Chronic pain is a common, costly, and disabling medical condition in the United States (1–4). It has been estimated that nearly 50 million adults experience chronic pain on most days or every day (5). Pain is also associated with approximately 20% of all ambulatory primary care and specialty visits in the United States (2, 6, 7). Beginning in the late 1990s until 2008, the proportion of pain-related visits during which patients were prescribed opioids substantially increased, as did opioid-related morbidity and mortality, overdose death, and admissions for treatment of substance use disorder (7–9). From 2000 until 2010, approximately 1 in 5 patients with noncancer pain or pain-related diagnoses were prescribed opioids in an outpatient setting (7–11). According to the Centers for Disease Control and Prevention (CDC), an increase in the national opioid dispensing rate started in 2006 and peaked in 2012, with more than 255 million prescriptions and 81.3 opioid prescriptions dispensed per 100 persons (12). The overall national rate of opioid dispensing decreased from 2012 to 2020 to its lowest point in 15 years, a rate of 43.3 prescriptions per 100 persons (12). The absolute number of deaths associated with the use of prescribed and illicit opioids increased 400% between 2000 and 2014 (13). The increase in illicit opioid use and overdose has also involved heroin and fentanyl (a synthetic opioid). In 2019, nearly 50,000 persons in the United States died of opioid-involved overdoses (14). Of those 50,000 persons, 14,019 (28%) died of a heroin overdose (14). This is a very large increase from the 1960 overdose deaths involving heroin in 1999 (14). The connection between heroin use and prescription opioids is important; it has been estimated that about 80% of persons who use heroin first misused prescription opioids (15). The thoughtful and judicious prescribing of opioids is important for many reasons, including to decrease the number of patients who transition to illicit drug use, but also to minimize risk and maximize safety and quality of life for those with chronic pain. This 2022 U.S. Department of Veterans Affairs (VA) and U.S. Department of Defense (DoD) guideline provides an update on opioid prescribing practices from the previous 2017 guideline. The VA/DoD guidelines are updated every 5 years or more frequently as important new evidence emerges.
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guidelines. This team emphasized strict adherence to the standards for trustworthy guidelines set by the National Academy of Medicine (16). The Evidence-Based Practice Work Group, in conjunction with VA and DoD leaders in pain management, selected a multidisciplinary panel of practicing clinician stakeholders and treatment researchers to update this guideline. This panel of subject experts was called the guideline development group. The group included various disciplines, including internal medicine, family medicine, neurology, nursing, pharmacy, psychology, physical therapy, social work, acupuncture and Chinese medicine, and chiropractic and interventional medicine. The Lewin Group, a contracted third party with expertise in clinical practice guideline development, facilitated meetings and the development of key research questions using the PICOTS (population, intervention, comparator, outcomes, timing of outcomes measurement, and setting) format. Through a consensus process, 12 key questions were framed to guide the evidence review. To manage conflicts of interest, the guideline development team was polled at the onset of the project and before each meeting to identify any conflicts. The guideline development group did not have any financial or intellectual conflicts of interest. An independent third party, ECRI, conducted a systematic evidence review that the guideline panel used to develop recommendations using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) method (17–19). The search methods and results are detailed in Appendix F and Appendix I of the full guideline (www.healthquality.va.gov).

Below we summarize some key updates of the 2022 VA/DoD Guideline for the Use of Opioids in the Management of Chronic Pain (20). The VA and DoD have broadly defined chronic pain as persistent and recurrent pain lasting longer than 90 days and long-term opioid therapy as opioid therapy continuing for longer than 3 months. The guideline also contains 2 recommendations addressing issues related to the use of opioids for acute pain because of the potential effect on transitioning to long-term opioid use.

