In 2009, the latest year for which data are available, an estimated 7 million Americans were abusing prescription drugs – more than the number abusing cocaine, heroin, hallucinogens, and inhalants, combined.6 Emergency-room visits related to nonmedical use of opioids rose 111 percent between 2004 and 2008.7 Between 1998 and 2008, the rate of opioid misuse increased 400 percent.4 Drug overdose is now the second-leading cause of accidental death in America, exceeded only by car crashes.3 This rising tide of abuse, addiction, overdose, and death has led to calls for tighter regulation of opioid pain medications and for greater prudence in prescribing on the part of clinicians. In July 2012, the U.S. Food and Drug Administration (FDA) released its final Risk Evaluation and Mitigation Strategies (REMS) content guidelines for prescriber education related to extended-release (ER) and long-acting (LA) opioid analgesics.10 The previous year, the White House Office of National Drug Control Policy, in collaboration with other branches of the federal government, introduced the “Action Plan To Address National Prescription Drug Abuse Epidemic.”11 These initiatives, echoing statements in recent clinical guidelines, seek to balance a crack-down on non-medical use of opioids while simultaneously protecting the delivery of effective pain management to legitimate patients.1

This CME monograph on best practices for prescribing opioids for chronic noncancer pain is in step with these important efforts, covering the educational themes emphasized by the FDA and the new federal plan to combat prescription drug misuse. This program offers clinicians a solid foundation for responsible and vigilant opioid prescribing.

The International Association for the Study of Pain defines chronic pain as “pain that persists beyond normal tissue healing time, which is assumed to be three months.”12 Numerous diseases and syndromes can result in chronic pain. For the purposes of this monograph, all chronic pain disorders outside of cancer pain or pain at end of life are collectively labeled “chronic noncancer pain” (CNCP).

Many treatment modalities exist for CNCP – opioid pain medications are only one of many tools in the pain management armamentarium. Not all patients are appropriate candidates for opioid medications, either because of the nature of their condition, the existence of relevant comorbid conditions, or their assessed risk for opioid abuse. Opioid therapy may be a useful component of a pain management plan, but in selecting patients for an opioid trial, clinicians must weigh the potential benefits of opioids against the risk of significant harms, including a wide range of adverse effects as well as adverse outcomes associated with abuse potential.

The challenge of pharmacovigilance
In their daily practice, clinicians who treat patients with chronic non-cancer pain face must balance pain relief with the risks associated with opioid analgesics. The term “pharmacovigilance” refers to the range of procedures and processes used to achieve this balance. As will become clear throughout this monograph, such procedures need not be burdensome and are not unlike the kinds of balancing acts required in the prescription of a great many other therapeutic agents. What makes opioids of particular concern is the fact that not only are they potentially dangerous for patients, they are also highly sought-after by recreational drug users and criminal elements in society.

In their efforts to find the appropriate, effective middle ground between relieving pain and preventing diversion and misuse of prescription opioids, clinicians must bear in mind the fact that the problem of unrelieved pain remains as urgent as ever. Chronic pain was estimated in a 2011 study to affect approximately 100 million Americans and to cost roughly $635 billion annually in treatment and lost productivity.13 In fact, the incidence of chronic pain in the U.S. is greater than that of diabetes, heart disease, and cancer combined.14,15

At the same time, opioids are subject to abuse, as previously mentioned, and also have a wide range of potential adverse effects that can predispose a patient to serious morbidity and even mortality. Risk is increased among older adults; those with impaired renal or hepatic function; individuals with obesity, cardiopulmonary disorders, sleep apnea, or mental illness; and in patients who combine opioids with other respiratory depressants such as alcohol, sedative-hypnotics, benzodiazepines, or barbiturates.

The Centers for Disease Control and Prevention (CDC) in 2010 issued recommendations aimed at helping clinicians find a balance between responsible opioid prescribing and minimizing the risks of abuse, addiction, and drug diversion, though the recommendations were acknowledged to be based on promising interventions and expert opinion, not rigorous evidence-based research.16 Use opioid medications for acute or chronic pain only after determining that alternative therapies do not deliver adequate pain relief. The lowest effective dose of opioids should be used.

In addition to behavioral screening and use of patient contracts, consider random, periodic, urine testing for opioids and other drugs for any patient less than 65 years old with non-cancer pain who is being treated with opioids for more than six weeks.

Do not prescribe ER/LA opioids for acute pain.

If your state has a prescription drug monitoring program (PDMP) periodically request a report on the history of opioid prescriptions to your patients by other providers.
The rest of this monograph details how to implement these general guidelines in ways that are consistent with the time and budgetary constraints often found in modern practice settings.

**Case study: Initial presentation**

Matt Davidson, 69, is a retired high school physical education teacher. He has come to his primary care physician for his annual physical. He has a history of hypertension, osteoarthritis, and prostate cancer, for which he was treated 2 years ago with a combination of external beam radiation and chemotherapy. His PSA is now near zero and he has no signs of disease, although he continues to be troubled by mild urinary incontinence and erectile dysfunction. On this visit, Mr. Davidson complains of joint pain, as well as a burning, tingling pain in his hands and feet and asks if anything can be done for it. He says he has been taking between 800 and 1200 mg ibuprofen daily for the pain, which he rates as 7-8 on a 10-point scale, but has also been having heartburn as a result.

A full evaluation of the patient’s pain leads to a dual diagnosis of osteoarthritis and peripheral neuropathy secondary to chemotherapy. As part of the evaluation, the patient is asked how his pain is affecting his life and whether it is preventing him from engaging in any activities. He reports disturbed sleep, which he says makes him more irritable during the day. He also says he no longer plays tennis, walking has begun to hurt, and it is becoming difficult to use the computer keyboard.

This information is used to create a treatment plan with the functional goals of reducing night time awakenings to no more than 1 per night; walking daily at least 1 mile without pain; using the computer without pain. A return to tennis is left as a possible goal if less strenuous goals are achieved first. An extended-release oxycodone product is prescribed, as well as a prophylactic laxative. The patient is given printed information about the safe use, storage, and disposal of opioid medications.

**Assessing patients for opioid therapy**

Determining if an opioid medication is appropriate for a patient with chronic non-cancer pain involves assessing both the condition itself and the patient’s potential for misuse or abuse of the medications. The FDA has recommended that providers contemplating prescribing an opioid pain medication complete a “comprehensive history and physical examination, including assessment of psychosocial factors and family history of substance misuse, as well as special considerations for the elderly, women, children, and cultural/ethnic groups.” Regulators expect to see at least a basic physical examination as part of the evaluation that leads to treatment with controlled substances. The exact components of the examination, however, are left to the medical judgment of the clinician, who is expected to have performed an examination proportionate to the diagnosis that justifies a treatment.

Any basic pain assessment includes the familiar elements of: chief complaint; history of present illness; past medical, surgical, and psychosocial history; family history; physical examination; and examination of imaging and other diagnostic studies or tests. As when assessing any patient, clinicians should take the time to look beyond the specific complaint or body part/system and evaluate holistically the broader mental, cultural, and socioeconomic contexts within which the chief complaint is embedded.

**History and physical exam**

Physical exams conducted as part of an assessment of pain should include an evaluation of the patient’s nervous system, with focus on sensory function. Clinicians should assess for allodynia (pain from stimulation that would not normally evoke pain, such as light touch), hyperalgesia (amplified pain response to stimulation that would normally evoke only mild pain), or pain insensitivity. A sensory examination could include response to light touch, light pressure, pinprick, cold or vibration.

It is important for clinicians to avoid the mistake of assuming that if an organic pathology cannot be found, the patient’s pain is “all in their head.” As Goodwin and Bajwa (2004) note, “Pain is what the patient says it is.” Psychological factors may be important in a patient’s experience of pain, and the importance of such factors should be taken seriously and incorporated into the overall treatment plan.

A comprehensive evaluation of a patient in pain usually requires moving beyond the typical list of questions asked during a general history. It may be possible to gather this information before an in-person visit by using paper or online questionnaires. In most cases where pain is the chief complaint, it is appropriate to begin a conversation by asking about the pain, but then it is usually best to review the broader context and impact of that pain. Here are some points that may be useful to cover in an initial evaluation:

- Location of pain.
- Character of pain (i.e., shooting or stinging, continuous or intermittent, worse at night or in the morning).
- Lowest and highest pain on 0 to 10 scale in a typical day.
- Usual pain on 0 to 10 scale on a typical day (augmented by verbal descriptors).
- How and when pain started.
- Exacerbating and relieving factors (i.e., stress, alcohol, other medical concerns).
- Effect of pain on sleep.
- Effect of pain on mood.
- Effect of pain on functioning at work.
- Effect of pain on quality of personal life, such as relationships, sex, or recreation.
- Is the patient involved in a legal or protracted insurance process connected to his or her chronic pain, such as a motor vehicle accident or a disability case?
- What activities could the patient do before pain impacted his or her life that he or she can’t do now?
- What does the patient expect from medications or other treatments in terms of analgesia or recovered function?
- Review of past experience/exposure to opioids.
- Review of past medical/surgical history.
- Review of family medical history.
- Assessment of patient history of drug, alcohol, and tobacco use.
- Psychosocial evaluation (including history of mental illness).

During an initial evaluation, clinicians should be alert for signs that a patient is minimizing his or her pain. This may result from a variety of psychological or emotional factors. For example, some patients may worry that they will be labeled as a “complainer” if they mention pain, or that their health care provider will suspect they are addicted if they ask about opioid pain medications. Other patients may under-report pain because they fear that pain medications will dull their cognitive abilities, lead to addiction, or produce undesirable side effects. Clinicians should be empathic, supportive and honest, neither promising too much nor removing all hope, when evaluating a patient in chronic pain.

