INTRODUCTION

Opioids are just one of a large armament of tools to treat acute (days to weeks) and chronic (months to years) pain, to relieve the physical distress of patients, and to maximize their quality of life. Physicians wield the power to heal and relieve pain. However, the same power has the potential to contribute to harm, especially in the case of prescribed opioids.

Current prescribing patterns by many have contributed to large increases in abuse, drug overdoses, and deaths. More than 50 people die of opioid overdoses each day in the US, surpassing overdose deaths owing to all illicit drugs and motor vehicle crashes. Careless or criminal physicians are being investigated and prosecuted in increasing numbers by local, state, and federal law enforcement.

To accentuate the severity of the crisis, new action is occurring at the state and federal levels. Last year, the Centers for Disease Control and Prevention (CDC) released new opioid prescribing guidelines; the Food and Drug Administration (FDA) added a black box warning for prescribing opioids and benzodiazepines; US Surgeon General Vivek Murthy sent a letter to all US physicians asking them for commitment to “Turn the Tide” on the opioid crisis; and the White House convened a summit of national leaders on this subject.

Causes of the Crisis

Efforts to increase prescribing for pain were intense in the 1990s and early 2000s. Regulatory bodies, including The Joint Commission, called on pain to be “made visible,” resulting in many calls to implement pain as the fifth vital sign. National groups unrealistically recommended “getting pain to zero.” In addition, pharmaceutical companies developed stronger and long-acting opioids, with aggressive marketing to physicians, while minimizing potential risks. Nonlegitimate users found that short-acting opioids (hydromorphone, oxycodone) and long-acting opioids (when “broken” of their time-release coatings) may result in enhanced euphoria and potentiation of their addictive nature. “Pill mill” practices sprang up across the US. Many well-meaning physicians prescribed high-dose opioids because of a lack of, or erroneous, education and experience, being naïve or exceedingly busy, or not recognizing the dangers that existed. Sadly, some patients who were started on opioid therapy for pain ultimately abused these medications. Tragic for far too many, this resulted in drug overdoses and death. A very small proportion of patients began selling their prescribed opioid medications for profit (“diversion” of medications).

From 2000 to 2014 the rates of opioid sales greatly increased, resulting in a quadrupling of opioid overdoses and a similar rise in opioid prescription-related deaths. The Sidebar: Potential Side Effects of Opioid Medications lists serious and common potential side effects of opioid use.

Data from the CDC document that more than 47,000 people in the US died of drug overdose in 2014, of which 60.9% involved an opioid. According to the CDC, approximately 44 people per day die in the US of opioid prescription overdoses, resulting in more than 16,000 deaths annually, with benzodiazepine overdoses contributing another 8000 deaths. In addition, drug use and misuse annually result in more than 2.5 million Emergency Department visits, of which 56% are for prescription

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Physician Guide to Appropriate Opioid Prescribing for Noncancer Pain

The approach to a patient’s pain must be individualized and multimodal. A thorough history, physical examination, and evaluation is needed to reach as specific a diagnosis as possible. One must weigh the potential benefit of a treatment with the potential risk. A physician’s efforts to relieve pain must not violate the mandate to “do no harm.” Depending on the pain severity, treatment must be tailored using multiple tools. Such tools include 1) nonpharmacologic (eg, physical therapy, heat, ice, massage, rest, exercise, meditation, cognitive-behavioral therapy; 2) pharmacologic, including topical medications, nonopioid medications (eg, acetaminophen, nonsteroidal anti-inflammatory drugs, tricyclic antidepressants); 3) opioids; 4) procedures (eg, joint and trigger point injections, nerve blocks, epidural injections); and 5) devices (eg, transcutaneous electrical nerve stimulation, implanted neurostimulators).