**Highlighted 2022 Guideline Updates**

This guideline has important changes from the previous 2017 document. The amount of research on long-term and short-term opioid use for pain conditions has grown each year. This updated guideline has important new recommendations for behavioral health assessment in all patients. These include assessing all patients with chronic pain for co-occurring behavioral health conditions before opioid initiation and periodically during treatment with opioids (Table, recommendation 15). It also includes a recommendation to screen patients with acute pain for pain catastrophizing when opioids are considered (Table, recommendation 16). A recommendation for preoperative opioid and pain management education is provided (Table, recommendation 20) and, notably, a recommendation to use buprenorphine instead of a full agonist opioid for patients who are receiving daily opioids for chronic pain (Table, recommendation 5). Finally, the treatment algorithms, which help guide clinicians through decision-making processes, have been updated and condensed so that there are now 3 rather than 4 as in the previous 2017 guideline (Supplement Figures 1 to 3, available at Annals.org).

**Initiation and Continuation of Opioids**

The guideline development group recommends against the initiation of opioid therapy for the management of chronic noncancer pain (Table, recommendation 1). Compared with the 2017 recommendation against initiation of long-term opioid therapy, the updated recommendation against opioid therapy in general for chronic pain is broader and reflects the evidence that opioid therapy for any duration may be harmful. Updated evidence for this recommendation included a 2018 systematic review by Busse and colleagues (21) that included 26,000 patients from 96 randomized controlled trials, which, consistent with the previous evidence, found that patients with chronic noncancer pain who were prescribed oral or transdermal opioids had small, but not clinically significant, improvement in pain and physical functioning when compared with nonopioid control participants. Although opioids can improve pain severity and functional status in some patients with musculoskeletal pain, including chronic low back pain (22) and osteoarthritis (23, 24) in studies of 4 to 24 weeks’ duration, the effects are small, are accompanied by adverse events, and are generally believed to be without important benefit on pain or function (23, 24). Sommer and colleagues (25) and Derry and colleagues (26) also found that treatment with an opioid was associated with small improvements for those with noncancer neuropathic pain. As with all clinical decisions, the limited relief and small improvement in function must be weighed against the known risks associated with opioids. Ultimately, despite finding some evidence for a small improvement in musculoskeletal and noncancer neuropathic pain, the guideline development group maintained that the potential for catastrophic harms of opioids and serious adverse events (27–30, 75), especially with long-term use, outweighed any potential benefits of temporarily improved pain severity and functional status in patients with chronic pain.

