CONNECTICUT MEDICAL ASSISTANCE PROGRAM
DEPARTMENT OF SOCIAL SERVICES
&
KEPRO
QUARTERLY NEWSLETTER

The CDC Clinical Practice Guideline for Prescribing Opioids for Pain - 2022.[1]

The Center for Disease Control and Prevention (CDC) published its Guideline for Prescribing Opioids for Chronic Pain in 2016, in response to the national opioid epidemic.[1] Although the height of the opioid epidemic occurred in the late 90s and early 2000s, prescribers needed a blueprint to aid in safe prescribing and deprescribing of opioids for the American people. Despite the decline in utilization, opioids continue to be the most misused medication in the United States.[2]

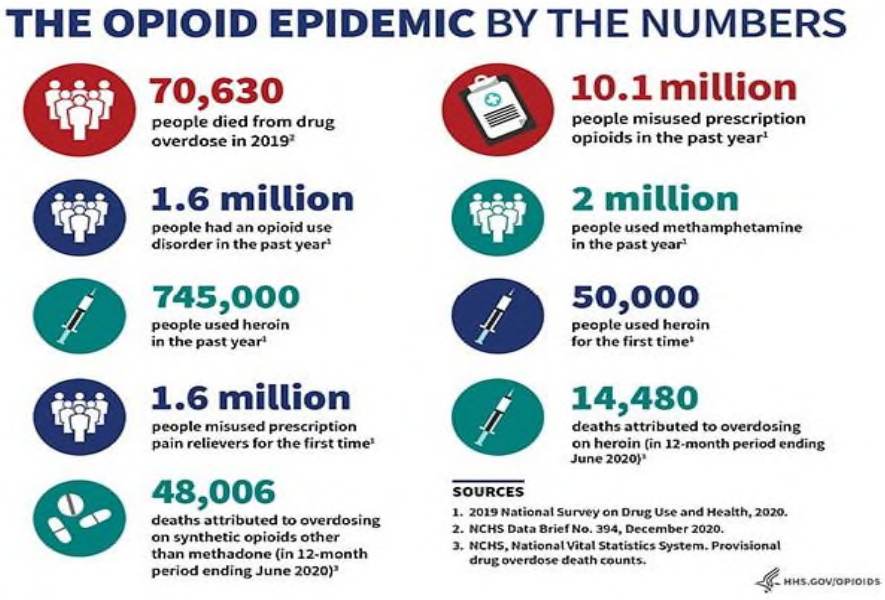
The 2016 guideline was grouped into three areas of consideration and contained twelve recommendations. The intent of this publication was to provide recommendations for prescribing opioids for chronic pain by primary care providers while establishing safeguards for clinicians to rely on and reference when treating patients. The guideline was developed to help improve patient outcomes and decrease the incidence of opioid adverse drug events (ADEs) including but not limited to the development of opioid use disorder (OUD), overdose, and death.

In response to the CDC's 12 recommendations, new laws and regulations were enacted at the federal and state level which shaped current public and private health care policy around opioids. The Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT) for Patients and Communities Act, also known as the SUPPORT Act, is just one example of this. Signed into law on October 24, 2018, the SUPPORT Act impacted state Medicaid programs, requiring new restrictions on opioid Medicaid claims for early refill, days' supply, quantity limits, therapeutic duplication, morphine milligram equivalency (MME), and concurrent therapies. While the CDC acknowledges that some legislative changes reinforced their recommendations and may provide benefit to some, these mandates caused harm to patients by increasing incidence of withdrawal, undertreated or untreated pain, overdose, suicidality, and worsening outcomes. The CDC is especially concerned with the following mishandlings:

- "Extension to patient populations not covered in the 2016 CDC Opioid Prescribing Guideline (e.g., cancer and palliative care patients).[2]"
- "Rapid opioid tapers and abrupt discontinuation without collaboration with patients.[2]"
- "Rigid application of opioid dosage thresholds.[2]"
- "Application of the guideline's recommendations for opioid use for pain to medications for opioid use disorder treatment (previously referred to as medication assisted treatment).[2]"
- "Duration limits by insurers and pharmacies.[2]"
- "Patient dismissal and abandonment.[2]"

