Cautious, Responsible Opioid Prescribing

Despite low-quality evidence supporting practice change, 1-6 use of chronic opioid therapy (COT) for chronic non-cancer pain increased dramatically over the past two decades. 34-36

Concurrently, opioid diversion, prescription opioid addiction/misuse, and fatal overdose involving prescription opioids increased markedly.^{20,37}

To reduce these and other problems related to COT, it is essential that clinicians adhere to cautious, responsible practices when considering opioids for chronic pain.

Myths and Facts about Chronic Opioid Therapy (COT):

Myth: COT for chronic pain is supported by strong evidence.	Fact: Evidence of long-term efficacy for chronic non-cancer pain (≥16 weeks) is limited, 1.2.3 and of low quality.4.5 Opioids are effective for short-term pain management. But, for many patients with chronic pain, analgesic efficacy is not maintained over long time periods.6
Myth: Physical dependence only happens with high doses over long periods of time.	Fact: With daily opioid use, physical dependence and tolerance can develop in days or weeks. ^{7,8}
Myth: Patients who develop physical dependence on opioids can easily be tapered off.	Fact: Successfully tapering chronic pain patients from opioids can be difficult — even for patients who are motivated to discontinue opioid use. ³³
Myth: Addiction is rare in patients receiving medically prescribed COT.	Fact: Estimates vary. Between 4% and 26% of patients receiving COT have an opioid use disorder. Among patients without an opioid use disorder, more than one in ten misuse opioids by: intentional over-sedation; concurrently using alcohol for pain relief; hoarding medications; increasing dose on their own; and borrowing opioids from friends. 9,15
Myth: Addiction is the main risk to be concerned about when prescribing opioids.	Fact: Opioids have significant risks besides addiction and misuse. ^{18,19} These risks include respiratory depression and unintentional overdose; ^{20,21} serious fractures from falls; ^{22,23} hypogonadism and other endocrine effects that can cause a spectrum of adverse effects; ²⁴ increased pain sensitivity, ²⁵ sleep-disordered breathing, ²⁶ chronic constipation and serious fecal impaction, ^{27,28} and chronic dry mouth which can lead to tooth decay. ²⁹
Myth: Extended-release opioids are better than short-acting opioids for managing chronic pain.	Fact: Extended-release opioids have not been proven to be safer or more effective than short-acting opioids for managing chronic pain. ³⁰
Myth: Prescribing high-dose opioid therapy (≥120 mg morphine equivalents/day) is supported by strong evidence that benefits outweigh risks.	Fact: No randomized trials show long-term effectiveness of high opioid doses for chronic non-cancer pain. Many patients on high doses continue to have substantial pain and related dysfunction. ³² Higher doses come with increased risks for adverse events and side effects including overdose, fractures, hormonal changes, and increased pain sensitivity. ¹⁸⁻²⁶
Myth: Opioid overdoses only occur among drug abusers and patients who attempt suicide.	Fact: Patients using prescription opioids are at risk of unintentional overdose and death. ²⁰ This risk increases with dose and when opioids are combined with other CNS depressants like benzodiazepines and alcohol. ²¹
Myth: Dose escalation is the best response when patients experience decreased pain control.	Fact: When treating chronic pain, dose escalation has not been proven to reduce pain or increase function, but it can increase risks. ³²

Do's & Don'ts for Acute Pain Management

DO explain that opioids are for time-limited use. With the first opioid prescription, set expectations that opioids should be discontinued when the pain problem is no longer acute.

DON'T stock your patients' medicine cabinets with unused opioids. Limit all initial and refill prescriptions for acute pain. A 30-day supply is often excessive — many patients only take a pill or two then leave the rest in their medicine cabinet. This increases the risk of diversion, which in turn increases the risk of addiction and fatal overdose in families and communities. For those patients who use the medicine daily for several weeks, physiologic dependence develops within days or weeks. Due to

risks of accidental poisoning, it is important to store opioids in a medication lock box and flush unused opioids down a sink or toilet.

DON'T start long-term use of opioids by accident. Long-term opioid prescribing should only occur after careful patient evaluation, discussion of risks and realistic expectations of benefits, and clear explanation of rules for safe use. Routine authorization of refills may cause patients to expect the prescription to continue indefinitely.