The guideline development group recognizes that there may be patients for whom, based on a clinical assessment, long-term opioid therapy may be appropriate. Evidence supported a new recommendation for buprenorphine in patients receiving a daily opioid for the treatment of chronic pain (Table, recommendation 5). Buprenorphine is a partial μ-opioid receptor agonist with analgesic properties. For patients who are prescribed daily opioids for the treatment of chronic pain, we suggest the use of buprenorphine instead of full μ-opioid receptor agonist opioids because of a lower risk for overdose and misuse. Although the guideline development group found very little evidence on the comparative effectiveness of buprenorphine and other full agonist opioids for the management of chronic pain, buprenorphine has a superior safety profile, especially for respiratory depression, even in nondependent persons and fatal overdose. In addition, excluding those who are opioid-naïve, buprenorphine is less likely to cause euphoriant effects and is a first-line treatment of opioid use disorder.
**Table. Recommendations and Evidence Table**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>2017 Strength of Recommendation</th>
<th>2022 Strength of Recommendation</th>
<th>Recommendation Category</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. We recommend against the initiation of opioid therapy for the management of chronic noncancer pain (for nonopioid treatments of chronic pain, see the VA/DoD CPGs for Low Back Pain, Headache, and Hip and Knee Osteoarthritis†).</td>
<td>Strong against</td>
<td>Strong against</td>
<td>Reviewed, new replaced</td>
<td>(21-30, 32-37, 117)</td>
</tr>
<tr>
<td>2. We recommend against long-term opioid therapy, particularly for younger age groups, as age is inversely associated with the risk for opioid use disorder and overdose.</td>
<td>Strong against</td>
<td>Strong against</td>
<td>Reviewed, new replaced</td>
<td>(27-30, 32-34, 36, 38-46) Additional references: (19, 47-51)</td>
</tr>
<tr>
<td>3. We recommend against long-term opioid therapy, particularly for patients with chronic pain who have a substance use disorder (refer to the VA/DoD CPG for the Management of Substance Use Disorders†).</td>
<td>Strong against</td>
<td>Strong against</td>
<td>Reviewed, new replaced</td>
<td>(27, 29, 30, 33, 38, 39, 41, 42, 52-57) Additional reference: (19)</td>
</tr>
<tr>
<td>4. For patients receiving medication for opioid use disorder, there is insufficient evidence to recommend for or against the selection of any one of the following medications over the other for the management of their co-occurring chronic pain: methadone, buprenorphine, or extended-release naloxone injection. Treat the opioid use disorder according to the VA/DoD CPG for the Management of Substance Use Disorders†.</td>
<td>Strong for</td>
<td>Neither for nor against</td>
<td>Reviewed, new replaced</td>
<td>(58-60) Additional references: (57, 61)</td>
</tr>
<tr>
<td>5. For patients receiving daily opioids for the treatment of chronic pain, we suggest the use of buprenorphine instead of full agonist opioids due to lower risk for overdose and misuse.</td>
<td>Not applicable</td>
<td>Weak for</td>
<td>Reviewed, new added</td>
<td>(21, 22, 25, 31, 62) Additional references: (61, 63-73)</td>
</tr>
<tr>
<td>6. We recommend against the concurrent use of benzodiazepines and opioids for chronic pain (refer to recommendation 10 in the VA/DoD CPG for the Management of Substance Use Disorders† for further guidance related to tapering 1 or both agents).</td>
<td>Strong against</td>
<td>Strong against</td>
<td>Reviewed, amended</td>
<td>(29, 52) Additional references: (19, 74)</td>
</tr>
<tr>
<td>7. If prescribing opioids, we recommend using the lowest dose of opioids as indicated by patient-specific risks and benefits.</td>
<td>Strong for</td>
<td>Strong for</td>
<td>Reviewed, amended</td>
<td>(27-30, 32, 33, 34, 39, 52, 75, 76, 118) Additional reference: (19)</td>
</tr>
<tr>
<td>8. If considering an increase in opioid dosage, we recommend reevaluation of patient-specific risks and benefits and monitoring for adverse events, including opioid use disorder and risk for overdose with increasing dosage.</td>
<td>Strong for</td>
<td>Strong for</td>
<td>Reviewed, new replaced</td>
<td>(27-30, 32-34, 39, 52, 75, 76) Additional reference: (19)</td>
</tr>
<tr>
<td>9. When prescribing opioids, we recommend the shortest duration as indicated.</td>
<td>Strong for</td>
<td>Strong for</td>
<td>Reviewed, new replaced</td>
<td>(28, 30, 38-40) Additional references: (19, 77)</td>
</tr>
<tr>
<td>10. After initiating opioid therapy, we recommend reevaluation at 30 d or fewer and frequent follow-up visits if opioids are to be continued.</td>
<td>Strong for</td>
<td>Strong for</td>
<td>Reviewed, new replaced</td>
<td>(28, 30, 38-40) Additional references: (19, 77)</td>
</tr>
<tr>
<td>11. We recommend against prescribing long-acting opioids: For acute pain As an as-needed medication When initiating long-term opioid therapy</td>
<td>Strong against</td>
<td>Strong against</td>
<td>Reviewed, amended</td>
<td>(28, 30, 31, 42, 62, 78-84) Additional references: (19, 85)</td>
</tr>
<tr>
<td>12. We suggest a collaborative, patient-centered approach to opioid tapering.</td>
<td>Strong for</td>
<td>Weak for</td>
<td>Reviewed, new replaced</td>
<td>(86, 87)</td>
</tr>
<tr>
<td>13. There is insufficient evidence to recommend for or against any specific tapering strategies.</td>
<td>Strong for</td>
<td>Neither for nor against</td>
<td>Reviewed, new replaced</td>
<td>(86, 87)</td>
</tr>
</tbody>
</table>

*Continued on following page*
that buprenorphine had fewer adverse effects. Freynhagen and colleagues (31) also compared buprenorphine over tramadol for 30% reduction in pain (62). Oxymorphone, tramadol, and tapentadol; they found no difference in most cases and favored buprenorphine over tramadol for 30% reduction in pain (62). Freynhagen and colleagues (31) also compared buprenorphine and various other opioids and found that buprenorphine had fewer adverse effects.

