking opioids. However, providers may not have control over the specific panels of tests, and often fentanyl might not be included. This could lead to false assurance. A discussion of these nuances of urine drug tests is warranted.
- Interpretation of urine drug tests results can be complicated, and many providers lack this knowledge, which can lead to inappropriate negative consequences. In addition, because most urine drug tests are screening tests, false positive or false negative tests are not uncommon. Such inaccurate tests could lead to punitive action. Confirmatory testing is important but can also lead to financial issues for patients. Several workgroup members felt these potential harms are not fully addressed in the supporting text. In addition, the concept of a screening test should be included (e.g. with false positives and negatives).
- As mentioned in the overall themes, there are biases and disparities in which patients have urine drug tests. Several workgroup members felt that this issue should be more centrally addressed, as the recommendation statement could have substantial disproportionately negative consequences among Black and Latinx patients.
- Because substance use is associated with serious stigma, some workgroup members recommended reviewing the supporting text to ensure non-stigmatizing language is warranted (e.g., should the term recreational drug be used instead of illegal drug?).
- Several workgroup members discussed the importance of providers’ discussing why and how urine drug tests are used, and not taking a punitive approach. There is a potential ethical tension if the role of the provider is to police the patient behavior, as the provider’s duty is to the individual patient, and the policy makers’ duty is to the public.
- Some workgroup members were cautious regarding conducting urine drug tests prior to prescribing opioids, especially if this were to delay care. Some also felt that the recommended frequency of urine drug tests and the use

of opioid dose to guide the frequency were arbitrary.

- Some workgroup members were cautious about patients' potential financial implications of frequent urine drug testing and confirmatory drug testing.
- Recommendation Category: Category B is appreciated, though others felt that a category A could potentially reduce bias and disparities in which patients' clinicians order urine drug tests.

***Recommendation #11:*** *Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible and consider whether benefits outweigh risks of concurrent prescribing of opioids and other central nervous system depressants. (Recommendation Category: A, Evidence Type: 3)*

**OWG Observations:**

- Several workgroup members felt the words "avoid," and "whenever possible" are problematic as they can be interpreted as "never". Some proposed that a more appropriate phrase may be to use extreme caution. In specific situations, benzodiazepines can be beneficial, and stopping benzodiazepines can be destabilizing. Additionally, benzodiazepines may serve as a marker for risk of overdose due to underlying conditions. It's also important to differentiate between chronic stable prescribed use versus erratic unpredictable non-prescribed use.
- Some workgroup members felt including an entire class of medications (central nervous system depressants) was far-reaching and could lead to unintended negative consequences.
- Some workgroup members felt that this recommendation statement is not appropriate for the acute care setting.
- Including the FDA warnings regarding benzodiazepine use among people prescribed opioids and among people with opioid use disorder should be included in the supporting text.
- Recommendation Category: Several workgroup members recommended a recommendation category B.

**Recommendation #12:** *Clinicians should offer or arrange treatment with medication for patients with opioid use disorder. (Recommendation Category: A, Evidence Type: 2)*

**OWG Observations:**

- Many workgroup members agreed with the language of the recommendation, specifically the word "should".
- New regulations regarding buprenorphine prescribing should be included in the supporting text.
- Several workgroup members noted that the supporting text should better distinguish opioid agonist versus opioid antagonist treatment and questioned the framing as the medications being equal options. Opioid agonist treatment has stronger evidence for better outcomes, doesn't require abstinence, has less challenges with inductions, and is much more widely utilized.
- Some workgroup members noted a conflation regarding management of problematic opioid use versus OUD in the supporting text. Reassessing pain is important prior to deciding whether to taper or discontinue opioids.
- Several specific details about OUD treatment were felt to be inaccurate in the supporting text, and additional review by an OUD expert is warranted.
- Some workgroup members felt the evidence type should be 1.

**Introduction and Conclusions Sections of the Guideline**

**OWG Observations:**

In addition to the overarching comments at the beginning of this document, additional comments, and observations specific to the introduction and conclusions sections are as follows:

- The discussion regarding health equity and disparities isn't until the end of the document. Many workgroup members recommended that this discussion be much earlier in the guideline. In addition, attention to health equity and disparities should be throughout the entire document, and a discussion about how the recommendation may impact equity and disparities is warranted.
- Many workgroup members felt there should be an explicit statement that the guideline is a *clinical* guideline, and not payer or governmental policies. Similarly, the tension between risks and benefits for individual patients versus the public health should be explicitly addressed. A patient-centered approach should be strongly encouraged.
- A few workgroup members noted issues with authorship and reviewers. Specifically, there are a small number of peer reviewers who are not identified, input from patients and providers was solicited but it was not clear how their input was factored into the guideline, and many of the included references have a lead author who is also an author of the guideline. In addition, providing the areas of expertise of the opioid work group members is suggested.
- When describing benefits and harms, it is important to recognize real-world patients' lack of access to many non-opioid pain management strategies.

## Appendix A: Opioid Workgroup Guiding Principles

### Background

As described in the Opioid Workgroup (OWG) Roster document (https://www.cdc.gov/injury/bsc/opioid-workgroup-2019.html), the Opioid Workgroup (OWG) under the Board of Scientific Counselors, National Center for Injury Prevention and Control (BSC/NCIPC), Centers for Disease Control and Prevention (CDC) will be supplied draft text in March 2021. The OWG is tasked with performing the following activities with respect to the draft guideline:

1. Reviewing the quality and implications of clinical and contextual evidence reviews.
2. Reviewing each guideline recommendation statement and accompanying rationale.
3. Considering for each recommendation:
    a. The quality of the evidence supporting the recommendation (assessing the accuracy of the evidence quality rating; i.e., evidence "type");
    b. The balance of benefits and risks associated with the recommendation (including the degree to which the benefits of issuing the recommendation can be anticipated to outweigh the harms);
    c. The values and preferences of clinicians and patients related to the recommendation (including the degree to which there is variability or uncertainty in values and preferences);
    d. The cost feasibility of the recommendation (including the degree to which implementation is anticipated to be feasible for health systems and patients financially); and
    e. The category designation of the recommendation (whether Category A or Category B is justified). Category A recommendations apply to all patients; Category B recommendations require individual decision making where different choices will be appropriate for different patients so that clinicians must help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.
4. Developing a summary report, including points of agreement and disagreement, of the workgroup's observations associated with items #1-3 above for the draft updated/expanded 2022 Guideline.

### Purpose of the OWG Guiding Principles

The intention of the Guiding Principles document is to provide a procedural framework to approach the tasks described above, as well as to aid in the completion of the work, whereby ethics, principles and priorities are outlined. This document is intended to facilitate the OWG members in comprehensively addressing the draft materials, in completing the assigned tasks; and for guiding group discussion, deliberation, and creation of recommendations and the final summary document. The Guiding Principles may also serve as a public document and reference on the general process and principles by which the OWG approached their assigned tasks.

**PRINCIPLE 1: MINIMIZE BIAS**

Goal: Identify potential bias in the following:

A. Evidence reviews
    i. Authors
    ii. Studies that have been included or excluded within a review
B. CDC draft guideline
    i. Authors
    ii. Algorithms, methods, and grading metrics used to determine inclusion or exclusion of studies/evidence, or applied to evaluate and determine the strength of evidence.
    iii. Decisions to consider or not consider various types of evidence (outside of evidence reviews). Minimize bias by ensuring that clinical evidence and various data from real-world patients and real-world practice is

weighted appropriately within the broader guiding principles framework.

**PRINCIPLE 2: SCIENTIFIC INTEGRITY**

Goal: Ensure the strength of recommendations are appropriate for the level of supporting evidence

A. Review draft content and evidence grades given.
B. Review evidence to support MME classifications and other latent factors that could distort outcomes for primary opioid science (genetics and CYP enzymes, drug metabolism, and variability in bioavailability).
C. Examine the grounds given for strength of each recommendation, noting especially any role played by values in the GRADE methodology.

