# Review of Opioid Prescribing in the Osteopathic and Ambulatory Setting

Ahmad I. Hussein, MBS; Christopher F. Bekampis, OMS IV; Richard T. Jermyn, DO

From the NeuroMusculoskeletal Institute at Rowan University School of Osteopathic Medicine in Stratford, New Jersey.

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Address correspondence to: Richard T. Jermyn, DO, Rowan University School of Osteopathic Medicine NeuroMusculoskeletal Institute, 42 E Laurel Rd, Ste 1700, Stratford, NJ, 08084-1354.

Email: jermynrt@rowan.edu

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**The opioid epidemic in the United States is one of the largest modern health crises in the nation's history. The crisis has been cultivated in academic journals, driven by the medical-pharmaceutical complex, and fueled by campaigns representing the most prestigious health care organizations and advocacy groups. Comprehensive guidelines for proper prescribing have been released in addition to state-sponsored prescription drug–monitoring programs (PDMPs) in response to overprescribing habits. When considering opioid treatment for a patient, physicians should document a thorough history of pain, give an appropriate physical examination, and complete a risk assessment using the proper diagnostic tools. Considering the osteopathic philosophy and approach to chronic pain, physicians should account for an integrative treatment approach for improved patient outcomes when considering applying the osteopathic philosophy to chronic pain management. A successful treatment plan can integrate cognitive behavioral therapy and promote self-healing by treating somatic dysfunctions with osteopathic manipulative treatment. This literature review discusses how to treat patients with chronic pain and how to properly use and prescribe opioids. The researchers analyzed the history and current status of the opioid epidemic, examined opioid management in the outpatient setting, reviewed the current domestic and international opioid prescribing guidelines, and discussed the incorporation of the osteopathic philosophy to manage chronic pain.**

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The current opioid epidemic in the United States has shown irrepressible growth for the past 2 decades and has resulted in 200,000 deaths to date due to opioid-related drug overdoses—approximately 116 deaths per day.[1,2] Despite targeted efforts from an array of governing bodies and institutions, the United States was the largest per capita consumer of opioids in the world from 2013 to 2016, which has had a significant impact on the global disease burden.[3-5] Trends in the rate and daily dose of opioids used among commercial and Medicare Advantage beneficiaries from 2007 to 2016 showed that opioid use and average daily prescription dose have exhibited no significant decline from their peak levels, despite the systematic growth of prevention and awareness efforts by federal and state institutions.[6]

Pain is generated in the central nervous system (CNS) from nociceptive signals and processed by the cerebral cortex in the brain. The pathophysiology of chronic pain

involves repetitive and persistent nociception, which results in long-term synaptic changes that result in lower thresholds for pain and exaggerated pain perception, a process known as central sensitization.[7-9] This process expands on the connection between chronic pain and responses such as hyperalgesia and allodynia.[8,9] Over time, psychologic factors such as depression, anxiety, and reduced well-being tend to precipitate and alter patients' perceptions of their pain, which is why understanding these factors is crucial to proper diagnosis and treatment.[9,10]

A systemic overreliance on opioids for the management of chronic pain has spurred a need to rethink pain management strategies, possibly by adjusting the opioid management process and taking a more interdisciplinary approach.

## Background

In the 1960s and 1970s, physicians took a relatively conservative treatment approach and reserved opioid prescriptions for patients who were terminally ill.[1] However, in 1980, the perception of addiction was changed, with roots that stemmed from a 1-paragraph letter to the editor in the *New England Journal of Medicine*.[11,12] The 5-sentence letter catalyzed the notion that addiction resulting from chronic opioid therapy was a rare possibility. Subsequently, a retrospective study[13] of 38 patients was published, which concluded that opioid use for nonmalignant pain was both safe and a "humane alternative" to surgery or to no treatment. These findings can be argued as the initial stimulus for the epidemic.