DON'T prescribe extended-release opioids for acute pain or to opioid-naïve patients. Extended-release opioids are not appropriate for managing acute pain and should never be prescribed to an opioid-naïve patient.

Do's & Don'ts for Chronic Pain Management

DON'T initiate chronic opioid therapy (COT) before considering safer alternatives such as primary disease management, cognitive-behavioral therapy (CBT), participating in pleasant and rewarding life activities, physical therapy, non-opioid analgesics and exercise.

DO screen patients for depression and other psychiatric disorders before initiating COT. Patients with depression and other mental health problems often present with pain problems. They may not know that mental health problems can contribute to chronic pain. These patients are at higher risk of opioid addiction. They may be better served by mental health treatment.

DO talk with patients about therapeutic goals, opioid risks, realistic benefits, and prescribing ground rules. Therapeutic goals should include increased activity and improved quality of life, not just pain relief. Patients should understand the full range of opioid risks and the limited benefits they can reasonably expect. The rules for safe and appropriate use of opioids need to be explicit, preferably documented in a written treatment agreement.

DO realize that patients are reluctant to disclose a history of substance abuse. A history of substance abuse indicates greater risk of opioid addiction, but getting an accurate picture of past and current drug use can be difficult. If a patient denies past or current substance abuse, recognize that they may be afraid to tell you the truth. Consult the medical record, a Prescription Drug Monitoring Database, and third parties as needed.

DO perform a thorough medical evaluation and a urine drug screen before initiating COT. Starting chronic opioid therapy should be an affirmative decision based on adequate assessment of risk, urine drug screening, and use of a treatment agreement. Because it can be difficult to know if a patient is seeking opioids for addiction or diversion purposes, COT should only be considered by a physician who has an ongoing relationship with the patient. The prescribing physician should be willing to continue working with the patient if problems arise.

DO explain to patients that discontinuing opioids may be difficult. Some patients find it difficult to taper off of opioids, particularly from higher dose regimens, even when they are eager to do so. Patients can experience increased pain, insomnia, or anxiety when tapering from opioids. These unpleasant withdrawal symptoms can last for several weeks. Do not abandon chronic pain patients after discontinuing opioids.

DO perform random urine drug screens on patients receiving COT. Urine drug screening helps identify patients using illicit drugs or not taking the medicine as prescribed.

DON'T continue COT with patients who show no progress toward treatment goals defined by increased function and reduced pain.

DON'T assume patients know how to use opioids safely.

Opioids are powerful drugs that patients sometimes use in unsafe ways. Risks of unsafe use increase with prescribed dose and are greater for extended-release medications with long half-life. Patients often do not understand that it can be unsafe to take extended-release opioids "as-needed for pain." Take time to talk with patients about how they are using opioids. Ask patients about their problems and concerns.¹⁷

DON'T assume patients use opioids as you intend. Many patients vary their dose and use combinations of other CNS depressant drugs or alcohol in ways that you may not know about. Patients may also sell their medications or share them with others. Opioid misuse often occurs among patients who do not have an opioid use disorder.^{9,15} Vigilance for unsafe use is essential.

DON'T start a treatment that you are not prepared to stop.

Don't initiate COT without benchmarks for stopping, a procedure for tapering that you are willing and able to use, and an approach to managing physical and psychological withdrawal symptoms. If substance abuse is identified, taper opioids and make arrangements for substance abuse treatment.

DON'T assume patients are doing well with COT without careful evaluation. Careful and compassionate interviewing about opioid use and misuse, questions about your patients' problems and concerns, ¹⁷ screening questionnaires, urine drug screening, and information from Prescription Drug Monitoring Databases often reveal problems with prescription opioids that would otherwise be missed.

DON'T abandon patients with a prescription drug problem. For patients who are misusing or addicted to prescription opioids, offer help or referral to someone who can treat substance abuse.

