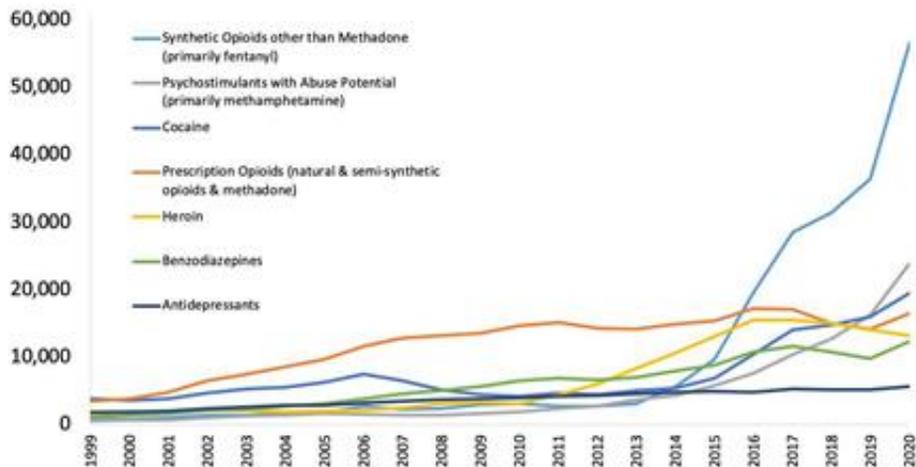


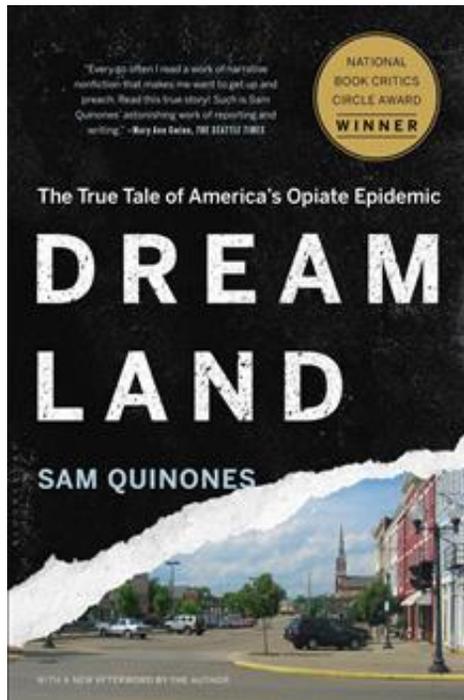
# **2022 CDC Opioid Prescribing Guidelines Updates**

Sarah Merritt, MD  
Lifestream Health Center  
Bowie, MD 20716

**Figure 2. National Drug-Involved Overdose Deaths\*, Number Among All Ages, 1999-2020**



\*Includes deaths with underlying causes of unintentional drug poisoning (X40-X44), suicide drug poisoning (X60-X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10-Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.



## WHY GUIDELINES FOR PRIMARY CARE PROVIDERS?

More than 60 million people in the United States are currently taking at least one prescription drug.

**50%** of people take at least one prescription drug.

**More than 2 million** people are currently taking at least one prescription drug.

- At least 15% of all prescriptions are for chronic conditions.
- More than 10% of all prescriptions are for chronic conditions.
- More than 10% of all prescriptions are for chronic conditions.

MYTH	TRUTH
<p><b>1</b> Prescriptions are too expensive for many patients.</p>	<p>More than 60 million people in the United States are currently taking at least one prescription drug. The average cost of a prescription drug is \$13.50 per month.</p>
<p><b>2</b> Most people do not take their medications as directed.</p>	<p>Only about 50% of people take their medications as directed. This is a major barrier to effective treatment.</p>
<p><b>3</b> Most people do not take their medications as directed.</p>	<p>Only about 50% of people take their medications as directed. This is a major barrier to effective treatment.</p>

## WHAT CAN PROVIDERS DO?

**Don't do no harm.** Long-term opioid use has significant benefits but also risks. Use the **2015 Guidelines for Prescribing Opioids for Chronic Pain** to support informed clinical decision-making, improved communication between patients and providers, and appropriate prescribing.

