THE JOURNAL OF FAMILY PRACTICE

Tips and tools for safe opioid prescribing

This review—with tables summarizing opioid options, dosing considerations, and recommendations for tapering—will help you provide rigorous Tx for noncancer pain while ensuring patient safety.

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The authors reported no potential conflict of interest relevant to this article.

PRACTICE RECOMMENDATIONS

› *Use a screening instrument such as the Opioid Risk Tool or the DIRE assessment to gauge a patient's risk of opioid misuse and determine the frequency of monitoring.* (C)

› *Give as much priority to improving functional activity and minimizing adverse opioid effects as you do to relieving pain.* (C)

› *Prescribe an immediate-release, short-acting agent at first instead of a long-acting formulation; start with the lowest effective dosage and calculate total daily dose in terms of morphine milligram equivalents (MME).* (C)

› *Reduce the original MME dose by 5% to 10% every week when discontinuing an opioid.* (C)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence

(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

CASE ▶

Marcelo G* is a 46-year-old man who presented to our family medicine clinic with a complex medical history including end-stage renal disease (ESRD) and hemodialysis, chronic anemia, peripheral vascular disease, venous thromboembolism and anticoagulation, major depressive disorder, osteoarthritis, and lumbosacral radiculopathy. His current medications included vitamin B complex, cholecalciferol, atorvastatin, warfarin, acetaminophen, diclofenac gel, and capsaicin cream. Mr. G reported bothersome bilateral knee and back pain despite physical therapy and consistent use of his current medications in addition to occasional intra-articular glucocorticoid injections. He mentioned that he had benefited in the past from intermittent opioid use.

How would you manage this patient's care?

**The patient's name has been changed to protect his identity.*

In 2013, an estimated 191 million prescriptions for opioids were written by health care providers, which is the equivalent of all adults living in the United States having their own opioid prescription.[1] This large expansion in opioid prescribing and use has also led to a rise in opioid overdose deaths, whether from prescribed or illicit use.[1] The Centers for Disease Control and Prevention (CDC) points out that each day, approximately 128 Americans die from an opioid overdose.[1] Deaths that occur from opioid overdose often involve the prescribed opioids methadone, oxycodone, and hydrocodone, the illicit opioid heroin, and, of particular concern, prescription and illicit fentanyl.[1]

The extent of this problem has sparked the development of health safety initiatives and research efforts. Through production quotas, the US Drug Enforcement Administration (DEA) reduced the number of opioids produced across all schedule I

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Family physicians write more opioid prescriptions than any other specialty, and they are therefore uniquely positioned to protect patients, improve the quality of their care, and ultimately produce a meaningful public health impact.

and schedule II lists in 2017 by as much as 25%.[2] The DEA again reduced the amounts produced in 2018.[3] For 2020, the DEA has determined that the production quotas and assessment of annual needs are sufficient.[4]

The CDC has also promoted access to naloxone and prevention initiatives; pharmacies in some states have standing orders for naloxone, and medical personnel and law enforcement now carry it.[1,5] Finally, new research has identified risk factors that influence one's potential for addiction, such as mental illness, history of substance and alcohol abuse, and a low income.[6] Interestingly, while numerous initiatives and strategies have been implemented across health systems, there is little evidence that demonstrates how implementation of safe prescribing strategies has affected overall patient safety and avoidance of opioid-related harms.

Nevertheless, concerns related to opioids are especially important for primary care providers, who manage many patients with acute and chronic diseases and disorders that require pain control.[7] Family physicians write more opioid prescriptions than any other specialty,[8] and they are therefore uniquely positioned to protect patients, improve the quality of their care, and ultimately produce a meaningful public health impact. This article provides a guide to safe opioid prescribing.

Use the patient interview to ensure that Tx aligns with patient goals

For patients presenting with chronic pain, conduct a complete general history and physical examination that includes a review of available records; a medical, surgical, social, family, medication, and allergy history; a review of systems; and documentation of any psychiatric comorbidities (ie, depression, anxiety, psychiatric disorders, personality traits). Inquiries about social history and current medications should explore the possibility of previous and current substance use and misuse.

