Chapter 1
The Clinician’s Dilemma:
Under-Treated Pain Versus
Prescription Drug Misuse

In recent years, two compelling public health trends have become entwined like the twin serpents in the caduceus: first came increased clinical attention across all medical specialties to the under-treatment of pain, generating increased prescribing of opioid analgesics. This was followed by a shift in patterns of drug misuse from illicit to prescription drugs—most notably a dramatic rise in diversion and non-medical use of opioid pain medications within the United States.

As the gatekeepers of prescription medications, clinicians are being enlisted to fight on two fronts: combating pain, while simultaneously defending against the misuse of and addiction to opioid pain medications. Some clinicians bristle at adding “pharmacovigilance” and “risk management” to their already lengthy task list. But the combination of potential therapeutic benefit and high risk associated with opioid analgesics leaves us no alternative but to become more committed and sophisticated risk managers.

The practice of medicine is often a balancing act. Nowhere is this truer than in the treatment of patients in pain. Pain is the most common reason patients seek care, and treating pain often presents clinicians with significant challenges—not least of which is the fact that pain is always subjective. None of us can prove that someone does or does not have pain. It is always an “untestable hypothesis.”

Opioids are potent and reliable pain relievers, but they are not a panacea. Opioids do not work for all pain, or for all patients, and they may cause adverse effects ranging from mild to life threatening. The primary clinical goal is to balance the legitimate need to treat the harm that comes with ongoing pain with the equally compelling need to minimize other risks of harm, to both the patient and society at large.

Over the past two decades, clinicians who treat patients in pain have been buffeted by the winds of both data and opinion, alternately pushing
pain management towards and away from opioid therapy. Prior to the 1990s, clinicians often viewed opioid pain medications with skepticism and avoided prescribing them, even when risks were thought to be low. This perspective gave way to the recognition that many patients were being under-treated for their pain, leading to increased interest in the clinical value of opioids and a dramatic rise in rates of opioid prescribing for pain. In her 2008 testimony to the U.S. Senate Committee on Judiciary, National Institute for Drug Abuse (NIDA) Director Nora D. Volkow, M.D., stated: “Prescriptions for opiates have escalated from around 40 million in 1991 to nearly 180 million in 2007, with the U.S. their biggest consumer. The U.S. has supplied 99 percent of the world total for hydrocodone (e.g., Vicodin) and 71 percent of oxycodone (e.g., OxyContin).”

Today, opioids are the most-prescribed class of prescription medications in the United States, with hydrocodone as the single most prescribed drug in the US. Factors contributing to the rise in opioid prescribing include the introduction of long-acting formulations and novel delivery systems, as well as prescriber concerns over the dangers of non-opioid analgesics such as non-steroidal anti-inflammatory drugs (NSAIDS).

Escalating opioid prescribing rates coincided with a dramatic rise in diversion and nonmedical use of these powerful drugs, perhaps due in part to the misconception by abusers that prescription medications are less dangerous than illicit drugs. Another potential contributory factor was the proliferation of hundreds of rogue Internet sites where consumers could purchase opioid medications without prescriptions, or via “online consultations” with real or bogus physicians. Meanwhile, “pill mills” where opioids are prescribed indiscriminately to anyone who would pay, proliferated in states such as Florida and Kentucky. Alarming spikes in addiction and unintended overdose deaths paralleled heightened prescribing rates of opioid medications.

It remains unclear exactly how much of this problem of misuse, addiction, and unintended overdose death is related to well-intended, but possibly under-informed or under-educated prescribers who over-prescribe opioids for legitimate patients in pain.

The winds of clinical, regulatory, and public opinion are now pushing clinicians toward a more cautious approach to opioid prescribing with a greater emphasis on risk management. This paradigm shift is being driven by undeniably dire statistics that reveal the scope of devastation caused by inappropriate use of opioid medications.
 Clinicians, however, still face the challenge of balancing the real need for pain control with the need to minimize and manage the risks associated with opioid analgesics. My view is that this balancing act is not so different from the decisions required when clinicians use many other potentially risky pharmacological therapies. Solid medical practice is founded upon making rational and individualized decisions based on risk-benefit analyses, and I believe we can make these medical decisions about controlled substances in a manner that best serves the interests of our patients and society at large. In the early days of general anesthesia use, anesthesia-related morbidity and mortality occurred at unacceptable rates. Many thought anesthesia was too dangerous because clinicians had not yet learned how to use this tool safely. Many indispensible drugs have high risks. But over time, the medical community has established safe parameters for their use in appropriate cases.