### PRACTICES AND ACTIONS

<p><b>USE WRITING THERAPY</b></p> <p>Consider an off-the-shelf writing therapy program (e.g., <i>MyHandwriting.com</i>) to help patients improve their handwriting skills. This can help them better understand and follow their medication instructions.</p>	<p><b>CONSIDER WHO IS ON YOUR TEAM</b></p> <p>Work with your pharmacist, nurse, or other healthcare professional to help you understand your medication and how to take it correctly.</p>
<p><b>USE A PHONE</b></p> <p>Use a mobile app to help you track your medication use and remind you when it's time to take your medication.</p>	<p><b>AVOID CONCURRENT PRESCRIPTIONS</b></p> <p>Ask your provider about potential interactions between your current medications and any new prescriptions.</p>
<p><b>IF YOU'RE TAKING OPIOIDS FOR CHRONIC PAIN</b></p> <p>Use a long-acting formulation (e.g., extended-release tablets) and avoid short-acting formulations (e.g., immediate-release tablets).</p>	

U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention

© 2015 CDC. All rights reserved. For more information, visit [www.cdc.gov/od/oc/opioidprescribingguidelines.html](http://www.cdc.gov/od/oc/opioidprescribingguidelines.html).

## **Chronic Pain and Prescription Opioids**

- At least 11% of Americans experience daily or chronic pain. Maybe as high as 20%
- Among those with chronic pain, 25% have taken an opioid in past 3 months for pain
- Opioids frequently prescribed for chronic pain around 3-4% of US adults take opioids for chronic pain

# MACS

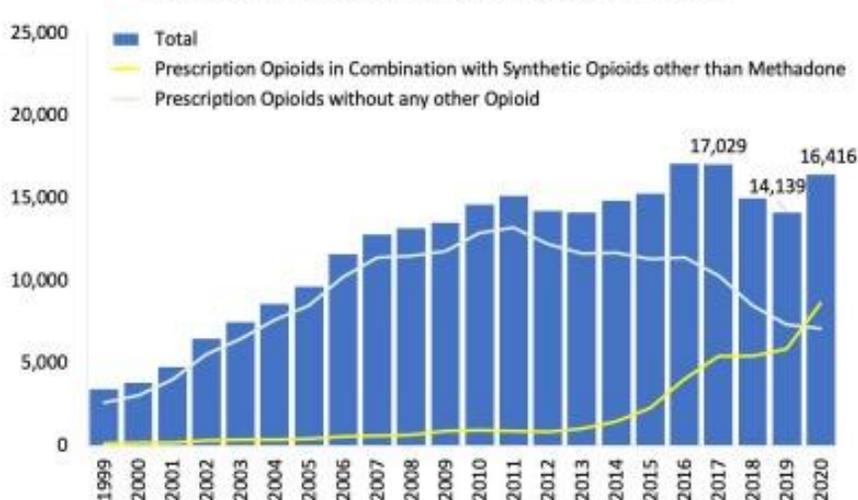
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*"I'm right there in the room, and no one even acknowledges me."*

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**Figure 4. National Overdose Deaths Involving Prescription Opioids\*, Number Among All Ages, 1999-2020**



\*Among deaths with drug overdose as the underlying cause, the prescription opioid subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2) or methadone (T40.3). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.



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## Perspective

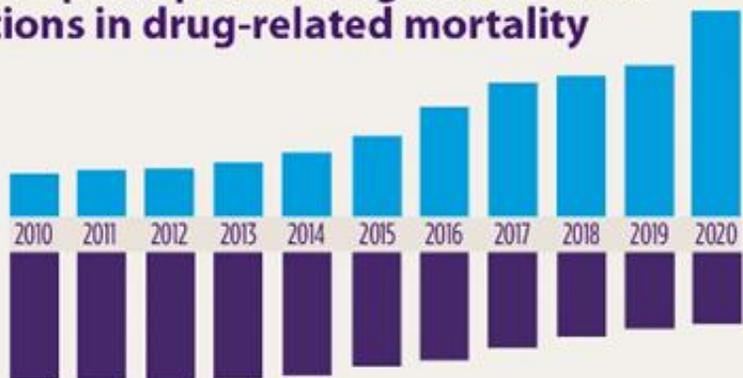
# No Shortcuts to Safer Opioid Prescribing

Deborah Dowell, M.D., M.P.H., Tamara Haegerich, Ph.D., and Roger Chou, M.D.

