Appropriate Use of Opioids in Managing Chronic Pain

A review of best practices for alleviating suffering, while avoiding risks.

ABSTRACT: Over the past two decades, the use of opioids to manage chronic pain has increased substantially, primarily in response to the recognized functional, emotional, and financial burden associated with chronic pain. Within this same period, unintentional death related to prescription opioids has been identified as a public health crisis, owing in part to such factors as insufficient professional training and medication overprescription, misuse, and diversion. The authors discuss current best practices for prescribing opioids for chronic pain, emphasizing patient assessment and essential patient teaching points regarding safe medication use, storage, and disposal.

Keywords: chronic pain, opioids, pain, prescription drug abuse, prescription drug diversion

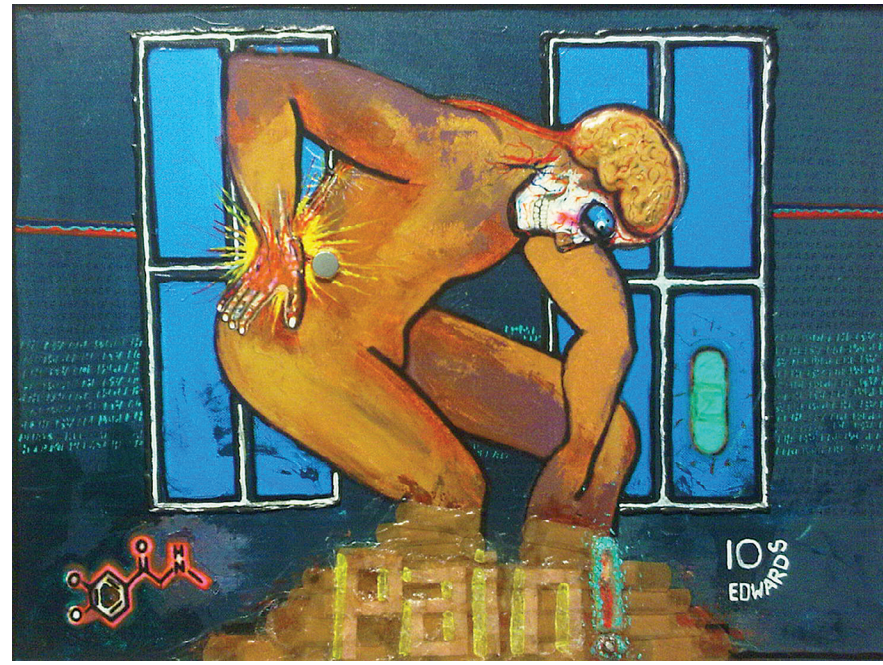
Chronic pain, also known as persistent pain, is any pain that continues beyond the period over which healing would normally occur (generally three to six months) and affects a person's function or quality of life.[1] Chronic pain includes persistent pain related to injury, surgery, or conditions such as arthritis, vascular insufficiency, cancer treatment–related neuropathy, or diabetic peripheral neuropathy. According to a 2015 study by the National Institutes of Health's National Center for Complementary and Integrative Health, an estimated 126 million U.S. adults have varying degrees of pain, ranging in persistence from "some days" to "every day" and in intensity from "a little" to "a lot."[2] Nearly 40 million of them experience the highest levels of pain intensity—categories 3 and 4 on the Washington Group on Disability Statistics' pain severity coding system, in which category 1 represents least severe pain and category 4 represents most severe pain—on "most days" or "every day."[2] In addition to the tremendous physical and emotional suffering chronic pain causes, it is also a significant public health problem that places an enormous financial burden on patients, their families, their employers, and health care systems.

In response to the recognized functional, emotional, and financial burden associated with chronic pain, the use of opioids in its management has increased substantially over the past two decades, with some opioid medications ranking among the most prescribed drugs in the United States.[3] Within this same period, unintentional death related to prescription opioids has been identified as a public health crisis.

While chronic pain can be alleviated through effective and compassionate treatment, it is rarely eliminated entirely. Treatment options may include nonpharmacologic modalities, such as physical therapy and cognitive–behavioral training; nonopioid analgesics; adjuvant medications, such as anticonvulsants and antidepressants; injection therapies, including trigger-point injections, large joint injections, and epidural steroid injections; central nervous system

stimulation; and, for carefully selected patients whose chronic pain and functional status does not improve with nonopioid therapies, opioids.

Although prescription opioids have been associated with misuse, abuse, diversion, and unintentional death, this is in part owing to such factors as insufficient provider education and professional training.[4] To address this problem, numerous organizations have published guidelines or position papers on the safe prescribing of opioids for chronic pain.[5-13] This article discusses current best practices for prescribing opioids for chronic pain, highlighting recent guideline recommendations. It emphasizes patient assessment and essential patient teaching points regarding safe medication use, storage, and disposal; describes potential adverse effects of opioids; and explains how to mitigate risk and promote adherence among patients using opioids to alleviate chronic pain.



This powerful expression of chronic pain was painted by patient Martin Edwards as part of the Paint Your Pain program initiated by the Pain Management Center at Overlook Medical Center, Atlantic Health System, Summit, New Jersey. To see the artwork of other patients in the program, go to http://bit.ly/1Ns0PxL.

