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Implementing Guidelines for Treating Chronic Pain with Prescription Opioids

Tools to help primary care nurses as they assume an ever-increasing role in medication management.

ABSTRACT: Chronic pain, stemming primarily from musculoskeletal conditions and severe headaches, is a growing problem in the United States, affecting as many as 43% of adults. Opioids are frequently prescribed to manage chronic pain despite limited data on their long-term efficacy and the potential risks of long-term use. In 2017, more than 47,000 people died as a result of an opioid overdose involving illicit opioids (such as heroin), illicitly manufactured opioids, diverted opioids, prescription opioids, or some combination thereof. Although it's been more than three years since the nationwide opioid crisis prompted the Centers for Disease Control and Prevention (CDC) to release a guideline outlining safe practices for prescribing opioids to patients with chronic pain (unrelated to active cancer or palliative and end-of-life care), opioid misuse remains a significant concern. Historically, physicians have been tasked with the primary responsibility for implementing opioid safety measures, but nurses in the primary care setting are being increasingly relied on to incorporate these measures as part of their practice. In this article, we discuss the use of five tools outlined in the CDC guideline: prescription opioid treatment agreements, urine drug screening, prescription drug monitoring program databases, calculation of morphine milligram equivalents, and naloxone kits. Primary care nurses can use these tools to promote opioid safety among patients receiving opioid therapy for chronic pain.

Keywords: chronic pain, opioids, opioid treatment guidelines, prescription drug monitoring programs, prescription opioids, primary care, treatment, urine drug screening

Chronic pain is often defined as pain that lasts longer than three months or past the time of normal tissue healing. In the United States, though estimates vary widely, the prevalence of chronic pain, manifesting primarily as persistent musculoskeletal pain or frequent headaches, has been estimated to be as high as 43% among U.S. adults.[1] Opioid medication has enabled many patients with chronic pain to live normal lives, giving them an opportunity to function efficiently and safely on fixed opioid doses. But while randomized controlled trials support the efficacy of opioid therapy in treating certain chronic pain syndromes for periods of up to 12 weeks, less is known about the efficacy of longer-term opioid therapy in the treatment of chronic pain.[1] Outside the context of cancer treatment and palliative or end-of-life care, the risks associated with long-term opioid use, including dependency and death from overdose, are well established. In the United States, more people died from drug overdose in 2014 than during any previous year on record—and 61% (28,647) of those deaths were due to opioids—either illicit, illicitly manufactured, diverted,

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Prescription opioid treatment agreements clarify the responsibilities of both provider and patient and may improve treatment adherence. Photo © Hinterhaus Productions.

prescription, or some combination thereof.[2] In 2016 and 2017, respectively, opioids were responsible for 66.4% (42,249) and 67.8% (47,600) of all fatal U.S. drug overdoses.[3,4]

In 2016, responding to growing concerns about opioid overprescription; opioid overdose; and widespread opioid dependency, misuse, and diversion, the Centers for Disease Control and Prevention (CDC) released a guideline that uses a risk–benefit approach to the prescription of opioids for chronic pain that is not associated with cancer treatment and palliative or end-of-life care: the *CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016*.[1] The guideline is directed specifically at primary care providers—that is, physicians, NPs, and physician assistants—because they are responsible for nearly half of all opioid prescriptions dispensed in the United States.[1] It's important, however, for all members of primary care teams to be well versed in opioid safety, particularly nurses, who spend more time with patients than primary care providers,[5,6] who are responsible for teaching patients about their medications, and who are anticipated to assume an even greater role in medication management for patients with chronic conditions as the U.S. population ages and the number of primary care physicians in the workforce continues to decline.[7]

This article provides primary care nurses with information needed to assist in implementing the 2016 CDC opioid safety guideline, focusing on five tools designed to improve safety for patients prescribed opioid therapy for chronic pain: prescription opioid treatment agreements, urine drug screening (UDS), prescription drug monitoring program (PDMP) databases, calculation of morphine milligram equivalents (MMEs), and naloxone kits.