In the 1990s, prescription opioids changed from a niche in the pain management community to a behemoth in the medical world through a combination of subsidization from pharmaceutical manufacturers, aggressive marketing campaigns, lack of physician education, and controlled disinformation.[1] "Opiophobia" campaigns led by pharmaceutical manufacturers cited numerous studies claiming the addiction risk for chronic opioid use was low and exaggerated the benefits of long-term use.[14,15] Overall, the 1990s brought forth an exponential increase in the frequency, duration, and dose of prescription opioids.[15,16]

This increase was exacerbated by the American Pain Society's 1997 proposal in conjunction with the American Academy of Pain medicine to measure pain as the "Fifth Vital Sign" and subsequently trademark the term. Various regulatory agencies and advocacy groups, including the Veterans Affairs Medical System and The Joint Commission joined in support of the campaign. These new pain management initiatives gradually shifted many physicians' pain treatment strategies to center around opioid therapy.[17]

Furthermore, physicians received higher patient satisfaction scores and reimbursement from the Centers for Medicare and Medicaid Services for treating patients' pain more aggressively with opioids.[18] The studies on the relationship between patient satisfaction scores and improved outcomes were dubious. Although a few studies[19,20] showed a positive correlation between patient experience and improved outcomes, several studies showed that patient experience scores did not correlate with significantly improved outcomes.[21-23] Many physicians who incorporated nonopioid approaches for pain management received subpar patient satisfaction scores for their lack of opioid and controlled-substance prescribing.[18] The subpar patient satisfaction scores led to a dramatic increase in the range of opioid prescribing for chronic pain, as well as for minor procedures and acute pain.[18] In response to nationwide efforts focused on responsible opioid prescribing, a paradigm shift occurred in 2011, in which the "Pain as the Fifth Vital Sign" campaign lost support, beginning a dramatic upshift in policies geared toward battling the epidemic.

### Trends and Metrics

A 2016 survey[24] conducted by the National Safety Council on physicians who spend more than 70% of their time seeing patients for pain found that 99% of physicians surveyed prescribed opioids longer than the 3-day Centers for Disease Control and Prevention (CDC) recommendation, and 74% of physicians incorrectly assumed that morphine and oxycodone are the

most effective pain treatments. Of note, 99% of physicians surveyed had seen a patient displaying evidence of opioid abuse, but only 32% referred the patient for treatment, and 67% continued to establish treatment protocols based on patient expectations.[24]

Despite this cycle, aggressive opioid prescribing remains entrenched within the medical community, which is highlighted by the fact that the number of opioids prescribed per person showed a 3-fold increase from 1999 to 2015.[25] The number of opioids prescribed in 2015 remained high across the country, from an average of 203 morphine milliequivalents (MME) per capita in the lowest quartile to 1319 MME per capita in the highest quartile. This variation suggests inconsistent practice patterns and a lack of consensus about appropriate opioid use, and it also reinforces the need for better application of treatment protocols and adherence to opioid prescribing practices.[25]

### Geographic Variation

A commonly overlooked lens into the epidemic is the geospatial data built around prescribing and overdose rates. The geographic variance in prescribing rates and doses on the growth of opioid abuse has received minor attention compared with the trends in increasing prescribing rates.[26,27] Jalal et al[26] broke down the overall drug epidemic into several drug-specific subepidemics and found that from 1996 to 2016, the spatial distribution of deaths attributed to prescription drugs, heroin, synthetic opioids (excluding methadone) had all increased. It was also observed that hotspots for prescription opioid abuse, which originally intensified in Appalachia and the southwestern United States, now encompassed most of the western United States, Florida, New England, and Oklahoma. The hotspots reflect the broad regional variance in opioid prescribing, which in turn contributes to the lack of standardization of patient treatment.

High prescribing and overdose rates likely indicate inadequate attention given to abuse and overprescribing, which can also radiate into surrounding areas from the epidemic hotspots.[27] Further inquiry is needed on why the states in the north central United States have been relatively vacant of drug overdose and overprescribing hotspots. The need for more standardized guidelines and education is highlighted by the increased patient demand for opioids and the arrival of more potent drug formulas that precipitate the need for more guidance about proper dosing and titration, among other aspects.

