

Safe and Practical: A Guide for Reducing the Risks of Opioids in the Treatment of Chronic Pain

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Health care providers often face the challenge of deciding when and how to prescribe opioids for patients with chronic noncancer pain. In patients for whom opioid treatment is appropriate, the risks can be mitigated by an initial risk assessment, informed consent, regular monitoring, and treatment within a medical home.

Health care providers often care for patients who are in pain, and choosing the correct therapeutic option can be daunting. Acute pain is less challenging, as it tends to have an easily identifiable cause and typically resolves when the inciting injury heals. Treating acute pain quickly is appropriate, and when nonsteroidal anti-inflammatory drugs (NSAIDs) and/or other over-the-counter regimens are insufficient to provide adequate analgesia, opioid therapy is often effective [1]. In this context, it is of paramount importance that clinicians set expectations for healing time and duration of therapy and consider adjuvant therapeutic options (such as referral for physical therapy). Unfortunately, it is not uncommon for pain to persist long after the acute illness or injury has healed, and deciding when to prescribe opioids for chronic pain is a difficult question.

Over the past 15 years, an overwhelming increase in the prescription of opioids for chronic noncancer pain has coincided with equally alarming increases in deaths due to opioid overdoses, emergency department visits related to nonmedical use of opioids, and substance abuse treatment for opioid addiction [1, 2]. Not surprisingly, these increases have occurred in parallel with the development of long-acting opioids, the aggressive marketing of opioids by the pharmaceutical industry, and leniency in the regulation of opioid prescribing on the part of state medical boards [1, 2].

Despite the abundance of opioids prescribed in the United States, many patients are still in pain. The Institute of Medicine's 2011 report *Relieving Pain in America* urges transformation of "prevention, care, education, and research, with the goal of providing relief for people with pain in America" [3]. However, the report also acknowledges the dangers and limitations of opioids in the setting of chronic pain [3]. Indeed, the consequences related to the misuse of opioids for the treatment of chronic noncancer pain are frightening: The number of deaths from opioid overdoses is increasing,

medication misuse and opioid addiction are soaring, and drug diversion remains alarming. Clearly these are challenging problems.

There is little published evidence to support the use of opioids for the treatment of chronic noncancer pain. According to the American Society of Interventional Pain Physicians (ASIPP), "the explosive use of therapeutic opioids ... is complicated by a lack of evidence regarding their effectiveness, long-term efficacy, and safety data in the treatment of chronic non-cancer pain, but there is irrefutable evidence of adverse consequences" [2]. A recent Cochrane review found only weak evidence to suggest that long-term opioid treatment yields clinically significant relief from chronic noncancer pain in appropriately selected patients [4].

In contrast, the risks of opioids are well established. The risk of opioid-related death is nearly 3 times higher in a patient who is taking a daily morphine-equivalent dose (MED) of 200 mg or more compared to someone taking a daily MED of less than 20 mg [5]. Adverse effects are common with opioid treatment. In addition, a condition known as opioid-induced hyperalgesia is gaining recognition; this condition is characterized by "persistent or increasing pain with increasing dose, pain worse on opioids than before, decreasing duration of analgesic effect and pain becoming increasingly diffuse or poorly localized with ongoing opioid use" [6].

Physicians are largely aware of the risks of long-term opioid therapy and therefore try to find other treatment options, both for patients who are newly diagnosed with chronic noncancer pain and for those who are already taking opioid medications. Alternatives and first-line medications often include NSAIDs, antidepressants, anticonvulsants, and topical agents. In addition, physical therapy, rehabilitation, cognitive behavioral therapy, and complementary medicine techniques may be helpful. For some patients, however, a trial of opioid therapy is a reasonable next step.

Patients must be carefully selected for an opioid trial

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Educating Medical Practitioners About Safe Opioid Prescribing: Training from the Governor's Institute on Substance Abuse

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There has been a great deal of speculation about what is causing the current epidemic of prescription medication abuse, with possible factors including sociocultural, economic, and medical issues [1]. One concern relates to the prescribing patterns of some clinicians—both primary care providers and specialists—particularly with regard to prescription of opioid analgesics. To address this concern, a number of national and state-level initiatives have aimed to promote safer opioid prescribing practices. In North Carolina, the Governor's Institute on Substance Abuse has played a lead role in these efforts, with the support of the North Carolina Division of Mental Health, Developmental Disabilities, and Substance Abuse Services (DMHDD-SAS); the Substance Abuse and Mental Health Services Administration (SAMHSA); and other funders.