CONCERNS ABOUT OPIOID THERAPY FOR CHRONIC PAIN

In addition to potential dependency and overdose, oral opioids are associated with the following adverse effects (about half of patients prescribed opioids experience at least one)[8]:

- nausea
- vomiting
- constipation
- thought and memory impairment
- drowsiness
- depression
- impaired sleep

- hormonal effects
- hyperalgesia
- immune system suppression
- respiratory depression
- urinary retention
- delayed recovery from surgery
- triggering or worsening of substance abuse or addiction

Investigators conducting a 13-year health care record review of 32,499 patients who were prescribed opioid therapy for chronic noncancer pain and continued its use for at least three months found that, over a median of 186 days, one of every 55 patients escalated to high-dose opioid therapy and, over a median of 2.6 years, one of every 550 patients died from an opioid-related cause.[9] For chronic pain unrelated to active cancer and treated outside the context of palliative or end-of-life care, the CDC recommends clinicians consider opioid therapy only if improvement in both pain and function are expected to outweigh associated risks; nonpharmacologic and nonopioid pharmacologic therapies are preferred. If opioids are prescribed, they should be used in conjunction with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.[1] When opioids are used to treat chronic pain in opioid-naive patients, the CDC recommends they be started at the lowest possible effective dosage, and when opioids are used to treat chronic pain in patients who are already taking opioids, the CDC advises clinicians to prescribe a dosage that's consistent with product labeling regarding tolerance.[1]

RESPONSE TO THE CDC GUIDELINE

Although the medical community has largely embraced the CDC guideline recommendations, it should be noted that they are not mandatory and have engendered some controversy concerning issues such as maximum opioid dosages; aggressive opioid tapering; and misapplication of the recommendations to patients outside the scope of the guideline, such as those with cancer, acute sickle cell crises, or postsurgical pain, resulting in pain exacerbation and other adverse effects.[10,11] As the Institute of Medicine has emphasized, "Effective pain management is a moral imperative, a professional responsibility, and the duty of people in the healing professions."[12] To this end, research suggests that it is essential for all primary care team members to familiarize themselves with the CDC guideline so as to avoid going beyond its recommendations and intent.[11] Primary care providers often lack confidence in treating patients prescribed long-term opioid therapy but have benefited from additional training in this area[13] and have expressed that working within multimodal, interdisciplinary teams that incorporate nurses, pharmacists, physical therapists, and mental health specialists help them to optimize chronic pain care, promote opioid safety, and reduce prescription opioid misuse.[14]

ASSESSING CHRONIC PAIN

A thorough pain assessment is the first step in safely managing any type of pain, and patient–provider trust is an essential component of that assessment. This is particularly true when assessing chronic pain in consideration of opioid therapy, because, in addition to determining pain location, quality, and intensity, as well as the efficacy or adverse effects of all pharmacologic and nonpharmacologic interventions, proper risk reduction requires transparency between patients and providers about a number of potentially sensitive topics, including[15]

- current medication use.
- history of substance use disorders (involving the patient or family members).
- lifestyle habits, including alcohol use.
- psychiatric history.

The goal of managing chronic pain is to improve the patient's pain levels and functional status while minimizing risks and adverse outcomes.

IMPLEMENTING THE SAFETY TOOLS

We recommend using universal risk reduction strategies when prescribing opioids for chronic pain, meaning that we use all five tools with every patient receiving opioids for chronic pain regardless of real or perceived risk of abuse or misuse. Nurses should explain to patients that the tools are used at least annually to ensure the safety and adherence of all patients receiving opioid therapy for chronic pain. Applying universal risk reduction strategies reduces both stigma and overall risk.[16,17] Engaging in this type of communication, which emphasizes a concern for patients' optimal pain relief and function, also serves to reinforce the trust that is so important for clinicians to establish and maintain when managing a patient's chronic pain with opioids.

Prescription opioid treatment agreements. These should be in place for all patients prescribed opioids or any other controlled substance, such as benzodiazepines, especially if taken concurrently with opioids. The purpose of the agreement is to improve medication adherence, outline prescribing policies, and mitigate risk. The agreement should address the goals of treatment and explain the following in lay terms[18]:

- patient responsibilities
- primary care provider responsibilities
- responsibilities shared by patient and primary care provider
- possible benefits and risks of opioids and nonopioid treatment options

The agreement should be written in a manner prioritizing safety and avoiding language that

stigmatizes patients. Avoid the use of words such as "narcotics" or "contracts," which may be perceived as coercive and erode trust.[18] Both the patient and clinician should sign and receive a copy of the agreement, and it should be placed in the medical record. Prescription opioid treatment agreements may be tailored to meet the patient's unique needs, but most require the patient to obtain opioids from a single provider (usually the provider initiating the agreement) and, in some cases, a specific, identified pharmacy. Agreements should further specify that the patient agrees to[15]

