



Interagency Guideline on Prescribing Opioids for Pain

Developed by the Washington State Agency Medical Directors' Group (AMDG) in collaboration with an Expert Advisory Panel, Actively Practicing Providers, Public Stakeholders, and Senior State Officials.

www.agencymeddirectors.wa.gov



AMDG agency medical directors' group

A collaboration of state agencies, working together to improve health care quality for Washington State citizens.

*Written for Clinicians who Care for People with Pain
3rd Edition, June 2015*

Table of Contents

| | |
|--|-----------|
| A MESSAGE FROM WASHINGTON’S SECRETARY OF HEALTH | 4 |
| COMPARISON OF 2010-2015 GUIDELINES | 5 |
| INTRODUCTION | 6 |
| Correct Diagnosis and Realistic Expectations | 6 |
| Uncertain Long-term Efficacy, Clear Evidence of Harm..... | 7 |
| Opioids and Chronic Disability | 8 |
| PART I. RECOMMENDATIONS FOR ALL PAIN PHASES | 9 |
| Clinically Meaningful Improvement in Function (CMIF) | 9 |
| Dosing Threshold | 11 |
| Non-opioid Options for Pain Management | 14 |
| PART II. PRESCRIBING OPIOIDS IN THE ACUTE AND SUBACUTE PHASE | 22 |
| Opioids in the Acute Phase | 22 |
| Opioids in the Subacute Phase | 23 |
| PART III. OPIOIDS FOR PERIOPERATIVE PAIN | 26 |
| Preoperative Period | 26 |
| Intraoperative Period..... | 27 |
| Immediate Postoperative Period | 27 |
| At Time of Hospital Discharge..... | 29 |
| PART IV. PRESCRIBING OPIOIDS FOR CHRONIC NON-CANCER PAIN | 32 |
| Opioids in the Chronic Phase | 32 |
| PART V. REDUCING OR DISCONTINUING CHRONIC OPIOID ANALGESIC THERAPY (COAT) | 36 |
| Reasons to Discontinue COAT and Considerations Prior to Taper | 36 |
| How to Discontinue Opioids | 37 |
| PART VI. RECOGNITION AND TREATMENT OF OPIOID USE DISORDER | 40 |
| PART VII. CHRONIC PAIN MANAGEMENT IN SPECIAL POPULATIONS | 42 |
| Managing Chronic Pain during Pregnancy; and Neonatal Abstinence Syndrome | 42 |
| Managing Chronic Non-cancer Pain in Children and Adolescents..... | 45 |
| Managing Chronic Pain in Older Adults | 47 |
| Managing Chronic Pain in Cancer Survivors | 49 |
| PART VIII. APPENDICES | 54 |
| Appendix A: Opioid Dose Calculations..... | 55 |
| Appendix B: Validated Tools for Screening and Assessment..... | 59 |
| Appendix C: How to use the Prescription Monitoring Program | 60 |
| Appendix D: Urine Drug Testing for Monitoring Opioid Therapy | 62 |
| Appendix E: Chronic Pain Syndromes in Cancer Survivors | 72 |
| Appendix F: Diagnosis-based Pharmacotherapy for Pain and Associated Conditions | 74 |
| Appendix G: Patient Education Resources..... | 76 |
| Appendix H: Clinical Tools and Resources | 78 |
| Appendix I: Guideline Development and AGREE II Criteria | 81 |
| ACKNOWLEDGEMENTS | 87 |
| REFERENCES | 89 |

Table of Figures and Tables

| | |
|--|----|
| Figure A. Three Item PEG Assessment Scale..... | 10 |
| Figure B. Two Item Graded Chronic Pain Scale..... | 10 |
| Figure C. Risk of Overdose Events in Four Different Populations..... | 12 |
| Figure D. Infant Hospitalizations for Neonatal Abstinence Syndrome in WA State 1990-2013..... | 44 |
| Figure E: UDT Algorithm for Monitoring COAT for CNCP..... | 67 |
| | |
| Table 1. Cognitive Behavioral and Non-pharmacological Therapies for Chronic Pain | 14 |
| Table 2. "Red Flags" Indicating Need for Further Patient Evaluation..... | 15 |
| Table 3. Recommended Sleep Hygiene Habits | 16 |
| Table 4. Risks for Over-sedation and/or Respiratory Depression from Postoperative Opioids..... | 29 |
| Table 5. Risks for Difficult-to-control Postoperative Pain..... | 30 |
| Table 6. How Often to Monitor Patients on COAT | 33 |
| Table 7. Prescribing Methadone for Pain Management..... | 34 |
| Table 8. When to Reduce, Taper, or Discontinue COAT | 36 |
| Table 9. Aberrant Behaviors..... | 38 |
| Table 10. Symptoms and Treatment of Opioid Abstinence Syndrome | 38 |
| Table 11. Common Pain Syndromes Resulting from Cancer Treatment | 51 |
| Table 12. Signs and Symptoms Associated with Recurrence of Malignancy..... | 53 |
| Table 13. Signs and Symptoms of Spinal Cord Compression | 53 |
| Table 14. Dosing Threshold for Selected Opioids | 55 |
| Table 15. MED for Selected Opioids | 57 |
| Table 16. MED for Methadone | 57 |
| Table 17. Morphine Equivalent Dose Calculation..... | 58 |
| Table 18. Recommended Frequency of PMP Checks during COAT | 61 |