As far back as 1994, the Governor's Institute, along with Duke University and the *Journal of Law, Medicine and Ethics*, cosponsored a conference devoted to prescription drug abuse and published 2 articles on the need for medical education to address this issue [1, 2]. In 2008, the Governor's Institute collaborated with SAMHSA to provide a series of workshops on safe opioid prescribing as part of a national training initiative. These workshops resulted in increased use of opioid risk screening tools and increased use of the North Carolina Controlled Substances Reporting System, and the success of these workshops demonstrated that prescribers were eager for training in this area. The Governor's Institute then began receiving requests for similar training, which resulted in additional trainings over the next 4 years.

In collaboration with the North Carolina Society of Addiction Medicine and other specialty groups, the Governor's Institute has provided or facilitated a number of

initiatives targeted at a broad range of North Carolina's medical practitioners. These trainings have focused on teaching core skills that will help practitioners balance the need for adequate pain management—including access to opioid medications, when needed—versus the need to minimize the risk of abuse. Topics that have been covered in these trainings include: the role and limitations of opioids in managing chronic pain; risk stratification as an element of treatment planning before initiation of a therapeutic trial; elements of adequate monitoring; and appropriate responses to aberrant medication behaviors, including when to discontinue opioids and when to refer patients for specialty care.

In 2009, with funding from the Kate B. Reynolds Charitable Trust, the Governor's Institute implemented a program for 10 counties in Eastern North Carolina. This initiative developed grassroots awareness of prescription drug abuse and included community awareness campaigns, medication turn-in days, and evening seminars for clinicians. Outreach within the medical community resulted in widespread attendance by primary care physicians, emergency medicine specialists, and pain management clinicians. Over the course of 2 years, 7 trainings were attended by a total of 260 health care providers. This training initiative also included the provision of onsite technical assistance in addressing systems barriers, which include organizational culture, workflow, and reimbursement issues.

The Governor's Institute has also hosted a series of highly successful, practice-oriented conferences every year for the past 4 years. These conferences are formatted to attract both addiction medicine specialists and primary care clinicians. Each conference has focused attention on

(Table 1). A thorough history and a physical examination are essential in determining whether opioids are a reasonable option. If the diagnosis is fibromyalgia, for example, opioids are not indicated [6]. Moreover, patients who have poorly defined pain, those with a somatoform disorder, and those who are receiving compensation (eg, workers' compensa-

tion or Social Security Disability) will likely have a poorer response to opioid therapy [7].

In addition to establishing a diagnosis, physicians should stratify patients according to their risk of addiction and opioid misuse. Risk stratification is key to mitigating these hazards, and it should be an ongoing process in patients with chronic noncancer pain (Table 2). Multiple patient screening tools are available, but these methods have not been compared directly, so it is unclear which is best [8]. Highly rated tools include the Diagnosis, Intractability, Risk, Efficacy (DIRE) Score; the Addiction Behaviors Checklist; and the Screener and Opioid Assessment for Patients with Pain (SOAPP) [1]. These screening tools and others, as well as treatment algorithms, can easily be found online. Community Care of North Carolina (CCNC) also provides online resources for providers who treat chronic pain (<https://www.communitycarenc.org/population-management/chronic-pain-project/>). Such tools can help physicians stratify patients into categories of

TABLE 1.
Steps in the Initial Assessment of Patients Who Are Being Evaluated for Long-Term Opioid Therapy

1. Take the patient's history and perform a physical examination.
2. Assess the risk that the patient will misuse the drug, perhaps by using a screening tool such as the Addiction Behaviors Checklist.
3. Check the North Carolina Controlled Substances Reporting System to see any controlled substance prescriptions the patient may have previously filled in North Carolina.
4. Perform baseline urine drug screening.
5. Have the patient sign a treatment agreement or a pain contract.

abuse of controlled medications, giving particular attention to abuse of opioids and benzodiazepines. Lectures have provided reviews of the literature and standards of treatment, and seminars have focused on in-depth discussions and on how standards of treatment can be implemented in real-world practice settings.

As an important part of responding to the current opioid epidemic, treatment needs to be provided for individuals who have moved beyond opioid misuse to opioid addiction. However, clinicians often receive little support in dealing with this problem. To address this need, the Governor's Institute, working with DMHDDSAS, has for the past 4 years facilitated an ongoing mentoring network for those working in opioid treatment programs (methadone clinics). This mentoring has included monthly conference calls that include case discussion, literature review, and emerging standards of care.