**Psychosocial evaluation**

Pain affects every aspect of a patient’s life. It is vital, therefore, to evaluate the ways pain may be impacting, or may be affected by, psychosocial elements of a patient’s life. Clinicians must be alert for signs of depression or anxiety, which are very common. Be particularly alert for suicidal thoughts since the risk of suicide is roughly double for patients with chronic pain. Some freely-accessible instruments for gathering a psychiatric history are available [see, for example, the Depression Anxiety & Positive Outlook Scale (ww.dapos.org) or the Patient Health Questionnaire (PHQ Screeners (www.phqscreeners.com))]. Referral to a mental-health professional is warranted if the clinician’s judgment suggests the patient has active psychological issues beyond his or her expertise.

---

<table>
<thead>
<tr>
<th>Numeric Pain Scale</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Pain</td>
<td>Moderate pain</td>
<td>Worst pain possible</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinicians should also probe for ways in which pain may be affecting the patient’s family system, work, or social activities. Pain can seriously erode these spheres of life and evaluating these challenges and addressing them during treatment (for instance by referral to a vocational counselor or social worker) is just as important as treating the more immediate medical issues that may be contributing to chronic pain.

### Evaluating patients for risk of opioid dependence or abuse

Whenever a clinician considers treating pain with a controlled substance, such as an opioid, risk of misuse or diversion is always a possibility, no matter how remote, and must be assessed. Exactly whom to suspect and when to be proactive in investigating risk factors is an area of great debate. To date, no convincing data exist to support the strategy of focusing on any one specific population or setting – which means that prescribers must be vigilant with all patients. The concept of “universal precautions” has been applied to this approach, which means that any patient in pain could have a drug misuse problem – just as any patient requiring a blood draw for a simple lab test could have HIV. Treating everyone with the same screens, diagnostic tests, and administrative procedures can help remove bias and level the playing field so everyone is treated equally and screened thoroughly.

Nonetheless, it is also true that some patient characteristics are predictive of a potential for drug abuse, misuse, or other aberrant behaviors. The factor that appears to be most strongly predictive in this regard is a personal or family history of alcohol or drug abuse. Some studies have also shown that younger age and the presence of psychiatric conditions are also associated with aberrant drug-related behaviors.

In evaluating patients with chronic pain for risk of addiction or signs that they may be abusing a controlled substance, it may be helpful to consider the sets of characteristics listed in Table 1.

### Written agreements

Written documentation of all aspects of a patient’s care, including assessments, informed consent, treatment plans, and provider/patient agreements, are a vital part of opioid prescription “best practices.” Such documentation provides a transparent and enduring record of a clinician’s rationale for a particular treatment and provides a basis for ongoing monitoring and, if needed, modifications of a treatment plan.

Many computerized systems are now available for the acquisition, storage, integration, and presentation of medical information. Most offer advantages that will benefit both patients and prescribers, such as maintaining up-to-date records, and providing instant availability of information relevant to prescribing or treatment. Although automation can help, clear documentation is not dependent on electronic record-keeping; it merely requires a commitment to creating clear and enduring communication in a systematic fashion. Good documentation can be achieved with the most elaborate electronic medical record systems, with paper and pen, or with dictated notes. Clinicians must decide for themselves how thoroughly, and how frequently, their documentation of a patient’s treatment should be.

### Informed consent

Informed consent is a fundamental part of planning for any treatment, but it is critically important in long-term opioid therapy, given the potential risks of such therapy. At its best, consent also fortifies the clinician/patient relationship.

Prescribers must be able to answer with confidence four key questions when obtaining informed consent in the context of treatment with opioids:

1. Does the patient understand the various options for treatment?
2. Has the patient been reasonably informed of the potential benefits and risks associated with each of those options?
3. Is the patient free to choose among those options, free from coercion by the healthcare professional, the patient’s family, or others?
4. Does the patient have the capacity to communicate his or her preferences – verbally or in other ways (e.g., if the patient is deaf or mute)?

Documentation related to these key areas can be accomplished by creating a separate paper or electronic informed consent form or by incorporating informed consent language into a larger treatment plan or patient/provider agreement.

### Table 1: Characteristics of chronic-pain patients v. addicted patients

<table>
<thead>
<tr>
<th>Chronic-pain patient</th>
<th>Addicted patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication use is not out of control.</td>
<td>Medication use is out of control.</td>
</tr>
<tr>
<td>Medication use improves quality of life.</td>
<td>Medication use impairs quality of life.</td>
</tr>
<tr>
<td>Wants to decrease medication if adverse effects develop.</td>
<td>Medication use continues or increases despite adverse effects.</td>
</tr>
<tr>
<td>Is concerned about the physical problem being treated with the drug.</td>
<td>Unaware of or in denial about any problems that develop as a result of drug treatment.</td>
</tr>
<tr>
<td>Follows the practitioner-patient agreement for use of the opioid.</td>
<td>Does not follow opioid agreement.</td>
</tr>
<tr>
<td>May have left over medication.</td>
<td>Does not have leftover medication.</td>
</tr>
<tr>
<td></td>
<td>Loses prescriptions.</td>
</tr>
<tr>
<td></td>
<td>Always has a story about why more drug is needed.</td>
</tr>
</tbody>
</table>

Adapted from: Webster LR, Dove B. Avoiding Opioid Abuse While Managing Pain. Sunrise River Press, North Branch, MN. 2007.

Many tools have been developed for the formal assessment of a patient’s risk of having a substance misuse problem, some of which are appropriate for routine clinical use because they are relatively brief and easily implemented. Table 2 lists the tools that appear to have good content, and face and construct validity for assessing patient risks related to chronic opioid therapy, although to date, no single tool has been widely endorsed or thoroughly validated.

### Table 2: Tools for patient risk assessment

<table>
<thead>
<tr>
<th>Tool</th>
<th>Use</th>
<th>Who administers?</th>
<th>Length</th>
<th>Access</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid Risk Tool (ORT)</td>
<td>Screen for risk of opioid addiction.</td>
<td>Clinician or patient self-report.</td>
<td>5 yes/no questions.</td>
<td><a href="http://www.opioidrisk.com/node/887">www.opioidrisk.com/node/887</a></td>
</tr>
</tbody>
</table>
Patient-provider agreements

A written agreement between a clinician and a patient about the specifics of their pain treatment with opioids can help clarify the plan with the patient, the patient’s family, and other clinicians who may become involved in the patient’s care. Such agreements can also reinforce expectations about the appropriate and safe use of opioids. Caution must be exercised, however, to ensure that patient/provider agreements are not used in a coercive way to unethically place patients in the position of having to agree to its terms or else lose an important component of their treatment (or even lose all treatment).22

Although evidence is lacking about the most effective methods to convey the information included in most patient-provider agreements, such agreements have been widely used and are recommended by regulators and many experts on treatment guidelines for long-term opioid therapy.21 Recently, the Veterans Administration and U.S. Department of Defense chartered an expert panel to undertake a systematic review of existing medical literature on this subject. In the clinical practice guidelines resulting from that work, the panel concluded that opioid treatment agreements are a standard of care when prescribing long-term opioid therapy.23

[Samples of several commonly-used agreements, including a low-literacy version, are available at: http://opioids911.org/media/doc/Opi911-OpioidRxAgreements.doc]

Provider/patient agreements have many potential advantages, including:17

- Allowing treatment to start on a note of mutual respect and partnership.
- Enhancing transparency.
- Engaging patients in a collaborative education and decision-making process.
- Helping to set functional goals and clarifying the clinician’s and patient’s roles and responsibilities in attaining these goals.
- Documenting acceptance of treatment risks and benefits.
- Documenting informed consent.
- Helping avoid misunderstandings that may occur over long treatment time periods.
- Providing a foundation for subsequent decisions about changes in medications or termination of treatment.

Clinicians should strive to craft agreements that serve their patients’ best interests and avoid coercive or punitive language. Thus, agreements should avoid:17

- Putting all burden on the patient rather than sharing it between patient and clinician.
- Framing the agreement in terms of punishments for possible future crimes or difficulties.
- Using language that is stigmatizing, dominating, or pejorative.
- Using coercion in any way.
- Imposing limitations for the clinician’s convenience without clear and substantial benefit for the patient.

- Insisting on behaviors unrelated to actual use of medications.
- Using the term “fired” to describe termination of treatment.
- Threatening abandonment or suggesting that patients will not have continued access to non-opioid pain relieving treatments if opioids are terminated.

To be effective, written agreements must be clearly understood by the patient. This may require the provision of agreements in multiple languages. All agreements should be written at the sixth- to seventh-grade level or even lower.24,25 Translators may need to be provided for speakers of other languages to ensure patient understanding and effective informed consent. A patient who does not fully understand the potential risks and benefits of a treatment cannot be truly “informed” as required by the legal and ethical guidelines for medical practice. Time must be allowed for patients to ask questions, and for prescribers to ensure patients understand what they are being told. Some, or all, of these tasks may be handled by trained personnel (or staff members) rather than clinicians.

Although the term “agreement” is generally perceived as being more patient-friendly than the word “contract,” clinicians should understand that, from a legal standpoint, any written or oral agreement between a prescriber and a patient may be considered a binding “contract.” Clinicians should ensure that the terms in any agreement are understood by the patient, and are acceptable, attainable, and consistent with high-quality practice.26

Creating function-based opioid treatment plans

Once a patient has been assessed and accepted as a candidate for treatment with an opioid pain medication, and after informed consent has been obtained for such treatment, a written plan for implementing the treatment should be drafted. Such plans typically include a statement of the goals of therapy. These goals should be written carefully in light of the inherent subjectivity of pain. Since pain itself cannot be measured objectively, framing treatment goals solely in terms of pain relief means that such goals cannot be objectively confirmed.

Although a patient’s subjective pain and suffering are obviously important factors, only the functional impact of the pain can be measured and used to create objective treatment goals. This impact takes many forms, but typically chronic pain erodes foundations of daily life, such as physical activity, concentration, emotional stability, interpersonal relationships, and sleep. This can, in turn, degrade functioning at work or in the home, which can lead to depression, anxiety, insomnia, and even suicide. Clinicians should know that even relatively modest reductions in pain can translate into significant functional improvements as pain rating declines.27

A 20 percent reduction in a pain score (i.e., roughly two points on the standard 0-10 pain scale) may be acceptable if it produces significant functional benefits for a patient.