## Reductions in opioid prescribing have not led to reductions in drug-related mortality

Overdose deaths:  
94,134\*

Opioid prescriptions:  
143,390,951<sup>1</sup>  
(44.4% decrease since 2011)



\*Provisional data for the 12-month period Jan. 2020–Jan. 2021

<https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

## Guideline changes:

Clinical audience

Initial vs Ongoing Therapy

Opioid Tapering

Considerations for Opioid Doseages

Nonopioid Therapies

## Clinical audience

The [2022 Clinical Practice Guideline](#) broadens the scope from primary care physicians to include additional clinicians whose practice areas include prescribing opioids in outpatient settings (upon discharge from hospital, emergency departments, and other facilities) for patients 18 years or older.

### Primary Care Clinicians

- Family physicians
- Nurse practitioners
- Physician assistants
- Internists

### Outpatient Clinicians

- Dental and other oral health clinicians
- Emergency clinicians providing pain management for patients being discharged from emergency departments
- Surgeons
- Occupational medicine physicians
- Physical medicine and rehabilitation physicians
- Neurologists
- Obstetricians and gynecologists

<https://www.cdc.gov/opioids/healthcare-professionals/prescribing/guideline/whats-changed.html>

## Initial and Ongoing Opioid Therapy

The guidance aims to clearly delineate recommendations that apply to patients who are:

1. Being considered for initial treatment with prescription opioids, or
2. Already receiving opioids as part of their ongoing pain management.

More information about opioid therapy as it relates to these two patient categories is available. Visit CDC's [Initiating Opioid Therapy](#) and [Continuing Opioid Therapy](#) web pages.

## Opioid Tapering

The benefits and the risks of opioid therapy change over time and should be re-evaluated periodically ([Recommendations 6](#) and [7](#)). In the [2022 Clinical Practice Guideline Recommendation 5](#) outlines situations when clinicians should consider tapering to a reduced opioid dosage or tapering and discontinuing opioid therapy and that these approaches should be discussed with patients prior to initiating changes. [Recommendation 5](#) also includes revised and expanded guidance on the following key topics to support opioid tapering when indicated:

- Determining whether, when, and how to taper opioids
- Providing advice to patients prior to tapering
- Pain management during tapering
- Behavioral health support during tapering
- Tapering rate
- Management of opioid withdrawal during tapering
- Challenges to tapering
- Continuing high-dosage opioids



## Considerations for Opioid Dosages

The recommendations related to opioid dosages are not intended to be used as an inflexible, rigid standard of care; rather, they are intended to be guideposts to help inform clinician-patient decision-making.

Guidance on opioid pain medication dosage thresholds was updated in the [2022 Clinical Practice Guideline](#). [Recommendation 4](#) states that if opioids are continued for subacute or chronic pain, clinicians should:

- Use caution when prescribing opioids at any dosage.
- Carefully evaluate individual benefits and risks when considering increasing dosage.
- Avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients.

These recommendations apply specifically to *starting* opioids or to *increasing* opioid dosages, and a different set of benefits and risks applies to reducing opioid dosage. Specific considerations to inform clinical decision-making and individualized patient care can be found in the supporting text of the recommendations.

Opioid dosage guidance was updated regarding:

- Suggestions for the lowest starting dose for opioid-naïve patients.
- Morphine milligram equivalent doses for commonly prescribed opioids.
- The approach to potential dosage increases, emphasizing principles of safe and effective pain treatment that allow for individual circumstances and flexibility in care.

## Nonopioid Therapies

All patients with pain should receive treatment that provides the greatest benefits relative to risks. This includes consideration of nonopioid therapies. The [2022 CDC Clinical Practice Guideline](#) has expanded guidance on nonopioid options for pain such as:

### Nonopioid Pharmacologic Therapies

- Topical or oral non-steroidal anti-inflammatory drugs (NSAIDs)
- Acetaminophen

### Nonpharmacologic Therapies

- Ice
- Heat
- Elevation
- Rest
- Immobilization and/or exercise

## What is a guideline?

- “Guidelines are recommendations intended to assist providers and recipients of care and other stakeholders to make informed decisions. Recommendations may relate to clinical interventions, public health activities, or government policies.”