While causes of pain can be assessed through physical examination and diagnostic tests, the patient interview is an invaluable source of information. No single means of assessment has consistently demonstrated superiority over another in measuring pain, and numerous standard assessment tools are available (**TABLE 1**[9-13]).[14] Unidimensional tools are often easy and quick ways to assess pain intensity. Multidimensional tools, although more time intensive, are designed to gather more subjective information about the pa-

tient's pain. Finally, use an instrument such as the 9-item Patient Health Questionnaire (PHQ-9) to screen patients for psychological distress.[15,16]

Provide an environment for patients to openly discuss their experiences, expectations, preferences, fears, and coping efforts, as well as the impact that pain has had on their lives.[17,18] Without this foundational understanding, medical treatment may work against the patient's goals. An empathic approach allows for effective communication, shared decision making, and ultimately, an avenue for individualized therapy.

Balancing treatment with risk mitigation

Use state prescription drug monitoring programs and urine drug testing to confirm patient compliance.

The challenge of managing chronic pain is to balance treating the patient with the basic principle of nonmaleficence (*primum non nocere*: "first, do no harm"). The literature has shown that risk factors such as a family history of substance abuse or sexual abuse, younger age, and psychological disease may be linked to greater risk for opioid misuse.[19,20] However, despite the many risk-screening tools available, no single instrument has reliably and accurately predicted those at higher propensity for prescription addiction. In fact, risk-screening tools as a whole remain unregulated by the US Food and Drug Administration (FDA) and other authorities.[21] Still, screening tools provide useful information as one component of the risk-mitigation process.

Screening tools. The tools most commonly used clinically to stratify risk prior to prescribing opioids are the 5-item Opioid Risk Tool (ORT),[22] the revised 24-item Screener and Opioid Assessment for Patients with Pain (SOAPP-R),[23] which are patient self-administered assessments, and the 7-item clinician-administered DIRE (Diagnosis, Intractability, Risk, Efficacy).[24] Given the subtle differences in criteria and the time required for each of these risk assessments, we recommend choosing one based on site-specific resources and overall clinician comfort.[25] Risk stratification helps to determine the optimal frequency and intensity of monitoring, not necessarily to deny care to "high-risk" patients.

In fact, just as the "universal precautions" approach has been applied to infection control, many have suggested using a similar approach to pain management. Risk screening should never be misunderstood as an attempt to diminish or undermine the patient's burden of pain. By routinely conducting thorough and respectful inquiries of risk factors for all patients, clinicians can reduce stigma, improve care, and contain overall risk.[26,27]

Monitoring programs and patient agreements. In addition to risk-screening tools, the CDC recommends using state prescription drug monitoring programs (PDMP) and urine drug testing (UDT) data to confirm the use of prescribed and illicit substances.[28] All 50 states have implemented PDMPs.[29] Consider incorporating these components into controlled-substance agreements, which ultimately aim to promote safety and trust between patients and providers. Of course, such agreements do not eliminate all risks associated with opioid prescribing, nor do they guarantee the absence of adverse outcomes. However, when used correctly, they can provide safeguards to reduce misuse and abuse. They also have the potential to preserve the patient-provider relationship, as opposed to providers cursorily refusing to prescribe opioids altogether. The term "controlled-substance agreement" is preferable to "pain contract" or "narcotic contract" as the latter 2 terms may feel stigmatizing and threatening.[30]

Risk evaluation and mitigation strategy (REMS). In an effort to ensure that benefits of opioid analgesics continue to outweigh the risks, the FDA approved the extended-release (ER)/long-acting (LA) opioid analgesics shared system REMS. Under this REMS, a consortium of ER/LA opioid manufacturers is mandated to provide prescriber education in the form of accredited continuing education and patient educational materials, available at https://opioidanalgesicrems.com/RpcUI/home.u.

