InTRoduCTI on
Chronic pain is defined as “pain that persists beyond normal tissue healing time, which is assumed to be three months”. When chronic pain is not associated with cancer or end of life care, it is often referred to as “chronic non-cancer pain” (CNP). Opioid prescriptions have increased substantially over the last 20 years, in large part due to increased use among patients with CNP. This trend has been accompanied by a substantial increase in prescription opioid misuse and mortality in adolescents and adults of all ages.

How can opioids be prescribed in a way that balances their ability to relieve pain and improve function, while mitigating their potential risks? The American Pain Society (APS), in partnership with the American Academy of Pain Medicine (AAPM), recently published evidence-based guidelines developed by a multidisciplinary panel on use of chronic opioid therapy (COT) for adults with CNP. This article reviews key clinical messages from this guideline. Additional details about the methods used to develop the guideline and the evidence review commissioned to inform the guideline have been published elsewhere.

TABLE 1 shows the recommendations covered in this article and TABLE 2 shows a list of the clinical tools included with the guideline.

Patient selection and risk stratification All clinicians prescribing opioids should be knowledgeable about risk factors for opioid abuse and methods for assessing risk. A thorough history and physical examination, including an assessment of psychosocial factors and family history, is essential for adequate risk stratification. The factor most
Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be used with caution. Clinicians should consider opioid rotation when patients on chronic opioid therapy experience intolerable adverse effects or inadquate benefit despite dose increases (weak recommendation, low-quality evidence).

A benefit-to-harm evaluation including a history, physical examination, and appropriate diagnostic testing, should be performed and documented prior to and on an ongoing basis during chronic opioid therapy (strong recommendation, low-quality evidence).

Clinicians may consider using a written chronic opioid therapy management plan to document patient and clinician responsibilities and expectations and assist in patient education (weak recommendation, low-quality evidence).

Opioid selection, initial dosing, and titration should be individualized according to the patient’s health status, previous exposure to opioids, attainment of therapeutic goals, and predicted or observed harms (strong recommendation, low-quality evidence). There is insufficient evidence to recommend short-acting versus long-acting opioids, or as-needed versus around-the-clock dosing of opioids.

Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be initiated and titrated cautiously, by clinicians familiar with its use and risks (strong recommendation, moderate-quality evidence).

Clinicians should reassess patients on chronic opioid therapy periodically and as warranted by changing circumstances. Monitoring should include documentation of pain intensity and level of functioning, assessments of progress towards achieving therapeutic goals, presence of adverse events, and adherence to prescribed therapies (strong recommendation, low-quality evidence).

In patients on chronic opioid therapy who are at high risk or who have engaged in aberrant drug-related behaviors, clinicians should periodically obtain urine drug screens or other information to confirm adherence to the chronic opioid therapy plan of care (strong recommendation, low-quality evidence).

In patients on chronic opioid therapy not at high risk and not known to have engaged in aberrant drug-related behaviors, clinicians should consider periodically obtaining urine drug screens or other information to confirm adherence to the chronic opioid therapy plan of care (weak recommendation, low-quality evidence).

Clinicians may consider chronic opioid therapy for patients with chronic noncancer pain and history of drug abuse, psychiatic issues, or serious aberrant drug-related behaviors only if they are able to implement more frequent and stringent monitoring parameters. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist (strong recommendation, low-quality evidence).

Clinicians should evaluate patients engaging in aberrant drug-related behaviors for appropriateness of chronic opioid therapy or need for restructuring of therapy, referral for assistance in management, or discontinuation of chronic opioid therapy (strong recommendation, low-quality evidence).

When repeated dose escalations occur in patients on chronic opioid therapy, clinicians should evaluate potential causes and re-assess benefits relative to harms (strong recommendation, low-quality evidence).

Clinicians should consider opioid rotation when patients on chronic opioid therapy experience intolerable adverse effects or inadequate benefit despite dose increases (weak recommendation, low-quality evidence).