A Message from Washington's Secretary of Health



STATE OF WASHINGTON
DEPARTMENT OF HEALTH

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May 29, 2015

To Whom it May Concern:

Washington and many other states are in the midst of an epidemic of opioid misuse, abuse and overdose. During the past ten years, the number of hospitalizations for opioid dependence, abuse, and overdose has each more than doubled. Statewide, annual unintentional prescription opioid-related overdose deaths climbed from 24 in 1995, to 512 in 2008.

Washington was one of the first states to recognize and respond to the opioid epidemic. The Agency Medical Directors Group (AMDG) collaborated with practicing clinicians to develop and implement the groundbreaking AMDG Opioid Dosing Guideline in 2007, the first attempt in the U.S. to reduce prescribing of high doses of opioids associated with unintentional overdose.

The AMDG Guideline, along with other key statewide efforts, has resulted in a 29% decrease in the rate of prescription opioid-related deaths between 2008 and 2013. Hospitalizations for prescription opioid overdose have also declined 29% between 2011 and 2013.

Although opioids can be a useful option for pain management, their inappropriate use can result in significant harms, including addiction and death. Please help us to improve the health of Washington residents by following this updated AMDG evidence-based practice guideline.

I would like to thank the Agency Medical Directors Group and participating clinicians for their leadership and continued efforts to address this public health issue.

Sincerely,

A handwritten signature in black ink, appearing to read "John Wiesman".

John Wiesman, DrPH, MPH
Secretary of Health

Comparison of 2010-2015 Guidelines

| 2010 Guideline | 2015 Guideline |
|---|---|
| Primary focus was on chronic non-cancer pain | Expands focus to include opioid use in acute, subacute, and perioperative pain phases and in special populations; includes sections on tapering and opioid use disorder. |
| <p>Two main sections:</p> <ul style="list-style-type: none"> I. Initiating, transitioning, and maintaining patients on chronic opioid analgesic therapy (COAT) with principles of safe prescribing, and II. Optimizing treatment for patients on > 120mg daily MED with brief sections on getting consultations, aberrant behaviors, tapering, and discontinuing COAT. | <p>New and modified sections:</p> <ul style="list-style-type: none"> I. Recommendations for All Pain Phases <ul style="list-style-type: none"> a. Clinically Meaningful Improvement in Function b. Expanded discussion on dosing threshold c. Non-opioid Options for Pain Management II. Opioids in the Acute and Subacute Phases III. Opioids for Perioperative Pain IV. Opioids for Chronic Non-cancer Pain (similar to previous guideline) V. New section on Reducing or Discontinuing COAT VI. New section on Recognition and Treatment of Opioid Use Disorder VII. New sections on opioid use in special populations (during pregnancy and neonatal abstinence syndrome, in children and adolescents, in older adults, and in cancer survivors). |
| <p>Appendices:</p> <ul style="list-style-type: none"> A. Opioid Dose Calculations & Calculator B. Screening Tools C. Tools to Assess Pain and Function D. Urine Drug Testing for COAT E. Consultative Assistance for WA State Payers F. Patient Education Resources G. Sample Doctor-patient Agreement for COAT H. Additional Resources to Streamline Clinical Care I. Emergency Department Opioid Guidelines | <p>Appendices:</p> <ul style="list-style-type: none"> A. Opioid Dose Calculations & Calculator B. <i>Renamed:</i> Validated Risk Factor Screening Tools and combines former appendices B and C. C. How to use the Prescription Monitoring Program D. Urine Drug Testing for COAT E. Chronic Pain Syndromes in Cancer Survivors F. Diagnosis-based Pharmacotherapy for Pain G. Patient Education Resources (updated) H. <i>Renamed:</i> Clinical Tools and Resources and combines former appendices G, H, and I I. Guideline Development and AGREE II Criteria |
| Recommended 120mg daily MED as a “yellow flag” dose as a strategy to prevent adverse events and overdose by advising providers to seek a consultation with a pain specialist. | Remains the same, plus adds guidance for safe prescribing <u>at any dose</u> , based on new studies showing significant risks occurring at lower doses. |
| Organized as narrative information and recommendations with evidence in citations. | Organized with each section having specific clinical recommendations with supporting narrative evidence sections with citations. |