CASE ▶

After reviewing Mr. G's chart and conducting a history, we learned that his bilateral knee osteoarthritis was atraumatic and likely due to overuse—although possibly affected by major trauma in a motor vehicle accident 5 years earlier. Imaging also revealed multilevel disc de-

TABLE 1
Validated pain assessment tools[9-13]

Type	Tool	Description	Validity	Advantages	Disadvantages
Unidimensional	Numerical Rating Scale (NRS)[9,10]	Self-report of pain level on a scale of 0 (no pain) to 10 (worst pain imaginable)	Validated and widely used	• Quick to administer • Easy for patients to understand • Can be given verbally	• Measures pain intensity only
	Verbal Rating Scale (VRS)[9,10]	Self-report to verbal questions, describing pain level using 5 descriptive categories	Correlates well with VAS (see below)[11]	• Quick to administer • Can be given verbally	• Subject to patient's interpretation of limited categories • Measures pain intensity only
	Visual Analog Scale (VAS)[9,10]	Self-report on a 100-mm line that indicates pain level	Validated and widely used	• Quick to administer • Easy for patients to understand	• Measures pain intensity only
Multidimensional	Brief Pain Inventory (BPI)[12]	Self-report of pain intensity and the impact of pain on daily functions	Validated and widely used	• Provides information on pain interference • Available in numerous languages	• More time consuming than unidimensional instruments
	Short-form McGill Pain Questionnaire (SF-MPQ-2)[13]	Self-report on 22 pain descriptors; patients score each on a scale of 0 to 10	Validated	• Provides information on subjective quality of pain	• More time consuming than unidimensional instruments

generation contributing to his radicular back pain, which seemed to be worse on days after working as a caterer. Poor lifting form at work may have contributed to his pain. Nevertheless, he had been consistent with medical follow-up and denied current or past use of illicit substances. Per the numeric rating scale (NRS), he reported 8 out of 10 pain in his knees and 6 out of 10 in his back. In addition to obtaining a PHQ-9 score of 4, we conducted a DIRE assessment and obtained a score of 19 out of a possible 21, indicating that he may be a good candidate for long-term opioid analgesia.

Criteria for prescribing opioids and for guiding treatment goals

Prescribing an opioid requires establishing a medical necessity based on 3 criteria:[31]

- pain of moderate-to-severe degree
- a physical diagnosis or suspected organic problem
- documented treatment failure of a noncontrolled substance, adjuvant agents, physician-ordered physical therapy, structured exercise program, and interventional techniques.

Treatment goals should be established and understood by the prescriber and patient prior to initiation of opioids.[28] Overarching treatment goals for all opioids prescribed are pain relief (but not necessarily a focus on pain scores), improvement in functional activity, and minimization of adverse effects, with the latter 2 goals taking precedence.[31]

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TABLE 2

PEG scale for assessing pain and function[32]

PEG score = average of 3 individual question scores
(30% improvement from baseline is clinically meaningful)

Q1: What number, from 0-10, best describes your pain in the past week?

0 = "no pain," 10 = "worst you can imagine"

Q2: What number from 0-10 best describes how, during the past week, pain has interfered with your enjoyment in life?

0 = "not at all," 10 = "complete interference"

Q3: What number from 0-10 describes how, during the past week, pain has interfered with your general activity?

0 = "not at all," 10 = "complete interference"

PEG, pain, enjoyment, general activity.

All pain management involving opioids should include nonpharmacologic components, such as exercise and weight loss.

To assess outcomes, formally measure progress toward goals from baseline evaluations. This can be achieved through repeated use of validated tools such as those mentioned earlier, or may be more broadly considered as progress toward employment status or increasing participation in activities.[31] All pain management plans involving opioids should include continued efforts with nonpharmacologic therapy (eg, exercise therapy, weight loss, behavioral training) and nonopioid pharmacologic therapy (eg, nonsteroidal anti-inflammatory drugs, tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, anticonvulsants).[28]

Have an "exit strategy." As part of goal setting, also consider how therapy will be discontinued if benefits do not outweigh the risks of harm.[28] Weigh functional status gains against adverse opioid consequences using the PEG scale (pain, enjoyment of life, and general activity) (**TABLE 2**[32]).[33] Improvements of 30% from baseline have been deemed clinically meaningful by some,[32] but not all benefits will be easy to quantify. At the start of treatment dialogue, use the term "therapeutic trial" instead of "treatment plan" to more effectively convey that opioids will be continued only if safe and effective, and will be prescribed at the lowest effective dose as one component of the multimodal approach to pain.[30]

Initiation of treatment: Opioid selection and dosing

When initiating opioid therapy, prescribe an immediate-release, short-acting agent instead of an ER/LA formulation.[28]

For moderate pain, first consider tramadol, codeine, tapentadol, or hydrocodone.[31] Second-line agents for moderate pain are hydrocodone or oxycodone.[31]

For severe pain, first-line agents include hydrocodone, oxycodone, hydromorphone, or morphine.[31] Second-line agents for severe pain are fentanyl and, with careful supervision or referral to a pain specialist, methadone or buprenorphine.[31]

Of special note, methadone should not be the first choice for ER/LA opioid due to its unique long half-life and ability to prolong the QT interval.[34] Only clinicians familiar with its use should prescribe methadone, while referring to the drug's clinical practice guideline for further advice.