**PRINCIPLE 3: ENHANCE INCLUSIVITY**

Goal: Identify ways in which the *current lens* is too narrow and therefore excluding key populations; find opportunities to extend the lens to enhance inclusivity

A. Types of studies included in published evidence reviews
   i. Identify the limits of their generalizability to outlying populations such as rare diseases.
   ii. Recommend additional types of information that should be included to ensure broad representation of all patients and circumstances.
   iii. Incorporation of supporting evidence even in the absence of direct evidence to ensure inclusion of marginalized populations.
B. Defining the target population.
   Chronic pain is not a monolith; it includes diverse conditions, etiologies, pain types, and severities. Appreciation of the diversity and complexity of chronic pain is required. We recognize a need to protect outliers, such as persons with rare diseases or progressive, degenerative conditions, who may not otherwise be captured in assessments of aggregate benefit vs. harm.
C. Considering the input of those whose lives are likely to be most affected and views that might be under-represented in the process.
   This type of inclusivity is important to both our internal processes and to ensuring adequate input of affected persons once the guideline is published in draft form. (Recognizing that the guideline is not subject to formal rulemaking requirements but, given the likely policy implications, robust provisions for notice and comment and efforts to include the viewpoints patients, providers and likely under-represented populations are important norms to follow before final adoption of the guideline by the agency).

**PRINCIPLE 4: PATIENT AND CLINICIAN CENTERED**

Goal: Establish patient and clinician centered care guidance that is accessible, comprehensive, and integrated.

A. Patient-Centeredness

   i. Identify barriers to care access including potential financial burden to the patient, use of internet-based medical records, and increased patient-provider communication via telephone or e-mail.
   ii. Treatment recommendations, whether pharmacologic or non-pharmacologic, must be *meaningfully accessible* to the individual patient when creating care plans. Citing efficacy evidence alone is insufficient.
   iii. Encourage providers to consider patient needs, desires, and limitations and avoid stigma when making treatment recommendations.
   iv. Recommend additional training and educational materials for providers on guideline concordant conservative care options.
   v. Establish strong interdisciplinary relationships, especially between providers with shared patient base.
   vi. Engage patients in the development of their care plans.

B. Clinician-Centeredness

i. Guidelines should support optimal patient care and shared decision-making for individual adjustment of all medications.
ii. Variation from guidelines should be expected for patient centered opioid prescribing. Variation from prescribing guidelines alone should not be considered evidence of suboptimal care.

**PRINCIPLE 5: HISTORICAL CONTEXT**

Goal: Mitigate harms from unintended consequences

A. Appreciate the historical context of the initial Guideline and its consequences into deliberations and recommendations, with a goal of preventing injury/harm in current and future patients.
   i. Recognize that all Guidelines have the potential for causing unintended side effects.
   ii. Incorporate lessons learned from the various misinterpretations of the 2016 Opioid Prescribing Guidelines in order to prevent similar unintended consequences.
   iii. Overreach of the guideline to exempted populations (e.g., patients with cancer, sickle cell disease, OUD).
   iv. Inflexible application of certain key recommendations, which were particularly problematic given the low evidence base to support them.
   v. Concreteness of the provision -- recommendations which could easily be lifted and enforced. While intended as supply and dosage recommendations, stated numbers were misapplied to define standards of care and policies. Despite the CDC's clarification, these numbers continue to define policies and drive inflexible care that is not patient-centered and has been shown to harm.
   vi. *Communication science* must be applied to ensure the conclusions of the Guideline are clear, without ambiguity, and with minimal ability to distort the information or create misunderstand, especially as it could pertain to local, state, or national policy.

## CDC's Response to OWG Observations

| OWG Observations | CDC's Response to OWG Observations |
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| ***Overall Observations and Overarching Themes*** | |
| Overall, many workgroup members felt that much of the supporting text of the guideline was not balanced and was missing key studies. Many workgroup members felt that the guideline focused heavily on the risks or potential harms of opioids, while less attention was focused on the potential benefits of opioids, or the risk of not taking opioids or undertreating pain. In addition, some workgroup members felt that the language of the recommendation statements or supporting text conveyed more certainty or was more absolute than warranted by the evidence. | CDC added studies and references to the revised guideline after the OWG review to address experts' concerns about missing studies (e.g., Sun et al. was a key missing study that informs the range of percentage of patients who used opioids long-term after surgery). Examples of studies added in supporting text include:<br>• Glanz, J. M., Binswanger, I. A., Shetterly, S. M., Narwaney, K. J., & Xu, S. (2019). Association Between Opioid Dose Variability and Opioid Overdose Among Adults Prescribed Long-term Opioid Therapy. JAMA Network Open, 2(4), e192613-e192613. Retrieved from https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2730786<br>• Oliva, E. M., Bowe, T., Manhapra, A., Kertesz, S., Hah, J. M., Henderson, P., . . . Trafton, J. A. (2020). Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. Bmj, 368, m283. Retrieved from https://www.bmj.com/content/368/bmj.m283<br>• Oliva, J. (2021). Dosing Discrimination: Regulating PDMP Risk Scores. 110 California Law Review __ (forthcoming 2022). Retrieved from https://dx.doi.org/10.2139/ssrn.3768774<br>• Sun, E. C., Darnall, B. D., Baker, L. C., & Mackey, S. (2016). Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the Postoperative Period. JAMA Internal Medicine, 176(9), 1286-1293. Retrieved from https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2532789 |
| Much of the discussion of the recommendations centered around the concern for misapplication of the guideline. Because of the consequences of misapplication of the 2016 guideline, many workgroup members were concerned about how the recommendation could be misapplied, leading to potential harm to patients. The workgroup discussion thus focused on how best to mitigate against this valid concern while preserving the benefits of the guideline. However, some were concerned that the workgroup may have been over-correcting and so much concern about future misapplication could potentially be detrimental to the greater good. | CDC added "Clinical Practice" to the Guideline title and throughout the document to reinforce messaging and the Guideline's intent. |
| | CDC added a callout box at the beginning of the revised guideline that clearly indicates up front "what the guideline is and is not" to help reinforce appropriate guideline implementation and prevent potential misapplication. |
| | CDC added five guiding principles in the "Recommendations" section to broadly inform implementation across recommendations. In addition, CDC added "Implementation Considerations" immediately below each recommendation statement. These bulleted implementation considerations offer practical insights meant to further inform clinician-patient decision-making for the respective recommendation and are not meant to be rigidly or inflexibly followed. |
| | CDC carefully considered observations and comments regarding language of the recommendation statements and supporting text and modified text, where appropriate; details are provided directly below and in later sections of this document. |