Dose, Duration, and Taper of Opioids
Consistent with the previous 2017 guideline, the guideline development group recommends that health care professionals use the lowest dose as indicated by patient-specific risks and benefits when prescribing an opioid (Table, recommendation 7). The risk for prescription opioid overdose and overdose death exists even at low opioid dosage levels and increases with increasing opioid doses (32, 33, 52, 118). There is a dose-related risk for OUD: Patients receiving 20 to 50 morphine milligram equivalents had a lower risk than those prescribed greater than 200 morphine milligram equivalents (32). Both the initiation of opioids in the opioid-naive patient (31) and opioid dose escalation in patients receiving long-term opioids (34, 38, 39) are associated with opioid misuse, development of OUD, and overdose.

Consistent with the previous 2017 guideline, the guideline development group recommends the shortest duration as indicated when prescribing opioids (Table,
recommendation 9). Current evidence suggests that a longer duration of opioid therapy is associated with a higher risk for subsequent treatment of OUD and a higher risk for fatal opioid overdose (28, 31, 40, 53, 85). A large retrospective cohort study provided moderate-quality evidence that a higher total day supply of opioids is associated with a higher risk for OUD (30). In addition to the dosage, a higher total day supply of opioids is also associated with increased risk for OUD. Risk is increased with an increased number of opioid doses dispensed, beginning with a greater than 10-day supply.

If the decision is made to initiate opioid therapy, follow-up is critical. This updated guideline still recommends reevaluation at 30 days or less after initiating opioid therapy and frequent follow-up visits if opioids are continued (Table, recommendation 10). Follow-up allows clinicians to review and adjust the pain care plan, including continuing the use of opioids. The timeline for follow-up is based on evidence of increased risk for OUD and fatal overdose with opioid use extending beyond 30 days (28, 30). Frequent follow-up visits after a new opioid prescription are also associated with a decreased risk for suicide attempt when compared with patients receiving less frequent follow-up visits (53).

This updated guideline continues to recommend against the use of long-acting opioids for treating acute pain, for as-needed pain, or when initiating long-term opioid therapy (Table, recommendation 11). This recommendation is based on the potential harms of OUD, overdose, and death. One large retrospective cohort study indicates that compared with short-acting opioids, long-acting opioids increased the risk for being treated for OUD (30). Evidence reflects that patients receiving long-acting and schedule II short-acting opioid formulations simultaneously were 4.7 times more likely to die of an overdose than those receiving non-schedule II opioids alone (28). Furthermore, the U.S. Food and Drug Administration has added the following warnings to extended-release opioid preparations:

Because of the risks for addiction, misuse, and misuse with opioids, even at recommended doses, and because of the greater risks for overdose and death with extended-release opioid formulations, reserve [extended-release opioid preparations] for use in patients for whom alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. [Extended-release opioid preparation] is not indicated as an as-needed (prn) analgesic. (85)

In general, however, no single opioid or opioid formulation is preferred over the others. There is limited evidence about the comparative effectiveness and safety of various opioid formulations.

Current evidence still supports using a collaborative, patient-centered approach when deciding to taper the opioid dosage or discontinue the opioid treatment (Table, recommendation 12). However, the guideline development group did not find evidence to recommend for or against any specific tapering strategies (Table, recommendation 13). Collaborative tapering strategies may include dose reduction or opioid treatment discontinuation. Potential benefits include risk reduction for overdose, OUD, and other adverse events. There were no direct harms identified when effective patient collaboration was used (86, 87). However, potential harms when tapering opioid dosages may include destabilization of patients and precipitation of opioid withdrawal. It may also be accompanied by worsening pain, loss of function, increased suffering, worsening depression, increased suicidal ideation and attempts, and use of other substances. The benefits of a collaborative, patient-centered approach to tapering were believed to outweigh the harms of this approach. Potential harms can be mitigated by using gradual tapering strategies at a rate that is slow enough to avoid withdrawal symptoms. If OUD is suspected at any point while treating a patient with chronic pain, appropriate treatment of OUD should be initiated. All providers can and should take a patient-centered, collaborative approach, with a focus on the patient’s goals, capabilities, prior treatments, and preferences. Providers should encourage patients to discuss previous experiences, including successes or difficulties, with the cessation or tapering of opioid dosages.