Framing treatment goals in terms of improved patient functioning, rather than merely pain relief, offers two primary advantages to clinicians:

- Prescribing decisions (or decisions to terminate treatment) are based on outcomes that can be objectively demonstrated to both clinician and patient (and, possibly, to the patient’s family)
- Individual differences in pain tolerance become secondary to the setting and monitoring of treatment goals, since subjectively perceived levels of pain are not the primary focus in determining functionality.

Basing treatment plans on functional goals is especially valuable in the context of prescribing opioid pain medications, because such goals may help differentiate a patient who is truly opioid addicted from one who merely seems to be addicted. This differentiation is possible because addiction often leads to decreased functioning, while effective pain relief typically improves functioning.

Functional decline itself may result from a range of problems, including inadequate pain relief, non-adherence to a regimen, function-limiting side effects, or untreated affective disorders. Sometimes impaired functioning is the result of addiction or misuse, and these objective results may shed valuable light on an otherwise confusing presentation of a patient’s pain symptoms.

Functional treatment goals should be realistic. Progress in restoring function is usually slow and gains are typically incremental. Chronic non-cancer pain is often marked by long-standing physical and psychological deconditioning, and recovery may require reconditioning that may take weeks, months, or years. It is much better to set goals that are slightly too low than slightly too high. Raising goals after a patient has “succeeded” in achieving them is far more motivational and encouraging than lowering goals after a patient has “failed.”
Table 3: Evidence for functional goals

<table>
<thead>
<tr>
<th>Functional goal</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Begin physical therapy</td>
<td>Letter from physical therapist</td>
</tr>
<tr>
<td>Sleeping in bed as opposed to lounge chair</td>
<td>Report by family member or friend (either in-person or in writing)*</td>
</tr>
<tr>
<td>Participation in pain support group</td>
<td>Letter from group leader</td>
</tr>
<tr>
<td>Increased activities of daily living</td>
<td>Report by family member or friend</td>
</tr>
<tr>
<td>Walk around the block</td>
<td>Pedometer recordings or written log of activity</td>
</tr>
<tr>
<td>Increased social activities</td>
<td>Report by family member or friend</td>
</tr>
<tr>
<td>Resumed sexual relations</td>
<td>Report by partner</td>
</tr>
<tr>
<td>Returned to work</td>
<td>Pay stubs from employer or letter confirming the patient is off of disability leave</td>
</tr>
<tr>
<td>Daily exercise</td>
<td>Gym attendance records or report from family member or friend</td>
</tr>
</tbody>
</table>

* Involving other persons requires explicit permission from the patient, and this permission should be documented, preferably in writing.


Table 3 illustrates some simple functional goals and ways they might be verified.

The responsibility for obtaining evidence of success in meeting a functional goal lies with the patient and should be made explicit in the prescribing agreement. If a patient is unable to document or achieve the progress outlined in a treatment plan, this may suggest a need for goal readjustment.

Components of an effective treatment plan

The creation of an effective function-based treatment plan must be a collaboration between patient and clinician. A patient’s pain score will be just one of many variables to be considered in framing goals. These goals should be realistic, meaningful to the patient, and verifiable. The details of a function-based treatment plan are necessarily specific to the patient, but one way to initiate the process is to begin with the question: “What do you hope to do as a result of treatment that you can’t do now?”

The treatment plan can include a discussion of, and the setting of expectations about, periodic re-assessment of goals. Patients may stabilize at a certain level of function, and the clinician and patient together must decide if this is acceptable or whether changes are needed.

As is the case in drafting other types of patient/provider documents, patients should be reminded of the benefits and risks of a chosen therapy. With opioids, these include the realities of tolerance and physical dependence and the potential need to taper the medication slowly to avoid withdrawal. Patients must also be educated about the possibility that opioids may be either ineffective or have intolerable adverse effects, and that there is also the possibility of psychological dependence, which could lead to misuse or, less commonly, addiction.

Another critical component of any treatment plan is a description of how treatment with an opioid medication might be terminated. Stopping opioid therapy in cases of chronic non-cancer pain is often more difficult than starting it. Being clear about the conditions under which opioid therapy will end is important because opioids are not curative, have no standard duration of treatment, and may be associated with substantial risks.

Termination may be required for many reasons, including:

- Healing or resolution of a specific pathology underlying the pain.
- The experience of intolerable side effects.
- Lack of adequate response to a medication in terms of either pain relief or functional improvement.
- Evidence of non-medical or inappropriate use of the medication(s).

If inappropriate use of a prescription medication is discovered, treatment must usually be suspended, although provisions should be in place for continuation of some kind of pain treatment and/or referral to other professionals or members of a pain management team. Some clinicians may be willing and able to continue a regimen of opioid therapy even after the discovery of aberrant behavior if done with intensified monitoring, patient counseling, and careful documentation of all directives. This level of vigilance and risk management, however, may exceed the abilities and resources of the average prescriber. In such cases, referral to a provider with specialized skill or experience in dealing with high-risk patients may be prudent.

Case Study: Treatment hits a roadblock

Mr. Davidson returns for a follow-up after 2 weeks. He reports that his arthritis pain has gotten only slightly better, but that he is still experiencing the burning/tingling pain in his hands and feet. He has not achieved any of his functional goals. Upon questioning, he reveals that he has not been taking the opioid medication as frequently as prescribed because he “doesn’t want to become an addict.”

This common patient fear is allayed with careful, compassionate education that explains the differences between addiction and tolerance and that communicates the key idea that proper use of an opioid may improve functioning and quality of life. The prescription for the ER-LA opioid is continued, and a prescription for 10 mg extended-release gabapentin is added.

Initiating treatment with opioids

Prior to an initial prescription of an opioid pain medication, clinicians should be certain that (1) all other potentially effective treatments that offer a more optimal benefit-to-risk profile have been considered or tried; (2) a complete evaluation has been performed and fully documented; (3) the patient’s level of opioid tolerance has been determined; and (4) informed consent and agreement to treat have been obtained. At the outset, both the clinician and the patient should view a new opioid prescription as a short-term trial of therapy. The goal of the trial is to provide data to guide decisions on the continued appropriateness of opioid medications and on the specific dose and formulation of medication used. Such a trial might be as brief as a few days or as long as several months.

Opioid selection, initial dosing, and titration must be individualized to the patient’s health status, previous exposure to opioids, and treatment plan. Although still not widely used, it is also becoming increasingly possible to use commercially-available genetic screening tools to assess for genetic variations in drug metabolism that could affect the way a patient responds to opioids. Caution should be exercised when using opioids in patients with conditions that may be complicated by adverse effects from opioids, including chronic obstructive pulmonary disease (COPD), congestive heart failure, sleep apnea, current or past alcohol or substance misuse, mental illness, advanced age, or patients with a history of renal or hepatic dysfunction. In addition, opioids should not be combined with other respiratory depressants, such as sedative-hypnotics (benzodiazepines or barbiturates) unless there is a specific medical and/or psychiatric indication for such a combination. In such cases, much more intensive monitoring is required.

A decision to continue opioid therapy after an appropriate trial should be based on careful review of the trial outcomes. Outcomes to consider include:

- Progress toward meeting therapeutic goals.
- Changes in functional status.
- Presence and nature of opioid-related adverse effects.
- Changes in the underlying pain condition.
- Changes in medical or psychiatric comorbidities.
- Degree of opioid tolerance in the patient.
- Identification of altered or aberrant behaviors, misuse, or diversion.

Dose titration

Patients who are opioid-naïve or have modest previous opioid exposure should be started at a low dose of a short-acting opioid and titrated slowly upward to decrease the risk of opioid-related adverse effects. If it is unclear whether a patient has recently been using opioids (either prescribed or non-prescribed), the clinician should assume that the patient is opioid-naïve (i.e., not tolerant) and proceed as just described.
Opioid tolerance should be established before prescribing an ER/LA opioid. The selection of a starting dose and manner of titration are clinical decisions that must be made on a case-by-case basis because of the many variables involved. Some patients, such as frail older persons or those with comorbidities, may require an even more cautious therapy initiation. Short-acting opioids are usually safer for initial therapy since they have a shorter half-life and may be associated with a lower risk of overdose from drug accumulation. Further studies are needed to confirm more consistent control of pain and improved adherence to prescribed therapy with use of ER/LA opioids. Although low-dose, short-acting opioids may offer the greatest safety for initiating opioid therapy, clinicians must recognize that short-acting opioids are not intrinsically safer than other formulations, and stress to their patients the importance of strict adherence to prescribed doses/administration.

**Considerations in opioid selection**

Opioids, as a class, comprise many specific agents available in a wide range of formulations. A given patient might be appropriate for ER/LA therapy only, short-acting only, or a combination of an ER/LA opioid with a short-acting opioid for breakthrough pain.

Short-acting, orally-administered opioids typically have rapid onset of action (10-60 min.) and relatively short duration of action (2-4 hours). They are used for acute or intermittent pain, or breakthrough pain that occurs against a background of a persistent level of pain. [Transmucosal immediate-release fentanyl is a special class of short-acting opioid that is only approved for breakthrough pain in cancer, and there is a separate FDA REMS devoted to this topic.] Combination products join an opioid with a non-opioid co-analgesic, usually for use in patients without moderate pain. Using a combination product when dose escalation is required risks increasing adverse effects from the non-opioid co-analgesic, even if an increase of the opioid dose is appropriate. In such cases, using a pure opioid may be preferable.

Unfortunately, at this time, no pharmaceutically manufactured single-agent option for hydrocodone is available, although clinical trials are underway as part of an effort to secure FDA approval for such an agent. Single-agent formulations are available for other types of opioids, such as codeine, morphine, oxycodone, oxymorphone, and hydrocodeine. In 2011, the FDA announced new rules that will limit to 325 mg the amount of acetaminophen allowed in opioid combination products in an attempt to limit liver damage and other ill effects from the use of these products with over-the-counter analgesics.