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| | CDC incorporated comments regarding concerns about potential misapplication by modifying some recommendation statements and moving details within statements to the supporting text, where more nuance and discussion was included and to avoid the perception of absolute or hard limits in some of the bolded recommendations. |
| Many workgroup members felt the guideline paid too little attention and had minimal discussion about racial/ethnic disparities and inequities in how pain is perceived, valued, and managed, and the potential implications of these disparities on implementation of the guideline, including disparities in access to recommended treatments, along with how the guideline could impact disparities. | CDC moved core content on health disparities from the "Conclusion" to the "Introduction" section to highlight these important issues up front. CDC also added more context and references regarding racial/ethnic disparities and inequities, health equity, and social determinants of health. In addition, CDC integrated more discussion regarding disparities in access and implementation considerations to mitigate and reduce disparities throughout the revised guideline. |
| | CDC added text to draw additional attention to and acknowledge that the risk of pain being differentially untreated or undertreated in racial/ethnic minority patients persists and demands immediate and sustained attention and action. CDC also added text to acknowledge that misapplications and actions not endorsed by the CDC or consistent with the 2016 Guideline, such as patient dismissal and abandonment, have occurred and contributed to patient harm, including untreated and undertreatment of pain, serious withdrawal symptoms, worsening pain outcomes, psychological distress, transitioning to illicit opioids, overdose, and suicidal ideation and behavior. |
| | CDC removed guidance referring to pain specialists throughout the guideline, as there is anecdotal evidence that a severe shortage of pain management specialists increases disparities in access to pain management, which could be alleviated if most clinicians (and not only pain specialists) take responsibility for and have or develop competency to manage pain. |
| Many workgroup members noted how the guideline has a constant tension between public health benefits versus patient benefits. This issue is minimally addressed in the guideline and comes very late. Workgroup members felt it is important to directly address this tension between risks and benefits to public health versus individual patients, and to contextualize how individual providers should use this guideline in caring for their patients versus considering potential public health consequences. In addition, several workgroup members felt that overall, the guideline was not sufficiently patient-centered. | CDC modified text in the introduction and rationale sections to address OWG comments about tension between public health benefits versus patient benefits and to further underline the guideline's focus on maximizing benefits and minimizing risks for individual patients. CDC also incorporated edits throughout the guideline to further highlight the importance of patient-centered care and decision-making. |

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| Many workgroup members were cautious about including specific opioid dose thresholds in the recommendations. Workgroup members acknowledged the importance of having benchmarks, but many felt that specific opioid doses would be misapplied as absolute cutoffs or thresholds for policies or practices. Many workgroup members felt the specific opioid dose thresholds belonged in the supporting text where the discussion could be more nuanced. In addition, there is no single standard formula for calculating MMEs. | CDC incorporated OWG observations about including specific opioid dose thresholds in the recommendations by moving specifics from the recommendation statements to "Implementation Considerations" in supporting text and adding nuance, where appropriate. |
| Many workgroup members noted a sense of exceptionalism throughout the guideline. Specifically, certain conditions were named in the text, while others were not. Naming of specific conditions may lead to interpretation regarding whether pain is "real" or "worthy" of certain types of treatment. In addition, while the guideline states it does not apply to sickle cell disease, cancer, palliative care, or end-of-life care, palliative care is not clearly defined. | CDC added a statement in the "Scope and Audience" section that exclusion of sickle cell disease, cancer, palliative care, and end-of-life care from the scope of this guideline does not imply that any other types of pain are less worthy of effective treatment. CDC also ensured that "palliative care" is clearly defined. |
| Many workgroup members felt that the recommendation category A was overutilized (11 of the 12 statements had recommendation category A). Members felt that this type of grading likely contributed to the misapplication of the 2016 guideline. | CDC carefully considered OWG comments and observations regarding grading categories of specific recommendations. As reflected in subsequent OWG report sections, many members stated that for most recommendations, category A would apply to the more general parts of the recommendation statements, while members were more divided regarding the category for specifics (e.g., dosage thresholds). CDC moved some of the specific language into "Implementation Considerations" and "Supporting Rationale" sections, took into consideration the more specific observations below each recommendation statement, and modified the grading of some recommendations. More details are provided under these recommendation sections in this document. |
| Many members of the workgroup developed a document that described the workgroup's guiding principles when providing observations on the guideline. Guiding principles include: minimize bias, ensure scientific integrity, enhance inclusivity, establish patient- and clinician-centered guidance, and mitigate harms from unintended consequences. The document is included as Appendix A. | CDC appreciates the OWG for developing and including "Guiding Principles" in their report as these provided additional guidance and context for incorporating OWG observations during the guideline revision process. CDC added reference to the OWG Guiding Principles in the revised draft updated Guideline. |

| ***Recommendation #1:*** *Nonopioid therapies are preferred for many common types of acute pain. Clinicians should only consider opioid therapy for acute pain only if benefits are anticipated to outweigh risks to the patient. (Recommendation Category: A; Evidence Type: 3)* | |
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| Several workgroup members recommended changing the wording of Recommendation #1—remove the second “only”, consider changing “preferred” to “effective”. | CDC removed the second “only” and changed “preferred” to “effective” in the recommendation statement. |
| Several workgroup members were concerned about the large and unclear category of acute pain, and felt further clarification is needed. For example, should post-surgical pain be in this category of acute pain? Several workgroup members felt the statement was an oversimplification and there were situations or conditions that should be exceptions. Workgroup members also felt that categorizing pain should be based on pathophysiology or severity, rather than time. Several members noted that it is often unclear when acute pain transitions to subacute pain, and when subacute pain transitions to chronic pain. In addition, there is little attention to acute-on-chronic pain. | CDC added “Implementation Considerations” immediately below the recommendation statement and moved up the definition of what is included in “many common types of acute pain” there. CDC also added text to clarify that the duration classifications of acute, subacute, and chronic pain are not absolute, but operational definitions based on time and are provided as rough guides for consideration in implementation. |
| Some workgroup members felt the recommendation does not consider shared decision-making. | CDC added a statement that clinicians "should involve patients in decisions about whether to start opioid therapy" in the “Implementation Considerations” directly following the recommendation statement. |
| Several workgroup members were concerned that the recommendation could be misinterpreted and translated into bad policy. There was particular concern about limited access to non-opioid pain management modalities, in part due to lack of availability or lack of coverage by payers. Improving access to non-opioid pain management modalities should be a priority. | CDC added more discussion about limited access, lack of coverage, and improving access to noninvasive, nonpharmacologic therapies. |
| Recommendation Category: Most, though not all, workgroup members felt this statement should be graded category B. | CDC added text to reiterate and highlight the limited scope of this recommendation and conditions to which this recommendation may not apply (e.g., major surgery, trauma).<br>CDC changed the recommendation category from “A” to “B” given heterogeneity in applicability of the recommendation across a broad range of acute pain conditions. |

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| ***Recommendation #2:*** *Nonopioid therapies are preferred for subacute and chronic pain. Clinicians should only consider initiating opioid therapy if expected benefits for pain and function are anticipated to outweigh risks to the patient. Before starting opioid therapy for subacute or chronic pain, clinicians should discuss with patients known risks and realistic benefits of opioid therapy, should establish treatment goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. If opioids are used, they should be combined with other therapies as appropriate. (Recommendation Category: A, Evidence Type: 3)* | |
| Several workgroup members voiced appreciation for this statement because of the attempt to be inclusive and comprehensive, take into account pain and function, and be realistic upfront with patients. In addition, the attention to de-prescribing and exit strategies is appreciated. | CDC added text in "Supporting Rationale" referring to experts' observations and appreciation for this recommendation statement. |
| Some workgroup members felt shared decision-making should be emphasized here and in other recommendations. | CDC added text to re-iterate and emphasize the importance of patient preferences and values being understood and used to inform clinical decisions and of involving patients in decisions about whether to start opioid therapy. |
| Several workgroup members noted that certain conditions for which this guideline does not apply feels like exceptionalism in terms of what's serious pain versus what's not and may reflect what types of pain conditions receive research funding or other attention. | CDC added a statement that exclusion of sickle cell disease, cancer, palliative care, and end-of-life care from the scope of this guideline does not imply that any other types of pain are less worthy of effective treatment. |
| Some workgroup members felt the language in this recommendation is somewhat too strong, given problems with some of the cited evidence. Words like "are preferred" might be softened to "may be preferred" or "may be effective". Although the harms of opioids are very well-defined, the benefits (especially long-term) are not well understood and difficult to study. | CDC added text in "Supporting Rationale" referring to some experts' observations regarding specific language for this recommendation statement. |
| Recommendation Category: Some workgroup members felt the recommendation category should be B. | CDC kept the recommendation category grading as the guideline authors and many workgroup members felt the recommendation category should be "A". |
| ***Recommendation #3:*** *When starting opioid therapy for acute, subacute, or chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids. (Recommendation Category: A and Evidence Type: 3)* | |
| Most workgroup members overall agreed with the statement. Some felt the need to define "starting" and opioid- naïve more clearly, particularly given patients' historical context of prior pain management strategies. | CDC reinforced language in "Implementation Considerations" stating that "Clinicians should not treat acute pain with ER/LA opioids or initiate opioid treatment for subacute or chronic pain with ER/LA opioids" and also providing specific parameters for ER/LA opioid use, consistent with FDA guidance (ER/LA opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least 1 week). |