UNDERSTANDING CHRONIC PAIN

Acute pain alerts the patient to risk of tissue damage or injury. Chronic pain may start with an acute pain episode that persists long beyond the time of expected healing, or it may occur spontaneously, as is the case with fibromyalgia and various types of neuropathy. In either case, chronic pain may cause permanent damage to the nervous system. Patients with chronic pain are often socially isolated and stigmatized; they have more disability than the general population, and their pain is often inadequately managed.[5]

While guideline recommendations for using opioids to treat chronic pain differ in some respects, most agree on general assessment and management principles, noting that opioids remain a necessary option for managing chronic pain in selected patients and that they should be used not as monotherapy, but as part of a comprehensive multimodal plan of care that includes nonpharmacologic interventions and nonopioid medications as first-line therapy (see *General Guidelines for Assessing and Managing Chronic Pain*[5-13]). The goal of chronic pain management is to achieve improvements in both pain intensity and functional status, with the emphasis on functional improvement. Both initial and ongoing comprehensive assessments are essential to appropriate chronic pain management.

ASSESSING PATIENTS WITH CHRONIC PAIN

Initial and follow-up assessments are often a nursing responsibility. In addition to performing a complete physical examination and taking a thorough medical, psychosocial, and mental health history, the initial assessment of patients with chronic pain should include detailed questions about the following:

- pain location, quality, and intensity
- pain relief provided by all treatment interventions, both pharmacologic and nonpharmacologic
- effects of pain on the patient
- history of substance use disorders
- current and past functional abilities
- adverse effects of current treatments
- ability to perform activities of daily living, such as driving, working, going to school, performing housework, exercising, walking long distances, and climbing stairs
- psychiatric history
- quality of sleep, mood, and energy

People with chronic pain commonly report having difficulty falling asleep and maintaining sleep. They often experience fatigue and daytime drowsiness. Patients who report poor quality of sleep also tend to report significantly higher pain intensity.[14] Early identification and treatment of sleep disorders

General Guidelines for Assessing and Managing Chronic Pain[5-13]

Consider the use of opioid medications for chronic pain only when

- the benefits clearly outweigh the risks.
- nonopioid therapies do not provide adequate pain relief and improve function.
- they are used as part of a comprehensive pain management plan that includes nonpharmacologic therapy and, if appropriate, nonopioid pharmacologic therapy.

Before prescribing opioid therapy,

- obtain and record a complete patient history, including medical, psychosocial, functional, family, mental health, and medication considerations.
- consult the state's prescription drug monitoring program (PDMP) to determine the patient's history of past opioid prescriptions or other prescribed drugs that may interact adversely with opioids or increase the risk of overdose. If opioid therapy is prescribed, review PDMP data on a regular basis. (Guideline recommendations vary as to optimal frequency of PDMP review.)
- conduct a thorough physical examination, review past test and imaging results, and obtain additional tests as indicated. Contact previous or current providers who may have relevant information about the patient's care.
- evaluate and document the risks of misuse or abuse of opioids, including alcohol and drug use by both the patient and family members.
- document one or more clinically recognized indications for prescribing opioids.
- identify and document specific, measurable treatment goals for improvement in pain and function.
- discuss its known risks and benefits, as well as patient and provider expectations and responsibilities for ensuring safe administration. Document the content of the discussion in a printed patient–provider agreement that specifies the need for random, periodic urine drug testing; policies for refills and dose adjustments; and the importance of adhering to all aspects of the multimodal plan.

Begin opioid therapy

- as a trial with an exit plan if treatment goals are not met.
- using the lowest effective dose of an immediate-release rather than an extended-release or long-acting opioid and increase the dose only if pain relief is determined to be insufficient, and clear and objective outcomes can be achieved at a higher dose. (Guideline recommendations vary as to the dosage level at which prescribers should exercise greater caution, with suggested levels ranging from 50 to 200 morphine milligram equivalents per day.)
- with the understanding that therapy can continue only as long as measurable outcomes and expectations, including functional goals, are met.

Assess and document outcomes within four weeks of starting therapy, prior to any dose escalation, and at least every three months thereafter.

Avoid prescribing opioids for chronic pain in patients concurrently using benzodiazepines.

Monitor patients prescribed long-term opioid therapy for

- analgesic efficacy.
- function.
- adverse effects.
- aberrant behavior.
- safe use of the medication.

Consult with a pain specialist through a telemedicine program or by phone, or refer patients for consultation with a pain specialist,

- any time problems arise that cannot be readily solved between provider and patient.
- if recommended or required by state guidelines.

For patients with chronic pain who have difficulty using prescribed opioids safely:

- Remain nonjudgmental.
- Do not discharge the patient from care.
- Try increasing monitoring and support through more frequent clinical visits or by involving social work or counseling services.
- Offer referral for medication-assisted treatment if indicated and available.

can minimize the risk of medication misuse during opioid therapy.

Improved function and quality of life is the focus of follow-up visits. At every subsequent visit throughout treatment, patients with chronic pain should be questioned about

- any changes in pain level, location, or quality.
- any changes in medications.
- adherence to the management plan.
- adverse effects of opioids, particularly constipation.
- personal health.
- mood, sleep, and functional status.
- adverse health behaviors.