Clinicians should taper or wean patients off of chronic opioid therapy who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress towards meeting therapeutic goals, or experience intolerable adverse effects (strong recommendation, low-quality evidence).

Clinicians should anticipate, identify, and treat common opioid-associated adverse effects (strong recommendation, moderate-quality evidence).

As chronic noncancer pain is often a complex biopsychosocial condition, clinicians who prescribe chronic opioid therapy should routinely integrate psychotherapeutic interventions, functional restoration, interdisciplinary therapy, and other adjunctive non-opioid therapies (strong recommendation, moderate-quality evidence).

Clinicians should counsel patients on chronic opioid therapy about transient or lasting cognitive impairment that may affect driving and work safety. Patients should be counseled not to drive or engage in potentially dangerous activities when impaired or if they describe or demonstrate signs of impairment (strong recommendation, low-quality evidence).

### Recommendations from the American Pain Society/American Academy of Pain Medicine guideline for use of chronic opioid therapy for chronic noncancer pain

<table>
<thead>
<tr>
<th>Topic area</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>patient selection and risk stratification</td>
<td>Prior to initiating chronic opioid therapy, clinicians should conduct a history, physical examination and appropriate testing, including an assessment of risk of substance abuse, misuse, or addiction (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>informed consent and opioid management plans</td>
<td>Clinicians may consider a trial of chronic opioid therapy as an option if chronic noncancer pain is moderate or severe, pain is having an adverse impact on function or quality of life, and potential therapeutic benefits outweigh or are likely to outweigh potential harms (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>initiation and titration of chronic opioid therapy</td>
<td>When starting chronic opioid therapy, informed consent should be obtained. A continuing discussion with the patient regarding chronic opioid therapy should include goals, expectations, potential risks, and alternatives to chronic opioid therapy (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>methadone</td>
<td>Clinicians may consider using a written chronic opioid therapy management plan to document patient and clinician responsibilities and expectations and assist in patient education (weak recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>monitoring</td>
<td>Clinicians and patients should regard initial treatment with opioids as a therapeutic trial to determine whether chronic opioid therapy is appropriate (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>high-risk patients</td>
<td>Opioid selection, initial dosing, and titration should be individualized according to the patient’s health status, previous exposure to opioids, attainment of therapeutic goals, and predicted or observed harms (strong recommendation, low-quality evidence). There is insufficient evidence to recommend short-acting versus long-acting opioids, or as-needed versus around-the-clock dosing of opioids.</td>
</tr>
<tr>
<td>aberrant drug-related behaviors</td>
<td>Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be initiated and titrated cautiously, by clinicians familiar with its use and risks (strong recommendation, moderate-quality evidence).</td>
</tr>
<tr>
<td>dose escalations and high-dose therapy</td>
<td>Clinicians may consider chronic opioid therapy for patients with chronic noncancer pain and history of drug abuse, psychiatric issues, or serious aberrant drug-related behaviors only if they are able to implement more frequent and stringent monitoring parameters. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>opioid rotation</td>
<td>In patients on chronic opioid therapy, clinicians should periodically obtain urine drug screens or other information to confirm adherence to the chronic opioid therapy plan of care (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>indications for discontinuation of therapy</td>
<td>In patients on chronic opioid therapy not at high risk and not known to have engaged in aberrant drug-related behaviors, clinicians should consider periodically obtaining urine drug screens or other information to confirm adherence to the chronic opioid therapy plan of care (weak recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>opioid-related adverse effects</td>
<td>Clinicians should evaluate patients engaging in aberrant drug-related behaviors for appropriateness of chronic opioid therapy or need for restructuring of therapy, referral for assistance in management, or discontinuation of chronic opioid therapy (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>use of psycho-therapeutic co-interventions</td>
<td>When repeated dose escalations occur in patients on chronic opioid therapy, clinicians should evaluate potential causes and re-assess benefits relative to harms (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>driving and work safety</td>
<td>Clinicians should consider opioid rotation when patients on chronic opioid therapy experience intolerable adverse effects or inadequate benefit despite dose increases (weak recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>use of psycho-therapeutic co-interventions</td>
<td>Clinicians should taper or wean patients off of chronic opioid therapy who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress towards meeting therapeutic goals, or experience intolerable adverse effects (strong recommendation, low-quality evidence).</td>
</tr>
<tr>
<td>opioid-related adverse effects</td>
<td>Clinicians should anticipate, identify, and treat common opioid-associated adverse effects (strong recommendation, moderate-quality evidence).</td>
</tr>
<tr>
<td>use of psycho-therapeutic co-interventions</td>
<td>As chronic noncancer pain is often a complex biopsychosocial condition, clinicians who prescribe chronic opioid therapy should routinely integrate psychotherapeutic interventions, functional restoration, interdisciplinary therapy, and other adjunctive non-opioid therapies (strong recommendation, moderate-quality evidence).</td>
</tr>
<tr>
<td>driving and work safety</td>
<td>Clinicians should counsel patients on chronic opioid therapy about transient or lasting cognitive impairment that may affect driving and work safety. Patients should be counseled not to drive or engage in potentially dangerous activities when impaired or if they describe or demonstrate signs of impairment (strong recommendation, low-quality evidence).</td>
</tr>
</tbody>
</table>