For physicians who provide in-office treatment with buprenorphine or naloxone (agonist and antagonist therapies for opioid addiction), the Governor's Institute has sponsored training updates at yearly addiction medicine conferences. These workshops have attracted a majority of the physicians in North Carolina who are treating opioid addiction with buprenorphine or naloxone.

The leaders of Community Care of North Carolina (CCNC) have long been aware of the public health impact of prescription drug abuse. Building on the impressive success of Project Lazarus in Wilkes County [3], CCNC recently initiated the statewide Project Lazarus: Chronic Pain Initiative. As part of this initiative, the Governor's Institute has been asked to develop and implement training for clinicians. This 2-year project, funded by the Kate B. Reynolds Charitable Trust and the North Carolina Office of Rural Health and Community Care, will be the largest training initiative ever implemented in this clinical area in North Carolina. In collaboration with the North Carolina Academy of Family Physicians, 40 training sessions will be provided for approximately 2,500–3,000 clinicians, and

ongoing site-specific case-discussion conferences will be facilitated. The trainings will cover the multidimensional character of chronic pain; the role of opioids in safe and effective management of chronic pain; screening and risk stratification to minimize misuse or abuse; intervening if or when misuse occurs; and networking with local pain management and behavioral health experts.

Ancillary materials for this project will be posted on a Governor's Institute-sponsored Web page that is devoted to providing substance abuse resources for health care providers (<http://www.sa4docs.org/>). This Web page provides training updates and links to other clinical resources, and last year it was visited by 12,805 unique visitors—not only from North Carolina but also from 49 other states and 17 countries. NCMJ

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References

1. Wilford BW, Finch J, Czechowicz J, Warren D. An overview of prescription drug misuse and abuse: defining the problem and seeking solutions. *J Law Med Ethics*. 1994;22(3):197-203.
2. Schnoll SH, Finch J. Medical education for pain and addiction: making progress toward answering a need. *J Law Med Ethics*. 1994;22(3):252-256.
3. Albert S, Brason FW 2nd, Sanford CK, Dasgupta N, Graham J, Lovette B. Project Lazarus: community-based overdose prevention in rural North Carolina. *Pain Med*. 2011;12 suppl 2:S77-S85.

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high, moderate, or low risk, which can help to guide management. High-risk patients and those who have significant psychiatric comorbidities or a history of drug abuse should be managed only by providers who have experience treating this population, and comanagement with a psychiatrist or an addiction specialist is strongly recommended [7].

Patients should give informed consent before opioid treatment is initiated. Adverse effects of opioids are common, and providers should develop a plan for dealing with these issues before starting opioid treatment. Nausea can affect up to 25% of patients but typically resolves with time; if treatment of nausea proves necessary, antihistamines or metoclopramide can often provide relief [9]. Constipation should be prevented with stool softeners and a stimulant laxative. Cognitive impairment and sedation are major risks when starting treatment with opioids, when the dosage is being increased, or when opioids are being taken with other sedating substances (such as alcohol). Patients should be

instructed not to drive when they are feeling impaired [7]. The risk of respiratory depression is much higher when a patient's dosage is increased or when an opioid is combined with another drug, such as a benzodiazepine. Patients also need to be aware of the risks of physical dependence and withdrawal before starting opioid therapy.

Expectations should be clearly agreed upon at the start of opioid therapy, and patients need to understand that total pain relief with opioids is not a realistic goal. The average benefit with opioid therapy is a reduction of 2 or 3 points on a 10-point pain scale [7]. A reasonable expectation is that a successful opioid trial will result in a 30% reduction in pain or a 30% improvement in function [8].

Treatment agreements or pain contracts can be used to document informed consent and expectations. There is fair evidence that treatment agreements may improve compliance [8]. These agreements also set expectations for random urine drug screening, pill counts, and avoidance of excessive

TABLE 2.
Guidelines for Monitoring Patients Who Are Receiving Long-Term Therapy for Chronic Noncancer Pain

■ For patients at low risk of misusing opioids: ● Urine drug screening should be performed every 1–2 years. ● The NCCSRS should be checked twice per year. ● A daily MED of 50 mg or more can be used if necessary.
■ For patients at medium risk of misusing opioids: ● Urine drug screening should be performed every 6–12 months. ● The NCCSRS should be checked 3 times per year. ● A daily MED of 50 mg or more can be used occasionally.
■ For patients at high risk of misusing opioids: ● Comanagement of care with a psychiatrist or an addiction specialist is highly recommended and is likely to be necessary. ● Urine drug screening should be performed every 3–6 months. ● The NCCSRS should be checked 4 times per year. ● Opioids should be avoided if possible, or used at a daily MED of 10 mg or less. ● Dose escalations should be avoided.
Any patient receiving long-term opioid therapy who displays aberrant behaviors should be counseled, and opioid therapy should be reconsidered.
Note. MED, morphine-equivalent dose; NCCSRS, North Carolina Controlled Substances Reporting System. Source: Guidelines are from [1].