Acute and chronic pain are not identical actions, with 37% accounted for by opioids or benzodiazepines.11

Physicians prescribing opioids and other controlled substances are being scrutinized with greater intensity and numbers. The Medical Board of California reported a 195% increase in disciplinary action outcomes related to controlled substance prescribing between the reporting years 2009 to 2010 and 2014 to 2015.12,13

Responses by Government and Health Systems

Government agencies and individual health care organizations are attempting to intervene in the opioid oversuse crisis. The CDC, FDA, and US Surgeon General have become active participants in responding to this problem.24

Local health care organizations are attempting to provide an infrastructure to promote safe prescribing and monitoring of opioid pain medications. For instance, in 2010, Kaiser Permanente Southern California (KPSC) took carisoprodol (Soma) and oxycodone (OxyContin) off the formulary because of the highly addictive and dangerous nature of the medications. Recently KPSC adopted the following opioid prescribing goals:

1. Protect our community and schools by decreasing the supply of opioid prescriptions to patients at high risk of diversion
2. Help avoid new patients becoming addicted to or dependent long term on opioids
3. Help reduce risk of overdose and death in our current patients who are receiving higher-dose opioids
4. Treat patients’ pain in a safe and effective manner, using medications (including opioids and pain-modulating drugs) and other treatments as applicable.

Thus far, these actions have resulted in a reduction in OxyContin prescribing by more than 85%; reduction of all brand-name opioid prescribing (these have a higher street value when diverted) by more than 95%; and a decrease in the number of patients receiving more than 120 mg/d morphine equivalent dosing (MED) by 31%.14

In late 2016, California passed legislation15 that, once enacted, will require physicians to check the state’s prescription drug monitoring program, called Controlled Substance Utilization Review and Evaluation System (CURES 2.0), before prescribing opioids. Similar requirements are being considered in other states.

Legal Implications

The Drug Enforcement Administration (DEA) and local law enforcement have begun to conduct sting operations in which undercover agents present to physicians in the office requesting opioid prescriptions without medically legitimate reasons. Through these and additional efforts, a small number of physicians have been found to have engaged in criminal activity, with other careless physicians noted to have departed from the standard of care. This has subsequently resulted in incarceration, loss of license, or other practice restrictions.

Physicians and health systems may reduce their exposure to investigation and prosecution by adhering to best practices and standards of care in pain control and opioid prescribing within their specialty. When prescribing opioids, physicians are bound by medical and legal regulations. Federal law16 states that a controlled substance prescription must be issued for a “legitimate medical purpose by an individual practitioner acting in the usual course of his [or her] professional practice” [emphasis the author’s].16 To comply, one must follow the standard of care based on one’s general specialty (eg, primary care, emergency medicine). For opioid prescribing specifically, substantial compliance with opioid prescribing guidelines is the accepted standard of care and satisfies adherence to the many state and federal laws governing this. Failure to follow the standard of care and guidelines puts both patients and physicians at risk.

Potential Side Effects of Opioid Medications

<table>
<thead>
<tr>
<th>To the user</th>
<th></th>
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<tbody>
<tr>
<td>Misuse</td>
<td></td>
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<tr>
<td>Substance use disorder (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition)</td>
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<tr>
<td>Overdose death</td>
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<tr>
<td>Respiratory depression</td>
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<tr>
<td>Somnolence and sedation</td>
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<tr>
<td>Withdrawal if abruptly stopped</td>
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<tr>
<td>Constipation</td>
<td></td>
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<tr>
<td>Androgen deficiency</td>
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<tr>
<td>Depression and anxiety</td>
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<tr>
<td>Opioid-induced hyperalgesia</td>
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<tr>
<td>Urinary retention</td>
<td></td>
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<tr>
<td>Nausea and vomiting</td>
<td></td>
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<tr>
<td>Hypotension</td>
<td></td>
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<tr>
<td>Liver toxicity</td>
<td></td>
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<tr>
<td>Pruritus</td>
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</tbody>
</table>

To the pregnant user’s fetus or newborn

| Preterm delivery                                  |   |
| Congenital defects: heart, neural tube, etc       |   |
| Neonatal abstinence syndrome                      |   |
| Multiple other possible effects                   |   |


**Safe Prescribing Policies**

Initiation of systemwide, clinic-wide safe-prescribing practices support the physician and patient such that the patient’s well-being is at the heart of all pain management decisions. Policies should emphasize the partnership and commitment of the physician and patient in working for the patient’s overall well-being; using and following pain agreements; initiating prescribing and refill details; appropriate monitoring; subspecialist referrals for those not improving or deteriorating; and tapering strategies when possible.

**OPIOID-PRESCRIBING GUIDELINES**

The Medical Board of California has published detailed but nondirective guidelines. Other guidelines containing similar key elements include those from the American Academy of Pain Management, the American Pain Society, and the Washington State Agency Medical Directors’ Group.