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| Several workgroup members appreciated the support text discussion regarding abuse-deterrent formulations. | CDC added text in “Supporting Rationale” referring to experts’ observations. |
| Recommendation Category: Most workgroup members agreed with the recommendation category A. | CDC kept the recommendation category grading as “A”. |
| ***Recommendation #4:*** *When opioids are started for opioid-naïve patients with acute, subacute, or chronic pain, clinicians should prescribe the lowest effective dosage. If opioids are continued for subacute or chronic pain, clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to >90 MME/day. (Recommendation Category: A and Evidence Type: 3)* | |
| Many workgroup members voiced concern about the dose thresholds written into the recommendation. Many were concerned that this recommendation would lead to forced tapers or other potentially harmful consequences. Though workgroup members recognized the need to have thresholds as benchmarks, many felt that including these thresholds in the supporting text could serve to de-emphasize them as absolute thresholds, and thus recommended removing the specific MME range from the recommendation. In addition, these thresholds are felt to be arbitrary to some degree and could be calculated differently based on different conversion formulas, but when they appear in the statement, they appear to be authoritative. | CDC moved text regarding dosage thresholds from the recommendation statement to “Implementation Considerations” and supporting text and included additional nuance. The implementation considerations offer practical insights meant to further inform clinician-patient decision-making for the recommendation and are not meant to be rigidly or inflexibly followed. |
| Several workgroup members appreciated the split of recommendations #4 and #5, which differentiated those who were starting opioids from those who were already receiving higher doses of opioids. | CDC added text in “Supporting Rationale” referring to experts’ observations. |
| Some workgroup members noted that the term “justify” was concerning, as it reflects legal language. To whom should providers be justifying their management decisions? Terms like “evaluating” benefits seemed more appropriate to the treatment context. In addition, some were concerned about the term “avoid” being too strong as well. | CDC changed "justify" to “evaluate” in the recommendation statement. |
| Recommendation Category: Several workgroup members felt the grading should be a B, but if the specific dose thresholds were removed from the text, then the grade should be an A. | CDC kept the recommendation category grading as “A”. |

| ***Recommendation #5:*** *For patients already receiving higher opioid dosages (e.g., >90 MME/day), clinicians should carefully weigh benefits and risks and exercise care when reducing or continuing opioid dosage. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids. (Recommendation Category: A and Evidence Type: 4)* | |
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| Many opioid workgroup members appreciated the language that acknowledged the complexity of the situation. | CDC added text in “Supporting Rationale” referring to experts’ observations. |
| Similar to the observations noted for recommendation #4, many workgroup members felt that the threshold dose should be removed from the statement and included in the supporting text. | CDC removed text regarding specific dosage threshold from the recommendation statement and retained in the supporting text. |
| Several workgroup members noted that the framing of this recommendation is not balanced – that it does not include the risk/benefit calculation of continuing opioids. For example, a more balanced approach is to have one sentence about continuing opioids and one sentence about tapering opioids in terms of risk/benefit analyses. Also, not fully acknowledged is that continuing opioids and not tapering opioids avoids risks of poor analgesia, worsening functioning, and suffering, and potentially illicit opioid use. | CDC added a statement in the discussion of benefits and risks that "Because tapering opioids can be harmful in some circumstances, benefits of continuing opioids in patients who have already received them long term might include avoiding risks of tapering and discontinuing opioids”. |
| | CDC changed "if benefits do not outweigh harms" to "if risks outweigh benefits" in the recommendation statement, which leaves more flexibility when risks and benefits are closely balanced. |
| Some workgroup members felt more discussion is needed regarding working with patients or obtaining consent from patients when prior to initiating and prior to tapering opioids, and limiting involuntary tapering. Others felt that consent should occur prior to initiating opioids, and that it may not be feasible to obtain consent at each point in which clinical management is changed. | CDC added text in "Supporting Rationale" noting this difference in expert opinion. CDC also added a statement that "In situations where benefits and risks of continuing opioids are considered to be close, shared decision-making with patients can be helpful." |
| Some workgroup members noted that the supporting text for recommendation #5 and other areas of the guideline document flips back and forth between “harm” and “risk”. Some felt that the document should use “risk”, as assessing risk is one of the biggest challenges providers face. | CDC replaced the term “harms” with “risks” throughout the revised guideline, where appropriate. Generally, “risk” is used to refer to potential harm while “harm” is used (intentionally) to refer to actual harm. |
| Several workgroup members felt an explicit and fuller discussion regarding benefits to society versus individual patients was warranted with this recommendation. | CDC modified text in the “Introduction” and “Rationale” to further underline the guideline’s focus on maximizing benefits and minimizing risks for individual patients. |
| Many workgroup members appreciated the supporting text. However, there were some specific issues that were noted as concerning | CDC would like to clarify that the draft states “Tapers should not be reversed without careful assessment of benefits and risks of increasing |

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| by some members, these included: never going back up in dosage during opioid tapering; lack of inclusion of observational studies showing potential dangers of tapering; minimal discussion about risk of tapering; role of patient-centeredness approach; representing the role of buprenorphine as established rather than emerging; an explicit discussion of goals of tapers is needed, particularly related to public health versus individual patient outcomes; there seems to be an underlying assumption that the goal is to get to zero MME, but perhaps it should be to get to a safer dose or better symptoms or function; a section on iatrogenic harms of tapering may be warranted. | opioid dosage or without maximizing nonopioid treatments for pain and for behavioral distress". |
| | CDC included multiple observational studies showing potential dangers of tapering:<br>• Gordon, K. S., Manhapra, A., Crystal, S., Dziura, J., Edelman, E. J., Skanderson, M., . . . Becker, W. C. (2020). All-cause mortality among males living with and without HIV initiating long-term opioid therapy, and its association with opioid dose, opioid interruption and other factors. Drug Alcohol Depend, 216, 108291. doi:10.1016/j.drugalcdep.2020.108291<br>• James, J. R., Scott, J. M., Klein, J. W., Jackson, S., McKinney, C., Novack, M., . . . Merrill, J. O. (2019). Mortality After Discontinuation of Primary Care-Based Chronic Opioid Therapy for Pain: a Retrospective Cohort Study. J Gen Intern Med, 34(12), 2749-2755. doi:10.1007/s11606-019-05301-2<br>• Mark, T. L., & Parish, W. (2019). Opioid medication discontinuation and risk of adverse opioid-related health care events. J Subst Abuse Treat, 103, 58-63. doi:10.1016/j.jsat.2019.05.001<br>• U.S. Food and Drug Administration. (2019c). FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering. Retrieved from https://www.fda.gov/drugs/drug-safety-and-availability/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes |
| | CDC also added the following references:<br>• Glanz, J. M., Binswanger, I. A., Shetterly, S. M., Narwaney, K. J., & Xu, S. (2019). Association Between Opioid Dose Variability and Opioid Overdose Among Adults Prescribed Long-term Opioid Therapy. JAMA Network Open, 2(4), e192613-e192613. doi:10.1001/jamanetworkopen.2019.2613<br>• Oliva, E. M., Bowe, T., Manhapra, A., Kertesz, S., Hah, J. M., Henderson, P., . . . Trafton, J. A. (2020). Associations between stopping prescriptions for opioids, length of opioid treatment, and overdose or suicide deaths in US veterans: observational evaluation. Bmj, 368, m283. doi:10.1136/bmj.m283 |
| | CDC added a statement that "Whether goal of the taper is stopping opioids or reducing opioids to a point where benefits outweigh risks depends on the individual patient's circumstances and individualized assessment of benefits and risks, informed by open discussion between the patient and clinician." |
| | CDC added clarification in section on "Tapering Rate" that opioids can be stopped once taken less than once/day if the goal is to stop. |
| | CDC emphasized in the supporting text that the transition to buprenorphine is an emerging approach to reducing long-term opioid use. |