### TABLE 1

<table>
<thead>
<tr>
<th>Topic area</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to initiating chronic opioid therapy, clinicians should conduct a history, physical examination and appropriate testing, including an assessment of risk of substance abuse, misuse, or addiction (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians may consider a trial of chronic opioid therapy as an option if chronic noncancer pain is moderate or severe, pain is having an adverse impact on function or quality of life, and potential therapeutic benefits outweigh or are likely to outweigh potential harms (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>When starting chronic opioid therapy, informed consent should be obtained. A continuing discussion with the patient regarding chronic opioid therapy should include goals, expectations, potential risks, and alternatives to chronic opioid therapy (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians may consider using a written chronic opioid therapy management plan to document patient and clinician responsibilities and expectations and assist in patient education (weak recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians and patients should regard initial treatment with opioids as a therapeutic trial to determine whether chronic opioid therapy is appropriate (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Opioid selection, initial dosing, and titration should be individualized according to the patient’s health status, previous exposure to opioids, attainment of therapeutic goals, and predicted or observed harms (strong recommendation, low-quality evidence). There is insufficient evidence to recommend short-acting versus long-acting opioids, or as-needed versus around-the-clock dosing of opioids.</td>
<td></td>
</tr>
<tr>
<td>Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be initiated and titrated cautiously, by clinicians familiar with its use and risks (strong recommendation, moderate-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians should reassess patients on chronic opioid therapy periodically and as warranted by changing circumstances. Monitoring should include documentation of pain intensity and level of functioning, assessments of progress towards achieving therapeutic goals, presence of adverse events, and adherence to prescribed therapies (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>In patients on chronic opioid therapy who are at high risk or who have engaged in aberrant drug-related behaviors, clinicians should periodically obtain urine drug screens or other information to confirm adherence to the chronic opioid therapy plan of care (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>In patients on chronic opioid therapy not at high risk and not known to have engaged in aberrant drug-related behaviors, clinicians should consider periodically obtaining urine drug screens or other information to confirm adherence to the chronic opioid therapy plan of care (weak recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians may consider chronic opioid therapy for patients with chronic noncancer pain and history of drug abuse, psychiatic issues, or serious aberrant drug-related behaviors only if they are able to implement more frequent and stringent monitoring parameters. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians should evaluate patients engaging in aberrant drug-related behaviors for appropriateness of chronic opioid therapy or need for restructuring of therapy, referral for assistance in management, or discontinuation of chronic opioid therapy (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>When repeated dose escalations occur in patients on chronic opioid therapy, clinicians should evaluate potential causes and re-assess benefits relative to harms (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>In patients who require relatively high doses of chronic opioid therapy clinicians should evaluate for unique opioid-related adverse effects, changes in health status, and adherence to the chronic opioid therapy treatment plan on an ongoing basis, and consider more frequent follow-up visits (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians should consider opioid rotation when patients on chronic opioid therapy experience intolerable adverse effects or inadequate benefit despite dose increases (weak recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians should taper or wean patients off of chronic opioid therapy who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress towards meeting therapeutic goals, or experience intolerable adverse effects (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians should anticipate, identify, and treat common opioid-associated adverse effects (strong recommendation, moderate-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>As chronic noncancer pain is often a complex biopsychosocial condition, clinicians who prescribe chronic opioid therapy should routinely integrate psychotherapeutic interventions, functional restoration, interdisciplinary therapy, and other adjunctive non-opioid therapies (strong recommendation, moderate-quality evidence).</td>
<td></td>
</tr>
<tr>
<td>Clinicians should counsel patients on chronic opioid therapy about transient or lasting cognitive impairment that may affect driving and work safety. Patients should be counseled not to drive or engage in potentially dangerous activities when impaired or if they describe or demonstrate signs of impairment (strong recommendation, low-quality evidence).</td>
<td></td>
</tr>
</tbody>
</table>
The Screener and Opioid Assessment for Patients with Pain Version 1