Introduction

This is the 3rd Edition of the Washington State Agency Medical Directors' Group's (AMDG) interagency opioid guideline. First developed in 2007 and updated in 2010, all guidelines were developed in collaboration with a broad advisory group of the state's academic leaders, pain experts, and clinicians in both primary care and specialty areas in response to the growing epidemic of opioid-related unintentional overdoses.¹¹ This guideline followed a rigorous and transparent development process and is designed as an easy-to-use reference to help primary care clinicians; each section includes a set of clinical recommendations, followed by supporting evidence, and there are several resources in the appendices.

This guideline offers a **balanced approach** to pain management that includes recommendations for using opioids when appropriate, such as with acute injuries and flare ups, for postoperative pain management, and during painful procedures; and recommending multimodal therapies in general for all chronic pain patients. This guideline supplements the Washington State Department of Health's pain management rulesⁱ requiring best practices in the prescribing of opioids for chronic non-cancer pain. In keeping with these rules, use of opioids for patients receiving hospice and palliative care during active cancer or terminal conditions is outside the scope of this guideline.

Monitoring and vigilance are critical to ensure effective and safe use of opioids for the thousands of Washington residents who are on opioids chronically, especially for those on high doses.

Correct Diagnosis and Realistic Expectations

Effective treatment of pain begins with an accurate diagnosis. Beyond the acute injury, the underlying cause of ongoing pain can be difficult to identify. Pain is generally described as either nociceptive (somatic) or neuropathic, but symptoms may not fit neatly into one group, often overlap and may change over time. Another common way to categorize pain is based on chronicity. Acute pain, whether related to disease, injury, or recent surgery, usually diminishes with tissue healing, whereas chronic pain typically lasts >3 months and involves neurological, emotional, and behavioral features that often impact a patient's quality of life, function, and social roles.¹²

Studies of interventions for chronic pain have often been of low quality, including problems associated with an increased risk of bias including difficulty with randomization and inadequate blinding.¹³ The best recent systematic reviews have shown only modest benefits.^{14,15} Patient expectations regarding expected outcomes may be unrealistic; expected outcomes should be balanced by potential risk of harm. Pursuing greater pain reduction via escalating opioid doses may contribute further to unrealistic expectations and even iatrogenic injury.

ⁱ WAC Chapter 246, authorized by ESHB 2876, Chapter 209 Laws of 2010

Uncertain Long-term Efficacy, Clear Evidence of Harm.

While the earlier guidelines focused on how prescribers could safely and effectively prescribe and manage chronic opioid analgesic therapy (COAT), more recent data suggests that the focus should also be on preventing the inappropriate transition from acute and subacute opioid use to chronic opioid use and to avoid COAT altogether when other alternatives for treating pain may be equally effective and safer in the long-term.

Three recently published systematic reviews which examine the effectiveness of opioids for chronic pain provide little support for COAT: A review of randomized controlled trials (RCTs) of opioids for chronic non-cancer pain concluded that the overall effectiveness of opioids for pain was only modest, and that the effect on function was small.¹⁶ In a Cochrane review of observational studies of cases on longer duration treatment¹⁷ the authors concluded, “The findings of this systematic review suggest that proper management of a type of strong painkiller (opioids) in well-selected patients with no history of substance addiction or abuse can lead to long-term pain relief for some patients...However, the evidence supporting these conclusions is weak, and longer-term studies are needed to identify the patients who are most likely to benefit from treatment”. The Agency for Healthcare Research and Quality’s (AHRQ) recent report, “The Effectiveness and Risks of Long-term Opioid Treatment of Chronic Pain,” which focused on studies of effectiveness measured at >1 year of COAT use, found *insufficient* data on long-term effectiveness to reach any conclusion.¹⁸