At the start, prescribe the lowest effective dosage (referring to the product labeling for guidance) and calculate total daily dose in terms of morphine milligram equivalents (MME) (**TABLE 3**[35-37]).[28] Exercise caution when considering opioids for patients with respiratory sleep disorders and for patients ≥ 65 years due to altered pharmacokinetics in the elderly population.[38] Also make dose adjustments for renal and hepatic insufficiency (**TABLE 4**[35]).

Doses between 20 to 50 MME/d are considered relatively low dosages.[28] Be cautious when prescribing an opioid at any dosage, and reassess evidence of individual benefits and risks before increasing the dosage to ≥ 50 MME/d.[28] Regard a dosage of 90 MME/d as maximal.[28] While there is no analgesic ceiling,

TABLE 3

Commonly prescribed opioid dosing and morphine equivalence information[a, 35-37]

Medication	Opioid-naive patient initial dosing	MME[b] (equivalent to 1 mg PO morphine)	Dosage forms available
Morphine IR (mg)	Parenteral: 2-5 mg q4h Oral: 10-15 mg q4h	1	PO (ER/IR), rectal, intrathecal, epidural, IM, IV, SQ
Morphine ER (mg)	Oral: 15 mg q8-12h	1	PO (ER/IR)
Codeine (mg)	Parenteral: 10 mg q3-4h Oral: 15-60 mg q4h	0.15	PO (tablet/solution), IM, SQ
Hydrocodone bitartrate ER (mg)	Chronic oral: 10 mg q12h or 20 mg q24h	1	PO
Hydrocodone bitartrate/ acetaminophen (mg)	Oral: 5-10 mg q4-6h	1	PO
Hydromorphone (mg)	Parenteral: 0.2-1 mg q2-3h Oral: 2-4 mg q4-6h	4	PO (ER/IR), IV, PCA, epidural PCA, IM, SQ, rectal
Hydromorphone ER (mg)	Not indicated for use in opioid-naive patients	4	PO (ER/IR)
Oxycodone IR (mg)	Oral: 5-15 mg q4-6h	1.5	PO (tablet/capsule)
Oxycodone/acetaminophen (mg)	Oral: 5-15 mg q4-6h	1.5	PO (tablet/capsule)
Oxycodone ER (mg)	Oral: 10 mg q12h	1.5	PO (tablet/capsule)
Oxymorphone (mg)	Parenteral: 0.5 mg q4-6h Acute oral: 10-20 mg q4-6h Chronic oral: 5-10 mg q8-12h, or 5-10 mg q4-6h	3	IM, IV, SQ, PO (ER/IR)
Methadone (mg)	Not indicated for use in opioid-naive patients	0-20 mg = 4 21-40 mg = 8 41-60 mg = 10 > 60 mg = 12	IM, IV, SQ, PO
Meperidine (mg)	Not recommended for use in opioid-naive patients	0.1	IM, SQ, IV

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doses greater than 90 MME/d are associated with risk for overdose and should prompt referral to a pain specialist.[31] Veterans Administration guidelines cite strong evidence that risk for overdose and death significantly increases at a range of 20 to 50 MME/d.[33] Daily doses exceeding 90 MME/d should be documented with rational justification.[28]

CASE ▶

Noncontrolled medications are preferred in the treatment of chronic pain. However, the utility of adjuvant options such as NSAIDs, duloxetine, or gabapentin were limited in Mr. G's case due to his ESRD. Calcium channel $\alpha 2$-δ ligands may have been effective in reducing symptoms of neuropathic pain but would have had limited efficacy against osteoarthritis. Based on his low risk for opioid misuse, we decided to start Mr. G on oxycodone 2.5 mg PO, every 6 hours as needed for moderate-to-severe pain, and to follow up in 1 month. We also explained proper lifting form to him and encouraged him to continue with physical therapy.