- take medications only as prescribed.
- limit refills.
- keep medications stored in a safe location.
- not share medications with others.
- participate in regular UDS and prescriber follow-up.

therapy.[1] Any UDS results that meet or exceed a predetermined cutoff point are deemed positive, while any below that cutoff are deemed negative. But this interpretation need not be applied rigidly. Patients with chronic pain vary their opioid intake depending on their pain levels. Patients should be taught to use nonopioid analgesics and nonpharmacologic therapies when their pain is under control and to take opioids as prescribed only when needed to control pain. Opioid prescriptions usually take these variations into account, with directions such as, "Take one to two hydrocodone tablets every six hours as needed for pain." The prescription also includes the maximum number of tablets to be taken over a 28- or 30-day period. Patients should not be penalized for taking less than the maximum dosage as if they were diverting the drugs. If the patient's UDS result is below the threshold and

Patients should be taught to use nonopioid analgesics and nonpharmacologic therapies when their pain is under control and to take opioids as prescribed only when needed.

When patients being treated for chronic pain do not have an opioid agreement in place, nurses should recommend that they schedule an appointment specifically to discuss treatment goals and establish such an agreement. (For a sample agreement from the American Academy of Pain Medicine, go to www.nhms.org/sites/default/files/Pdfs/Opioid-Tx-Agreement-AAPM2001.pdf.) Should a patient express unwillingness to sign a treatment agreement, the nurse's role is to answer patient questions and address patient concerns, further explaining that opioid medications are controlled substances, the risks with which they are associated, and that the completion of a treatment agreement–informed consent is a prerequisite for all patients whose chronic pain is to be treated with opioid therapy. Generally, opioids are initiated on a trial basis, and it is ultimately the prescribing clinician who determines whether the potential benefits of opioid therapy outweigh the risks for a particular patient.

UDS. UDS immunoassays are conducted to confirm the presence of prescribed substances and to detect undisclosed prescription drug or illicit substance use. The CDC recommends that patients with chronic pain be screened before starting opioid therapy and at least annually while taking opioid

deemed negative, the nurse should discuss this result with the patient, confirming the accuracy of the last opioid dose taken before the urine sample was collected and arranging for a confirmatory test to be ordered.

If, however, a patient reports increased pain requiring increased pain medication, the patient should be reminded (as instructed in the prescription opioid treatment agreement) to notify the primary care nurse, who can conduct a complete pain assessment, develop an appropriate pain management plan, and alert the prescriber. Cutoff points vary depending on the substances for which urine is being tested and the laboratory conducting the testing. Nurses should be familiar with the substances typically included in the screening panel used by their practice, how to retrieve results, and how to request confirmatory testing.[1] Most urine drug screens test for the following substances, with some variation:

- opioids (morphine and morphine derivatives, but not necessarily the semisynthetic or synthetic opioids oxycodone and fentanyl)
- tetrahydrocannabinol (THC)
- barbiturates
- methadone
- cocaine

- amphetamines
- benzodiazepines
- phencyclidine
- alcohol (if specified)

To test for oxycodone or fentanyl, the provider usually needs to order specific confirmatory tests. In addition, at low dosages hydrocodone may not be detected by UDS.

Random versus scheduled UDS. Random UDS, though not always feasible in the primary care setting, is preferred over scheduled UDS, as patients who receive advance notice can make medication or lifestyle changes prior to screening. Some clinicians obtain urine specimens at every visit but send it for testing on a random schedule.[1]

Ideally, PDMP data on all patients should be reviewed prior to writing or refilling an opioid prescription.

UDS results are often preliminary or 'presumptive.' If a positive UDS result is unexpected based on the patient's current medications, confirmatory testing should be conducted to rule out false-positive immunoassay results, possibly reflecting the metabolites from the patient's prescribed opioids.[1,19] Laboratories vary as to how long they keep specimens, so if additional testing is necessary, ask the laboratory if the patient's sample is still available (some laboratories retain specimens for up to two weeks). As soon as confirmatory testing has been performed, the next step should be to discuss the results with the patient. Although UDS follow-up is recommended, research suggests that unexpected UDS results are often not addressed by providers.[20] In a retrospective cohort study by Morasco and colleagues, nearly one-third of unexpected UDS results went unacknowledged by primary care providers, more than half of prescribed changes were not carried out, and 16% of primary care providers made no changes in treatment plans despite documented aberrant UDS results.[20]