Adverse events most commonly reported in randomized trials include constipation, nausea and vomiting, dizziness, and drowsiness.¹⁹ More serious long-term consequences have only been identified from observational and epidemiological investigations; these include abuse, inhibition of endogenous sex hormone production with resulting hypogonadism and infertility,²⁰ immunosuppression,²¹ falls and fractures in older adults,²² neonatal abstinence syndrome,²³ cardiac arrhythmia related to methadone,²⁴ sleep disordered breathing,²⁵ opioid-induced hyperalgesia,²⁶ nonfatal overdose hospitalizations,²⁷ emergency department visits,²⁸ and death from unintentional poisoning.²⁹

Opioid therapy is also associated with the development of physical dependence and addiction³⁰ ([DSM 5 Opioid Use Disorder](#)). The true incidence of these serious complications is unknown but is likely to affect more patients than was previously reported.^{18,31,32} In addition, the lack of a useful case definition for any of these dependent states makes it challenging for a primary care provider to identify and intervene appropriately.²⁶ Even with acute low dose opioids (1 – 36 mg/day morphine equivalent dose or MED), patients are at increased risk for developing opioid use disorder (OUD). The likelihood of developing OUD ranges from a 3-fold increase for acute low dose opioids, to a 122-fold increase for chronic high dose opioids (≥ 120mg/day MED) compared to patients who are not prescribed opioids.³²

Because there is little evidence to support long term efficacy of COAT in improving function and pain, and there is ample evidence of its risk for harm, prescribers should proceed with caution when considering whether to initiate opioids or transition to COAT.

Opioids and Chronic Disability

Despite evidence based guidelines recommending against their use, opioids are frequently prescribed as first line agents for low back sprain and other routine musculoskeletal conditions.^{15,33-35} In addition, there is evidence in the workers' compensation population that early opioid use increases the risk of disability⁶ and it is difficult to discontinue COAT once initiated, as over 60% of patients taking opioids for at least 3 months are still on opioids 5 years later.¹ More effective early intervention strategies for acute low back pain, such as physical activity and emphasizing options for staying at or returning to work, are recommended to avoid transitioning to chronic low back pain.³⁶ Routine musculoskeletal conditions are among the top causes of disease burden in the US as measured by Years Lived with Disability (YLD), accounting for nearly 8 million YLD in 2010.³⁷ By 2011, nearly 25% of disabled Medicare beneficiaries under 65 were on opioids chronically. Preventing a transition from acute and subacute pain to chronic pain and disability could have a significant impact on saving productive lives.³⁸

Although opioids benefit some patients if prescribed and managed properly for appropriate conditions, from a public health perspective, preventing the next group of Washington residents from developing chronic disability due to unnecessary, ineffective, and potentially harmful COAT is a key objective of this guideline.

Part I. Recommendations for All Pain Phases

Clinically Meaningful Improvement in Function (CMIF)

Tracking function as well as pain is critical in determining the patient's ongoing response to opioids and whether any improvement is consistent with potential changes in opioid dosing. Because of the well documented evidence of risk and the limited evidence of effectiveness beyond the period of acute pain, the use of opioids should result in clinically meaningful improvement in function and pain and therefore, quality of life.

Clinically meaningful improvement is defined as an improvement in pain AND function of at least 30% as compared to the start of treatment or in response to a dose change. **A decrease in pain intensity in the absence of improved function is not considered meaningful improvement except in very limited circumstances such as catastrophic injuries (e.g. multiple trauma, spinal cord injury, etc.).**

COAT that focuses only on pain intensity can lead to rapidly escalating dosage with deterioration in function and quality of life. During the chronic phase, providers should routinely review the effects of opioid therapy on function to determine whether opioid therapy should continue. A brief but effective way to assess function is to determine the degree to which pain interferes with a patient's activities, as this is highly correlated with pain intensity when changes are tracked over time ([Figure A](#) and [Figure B](#)).

Continuing to prescribe opioids in the absence of clinically meaningful improvement in function and pain, or after the development of a severe adverse outcome (e.g. overdose event) is not considered appropriate care. In addition, the use of escalating doses to the point of developing opioid use disorder, as defined by DSM 5, is not appropriate.