Pain Assessment and Documentation Tool

sample form developed by the American Academy of Pain Medicine

Clinical tools included with the American Pain Society/American Academy of Pain Medicine guideline for use of chronic opioid therapy for chronic noncancer pain

<table>
<thead>
<tr>
<th>Type of clinical tool</th>
<th>Clinical tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>risk assessment tools</td>
<td>The Screener and Opioid Assessment for Patients with Pain Version 1</td>
</tr>
<tr>
<td></td>
<td>The Revised Screener and Opioid Assessment for Patients with Pain</td>
</tr>
<tr>
<td></td>
<td>The Opioid Risk Tool</td>
</tr>
<tr>
<td></td>
<td>Diagnosis, Intractability, Risk, Efficacy Tool</td>
</tr>
<tr>
<td>monitoring tools</td>
<td>Pain Assessment and Documentation Tool</td>
</tr>
<tr>
<td></td>
<td>Current Opioid Misuse Measure</td>
</tr>
<tr>
<td>sample informed consent form</td>
<td>sample form developed by the American Academy of Pain Medicine</td>
</tr>
<tr>
<td>sample opioid management plan</td>
<td>sample form developed by the American Academy of Pain Medicine</td>
</tr>
</tbody>
</table>

...
aberrant drug-related behaviors. To avoid unrealistic expectations regarding likely benefits, patients should be counseled that total pain relief with opioids is rare. Indeed, trials suggest that improvement averages less than 2–3 points on a 0 to 10 scale. Written documentation can help clarify the opioid management plan, particularly in patients at higher risk for misuse of opioid analgesics.

**Initiation and titration of chronic opioid therapy**

An initial course of treatment with opioids for CNCP should be viewed as a short-term, therapeutic trial. The decision to proceed with COT should be made after careful consideration of whether the patient has made progress toward meeting therapeutic goals, presence and severity of opioid-related adverse effects, changes in psychiatric or medical co-morbidities, and identification of aberrant drug-related behaviors, addiction, or diversion. In patients who experience mild or moderate opioid-related adverse effects, a longer trial may be indicated because some adverse effects decrease with longer exposure.

In patients who are opioid-naïve, or have modest previous opioid exposure, opioids should be started at a low dose and titrated slowly, to decrease risk of opioid-related adverse effects. Frail older persons or those with co-morbidities may benefit from particularly cautious initiation and titration of therapy. Short-acting opioids are probably safer for initial therapy since they have a shorter half-life and may be associated with a lower risk of inadvertent overdose. Proposed benefits of transitioning to long-acting opioids with around-the-clock dosing include more consistent control of pain, improved adherence, and lower risk of addiction or abuse, but well-conducted studies have not proven these benefits. A transition to long-acting, sustained-release opioids is a reasonable goal in most patients, but there is no compelling reason to require low-risk patients on stable doses of short-acting, as-needed opioids to switch regimens.