**Key Elements of Opioid Prescribing Guidelines**

The Sidebar: Checklist for Prescribing Opioids provides a detailed checklist of key elements critical in the evaluation and management of a patient when the prescribing of opioids is believed to be indicated. More specifics are expanded on in this section.

**History**

This must be detailed and include current and past information. Physicians ought to “trust but verify” which should be done by reviewing old records, urine drug screening, and checking information from a prescription drug monitoring program. These will confirm or refute the story given by the patient. In light of the large amount of abuse and diversion, physicians must be on the alert for “red flags” (see Sidebar: Red Flags for Drug Abuse, Addiction, or Diversion).

Addiction risk screening is vital and should include personal and family history of alcohol, illegal and/or prescription drug substance abuse (including tobacco, age, history of sexual abuse), and a personal mental health history. Tools include the

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**Checklist for Prescribing Opioids**

- **History**
  - Current specific pain symptoms
  - Past pain, imaging, treatment, consultations, procedures, etc. (get old records)
  - Chronic medical problems
  - Medications: All including over-the-counter; verify via a prescription drug monitoring program (PDMP)—e.g., the California Controlled Substance Utilization Review and Evaluation System (CURES)—or via urine drug screening
  - Alcohol and drugs: Current and past
  - Mental health
  - Opioid Risk Tool (ORT), Screener and Opioid Assessment for Patients with Pain (SOAPP), or similar

- **Physical examination**
  - Vital signs
  - General examination
  - Specific detailed examination: Area of symptoms

- **Additional diagnostic evaluation as indicated**
  - Imaging: Consider on the basis of pain level, injury, chronicity
  - Laboratory tests (including urine drug testing, renal and liver function)
  - Additional testing as needed

- **Assessment: As specific as possible**
  - Treatment plan with goals (must be medically justified): Individualized
  - Informed consent about risks and benefits

- **Controlled substance agreement (optional but a good idea)**

- **Medical records documentation: Be thorough**

- **Consultation: When there is failure to improve or deterioration**

- **Periodic review (follow-up visits)**
  - Analgesia: Pain control
  - Activities of daily living
  - Adverse effects
  - Affect
  - Aberrant behaviors

- **Monitoring**
  - CURES or other PDMP
  - Urine drug screening
  - Laboratory testing: As indicated; patient specific
  - Updated brief history, examination, assessment
  - Morphine equivalent dosing (MED) calculation and monitoring

- **Prescribing to addicts**
  - Specific state and federal laws and statutes
  - “Trust but verify”: Be on the lookout for red flags of abuse, misuse, or diversion; addicts will say anything to get the drugs desired
  - Drug combinations: Common among those abusing or diverting: Opioids plus benzodiazepines with or without carisoprodol

- **Excessive or high-dose opioids**: 100 mg/d MED, also referred to as morphine milli equivalents

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Red Flags for Drug Abuse, Addiction, or Diversion

- Early refills/claims that the medications were lost or stolen—even with a police report
- Age 35 years or younger, especially combined with other red flags
- Concurrent use of multiple pharmacies
- Obtaining controlled substances from multiple physicians or “doctor shopping”
- Excessive amounts or drug combinations
- Obtaining or buying controlled substances from family, friends, or others
- Giving or selling controlled substances to family, friends, or others
- Use/abuse of alcohol or drugs—current or past
- Use of tetrahydrocannabinol/marijuana, even with a medical marijuana card
- Use of drug culture street lingo for the names of the medications or other drugs
- Inconsistent results from urine drug screens or the prescription drug monitoring program report
- Patients driving long distances to see the physician for controlled substances
- Multiple family members or those residing in the same household receiving identical or similar controlled substances
- Similar or identical prescribing (eg, medication selection, strengths) regardless of specifics of symptoms such as pain severity, examination findings, diagnosis, etc (lack of individual management plans)
- Failure to improve without adjustment of management plan
- Drug overdoses

Note: Presence of any red flag necessitates additional information to confirm.

### Morphine Equivalent Dosing

Patients receiving opioids should have their MED calculated (mg/d) using an opioid calculator and documented (Table 1). Overdose risk increases by 3.7% in patients taking an MED of 50 to 99 mg/d. This risk increases to 8.9%, with an annual overdose death rate of 1.8%, when the MED is 100 mg/d or greater. When higher dosages are necessary, documentation of specific informed consent by the patient, closer monitoring, and periodic comanagement by an appropriate subspecialist is required. Home naloxone rescue preparations may be warranted if the patient is at higher risk of overdose and death. Patients build tolerance to opioids over time and are at higher risk of overdose and death when there is a gap in opioid medication use (eg, incarceration, rehabilitation), especially if placed back on previous opioid dosages.