Patients who used opioids for at least 90 days were greater than 60% more likely to still be on chronic opioids in 5 years.¹

Clinical Recommendations

1. Assess and document function and pain using validated tools ([Figure A](#) and [Figure B](#)) at each visit where opioids are prescribed.
2. Expect patients to improve in function and pain and resume their normal activities in a matter of weeks after an acute pain episode. Strongly consider re-evaluation for those who do not follow the normal course of recovery.
3. Evaluate function and pain using brief validated instruments at these critical decision-making phases:
 - a. At the end of the acute phase (6 weeks following an episode of pain or surgery), to determine whether continued opioid therapy is warranted.
 - b. At the end of the subacute or perioperative phase (12 weeks following an episode of pain or surgery), to determine whether non-opioid treatment will help or if prescribing COAT is warranted.
 - c. During chronic use with regular assessment and documentation of function and pain.

4. Use only validated instruments to measure clinically meaningful improvement in function and pain. The following tools have been validated and are easy ways to track function and pain:
 - a. PEG – A 3-item tool to assess Pain intensity, interference with Enjoyment of life, and interference with General activity.³⁹
 - b. Graded Chronic Pain Scale – A 2-item tool to assess pain intensity and pain interference.⁴⁰

Figure A. Three Item PEG Assessment Scale

| | | | | | | | | | | | |
|---|---|---|---|---|---|--------------------------------|---|---|---|----|--|
| 1. What number best describes your <u>pain on average</u> in the past week: | | | | | | | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| No pain | | | | | | Pain as bad as you can imagine | | | | | |
| 2. What number best describes how, during the past week, pain has interfered with your <u>enjoyment of life</u>? | | | | | | | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| Does not interfere | | | | | | Completely interferes | | | | | |
| 3. What number best describes how, during the past week, pain has interfered with your <u>general activity</u>? | | | | | | | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| Does not interfere | | | | | | Completely interferes | | | | | |

Krebs 2009

Figure B. Two Item Graded Chronic Pain Scale

| Graded chronic pain scale: a two-item tool to assess pain intensity and pain interference | | | | | | | | | | | |
|---|---|---|---|---|---|--|---|---|---|----|--|
| <p>In the last month, on average, how would you rate your pain? Use a scale from 0 to 10, where 0 is "no pain" and 10 is "pain as bad as could be"? <i>[That is, your usual pain at times you were in pain.]</i></p> | | | | | | | | | | | |
| No pain | | | | | | Pain as bad as could be | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| <p>In the last month, how much has pain interfered with your daily activities? Use a scale from 0 to 10, where 0 is "no interference" and 10 is "unable to carry on any activities."</p> | | | | | | | | | | | |
| No interference | | | | | | Unable to carry on any activities | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |

Evidence

There is a broad consensus in published studies that a combination of outcome measures is superior to any single measure.^{41,42} A major emphasis in earlier studies has been on the MINIMUM clinically important difference (MCID) in outcome. This measure has been tailored to clinical trials of drugs and other interventions. However, more robust definitions may be necessary to clearly define outcomes important to patients. For example, one study prospectively defined a minimally acceptable degree of improvement in patients undergoing lumbar fusion and found that these predefined outcomes established by patients themselves were not achieved.^{43,44} For this cohort of patients, a combination of four outcomes included:

1. At least a 3/10 decrease in pain, AND
2. An improvement of at least 20 points on the Oswestry Disability Index, AND
3. Discontinuation of opioid medications, AND
4. Return to some occupational activity.

Based on the literature and expert consensus for low back pain, a 30% improvement in principal outcome measures (pain and function) is considered clinically meaningful.⁴⁵ This degree of improvement has also been validated in low back pain compared to actual measures of physical function.⁴⁶ For acute postoperative pain, a 35-45% decrease in pain was associated with reported acceptable improvement to patients.⁴⁷ In a short term prospective study of patients with arthritis undergoing steroid injections, patient-perceived satisfactory improvement was associated with a 55% improvement on a visual analogue scale.⁴⁸ Considering the potential long-term risks of opioid therapy and based on the published literature and expert consensus, two other groups have chosen a 30% improvement in pain and function to be critical for assessing changes from baseline for both acute/subacute and for chronic pain in patients placed on opioids: Washington (final) and California (draft) State Workers' Compensation Programs.ⁱⁱ