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TABLE 3

Commonly prescribed opioid dosing and morphine equivalence information[a, 35-37] (*cont'd*)

Medication	Opioid-naive patient initial dosing	MME[b] (equivalent to 1 mg PO morphine)	Dosage forms available
Fentanyl buccal or SL tablets, or lozenge/troche (mcg)	Not indicated for use in opioid-naive patients	0.13	Buccal, SL tablets, or lozenge/troche
Fentanyl film or oral spray (mcg)	Not indicated for use in opioid-naive patients	0.18	Film or spray
Fentanyl nasal spray (mcg)	Not indicated for use in opioid-naive patients	0.16	Nasal spray
Fentanyl patch (mcg)	Not indicated for use in opioid-naive patients	7.2	Patch
Buprenorphine tablet (mg)	8 mg/d x 4 d; titrate to 16 mg/d	30	SL tablet
Buprenorphine patch (mcg/hr)	5 mcg/h, applied once weekly	12.6	Patch
Buprenorphine film (mcg)	75 mcg once daily or q12h	0.03	Film
Buprenorphine/naloxone	Buccal: 2.1/0.3 mg Sublingual: 2/0.5 mg	—	Film
Tapentadol (mg)	Oral: 50-100 mg q4-6h	0.4	PO (ER/IR)
Tapentadol ER (mg)	Oral: 50 mg bid	0.4	PO (ER/IR)
Tramadol (mg)	Oral: 50 mg q4-6h	0.1	PO (ER/IR)

ER, extended release; IM, intramuscular; IR, immediate release; IV, intravenous; PCA, patient-controlled analgesia; PO, by mouth; SL, sublingual; SQ, subcutaneous.

[a] This table is a reference and is not meant to supercede the treating provider's recommendations.
[b] MME (morphine milligram equivalents) is used for PO conversions.

Deciding to continue therapy with opioids

There is a lack of convincing evidence that opioid use beyond 6 months improves quality of life; patients do not report a significant reduction in pain beyond this time.[28] Thus, a repeat evaluation of continued medical necessity is essential before deciding in favor of ongoing, long-term treatment with opioids. Continue prescribing opioids only if there is meaningful pain relief and improved function that outweighs the harms that may be expected for a given patient.[31] With all patients, consider prescribing naloxone to accompany dispensed opioid prescriptions.[28] This is particularly important for those at risk for misuse (history of overdose, history of substance use disorder, dosages ≥ 50 MME/d, or concurrent benzodiazepine use). Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org. Due to the established risk of overdose, avoid, if possible, concomitant prescriptions of benzodiazepines and opioids.[31]

Follow-up and monitoring

Responsiveness to opioids varies greatly among individuals.[38,39] An opioid that leads to a therapeutic analgesic effect in one patient may cause adverse events or toxicity in another. Periodically reassess the appropriateness of chronic opioid therapy and modify

TABLE 4

Dosing considerations and adverse effects of common opioids[35]