Employing effective risk management is simply good medicine. Clinicians routinely use dangerous treatments—such as NSAIDS, carbamazepine, chemotherapy, and even insulin, to cite just a few examples—and we do so only when the potential benefits outweigh the risks. We use great care to deliver these risky therapies safely. The challenge posed by opioid analgesics is that not only are they potentially dangerous for patients, they are highly sought-after for misuse.

Prescribing opioid analgesics responsibly should not require that clinicians stake out polarized positions on the issues. Opioids are neither inherently “good” nor inherently “bad.” Nor is there any need to be “pro” or “con” when it comes to opioids. All clinicians can agree that we must support the use of opioids in those cases where it is in the patient’s best interest and oppose it when it is not. Your medical judgment, founded on prudent and shared medical decision-making, must weigh the potential risks and benefits of opioid therapy against alternative treatment options. The risk of non-treatment must also be included in this risk-benefit analysis. In daily practice, that means a prescriber may be “pro” opioid for one patient and “con” for another. This book provides a practical foundation for clinicians to perform the balancing act required in opioid management for persistent pain.

Prescription Drug Misuse
The chapters to come will describe how clinicians can implement responsible opioid prescribing in their busy daily practices. But first,
I want to be sure you fully appreciate the magnitude of the current problems with prescription drug misuse. Let’s be clear: the misuse of prescription opioid drugs in the United States has created a significant and growing public health crisis of addiction, overdose, and death. The opioid medications associated with these problems include immediate and extended release products, as well as methadone. Many people directly affected by the crisis have been previously healthy and have had no history of substance misuse.4

If nothing you’ve read or heard so far has focused your mind on this public health crisis, the following statistics should:

- Between 1998 and 2008, the rate of opioid misuse increased 400%.5
- More than 6 million Americans are abusing prescription drugs—more than the number abusing cocaine, heroin, hallucinogens, and inhalants, combined.6
- Emergency-room visits related to pharmaceutical opioids doubled between 2004 and 2008.7
- Between 1998 and 2008, there was a fivefold increase in drug treatment admissions for prescription opioids.8
- The number of deaths nationwide attributable to prescription opioid analgesics quadrupled between 1999 and 2007.7
- From 1999 to 2005 the number of hospital records related to poisoning deaths mentioning methadone increased 468%.9
- Opioid overdose is now the second-leading cause of accidental death in America, exceeded only by car crashes; in 17 states opioid overdose is the leading cause of accidental death.10

Behind these figures lie millions of tragic stories of untimely death, fractured families, shattered dreams, and wasted lives. The same spectrum of ills can be found in the wake of any abused drug, including alcohol, tobacco, heroin, and cocaine, to name just a few. But the fact that opioids are prescription drugs makes it imperative that prescribers become more vigilant risk managers as they care for patients in pain.

**The Continuing Need for Pain Management**

Given the magnitude of the problems related to opioid analgesics, it can be tempting to resort to draconian solutions: clinicians may simply stop prescribing opioids, or legislation intended to improve pharmacovigilance may inadvertently curtail patient access to care.
As we work to reduce diversion and misuse of prescription opioids, it’s critical to remember that the problem of unrelieved pain remains as urgent as ever.

Medicine and public health measures have succeeded in greatly increasing longevity. But although we live longer as a population, we do not necessarily live better. A 2011 congressionally mandated study by the Institute of Medicine Committee on Advancing Pain Research, Care, and Education reported that 116 million Americans suffer from chronic pain, costing up to $635 billion annually in treatment and lost productivity.11

Other surveys set the problem of chronic pain in stark relief:
- Among all adults 65 years of age and over who reported pain lasting more than 24 hours, 60% stated that it lasted more than one year.11
- In 2004, more than 25% of adults 18 years of age and over reported low back pain in the past 3 months, with high rates of limited activity and serious psychological distress.12
- Low back pain is the second most common neurological ailment in the US behind headache (when every type and severity level of headache are lumped together).13
- The incidence of pain in the US is greater than that of diabetes, heart disease and cancer combined.13, 14
- Tragically, research shows that 50-70% of patients die in moderate to severe pain, despite the availability of opioids and other therapies to control pain.15

Without doubt, there have been improvements in pain treatment in recent years. Significant efforts have begun to reduce the incidence of untreated or under-treated pain in children, older patients, and in all other vulnerable patient populations. The following general principles are now widely accepted for pain management, according to current clinical guidelines, policy statements, and organizational goals:16
- Pain management is integral to good medical practice for all patients.
- Opioid therapy to relieve pain and improve function is legitimate medical practice for acute and chronic pain of both cancer and non-cancer origins.
- Patients should not be denied opioid medications except when the risks outweigh the potential benefits.
• The use of opioids for other than legitimate medical purposes poses a threat to the individual and society.
• Prescribers have a responsibility to minimize the potential for the misuse and diversion of controlled substances.

