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Perspective

Reducing the Risks of Relief — The CDC Opioid-Prescribing Guideline

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Deaths from prescription-opioid overdose have increased dramatically in the United States, quadrupling in the past 15 years. Efforts to improve pain management resulted in quadrupled rates of opioid prescribing, which propelled a tightly correlated epidemic of addiction, overdose, and death from prescription opioids that is now further evolving to include increasing use and overdoses of heroin and illicitly produced fentanyl.

The pendulum of opioid use in pain management has swung back and forth several times over the past 100 years. Beginning in the 1990s, efforts to improve treatment of pain failed to adequately take into account opioids' addictiveness, low therapeutic ratio, and lack of documented effectiveness in the treatment of chronic pain. Increased prescribing was also fueled by aggressive and sometimes misleading marketing of long-acting opioids to physicians.[1] It has become increasingly clear that opioids carry substantial risks and uncertain benefits, especially as compared with other treatments for chronic pain.

On March 15, 2016, the Centers for Disease Control and Prevention (CDC) released a "Guideline for Prescribing Opioids for Chronic Pain" to chart a safer, more effective course.[2] The guideline is designed to support clinicians caring for patients outside the context of active cancer treatment or palliative or end-of-life care. More research is needed to fill in critical evidence gaps regarding the effectiveness, safety, and economic efficiency of long-term opioid therapy. However, given what we know about the risks associated with long-term opioid therapy and the availability of effective nonpharmacologic and nonopioid pharmacologic treatment options, the guideline uses the best available scientific data to provide information and recommendations to support patients and clinicians in balancing the risks of addiction and overdose with the limited evidence of benefits of opioids for the treatment of chronic pain.

Most placebo-controlled, randomized trials of opioids have lasted 6 weeks or less, and we are aware of no study that has compared opioid therapy with other treatments in terms of long-term (more than 1 year) outcomes related to pain, function, or quality of life.[2] The few randomized trials to evaluate opioid efficacy for

longer than 6 weeks had consistently poor results. In fact, several studies have showed that use of opioids for chronic pain may actually worsen pain and functioning, possibly by potentiating pain perception. A 3-year prospective observational study of more than 69,000 postmenopausal women with recurrent pain conditions showed that patients who had received opioid therapy were less likely to have improvement in pain (odds ratio, 0.42; 95% confidence interval [CI], 0.36 to 0.49) and had worsened function (odds ratio, 1.25; 95% CI, 1.04 to 1.51).[3] An observational case–control study of patients undergoing orthopedic surgery showed that those receiving long-term opioid therapy had significantly higher levels of preoperative hyperalgesia.[4] After surgery, patients who had received long-term opioid therapy reported higher pain intensity (a rating of 7.6 vs. 5.5 out of 10) in the recovery room than patients who had not been taking opioids.

Whereas the benefits of opioids for chronic pain remain uncertain, the risks of addiction and overdose are clear. Although partial agonists such as buprenorphine may carry a lower risk of dependence, prescription opioids that are full mu-opioid–receptor agonists — nearly all the products on the market — are no less addictive than heroin. Although abuse-deterrent formulations may reduce the likelihood that patients will inject melted pills, these formulations are no less addictive and do not prevent opioid abuse or fatal overdose through oral intake.

The prevalence of opioid dependence may be as high as 26% among patients in primary care receiving opioids for chronic non–cancer-related pain.[2] Risk-stratification tools do not allow clinicians to predict accurately whether a patient will become addicted to opioids, although persons with a history of mental illness or addiction are at higher risk.[2] Overdose risk increases in a dose–response manner, at least doubling at 50 to 99 morphine milligram equivalents (MME) per day and increasing by a factor of up to 9 at 100 or more MME per day, as compared with doses of less than 20 MME per day.[2] Overall, 1 of every 550 patients started on opioid therapy died of opioid-related causes a median of 2.6 years after the first opioid prescription; the proportion was as high as 1 in 32 among patients receiving doses of 200 MME or higher.[5] We know of no other medication routinely used for a nonfatal condition that kills patients so frequently.

The new CDC guideline emphasizes both patient care and safety. We developed the guideline using a rigorous process that included a systematic review of the scientific evidence and input from hundreds of leading experts and practitioners, other federal agencies, more than 150 professional and advocacy organizations, a wide range of key patient and provider groups, a federal advisory committee, peer reviewers, and more than 4000 public comments.

Three key principles underlie the guideline's 12 recommendations (see box). First, nonopioid therapy is preferred for chronic pain outside the context of active cancer, palliative, or end-of-life care. Opioids should be added to other treatments for chronic pain only when their expected benefits for both pain and function are likely to outweigh the substantial risks inherent in this class of medication.

Nonpharmacologic therapies can ameliorate chronic pain while posing substantially less risk to patients. In some instances, other therapies result in better outcomes than opioids. These therapies include exercise therapy, weight loss, psychological therapies such as cognitive behavioral therapy, interventions to improve sleep, and certain procedures. The evidence review conducted in developing the guideline revealed that exercise therapy helped improve, and sustain improvements in, pain and function in patients with osteoarthritis. It did not find evidence that opioids were more effective for pain reduction than nonopioid treatments such as nonsteroidal anti-inflammatory drugs for low back pain or antidepressants for neuropathic pain, but it did find that nonopioid treatments could be better tolerated and superior for improving physical function while conferring little or no risk of addiction and substantially lower risks of overdose and death.[2]

Second, when opioids are used, the lowest possible effective dose should be prescribed to reduce the risks of opioid use disorder and overdose. Clinicians should carefully reassess individual benefits and risks when increasing a dose to 50 MME or more per day. Doses of 90 MME or more should be avoided, or the decision to titrate above this level should be carefully considered and justified. When prescribing opioids, the rule of thumb is to "start low and go slow."

Third, clinicians should exercise caution when prescribing

opioids and should monitor all patients closely. Prescribers should mitigate risk by, for example, avoiding concurrent use of benzodiazepines if possible, reviewing data from a prescription-drug monitoring program when deciding whether to start or continue opioid therapy, offering naloxone at least to patients who are at greater risk for overdose, having a clear "off-ramp" plan to taper and discontinue therapy, reevaluating the dosage and necessity of opioid treatment regularly, and obtaining urine toxicology screening at the initiation of treatment and, for some patients, periodically thereafter. For patients who become addicted to opioids, treatment with methadone, buprenorphine, or naltrexone improves outcomes.

Initiation of treatment with opioids is a momentous decision and should be undertaken only with full understanding by both the physician and the patient of the substantial risks involved. Clinicians need to recognize the risk associated with any treatment with opioids and should prescribe only the shortest course needed. Although the guideline addresses chronic pain, many patients become addicted to opioids after being treated for acute pain. Three days of treatment or less will often be sufficient; more than 7 days will rarely be required. Some trauma and surgery may require longer courses; treatment of postsurgical pain is beyond the scope of this guideline. Furthermore, it is important to discuss storage of opioids in a secure location to prevent diversion, as well as to counsel patients regarding the overdose risk posed to household members and other persons.

Management of chronic pain is an art and a science. The science of opioids for chronic pain is clear: for the vast majority of patients, the known, serious, and too-often-fatal risks far outweigh the unproven and transient benefits.

The CDC Opioid-Prescribing Guideline.

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and provider responsibilities for managing therapy.
4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME) per day, and should avoid increasing dosage to ≥90 MME per day or carefully justify a decision to titrate dosage to ≥90 MME per day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than 7 days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1–4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. 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.
8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use are present.
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 chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid-use disorder.

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