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References

- 1. Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. Pain. 2004;112:372-80.
- Papaleontiou M, Henderson CR, Turner BJ, Moore AA, Olkhovskaya Y, Amanfo L, Reid MC. Outcomes associated with opioid use in the treatment of chronic noncancer pain in older adults: A systematic review and meta-analysis. JAGS 2010; 58:1353-1369.
- Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, Kosten TR, et al. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction.
 Ann Intern Med. 2007;146:116-27.
- 4. Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, Donovan MI, Fishbain DA, Foley KM, Fudin J, Gilson AM, Kelter A, Mauskop A, O'Connor PG, Passik SD, Pasternak GW, Portenoy RK, Rich BA, Roberts RG, Todd KH, Miaskowski C; American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain 2009; 10:113-130.
- 5. American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. Pharmacological Management of Persistent Pain in Older Persons. JAGS 2009; 57:1331-1346, 2009.
- 6. Ballantyne JC, Shin NS. Efficacy of opioids for chronic pain: a review of the evidence. Clin J Pain 2008;24:469-78.
- 7. McQuay H. Opioids in pain management. Lancet 1999, 353: 2229-2232.
- 8. Baily CP and Connor M. Opioids: Cellular mechanisms of tolerance and physical dependence. Current Opinion in Pharmacology 2005; 5:60-80.
- 9. Fleming MF, Balousek SL, Klessig CL, Mundt MP, Brown DD. Substance Use Disorders in a Primary Care Sample Receiving Daily Opioid Therapy. *J Pain* 2007; 8:573-582. Banta-Green CJ, Merrill JO, Doyle SR, Boudreau DM, Calsyn DA. Measurement of opioid problems among chronic pain patients in a general medical population. *Drug and Alcohol Dependence* 2009; 104:43-49. Becker WC, Fiellin DA, Gallagher RM, Barth KS, Ross JT, Oslin DW. The association between chronic pain and prescription drug abuse in Veterans. *Pain Medicine* 2009; 10:531-536.
- 10. Banta-Green CJ, Merrill JO, Doyle SR, Boudreau DM, Calsyn DA. Measurement of opioid problems among chronic pain patients in a general medical population. Drug and Alcohol Dependence 2009; 104:43-49.
- 11. Becker WC, Fiellin DA, Gallagher RM, Barth KS, Ross JT, Oslin DW. The association between chronic pain and prescription drug abuse in Veterans. Pain Medicine 2009; 10:531-536.
- Boscarino JA, Rutstalis M, Hoffman SN, Han JJ, Erlich PM, Gerhard GS, Stewart WF. Risk factors for drug dependence among out-patients on opioid therapy in a large US health-care system. Addiction 2010: 105:1776-1782.
- 13. Manchikanti L., Fellows B., Damron K.S., Pampati V., McManus C.D. Prevalence of illicit drug use among individuals with chronic pain in the Commonwealth of Kentucky: an evaluation of patterns and trends.