Managing unexpected results. There are many reasons for unexpected results, including the sensitivity of the test, limited quantitation, laboratory cutoff levels, diluted urine (either the result of physiological causes or tampering), rapid metabolism, nonuse, or diversion.[21] Unexpected negative results may occur as the result of a missed dose (potentially because of adverse effects, limited benefit of the medication, or other factors). If unexpected UDS results are confirmed, the nurse should ensure that the primary care provider is aware of the findings and let the patient know they will need to schedule a visit to address the problem. Next steps may include the following[1]:

- discussing medication practices with the patient
- scheduling more frequent evaluation
- considering opioid tapering if misuse or abuse is evident
- considering opioid discontinuation or transition to a different opioid
- offering naloxone
- offering referral for substance use disorder treatment as appropriate

Before sending urine specimens for screening, it is important to document the medication doses the patients last took and the times at which they took them. This can help clinicians interpret results. UDS and appropriate follow-up help clinicians manage their patients' prescribed controlled substances and provide patients greater protection from drug misuse. UDS should be interpreted in the context of all available clinical information. UDS results alone should not be used as the basis for discharging a patient from care or discontinuing opioid therapy.[21]

PDMP databases. These are statewide electronic databases that track all controlled substance prescriptions distributed within a given state. They are currently available or in development in 49 states—all except Missouri, whose opioid-related overdose death rate exceeds the national average.[22] Prescription records include information on the dispensers and prescribers, drug names, and quantities. Use of the PDMP alerts providers of a patient's use of multiple providers or multiple pharmacies, making it an essential tool for ensuring safer prescribing. Use of PDMPs has been found to reduce "doctor shopping," prescription abuse, and diversion.[23] A data analysis of PDMPs and opioid-related overdose deaths demonstrated that PDMP use was associated with an annual decrease of 1.12 opioid-related overdose deaths per 100,000 population.[22] The investigators estimated that if all state PDMPs monitored at least four categories of scheduled drugs and updated program data weekly—and if Missouri had developed a PDMP with similar standards—more than 600 deaths could have been prevented in 2016, the year the analysis was published.

Ideally, PDMP data on all patients should be reviewed prior to writing or refilling an opioid prescription. State policies regarding PDMP access vary, but in most states, physicians (including residents), NPs, dentists, pharmacists, and licensed delegates, such as nurses and social workers, may

register for access. Any unexpected PDMP findings should prompt a patient visit.

Calculation of MMEs. The MME is a value that allows for comparison between morphine and other opioid pain medications, enabling clinicians to estimate oral equianalgesic doses. Calculating the total daily MME helps clinicians identify patients who may benefit from closer monitoring or tapering of opioids, prescribing of naloxone, or other measures. (See *A Step-by-Step Guide to Calculating Morphine Milligram Equivalent Dosages.*[24,25]) Nurses should document the MME in the patient's medical record and discuss any associated risks with the patient, particularly if the patient concurrently uses other medications that increase risk of overdose, such as benzodiazepines, muscle relaxants, or hypnotics, or uses alcohol. It is important for the entire primary care team to be aware of a patient's MME, as MMEs at or above 50 per day are associated with greater risks than lower MMEs, and MMEs below

A Step-by-Step Guide to Calculating Morphine Milligram Equivalent Dosages

Due to the varying potencies of opioid medications, a conversion factor is required to determine the morphine equivalency of the opioid component of any opioid-based medication (see Table 1).

This equation is used to calculate a patient's MME dose: **pill strength (mg) × pills/day × conversion factor = MME**.

Nurses can calculate a patient's MME dose based on conversion factors available on government websites such as that of the Centers for Disease Control and Prevention (CDC)[24] or use one of the several online MME calculators, such as the CDC's Opioid Guideline Mobile App (www.cdc.gov/drugoverdose/prescribing/app.html), which providers may find particularly helpful when caring for patients prescribed more than one opioid medication. It should be noted that, since there is no universally accepted conversion method, there are variations among MME calculators and conversion charts, particularly with regard to the conversions of methadone and fentanyl.[25]

The following scenarios illustrate how MMEs would be calculated for various types of prescriptions:

- **Calculating the MME for a dose-steady prescription.** A patient has been instructed to take five 10-mg pills of hydromorphone daily for 30 days. The equation is: 10 mg × 5 pills/day × 4 (the hydromorphone conversion factor) = 200 MME.
- **Calculating the MME for a dose-variable prescription.** A patient has been instructed to take five 10-mg pills of hydromorphone daily for 30 days but has been given an additional 15 pills to use as needed for breakthrough pain. First, calculate the total number of pills in the prescription: 5 pills × 30 days + 15 pills = 165 pills. Then, calculate the average number of pills per day: 165 (total number of pills) ÷ 30 (number of days covered) = 5.5 (average pills/day). Now substitute "average pills/day" for "pills/day" in the standard MME equation: 10 mg × 5.5 average pills/day × 4 (the hydromorphone conversion factor) = 220 MME.
- **Calculating the MME for multiple opioid prescriptions.** If a patient is taking multiple opioids, calculate the MME for each drug and then add them together to calculate the total MME. For example, a patient is taking five 10-mg pills of hydromorphone daily for 30 days, but then two 30-mg pills of codeine per day—one every 12 hours—are added to the regimen. The MME for the hydromorphone has already been established as 200 MME; for the codeine, calculate: 30 mg × 2 pills/day × 0.15 (the codeine conversion factor) = 9 MME. The patient's total MME is 209 (200 MME from hydromorphone plus 9 MME from codeine).

Table 1. Calculating Morphine Milligram Equivalents (MMEs)[24]

Opioid, mg/day	Conversion Factor
Codeine	0.15
Fentanyl transdermal (mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1–20	4
21–40	8
41–60	10
61–80	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

Note: These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.

20 per day are safer still. The CDC guideline thus advises clinicians to carefully assess risks and benefits when considering increasing opioid dosages as high as 50 MME per day.[1] It should be noted, however, that abrupt cessation of opioids may lead to physical withdrawal and cessation of analgesia. The CDC guideline does not support abrupt discontinuation of opioids, though in the aftermath of an overdose, a rapid taper may be necessary.[11]

Naloxone is especially recommended for patients at elevated risk for respiratory depression.

Naloxone kits. Naloxone (Narcan, Evzio) is an opioid antagonist used to reverse life-threatening opioid overdoses. Naloxone displaces opioids from receptor sites in the brain, thereby reversing respiratory depression.[26] Overdose education should be provided and naloxone offered as an antidote to all patients at risk for opioid overdose, including those in the process of opioid tapering. Opioid overdose–related deaths can be prevented when naloxone is administered as soon as possible. Between 1996 and 2014, naloxone successfully reversed a reported 26,463 opioid overdoses.[27] Even with as little as 10 minutes of training, laypersons can recognize an opioid overdose and initiate naloxone rescue.

Naloxone can be given intramuscularly, subcutaneously, or intravenously, and can be easily administered intranasally by friends or family members of patients using opioid medications.[26] The U.S. surgeon general advises primary care providers and pharmacists to prescribe or dispense naloxone to all patients at elevated risk for opioid overdose, including those receiving opioids to manage chronic pain, and to make naloxone available to the patients' friends and family members.[28] Naloxone is especially recommended for patients at elevated risk for respiratory depression, such as those who

- are taking 50 or more MME per day.
- are taking concurrent opioids and benzodiazepines.
- are using alcohol while taking opioids.
- have been diagnosed with a current or previous opioid use disorder.
- have received a current or previous diagnosis of sleep apnea.
- have a history of renal or hepatic impairment.
- have a history of possible overdose in the past three years.

Incorporating risk reduction tools into practice. To reduce the workload on both nurses and primary care providers, the primary care team can develop a process that helps prepare them for upcoming appointments of patients being treated with opioids for chronic pain. It would involve ordering in advance any UDS or PDMP reports or laboratory tests relevant to all patient visits scheduled for the week. The team can then review the results and, if any are unexpected, consider whether treatment changes or increased monitoring would best address aberrant behaviors, all of which they can discuss with the patient at the scheduled visit. Primary care teams can also collaborate with their information technology departments to develop a note template specific to continuing pain management in patients receiving opioid therapy for chronic pain, which would include the following information:

- date on which the opioid agreement is signed
- date of the most recent UDS
- date of last PDMP access
- patient's current MME
- whether a naloxone prescription has been dispensed

Such note templates can quickly relay information and key care considerations to the primary care provider and nurses prior to the filling of each opioid prescription. ▼

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