**Methadone**

Clinicians who prescribe methadone should be familiar with its clinical pharmacology and associated risks. The observed increase in methadone-associated deaths that occurred in conjunction with its increased use for CNCP could be related in part to its association with cardiac arrhythmias (particularly at higher doses) or to inadvertent overdose related to the very long and highly variable half-life of this drug.

The half-life of methadone is usually estimated at 15–60 hours. At a half-life of 60 hours, it would take almost 12 days on a stable dose of methadone to reach steady state (five half-lives). Methadone should therefore be started at low doses and titrated slowly. A safe starting dose in most opioid-naïve patients is 2.5 mg every 8 hours, with dose increases occurring no more frequently than weekly. In older patients or those with renal or hepatic co-morbidities, less frequent dosing and more cautious dose titration are recommended. The utility of routine electrocardiograms for preventing methadone-induced arrhythmias by identifying those at higher risk for this adverse event is unknown.

In opioid-tolerant patients, conversion to methadone should be performed cautiously. Equianalgesic dose ratios for methadone relative to other opioids are variable and decrease at higher doses. Starting methadone doses should generally not exceed 30 to 40 mg a day even in patients on high doses of other opioids. Several algorithms are available for converting from other opioids to methadone. Due to its long half-life, methadone is not recommended for breakthrough pain or as an as-needed medication.

**Monitoring**

Regular monitoring is recommended for all patients on COT. In patients at low risk for adverse outcomes and on stable doses of opioids, monitoring at least once every 3 to 6 months may be sufficient. More frequent monitoring is suggested after initiation of therapy or changes in opioid doses and in patients at higher risk for aberrant drug-related behaviors, those in an occupation demanding mental acuity, and in older adults or patients with co-morbid medical conditions. For patients at high risk for adverse outcomes, monitoring on a weekly (or more frequent) basis may be required.

Monitoring should routinely include the assessment and documentation of pain severity and functional ability, progress towards achieving therapeutic goals, presence of adverse effects, and presence of aberrant drug-related behaviors. Because patient self-report may be unreliable, pill counts, family member or caregiver interviews, and use of prescription monitoring program data can be useful supplements. Use of monitoring tools such as the Pain Assessment and Documentation Tool and the Chronic Opioid Misuse Measure is suggested as an efficient method of assessment and documentation.

Periodic urine drug screening is recommended in all high risk patients. The absence of prescribed opioids or presence of unprescribed opioids or illicit drugs can be a marker for problematic issues that would not be apparent without urine drug screening. In low risk patients, clinicians are advised to consider urine drug screening, but may exercise their clinical judgment because the yield may be too low to justify the costs in some patients. Random urine drug screens may be more informative than scheduled or routine testing, as patients may alter behaviors when they expect to be tested. Interpretation of urine drug screens requires an understanding of opioid drug metabolism, pharmacokinetics and limitations of laboratory testing methods.

Urine drug screen results usually do not suggest a definitive course of action, and should be interpreted in the context of individual patient circumstances. A differential diagnosis for abnormal urine
drug screen results includes drug abuse or addiction, self-treatment of poorly controlled pain or psychological issues, and diversion.

**High-risk patients** Use of COT in patients with suspected aberrant drug-related behaviors, psychosocial comorbidities, or history of substance abuse is only recommended if potential risks can be minimized. Suggested strategies include implementation of more frequent and intense monitoring, authorization of limited prescription quantities, and consultation or co-management with persons who have expertise in addiction or mental health issues.

**Aberrant drug-related behaviors** The occurrence of aberrant drug-related behavior always requires evaluation. The response to aberrant drug-related behavior reflects a clinical judgment about its seriousness, its cause or causes, the likelihood that behaviors of this type will recur, and the clinical context. Patients who engage in a relatively non-serious aberrant behavior, such as one or two episodes of unauthorized minor opioid escalations, can often be managed with patient education and enhanced monitoring. Patients who are repeatedly nonadherent or who engage in more serious aberrant behaviors (such as use of cocaine or methamphetamine, use of unprescribed opioids, or obtaining opioids from multiple outside sources) may require consultation, major restructuring of therapy, and in many cases discontinuation of opioids. Patients who meet criteria for a substance use disorder should be referred for treatment of this serious co-morbidity.