Although pain remains the most common reason a patient seeks medical attention, most clinicians are grossly under-trained in pain assessment, pain management, and appropriate use of controlled substances. Four factors contribute to the ongoing problem of both undertreated pain and opioid over-prescribing:
1. Lack of knowledge among prescribers about current pain management guidelines, risk management practices, and research in pain medicine.
2. Lack of knowledge among prescribers about addiction, dependence, and misuse.
3. The perception that prescribing adequate amounts of opioids (high or low dosages) will result in unnecessary scrutiny by regulatory authorities.
4. Lack of understanding of regulatory policies and processes.

To these factors might be added a fifth: the absence of a clearly stated overview of how government regulations and professional guidelines for prescribing can be incorporated into the hectic daily practice of clinicians. This book answers this critical need.

**Responsible Prescribing With Incomplete Data**
Although both the problem of prescription drug misuse and the need for adequate pain relief are evident, clear clinical data to guide practitioners in balanced and responsible opioid prescribing remain elusive. But the absence of complete information about the risks and benefits of opioids does not relieve practitioners of the obligation to treat patients as safely and effectively as possible. Practicing medicine with incomplete and sometimes conflicting data is familiar territory for primary care and specialist clinicians alike, whether treating cardiac disease, cancer, or chronic pain. We remain obliged to treat pain as best we can, given the state of research, and to become and remain as well-informed as possible about the risks and benefits of specific medications. That’s what this book is all about.
Many difficult issues regarding the use of opioids remain poorly supported, one way or the other, by clear science. In the chapters to come, I’ll deal with many of the challenges presented by vexing questions that have limited science in guiding clinical practice, such as the efficacy of opioids in chronic pain, rates of and concerns about addiction and misuse, and dose escalation and discontinuation.

The evidence supporting long-term efficacy for opioid use in chronic noncancer pain is limited and of low quality. The 2009 APS-AAPM Clinical Guidelines For the Use of Chronic Opioid Therapy in Chronic Noncancer Pain concluded that clinical data on efficacy are currently not adequate to support or refute the role this treatment should play for any given individual (Appendix B). In addition, the rate of addiction or misuse in patients given opioids for chronic pain is commonly questioned. It was previously believed that addiction associated with opioids for chronic pain was rare. The data upon which these conclusions were drawn, however, have been found to be inadequate and seriously flawed. Although we currently do not know the exact rate of addiction in patients legitimately prescribed opioids for pain or the rate of overall misuse, we know that rates are high enough that they should be considered a significant potential adverse effect.

Addiction and misuse are often a major concern associated with opioid use. Opioids, however, have a wide range of potential adverse effects that can predispose a patient to serious morbidity and mortality. Much of this risk relates to respiratory depression, potentially leading to unintended overdose, negative impact on endocrine function, and possibly, heightened fracture risk related to effects on bone metabolism and from falls. Risk is increased among the elderly; those with impaired renal or hepatic function; individuals with cardiopulmonary disorders, such as chronic obstructive pulmonary disease (COPD); congestive heart failure (CHF), sleep apnea, or mental illness; and in patients who combine opioids with other respiratory depressants such as alcohol, sedative-hypnotics, benzodiazepines, or barbiturates.

In cases where patients do not respond to long-term opioid therapy, some clinicians routinely escalate the dose, hoping that higher doses will either achieve the desired analgesia or overcome pharmacological tolerance. Many clinicians were taught that there was no ceiling dose with opioids, and to titrate up until pain was relieved (or there were intolerable side effects). Escalating dosages as a reflexive response to poor
efficacy, however, is a serious mistake. Patients who do not respond to a trial of opioids, with structured dose titration and monitoring, must be evaluated to determine whether or not the pain is responsive to opioids, whether efficacy is limited because of side effects or inadequate dosing, or whether misuse or diversion is possible. Scientific data are inadequate to guide us in one direction or another but common sense can help to a great extent. We know that dose escalation comes with increased risk, so when increased dosing is thought to be warranted, we must proportionately raise our vigilance, with a clear view toward indicators of efficacy in the absence of indicators of adverse effects or aberrant use. Prescribers must develop distinct, measurable end-points for their treatment plans (e.g., functional capacities, exercise tolerance, sleep, mood, social interaction), and they must be as willing to discontinue therapy as they are to initiate it. A structured approach to discontinuing opioid therapy (commonly referred to as an “exit strategy”) should be part of treatment planning at dose initiation.