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| Some workgroup members were concerned that much of the discussion was about over-correcting for possible misapplication of the guideline, which could lead to the detriment of the greater good. | CDC added text in "Supporting Rationale" referring to experts' observations. |
| Recommendation Category: Many workgroup members felt that grade B is more appropriate. In addition, several noted that there is a bit of a mismatch in grading. For example, when there are several caveats and individualization in the language in the statement, how can it be recommended for all people? | CDC changed the recommendation category grading from "A" to "B" given that this recommendation includes caveats on tapering and requires clinicians and patients to decide together whether benefits outweigh risks with respect to tapering. |
| ***Recommendation #6:*** *When opioids are used for acute pain, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. One to three days or less will often be sufficient; more than seven days will rarely be needed. (Recommendation Category: A and Evidence Type: 4)* | |
| Several workgroup members were concerned about the potential application of this recommendation. Some felt that removing the last sentence would reduce risk of misapplication and questioned the evidence supporting the statement (evidence type = 4). The challenges of defining acute pain were noted again (see observations for statement #1 - e.g., it is not a diagnosis, it does not reflect pathophysiology), and some workgroup members felt many potential exceptions may require more than 3 days of opioids (and that "rarely" doesn't seem accurate). However, others felt differently, and did not want to water down this statement so much that it doesn't help improve excess opioid prescribing that exists. | CDC removed the second sentence from the recommendation statement. CDC also added text regarding days' supply in "Implementation Considerations" and in supporting text, where there is more room to discuss the scope of guidance and nuance. |
| Some workgroup members wanted clarification and discussion in the text about the goal of this statement— whether it is about patients versus public health outcomes. | CDC modified text in the "Introduction" and "Rationale" to further underline the guideline's focus on maximizing benefits and minimizing risks for individual patients. |
| Some workgroup members discussed how implementation of this guideline can have differential outcomes on patients based on their sociodemographic characteristics. For example, some patients will navigate the health care system to get refills as needed, while for others it will be impossible, thereby leading to potential different consequences. | CDC added text in "Supporting Rationale" referring to experts' observations.<br>CDC added statements in the "Implementation Considerations": "To minimize unintended impact on patients with an unexpectedly prolonged duration of severe acute pain, clinicians, practices, and health systems should have mechanisms in place to provide timely re-evaluation for the subset of patients who experience severe acute pain that continues longer than the expected duration to confirm or revise the initial diagnosis and to adjust management accordingly. In particular, clinicians, practices, and health systems should attend to minimizing |

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| | disparities across patients based on access to care and affordability of refills to ensure patients can access additional evaluation and treatment as needed. " |
| Several workgroup members recommended moving the last sentence into the supporting text rather than the recommendation (e.g., not including 3-7 days in the statement), or adding qualifiers like "most patients" or "many patients" or "initial prescription", and felt that doing so would allow for more flexibility and patient centeredness. | CDC removed the second sentence from the recommendation statement. CDC also added text regarding days' supply in "Implementation Considerations" and in supporting text, where there is more room to discuss the scope of guidance and nuance. |
| Recommendation Category: Several workgroup members felt that the first sentence was category A, but not the second sentence. And that category A for the second sentence was out of step with the evidence type 4, and the qualifiers that are necessary to describe the exceptions. | CDC kept the recommendation category grading as "A" given the second sentence in the statement was removed. |
| ***Recommendation #7:*** *Clinicians should continue opioid therapy for subacute or chronic pain only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for subacute or chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. (Recommendation Category: A, Evidence Type: 4)* | |
| Overall, many workgroup members felt ok with the statement in general and the recommendation category. They noted that there is little evidence to support it, particularly the specific time frames of 1-4 weeks and 3 months; however, it was reasonable and reflects common practice. | CDC added text in "Supporting Rationale" referring to experts' observations. |
| As mentioned in overall themes, several group members observed that the use of "risks" and "harms" in this recommendation is inconsistent and recommend more careful and consistent consideration of these terms. Several members felt that using the term risk would be more appropriate than harms, as harms are typically not currently present. | CDC replaced the term "harms" with "risks" throughout the revised guideline, where appropriate. Generally, "risk" is used to refer to potential harm while "harm" is used (intentionally) to refer to actual harm. |
| In the supporting text, there is discussion about 50 MME, while in other places the threshold is 90 MME. 50 MME as a threshold to increase the frequency of visits is a bit arbitrary. | CDC added language in supporting text referencing doubling in overdose risk above 50 MME/day (50-100 MME/day) relative to below 20 MME/day across several studies. In many ways, 50 MME/day has more justification as a threshold than 90 MME/day as risk increases continually but benefits do not appear to increase above 50 MME/day for most patients. Other guidelines since 2016 (e.g., ACOEM 2017) have emphasized 50 MME/day rather than 90 MME/day as a benchmark for caution and increased visits. Most other discussion of risk related to dosage thresholds in this update now highlights 50 MME/day rather than 90 MME/day. |

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| As mentioned in overall themes, many workgroup members noted that the issue of health disparities and health equity should be more central in the supporting text for this recommendation. These issues, including social determinants of health, are important and have real consequences when recommending frequent visits. For example, the duration of prescriptions or the frequency of visits may need to be guided more by social determinants of health or payer issues (e.g., co-pays) than by opioid dose. | CDC added more context and references regarding racial/ethnic disparities and inequities, health equity, and social determinants of health throughout the revised guideline. In addition, CDC integrated more discussion regarding disparities in access and implementation considerations to mitigate and reduce disparities. For this recommendation, CDC added payer and access considerations to "Implementation Considerations". |
| ***Recommendation Statement #8:*** *Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk for opioid-related harms and discuss with patients. Clinicians should incorporate into the management plan strategies to mitigate risk, including offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present. (Recommendation Category: A, Evidence Type: 4)* | |
| Several workgroup members noted concern about naming specific conditions that increase risk; it suggests a parity among them. There is concern that listing these conditions implies that they carry equal risk, and that other conditions that are not listed carry less risk. In addition, specifying the 50 MME dose threshold is concerning, and conveys similar risk as the other conditions. The dose threshold is arbitrary and inconsistent with other sections of the guideline (50 vs. 90 MME). As noted in overarching themes, many members recommended that these specific conditions be removed from the recommendation. | CDC moved the specific conditions from the recommendation statement to "Implementation Considerations". |
| | CDC added language in supporting text referencing the doubling in overdose risk above 50 MME/day (50-100 MME/day) relative to below 20 MME/day across several studies. In terms of benefits vs. risks of opioids, 50 MME/day has more justification as a threshold than 90 MME/day as risk increases continually, but benefits do not appear to increase above 50 MME/day for most patients. Other guidelines since 2016 (e.g., The American College of Occupational and Environmental Medicine Chronic Pain Guideline, 2017) have emphasized 50 MME/day rather than 90 MME/day as a benchmark for caution and increased visits. Most other discussion of risk related to dosage thresholds in this update now highlights 50 MME/day rather than 90 MME/day. |
| | CDC added sleep-disordered breathing to the list of factors prompting offering of naloxone in "Implementation Considerations" and in supporting text. |
| A few members noted concerns with potential downstream effects of offering naloxone for patients of limited means, with concerns specifically about the cost of purchasing naloxone (e.g., in some areas, patients were required to fill and pay for naloxone). | CDC added text in "Supporting Rationale" referring to experts' observations. |
| | CDC added text regarding access to naloxone in "Implementation Considerations" to address concerns about potential downstream effects of offering naloxone for patients of limited means, including that this is part of the rationale for the recommendation to specify that naloxone is "offered" to patients (patients are not required to fill). |
| Some members noted specific conditions that were concerning:<br>• Pregnancy seems to be missing as a risk factor, though there is a different framework for pregnant women with OUD. There is concern about the framing that benefits | CDC added more discussion of benefits vs. risks of opioids for acute and chronic pain to address concerns related to pregnant individuals, including references to the American College of Obstetricians and Gynecologists (ACOG) recommendations on these. In addition, CDC addressed concerns about not prescribing opioids leading to withdrawal in the cautions regarding tapering in pregnant individuals. |