 J Kv Med Assoc 2005: 103: 55-62.
- Ives TJ, Chelminski PR, Hammett-Stabler CA, Malone RM, Perhac JS, Potisek NM, Shilliday BB, DeWalt DA, Pignone MP. Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. BMC Health Services Research 2006; 6:46-55.
- Banta-Green CJ, Merrill JO, Doyle SR, Boudreau DM, Calsyn DA. Opioid use behaviors, mental health and pain Development of a typology of chronic pain patients. *Drug and Alcohol Dependence* 2009; 104:34-42.
- 16. Goldsworthy RC, Schwartz NC, Mayhorn CB. Beyond Abuse and Exposure: Framing the Impact of Prescription-Medication Sharing. Am J Public Health. 2008;98:1115–1121.
- 17. Sullivan MD, Von Korff M, Banta-Green C, Merrill JA, Saunders K. Problems and concerns of patients receiving chronic opioid therapy for chronic non-cancer pain. Pain 2010; 149:345-353.
- 18. Ballantyne JC, Mao J. Opioid therapy for chronic pain. N Engl J Med 2003;349:1943-53.
- 19. Von Korff M. Commentary on Boscarino et al. (2010): Understanding the spectrum of opioid abuse, misuse and harms among chronic opioid therapy patients. Addiction 2010; 105:1783-1784.
- 20. Paulozzi LJ, Ryan GW. Opioid analgesics and rates of fatal drug poisoning in the United States. Am J Prev Med. 2006;31:506-11.
- 21. Dunn KM, Saunders KW, Rutter CM, Banta-Green CJ, Merrill JO, Sullivan MD, Weisner CM, Silverberg MJ, Campbell Cl, Psaty BM, Von Korff M. Opioid prescriptions for chronic pain and overdose: a cohort study. Annals of Internal Medicine 2010; 152:85-92.
- 22. Saunders KW, Dunn KM, Merrill JO, Sullivan MD, Weisner CM, Braden JB, Psaty BM, Von Korff M. Relationship of opioid use and dosage levels to fractures in older chronic pain patients. Journal of General Internal Medicine 2010: 25:310-315.
- 23. Takkouche B, Montes-Martinez A, Gill S, Etminan M. Psychotropic medications and the risk of fracture. Drug Safety. 2007;30(2):171-84.
- 24. Vuong C, Van Uum SH, O'Dell LE, Lutty K, Friedman TC. The effects of opioids and opioid analogs on animal and human endocrine systems. Endocr Rev. 2010; 31:98-132.
- 25. Zhou HY, Chen SR, Chen H, Pan HL. Opioid-induced long-term potentiation in the spinal cord is a presynaptic event. Neuroscience 2010; 30:4460-4466.
- 26. Walker JM, Farney RJ, Rhondeau SM, Boyle KM, Valentine K, Cloward TV, Shilling KC, Chronic Opioid Use is a Risk Factor for the Development of Central Sleep Apnea and Ataxic Breathing. J Clin Sleep Medicine 2007; 3:455-461.
- 27. Tuteja AK, Biskupiak J, Stoddard GJ, Lipman AG. Opioid-induced bowel disorders and narcotic bowel syndrome in patients with chronic non-cancer pain. Neurogastroenterol Motil 2010; 22:424-30.
- 28. Bell TJ, Panchal SJ, Miaskowski C, Bolge SC, Milanova T, Williamson R. The prevalence, severity and impact of opioid-induced bowel dysfunction: results of a US and European Patient Survey (PROBE 1). Pain Medicine 2009; 10:35-42.
- 29. Murray Thomson W, Poulton R, Mark Broadbent J, Al-Kubaisy S: Xerostomia and medications among 32-year olds. Acta Odontol Scand 64:249-254, 2006
- 30. Chou R, Clark E, Helfand M. Comparative efficacy and safety of long-acting oral opioids for chronic non-cancer pain: a systematic review. J Pain Symptom Manage 2003;26:1026-1048.
- 31. Lusher J, Elander J, Bevan D, Telfer P, Burton B: Analgesic addiction and pseudoaddiction in painful chronic illness. Clin J Pain 2006; 22:316–324.
- 32. Franklin GM, Rahman EA, Turner JA, Daniell WA, Fulton-Kehoe D. Opioid use for chronic low back pain. A prospective, population-based study among injured workers in Washington State, 2002–2005. Clin J Pain 2009; 25:743-751.
- 33. Blondell RD, Ashrafioun L, Dambra CM, Foschio EM, Zielinski AL, Salcedo DM. A clinical trial comparing tapering doses of buprenorphine with steady doses for chronic pain and co-existent opioid addiction.

 J Addict Med 2010: 4:140-146.
- 34. Caudill-Slosberg MA, Schwartz LM, Woloshin S. Office visits and analgesic prescriptions for musculoskeletal pain in US: 1980 vs 2000. Pain. 2004;109(3):514-519.
- 35. Boudreau D, Von Korff M, Rutter CM, et al. Trends in long-term opioid therapy for chronic non-cancer pain. Pharmacoepidemiol Drug Saf. 2009;18(12):1166-1175.
- 36. Sullivan MD, Edlund MJ, Fan MY, et al. Trends in use of opioids for non-cancer pain conditions 2000-2005 in commercial and Medicaid insurance plans: the TROUP study. Pain. 2008;138(2):440-449.
- 37. Zacny J, Bigelow G, Compton P, Foley K, Iguchi M, Sannerud C. College on Problems of Drug Dependence taskforce on prescription opioid non-medical use and abuse: position statement. Drug and alcohol dependence 2003;69:215-232.