Screening Assessment and Evaluation

Assessing patient risk for adverse events is important when using opioids to manage pain. As with the 2017 guideline, the guideline development group recommends assessing risk for suicide and self-directed violence when initiating, continuing, changing, or discontinuing long-term opioid therapy (Table, recommendation 14). Specific populations, including those with psychotic disorders, mood disorders, pain disorders, headache, pain, neuropathy, or a cancer diagnosis, may be at an elevated risk for self-harm (27). According to a large retrospective study, veterans receiving long-term opioids for chronic noncancer pain are at increased risk for suicide (27). Both escalation of opioid dose and discontinuation of an opioid prescription increased the risk for adverse events. The risk was higher the longer the patients had been receiving opioid therapy before discontinuation (27). Hayes and colleagues (75) found that dose escalation increased the risk for substance use disorder and opioid-related adverse outcomes, including self-directed harm in veterans prescribed opioids for chronic noncancer pain. A study by Oliva and colleagues (88) concluded that veterans were at greater risk for death from overdose or suicide after discontinuing opioid treatment. Clinicians should consider patient history of suicidal behaviors when assessing risk. Alternatives to long-term opioid therapy should be considered, and behavioral health providers should be involved in care when a patient endorses suicidal ideation or becomes destabilized because of a medically appropriate decision to taper the opioid dosage or cease long-term use.

This guideline includes a new recommendation to screen for additional mental health conditions that potentially increase risk in patients with chronic pain when considering long-term opioid therapy (Table, recommendation 15). The guideline development group recommends

mendation 12). However, the guideline development
assessing for behavioral health conditions, history of traumatic brain injury, and psychological factors (for example, negative affect, pain catastrophizing) because these conditions are associated with a higher risk for harm. This recommendation is based on evidence suggesting mood disorders were associated with a higher risk for death by intentional opioid overdose (27). Similarly, one study (30) suggests an association between psychotic disorders and a higher risk for intentional overdose; therefore, screening for psychotic disorders is recommended. The guideline also recommends screening for a history of a concussive event associated with mental, emotional, or physical symptoms. A large retrospective cohort study suggested that traumatic brain injury was associated with an increased risk for opioid overdose among veterans (97). The work group recognizes that this recommendation may be challenging to implement, as it could result in more referrals to behavioral health providers in areas where availability is already critically low. In addition, there is the risk that some patients may associate their mental health symptoms with their chronic pain. Virtual behavioral health services are an opportunity to support patients who cannot access in-person behavioral health assessment, yet are willing to engage in services through a virtual platform.

This updated guideline includes a new recommendation for screening for pain catastrophizing and co-occurring behavioral health conditions to identify those at higher risk for negative outcomes when opioids are being considered in patients with acute pain (Table, recommendation 16). Evidence from 4 large retrospective and retrospective cohort studies suggests that patients with acute pain and co-occurring behavioral health conditions are at increased risk for opioid dependence, overdose, death, and potentially obtaining inappropriate prescriptions (41, 99–101). In addition, 2 smaller prospective cohort studies showed that when patients catastrophize, or anticipate that their pain will last longer than 1 week, they have higher rates of persistent pain (102, 112). For screening of catastrophizing in an acute pain setting, brief versions of the Pain Catastrophizing Scale (119) may be preferred (3- to 4-item vs. the full 13-item version) (120, 121). When patients have a positive screen result, the clinician may consider nonopioid analogs. There are some risks associated with screening patients for pain catastrophizing and co-occurring behavioral health conditions. Some patients may feel a stigma associated with this type of diagnosis. This is especially true for military patients where there may be career implications for a positive screen result.