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| outweigh risks for pregnant patients receiving MOUD, but not those with pain, despite the fact that not prescribing opioids could lead to withdrawal. In addition, pregnancy statements were overgeneralized, and there was concern that with the supporting text, pregnant women undergoing procedures could be at risk of not receiving adequate treatment.<br>• Because buprenorphine has a very high MME, it's not clear what the implications would be. | CDC noted in the MME table that "Buprenorphine products approved for the treatment of pain are not included in the table due to their partial mu receptor agonist activity and resultant ceiling effects compared to full mu receptor agonists." and that "These conversion factors should not be applied to dosage decisions related to the management of opioid use disorder." |
| | CDC also added supporting text for Recommendation 4, where MME dose-overdose relationship is first discussed: "Note that these studies examined dose-response risk of overdose for full-agonist opioids and not for partial agonist opioids such as buprenorphine, which is unlikely to have the same continuous association between dosage and overdose risk because respiratory depressant effects of buprenorphine reach a plateau." |
| Many workgroup members noted that the supporting text was not balanced, and a full discussion of risks and benefits are needed – that address risk/benefits of prescribing opioids and of not prescribing or limiting opioids. For example, the discussion about older adults focuses on risks of opioids, but there is no discussion about risks of untreated or undertreated pain in this population (e.g., potential worsening of blood pressure, mood, cognition). A similar point was made regarding individuals with psychiatric conditions, and the possibility of destabilization with untreated or undertreated pain. Likewise, the discussion about people with substance use disorders was unbalanced, with little discussion regarding the challenges of pain management (and buprenorphine's analgesic effect was missing). This issue of an unbalanced discussion in the supporting text is noted as an overall theme throughout the guideline. | CDC added language to emphasize that persons aged ≥65 and with cognitive impairment can be at risk for inadequate pain treatment and that clinicians should ensure pain is addressed. CDC also added language that clinicians should ensure that treatment for pain is optimized in patients with depression and other mental health conditions. |
| | CDC added language that patients with co-occurring pain and substance use disorder require ongoing pain management that maximizes benefits relative to risks, along with reference to see "Pain management in patients with opioid use disorder" section of Recommendation 12 for additional guidance specific to patients with opioid use disorder (this section includes discussion of buprenorphine's analgesic effect). |
| Some workgroup members noted that there is little consideration about the problem of lack of access to alternative pain treatments. | CDC clarified that Recommendation 8 is focused on risk mitigation when prescribing opioids. Lack of access to alternative pain medications is addressed, and text has been modified to emphasize the importance of improving access to nonopioid pain treatments, in the "Introduction", other Recommendations that discuss nonopioid pain management strategies (e.g., Recommendation 2), and the "Conclusions". |
| While many workgroup members noted that naloxone should remain in the recommendation, some felt that taking a more comprehensive risk mitigation approach is warranted. | CDC added "Implementation Considerations" directly below the recommendation statement, including a more comprehensive risk reduction approach and including additional risk intervention strategies. |

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| Recommendation Category: Several workgroup members noted that evidence category A was appropriate if the list of conditions were removed. However, if the list of conditions remains in the recommendation statement, then the recommendation category should be B. Some workgroup members disagreed and felt the evidence category should remain A regardless of the list of conditions. | CDC kept the recommendation category grading as "A". |
| ***Recommendation #9:*** *Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for acute or chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months. (Recommendation Category: A, Evidence Type: 4)* | |
| Several workgroup members felt that the word "dangerous" may be too strong and too binary. Some felt "high-risk" may be more appropriate, noting that there are nuances to deciding whether specific combinations of medications put individuals at risk. In addition, some workgroup members noted that it would be important to check the PDMP for risks that are broader than overdose. | CDC deleted "dangerous" from the recommendation statement. CDC also added text regarding considerations beyond overdose risk (e.g., OUD/SUD evaluation) in the "Implementation Considerations". |
| There were conflicting opinions regarding checking the PDMP for acute pain. Some workgroup members felt that prior to prescribing opioids for a small number of days, checking the PDMP may not be warranted or feasible, and therefore, the word "acute" should be removed or a qualifying term like "when possible" should be added. Others disagreed and felt acute pain should remain in the recommendation statement. | CDC kept "acute pain" in the recommendation statement and moved the timing guidance from the recommendation statement to "Implementation Considerations", where there is more room for nuance. |
| Some workgroup members expressed caution regarding potential harms of the PDMP, particularly when algorithms are used to create risk scores that lack evidence without qualifications. Some mentioned the cost to the patient- provider relationship; however, others discussed that when protocols are standardized, there is less risk to negatively impacting the patient-provider relationship and less risk of bias. | CDC added reference to and discussion of algorithms and potential harms. CDC added text in "Supporting Rationale" referring to experts' observations. |

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| Some workgroup members appreciated the recommendation that patients are not dismissed due to PDMP information. Perhaps this declaration should be more prominent, given this real risk to patients. | CDC emphasized the importance of patients not being dismissed due to PDMP information in “Implementation Considerations” added immediately below recommendation statement. |
| Some workgroup members felt the supporting text needs to be re-worked, especially regarding acute pain. | CDC reviewed supporting text to confirm applicability to acute pain. Although much of the guidance will not apply if the patient has no other prescriptions, in the case of a patient with multiple opioid prescriptions from acute pain presentations with different providers, a new encounter with a clinician for acute pain can provide an important opportunity for communication and intervention to improve patient safety. CDC changed "when starting opioid therapy for acute or chronic pain" to "when prescribing initial opioid therapy for acute or chronic pain" to make it clearer that this would not apply to medications provided to the patient in the emergency department, but to prescriptions for the patient to take following the clinical encounter (whether in the emergency department or elsewhere). |
| Recommendation Category: The workgroup was split regarding the recommendation category. Some felt that category A is appropriate. Others felt category A is appropriate only if acute pain were removed and/or if there were qualifying language like “when possible” or “when available”. As with several other recommendation statements, several members of the workgroup felt it was difficult to assign a recommendation category to the statement while recommending changes to the statement. It becomes unclear if the category would/should be applied to a modified statement or the existing statement. | CDC changed the recommendation category from “A” to “B” given that acute pain was kept in the recommendation statement. |
| ***Recommendation #10:*** *When prescribing opioids for chronic pain, clinicians should use drug testing before starting opioid therapy and consider drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs. (Recommendation Category: B, Evidence Type: 4).* | |
| Illicit drugs are not defined, which is particularly problematic for cannabis. The issues around cannabis create challenges for providers, which vary by state. Perhaps cannabis should be approached similarly to | CDC changed "illicit" to "nonprescription controlled substances" in the recommendation statement and supporting text. |
| | CDC added a statement that "Testing for fentanyl is not currently available in widely-used toxicology assays, potentially leading to false assurance." |