ER/LA opioids usually have a relatively slow onset of action (typically between 30 and 90 min.) and a relatively long duration of action (4 to 72 hrs). Such agents are typically used for patients with constant background pain. These agents achieve their extended activity in various ways. Methadone and levophanol have intrinsic pharmacokinetic properties that make their effects more enduring than many short-acting opioids. ER/LA agents such as controlled-release morphine, oxycodone, or transdermal fentanyl achieve their prolonged time course via a delivery system that is modified to slow absorption or to slow the release of the active ingredient. Clinicians should warn patients that unless specifically instructed otherwise, oral ER/LA opioids should not be broken, chewed, or crushed, and patches should not be cut or torn prior to use, since this may lead to rapid release of the opioid and could cause overdose or death.

Prescribers should educate themselves about the general characteristics, toxicities, and drug interactions for ER/LA opioid products. [For detailed information on current ER/LA opioid analgesics, see the FDA Blueprint for Prescriber Education, available at: http://www.er-la-opiodrems.com]. Respiratory depression is the most serious adverse effect of opioids as it can be immediately life-threatening. The risk of respiratory depression or respiratory arrest is higher in patients with an upper respiratory infection, asthma or other respiratory problem, hence, if these conditions arise, the opioid dose needs to be reduced. Constipation is the most common long-term side-effect but can often be managed. Drug-drug interaction profiles vary among the products. Knowledge of particular opioid-drug interactions, and the underlying pharmacokinetic and pharmacodynamic mechanisms, allows for the safer administration of opioid analgesics.

Central nervous system depressants (sedatives, hypnotics, tranquilizers, tricyclic antidepressants and alcohol) can have a potentiating effect on the sedation and respiratory depression due to opioids. Alcohol consumption should be avoided entirely with some oral products (e.g. morphine, hydromorphone, oxymorphone) because ethanol increases the plasma concentration of the opioid. Opioids may enhance the neuromuscular blocking action of skeletal relaxants and produce an increased degree of respiratory depression. Using opioids with monoamine oxidase inhibitors (MAOIs) may result in possible increase in confusion, anxiety, and respiratory depression. Opioids can reduce the efficacy of some diuretics by inducing the release of antidiuretic hormone (ADH). In addition, some opioids interact with various cytochrome P450 enzyme inhibitors and inducers and thus may result in higher or lower than expected blood levels of the drug. Methadone can be an effective opioid, but it must be prescribed carefully and with full knowledge of its highly variable pharmacokinetics and pharmacodynamics.

**Abuse-deterrent formulations**

As concern has risen about opioid misuse and abuse, efforts have been made to create abuse-deterrent and tamper-resistant opioid formulations. One class of deterrent formulation incorporates an opioid antagonist into a separate compartment deep within a single capsule; crushing the capsule releases the antagonist and neutralizes the opioid effect. The central opioid antagonist compartment is eliminated from the body unchanged if the capsule is consumed normally without tampering. Another strategy is to modify the physical structure of tablets or incorporate compounds that make it difficult or impossible to liquefy, concentrate, or otherwise transform the tablets. Transdermal opioid formulations have been perceived in the past as less vulnerable to misuse, but such formulations can be abused. For example, a transdermal, 7-day duration formulation of buprenorphine has been reported to be an increasingly misused opioid, particularly in prison populations. As a partial opioid agonist, buprenorphine was thought to be a lower-risk agent than full agonist opioids, however it is clear that this medication can be as susceptible to abuse as full-opioid agonists.

Abuse-deterrent opioid formulations, of course, do not prevent users from simply consuming too much of a medication. These formulations may help reduce the public health burden of prescription opioid abuse, but the evidence to date is inadequate to project whether this potential will actually be achieved.

**Case study: Progress**

At the next scheduled follow-up visit, Mr. Davidson reports reduced pain and improved functioning. He says his pain is now 3-4 on a 10-point scale. He can now walk his dog twice daily, and is using the computer without pain. He says his sleep has improved as well. Mr. Davidson asks for a higher dose of the opioid “to see if I can get the pain down to zero.” Although seemingly reasonable, it is explained to Mr. Davidson that, in fact, “zero pain” is an unrealistic goal for anyone, and that increasing the dose to achieve that goal would likely incur a range of side effects that would erode his overall quality of life.

**Periodic review and monitoring**

If a trial of an opioid medication is deemed successful and opioid therapy is continued, periodic review and monitoring should be performed for the duration of treatment. The tests performed, questions asked, and evaluations made should be tailored to the patient as guided by the physician’s clinical judgment. For example, a physical examination may or may not be required at each follow-up visit. Clinicians must evaluate progress against agreed-upon treatment goals and assess for a wide range of potential adverse effects, ranging from physical side effects such as constipation or sedation, to behavioral side effects such as mood changes, signs of drug craving or seeking, or impaired behavior.
function in various domains of daily living. As part of routine practice, clinicians who prescribe opioids should perform medication reconciliation at each patient visit. The American Medical Association defines “medication reconciliation” as “…making sense of a patient’s medications and resolving conflicts between different sources of information to minimize harm and maximize therapeutic effects.”

The intensity and frequency of monitoring is dependent on an assessment of the patient’s risk for abuse, diversion, or addiction. Tools and techniques similar or identical to those used during an initial assessment of a patient’s risk can be used to re-assess or monitor risk on an on-going basis.

States vary in their requirements for intervals at which follow-up visits are required when controlled substances such as opioid medications are prescribed. Although federal law allows for a 90-day supply of prescriptions for patients receiving schedule II drugs (who are otherwise deemed safe to have this amount), state law can vary from 30 days to 6 months. In cases where state and federal law conflict, the most restrictive rule prevails.

Relatively infrequent monitoring may be appropriate for low-risk patients on a stable dose of opioids. More frequent or intense monitoring is appropriate for patients during the initiation of therapy or if the dose, formulation, or opioid medication is changed. Patients who may need more frequent or intense monitoring include:

- Those with a prior history of an addictive disorder, past abuse, or other aberrant use.
- Those in an occupations demanding mental activity over sustained periods of time.
- Those with comorbid psychiatric or medical conditions.
- Daily or weekly monitoring may be necessary for patients at very high risk for adverse outcomes.

**Reviewing functional goals**

A key part of periodic monitoring is a careful review of previously-agreed-upon functional goals. Patients should come to appointments ready to provide the evidence upon which an evaluation of progress can be made. This evidence should span as many domains of a person’s life as possible: personal and social relationships, employment, physical activities, health, hobbies, and spiritual activities.

Functional goals that are not attained require investigation, possible adjustment, and encouragement that future progress is possible. If the goals have been attained, clinicians should be supportive and positive, while setting new goals to motivate further progress.

Functional goals related to physical activity are sometimes not achieved by patients because they report that the agreed-upon activity hurts too much. Such cases should be carefully evaluated before a decision is made to increase the dose of an opioid medication. All patients – even those with end-stage disease – can engage in some kind of physical activity at least some time during the day. The motions or activity may be extremely modest, yet they may nonetheless serve as effective functional goals. Patients with chronic pain often require such micro-level goals and controlled, gradually-increasing motion or activity over sustained periods of time.

**Managing breakthrough pain**

Patients with chronic pain receiving a steady dose of an opioid medication may experience episodes of pain that “break through” the analgesic effects of the steady-state drug (regardless of the route of administration). Close monitoring of breakthrough episodes is key to helping patients reduce pain and facilitate functioning. Providing patients either paper or electronic pain diaries can help them track breakthrough episodes and spot correlations between the episodes and variables in the patient’s life. If specific triggers are identified, this may provide opportunities for changes that will reduce the prevalence of breakthrough episodes without recourse to increased reliance on medication.

Non-opioid methods of dealing with breakthrough pain (i.e., cold or warmth, massage, yoga, acupuncture, meditation, electrical stimulation) might be considered prior to any increases in opioid medication; although research evidence regarding many CAM (complementary and alternative medicine) approaches is inconclusive. If a short-acting opioid preparation is prescribed for breakthrough pain, clinicians should remind patients about the potentials problems of diversion and misuse of these agents.

As with the management of the underlying chronic pain condition, clinicians should use an agreed-upon set of functional goals as a way to monitor, and if necessary, adjust, the use of as-needed opioid medications for breakthrough pain.

**Monitoring adherence**

Trust is a necessary part of any patient/clinician relationship, but studies suggest that in the context of controlled substances, it is unwise to rely on a patient’s word that medications are being consumed as prescribed. Although the use of more objective ways to monitor adherence to medication regimens is an imperfect science, such methods remain an essential component of periodic review. Multiple objective methods to assess adherence exist, but there is no single “best” approach and all such methods have both advantages and potential drawbacks.

Drug testing should be approached in a consensual manner as part of an agreed-upon treatment plan and with the idea that such testing benefits both the patient and the provider. The potential benefits of clinical drug testing include:

- Serving as a deterrent to inappropriate use.
- Providing objective evidence of abstinence from drugs of abuse.
- Assisting with a diagnosis.

- Helping patients allay concerns by family members, employers, or law-enforcement.
- Demonstrating to regulatory authorities a clinician’s dedication to monitoring “best practices”.

In the context of family practice settings, unobserved urine collection is usually an acceptable procedure for drug testing. Prescribers, however, should be aware of the many ways in which urine specimens can be adulterated. Specimens should be shaken to determine if soap products have been added, for example. The urine color should be noted on any documentation that accompanies the specimen for evaluation, since unusually colored urine could indicate adulteration. If possible, urine temperature and pH should be measured immediately after collection.

One way to reduce the risk of urine test false positives or false negatives is to develop a relationship with a single laboratory, become familiar with its testing tools and threshold values, and use the same screening and confirmatory tests regularly to build familiarity with the range of normal results.