Valid and reliable assessment tools can help nurses identify the effects of pain on the patient; track progress during treatment; evaluate adherence to medications; and recognize misuse, overuse, or illicit use. These include the following:

- the Two-Item Graded Chronic Pain Scale, which is used to assess patient perception of both pain intensity and impact of pain on function (see Figure 1)[13]
- the Brief Pain Inventory[15]
- the Pain Assessment and Documentation Tool, available at www.prescriberesponsibly.com/sites/default/files/pdf/pain/PADT.pdf
- the Quality of Life Scale, which measures function in people with chronic pain, available from the American Chronic Pain Association at http://theacpa.org/uploads/documents/Quality_of_Life_Scale.pdf

When patients report unrelieved pain, the possibility of a new or progressive problem should be considered and fully evaluated.

POTENTIAL ADVERSE EFFECTS OF OPIOIDS

Opioid-induced constipation is nearly universal and does not diminish with time. For most patients, management requires regular use of a stimulant or osmotic laxative as well as a stool softener. Patient teaching should include a plan to prevent and treat constipation. Sedation, nausea, and urinary retention may also occur when opioid therapy is initiated, but these effects usually diminish with time.

Long-term opioid use may cause some patients to exhibit symptoms of hypogonadism[16] or to become more sensitive to painful stimuli, a condition known as opioid-induced hyperalgesia.[17-19] Decreases in testosterone and estrogen may adversely affect sexual drive and function and have long-term negative effects on muscle mass and bone density. Less common adverse effects include delirium, hallucinations, delayed gastric emptying, bowel obstruction, immunologic and hormonal dysfunction, and muscle rigidity or myoclonus. These potential problems should be discussed with the patient when obtaining informed consent. Both patient education and family support and education are essential to minimizing adverse events when managing chronic pain (see *Enlisting Family Support*).

Physical dependence is an adaptation to a drug that manifests in withdrawal symptoms upon the drug's abrupt cessation or rapid dose reduction.[20] Physical dependence is an expected effect of opioid therapy and also occurs with many other psychoactive drugs, such as antidepressants and benzodiazepines. If a person taking opioids stops the medication abruptly, symptoms of withdrawal will occur within approximately 12 hours. When opioids are no longer

Figure 1. The Two-Item Graded Chronic Pain Scale

Graded chronic pain scale: a two-item tool to assess pain intensity and pain interference

In the last month, on average, how would you rate your pain? Use a scale from 0 to 10, where 0 is "no pain" and 10 is "pain as bad as could be." [*That is, your usual pain at times you were in pain.*]

No pain										Pain as bad as could be
0	1	2	3	4	5	6	7	8	9	10

In the last month, how much has pain interfered with your daily activities? Use a scale from 0 to 10, where 0 is "no interference" and 10 is "unable to carry on any activities."

No interference										Unable to carry on any activities
0	1	2	3	4	5	6	7	8	9	10

Reprinted from the Washington State Agency Medical Directors' Group. *Interagency Guideline on Prescribing Opioids for Pain*. 3rd edition; June 2015.[13]

Enlisting Family Support

- Encourage family involvement in pain management in a manner consistent with Health Insurance Portability and Accountability Act (HIPAA) regulations.
- Ensure that patients and their families have realistic expectations for opioid therapy. Patients rarely achieve more than a 30% to 50% reduction in chronic pain through opioid therapy alone.
- Remind patients and family members that multimodal plans of care, including self-care strategies and nonpharmacologic interventions, are most effective.
- Include family members in discussions of the patient's function, mood, activity, and progress toward specific goals.
- Identify and address patient and family concerns regarding adherence to the treatment plan.

indicated, slowly tapering off the drugs will prevent withdrawal symptoms.

Opioid tolerance. Tolerance to sedation, nausea and vomiting, euphoria, and anxiolytic effects of opioids develops rapidly.[21] Tolerance develops more slowly to the analgesic effects of opioids, but when it occurs, it results in less analgesic efficacy.[21] Tolerance can develop regardless of the route, dose, or type of opioid. A thorough assessment is indicated any time a patient requests a dose increase. Ask the patient whether there is a new problem causing the pain, if the pain has worsened, or if the opioid is being used for purposes other than analgesia, such as for sleep problems or reducing anxiety, both of which are best treated with other strategies. Depending on the patient's particular problem, the dosage may be increased within recommended levels, the opioid may be changed, or the nonpain symptoms (of insomnia or anxiety) may be managed by other means. When one opioid is exchanged for another, cross-tolerance is rarely complete. The change may result in greater efficacy at lower doses. To avoid adverse effects, exercise caution when changing opioid medications, dosage, or scheduling and do so only after a thorough patient reassessment.

Opioid withdrawal. Any person taking opioids for several weeks or longer may experience symptoms of withdrawal (also called opioid abstinence syndrome) if the opioid dosage is rapidly decreased or if opioids are abruptly stopped. Opioid withdrawal is characterized by sympathetic arousal with elevated heart rate and blood pressure, pupillary dilation, goose bumps, anxiety, jittery behavior, and additional symptoms such as nausea, diarrhea, runny nose, yawning, myalgia, and insomnia. Symptoms of withdrawal are treated by resuming opioid therapy at a lower dose and providing a less drastic tapering schedule, or with an α-blocking agent, such as clonidine (Catapres and others).[22]

Opioid-induced hyperalgesia occurs when repeated or prolonged exposure to opioids makes the person increasingly sensitive to painful events or causes the chronic pain to intensify, spread, change in quality, or increase in frequency. The prevalence and underlying mechanisms of opioid-induced hyperalgesia are largely unknown. It is suspected when increases in opioid doses are paradoxically accompanied by an increase in pain or by the pain becoming more diffuse and less manageable.[18,21,23] It differs from opioid tolerance in this respect. The treatment for opioid-induced hyperalgesia is to gradually reduce the opioid dose while transitioning the patient to an effective nonopioid alternative.[23]