Restructuring of therapy may include more frequent or intense monitoring strategies, temporary or permanent tapering of opioid doses, or the addition of psychological therapies or other non-opioid treatments. In patients with opioid addiction, structured opioid agonist treatment with methadone or buprenorphine by a licensed program may be an appropriate option. COT must be discontinued in patients who are known to be diverting opioids or in those engaging in seriously aberrant behaviors (such as injecting an oral formulation).

**Dose escalations and high dose opioids** Theoretically, opioids have no maximum or ceiling dose. In practice, progressively higher opioid doses may improve symptom control in some patients, but can also result in additional adverse effects with little incremental benefit, or be a marker for substance abuse or diversion. The guideline defines high dose opioid therapy as >200 mg daily of oral morphine (or equivalent). These doses are outside the ranges evaluated in randomized trials and prescribed in only a small minority of patients in observational studies. When opioid doses reach this threshold, more frequent and intense monitoring is recommended. Clinicians should consider weaning or discontinuation of chronic opioid therapy if assessments indicate reduced analgesia, function, or quality of life; aberrant drug-related behaviors; or the presence of intolerable adverse effects.

**Opioid rotation** There is insufficient evidence to make recommendations about opioid rotation (the practice of switching from one opioid to another opioid) as a strategy for managing intolerable opioid-related adverse effects or inadequate symptom relief. If opioid rotation is tried, switches should generally be accompanied by a moderate reduction in the calculated equianalgesic dose.

**Discontinuation of opioid therapy** Patients should be tapered or weaned off COT when they engage in serious or repeated aberrant drug-related behaviors or diversion, experience intolerable adverse effects, or make no progress towards meeting therapeutic goals. A taper or wean can often be achieved in the outpatient setting in patients without severe medical or psychiatric co-morbidities. In more complex cases, detoxification in a rehabilitation setting can be helpful, especially for patients unable to reduce their opioid dose in a less structured setting. If the aberrant behaviors are related to addiction, addiction treatment resources should be made available.

Symptoms of opioid withdrawal can be very unpleasant, but are generally not life threatening. Approaches to weaning range from a slow, 10% dose reduction per week to a more rapid 25–50% reduction every few days. Anecdotal clinical experience suggests that at high doses (e.g., over 200 mg/day of morphine or equivalent), the initial wean can be more rapid. The rate of dose reduction often must be slowed when relatively low daily doses, such as 60 to 80 mg daily of morphine (or equivalent), are reached, due to occurrence of more withdrawal symptoms. Patients may experience pain hypersensitivity during initial opioid withdrawal. Clinicians should continue to treat patients who are taken off opioids for their painful condition as well as for substance use or psychiatric disorders.

**Opioid-related adverse effects** Clinicians should anticipate and treat common opioid-associated adverse effects. Because constipation is so frequent and persistent following initiation of COT, it is recommended that clinicians routinely consider a bowel regimen when opioids are started. Bowel regimens including increased fluid and fiber intake, stool softeners, and laxatives are often effective. A number of anti-emetic therapies are available to treat nausea or vomiting that develops after initiation of therapy. Patients with sleep apnea or other underlying pulmonary conditions may be at higher risk for respiratory depression and should have opioids initiated and titrated carefully. Although there is insufficient evidence to recommend routine monitoring for hypogonadism or other hormonal deficiencies, patients should be tested if they report symptoms.
such as decreased libido, sexual dysfunction, or fatigue.\textsuperscript{24,25,51}

**Use of psychotherapeutic co-interventions** When chronic pain is accompanied by comorbidities, impaired function, or psychological disturbances, COT is likely to be most effective as part of multimodality treatment that addresses all of these domains.\textsuperscript{52} Clinicians should routinely integrate therapies such as cognitive-behavioral therapy, functional restoration, and interdisciplinary rehabilitation\textsuperscript{53-60} that target the psychosocial and functional factors that contribute to or are affected by CNCP.