### Status of Nationwide Prescription Drug–Monitoring Programs

In response to the growing rate of opioid abuse, prescription drug–monitoring programs (PDMPs) have been enacted at the state level. Currently, 49 states (along with St Louis county and 71 jurisdictions in Missouri) have operational PDMPs. The types of drugs tracked by each state usually include Schedule II and III opioids, which have a high potential for abuse and are only available through prescription.[28,29] Prescription drug–monitoring programs are regarded as one of the most integral policy mechanisms for combating illicit controlled and dangerous substance (CDS) use and associated mortality. Bao et al[30] observed that PDMPs were associated with a reduction in the prescribing of Schedule II opioids in a 9-year study across 24 states. In addition, opioid-related mortality was lower in states with a functional PDMP as opposed to those who lacked the proper implementation and infrastructure.[31] Ali et al[28] found a significant association with PDMP implementation and a reduction in "doctor-shopping," which is the practice of visiting multiple physicians with the goal of obtaining prescriptions for otherwise illegal drugs or receiving the medical opinion that the patient wants to hear. These trends note that operational PDMPs have a significant influence on macro- and microlevel outcomes.

## Overview of Guidelines

On March 15, 2016, the CDC released the CDC Guideline for Prescribing Opioids for Chronic Pain[32] with the intent of providing a more structured and effective strategy for proper opioid prescribing. The

guideline is designed for patients with chronic pain who are not undergoing active cancer treatment or receiving palliative, end-of-life care. The scope of research on opioid therapy and patient outcomes remains limited, and the CDC guidelines provide treatment options using evidence obtained from randomized controlled trials. From the CDC prescribing guidelines,[32] 3 key points stand out:

1. Alternatives to opioid therapy are preferred for chronic pain. Opioids should be used as a final option, only when their expected benefits are likely to outweigh their substantial risks.
2. When initiating opioid therapy, the provider should "start low and go slow." In other words, the provider should begin with the lowest effective dose when initiating opioid therapy.
3. All patients taking opioid therapy require strict and periodic monitoring.

Recently, many other guidelines have been released both nationally and internationally, most notably by the National Pain Centre[33] in Canada and the US Department of Veterans Affairs and Department of Defense,[34] as well as multiple studies comparing different guidelines.[35,36] Nuckols et al[37] assessed the degree of quality of guidelines and found that several guidelines have a consensus on numerous prescribing risk mitigation strategies, such as attention to polypharmacy, comorbidities, and dosing ranges. The study[37] also noted that these agreed-upon strategies must be evaluated for their efficacy, individually or as a whole. **Figure 1** depicts a prescribing algorithm that complies with New Jersey state and federal guidelines that can be applied and modified as a template for opioid prescribing depending on local regulations.[38]

## Opioid vs Nonopioid Therapy

Research comparing opioid with alternative analgesic therapies remains limited, and most studies focus on one aspect of nonopioid therapy, such as the use of cannabis[39] or physical therapy.[40] However, the Strategies for Prescribing Analgesics Comparative Effectiveness clinical trial[41] studied 240 randomized patients with chronic neck, back, and osteoarthritis pain recruited from Veteran's Affairs primary care clinics. Krebs et al[41] found that over a 12-month period, improvement in pain-related function was not significantly different in patients treated with opioids compared with patients treated with nonopioid medications. Additionally, pain in patients who were not prescribed opioids showed slightly more improvement relative to patients who were prescribed opioids.[41]

Physicians should focus on using nonopioid and nonpharmacologic treatments, applying interdisciplinary approaches, and encouraging patient's active engagement in their treatment. Further research, especially in long-term studies comparing various dose thresholds and other risk mitigation strategies, is needed. An overview of nonpharmacologic and nonopioid pain management approaches is shown in **Table 2.**

Buprenorphine is one alternative medication that has gained popularity, albeit for the management of opioid use disorder. Like opioids, buprenorphine also acts on the μ receptor, and it exerts similar effects to that of morphine and its equivalents. However, buprenorphine has a "ceiling effect" and thus does not cause the adverse effects of CNS depression. Transdermal formulations of buprenorphine have been found to have the lowest rates of abuse and diversion compared with other opioids and buprenorphine formulations with regard to chronic pain.[42] Research[43-45] is also being conducted on long-acting delivery systems of buprenorphine, with a goal of addressing issues of patient adherence and diversion in treatment. In theory, this long-acting option would reduce the number of doses to increase patient adherence and put more control of the treatment in the hands of the physician to reduce diversion. Some of these novel systems have showed promise in their trials, particularly depot preparations and implantable buprenorphine.[46] By addressing some of the primary impedances to successful pharmacologic treatment, these future directions can have a significant