DRUG–DRUG INTERACTIONS

All opioids can cause respiratory depression and thus present a potential risk of unintentional overdose and death due to respiratory failure. For this reason, providers are advised to initiate opioid therapy at the lowest effective dose, titrate the dose upward slowly as necessary, and advise patients of the risks of mixing opioids with other sedating drugs, such as benzodiazepines, carisoprodol (Soma), zolpidem (Ambien and others), butalbital (found in some combination headache medications, including Fiorinal), gabapentin (Neurontin and others), pregabalin (Lyrica), hydroxyzine (Vistaril and others), promethazine (Phenadoz and others), and alcohol. Such combinations raise the risk of falls, accidents, cumulative sedation, hypoventilation, and unintentional death.

Methadone (Dolophine and others) interacts with a number of other drugs.[24,25] Phenytoin (Dilantin and others), carbamazepine (Tegretol and others), rifampin (Rifadin), erythromycin (Eryc and others), and several antiviral agents increase methadone metabolism, thereby decreasing circulating drug levels and, potentially, efficacy, and possibly bringing on symptoms of withdrawal. Antifungal drugs and selective serotonin reuptake inhibitors or tricyclic antidepressants may increase methadone levels, causing adverse events.[26] High doses of methadone alone or moderate doses in combination with other potentially cardiotoxic medications may be associated with QT prolongation and torsades des pointes, which is potentially fatal. Specific classes of drugs associated with QT prolongation include antiarrhythmic medications, antihistamines, fluoroquinolones, macrolide antibiotics, tricyclic antidepressants, and antipsychotics. Because of this risk, a baseline electrocardiogram should be performed at the start of methadone therapy and periodically throughout treatment, accompanied by frequent assessment and monitoring.[25]

Tramadol (Ultram, ConZip), a partial opioid agonist, also has norepinephrine and serotonergic properties. In combination with other serotonergic drugs, tramadol may precipitate the serious adverse effect of serotonin syndrome. Patients should be fully informed

of this risk, particularly when adding or increasing the dose of any serotonergic drug.

MANAGING RISK AND PROMOTING ADHERENCE

Initial opioid risk assessment. Current recommendations and U.S. Food and Drug Administration (FDA) opioid labeling suggest that, for chronic pain, opioid therapy should be administered only to patients whose pain is moderate to severe and unmanageable without it. Other medications and modalities should be tried and optimized first. Before deciding to initiate a trial of opioid therapy or to continue using opioid therapy as a component in the care plan of a patient with chronic pain, it's necessary to conduct a thorough risk assessment of the patient's ability to use opioids safely. Opioid risk screening tools, such as the Opioid Risk Tool (ORT), may be helpful in determining the type and intensity of monitoring the patient requires and the patient's need for referral to additional supportive services. The ORT is a simple, validated, five-question survey that may be used to stratify patients into categories of low, moderate, and high risk before starting therapy (see Figure 2).[27,28] The patient's initial risk category should always be modified to incorporate actual

Figure 2. The Opioid Risk Tool

		Mark each box that applies	Item Score If Female	Item Score If Male
1. Family History of Substance Abuse	Alcohol	[ ]	1	3
	Illegal Drugs	[ ]	2	3
	Prescription Drugs	[ ]	4	4
2. Personal History of Substance Abuse	Alcohol	[ ]	3	3
	Illegal Drugs	[ ]	4	4
	Prescription Drugs	[ ]	5	5
3. Age (Mark box if 16 – 45)		[ ]	1	1
4. History of Preadolescent Sexual Abuse		[ ]	3	0
5. Psychological Disease	Attention Deficit Disorder	[ ]	2	2
	Obsessive Compulsive Disorder			
	Bipolar Schizophrenia			
	Depression	[ ]	1	1
TOTAL		[ ]		
Total Score Risk Category	Low Risk 0 – 3	Moderate Risk 4 – 7		High Risk ≥ 8

Reprinted from the Washington State Agency Medical Directors' Group. *Interagency Guideline on Opioid Dosing for Chronic Non-Cancer Pain, 2010 Update*. http://www.agencymeddirectors.wa.gov/files/opioidgdline.pdf.

behavior over the course of opioid therapy, as ORT results may be misleading.[29] For example, a patient with a very distant history of recreational cocaine use whose family history includes alcohol dependence would be identified as high risk on the ORT. This same patient, however, may demonstrate excellent adherence to opioid therapy over time, and this should be acknowledged. By the same token, patients who are initially assessed as low risk on the ORT but demonstrate high-risk behaviors over the course of opioid therapy should be monitored more frequently.

Other validated screening tools that may be used before initiating a trial of opioids include the revised Screener and Opioid Assessment for Patients with Pain[30] and the Diagnosis, Intractability, Risk, Efficacy Score.[31] For patients currently receiving opioid therapy, the Current Opioid Misuse Measure may be used to monitor and document continued medication adherence.[32]

Opioid agreements. Several guidelines recommend the use of opioid agreements when opioids are considered for patients with chronic pain.[9, 10, 13, 21] These agreements specify expectations such as, that the patient

- will obtain opioids from a single provider and a named pharmacy.
- understands that medication refills will be limited, even in the case of loss or theft.
- will take medications exactly as prescribed, without unauthorized dose escalation.
- will safeguard medications and prescriptions at all times, never sharing or allowing others access to the medications.
- will meet agreed-upon expectations for regular follow-up visits, random urine drug testing, pill counts, and other risk management requirements.