-WHO 2003, 2007

## What is EBM?

“Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research. By individual clinical expertise we mean the proficiency and judgment that individual clinicians acquire through clinical experience and clinical practice. Increased expertise is reflected in many ways, but especially in more effective and efficient diagnosis and in the more thoughtful identification and compassionate use of individual patients’ predicaments, rights, and preferences in making clinical decisions about their care.”

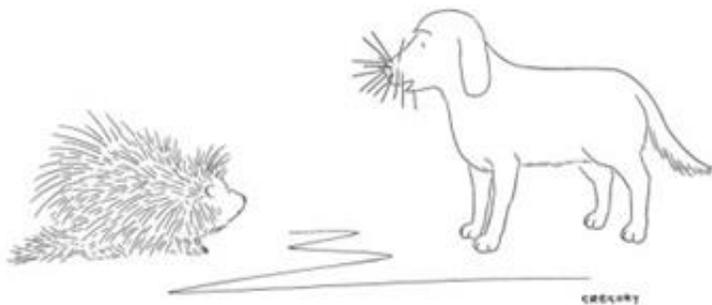
- Sackett, et al. BMJ January 1996

## Clinical Evidence Summary

- No long-term ( $\geq 1$  year) outcomes in pain/function; most placebo-controlled trials  $\leq 6$  weeks
- Opioid dependence in primary care: 3%-26%
- Dose-dependent association with risk of overdose/harms
- Inconsistent results for different dosing protocols; initiation with LA/ER increased risk of overdose
- Methadone associated with higher mortality risk
- No differences in pain/function with dose escalation
- Risk prediction instruments have insufficient accuracy for classification of patients
- Increased likelihood of long-term use when opioids used for acute pain

# MACS

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*"On the plus side, you've cured my back pain."*

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## CDC Guidelines at a Glance 2022 (needs edit)

1. Nonopioid treatments are often effective
2. Maximize nonopioid treatments and discuss benefits and risks
3. Periodically review risk/benefit & responsibilities
4. Start with immediate release preparations
5. Use lowest effective dose (<90 MME preferred)
6. Acute pain: Use shortest duration (3-7 days)
7. Chronic pain: Reassess within 1-4 weeks
8. Consider naloxone & other risk reduction strategies
9. Review PDMP
10. Urine screening prior to initiation and at least annually
11. Avoid prescribing opioids and benzodiazepines together
12. Offer or arrange evidence-based treatment for opioid use disorder (MAT, buprenorphine)

## Determining Whether or Not to Initiate Opioids for Pain (Recommendations 1 and 2)

- Nonopioid therapies are at least as effective as opioids for many common types of acute pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider opioid therapy for acute pain if benefits are anticipated to outweigh risks to the patient. Before prescribing opioid therapy for acute pain, clinicians should discuss with patients the realistic benefits and known risks of opioid therapy (recommendation category: B; evidence type: 3).
- Nonopioid therapies are preferred for subacute and chronic pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and 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 the realistic benefits and known risks of opioid therapy, should work with patients to establish treatment goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks (recommendation category: A; evidence type: 2).

## Selecting Opioids and Determining Opioid Dosages (Recommendations 3, 4, and 5)

- When starting opioid therapy for acute, subacute, or chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release and long-acting (ER/LA) opioids (recommendation category: A; evidence type: 4).
- When opioids are initiated 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 evaluate individual benefits and risks when considering increasing dosage, and should avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients (recommendation category: A; evidence type: 3).
- For patients already receiving opioid therapy, clinicians should carefully weigh benefits and risks and exercise care when changing opioid dosage. If benefits outweigh risks of continued opioid therapy, clinicians should work closely with patients to optimize nonopioid therapies while continuing opioid therapy. If benefits do not outweigh risks of continued opioid therapy, clinicians should optimize other therapies and work closely with patients to gradually taper to lower dosages or, if warranted based on the individual circumstances of the patient, appropriately taper and discontinue opioids. Unless there are indications of a life-threatening issue such as warning signs of impending overdose (e.g., confusion, sedation, or slurred speech), opioid therapy should not be discontinued abruptly, and clinicians should not rapidly reduce opioid dosages from higher dosages (recommendation category: B; evidence type: 4).