In recent months, the CDC released an update to the 2016 guideline titled: The CDC Clinical Practice Guideline for Prescribing Opioids for Pain - 2022.[2] The motivation for the update is twofold, to include new scientific evidence for opioids and to respond to the misinterpretation of the original guidance. Throughout the document, the CDC vehemently defends their intent that recommendations are voluntary, flexible, and not meant to take the place of clinical judgement or aid in the creation of strict protocols. They did not intend for the development of laws, regulations, and policies, specifically citing the SUPPORT Act promoting non-opioid medications for pain, state laws limiting initial opioid prescriptions to ≤ a 7-day supply, and state laws requiring the co-prescribing of naloxone with an opioid prescription in high-risk patients.[2]

The 2022 guidance contains 12 updated recommendations grouped into 4 areas of consideration (listed below) intended for primary care practitioners treating patients ≥ 18 years of age with acute, subacute, or chronic pain not caused by malignancy, sickle cell disease, palliative, or end of life associated pain.[2] The authors define acute pain as pain caused by injury or trauma, with a sudden onset with limited duration (typically < 1 month). Subacute pain is defined as unresolved acute



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pain or persistent pain of 1-3 months in duration. Chronic pain is further defined as pain lasting > 3 months and can be caused by underlying disease states, inflammation, injury, or unknown causes.[2] These recommendations are voluntary and meant to help practitioners provide patient centered, flexible care.

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

"1. 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.[2]"

Acute pain situations include but are not limited to the following types of pain: back, neck, musculoskeletal, neuropathic, dental, kidney stones, migraines, minor surgery, and postoperative pain. Nonpharmacologic options to treat acute pain can consist of heat, ice, rest, massage, acupressure, spinal manipulation, exercise, stretching, physical therapy, yoga, meditation, and mindfulness. While these options are safe and effective, barriers exist, making pharmacologic therapies easier to obtain. Insurance may not reimburse for nonpharmacologic therapies, or patients living in rural settings or who have a lack of transportation may have difficulty with access. It is important to recognize and address potential barriers.

Nonopioid medications have a low cost, high return, similar efficacy compared to opioids, and should be maximized in the treatment of acute pain. Nonopioid therapies can include NSAIDs, acetaminophen, antidepressants and anticonvulsants for neuropathic pain, topical medications (capsaicin and lidocaine), and antimigraine therapies. When considering acute pain, NSAIDs cause less harm and are just as effective as opioids for acute pain.[3,4] Selection of nonopioid medications requires assessment of the entire clinical situation and risk for ADEs. Evaluate patients for renal and hepatic impairment and use caution when prescribing oral NSAIDs in patients with cardiovascular or gastrointestinal issues.

If opioids are warranted for severe acute pain (burns, crush injuries, invasive surgery), it is recommended to use the lowest dose and shortest duration of an immediate release (IR) product. Directions for use should be "as needed" rather than scheduled or around the clock. Assess and discuss the risks versus benefits of opioid use with the individual patient prior to beginning therapy.

"2. 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.[2]"

Opioids are not considered first line treatment for subacute or chronic pain. Nonpharmacologic and nonopioid options are the preferred treatment option, however, if opioid therapy is deemed appropriate, assess the risk versus benefit, use the lowest dose and shortest duration of IR opioids, and establish a discontinuation strategy. Providers should work to diagnose the underlying cause of pain. If patients are to continue on opioids for > 30 days, there should be a clear indication of the source of chronic pain, prescriber assessment, and plan prior to continuing therapy past 30 days. Long term therapy with opioids needs to be an intentional decision, preferably made within an integrated pain management team.

Selecting Opioids and Determining Opioid Dosages (Recommendations 3 – 5)

"3. 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.[2]"

IR opioids are preferred over extended release (ER) and long acting (LA) formulations except in patients who experience severe continuous pain and who are opioid tolerant, (i.e.: patients receiving the equivalent of 60 mg/day of oral morphine or 30 mg/day of oral oxycodone for ≥ 1 week).[2] Examples of ER/LA opioids include transdermal fentanyl, oxycodone ER, morphine ER, and methadone. Methadone should not be considered the first choice for a long-acting agent as it has inconsistent pharmacokinetics, can accumulate in the body, and can cause QTc prolongation.