Prescribers should be familiar with the metabolites associated with each opioid that may be detected in urine, since the appearance of a metabolite can be misleading. A patient prescribed codeine, for example, may test positive for morphine because morphine is a metabolite of codeine. Similar misunderstandings may occur for patients prescribed hydrocodone who appear positive for hydromorphone or oxycodone and oxymorphone (see Table 4).

| Table 4: Urinary analytes of common opioid pain medications |
|-----------------|-----------------|
| Drug            | Urinary analytes |
| Morphine        | Morphine        |
| Hydrocodone     | Hydrocodone     |
| Hydrocodone     | Hydromorphone   |
| Hydrocodone     | Oxycodone       |
| Hydromorphone   | Oxymorphone     |
| Hydrocodone     | Hydrocodone     |

**Case study: A caution light**

After 3 weeks, the physician is given a message that a young woman has called requesting an early refill of Mr. Davidson’s opioid “because he’s suffering.” This raises the physician’s suspicions. He accesses his state Prescription Drug Monitoring Program to see if Mr. Davidson might be getting prescriptions from another provider. He is not, and nothing appears unusual. The physician calls Mr. Davidson.
directly and Mr. Davidson confirms that he did ask his granddaughter to call for the prescription because he was having increased pain after playing tennis for an hour. Mr. Davidson is advised to temporarily use an OTC NSAID (not more than 600 mg) and is asked to return for an in-person visit within a week. At that visit, a range of non-pharmacological strategies are reviewed to provide additional pain relief (i.e. post-exercise cold/warm treatments; exercises to improve flexibility; massage; and the use of an elbow brace to be used for tennis).

**Using Prescription Drug Monitoring Programs (PDMPs)**

PDMPs can serve an important clinical monitoring role. PDMPs use secure Internet sites to offer point-of-care access to records of controlled substances from other prescribers and dispensing pharmacies. From these, clinicians can quickly glean patterns of prescription drug use that can be helpful in confirming or refuting suspicions of aberrant behaviors. Information from a PDMP may also be clinically relevant in that it may reveal that a patient is being prescribed medications whose combinations are contraindicated.

There is currently little uniformity, information-sharing, or cooperation among state PDMPs, but efforts are under way to improve this situation. An advisory committee of the Council of State Governments has endorsed the formation of an interstate PDMP compact, and legislation to accomplish this goal is currently being drafted. By checking PDMP data (particularly for high-risk patients), clinicians can get a sense of the controlled substances that the patient has been receiving from other prescribers and other pharmacies. Individuals may have perfectly acceptable reasons for multiple prescribing episodes, but the existence of such a pattern should always trigger inquiry.

**Common issues related to opioid pain medications**

**Preventing and managing opioid-related side effects**

Many patients treated with an opioid will experience side effects, the most common of which is constipation. Other possible effects include:

- Respiratory depression.
- Sedation.
- Urinary hesitancy or retention.
- Dry mouth.
- Nausea/vomiting.
- Itching.
- Sweating.
- Hypogonadism.
- Myoclonus.

Some side effects, such as sedation, may lessen over time after treatment initiation. Others, such as constipation, rarely become less problematic. Constipation is so common, in fact, that when patients use opioids and do not have constipation, clinicians should consider possible reasons ranging from rapid bowel transit time to diversion. Constipation requires proactive treatment, with stimulating laxatives prescribed at the time of initiating opioids, and frequent re-evaluation. With the exception of constipation, uncomfortable or unpleasant side effects may potentially be reduced by switching to another opioid or route of administration (such side effects may also be alleviated with adjunctive medications).

**Opioids and pregnancy**

Some data suggest an association between the use of long-term opioid therapy during pregnancy and adverse outcomes in newborns, including low birth weight and premature birth, though correlated maternal factors may play a role in these associations and causality is not certain. Higher doses of antenatal methadone in tolerant mothers do not seem to increase complication rates. Importantly, opioid withdrawal can be expected in up to half of newborns of opioid-dependent mothers. If a mother is receiving long-term opioid therapy at or near the time of delivery, a professional experienced in the management of neonatal withdrawal should be available.

Nonetheless, given the potential risks of opioids during pregnancy, current American Pain Society-American Academy of Pain Medicine (APS-AAPM) guidelines suggest that clinicians should encourage minimal or no use of opioids during pregnancy unless the potential benefits outweigh risks. If opioid medications are prescribed, clinicians should thoroughly counsel pregnant women about the potential risks and benefits, and clinicians should be prepared to anticipate and manage risks to the patient and newborn.

**Driving and work safety**

Driving while using opioid medications remains a controversial issue. Particularly at the initiation of therapy, opioid medications may cause sleepiness, clouded thinking, decreased concentration, slower reflexes, or incoordination, all of which may pose a danger to the patient and others when driving or operating machinery.

On the other hand, a number of epidemiologic studies failed to show an association between long-term opioid use and motor vehicle accidents, fatalities, or citations for impaired driving. Since at least some of the cognitive and motor-impairing effects of opioids resolve with steady use and a consistent dose, some activities or driving may be allowable at the discretion of the clinician’s medical judgment and in the absence of signs of impairment.

Current APS-AAPM guidelines recommend that all patients who are initially prescribed opioid medications, or those who have their dose increased, be advised not to drive or engage in potentially dangerous work or other activities. There is no consensus on exactly how long they should abstain from driving. Patients should be educated about the increased risk of impairment when starting opioid therapy, when increasing doses, and when taking other drugs or substances (such as, alcohol, benzodiazepines, or even some cold remedies) that may exacerbate cognitive and motor impairment. Clinicians should be aware that certain professions (i.e., school bus drivers and pilots) may be subject to restrictions in the use of opioid medications. Clinicians should check with their state medical society or the Federation of State Medical Boards to obtain up-to-date information in this regard.

**Screening for endocrine function**

Both male and female patients on long-term opioid therapy are at risk for hypogonadism, thus the endocrine function of all patients should be assessed at the start of long-term opioid therapy and at least annually thereafter. The symptoms of hypogonadism in both genders may include fatigue, mood changes, decreased libido, loss of muscle mass, and osteoporosis. Although there are insufficient data to recommend routine endocrine screening of asymptomatic patients, current guidelines do recommend such testing for patients exhibiting any of the aforementioned signs and symptoms.

**Opioid rotation**

“Opioid rotation” means switching from one opioid to another in order to better balance analgesia and side effects. Rotation may be needed because of a lack of efficacy (often related to tolerance), bothersome or unacceptable side effects, increased dosing that exceeds the recommended limits of the current opioid, or inability to absorb the medication in its present form (i.e., if there is a change in the patient’s ability to swallow, switch to a formulation that can be absorbed by a different route such as transdermal).

Because of the large number of variables involved in how any given opioid will affect any given patient, opioid rotation must be approached cautiously, particularly when converting from an immediate-release formulation to an ER/LA product. An equianalgesic chart should be used when changing from one opioid to another or from one route of administration to another. Such charts must be used carefully, however. A high degree of variation has been found across the various charts and online calculator tools, and may account for some overdoses and fatalities.

The optimal dose for a specific patient must be determined by careful titration and appropriate monitoring, and clinicians must be mindful that patients may exhibit incomplete cross-tolerance to different types of opioids because of differences in the receptors or receptor sub-types to which different opioids bind.

In some cases, because of the risk of potential harm during the time of rotating from one chronic opioid regimen to another, it may be wise to initially use lower doses of an ER/LA opioid than might be suggested by equianalgesic charts, while temporarily liberalizing, as needed, the use of a short-acting opioid. This would then be followed by gradual titration of the LA opioid to the point where the as-needed short-acting opioid is incrementally reduced, until no longer necessary.
Managing non-adherent patients

Patients who begin to exhibit aberrant drug-related behaviors or non-adherence to a prescription should be monitored more strictly than compliant patients. Suspicions that a patient is non-adherent should prompt a thorough investigation of the situation, including an honest evaluation of the patient/provider relationship. The way clinicians interact with patients can affect the relationship (for better or worse) and influence treatment outcomes. A clinician’s negative reactions to non-adherence might include anger at the patient, disappointment and sadness at the apparent betrayal of trust, or fear that the patient’s behavior could expose the provider to legal jeopardy. Before accusing a patient of not adhering to a prescribed regimen, clinicians should assess the situation fully. Possible reasons for non-adherence include:

- Inadequate pain relief.
- Misunderstanding of the specifics of the prescription.
- Misunderstandings related to lack of fluency with English.
- Attempts to “stretch” a medication in order to save money.
- Cultural or familial pressure not to take a medication.
- Stigma about taking a pain medication.
- Overmedication and fears about addiction.
- Misunderstanding of a prescription by a caregiver who has taken responsibility for daily apportioning of medications.
- Confusion between two medications that look very similar to each other.

The use of patient–provider agreements and/or informed consent documents can help clinicians navigate the uncertainties that can arise in cases of real or apparent non-adherence, and may help make the process less confrontational. Consultation with an addiction medicine specialist or psychiatrist may be necessary if addiction is suspected or if a patient’s behavior becomes so problematic that it jeopardizes the clinician/patient relationship.

Case study: Stable improvement

After a slight dose adjustment of the gabapentin, Mr. Davidson reports continued functional progress and acceptable levels of pain. He has increased his level of physical activity and reports that his mood and general health is better as a result. He says he would like to try to taper down his use of the opioid, and he is given clear and specific instructions for how to do that.

Treatment termination

Reasons for discontinuation of an opioid analgesic can include the healing of or recovery from an injury, medical procedure, or condition; intolerable side effects; lack of response; or discovery of misuse of medications. Regardless of the reason, termination should be accomplished so as to minimize unpleasant or dangerous withdrawal symptoms by tapering the opioid medication slowly, or by carefully changing to a new formulation. Approaches to weaning range from a slow 10 percent reduction per week to a more aggressive 25 to 50 percent reduction every few days. In general, a slower taper will produce fewer unpleasant symptoms of withdrawal.

In general, opioid therapy must be discontinued or re-evaluated whenever the risk of therapy is deemed to outweigh the benefits being provided. A clinician may choose to continue opioid treatment with intensified monitoring, counseling, and careful documentation if it is deemed in the best interest of the patient. This requires, however, careful consideration and a well-documented risk management plan that addresses the greater resources necessary for opioid continuation following evidence of misuse.