## Deciding Duration of Initial Opioid Prescription and Conducting Follow-Up (Recommendations 6 and 7)

- When opioids are needed for acute pain, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids (recommendation category: A; evidence type: 4).
- Clinicians should evaluate benefits and risks with patients within 1–4 weeks of starting opioid therapy for subacute or chronic pain or of dosage escalation. Clinicians should regularly reevaluate benefits and risks of continued opioid therapy with patients (recommendation category: A; evidence type: 4).

## Assessing Risk and Addressing Potential Harms of Opioid Use (Recommendations 8, 9, 10, 11, and 12)

- Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk for opioid-related harms and discuss risk with patients. Clinicians should work with patients to incorporate into the management plan strategies to mitigate risk, including offering naloxone (recommendation category: A; evidence type: 4).
- When prescribing initial opioid therapy for acute, subacute, or chronic pain, and periodically during opioid therapy for chronic pain, 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 combinations that put the patient at high risk for overdose (recommendation category: B; evidence type: 4).
- When prescribing opioids for subacute or chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances (recommendation category: B; evidence type: 4).
- Clinicians should use particular caution when prescribing opioid pain medication and benzodiazepines concurrently and consider whether benefits outweigh risks of concurrent prescribing of opioids and other central nervous system depressants (recommendation category: B; evidence type: 3).
- Clinicians should offer or arrange treatment with evidence-based medications to treat patients with opioid use disorder. Detoxification on its own, without medications for opioid use disorder, is not recommended for opioid use disorder because of increased risks for resuming drug use, overdose, and overdose death (recommendation category: A; evidence type: 1).

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**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)

## **For Recommendation #1**

Several workgroup members recommended changing the wording of Recommendation #1—remove the second “only”, consider changing “preferred” to “effective”.

**CHANGE:** CDC removed the second “only” and changed “preferred” to “effective” in the recommendation statement.

## For Recommendation #1

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.

**CHANGE:** 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.

## **For Recommendation #1**

Some workgroup members felt the recommendation does not consider shared decision-making.

**CHANGE:** 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.

## For Recommendation #1

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.

**CHANGE:** CDC added more discussion about limited access, lack of coverage, and improving access to noninvasive, nonpharmacologic therapies.

## For Recommendation #1

Recommendation Category: Most, though not all, workgroup members felt this statement should be graded category B.

**CHANGE:** 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).

CDC changed the recommendation category from “A” to “B” given heterogeneity in applicability of the recommendation across a broad range of acute pain conditions.

**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)

## **For Recommendation #2**

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.

**CHANGE:** CDC added text in “Supporting Rationale” referring to experts’ observations and appreciation for this recommendation statement.

## **For Recommendation #2**

Some workgroup members felt shared decision-making should be emphasized here and in other recommendations.

**CHANGE:** 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.

## For Recommendation #2

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.

**CHANGE:** 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.

## For Recommendation #2

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.

**CHANGE:** CDC added text in “Supporting Rationale” referring to some experts’ observations regarding specific language for this recommendation statement.

## **For Recommendation #2**

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

**CHANGE:** 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)

## For Recommendation #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.

Change: 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).

## For Recommendation #3

Several workgroup members appreciated the support text discussion regarding abuse deterrent formulations.

UNITE CDC added text in "Supporting Rationale" referring to experts' observations.

## **For Recommendation #3**

Recommendation Category: Most workgroup members agreed with the recommendation category A.

workgroup 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  $\geq 50$  morphine milligram equivalents (MME)/day, and should avoid increasing dosage to  $\geq 90$  MME/day or carefully justify a decision to titrate dosage to  $> 90$  MME/day. (Recommendation Category: A and Evidence Type: 3)

## **For Recommendation #4**

Recommendation Category: Most workgroup members agreed with the recommendation category A.

CHANGE: CD kept the recommendation category grading as "A".

## For Recommendation #4

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.

**CHANGE:** 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.

## For Recommendation #4

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.