**Driving and work safety** In the absence of signs or symptoms of impairment, there is no evidence that patients maintained on stable doses of COT should be restricted from driving.\textsuperscript{61,62} Nonetheless, opioids may cause somnolence, clouded mentation, decreased concentration, and slower reflexes or incoordination. Clinicians should counsel all patients initially prescribed COT not to drive or engage in potentially dangerous work or other activities when impaired. Patients should be educated about the greater risk of impairment when starting opioid therapy, when increasing doses, and when taking other drugs or substances that may have central nervous effects, including alcohol. Clinicians should counsel patients not to drive or engage in potentially dangerous activities if they describe or demonstrate signs of impairment, and should refer to state laws regarding physician-reporting requirements to local authorities in these situations. Certain professions (such as bus drivers and pilots) may be subject to additional regulations and laws regarding use of opioids.

**Identifying a medical home and when to obtain consultation** Patients do better when they have continuous access to a clinician who provides comprehensive care for the large majority of their health care needs and who coordinates care when the services of other health care professionals are needed.\textsuperscript{53} The attributes of effective primary care were described recently in a model known as the patient-centered primary care medical home.\textsuperscript{64} With their multiple and complex health care needs, patients with CNCP require the coordinated and comprehensive services offered through a medical home. The medical home model does not necessarily require the primary care clinician to prescribe and monitor COT. In fact, patients with CNCP may need additional or special services that may not be available in their medical home. In such cases, consultation with other professionals is essential. In particular, pain centers that provide access to an array of pain therapies and specialists trained to assess, prescribe, and monitor COT can be highly valuable. Nonetheless, the primary care clinician should continue to coordinate consultation and communication among all clinicians involved in the patient’s treatment.

**Breakthrough pain** Patients prescribed stable doses of around-the-clock COT for CNCP frequently experience periods of increased pain (i.e., breakthrough pain).\textsuperscript{65,66} Appropriate evaluation of breakthrough pain may require additional diagnostic testing, follow-up visits, or consultation in order to identify the etiology of the pain or the factors precipitating it. Clinicians should carefully weigh the potential benefits vs. risks when considering the addition of an as-needed opioid for treatment of breakthrough pain, and consider both non-opioid drug therapies and non-pharmacologic treatments as other options. In patients at high risk for aberrant drug-related behaviors, access to a short-acting drug for breakthrough pain may increase the risk of such behaviors. A trial of an as-needed opioid should only occur in conjunction with more frequent monitoring and follow-up, and may not be indicated. In patients at low risk for aberrant drug-related behaviors, a trial of an as-needed opioid with routine follow-up and monitoring may be a reasonable strategy. In all cases, clinicians should periodically re-assess relative benefits to risks of the as-needed opioid to make appropriate decisions regarding continuation of this therapy.

**CONCLUSIONS** Use of COT for CNCP is steadily increasing. Guidelines based on the best available evidence and developed by multidisciplinary panels of experts are critical for promoting the effective and safe use of COT for CNCP. An expert panel convened by APS and AAPM concluded that COT can be an effective therapy for carefully selected and monitored patients with CNCP.\textsuperscript{5} However, opioids are also associated with potentially serious harms, including opioid-related adverse effects and outcomes related to the abuse potential of opioids. The guidelines summarized in this article are based on the underlying assumption that safe and effective therapy requires clinical skills and knowledge in the principles of opioid prescribing and on the assessment and management of risks. An appropriate balance between benefits and risks of COT for CNCP is dependent on careful patient evaluation and structuring of opioid therapy to accommodate identified risk, appropriate initiation and titration of COT, regular and comprehensive monitoring while on COT, and anticipation and management of opioid-related adverse effects.

**REFERENCES**