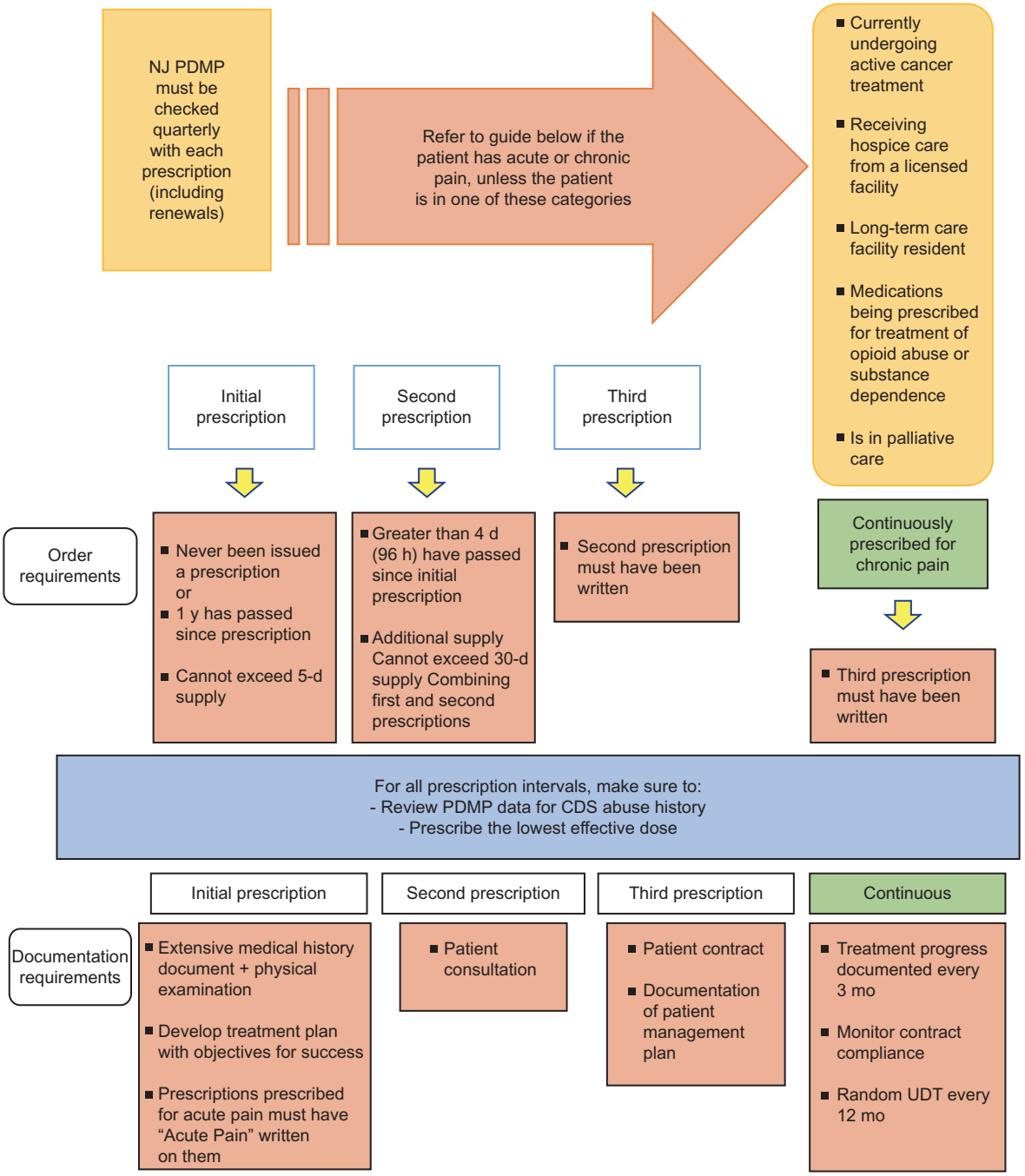


**Figure 1.**
The New Jersey opioid prescribing algorithm. Adapted from Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep*. 2016;65(No. RR-1):1-49. doi:10.15585/mmwr.rr6501e1. *Abbreviations*: CDS, controlled and dangerous substance; PDMP, prescription drug monitoring program; UDT, urine drug testing.

effect on both the patient population with chronic pain and the opioid crisis.