alcohol consumption, and they establish the consequences if a prescription is lost or stolen. Examples of such agreements can be found on the CCNC Web page cited previously and on the Web site of the Washington State Department of Labor & Industries (<http://www.lni.wa.gov/ClaimsIns/Files/OMD/agreement.pdf>).

The North Carolina Controlled Substances Reporting System (NCCSRS) is a superb resource, and it should be accessed prior to prescribing opioids for any patient. [Editor's note: For more information on the NCCSRS, please refer to the commentary by Bronson on pages 249–253.] Using the NCCSRS, providers can learn where in North Carolina and when patients have filled prescriptions for a controlled substance. Currently 43 other states also have prescription monitoring programs, and work is progressing to link these systems. Prescription monitoring programs can reduce doctor shopping and prescription drug abuse [8]. More information on accessing the NCCSRS can be found at <http://www.ncdhhs.gov/mhddsas/controlledsubstance/implementation-guide2-11.pdf>. Unfortunately, prescription monitoring programs are grossly underutilized [1].

Urine drug screening should be conducted for every patient who is receiving long-term opioid therapy [8]. However, the results of such screening should be interpreted in the context of the patient's behavior and overall compliance [7]. Unexpected positive results should be confirmed by more specific means such as gas chromatography-mass spectrometry. False-negative results are also possible. If an opioid is present at a concentration lower than the laboratory's threshold value, then a negative result will be reported.

In addition, some assays do not detect oxycodone, fentanyl, or methadone; these tests may need to be requested specifically. The numerous available assays each have variable test characteristics that are not equivalent across all drug classes. For example, pseudoephedrine not infrequently results in a false-positive result on an amphetamine screening test, whereas a positive result when testing for cocaine is much more specific. Consultation with the laboratory can be helpful in these cases.

Opioid selection is primarily based on cost, side effects, and patient comorbidities. There is no evidence to suggest that one opioid is better than another, nor is there evidence that long-acting opioids are any better or any worse than short-acting opioids for relieving chronic noncancer pain [7]. In particular, there is no compelling evidence to support prescribing both a long-acting opioid plus a short-acting opioid for "breakthrough pain" [7]. If a patient's pain is well controlled by a short-acting medication that is taken 4 times a day, then there is no reason to change that regimen [10].

The use of methadone to treat chronic noncancer pain has been increasing, perhaps because of the low cost of such therapy [11]. This trend is a cause for concern given the specific risks associated with methadone therapy. The long and variable half-life of methadone makes titration difficult, and methadone therapy is associated with a significant risk that the patient's corrected Q-T (QTc) interval will be prolonged. Thus, I feel methadone should be a medication of last resort. Patients who require a trial of methadone can start therapy at a dosage of 2.5 mg orally every 8 hours. Dosage increases should occur no more frequently than once per week [7]. Even if a patient has been taking high doses of other opioids, the starting dose of methadone should be no higher than 30–40 mg per day [7]. An electrocardiogram should be performed to monitor the QTc interval prior to starting methadone therapy, again after 1 month of therapy, and then yearly while therapy continues. Providers should avoid prescribing other medications that prolong the QTc interval and should increase electrocardiogram monitoring if necessary. Methadone should not be used to treat breakthrough pain, nor should it be used on an as-needed basis [7].

Given the well-established risks of opioids, use of high-dose opioid therapy should be reconsidered. Good evidence shows that dose limits are associated with a reduction in the total daily dosage of opioids and with a reduction in the number of deaths due to opioid overdose [8]. Multiple guidelines support opioid dosage limits, but they do not necessarily agree on what the upper limit should be [8]. According to guidelines from the ASIPP, patients who do not experience a response to low-dose opioid therapy (a daily MED up to 40 mg) or moderate-dose therapy (a daily MED of 40–90 mg) are unlikely to respond to higher doses of opioids [8]. Patients who require high doses of opioids (a daily MED of 100 mg or more) should be re-evaluated to determine the cause of their pain, and providers should evaluate adherence to the treatment plan, consider the use of more frequent

monitoring, and possibly refer the patient to a pain specialist [7, 8]. Several studies have shown that some patients who experience severe pain despite receiving high doses of opioids actually achieve improvement of pain and mood with a decrease in dosage [8].