Previous opioid guidelines have suggested periodic reevaluation of patients at specific intervals when prescribed an opioid; however, there is a lack of evidence to support a specific time period, and instead, the guideline development group recommends ongoing reevaluation of the benefits and harms of continued opioid prescribing based on individual patient risk characteristics (Table, recommendation 17). The guideline development group encourages clinicians to use the CDC guidance of reevaluation every 90 days as a starting point, while recognizing that some patients may need more frequent reevaluation of risks and benefits. Reevaluation may capture changes within an individual’s health presentation or lifestyle that would identify a risk factor not previously known or present.

**Risk Mitigation**

Although there are various known factors that increase the risk for adverse outcomes among patients receiving long-term opioid therapy, evidence to support specific risk mitigation strategies to improve outcomes is lacking. The guideline development group specifically looked for evidence to support the effectiveness or comparative effectiveness of informed consent, risk assessment instruments, pill counts or limited pills per prescription, the use of misuse deterrent formulations, diversion prevention interventions, pharmacogenetic testing, random callbacks, monitoring for aberrant or high-risk behaviors, or naloxone prescriptions to improve outcomes, but evidence was lacking for these strategies. Thus, the recommendations in the 2017 guideline for checking prescription drug monitoring programs and prescribing naloxone rescue and accompanying education had to be removed from the recommendation list; nevertheless, these continue to be the standard of care for patients receiving long-term opioid therapy for both VA and DoD health care systems, as is the requirement for written informed consent. The 2022 guideline maintains the recommendation for urine drug testing for patients receiving long-term opioids, as the evidence showed decreased risk for self-directed violence and thus improved safety (53).

Recent evidence supports education as a new strategy to decrease opioid use for postoperative pain. Cheesman and colleagues (112) conducted a randomized controlled trial that compared patients who received preoperative pain management and opioid education versus a control group. The study found that preoperative patient education resulted in a decrease in the number of opioid prescription refills and reduced opioid use both in the short term and over a 2-year follow-up. As this result indicates a reduced risk for transitioning to long-term opioid use, the guideline development group included a new recommendation to provide patients with preoperative opioid and pain management education to reduce the risk for prolonged opioid use for postsurgical pain (Table, recommendation 20).

**Comparison With Other Guidelines**

The CDC has also recently released an updated opioid guideline (122). The VA/DoD and the CDC use different methods for development, which results in some variation in the recommendation language. However, both guidelines recommend against the use of opioids for the treatment of chronic pain, and both guidelines recommend against the use of extended-release opioids. Both the VA/DoD guideline and the CDC guideline recommend that, when opioids are prescribed, clinicians prescribe the lowest dose possible for the shortest time based on an assessment of the patient. Both support ongoing evaluation of benefits and harms when opioids are used to manage pain. Although there are differences in the scope and aspects of pain management, the VA/DoD guideline and the CDC guideline do not have any contradictory recommendations.
Future Research

The systematic evidence review done as part of the development of this guideline revealed areas where more research is needed. These include areas that require more evidence to support our current recommendations as well as other areas where we did not find evidence. The guideline development group identified that more studies are needed examining the comparative effectiveness of different analgesic agents, the effectiveness of different tapering strategies, and the effectiveness of different risk mitigation strategies on the management of patients receiving long-term opioid therapy.

Conclusion

Chronic pain is common in the United States and continues to burden individuals, families, and society. The decision to use an opioid to manage pain should be made with a great deal of caution. The guideline development group does not recommend use of opioid analgesics in the daily management of chronic pain. The benefits that opioids can provide are small and are outweighed by the risks to the patient. If the decision is made to use long-term opioid therapy for a patient, then buprenorphine should be considered because of its lower risk profile. Clinicians can further reduce risk by screening for underlying mood disorders and a history of traumatic brain injury. Although risk mitigation strategies have also been used to lower risk in patients receiving opioids, the guideline development group was surprised to find little evidence in this area.

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Author contributions are available at Annals.org.

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Clinical Guideline

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