## Clinical Presentation

### Patient History and Physical Examination

A thorough documentation of patients' medical history is required before and periodically during therapy for patients with acute or chronic pain who are considering opioid analgesic or CDS therapy. By taking a comprehensive history, physicians can identify what type of pain they have (eg, myofascial, viscerosomatic, or neuropathic), the possible cause(s), whether there is a psychosomatic component, what has or has not worked, and whether there are signs of opioid dependency or opioid-seeking behavior. Categorically, health care professionals should look for evidence of prescribed and nonprescribed opioid use and abuse. A thorough physical examination should also be performed.

### Risk Assessment

For patients with acute and chronic pain, risk assessment and stratification is an integral part of each patient's treatment plan and has become a national standard of care. To design a patient's treatment plan, physicians are generally recommended to use a validated addiction risk assessment screening tool, such as the Opioid Risk Tool (ORT) and Screener and Opioid Assessment for Patients with Pain–Revised (SOAPP-R).[47,48]

The ORT has various categories, such as age, family history of substance abuse, and personal history of substance abuse, that are given number scores based on certain responses. The end results can be placed into 3 categories: low risk (0-3), moderate risk (4-7), and high risk (8+).[47] The SOAPP-R tool is used to determine how much monitoring a patient taking long-term opioid therapy might require. The tool includes a brief questionnaire and 24 items that are scored and help to justify the type of therapy a patient receives or their referral to a pain specialist. The SOAPP-R cannot detect any misrepresentation by patients, and it should not be the only means on which treatment should be based. The SOAPP-R does come with treatment recommendations based on the tabulated SOAPP-R score and corresponding risk level.[48] A study[48] evaluating the feasibility of the SOAPP-R tool found that the tool had an 83% success rate of predicting opioid misuse in the cohort (n=25). The SOAPP-R is scored by adding all of the ratings from all of the questions. Similar to the ORT assessment, the SOAPP-R is scored numerically and, depending on the value, the patient may be low, medium, or high risk for opioid abuse; a score of 18 or higher is considered positive for risk of opioid abuse.[48]

## Initiating Opioid Therapy

### Patient Contract

Communication between physicians and patients is one of the most important components of meeting treatment goals. To foster clear communication, a written document called an opiate agreement can be used to outline both physician and patient expectations and should be used with patients who are beginning long-term treatment with opioid analgesics or other controlled substances. Opiate agreements synthesize the treatment plan and objectives into a manner that will help patients understand their role and responsibilities in achieving successful treatment (eg, obtaining refills or urine drug screenings) and the responsibilities of the health care professional governing their treatment. An opiate agreement can help facilitate communication between patients and health care professionals and resolve any unknowns or concerns before starting long-term CDS treatment.

### Urine Drug Testing

An established standard in pain management practice, urine drug testing (UDT) can help identify controlled substance abuse, patient compliance and aberrant behaviors, and the presence of substances in situations of overdose. Notwithstanding the importance of UDT in patient treatment, 2 studies[49,50] have observed a lack of knowledge in some health care professionals in maintaining accurate UDT interpretation. Furthermore, not all opioids are detected equally by UDTs, and proper

knowledge of opiate metabolism and the specific substances to which the UDT tests for is strongly recommended for health care professionals.[50] One limitation of standard immunoassays is that morphine is used to set the threshold for distinguishing between positive and negative test results, which may result in false-negative results.[49] Confirmation by liquid or gas chromatography separation and specific detection by mass spectrometry tend to minimize this risk, and they increase diagnostic accuracy.[50,51] Physicians should also be aware that standard UDTs may not test for synthetic or semisynthetic opioids. Frequency recommendations for UDT can vary depending on patients' risk scores and can be done once annually to numerous times per year for some patients (Table 1).[52]