Both the prescriber and patient review and sign the agreement, which serves as an educational tool, a written reminder of mutual expectations, and a way to build patient and provider trust. Sample agreements may be found at: www.lni.wa.gov/Forms/pdf/F252-095-000.pdf and www.aafp.org/fpm/2001/1100/fpm20011100p47-rt1.pdf.

Patients are encouraged to make appointments to discuss any problems they have following the plan, and they are expected to tell other providers that they have an opioid agreement so as to avoid confusion should another provider inadvertently prescribe another opioid. Deviations from the agreement require a discussion between the provider, patient, and family to review the plan and determine the reasons for nonadherence. Depending on the patient's adherence history and the severity of any aberrant behavior, consequences for a one-time deviation may range from additional education and support with more frequent monitoring to discontinuation of opioid therapy. If it is determined that the patient should stop opioid therapy, she or he should not be discharged from care, but should be offered nonopioid pain management options.

Random urine drug testing is used to determine whether patients are taking prescribed medications as directed and not illicit or prescription drugs that have not been prescribed. Random urine testing is requested at unpredictable intervals one to four times per year, depending on the patient's risk stratification. Some practices computerize the randomization for low-risk patients and adhere to more vigilant and frequent testing for those at moderate or high risk. Urine drug panels are not all the same. When testing a patient's urine for adherence to the treatment plan, the test panel should include illicit drugs, controlled medications, and the specific medications that are prescribed. Urine testing may also detect cannabinoids and alcohol.[33]

Initial screening is usually accomplished with a urine dipstick point-of-care test called an immunoassay. Patients are not usually observed or monitored while giving specimens in primary care settings. Drug screening should be seen as a routine test and a normal part of care for all patients taking opioids. An immunoassay identifies only general classes of drugs rather than specific drugs. Results are reported as either positive or negative. Both false-positive and false-negative results are common with immunoassay testing. It is inappropriate to draw conclusions or confront patients about nonadherence based on immunoassay results alone. When immunoassay results do not conform to expectations, confirmatory testing using highly reliable and drug-specific gas chromatography–mass spectrometry or liquid chromatography–tandem mass spectrometry testing at outside laboratories is required. When such testing is treated and explained as a universal part of the evaluation process, rather than as one in which certain patients are singled out, most patients are cooperative. Providers must know how to correctly interpret the results. Communication with the testing laboratory is essential.

When a confirmatory test shows unexpected results, the patient should be seen in person to discuss the results and the possible reasons for the surprise findings. A positive, supportive approach that keeps the patient engaged in care is most helpful. When correctly interpreted and confirmed, red flag results include those that are

- negative for prescribed medications, suggesting that patients are not taking their medications because of a misunderstanding of directions, nonadherence, diversion, sharing or selling medications, unreported lost or stolen medications, or early overuse and depletion.
- positive for controlled medications that are not prescribed, suggesting that patients are taking unauthorized medications or obtaining medications from multiple sources.
- positive for illicit drugs.

Table 1. Commonly Prescribed Oral and Transdermal Opioids Used in the Treatment of Chronic Pain

Classification	Generic Name	Trade Names and Formulations		
		Immediate release	Extended release	Transdermal patch
Agonists	Morphine	Morphine, MSIR	Morphine ER, Avinza, Kadian, MS Contin, Embeda (with naltrexone)	
	Hydromorphone	Dilaudid	Exalgo	
	Hydrocodone	Norco (with APAP), Vicodin (with APAP)	Zohydro, Hysingla	
	Oxycodone	Percocet (with APAP), Endocet (with APAP), Roxicet (with APAP)	OxyContin, Xartemis XR (with APAP)	
	Oxymorphone	Opana	Opana ER	
	Methadone	Dolophine, Methadose (has long-acting properties)		
	Fentanyl			Duragesic (48–72 hour)
Partial agonists	Buprenorphine			Butrans (7 day)
Atypical partial agonists	Tramadol	Ultram, Ultracet (with APAP)	Ultram ER, ConZip	
	Tapentadol	Nucynta	Nucynta ER	

APAP = acetaminophen.

If the confirmatory test is positive for illicit drugs, the provider may choose to increase supervision and support for the patient to continue to use opioids or decide that the patient should taper off of opioids safely and rely on other strategies for pain management. Referral for addiction services is indicated in some cases.

Prescribers may immediately discontinue opioids or begin tapering opioids to discontinuation if there is credible evidence that a patient is

- selling the medications.
- forging prescriptions.
- getting opioids dishonestly from several providers.
- making aggressive or threatening demands during clinic visits or by phone.
- persistently using nonprescribed medications, illicit drugs, or alcohol.
- persistently losing medications, running out early, or sharing medications with family members or others.

Tapering opioids is best conducted under the supervision of a knowledgeable provider.

Pill counts. Pill or patch counts performed at regular visits or at random are another means of monitoring adherence. For the count, patients should bring their medications in the containers in which they were dispensed. A random pill count may uncover poor adherence for a variety of reasons, including financial difficulty obtaining the medications, poor understanding of the care plan, misuse, or diversion. A pill count may reveal that a patient is taking more than has been prescribed because of increasing pain, running out early, and then "toughing it out" until the next prescription.