Starting opioid therapy can be easier than stopping it. But, if you are not prepared to stop the treatment—if it does not work, if the chronic pain syndrome subsides, or if its risk outweighs its benefits—you probably should not start it. Discontinuing a long-term opioid regime is easiest at the earliest signs of ineffectiveness, intolerance, or aberrant use. Assessment of efficacy and safety should occur before dosages rise to high levels, as high dosages require clear evidence of benefit without adverse outcomes or aberrant patient behavior. Long-term opioid therapy that continues without clear evidence of benefit, or despite evidence of adversity or aberrant use, may contribute to an iatrogenic problem where tapering becomes more difficult, or requires protracted periods of time or specialized intervention.

In an effort to guide healthcare providers in the context of unanswered research questions, the Centers for Disease Control and Prevention (CDC) in 2010 issued the following recommendations, which it acknowledged are based on promising interventions and expert opinion, not rigorous evidence-based research:10

- 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 noncancer pain who is being treated with opioids for more than six weeks.

- If a patient’s dosage has increased to ≥120 morphine milligram equivalents per day without substantial improvement in pain and function, seek a consult from a pain specialist.
- Do not prescribe long-acting or controlled-release opioids (e.g., OxyContin®, fentanyl patches, and methadone) for acute pain.
- Periodically request a report from your state prescription drug monitoring program on the prescribing of opioids to your patients by other providers.

All of these points will be explored in more depth in later chapters. For now, let me briefly summarize the fundamental tenets of responsible opioid prescribing, as presented in this book, which expand upon the CDC recommendations:

**Summary**

**PATIENT EVALUATION AND SELECTION**

- Reserve long-term opioid therapy for patients who have tried other potentially effective treatments that pose less risk, including physical therapy, exercise, cognitive-behavioral therapy, and non-opioid analgesics.
- Screen patients before and during treatment for risks of all adverse outcomes, including those with mental illness and substance misuse, cardiopulmonary disease, and endocrine disorders.
- Understand that patients may be reluctant to disclose a history of substance misuse. Always check the medical record, a prescription drug-monitoring database, and third parties within the allowable circle of care.
- Don’t start long-term use of opioids by default. Long-term opioid prescribing should generally be reserved for persistent or chronic pain and should only occur after careful patient selection, discussion of risks, and the setting of realistic expectations and functional goals.
- Educate patients about the risks and benefits of opioid medications, as well as about their proper storage and disposal, so that they can make informed decisions about choosing or rejecting opioid therapy.
TREATMENT PLANS

• Be sure that the decision to start treatment is clearly agreed to by the patient and prescriber, and that each is informed about (and is willing to work toward) treatment continuation or termination based on functional goals and safety.

• Explain to patients that opioids used to treat acute pain are for time-limited use. At the outset, set expectations that opioids should be discontinued when the pain problem is no longer acute.

• Avoid dispensing more medication than necessary. A 30-day supply for acute pain may be more than necessary. In treating acute pain with opioids, give only the amount believed to be needed. Be aware that excess medication may serve to stock an uncontrolled medicine cabinet and increase the risks of accidental toxicity or diversion.

PERIODIC REVIEW AND MONITORING

• Never continue long-term opioid therapy with patients who, after reasonable efforts, show inadequate progress toward functional goals.

• Consult with more specialized healthcare providers if a patient’s problems exceed your range of expertise. Do not accept unmanageable risk just because the appropriate consultant may not be available.

• Don’t abandon patients with aberrant behaviors or a prescription drug problem. Consider all possible causes for the behavior and remain open to employing other potentially safe treatments.

• Question how your patient is using his or her opioids. Some patients may not use the drugs you prescribe as directed. They may vary the dosing or combine them with other dangerous substances, drugs, or alcohol in ways that are not advisable.

• Have clear treatment parameters beyond which continued use requires re-evaluation. For instance, acute pain that continues to require opioid therapy should be fully re-evaluated.

• Exercise compassion and trust—but verify. Recognize that misuse and addiction often coincide with denial and a striking lack of insight. Clinicians, therefore, must use all available tools to discern these problems as early as possible. This includes closely monitoring functional and behavioral status, utilizing urine toxicity screens and prescription drug monitoring systems, and remaining engaged in care before and after any potential adverse outcomes.
In the rest of this book I will “unpack” these bullet points with an eye to the real-world, day-to-day demands made on clinicians like you and me. Although the challenges of balancing the potential benefits and risks of opioids are real, they’re no different than the choices presented by potentially risky treatments in other spheres of medical practice. As you will see, responsible opioid prescribing often relies on subtle changes of attitude, relatively simple changes to policies or procedures, and a willingness to examine one’s current approach to opioids. When opioids are prescribed responsibly, both patients and clinicians benefit.