"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.[1]"

The incidence of opioid related overdose and death increase as the dose of the opioid increases.[2] While not included in the high-level summary of recommendations, the CDC does cite certain morphine milligram equivalent (MME) dosages within the supporting rationale. These thresholds are not meant to be

Year	Quantity of Opioids Dispensed	Unique Recipients Receiving an Opioid Prescription	Unique Recipients Experiencing an Opioid Overdose	Unique Recipients Diagnosed with Opioid Use Disorder
2016	26,236,289	140,073	3,540	35,173
2018	18,510,115	102,741	3,796	36,835
2020	14,282,086	75,151	3,937	36,028
2022	11,989,937	74,117	3,897	35,533

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firm stopping points and should not take the place of clinical judgement. The guideline states that "The lowest starting dose for opioid -naïve patients is often equivalent to a single dose of approximately 5–10 MME or a daily dosage of 20–30 MME/day.[2]"

Doses above 50 MME/day provide little benefit to patient pain and function and increase the risk of opioid related ADEs. If prescribers choose to increase the dose, it is recommended to do so slowly and continue to measure the risk versus benefit to the individual patient. While studies have used specific dosing thresholds to indicate risk of overdose, there is no exact dose below which overdose from opioids is not a risk, essentially advising that overdose can occur at any dose.

"5. 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.[2]"

It is recommended to avoid rapidly tapering and/or abruptly discontinuing opioid therapy. New patients within a practice who are already established on opioids should have a plan and goals for therapy. If a patient is not experiencing ADEs or in danger of overdose, tapering does not have to occur right away. Be transparent about clinically meaningful improvements while setting expectations appropriately. If there is no improvement on opioids, have an exit strategy. Collaboration with the patient is of upmost importance because if they don't agree with a tapering plan, it likely will not work. Discuss the goal of tapering with the patient to determine if it is to decrease the dose or to stop the opioid completely. The

longer the patient is on opioid therapy, the longer the taper should be. Guidelines recommend a 10% taper per month, or slower, for patients who have received chronic opioid therapy for ≥ 1 year, until 30% of the original dose is reached, and then a weekly decrease by 10% of that dose.[2] The key is to monitor the individual patient for signs of success with the taper or emerging signs of withdrawal and adjust accordingly. Weekly check-ins with patients have been found to be beneficial and nonpharmacologic or nonopioid therapies can be considered when appropriate. Patients can also be transitioned to buprenorphine indicated for the treatment of pain, rather than continuing with a full opioid agonist. Always weigh the risk versus benefit with opioid therapy as some patients do benefit from continued treatment with high dose opioids.

The Health and Human Services (HHS) Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesia recommends tapering, reducing dose, and discontinuing opioids in the following situations:[5]

- Patient requests to taper or discontinue opioid therapy
- Improvement in patient pain
- Opioid treatment did not reduce pain or improve patient function
- Unclear risk v. benefit in chronic opioid patients
- Patients receiving large doses without benefit
- Side effects that impair function or impact quality of life (QOL)
- Patient misusing opioid therapy
- Overdose or evidence of impairment from opioids
- Patients with concurrent medications or disease states that can increase opioid related ADEs

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

"6. 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.[2]"

It is recommended to limit the duration and quantity of opioids prescribed. For acute pain, a few days duration is appropriate, longer durations may be needed for subacute pain. Prescriber follow-up should match duration of therapy and occur at least every 2 weeks for subacute pain requiring opioids. If a patient receives opioid therapy for ≥ 1 month, prescribers must ensure this is intentional, set goals, attempt to diagnosis the cause of pain, and have a plan for the individual patient. A tapering strategy should be in place for any patient who receives around the clock opioid therapy for longer than a few days.