Prescription drug monitoring programs (PDMPs) are electronic databases through which providers licensed by the U.S. Drug Enforcement Administration (DEA) have access to information on when, where, and by whom prescriptions are dispensed for their patients. These programs collect information on controlled medications dispensed by pharmacies throughout the state. At press time, all states but Missouri have operational PDMPs,[34, 35] and the Prescription Monitoring Information Exchange (PMIX) provides a platform through which PDMPs may exchange data across state borders, giving clinicians an even broader look at patients' prescription-filling histories,[36] though the operation and complexity of PDMPs vary from state to state. Any unexpected findings revealed through access to a PDMP or PMIX should prompt a patient visit and conversation, as data entry errors may occur and names can be entered in multiple ways.

Medication safety, storage, and disposal. Patient education should include proper security and disposal of unused medications. Between 2012 and 2013, prescription pain relievers used for nonmedical reasons were most frequently obtained from friends or relatives for free.[37] Patients receiving controlled medications such as opioids are responsible for keeping their medications secure at all times—safely stored in a concealed location or kept in a locked safe. Sharing medications with others is dangerous and illegal. For this reason, the pharmacy or provider will seldom replace lost, missing, or stolen medications. The safety of children and adolescents is of concern, as these groups are vulnerable to experimentation and accidental ingestion. Pets, too, may ingest medications that are not well secured.

"Saving medications for later" also increases the risk of misuse and intentional or accidental ingestion by another person. The FDA recommends the disposal of expired, unwanted, or unused medications through take-back programs sponsored by local law enforcement through DEA-authorized collectors. (To find local authorized collectors, call the DEA Office of Diversion Control's Registration Call Center at 1-800-882-9539.) In addition, some pharmacies provide patients with mail-back envelopes. If such programs are not available locally, instruct patients not to crush tablets or capsules, but to mix medicines with an unpalatable substance such as kitty litter or used coffee grounds, place the mixture in a sealed plastic bag, and put it in the household trash. Before throwing out empty pill bottles or other empty medicine packaging, remove all information on the prescription label to prevent access to personal health information or identity theft.

To avoid water supply contamination, the U.S. Environmental Protection Agency has cautioned against flushing medications down a sink or toilet, but the FDA continues to recommend the flushing of certain medications, including fentanyl (Duragesic, Ionsys) and buprenorphine (Butrans) transdermal patches, which may contain a potentially lethal dose of medication even after use. For more information on these recommendations, visit the FDA Web site at http://1.usa.gov/1eq6jVz.

Table 2. Approximate Morphine Equivalents of Selected Oral Opioids[a]

Oral Opioid Dose	Oral Morphine Dose
15 mg tramadol	1.5 mg
15 mg codeine	2.25 mg
15 mg tapentadol	6 mg
15 mg hydrocodone	15 mg
15 mg oxycodone	22.5 mg
15 mg oxymorphone	45 mg
15 mg hydromorphone	60 mg

[a]These ratios are for information only. Actual conversion from one opioid to another requires a number of clinical considerations. These ratios do not apply to parenteral dosing.
Doses were calculated at: www.agencymeddirectors.wa.gov/opioiddosing.asp.

SELECTING THE RIGHT OPIOID

Several opioids are commonly used to manage chronic pain (see Table 1). When selecting an opioid for a patient with chronic pain, the prescriber considers the patient's health status, age, and previous exposure to opioids; the potential for drug–drug interactions; and the treatment plan. The oral or transdermal routes are preferred for chronic pain, but in some cases intrathecal pumps or other invasive routes are used. Oral opioids may be short acting, with an onset of 45 to 60 minutes and a duration of three to six hours; or long acting, with a duration ranging from eight hours to seven days, depending on the product. Opioid-naïve patients should *never* begin therapy with long-acting or extended-release opioids, but may be converted to these medications once a stable dose of short-acting opioids has been established.[9] When combination products containing an opioid and acetaminophen, aspirin, or ibuprofen are prescribed, it is important to recognize and educate patients on the safe daily and long-term dose limits of the nonopioid component of the medication.

If a patient has had prior opioid treatment, morphine equivalency ratios may be considered (see Table 2), though actual conversion from one opioid to another requires a number of clinical considerations.[38] Methadone dosing is unique and dose dependent. For example, 10 to 20 mg of methadone is considered the equivalent of 40 to 80 mg of morphine, while 30 to 40 mg of methadone is considered the equivalent of 240 to 320 mg of morphine. The ratio increases to 10:1 or more for methadone doses of 60 mg and higher.[13] These equivalencies are not based on analgesic efficacy, but rather on the very long and unpredictable half-life of methadone that results in accumulation and adverse effects.[24] To prevent death from overdose and accumulation, methadone should be prescribed only if the provider understands the additional monitoring required with its use and is knowledgeable about methadone's pharmacokinetics, unpredictable clearance, and potential for multiple drug interactions.[13]

Specific conversion values are not available for buprenorphine patches. Buprenorphine displaces full mu-opioid receptor agonists, such as morphine (MS Contin and others), hydromorphone (Dilaudid, Exalgo), and oxycodone (OxyContin and others), causing acute withdrawal symptoms and increased pain. Buprenorphine patches should not be used in conjunction with these opioids. As with methadone,

buprenorphine should be prescribed only by providers familiar with its use. Oral buprenorphine is reserved for use in addiction and can be prescribed only by certified physicians.