Medication	Renal impairment dosing considerations	Hepatic impairment dosing considerations	Adverse effects
Morphine IR	None[a]	None[a]	CNS adverse effects, headache, respiratory depression, histamine release, hypotension, GI adverse effects, urinary retention
Morphine ER	None[a]	None[a]	CNS adverse effects, headache, respiratory depression, histamine release, hypotension, GI adverse effects, urinary retention
Hydromorphone	Consider 25%-50% of the starting dose depending on the impairment level. Monitor patient closely.	Consider 25%-50% of the starting dose depending on the impairment level. Monitor patient closely.	CNS adverse effects, respiratory depression, hypotension, phenanthrene hypersensitivity
Hydromorphone ER	**CrCl > 60 mL/min:** None[a] **CrCl 40-60 mL/min:** Consider 50% of the starting dose **CrCl < 30 mL/min:** Consider 25% of the starting dose	**Mild impairment:** None[a] **Moderate impairment:** Consider 25% of the starting dose **Severe impairment:** Use a different therapy	CNS adverse effects, respiratory depression, hypotension, phenanthrene hypersensitivity
Oxycodone IR	**CrCl ≥ 60:** None[a] **CrCl < 60:** Use lower end of dosage range or consider 33%-50% of starting dose	Consider 33%-50% of starting dose. Titrate slowly	CNS adverse effects, pruritus, headache, respiratory depression, GI adverse effects, fever, phenanthrene hypersensitivity
Oxycodone/ acetaminophen	IR: None[a] ER: 1 tablet q12h	IR: None[a] ER: 1 tablet q12h	Dizziness, GI adverse effects, rash, CNS adverse effects, respiratory depression, phenanthrene hypersensitivity
Oxycodone ER	**CrCl ≥ 60:** None[a] **CrCl < 60:** Use lower end of dosage range or consider 33%-50% of starting dose. If intended dose is smaller than available dosage, consider a different therapy	Consider 33%-50% of recommended dose If intended dose is smaller than available dosage, consider a different therapy	CNS adverse effects, pruritus, headache, respiratory depression, GI adverse effects, fever, phenanthrene hypersensitivity
Oxymorphone	**CrCl ≥ 50 mL/min:** None[a] **CrCl < 50 mL/min:** Use caution; bioavailability is increased **ER PO:** Opioid naive: 5 mg/dose Opioid experience: 50% lower than starting dose **IR PO:** 5 mg/dose Parenteral: Use a lower dose For all: Titrate slowly and monitor closely	**Mild impairment:** Use caution **ER PO:** Opioid naive: 5 mg/dose Opioid experience: 50% lower than starting dose **IR PO:** 5 mg/dose Parenteral: Use a lower dose For all: Titrate slow and monitor closely **Moderate-to-severe impairment:** Use is contraindicated	CNS adverse effects, pruritus, headache, respiratory depression, GI adverse effects, fever, phenanthrene hypersensitivity

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TABLE 4

Dosing considerations and adverse effects of common opioids[35] (*cont'd*)

Medication	Renal impairment dosing considerations	Hepatic impairment dosing considerations	Adverse effects
Hydrocodone bitartrate ER	**Mild impairment:** None[a] **Moderate-to-severe impairment:** Consider decreasing dose by 50%; titrate slowly and monitor closely **ESRD:** Consider decreasing dose by 50%; titrate slowly and monitor closely (manufacturer dependent)	**Mild-to-moderate impairment:** None[a] Consider decreasing dose by 50%, titrating slowly, and monitoring closely **Severe impairment:** Consider decreasing dose by 50%, titrating slowly, and monitoring closely; or start at 10 mg q12h and monitor closely or avoid (manufacturer dependent)	GI adverse effects, CNS adverse effects, respiratory depression, hypertension, phenanthrene hypersensitivity
Hydrocodone bitartrate/ acetaminophen	None[a]	None[a]	GI adverse effects, CNS adverse effects, respiratory depression, phenanthrene hypersensitivity
Codeine	None[a]	None[a]	GI adverse effects, CNS adverse effects, respiratory depression, hypertension, histamine release, rash, phenanthrene hypersensitivity
Methadone	None[a]	None[a]	QTc prolongation, CNS adverse effects, respiratory depression, GI adverse effects, rash
Meperidine	Avoid use in impairment	None[a]	CNS adverse effects, respiratory depression, histamine release, hypotension, anaphylaxis, GI adverse effects
Fentanyl	None[a]	None[a] **Patch** **Mild-to-moderate impairment:** Reduce dose by 50% **Severe impairment:** Avoid use	CNS adverse effects, headache, dehydration, dyspnea, muscle weakness, application site erythema, respiratory depression

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treatment based on its ability to meet therapeutic goals. While practice behaviors and clinic policies vary across institutions, risk stratification can provide guidance on the frequency and intensity of follow-up and monitoring. Kaye et al[21] describe a triage system in which low-risk patients may be managed by a primary care provider with routine follow-up and reassessment every 3 months.[21] Moderate-risk patients may warrant additional management by specialists and a monthly follow-up. High-risk patients may need referrals to interdisciplinary pain centers or addiction specialists.[21]

Along these lines, the CDC recommends conducting a PDMP review and UDT before initiating therapy, followed by a periodic PDMP (every 1-3 months) and a UDT *at least* annually. Keep in mind, providers should follow their state-specific regulations, as monitoring requirements may vary. In addition, clinicians should always be alert to adverse reactions (**TABLE 4**[35]) and sudden behavior changes such as respiratory depression, nausea, constipation, pruritus, cognitive impairment, falls, motor vehicle accidents, and aberrant behaviors. Under these circumstances, consider a dose reduction and, in certain cases, discontinuation.