A patient's opioid dose should be tapered off if the patient experiences intolerable adverse effects, fails to progress toward treatment goals, and/or shows signs of repeated aberrant behavior [7]. According to the ASIPP, "minimal requirements for continued opioid therapy are analgesia of at least 30%, and/or activity improvement of 30% without misuse/abuse, or major adverse effects" [8].

Opioid withdrawal is very unpleasant but is not life threatening. To decrease the symptoms of withdrawal, the total opioid dose can be decreased by 10% of the original dose weekly [8]. However, some patients can tolerate more rapid tapering. Importantly, therapy does not need to be tapered if patients have not been taking opioids for more than 3 months nor if they have been diverting medications. Symptoms of withdrawal (abstinence syndrome) can be managed with clonidine: 0.1–0.2 mg can be taken orally every 6 hours, or a 0.1-mg transdermal patch can be applied weekly. Patients should be monitored for hypotension while they are taking clonidine [8]. If patients develop withdrawal symptoms during tapering, treatment with clonidine, sedating antidepressants such as trazodone, and nonsteroidal anti-inflammatory medications is preferable to using benzodiazepines [8]. The speed of tapering can be adjusted for the individual patient, but patients who do not comply with the tapering regimen or who abuse their medication should be referred for detoxification [8].

Addiction resources should be offered to all patients who exhibit aberrant behavior such as using unprescribed opioids, using cocaine, altering prescriptions, harassing members of the physician's staff, requesting multiple early refills, or losing prescriptions [7]. Patients with dependency can be offered office-based treatment with buprenorphine/naloxone (Suboxone, Reckitt Benckiser Pharmaceuticals Inc.), which is a reasonable alternative to methadone maintenance therapy for some patients. Primary care providers can offer this treatment if they have obtained special training and have been granted a waiver by the Drug Enforcement Administration. More information can be found at <http://www.pcsub.org/>.

Treatment of chronic noncancer pain is complex and involves numerous aspects of the patient's life; in these respects chronic pain resembles other chronic diseases that are treated by primary care physicians. The Institute of

Medicine of the National Academies notes that all patients who are being treated for pain, including those who are being seen by a pain specialist, can benefit from having a primary care practitioner (or a medical home) to help coordinate care from various providers [3]. Coordination of care is essential, because a simple medical model in which a physician attempts to cure the disease does not work for chronic noncancer pain. A chronic disease model—including risk assessment, a team approach, patient self-management, and care coordination across specialties—will benefit all patients with chronic noncancer pain, whether or not they are being treated with opioids. **NCMJ**

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References

1. Atluri S, Akbik H, Sudarshan G. Prevention of opioid abuse in chronic non-cancer pain: an algorithmic, evidence based approach. *Pain Physician*. 2012;15(3 suppl):ES177-ES189.
2. Manchikanti L, Abdi S, Atluri S, et al. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 1—evidence assessment. *Pain Physician*. 2012;15(3 suppl):S1-S65.
3. Committee on Advancing Pain Research, Care, and Education; Board on Health Sciences Policy; Institute of Medicine of the National Academies. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington, DC: The National Academies Press; 2011.
4. Noble M, Treadwell JR, Tregear SJ, et al. Long-term opioid management for chronic noncancer pain. *Cochrane Database Syst Rev*. 2010;(1):CD006605.
5. Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN. Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med*. 2011;171(7):686-691.
6. Painter JT, Crofford LJ. Chronic opioid use in fibromyalgia syndrome: a clinical review. *J Clin Rheumatol*. 2013;19(2):72-77.
7. Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113-130.
8. Manchikanti L, Abdi S, Atluri S, et al. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2—guidance. *Pain Physician*. 2012;15(3 suppl):S67-S116.
9. Swegle JM, Logemann C. Management of common opioid-induced adverse effects. *Am Fam Physician*. 2006;74(8):1347-1354.
10. Bloodworth D. Opioids in the treatment of chronic pain: legal framework and therapeutic indications and limitations. *Phys Med Rehabil Clin N Am*. 2006;17(2):355-379.
11. Center for Substance Abuse Treatment. *Methadone-Associated Mortality: Report of a National Assessment, May 8–9, 2003*. Rockville, MD: Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration; 2004. http://pain-topics.org/pdf/CSAT_Methadone_Report.pdf. Accessed March 18, 2013.