PATIENTS REQUIRING SPECIAL CONSIDERATION

Some patients with chronic pain should be given special consideration during assessment for opioid therapy, as their age, physical condition, or health behaviors may significantly affect treatment.

Older adults. Persistent pain is common and undertreated in patients 65 and older, leading in many cases to adverse outcomes such as impaired function, sleep, quality of life, and mobility (with the attendant risk of falls).[6, 39, 40] Nonsteroidal antiinflammatory drugs are often contraindicated or used with caution in this age group. While older patients may benefit from judicious use of long-term opioid therapy,[6] metabolic changes that occur with aging may slow drug metabolism and excretion, potentially leading to higher than expected serum drug levels. Oversedation can increase the risk of falling in this population, as can unrelieved pain. "Start low and go slow" when initiating opioid therapy in older adults, and monitor outcomes frequently.

Patients with compromised renal and hepatic function. Evaluate renal and hepatic function to determine safe dosages and dosing intervals. Patients with significant liver dysfunction should avoid products containing acetaminophen. The estimated glomerular filtration rate is used to determine medication dose reductions in patients with significant renal insufficiency. Certain opioids, such as morphine and codeine, should be avoided in the treatment of patients with renal dysfunction, as they have active and potentially toxic metabolites that tend to accumulate in the presence of impaired renal clearance.[41] Others, including tramadol, hydromorphone, and oxycodone, may be used in such patients with close monitoring, but the safest opioid options are those that are not excreted renally: transdermal buprenorphine, methadone, fentanyl, and sufentanil (Sufenta).[42]

Pregnant women. Between 2001 and 2009, there was an estimated three-to-four-fold rise in opioid use during pregnancy, including both illicit and prescribed opioids.[43] Both opioid physical dependence and opioid withdrawal during pregnancy are associated with adverse perinatal outcomes. It is important to alert women of childbearing age to these risks. Effective birth control is essential when opioid therapy is considered in a woman of childbearing age. It is critical to refer women who discover a pregnancy while using opioid therapy to a high-risk obstetric program. At present, supervised opioid maintenance therapy for women taking opioids for any reason during pregnancy is the recommended treatment approach.[44]

Patients with sleep disorders or obstructive sleep apnea. Opioid use in patients with untreated sleep apnea, whether diagnosed or undiagnosed, raises concerns since the combined effects of obstructive apnea due to airway collapse and central apnea due to opioid use could increase the risk of hypoventilation or respiratory depression during sleep.[45, 46] For this reason, patients with symptoms of obstructive sleep apnea who are using opioid therapy should be referred for appropriate sleep evaluation. The STOP-Bang questionnaire, which is a validated screening tool for identifying obstructive sleep apnea in surgical patients, may facilitate initial assessment.[47-49] The questionnaire focuses on eight correlates of obstructive sleep apnea: loud snoring, tiredness, observed apneas, high blood pressure, body mass index, age, neck circumference, and gender. (For a copy of the questionnaire, go to www.stopbang.ca/osa/screening.php.)

Patients with depressed mood or anxiety. Chronic pain may adversely affect mood; conversely, depressed or anxious mood can increase pain perception. Identifying and treating depression and anxiety are part of a comprehensive pain management plan. The Patient Health Questionnaire-9, available at www.phqscreeners.com/sites/g/files/g10016261/f/201412/PHQ-9_English.pdf, is a validated, self-administered nine-item tool commonly used to assess patients for depressed mood.[50, 51] The Generalized Anxiety Disorder 7-Item scale, available at www.integration.samhsa.gov/clinical-practice/GAD708.19.08Cartwright.pdf, is used to monitor the effect of anxiety on chronic pain.[52] Mental health disorders should be treated concurrently with chronic pain.

Patients with adverse health behaviors should be offered nonjudgmental support, educational materials, and referrals to specialists to support behavioral change.

Tobacco use. The interrelationship between smoking behavior and severity of chronic pain is mediated by complex biopsychosocial factors. While several studies have found an association between smoking tobacco and high-intensity chronic pain scores, it is not clear whether people with chronic pain smoke as a means of coping with or reducing their pain, or whether smoking actually exacerbates their pain.[53-55] While assessing patients for readiness to quit, offering ongoing support and assistance with smoking cessation may help them meet their smoking cessation goals.

Alcohol use. Any alcohol use is contraindicated in patients using opioid therapy, as alcohol greatly increases the risk of adverse outcomes, including central nervous system and respiratory depression, aspiration, overdose, and death.[56] Many tools are available to screen patients for risky drinking patterns. Providing ongoing nonjudgmental monitoring for alcohol use and supportive guidance is critical in keeping patients with chronic pain safe.

Obesity. Several studies show associations between obesity and fibromyalgia, chronic headaches, abdominal pain, and osteoarthritis.[57] Obesity may also be an

Resources

American Chronic Pain Association
www.theacpa.org

American Pain Society
www.ampainsoc.org

American Society for Pain Management Nursing
www.aspmn.org

National Headache Foundation
www.headaches.org

National Sleep Foundation
www.sleepfoundation.org

PainEDU: Improving Pain Treatment Through Education
www.PainEDU.org

Washington State Department of Health
Health Education Resource Exchange
Safe Use of Prescription Pain Medication patient education poster
http://here.doh.wa.gov/materials/safe-use-of-prescription-pain-medication

Washington State Department of Social and Health Services
Health and Recovery Services Administration
Tapering Plan for Client with Chronic, Non-Cancer Pain
www.hca.wa.gov/medicaid/pharmacy/Documents/taperschedule.xls

obstacle to exercise. Providing compassionate support and referrals for assistance in weight management are important strategies in helping obese patients alleviate chronic pain.