Additionally, in cases of pain unre-

TABLE 4

Dosing considerations and adverse effects of common opioids[35] (*cont'd*)

Medication	Renal impairment dosing considerations	Hepatic impairment dosing considerations	Adverse effects
Buprenorphine	None[a]	**Patch** None[a] **Sublingual** **Mild and moderate impairment:** None[a] **Severe:** Consider decreasing start and titration doses by 50% **Buccal** **Mild and moderate impairment:** None[a] **Severe:** Consider decreasing start and titration doses by 50%	CNS adverse effects, hypertension, hypotension, anemia, nausea, GI adverse effects
Buprenorphine/ naloxone	None[a]	**Mild impairment:** None[a] **Moderate impairment:** Caution with maintenance dosing **Severe impairment:** Avoid use	Headache, pain, GI adverse effects, vasodilation, palpitations, insomnia, withdrawal syndrome
Tapentadol	Avoid use in severe impairment	Avoid use in severe impairment	CNS adverse effects, GI adverse effects, pruritus
Tapentadol ER	Avoid use in severe impairment	Avoid use in severe impairment	CNS adverse effects, GI adverse effects, pruritus
Tramadol	**IR:** **CrCl ≥ 30 mL/min:** None[a] **CrCl < 30:** Use q12h dosing schedule **ER:** **CrCl ≥ 30 mL/min:** None[a] **CrCl < 30:** Use is discouraged	**IR:** None[a] If patient has cirrhosis: 50 mg q12h **ER:** **Mild impairment:** None[a] **Moderate-to-severe impairment:** Use is discouraged	Respiratory depression, muscle weakness, CNS adverse effects, GI adverse effects, flushing, diaphoresis,

CNS, central nervous system; CrCl, creatinine clearance; ER, extended release; ESRD, end-stage renal disease; GI, gastrointestinal; IR, immediate release.

[a] Manufacturer's label makes no specific dosage adjustment recommendations. However, some articles in the literature recommend starting at very low doses, titrating upward slowly, and closely monitoring the patient.

sponsive to escalating opioid doses, include opioid-induced hyperalgesia (OIH) in the differential. Dose reductions, opioid rotations, and office-based detoxifications are all options for the treatment of OIH.[40] Assessment of pain and function can be accomplished using the PEG scale (**TABLE 2**).[32]

CASE ▶

Two weeks into Mr. G's initial regimen, he called to report no change in pain or functional status. We increased his dose to 5 mg PO every 6 hours as needed. At his 1-month follow-up appointment, he reported his pain as 6/10 and no adverse effects. We again increased his dose to 10 mg PO every 6 hours as needed, with follow-up in another month.

Discontinuation and tapering of opioids

Indications for discontinuing opioids are patient request, resolution of pain, doses

TABLE 5

Recommendations for discontinuing and tapering opioids[1,31,41,43,44]

1. Engage the patient in all discussions regarding discontinuation/tapering.
2. Consider switching patient from IR to ER opioids on a fixed-dose schedule to assist some patients in adhering to the taper/discontinuation plan.
3. Collaborate with a multidisciplinary team to assist with scheduling dose reductions.
4. Gradually reduce 5%-10% of the original MME every 1-4 weeks until 30% of the original dose is reached, followed by a weekly reduction of 10% of the remaining dose.
5. Increase the taper rate when opioid doses reach a low level (eg, < 15 mg/d MME), since formulations of opioids may not be available to allow smaller decreases.
6. Use a schedule for tapering, including planned dates, doses, frequency, total dose/d, and quantities that will be required for the prescription.
7. Do not reverse the taper in cases of withdrawal symptoms; rate may be slowed or paused while monitoring for and managing withdrawal symptoms.
8. Manage opioid abstinence syndrome with clonidine 0.1-0.2 mg orally every 6 h or transdermal clonidine patch 0.1 mg/24 h weekly during the taper.