## Opioid Dosing and Tapering

A study that compared a German opioid dosing guideline with high-dose long-term opioid therapy for chronic noncancer pain found that the opioid therapy guideline was associated with improved health outcomes (eg, lower rates of high-risk opioid therapy and hospital admissions for abuse or dependence and decreased health care costs) in a large sample that was representative of the German population.[53,54]

The CDC and Canadian opioid guidelines recommended to begin treatment with immediate-acting opiates vs extended-release or long-acting opiates.[32,33] Treatment should be started at the lowest effective dose, with a maximum of 50 MMEs per day to reduce the risk of fatal overdose[32]; MMEs are determined by the dose multiplied by the conversion factor of the medication to morphine (Figure 2). Careful assessment of risks and benefits, as well as consultation with a pain specialist, should be completed if a physician is considering titrating above this threshold.

After initiation, physicians should evaluate the benefits and harms of continued opioid therapy within 1 to 4 weeks of initiation or dose escalation.[32,34] Physicians should reevaluate patients at least every 3 months, with a focus on benefits specifically pertaining to

**Table 1.**
**Recommended Frequency of Urine Drug Testing Per Year Depending on Patient Opioid Risk Level**

| Risk Level[a] | Urine Drug Test Frequency Recommendation, y |
|---|---|
| Low | 1 |
| Moderate | 2 |
| High (or opioid dose >120 MMEs) | 3-4 |
| Aberrant | At time of visit |

[a] Determined by Opioid Risk Tool score.

**Abbreviation**: MME, morphine milliequivalents.

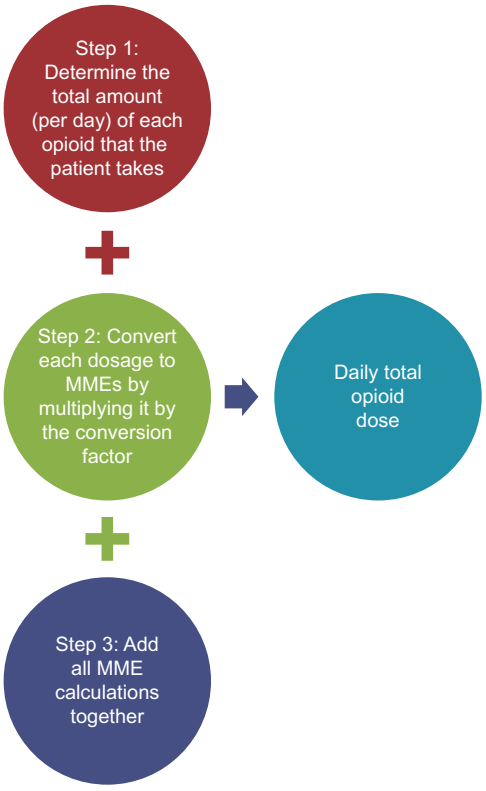


**Figure 2.**
A guide to calculate the total daily opioid dose. Adapted from Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep. 2016;65(No. RR-1):1-49. doi:10.15585/mmwr.rr6501e. *Abbreviation*: MME, morphine milliequivalent.

functionality, pain control, and quality of life.[32] Reevaluation can be completed by interviewing the patient or using tools such as the average pain intensity, interference with enjoyment of life, and interference with general activity, or PEG, assessment scale. If the harm begins to outweigh the benefits of opioid treatment, physicians should consider tapering the dose and incorporating other therapies to optimize pain control.

To the authors' knowledge, the CDC has not found any high-quality evidence toward an optimal taper rate.[32] Upon their review of guidelines from multiple organizations between 2009 and 2012, dose-reduction percentages and intervals greatly varied.[35] The guidelines[32] concluded that a 10% decrease in original dose per week is a reasonable starting point but noted that the plans may need to be individualized based on patient goals and concerns.[53,54] The Canadian guidelines[33] are more rigid and suggest a gradual reduction of 5% to 10% of the MME dose every 2 to 4 weeks with frequent follow-up. The 2017 United States Veteran Affairs/Department of Defense guideline[34] agrees with individualizing opioid tapering and lists considerations for determining a rapid vs gradual taper but with a reduction of 5% to 20% weekly (rapid) or every 4 weeks (gradual). However, among all 3 guidelines, the problem of low-quality evidence among studies remains, and issues with the research include imprecision, bias, and indirectness. As such, these guidelines cannot be used as rigid, evidence-based protocols, but rather as a framework that can be individualized for each patient.