Substance use history. A history of illicit drug use should not prevent patients who have undergone a significant period of abstinence and participated in abstinence support from receiving safe and effective treatment for chronic pain, including opioid therapy. On the other hand, for patients with an active substance use disorder or a history of diverting drugs, chronic pain is best treated by a pain management and addiction specialist. The practitioner and patient should develop a clear, collaborative plan of care that includes previous support strategies and frequent monitoring to evaluate medication adherence and support.

Before initiating opioid therapy for chronic pain, and periodically throughout treatment, clinicians should consult their state's PDMP.[9] In the primary care setting, neither opioids nor benzodiazepines should be prescribed to treat chronic pain in patients with active substance use disorders or a history of drug diversion. The risk of accidental death from overdose outweighs any possible benefit. Instead such patients should be referred to pain and addiction specialists for care.

It is not uncommon for providers to "discharge" from their practice patients found to be using street drugs; but unless the patient represents a threat to clinic staff, there is no justification for doing so. For these patients, nonopioid pharmacologic and nonpharmacologic strategies can be used to reduce chronic pain.

Although marijuana has been legalized in some form (for medical use or for medical and recreational use) in 23 states, the District of Columbia, Canada, and some European countries, it is still illegal by federal law in the United States.[58] This creates legal and ethical issues for providers. Although marijuana is sometimes prescribed for chronic pain, its use remains controversial and research-based recommendations are lacking. In states in which only medical marijuana is legal, providers should make treatment decisions on a case-by-case basis, taking into account their own preference and comfort.

LEGAL AND PRACTICAL CHALLENGES TO PRESCRIBING OPIOIDS

In the United States, opioids are controlled substances, which are assigned by the DEA to one of five "schedules," according to their perceived potential for abuse—the lower the schedule number, the higher the associated risk of abuse and dependency. Schedule I drugs are considered by the DEA to have a high potential for abuse and no currently accepted medical use. These include heroin, LSD, and currently, marijuana.[59] Most opioids are schedule II drugs, though codeine is schedule III and tramadol is schedule IV.

In an attempt to reduce abuse and diversion, recent federal and state laws have increased restrictions regarding opioid prescribing practices. For example, in August 2014, the DEA reclassified hydrocodone combination products, formerly schedule III drugs, as the more tightly controlled schedule II drugs, which can be prescribed only with an original signed and dated paper prescription in quantities intended for no more than 30 days of use.[60] The effect of this change and of other restrictions on opioid prescribing for people with pain is not yet clear. Prescribers are not allowed to postdate prescriptions; each prescription must be dated on the day it is written. However, for patients at low risk for opioid misuse, and who are on a stable opioid dosage, a "fill date" can be entered in the directions to the pharmacist. In this way, a provider may choose to issue up to three separate prescriptions (that is, prescribe a 90-day supply) during one visit. Some providers prefer to see patients monthly to evaluate their progress and dispense written prescriptions after each assessment, even though this practice can be burdensome for low-risk patients and can clog

the provider's schedule. However, dispensing three prescriptions at one time may lead to misplaced or lost prescriptions and poor follow-up. Some practices address this issue by having a nurse assess the patient, dispense monthly written prescriptions, and schedule patient visits with the prescriber every three months.

Few public or professional resources are available in most communities to support patients with chronic pain and their pain management providers. Ineffective and conflicting regulations present challenges to optimal and safe opioid use. Payer policies, preferred drug formularies, lack of reimbursement for such integrative therapies as acupuncture or massage, and poor coordination of education for health care professionals contribute to the challenges of prescribing opioids to manage chronic pain.[5] Insurance coverage that limits the number of pills allowed in total, per month, or per prescription undermines provider decision making and patient care. Some state-funded insurance plans for low-income patients include formularies that require prescribing methadone as a first-line opioid. While methadone is inexpensive, many providers are inexperienced in its safe use, and deaths have resulted from unsafe prescribing.[24, 25] Burdensome prior authorization requirements by insurers create time-consuming hurdles to prescribing specific medications, including some opioids, anticonvulsants, and anesthetic patches for pain. Clinicians lose precious time in paperwork while patients wait, often in pain, for authorization.

Managing chronic pain is hard work and time consuming for both patients and clinicians. It's common for both to become discouraged. This can cause patients to become angry or demanding and clinicians to minimize or dismiss the reports of pain from patients who need care. Lack of professional, patient, family, and community education perpetuates common myths and misperceptions about chronic pain and opioid use as part of pain management.

Both unrelieved chronic pain and misuse or abuse of opioids can reduce a patient's quality of life. Nurses are essential in helping patients effectively manage chronic pain while avoiding the risks opioid treatment may pose. Nurses can access online resources to help them care compassionately and competently for people with chronic pain (see *Resources*). If pain management is a moral imperative, as the Institute of Medicine (now the Health and Medicine Division of the National Academies of Sciences, Engineering, and Medicine) has asserted,[1] then nurses have a responsibility to take the lead in directing safe and effective pain management practices. ▼

For 15 additional continuing nursing education activities on the use of opioids, go to www.nursingcenter.com/ce.

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