### Case Example: Appropriate Care of an Acute Injury

A 50-year-old athletic woman sustained an injury while snow skiing, resulting in pain at the distal lateral aspect of the left knee that she described as 10 on a 10-point pain scale. Within 2 hours of the injury, the patient was evaluated, which included a thorough history, examination, and radiographs that confirmed a small proximal fibular fracture. The patient had no history of substance abuse. She was prescribed hydrocodone-acetaminophen, 10/325 mg tablets, to be used up to every 6 hours (4 maximum in 24 hours) for severe pain, ice off and on for 48 hours, knee brace, and crutches or cane as tolerated, with phone advice from orthopedics. Within 48 hours, and after taking a total of 5 opioid tablets, the patient limped with a cane, and the pain level ranged from 5 to 7. As advised, the patient changed her medication to over-the-counter nonsteroidal anti-inflammatory drugs. Physical therapy was started to assist further rehabilitation after 2 weeks. The remaining 5 hydrocodone tablets were appropriately destroyed.

This case exemplifies appropriate evaluation and management, including low-dose, short-course opioids, alternative pharmacologic and nonpharmacologic management, and destruction of leftover opioids.

### SPECIAL PRESCRIBING CIRCUMSTANCES

#### Prescribing to Patients with Substance Use Disorder

Patients with substance use disorder with medically legitimate pain sufficient to justify opioids must be closely monitored, including through random urine drug screening, reviews using a prescription drug monitoring program, appointment visits, and consultation with a subspecialist. Addiction medicine comanagement may be necessary. Detailed documentation is vital.

### Response to Potentially Aberrant Behavior

Patient treatment must be individualized, including responses to potential aberrant behavior, on the basis of the entirety of the information. Prescription forgery or theft would generally require involvement of law enforcement. Overdose would require treatment modification and at times medication discontinuation. At the other end of the spectrum, rare diversion of a few tablets to a family member for emergent, acute pain or a one-time aberrant finding on a urine drug screen may warrant a documented discussion with the patient and closer monitoring.

If it becomes apparent that the patient is not using these medications for medically legitimate purposes, the opioid dosage must be rapidly tapered. Abusive or violent behavior by the patient also requires immediate intervention. Options include addiction medicine specialists and buprenorphine treatment. Tapering of opioid dosages and the management of substance use disorder are difficult issues and beyond the scope of this article.

### Kidney, Liver, Heart, and Lung Disease

Diseases of each of these organ systems may affect or be affected by treatment with opioids and other controlled substances. Liver disease makes using acetaminophen difficult, and renal disease often prevents the use of nonsteroidal anti-inflammatory medications. When possible, use noncontrolled substance medications, and when opioids are necessary, use lower dosage strengths and quantities with very close monitoring. Additional treatments to consider may include heat or ice, exercise, physical therapy, topical analgesic creams, and alternative medicine approaches.

### Dangerous Drug Combinations

Physicians must beware of dangerous drug combinations. Sometimes dangerous combination are prescribed for medically legitimate reasons, without recognition of the dangers. However, other times they are requested by the patient because they are popular in the recreational drug community and commonly diverted. These combinations place the patient at additional risk of overdose and death, as does concurrent use of alcohol and other sedating medications (both prescriptions and over-the-counter). The use of fentanyl transdermal patches and long-acting opioids in opioid-naïve patients also places the patient at a higher risk of oversedation and overdose. Dangerous drug combinations also include the following:

- **“Trinity” or “Holy Trinity”:** Opioid plus benzodiazepine plus carisoprodol
- **“Sizzurp”:** Promethazine with codeine cough syrup plus Jolly Rancher fruit-flavored hard candy (The Hershey Company, Hershey, PA) plus fruit-flavored soda (eg, Sprite [The Coca Cola Company, Atlanta, GA])
- **Opioids and benzodiazepines (FDA black box warning).**