**CHANGE:** CDC added text in “Supporting Rationale” referring to experts’ observations.

## For Recommendation #4

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.

**CHANGE:** CDC changed "justify" to “evaluate” in the recommendation statement.

## For Recommendation #4

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.

**CHANGE:** 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)

## **For Recommendation #5**

Many opioid workgroup members appreciated the language that acknowledged the complexity of the situation.

**CHANGE:** CDC added text in “Supporting Rationale” referring to experts’ observations.

## For Recommendation #5

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.

**CHANGE:** CDC removed text regarding specific dosage threshold from the recommendation statement and retained in the supporting text.

## For Recommendation #5

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.

**CHANGE:** CDC removed text regarding specific dosage threshold from the recommendation statement and retained in the supporting text.

## For Recommendation #5

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.

**CHANGE:** 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.

## For Recommendation #5

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.

**CHANGE:** 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."

## For Recommendation #5

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.

**CHANGE:** 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.

## **For Recommendation #5**

Several workgroup members felt an explicit and fuller discussion regarding benefits to society versus individual patients was warranted with this recommendation.

**CHANGE:** CDC modified text in the “Introduction” and “Rationale” to further underline the guideline’s focus on maximizing benefits and minimizing risks for individual patients.

## For Recommendation #5

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.

**CHANGE:** CDC would like to clarify that the draft states “Tapers should not be reversed without careful assessment of benefits and risks of increasing opioid dosage or without maximizing nonopioid treatments for pain and for behavioral distress”.

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."

## For Recommendation #5

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.

**CHANGE:** CDC emphasized in the supporting text that the transition to buprenorphine is an emerging approach to reducing long-term opioid use.

## For Recommendation #5

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.

**CHANGE:** CDC added text in “Supporting Rationale” referring to experts’ observations.

## For Recommendation #5

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?

**CHANGE:** 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)

## For Recommendation #6

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.

**CHANGE:** 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.

## For Recommendation #6

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.

**CHANGE:** CDC modified text in the “Introduction” and “Rationale” to further underline the guideline’s focus on maximizing benefits and minimizing risks for individual patients.

## For Recommendation #6

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.

**CHANGE:** CDC added text in “Supporting Rationale” referring to experts’ observations.

## For Recommendation #6

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.

**CHANGE:** 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 disparities across patients based on access to care and affordability of refills to ensure patients can access additional evaluation and treatment as needed."

## For Recommendation #6

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.

**CHANGE:** 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.

## For Recommendation #6

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.

**CHANGE:** 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)

## For Recommendation #7

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.

**CHANGE:** CDC added text in “Supporting Rationale” referring to experts’ observations.

## For Recommendation #7

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.

**CHANGE:** 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.

## For Recommendation #7

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.

**CHANGE:** 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.

## For Recommendation #7

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.

**CHANGE:** 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 #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 ( $\geq 50$  MME/day), or concurrent benzodiazepine use, are present.  
(Recommendation Category: A, Evidence Type: 4)

## For Recommendation #8

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 50MME 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.

**CHANGE:** CDC moved the specific conditions from the recommendation statement to “Implementation Considerations”.

## For Recommendation #8

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 50MME 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.

**CHANGE:** 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.

## For Recommendation #8

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 50MME 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.

**CHANGE:** CDC added sleep-disordered breathing to the list of factors prompting offering of naloxone in “Implementation Considerations” and in supporting text.

## For Recommendation #8

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).

**CHANGE:** 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).

## For Recommendation #8

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.

**CHANGE:** 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."

## For Recommendation #8

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.

**CHANGE:** 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."

## For Recommendation #8

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.

**CHANGE:** CDC added language to emphasize that persons aged  $\geq 65$  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.

## For Recommendation #8

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.

**CHANGE:** 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).

## For Recommendation #8

Some workgroup members noted that there is little consideration about the problem of lack of access to alternative pain treatments.

**CHANGE:** 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”.

## For Recommendation #8

While many workgroup members noted that naloxone should remain in the recommendation, some felt that taking a more comprehensive risk mitigation approach is warranted.

**CHANGE:** CDC added “Implementation Considerations” directly below the recommendation statement, including a more comprehensive risk reduction approach and including additional risk intervention strategies.

## For Recommendation #8

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.