While tapering opioid use, physicians should monitor for and manage withdrawal symptoms (**Table 3**), which can be critical to a patient's compliance with the taper (**Figure 1**). Additionally, multidisciplinary programs that address functional or psychological impairment and aberrant behaviors that develop while tapering use are strongly recommended.[33,34] A 2017 randomized controlled trial[55] of 35 patients found that a taper support intervention can help with this process.

**Table 2.**
**Overview of Suggested Nonpharmacologic and Nonopioid Pain Management Approaches[a]**

| Diagnosis | First-Line Treatment | Second-Line Treatment |
|---|---|---|
| Low back pain | Self-care, exercise, OMT, NSAIDs | SNRIs, TCAs |
| Osteoarthritis | Exercise, weight loss, NSAIDs | Intra-articular hyaluronic acid, capsaicin, OMT |
| Fibromyalgia | Low-impact aerobic exercise, pregabalin, duloxetine, milnacipran, TCAs, gabapentin, OMT | NA |
| Migraine | Preventative: β-blockers, TCAs, calcium channel blockers<br>Acute: NSAIDs, antinausea medications, triptans (migraine-specific), OMT | NA |
| Neuropathic pain | TCAs, SNRIs, gabapentin/pregabalin, topical lidocaine, OMT | NA |

[a]Adapted from CDC Guidelines for Prescribing Opioids for Chronic Pain.[26]

**Abbreviations**: NSAIDs, nonsteroidal anti-inflammatory drugs; OMT, osteopathic manipulative treatment; SNRIs, serotonin-norepinephrine reuptake inhibitors; TCAs, tricyclic antidepressants.

## Aberrant Behavior and Symptoms of Toxicity

Aberrant patient behaviors should be met with risk mitigation strategies in short- and long-term settings to increase the likelihood of a successful treatment and decrease the long-term reliance on opioid therapy. Random or routine pill counts are one strategy to enforce medication adherence and reduce the risk of treatment diversion. The most effective pill count method is to compare the number of pills on all prescriptions with that of the instructions on the medication label and with the date the medication was filled. The highest-risk patients may require unscheduled returns to the office, where they must bring their medications in within 24 to 36 hours from the time of contact. Another strategy is the use of warning letters, which are initially given to patients who violate any terms of their opiate agreement.

**Table 3.**
**Opioid Symptom Withdrawal and Corresponding Pharmacologic Treatment Option**[a]

| Opioid Withdrawal Symptom | Pharmacologic Treatment |
|---|---|
| **Sympathetic**<br>Restlessness<br>Sweating<br>Tremors | α-2-agonist (eg, clonidine) |
| **Nausea** | Antiemetic |
| **Diarrhea** | Loperamide, antispasmodic |
| **Muscle pain** | NSAIDs |
| **Neuropathic Pain** | Gabapentin |
| **Myoclonus** | Muscle relaxants |
| **Insomnia**[b] | Sedating antidepressants (eg, nortriptyline, mirtazapine, trazodone) |

[a] This table is adapted from Agency Medical Director's Group 2015 interagency guideline on prescribing opioids for pain.[46]
[b] Benzodiazepines should not be used.

**Abbreviation**: NSAIDs, nonsteroidal anti-inflammatory drugs.

Physicians must watch for signs and symptoms indicative of acute toxicity or dependence. The primary symptoms reflect its effect on CNS depression. These symptoms are commonly referred to as the "opioid overdose triad" and consist of pinpoint pupils, unconsciousness, and respiratory depression. Pulmonary edema (in patients with apnea or severe bradypnea), with rales and frothy sputum, is usually a late sign of severe opioid toxicity.[56] Other common findings of acute toxicity or dependence can be found in other body systems, indicated by hypotension, bradycardia, nausea, vomiting, and evidence of needle use (**Figure 3**).[57,58]

## Integrating the Osteopathic Philosophy

In accordance with the first tenet of osteopathic medicine that states, "the body is a unit; the person is a unit of body, mind, and spirit,"[58] cognitive behavioral therapy can help patients understand their pain, take an active role in their management plan, and use pain-coping behaviors.[59] A review[60] of 40 trials concluded that cognitive behavioral approaches used to manage chronic pain related to rheumatoid arthritis decreased overall pain score and improved mood and function. Moreover, the conversation helps promote active communication and builds trust between the patient and the physician.