If termination of the provider/patient relationship is deemed necessary, clinicians must ensure that the patient is transferred to the care of another provider and ensure that the patient has adequate medications to avoid unnecessary risk, such as from uncontrolled or potentially dangerous withdrawal. Practitioners can be held accountable for patient abandonment if medical care is discontinued without justification or adequate provision for subsequent care.

Methadone

Methadone has recently received growing attention and concern because it is frequently involved in unintentional overdose deaths. These deaths have escalated as methadone has increasingly been used as an analgesic drug for chronic pain. At one time, methadone had been used almost exclusively in opioid maintenance therapy programs to treat addiction. Its relatively long plasma elimination half-life compared to its relatively short analgesic half-life makes it optimal for maintenance, allowing for once-daily dosing. But methadone only exerts potent analgesic effects in the early phase of its elimination half-life, and this, along with the fact that it is among the least expensive opioids, has led to a dramatic increase in its use for alleviating chronic non-cancer pain.

Methadone has unique pharmacokinetic and pharmacodynamic characteristics that add substantial risk to its use. Although its chemical structure is different from classic opioids such as morphine, methadone acts on the same set of opioid receptors, though with different affinities for the various opioid receptor subtypes. In addition, methadone possesses non-opioid receptor effects that may explain some of its potential special efficacy. These varied effects across opioid receptors, along with its non-opioid properties, have garnered methadone the reputation of being a “broad spectrum opioid.”

For a number of reasons, however, methadone must be titrated very carefully in order to avoid overdose. These reasons include:

- An analgesic half-life much shorter than its elimination half-life (leading to accumulation)
- Metabolism by a group of liver enzymes that differ from those associated with most other opioids, hence leading to unexpected drug-drug interactions
- Significant genetic variations in the liver enzymes that metabolize methadone, which contribute to the unpredictability of methadone’s effects and side effects
- Metabolism may be affected by cigarette smoking (which accelerates elimination) and alcohol consumption (which can augment methadone toxicity acutely and accelerate metabolism with chronic use)

The APS/AAPM guidelines recommend a starting dose in most opioid-naive patients of 2.5 mg every 8 hours, with dose increases occurring no more frequently than weekly. The lowest possible dose titration should be followed even in opioid-tolerant patients because methadone appears to be more potent in patients who have been using higher doses of the pre-switch opioid. The total daily dose of methadone on the first day of treatment should not ordinarily exceed 30-40 mg/d regardless of prior exposure. In older patients or those with renal or hepatic comorbidities, lower starting doses, less frequent dosing, and more cautious dose titration are recommended. Because of its long half-life and variable pharmacokinetics, methadone is not recommended to treat breakthrough pain or an as-needed medication.

When rotating from another opioid to methadone, extreme caution must be used when referring to equianalgesic conversion tables. The consensus recommendations from an expert panel suggest a 75 to 90 percent decrement in the equianalgesic dose from conventional conversion tables when a switch is made from another opioid to methadone.

Because the risk of overdose is particularly acute with methadone, patients should be educated about these risks and counseled to use methadone exactly as prescribed. They should also be warned about the dangers of mixing unauthorized substances with their medication. Benzodiazepines, in particular, pose a threat. Death investigations often find that benzodiazepines have been used in combination with methadone and other opioids. Other respiratory depressants, including alcohol, pose similar risks. Dosing should, therefore, be conservative and cautious until patients demonstrate the ability to tolerate and use the drug safely.

In 2006, the FDA issued a public health advisory warning that methadone can cause serious cardiac conduction disturbances, including QT interval prolongation and Torsades de Pointes, a potentially fatal ventricular arrhythmia. It appears that methadone-related corrected QT (QTc) interval prolongation and cardiac arrhythmias can occur at any dose but are more likely at higher doses or with concomitant use of drugs that interact with methadone or that themselves prolong QTc. Although uncommon,
the cardiac arrhythmias that can be induced by methadone can be lethal if not detected. The cardiac health of patients who are candidates for methadone should be assessed, with particular attention paid to any history of heart disease or arrhythmias. An initial ECG may be advisable prior to starting methadone, particularly if a patient has a specific cardiac disease or cardiac risk factors or is taking agents that may interact with methadone.

**Required patient education**

Thorough patient education about the safe use, storage, and disposal of opioid medications is an essential part of “best practices” opioid prescribing. This education can be partially integrated into standard patient/provider agreements or informed consent documents. As with other patient-directed materials, education must be provided in a language and at a reading level (typically 6th-7th grade) appropriate for a clinician’s patient population. Examples of effective patient education can be found at websites, such as Opioids911-Safety (www.opoids911.org).

Safe use of opioid medications means that patients carefully follow clinician instructions, including special directions about timing of doses and whether to administer the medication with food or without. Clinicians should be mindful of any physical limitations (i.e. poor eyesight) that a patient might have that could interfere with accurate and timely administration of prescribed opioids.

Here are some key ideas to convey to patients about proper use:
- Read the prescription container label each time to check dosage.
- Never use medicines after expiration date.
- Never share medicines with others.
- Do not take a pain medicine with alcohol or other sedatives.
- Do not take a pain medicine to promote sleep.
- Never break, chew, or crush medicines, particularly ER/LA opioid medications.
- For transdermal products, external heat, fever, and exertion can increase absorption, leading to a potentially fatal overdose.
- Transdermal products with metal foil backings are not safe for use in MRI scanners.
- Do not use transdermal products if they are broken or torn.

**Safe storage**

Patients need to be reminded that even children or close relatives can be tempted to use pain medications they have not been prescribed. Opioids are often obtained by teens, for example, from un-secured medicine cabinets of family and friends.

If possible, opioid pain medications should be stored in a locked cabinet or other secure storage unit. Storage areas should be cool, dry, and out of direct sunlight. Remind patients not to store medications in their car, to keep medications in the original containers, and to avoid storing medications in the refrigerator or freezer unless specifically directed to do so by a healthcare provider or pharmacist.

**Proper disposal**

The Office of National Drug Control Policy currently recommends that unused opioid pain medications be flushed down a toilet. Some states, however, may have different or more stringent guidelines. California, for example, instructs consumers not to flush any medicines down the toilet or drain. If flushing medicines is not allowed in your state, instruct patients to follow the instructions of a pharmacist for disposal or to mix the medicines with an undesirable substance, such as used coffee grounds, put the mixture into a disposable container with a lid or a sealable bag, and place it in the trash.

Before they are thrown out, personal information, including the prescription number, should be removed from empty medication containers. Patients should also be encouraged to use any drug take-back programs available in the local community. [Note: the Drug Enforcement Administration maintains up-to-date information on national take-back programs, as well as ways to find drug collection sites in any given locale. Information can be accessed at: www.deadiversion.usdoj.gov/drug_disposal/takeback/index.html.]

**Take-home naloxone**

In the future it may become more common to provide patients and their caregivers with the intranasal preparation of the opioid antagonist medication naloxone as a way to reverse the complications associated with accidental overdose. Although naloxone was FDA-approved in 1971 and has been used for decades by emergency medical services personnel, intranasal administration of naloxone is not currently approved by the FDA for at-home use as an antidote for opioid overdose so, as of this writing, this represents an off-label use of this medication. Numerous studies and community initiatives have attested to the safety, convenience, and effectiveness of providing intranasal naloxone to patients who may be at risk of overmedication or overdose. This includes patients who:
- Receive prescriptions of more than 50 mg of morphine equivalent/day.
- Are being rotated from one opioid to another when there may be incomplete cross-tolerance.
- Are opioid naïve and who have been prescribed methadone or who are rotated from another opioid to methadone.
- Are released after emergency medical care involving opioid intoxication or poisoning.
- Have a suspected history of substance abuse, dependence, or nonmedical opioid use.
- Have known or suspected concurrent heavy alcohol use.
- Have a respiratory infection or illness.
- May have difficulty accessing emergency medical services.

Efforts are underway in several states to make intranasal naloxone more widely available to the public and to train health care and emergency service providers in its use.

**Dealing with opioid overdose**

Because respiratory depression is the most serious potential harm from opioids, it is incumbent on clinicians to fully inform patients of this fact and educate them (and their home caregivers, if possible) on recommended steps to take in an emergency. Respiratory depression might occur because a patient takes more than the prescribed amount, either intentionally or unintentionally, or because the patient was mistakenly given too much medication by a caregiver. Point out that respiratory depression typically takes some time to develop, hence there will be early warning signs of overdose including:
- Intoxicated behavior – confusion, slurred speech, stumbling;
- Feeling dizzy or faint;
- Acting very drowsy or groggy;
- Unusual snoring, gasping, or snorting during sleep; and
- Difficulty waking up from sleep or staying awake.

Patients and their caregivers should be counseled to immediately call 911 or an emergency service if they observe any of these warning signs. If naloxone has been provided for the patient, it should be administered immediately, which will reverse respiratory depression and should allow the patient to begin breathing more normally. If a person has stopped breathing, artificial respiration/cardio-pulmonary resuscitation (CPR, including rescue breathing) should be begun immediately until emergency help arrives.

**Conclusions**

This monograph has summarized “best practices” for the responsible prescribing of opioid pain medications for chronic non-cancer pain. More detailed information on many of these topics is available from the resources listed. The treatment of pain is a dynamic and evolving field, and clinicians should periodically refresh their knowledge through reading, attending seminars or other events, or by taking additional CME courses.