Additional resource:
www.cdc.gov/drugoverdose/pdf/clinical_pocket_guide_tapering-a.pdf

IR, immediate release; ER, extended release; MME, morphine milligram equivalents.

Methadone should not be the first choice for an extended-release/long-acting opioid due to its long half-life and ability to prolong the QT interval.

≥ 90 MME/d (in which case a pain specialist should be consulted), inadequate response, untoward adverse effects, and abuse and misuse.[1,31,41] However, providers may also face the challenge of working with patients for whom the benefit of opioid therapy is uncertain but who do not have an absolute contraindication. Guidance on this matter may be found in a 2017 systematic review of studies on reducing or discontinuing long-term opioid therapy.[42] Although evidence on the whole was low quality, it showed that tapering or discontinuing opioids may actually reduce pain and improve function and quality of life.

When working with a patient to taper treatment, consider using a multidisciplinary approach. Also, assess the patient's pain level and perception of needs for opioids, make clear the substantial effort that will be asked of the patient, and agree on coping strategies the patient can use to manage the taper.[31,43] While the evidence does not appear to support one tapering regimen over another, we can offer some recommendations on ways to individualize a tapering regimen (**TABLE 5**).[1,31,41,43,44]

General recommendations. Gradually reduce the original MME dose by 5% to 10% every week to every 4 weeks, with frequent follow-up and adjustments as needed based on the individual's response.[1,31,41,43] In the event that the patient does not tolerate this dose-reduction schedule, tapering can be slowed further.[31] Avoid abrupt discontinuation.[33] Opioid abstinence syndrome, a myriad of symptoms caused by deprivation of opioids in physiologically dependent individuals, although rare, can occur during tapering and can be managed with clonidine 0.1 to 0.2 mg orally every 6 hours or transdermal clonidine patch 0.1 mg/24 hours weekly during the taper.[31]

Tapering of long-term opioid treatment is not without risk. Immediate risks include withdrawal syndrome, hyperalgesia, and dropout, while ongoing issues are potential relapse, problems in increasing and maintaining function, and medicolegal implications.[43] Withdrawal symptoms begin 2 to 3 half-lives after the last dose of opioid, and resolution varies depending on the duration of use, the most recent dose, and speed of tapering.[43] In general, a patient needs 20% to 25% of the previous day's dose to prevent withdrawal symptoms.[31] Increased pain appears to be a brief, time-limited occurance.[43] Dropout and relapse tend to be attributed to

TABLE 6

Elements of optimal opioid prescribing[14,22-24,28,30-32]

1. Gather patient history (include patient interview) and conduct a physical exam.
2. Assess pain.
3. Employ risk-mitigation strategies.
4. Confirm use of prescribed and illicit substances using PDMP and UDT.
5. Clarify indications for opioid therapy and medical necessity.
6. Enact a controlled-substance agreement with the patient.
7. Set goals and optimize nonopioid and nonpharmacologic modalities.
8. Initiate appropriate agents at appropriate doses (prescribe naloxone to accompany opioid prescriptions).
9. Follow-up, monitor, and evaluate progress toward goal of therapy.
10. Discontinue therapy when indicated and follow tapering regimen.

UDT, urine drug testing; PDMP, prescription drug monitoring program.

patient factors such as depressive symptoms and higher pain scores at initiation of the taper.[43] Low pain at the end of tapering has been shown to predict long-term abstinence from opioids.[43]

CASE ▶

Two months into his oxycodone regimen, Mr. G reported improved functional status at his catering job and overall improved quality of life. He had improved his lifting form and was attending biweekly physical therapy sessions. His pain score was 3/10. He expressed a desire to "not get hooked on opioids," and mentioned he had "tried stopping the medicine last week" but experienced withdrawal symptoms. We discussed and prescribed the following 5-week taper plan: 2.5 mg reduction of oxycodone per dose, every 2 weeks x 2. Then 2.5 mg PO every 6 hours as needed x 1 week before stopping.

Organizing your approach

To optimize the chance for success in opioid treatment and to heighten vigilance and minimize harm to patients, we believe an organized approach is key (**TABLE 6**[14,22-24,28,30-32]), particularly since this class of medication lacks strong evidence to support its long-term use. JFP

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As part of goal setting, consider how therapy will be discontinued if benefits do not outweigh the risks of harm.

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