In line with the second and third osteopathic tenets,[58] osteopathic manipulative treatment (OMT) focuses on identifying and treating somatic dysfunctions to optimize biological structure and promote homeostatic function of the body. Two separate systematic reviews and meta-analyses that assessed OMT and low back pain by using either a single technique[61] or a variety of techniques based on clinical judgement[62] demonstrated that OMT provided a significant degree of pain relief vs no treatment or other nonpharmacologic intervention. The American Osteopathic Association released official guidelines[63] based on these studies and recommended that "OMT be utilized by osteopathic physicians for musculoskeletal causes of low back pain (ie, to treat the diagnoses of somatic dysfunctions related to low back pain)."

Moreover, a randomized control trial[64] that analyzed OMT and ultrasound therapy for chronic low back pain demonstrated a statistically significant decrease in prescription drug use in the OMT group vs the sham OMT group. No treatment comes without potential adverse events, and OMT is no exception. However, a large-scale analysis[65] of outcomes immediately after OMT demonstrated a 2.5% incidence of adverse events. Of these events, pain/discomfort was the most common, and the others included fatigue, lightheadedness, nausea and vomiting, headache, numbness and tingling, stiffness, and "other."[64] Whether OMT is used as a primary treatment or as an adjunct, it is a noninvasive option with minimal side effects that should be a key part of the treatment plan for patients with chronic pain.

| |
|---|
| **Pulmonary** |
| • Depressed respiratory rate |
| • Miosis and/or depressed consciousness[a] |
| • Pulmonary edema |
| • Rales and frothy sputum[b] |
| **Ophthalmologic** |
| • Decreased size and reactivity of pupils |
| • Constriction <2 mm in diameter |
| **Dermatologic** |
| • Recent needle marks (small erythematous, inflammed, show signs of bruising) |
| • Old needle marks (pigmentation and atrophy) |
| • Fentanyl patches |
| • Mucous membrane cyanosis |
| • Hypothermia |
| **Neurologic** |
| • Seizures (often caused by tramadol, propoxyphene, and meperidine overdoses) |
| **Cardiovascular** |
| • Hypotension |
| • Bradycardia |

**Figure 3.**
Physical examination for opioid toxicity and findings by system. [a] High risk indicators for acute opioid toxicity . [b] Indicator of severe opioid toxicity. Adapted from Boyer EW. Management of opioid analgesic overdose.[56] *Abbreviations*: CDS, controlled dangerous substances; PDMP, prescription drug monitoring program; UDT, urine drug testing.

## Limitations and Future Research

This review was limited by the restriction of the depth of analysis of the various prescribing guidelines presented, as well as a limitation of specific details regarding tapering, dosing, and physical examination for patients with chronic pain. Future studies could include an approach to an individual patient that focuses more on these individual steps and analyzes the guidelines and incorporation of osteopathic philosophy. Opioid treatment, as opposed to nonopioid alternatives, remains equivocal for the general population, and more research about individually tailored and integrative treatment approaches is required. Future research should also focus on evaluating the effectiveness of various risk-attenuating strategies and subsequently adjusting recommendations, in addition to nonopioid and nonpharmacologic pain management approaches.

## Conclusion

Physicians must adhere to the most current clinical protocols for opioid prescription and withdrawal to mitigate increased opioid misuse and overdose rates in any setting. Opioid management necessitates an integrative treatment approach that considers various factors, such as screening tools, physical examination findings, dosing and tapering strata for patients with chronic pain, and an extensive UDT process. Physicians must note that the guidelines only provide a general framework of proper treatment and that a specific care plan must be individualized to each patient.

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