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| alcohol, which is not routinely tested among individuals taking opioids. However, providers may not have control over the specific panels of tests, and often fentanyl might not be included. This could lead to false assurance. A discussion of these nuances of urine drug tests is warranted. | CDC addressed observations regarding cannabis and added to discussion about avoiding drug testing for THC unless it would make a difference in clinical management and moved content up to the background regarding problems for drug testing. Discussion now reads "Ideally, clinicians would not test for substances for which results would not affect patient management. For example, a drug test result for tetrahydrocannabinol (THC), which might be used therapeutically or recreationally, and is subject to laws that vary by U.S. jurisdiction, might not be needed to make decisions about opioid prescribing for most patients. However, it can be challenging or impossible for clinicians to tailor widely used drug screening panels to include the specific substances most relevant to clinical decisions for their patient." |
| Interpretation of urine drug tests results can be complicated, and many providers lack this knowledge, which can lead to inappropriate negative consequences. In addition, because most urine drug tests are screening tests, false positive or false negative tests are not uncommon. Such inaccurate tests could lead to punitive action. Confirmatory testing is important but can also lead to financial issues for patients. Several workgroup members felt these potential harms are not fully addressed in the supporting text. In addition, the concept of a screening test should be included (e.g. with false positives and negatives). | CDC expanded discussion of inaccurate drug screening results and of misinterpretation. CDC also modified recommendation statement language to be more conditional (i.e., "consider" drug testing). |
| As mentioned in the overall themes, there are biases and disparities in which patients have urine drug tests. Several workgroup members felt that this issue should be more centrally addressed, as the recommendation statement could have substantial disproportionately negative consequences among Black and Latinx patients. | CDC added text in “Supporting Rationale” referring to experts’ observations. CDC also added text regarding health equity considerations to address concerns about biases and disparities in which patients have urine drug tests. The supporting text includes a statement that "Toxicology testing costs are not always covered fully by insurance and can be a burden for patients, and clinician time is needed to interpret, confirm, and communicate results" and discussion of how to balance the importance of confirmatory testing with financial issues for patients. |
| Because substance use is associated with serious stigma, some workgroup members recommended reviewing the supporting text to ensure non-stigmatizing language is warranted (e.g., should the term recreational drug be used instead of illegal drug?). | CDC reviewed language in the supporting text and changed “illegal” drugs terminology throughout based on concerns about stigma. CDC also changed “drug testing” to “toxicology screening”. |
| Several workgroup members discussed the importance of providers’ discussing why and how urine drug tests are used, and not taking a punitive approach. There is a potential ethical tension if the role of the provider is to police the patient behavior, as the provider’s | CDC added a statement that results "will not be used punitively" to supporting text statement that "Clinicians should explain to patients that toxicology testing is intended to improve their safety...". The supporting text also discusses how drug tests will be used: "Clinicians should also explain expected results (e.g., presence of prescribed medication and absence of drugs, including illicit recreational drugs, not reported by the patient). Clinicians should ask patients about use of prescribed and other |

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| duty is to the individual patient, and the policy makers' duty is to the public. | drugs and ask whether there might be unexpected results. This will provide an opportunity for patients to provide information about changes in their use of prescribed opioids or other drugs." The supporting text and guidance are focused on use for patient safety, not on policing behavior. |
| Some workgroup members were cautious regarding conducting urine drug tests prior to prescribing opioids, especially if this were to delay care. Some also felt that the recommended frequency of urine drug tests and the use of opioid dose to guide the frequency were arbitrary. | CDC moved language regarding time frames from the recommendation statement to "Implementation Considerations", where additional nuance can be and is included. CDC also deleted a statement about testing frequency based on opioid dosage; Although this can be a more objective way to determine frequency, there is limited evidence to determine its utility. |
| Some workgroup members were cautious about patients' potential financial implications of frequent urine drug testing and confirmatory drug testing. | CDC included a statement in the supporting text that "Toxicology testing costs are not always covered fully by insurance and can be a burden for patients, and clinician time is needed to interpret, confirm, and communicate results". CDC also included discussion of how to balance the importance of confirmatory testing with financial issues for patients. |
| Recommendation Category: Category B is appreciated, though others felt that a category A could potentially reduce bias and disparities in which patients' clinicians order urine drug tests. | CDC added text in "Supporting Rationale" referring to experts' observations. CDC kept the recommendation category grading as "B". |
| ***Recommendation #11:*** *Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible and consider whether benefits outweigh risks of concurrent prescribing of opioids and other central nervous system depressants. (Recommendation Category: A, Evidence Type: 3)* | |
| Several workgroup members felt the words "avoid," and "whenever possible" are problematic as they can be interpreted as "never". Some proposed that a more appropriate phrase may be to use extreme caution. In specific situations, benzodiazepines can be beneficial, and stopping benzodiazepines can be destabilizing. Additionally, benzodiazepines may serve as a marker for risk of overdose due to underlying conditions. It's also important to differentiate between chronic stable prescribed use versus erratic unpredictable non-prescribed use. | CDC deleted "avoid" and "whenever possible" and instead included "use extreme caution" in the recommendation statement. CDC also added text in "Supporting Rationale" referring to experts' observations. |
| | CDC added the following to the supporting text: "Risks of concurrent opioid and benzodiazepine use can also vary. For example, long-term stable low-dose use is likely to be safer than erratic, unpredictable use, use of high-dose opioids and high-dose benzodiazepines in combination, or use with other substances including alcohol. In specific situations, benzodiazepines can be beneficial, and stopping benzodiazepines can be destabilizing." |
| Some workgroup members felt including an entire class of medications (central nervous system depressants) was far-reaching and could lead to unintended negative consequences. | CDC emphasized the importance of considering whether benefits outweigh risks of concurrent prescribing of opioids and other central nervous system depressants. |
| Some workgroup members felt that this recommendation statement is not appropriate for the acute care setting. | CDC modified the recommendation statement language as detailed above, ensuring the recommendation is applicable for the acute care setting. |

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| Including the FDA warnings regarding benzodiazepine use among people prescribed opioids and among people with opioid use disorder should be included in the supporting text. | CDC added the following FDA advisory information in the supporting text: “Importantly, as emphasized in an FDA advisory (U.S. Food and Drug Administration, 2017), buprenorphine or methadone for opioid use disorder should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system. While the combined use of these drugs increases risks, the harm caused by untreated opioid use disorder can outweigh these risks.” |
| Recommendation Category: Several workgroup members recommended a recommendation category B. | CDC changed the recommendation category grading from “A” to “B”. |
| ***Recommendation #12:*** *Clinicians should offer or arrange treatment with medication for patients with opioid use disorder. (Recommendation Category: A, Evidence Type: 2)* | |
| Many workgroup members agreed with the language of the recommendation, specifically the word “should”. | CDC added text in “Supporting Rationale” referring to experts’ observations. |
| New regulations regarding buprenorphine prescribing should be included in the supporting text. | CDC added references to new regulations and practice guidelines regarding buprenorphine prescribing published in April 2021 and to SAMHSA's updated related website. |
| Several workgroup members noted that the supporting text should better distinguish opioid agonist versus opioid antagonist treatment and questioned the framing as the medications being equal options. Opioid agonist treatment has stronger evidence for better outcomes, doesn’t require abstinence, has less challenges with inductions, and is much more widely utilized. | CDC notes that the supporting text describes the 3 FDA-approved medications for OUD, states that "Buprenorphine and methadone treatment of opioid use disorder have been associated with reduced overdose mortality (Krawczyk et al., 2020) and reduced overall mortality (Pearce et al., 2020)" and then briefly describes some of the limitations in evidence on naltrexone (including that it has not been evaluated in patients with pain and opioid use disorder) and potential challenges (including the requirement for abstinence before starting and challenges with induction) and considerations for patient selection relevant to those limitations. This strikes a balance between presenting all as options and also not as equivalent options given different limitations noted, and brief considerations for selection. Readers are referred to ASAM's National Practice Guideline for Treatment of Opioid Use Disorder and to various SAMHSA resources for more details. |
| Some workgroup members noted a conflation regarding management of problematic opioid use versus OUD in the supporting text. Reassessing pain is important prior to deciding whether to taper or discontinue opioids. | CDC revised language in the supporting text from "clinicians can offer to taper and discontinue opioids" to "should reassess the patient’s pain, ensure that therapies for pain management have been optimized (see Recommendation 2), discuss with patients, and carefully weigh benefits and risks of continuing opioids at the current dosage". |
| Several specific details about OUD treatment were felt to be inaccurate in the supporting text, and additional review by an OUD expert is warranted. | CDC further strengthened cautionary language regarding oral naltrexone, consistent with ASAM 2020 OUD treatment guideline update. CDC changed “oral film” to “sublingual film”. CDC also added language noting the limited evidence to date supporting buprenorphine microdosing. |
| | CDC will ensure that at least one subject matter expert with knowledge and experience with OUD treatment provides additional review of the revised guideline. |
| Some workgroup members felt the evidence type should be 1. | CDC changed the recommendation evidence type from “2” to “1”. |