Clinicians face the competing demands of relieving pain while minimizing potential harm to both patients and society. The steps and procedures described in this monograph provide a roadmap and structure by which clinicians can achieve these twin goals without incurring undue burdens of time or energy. Pharmacovigilance simply means that prescribers apply basic principles of prudent medicine to the needs of patients in pain. And because the evidence base for current guidelines remains sub-optimal, clinicians retain a great deal of latitude in deciding how that vigilance is best deployed on a day-to-day basis.
Table 5: Specific drug information for extended-release and long-acting opioid analgesics (ER/LA opioid analgesics)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
<th>Dosing interval</th>
<th>Key instructions</th>
<th>Specific drug interactions</th>
</tr>
</thead>
</table>
| Avinza    | Morphine Sulfate ER. Capsules, 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, and 120 mg. | Once a day. | ✷ Initial dose in opioid non-tolerant patients is 30 mg.  
✦ Titrating using a minimum of 3-day intervals.  
✦ Swallow capsule whole (do not chew, crush, or dissolve).  
✦ May open capsule and sprinkle pellets on applesauce for patients who can reliably swallow without chewing; use immediately.  
✦ Maximum daily dose: 1600 mg due to risk of serious renal toxicity by excipient, fumaric acid. | ✷ Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of morphine.  
✦ PGP inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold. |
| Butrans   | Buprenorphine. Transdermal System, 5 mcg/hr, 10 mcg/hr, 20 mcg/hr. | One transdermal system every 7 days | ✷ Initial dose in opioid non-tolerant patients when converting from less than 30 mg morphine equivalents, and in mild to moderate hepatic impairment - 5 mcg/hr dose.  
✦ When converting from 30 mg to 80 mg morphine equivalents - first taper to 30 mg morphine equivalent, then initiate with 10 mcg/hr dose.  
✦ Titrating after a minimum of 72 hours prior to dose adjustment.  
✦ Maximum dose: 20 mcg/hr due to risk of QTc prolongation.  
✦ Application:  
✦ Apply only to sites indicated in the Full Prescribing Information.  
✦ Apply to intact/non-irritated skin.  
✦ Skin may be prepped by clipping hair, washing site with water only.  
✦ Rotate site of application a minimum of 3 weeks before reapplying to the same site.  
✦ Do not cut.  
✦ Avoid exposure to heat.  
✦ Dispose of used/unused patches by folding the adhesive side together and flushing down the toilet. | ✷ CYP3A4 Inhibitors may increase buprenorphine levels.  
✦ CYP3A4 Inducers may decrease buprenorphine levels.  
✦ Benzodiazepines may increase respiratory depression.  
✦ Class Ia and III antiarrythmics, other potentially arrhythmogenic agents, may increase risk for QTc prolongation and torsade de pointe. |
| Dolophine | Methadone Hydrochloride. Tablets, 5 mg and 10 mg. | Every 8 to 12 hours. | ✷ Initial dose in opioid non-tolerant patients: 2.5 to 10 mg.  
✦ Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose and death. Use low doses according to the table in the full prescribing information.  
✦ High inter-patient variability in absorption, metabolism, and relative analgesic potency.  
✦ Opioid detoxification or maintenance treatment shall only be provided in a federally certified opioid (addiction) treatment program (Code of Federal Regulations, Title 42, Sec 8). | ✷ Pharmacokinetic drug-drug interactions with methadone are complex.  
✦ CYP 450 inducers may increase methadone levels.  
✦ CYP 450 inhibitors may decrease methadone levels.  
✦ Anti-retroviral agents have mixed effects on methadone levels.  
✦ Potentially arrhythmogenic agents may increase risk for QTc prolongation and torsade de pointe.  
✦ Benzodiazepines may increase respiratory depression. |
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<tr>
<th>Use in opioid-tolerant patients</th>
<th>Refer to full prescribing information.</th>
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| **Product-specific safety concerns** | • QTc prolongation and torsade de pointe.  
• Peak respiratory depression occurs later and persists longer than analgesic effect.  
• Clearance may increase during pregnancy.  
• False positive urine drug screens possible. |
| **Relative potency to oral morphine** | Varies depending on patient’s prior opioid experience. |
| **Duragesic** | Fentanyl.  
Transdermal System, 12, 25, 50, 75, and 100 mcg/hr. |
| **Dosing interval** | Every 72 hours (3 days). |
| **Key instructions** | • Use product specific information for dose conversion from prior opioid.  
• Use 50 percent of the dose in mild or moderate hepatic or renal impairment, avoid use in severe hepatic or renal impairment.  
• Application:  
  • Apply to intact/non-irritated/non-irradiated skin on a flat surface.  
  • Skin may be prepped by clipping hair, washing site with water only.  
  • Rotate site of application.  
  • Titrate using no less than 72 hour intervals.  
  • Do not cut.  
• Avoid exposure to heat.  
• Avoid accidental contact when holding or caring for children.  
• Dispose of used/unused patches by folding the adhesive side together and flushing down the toilet. |
| **Specific contraindications:** | • Patients who are not opioid-tolerant.  
• Management of acute or intermittent pain, or in patients who require opioid analgesia for a short period of time.  
• Management of post-operative pain, including use after out-patient or day surgery.  
• Management of mild pain. |
| **Specific drug interactions** | • CYP3A4 inhibitors may increase fentanyl exposure.  
• CYP3A4 inducers may decrease fentanyl exposure. |
| **Use in opioid-tolerant patients** | All doses of Duragesic are indicated for use in opioid-tolerant patients only. |
| **Product-specific safety concerns** | • Accidental exposure due to secondary exposure to unwashed/unclothed application site.  
• Increased drug exposure with increased core body temperature or fever.  
• Bradycardia.  
• Application site skin reactions. |
| **Relative potency to oral morphine** | See individual product information for conversion recommendations from prior opioid. |
| **Embeda** | Morphine Sulfate ER-Naltrexone.  
Capsules, 20 mg/0.8 mg, 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg, 100 mg/4 mg. |
| **Dosing interval** | Once a day or every 12 hours. |
| **Key instructions** | • Initial dose as first opioid: 20 mg/0.8 mg.  
• Titrate using a minimum of 3-day intervals.  
• Swallow capsules whole (do not chew, crush, or dissolve).  
• Crushing or chewing will release morphine, possibly resulting in fatal overdose, and naltrexone, possibly resulting in withdrawal symptoms.  
• May open capsule and sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately. |
| **Specific drug interactions** | • Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of morphine.  
• PGP inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold. |
| **Use in opioid-tolerant patients** | Embeda 100 mg/4 mg capsule is for use in opioid-tolerant patients only. |
| **Product-specific safety concerns** | None. |
| **Exalgo** | Hydromorphone Hydrochloride.  
Extended-Release Tablets, 8 mg, 12 mg or 16 mg. |
| **Dosing interval** | Once a day. |
| Key instructions | Use the conversion ratios in the individual product information.  
Start patients with moderate hepatic impairment on 25 percent dose that would be prescribed for a patient with normal hepatic function.  
Start patients with moderate renal impairment on 50 percent, and patients with severe renal impairment on 25 percent of the dose that would be prescribed for a patient with normal renal function.  
Titrate using a minimum of 3 to 4 day intervals.  
Swallow tablets whole (do not chew, crush, or dissolve).  
Do not use in patients with sulfa allergy—contains sodium metabisulfite. |
| Specific drug interactions | None. |
| Use in opioid-tolerant patients | All doses of Exalgo are indicated for opioid-tolerant patients only. |
| Drug-specific adverse reactions | Allergic manifestations to sulfa component. |
| Relative potency to oral morphine | Approximately 5:1 oral morphine to hydromorphone oral dose ratio, use conversion recommendations in the individual product information. |

**Kadian**

**Dosing interval** Once a day or every 12 hours.

| Key instructions | Product information recommends not using as first opioid.  
Titrate using a minimum of 2-day intervals.  
Swallow capsules whole (do not chew, crush, or dissolve).  
May open capsule and sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately. |
| Specific drug interactions | Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of morphine.  
PGP inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold. |
| Use in opioid-tolerant patients | Kadian 100 mg and 200 mg capsules are for use in opioid-tolerant patients. |
| Product-specific safety concerns | None. |

**MS Contin**

**Morphine Sulfate.**

**Controlled-release Tablets, 15 mg, 30 mg, 60 mg, 100 mg, and 200 mg.**

| Dosing interval | Every 8 hours or every 12 hours. |
| Key instructions | Product information recommends not using as first opioid.  
Titrate using a minimum of 2-day intervals.  
Swallow tablets whole (do not chew, crush, or dissolve). |
| Specific drug interactions | PGP inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold. |
| Use in opioid-tolerant patients | MS Contin 100 mg and 200 mg tablet strengths are for use in opioid-tolerant patients only. |
| Product-specific safety concerns | None. |

**Nucynta ER**

**Tapentadol.**

**Extended-Release Tablets, 50 mg, 100mg, 150 mg, 200 mg, and 250 mg.**

| Dosing interval | Every 12 hours |
| Key instructions | Use 50 mg every 12 hours as initial dose in opioid nontolerant patients.  
Titrate by 50 mg increments using a minimum of 3-day intervals.  
Maximum total daily dose is 500 mg.  
Swallow tablets whole (do not chew, crush, or dissolve).  
Take one tablet at a time and with enough water to ensure complete swallowing immediately after placing in the mouth.  
Dose once daily in moderate hepatic impairment with 100 mg per day maximum.  
Avoid use in severe hepatic and renal impairment. |
| Specific drug interactions | Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of tapentadol.  
Contraindicated in patients taking MAOIs. |
| Use in opioid-tolerant patients | No product-specific considerations. |
| Product-specific safety concerns | Risk of serotonin syndrome.  
Angioedema. |
| Relative potency To oral morphine | Equipotency to oral morphine has not been established. |
**West Virginia specific statistics and regulations**

Section 2.5.a West Virginia statistics on prescription drug abuse and resulting deaths

West Virginia had the second-highest rate of prescription drug overdose rates in the country—25.8 deaths per 100,000 people—in 2008, the latest year for which data are available. (New Mexico was first with 27 deaths per 100,000.) McDowell County had the 5th highest rate of drug poisoning deaths in the country in 2007-2008, at 38.3 deaths per 100,000 people.