#### Table 1. Morphine equivalent dosing (MED) summary calculator

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand</th>
<th>Relative strength</th>
<th>100 mg/d MED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>MS Contin, etc</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Norco, Vicodin</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>OxyCodeine, Roxycodone</td>
<td>1.5</td>
<td>66</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Dilaudid</td>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>Opana</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>Methadone</td>
<td>Methadose</td>
<td>8-12</td>
<td>10</td>
</tr>
<tr>
<td>Fentanyl transdermal patch</td>
<td>Methadose</td>
<td>100</td>
<td>42</td>
</tr>
</tbody>
</table>

* Sometimes referred to as morphine milliequivalents (MME). Oral administration unless otherwise specified. Calculations were made using the Washington State Agency Medical Directors’ Group’s Opioid Dose Calculator (available from www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm).29
**DISCUSSION AND RECOMMENDATIONS**

In light of the increase in opioid prescribing since 2012, and the opioid overdose death rates surpassing deaths caused by traffic accidents and illicit drugs, urgent actions are necessary. These actions must be taken by physicians, health plans, the government, and others. Most prescribing physicians feeding the opioid epidemic are well meaning, naïve, or just too busy to recognize the dangers.

Physicians must educate themselves and proactively do the right thing as far as opioid prescribing. Physicians and society must be reeducated that opioid pain medications for noncancer pain should be the rare exception, rather than the rule. Written visit checklists may be useful, especially in group practices where the patient may be seen over time by multiple physicians but also for physicians in smaller or one-physician offices. Electronic medical record systems are able to assist in many ways, including incorporating best practice alerts.

Practical actions physicians can take include:

- Recognize that the opioid crisis is ravaging families and communities
- Avoid opioid pain medications whenever possible; start with safer alternatives
- Follow the CDC opioid prescribing guidelines2 (see Sidebar: Centers for Disease Control and Prevention [CDC] 2016 Opioid Prescribing Guidelines Summary) for new patients with pain and for patients with chronic pain when possible
- Ensure that the opioid prescriptions are truly for medically legitimate purposes, with vigilance for red flags (see Sidebar: Red Flags for Drug Abuse, Addiction, or Diversion)
- Carefully follow in substantial compliance the Opioid Prescribing Guidelines described above, and in the Sidebar: Checklist for Prescribing Opioids—with the provision of detailed documentation in the medical record
- Follow the US Surgeon General’s call to action and consider taking the Surgeon General’s pledge at http://turnthetiderx.org:
  - Educate ourselves to treat pain safely and effectively
  - Screen patients for opioid use disorder and provide or connect them with evidence-based treatment
  - Talk about and treat addiction as a chronic illness, not as a moral failing.
  - Physicians, among others, played a major part in the current opioid crisis. Committed and caring physicians will also have a great impact in “turning the tide” of the opioid crisis.

**Disclosure Statement**

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**How to Cite this Article**


**References**


**Centers for Disease Control and Prevention [CDC] 2016 Opioid Prescribing Guidelines Summary**

Because of increasing risks of overdose and death of users of opioids, the CDC released its “Guideline for Prescribing Opioids for Chronic Pain”1 in March 2016. The guidelines can be used as a best practice guideline but are not the standard of care at this time.

- Avoid benzodiazepines with opioids (increases risk of overdose and death vs opioid-only use)
- Perform periodic benefit-risk evaluation, including prescription drug monitoring program database review and urine drug screen
- Prescribe nonpharmacologic and nonopioid treatment as first line
- For chronic pain, avoid opioids; risk outweighs benefits for most
- Discuss risk-benefits with patients and document
- Establish realistic goals before opioid therapy starts
- Start with immediate-release opioids; avoid methadone as first line because of higher risk
- Use additional precautions if dose exceeds morphine equivalent dosing [MED] of 50 mg/d
- Generally, avoid increasing the dosage to MED 90 mg/d
- Prescribe a maximum of only 3 days of opioids for acute pain for most nontraumatic, nonsurgical pain.

Concerns regarding the CDC guidelines are that they may limit access to opioids for some patients for whom opioids may benefit.

The monitor, and Rest the cure, are starting points for contemplation which should ever be present to the mind of the surgeon in reference to his treatment.

— John Hilton, FRCS, FRS, FZS, 1805-1878, English surgeon and Charter Fellow of the Royal College of Surgeons, professor of anatomy

Starting Points

Pain the monitor, and Rest the cure, are starting points for contemplation which should ever be present to the mind of the surgeon in reference to his treatment.