| *Introduction and Conclusions Sections of the Guideline* | |
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| The discussion regarding health equity and disparities isn't until the end of the document. Many workgroup members recommended that this discussion be much earlier in the guideline. In addition, attention to health equity and disparities should be throughout the entire document, and a discussion about how the recommendation may impact equity and disparities is warranted. | CDC moved the discussion about health equity and disparities from the "Conclusions" to the "Introduction". CDC also added more context and references regarding racial/ethnic disparities and inequities, health equity, and social determinants of health. In addition, CDC integrated more discussion regarding disparities in access and implementation considerations to mitigate and reduce disparities throughout the revised guideline. |
| Many workgroup members felt there should be an explicit statement that the guideline is a clinical guideline, and not payer or governmental policies. Similarly, the tension between risks and benefits for individual patients versus the public health should be explicitly addressed. A patient-centered approach should be strongly encouraged. | CDC added "Clinical Practice" to the Guideline title and throughout the document to reinforce messaging and the Guideline's intent. CDC also added five guiding principles in the "Recommendations" section to broadly inform implementation across recommendations. |
| | CDC added a callout box at the beginning of the Guideline to highlight up front that this clinical practice guideline is not:<br>• A replacement for clinical judgment or individualized, patient-centered care<br>• A law, regulation, or policy that dictates clinical practice<br>• Intended to be applied as inflexible standards of care across patient populations by health care professionals, health systems, third-party payers, or governmental jurisdictions |
| | CDC reiterates in the "Summary" and throughout the document that: "Special attention should be given to ensure high quality and equitable care across sociodemographic groups. This voluntary clinical practice guideline provides guidance only and is intended to be flexible to support, not supplant, clinical judgment and individualized, patient-centered decision-making. This guideline should not be applied as inflexible standards of care across patient populations by health care professionals, health systems, third-party payers, or governmental jurisdictions. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of pain treatment, including opioid therapy for pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death." |

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| A few workgroup members noted issues with authorship and reviewers. Specifically, there are a small number of peer reviewers who are not identified, input from patients and providers was solicited but it was not clear how their input was factored into the guideline, and many of the included references have a lead author who is also an author of the guideline. In addition, providing the areas of expertise of the opioid work group members is suggested. | CDC would like to clarify that at the time the OWG received the initial draft of the updated Guideline in March 2021, the peer review selection process was still ongoing and peer reviewers had not yet been identified. As of September 2021 and the time of developing this document, the selection process was still underway. As stated in the revised draft updated Guideline: "CDC will select peer reviewers based on scientific and subject-matter expertise, racial/ethnic diversity, diversity of experiences and perspectives, independence from the guideline development process, and consideration of conflicts of interest. Specific effort will be made to identify subject matter experts with knowledge and experience in topics such as: chronic and acute pain management; clinical practice; health equity; mental health and well-being; opioids and opioid therapies; opioid tapering; opioid use disorder treatment; pharmacological and non-pharmacological pain management; and surgical pain management. CDC will assess potential conflicts of interest with the same conflict of interest disclosure form used for selection of BSC/NCIPC OWG members. Conflict of interest forms will be reviewed by the NCIPC Associate Director for Science and confirmed by SBIU. CDC will post the names of peer reviewers on the CDC and the NCIPC Peer Review Agenda websites that are used to provide information about the peer review of influential government scientific documents. Peer reviewers will independently review the draft guideline to determine the reasonableness and strength of recommendations; the clarity with which scientific uncertainties were clearly identified; and the rationale, importance, clarity, and ease of implementation of the recommendations. CDC will review and carefully consider peer review comments when revising the draft guideline." |
| | CDC developed a supporting document, posted alongside this one in the Federal Register, entitled [placeholder] “Draft CDC Clinical Practice Guideline for Prescribing Opioids – United States, 2022: Public Comment, Community Engagement, and CDC Response” to further highlight how input from patients, caregivers, family members, and clinicians was solicited through multiple opportunities and incorporated into the revised draft Guideline. |
| | CDC notes that the following is included in the draft updated Guideline regarding the areas of expertise of the OWG members: “OWG members included patients with pain, caregivers, and family members of patients with pain. The OWG also comprised clinicians and subject matter experts, with the following perspectives represented: primary care, pain medicine, public health, behavioral health, pharmacy, emergency medicine, medical toxicology, obstetrics/gynecology, bioethics, orthopedic surgery, plastic surgery, dentistry, sickle cell disease, substance use disorder treatment, and research. Diversity in perspectives was also represented in regard to sex, race/ethnicity, and geographic region.” In addition, CDC developed a webpage to highlight information regarding the OWG, including the full roster of members and their affiliations. This information can be accessed at: https://www.cdc.gov/injury/bsc/opioid-workgroup-2019.html |

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| When describing benefits and harms, it is important to recognize real-world patients' lack of access to many non- opioid pain management strategies. | CDC modified text throughout the draft revised Guideline to further highlight and recognize patients' lack of access to many non-opioid pain management strategies. For example, text in the "Background" states: "The range of therapeutic options that might benefit patients has historically been inaccessible to many patients due to a variety of factors, including inadequate clinician education, training, and guidance, a shortage of pain management specialists, insufficient access to modalities such as behavioral therapy, siloed health systems, insurance coverage and reimbursement policies, and lack of clarity around the evidence supporting different pain treatments. Disparities in access are particularly pronounced for certain patient populations, including racial and ethnic minority persons, people living in rural areas, females, older persons, and those with disabilities." CDC also included text referring to related themes from community input, including "inconsistent access to effective pain management solutions and achieving reduced opioid use through diverse approaches". |
| | CDC will work with public and private payers to improve coverage for nonpharmacologic treatments, remove barriers to prescribing non-opioid pain medication, reimburse for patient counseling and coordination of care, increase access to evidence-based treatments of opioid use disorder, and enhance availability of multidisciplinary, multimodal care. |
| ***Appendix A: Opioid Workgroup Guiding Principles*** | |
| *See Appendix A in full report above.* | CDC appreciates the OWG for developing and including "Guiding Principles" in their report as these provided additional guidance and context for incorporating OWG observations during the guideline revision process. |
| | CDC added reference to the OWG Guiding Principles in the revised draft updated Guideline. |