Section 2.5.b Epidemiology of chronic pain and misuse of opioids

Pain remains the most common reason people seek health care. Chronic pain was estimated in a 2011 study to affect roughly 100 million Americans and to cost about $635 billion annually in treatment and lost productivity. In fact, the incidence of chronic pain in the U.S. is greater than that of diabetes, heart disease, and cancer combined. Inadequate pain management can cause many secondary health impacts including a heightened risk for complications (e.g., pneumonia, deep venous thrombosis), impaired recovery from injury or procedures, diminished quality of life, and a higher risk for anxiety, depression, and suicide.

Opioids are the most commonly-cited drugs among primary drug treatment admissions in West Virginia in 2010. “Other opiates” accounted for 34.9 percent of the total. Marijuana, the next-most-common admission, accounted for 12.3 percent of the total of 3803 reported admissions.

Section 2.5.e Pill counts

As part of routine practice, clinicians who prescribe opioids should perform medication reconciliation at each patient visit, which is defined by the American Medical Association as “…making sense of a patient’s medications and resolving conflicts between different sources of information to minimize harm and maximize therapeutic effects.” Random pill counts can be part of this effort and may be useful in cases of suspected abuse or diversion. A pill count is performed by notifying the patient a day before or on the day of the patient’s appointment that they should bring in any unused pills. Inability to provide pills, or providing either more or fewer than expected may suggest a problem, although physicians should not automatically presume that the problem is abuse or diversion. Many factors may be involved, and the situation should be explored with a non-judgmental, but firm, conversation with the patient.

Section 2.5.i Compliance with controlled substances laws and rules

Opioid pain medications are regulated by the U.S. Controlled Substances Act (CSA). All controlled substances have some degree of abuse potential or are immediate precursors to substances with abuse potential. Controlled substances are placed in their respective schedule based on whether they are determined to have a currently accepted medical use in the United States and on
their perceived abuse potential and/or likelihood of causing dependence. Schedule I substances are judged to have a high potential for abuse and no currently accepted medical use in the United States. Exemptions include heroin, LSD, and peyote. (Cannabis is currently listed in Schedule I, although there is considerable debate about this placement and many medical organizations advocate moving cannabis to a less restrictive schedule. 63) Schedule II substances are viewed as having a high potential for abuse or which may lead to psychological or physical dependence, and yet which also have an accepted medical use in the United States. Most opioid pain medications are Schedule II drugs. Other Schedule II drugs include amphetamine, methamphetamine, methylphenidate, and cocaine. Prescriptions for Schedule II drugs cannot be automatically refilled. Schedule III substances are considered to have a lower potential for abuse than substances in schedules I or II. Examples of Schedule III opioids include combination substances in schedules I or II. Examples of Schedule III opioids include combination substances containing more than 9 milligrams of codeine per dosage unit (i.e. Tylenol® with codeine®). Schedule IV and V drugs are considered to have even lower potentials for abuse than other schedules.

In addition to federal laws, the state of West Virginia has its own laws that relate to the issue of prescription drug abuse, misuse, and diversion. Most recently, law SB437 was signed into law in March of 2012 and contained several provisions seeking to address the epidemics of prescription drug abuse and diversion. 64 This legislation:

- Adds new regulations of opioid treatment centers prescribing methadone.
- Establishes licensing and regulation of Chronic Pain Clinics.
- Establishes review capabilities of the Controlled Substances Database to flag abnormal or unusual usage patterns of controlled substances by patients and unusual prescribing or dispensing patterns by licensed practitioners.
- Implements a requirement for continued education for physicians and other prescribers, dispenser and people who administer controlled substances.
- Regulates the pharmacy sale of pseudoephedrine.

Details of these regulations can be found at: www.wvems.com.

Section 2.5.7 Registration with and use of the West Virginia Controlled Substances Monitoring Program

West Virginia’s Controlled Substances Monitoring Program (CSMP) was established in 1995 by the state Board of Pharmacy for the monitoring of Schedule II-IV Controlled Substances. Data collection occurs once per week and collects an average of 3.3 prescriptions annually. 65 West Virginia received grants to fund its PDMP under the Harold Rogers Prescription Drug Monitoring Program Grants, administered by the Department of Justice of Bureau of Justice Assistance, in 2002 and 2004.

Law SB437 requires the use of the CSMP for health care providers who prescribe or dispense pain-relieving controlled substances to a patient for “chronic nonmalignant pain.” This is defined as “pain that has persisted after reasonable medical efforts have been made to relieve the pain or cure its cause and that has continued, either continuously or episodically for longer than 3 continuous months.” Licensed prescribers and dispenser must check the CSMP database to determine whether the patient has obtained any controlled substances from any source other than the current practitioner within the 12 month period immediately preceding the visit of the patient. Physicians and other prescribers must re-check the database at least annually if they continue to treat the patient with controlled substances for chronic pain. The prescriber or dispenser must promptly document in the patient’s medical record the rationale for prescribing or dispensing or administering the pain relieving controlled substance, information on controlled substances prescribed to the patient by another provider within the previous 12-month period, and a copy of the CSMP accessed report signed and dated. For more information about the CSMP, including how to register and access the database, visit www.wvbp.com.
1. Long-acting (LA) and extended-release (ER) formulations of opioids should typically not be used for which of the following?
   b. Treating acute pain.
   c. Treating end-of-life pain.
   d. Treating chronic non-cancer pain.

2. If an organic pathology cannot be found to explain a patient’s pain, what should a clinic infer?
   a. The pain is real, though unexplained.
   b. The pain is psychosomatic.
   c. The patient is seeking opioids for illegal use.
   d. The pain is the result of a mental health condition.

3. Which of the following is the appropriate use of “universal precautions” as it applies to patients with chronic pain?
   a. Exploring patients’ HIV status.
   b. Having all patients submit to frequent urine toxicology tests.
   c. Being vigilant about the possibility of misuse or abuse with all patients.
   d. None of the above.

4. The DIRE and the COMM are examples of which of the following assessments?
   a. Quantifying patients’ pain perceptions.
   b. Assessing patient risk of opioid misuse or abuse.
   c. Evaluating risk of physical adverse reactions to opioids.
   d. Determining a reason for opioid pain medications.

5. All of the following need to be documented in writing as part of an overall therapeutic approach to managing chronic pain patients EXCEPT:
   a. Informed consent.
   b. Patient/provider agreements.
   c. Treatment agreements.
   d. Answers to patient questions about insurance coverage.

6. All of the following are possible advantages of patient/provider agreements EXCEPT:
   a. Provides a foundation for subsequent decisions about treatment termination.
   b. Can help clinicians identify a patient’s level of risk for opioid abuse.
   c. Can help avoid misunderstandings between provider and patient.
   d. Can document informed consent.

7. Which of the following is correct regarding framing treatment goals solely around pain relief compared to functional goals?
   a. Framing around pain relief provides an objective means of measurement.
   b. It takes a significant reduction in pain to result in functional improvement.
   c. Functional goals help differentiate a patient who is truly addicted to opioids from one who seems to be addicted.
   d. None of the above.

8. The responsibility for obtaining evidence of success in meeting a functional goal lies with which of the following individuals?
   a. The clinician.
   b. The patient’s partner.
   c. The patient.
   d. Law enforcement officers.

9. When opioid treatment is initiated, both the patient and clinician should view the commitment as:
   a. Short-term trial of therapy.
   b. A long-term use of opioid therapy.
   c. A titration of the opioid to reach optimal pain relief.
   d. Continued therapy until adequate pain relief is achieved.

10. It can be particularly unsafe to combine opioids with which of the following other medicines?
    a. Stimulant medications.
    b. SSRI antidepressants.
    c. Benzodiazepines or barbiturates.
    d. Anti-hypertensive medications.

11. The duration of action of short-acting opioids is generally:
    a. 10 - 60 min.
    b. 2 hrs. maximum.
    c. 2 - 4 hrs.
    d. 8-10 hrs.

12. Short-acting opioids are most appropriate and commonly used for which of the following conditions?
    b. Breakthrough pain.
    c. Neuropathic pain.
    d. None of the above.

13. Combination products are those that include an opioid with which of the following elements?
    a. Non-opioid analgesic.
    b. Non-opioid narcotic medication.
    c. Opioid antagonist to prevent abuse.
    d. Caffeine.

14. What is the typical duration of action of the different ER/LA opioids?
    a. 30 – 90 min.
    b. 2 – 4 hrs.
    c. 4 – 12 hrs.
    d. 4 – 72 hrs.

15. All of the following types of patients need more frequent or intense monitoring EXCEPT:
    a. Those with a prior history of an addictive disorder.
    b. Adherent patients on a stable dose of opioid.
    c. Those with comorbid psychiatric conditions.
    d. Older adults.

16. Of the following tools, which one can help patients pinpoint triggers of breakthrough pain?
    a. Paper or electronic pain diary.
    b. Pill box organizers.
    c. Portable EEG monitors.
    d. Automated systems for sending patients reminders to take their medications.

17. Uncomfortable or unpleasant side effects (aside from constipation) may potentially be reduced by which two approaches?
    a. Switching to another opioid or taking the opioid with food.
    b. Switching to another opioid or using adjunctive medications to treat symptoms.
    c. Adding a non-opioid analgesic or trying a complimentary therapeutic technique.
    d. Changing the route of administration or advising patients to avoid alcohol consumption.

18. Which of the following is the APS-AAPM guideline regarding driving for patients prescribed opioid medication?
    a. Patients taking opioids should not drive for 1 month after starting them.
    b. There is no consensus on specifically how long patients should abstain from driving.
    c. Driving is at the discretion of the clinician.
    d. There are no driving restrictions.
19. One reason that methadone must be prescribed with particular caution is that:
   a. Methadone is only appropriate for opioid maintenance therapy programs.
   b. Methadone’s analgesic half-life is much shorter than its elimination half-life.
   c. Methadone has uniquely powerful respiratory depressive effects.
   d. Methadone may produce visual disturbances.

20. In 2006, the FDA added a caution to the “black box” warning that methadone may cause which of the following serious adverse effects?
   a. Respiratory depression.
   b. Cardiac conduction disturbances.
   c. Myoclonus.
   d. Renal failure.