"7. 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.[2]"

When daily opioid doses exceed 50 MME, overdose risk is doubled compared to patients taking <20 MME/day, therefore, follow up with

these patients is recommended at least within the first 2 weeks of therapy.[2] Follow-up for patients receiving < 50 MME/day of IR formulations should occur within 4 weeks of starting treatment. Continuation of opioids past 30 days must be intentional.

Assessing Risk and Addressing Potential Harms of Opioid Use (Recommendations 8 – 12)

"8. 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.[2]"

Prescribers should consider individual patient risks at the start of opioid therapy and throughout treatment. Pregnant patients who are prescribed opioids should receive the lowest effective dose for the shortest duration, as long as the benefits outweigh the risks. Comorbid disease states, such as renal and hepatic impairment, can decrease the metabolism of opioids and put patients at risk of adverse events. Established risk factors for overdose include a history of mental health disorders, history of substance abuse, history of breathing disorders, history of overdose, ≥50 MME/day, and use of concurrent CNS depressants. Use caution and increase monitoring in patients with renal and hepatic insufficiency, patients ≥ 65 years of age, patients with safety critical jobs, patients with mental health disorders, substance use disorders, or previous overdoses. Discuss the risk of respiratory depression with patients and offer naloxone to those who may be at risk of overdose.

"9. 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.[2]"

It is recommended that prescribers check the PDMP prior to initial opioid prescription and at least every three months for patients receiving chronic therapy. If the PDMP uncovers concurrent therapies or MMEs that increase a patient's risk, prescribers must work to mitigate those risks.

"10. 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.[2]"

Urine or other toxicology testing for patients receiving opioid therapy can be considered to improve patient safety, prior to starting therapy with opioids and then at least every year thereafter.

"11. 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.[2]"

It is recommended to use extreme caution in patients receiving concurrent therapy with opioids and benzodiazepines. Opioids used concurrently with gabapentin also carries an increased risk of overdose, especially when higher doses are used for one or both medications. Opioids used concurrently with other CNS depressants such as muscle relaxants or sedative hypnotics can potentiate the risk of respiratory depression. Offer naloxone to patients who are receiving concurrent therapy that increases the risk of respiratory depression and other ADEs.

"12. 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.[2]"

The DSM-5 defines opioid use disorder as a problematic pattern of opioid use leading to clinically significant impairment or distress.[6] Chronic opioid therapy increases the risk of OUD, especially in patients who receive > 90 days of opioid treatment. There are 3 FDA approved options available for treatment of OUD: buprenorphine, methadone, and naltrexone. These options range from partial agonist to full antagonist with positive and negative attributes associated with each choice. Selection of OUD treatment should be made on an individual case by case basis.

Pain is an individual experience influenced by psychology, biology, genetics, perception, and even social and demographic differences. The CDC recognizes inequality in the treatment of pain, noting that black and Hispanic patients are less likely to receive treatment for acute pain, and black patients are likely to receive lower doses of pain medication when compared to white patients.[1] Pain can negatively affect all aspects of life and should be assessed and treated no matter what race or ethnicity a patient is.

Throughout the guideline the principal theme is to establish safeguards around opioid therapy for clinicians to use when providing flexible and supportive care. The intent of the guideline was not for the development of rigid and strict policies around opioid utilization that are currently being implemented and used at the federal, state, and insurance payor level. Nonpharmacologic and nonopioid treatments can improve pain, patient functioning, and quality of life.

Opioids should only be used when the benefits of therapy outweigh the risks, and the lowest effective dose for the shortest duration of time. Patient treatment objectives should be clearly defined when moving from acute to subacute to chronic opioid use. When scaling back or discontinuing opioids, taper them. Chronic opioid therapy is associated with an increased risk of significant events such as overdose and occurrence of OUD. The CDC is clear to include that there is no way to define which patients will benefit from opioids and which will experience significant adverse events, and there is no dosage or threshold MME that can define absolutely no risk of overdose. While opioid prescription use, misuse, and OUD continue to decline, opioids are still the most misused prescription medication in the U.S. As a nation, we are still learning and healing from the opioid epidemic. It remains paramount that primary care providers, as well as federal and state stakeholders, have a gold standard guideline to rely on when providing patient care involving opioids.

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