**CHANGE:** 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)

## For Recommendation #9

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.

**CHANGE:** 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”.

## For Recommendation #9

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.

**CHANGE:** 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.

## For Recommendation #9

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.

**CHANGE:** CDC added reference to and discussion of algorithms and potential harms. CDC added text in “Supporting Rationale” referring to experts’ observations.

## **For Recommendation #9**

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.

**CHANGE:** CDC emphasized the importance of patients not being dismissed due to PDMP information in “Implementation Considerations” added immediately below recommendation statement.

## For Recommendation #9

Some workgroup members felt the supporting text needs to be re-worked, especially regarding acute pain.

**CHANGE:** 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).

## For Recommendation #9

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.

**CHANGE:** CDC changed the recommendation category from “A” to “B” given that acute pain was kept in the recommendation statement.

## For Recommendation #9

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.

**CHANGE:** 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).

## For Recommendation #10

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.

**CHANGE:** CDC changed "illicit" to "nonprescription controlled substances" in the recommendation statement and supporting text.

## For Recommendation #10

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.

**CHANGE:** CDC added a statement that "Testing for fentanyl is not currently available in widely-used toxicology assays, potentially leading to false assurance."

## For Recommendation #10

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.

**CHANGE:** 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."

## For Recommendation #10

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).

**CHANGE:** 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)."

## For Recommendation #10

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.

**CHANGE:** 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.

## **For Recommendation #10**

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?).

**CHANGE:** 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”.

## For Recommendation #10

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.

**CHANGE:** 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 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.

## For Recommendation #10

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.

**CHANGE:** 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.

## For Recommendation #10

Some workgroup members were cautious about patients' potential financial implications of frequent urine drug testing and confirmatory drug testing.

**CHANGE:** 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.

## For Recommendation #10

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.

**CHANGE:** 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)

## For Recommendation #11

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.

**CHANGE:** 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.

## For Recommendation #11

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.

**CHANGE:** 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.”

## For Recommendation #11

Some workgroup members felt including an entire class of medications (central nervous system depressants) was far-reaching and could lead to unintended negative consequences.

**CHANGE:** CDC emphasized the importance of considering whether benefits outweigh risks of concurrent prescribing of opioids and other central nervous system depressants.

## **For Recommendation #11**

Some workgroup members felt that this recommendation statement is not appropriate for the acute care setting.

**CHANGE:** CDC modified the recommendation statement language as detailed above, ensuring the recommendation is applicable for the acute care setting.

## For Recommendation #11

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.

**CHANGE:** 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.”

## **For Recommendation #11**

Recommendation  
Category: Several  
workgroup members  
recommended a  
recommendation  
category B.

**CHANGE:** 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)

## **For Recommendation #12**

Many workgroup members agreed with the language of the recommendation, specifically the word “should”.

**CHANGE:** CDC added text in “Supporting Rationale” referring to experts’ observations.

## **For Recommendation #12**

New regulations regarding buprenorphine prescribing should be included in the supporting text.

**CHANGE:** CDC added references to new regulations and practice guidelines regarding buprenorphine prescribing published in April 2021 and to SAMHSA's updated related website.

## For Recommendation #12

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.

**CHANGE:** 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.

## For Recommendation #12

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.

**CHANGE:** 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".

## For Recommendation #12

Several specific details about OUD treatment were felt to be inaccurate in the supporting text, and additional review by an OUD expert is warranted.

**CHANGE:** 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.

## For Recommendation #12

Several specific details about OUD treatment were felt to be inaccurate in the supporting text, and additional review by an OUD expert is warranted.

**CHANGE:** CDC will ensure that at least one subject matter expert with knowledge and experience with OUD treatment provides additional review of the revised guideline.

## **For Recommendation #12**

Some  
workgroup  
members felt the  
evidence type  
should be 1.

**CHANGE:** CDC changed the recommendation evidence type  
from “2” to “1”.

## References:

“No Shortcut to Safer Opioid prescribing”

<https://www.nejm.org/doi/full/10.1056/NEJMp1904190>

Overdose Death rates

<https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates>

What’s Changed

<https://www.cdc.gov/opioids/healthcare-professionals/prescribing/guideline/whats-changed.html>