Dosing Threshold

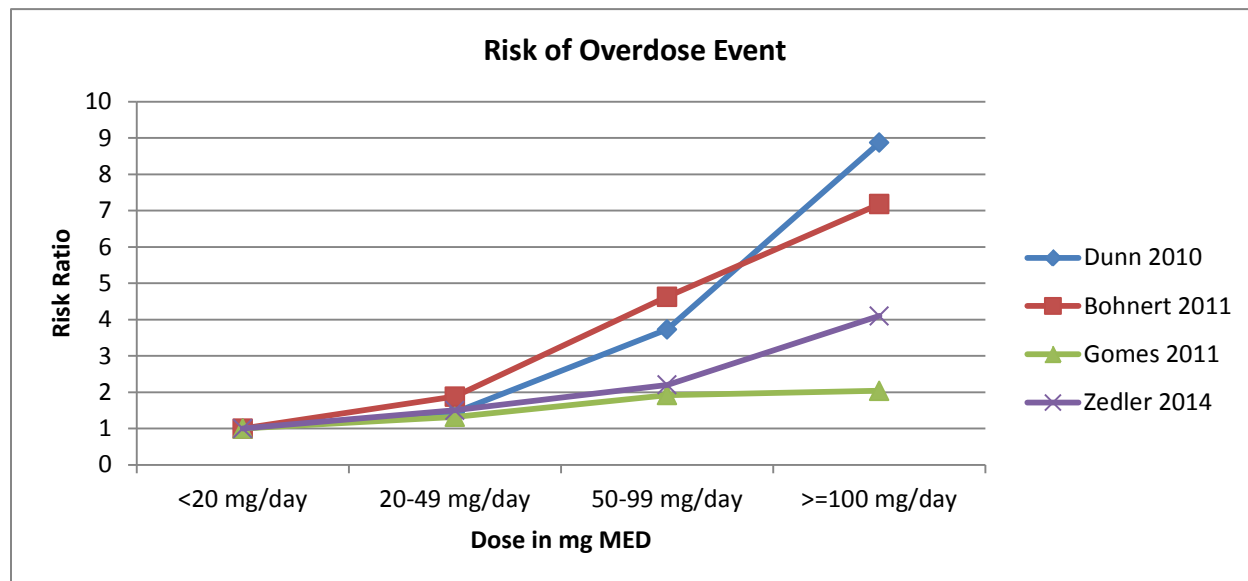
While there is evidence that opioids can provide significant pain relief in the short term, there is little evidence for sustained improvement in function and pain relief over longer periods of time. COAT is associated with the development of tolerance, a decrease in analgesic effect with the same dose over time. Providers must pay attention to the development of tolerance and avoid ongoing dose escalation to overcome this effect.

The 2010 edition recommended a 120 mg/day MED threshold to seek consultation with a pain specialist as a strategy to prevent serious adverse outcomes, including fatal overdoses. Group Health Cooperative (GHC), which implemented the best practices from the 2010 edition, has demonstrated a reduction in opioid doses for their COAT patients. For the last quarter of 2014, less than one-quarter of COAT patients seen by GHC providers received 50 mg/day MED or greater and only 7.3% exceeded 120 mg/day MED.

ⁱⁱ <http://www.lni.wa.gov/ClaimsIns/Files/OMD/MedTreat/FINALOpioidGuideline010713.pdf> and <http://www.dir.ca.gov/dwc/dwcwcabforum/Opioids.htm>

Recent studies support a dose-related risk and shed new light on significant risks occurring at doses lower than 120 mg/day MED. Overdose risk approximately doubles at doses between 20 and 49 mg/day MED, and increases nine-fold at doses of 100 mg/day MED or more (Figure C). Although the 2015 guideline maintains the 120 mg/day MED threshold for consultation and some guidelines have lower dose thresholds ranging from 50 to 90 mg/day MED, there is no completely safe opioid dose.

Figure C. Risk of Overdose Events in Four Different Populations



Providers should be especially cautious and assess risk for ongoing opioid therapy when a patient transitions from acute opioid use to COAT, continuing COAT at a dose to which a patient has already become accustomed, or escalating the opioid dose. Use the electronic [morphine equivalent dose \(MED\) calculator](#) for determining dose when a patient is on one or more opioids. The calculator should not be used to determine doses when converting a patient from one opioid to another.

There is a correlation between the amount of opioids prescribed for patients and their potential availability for diversion, with associated risks for individuals in the community. The recommendations below are intended to reduce the risks to both patients and the community.

There is no completely safe opioid dose.⁷ COAT patients should be routinely assessed for risk as medical conditions and life circumstances may change during treatment.

Clinical Recommendations

1. **Avoid** COAT if the patient has any of the following FDA or clinical contraindications:
 - a. Significant respiratory depression (e.g. respiratory failure), acute or severe asthma in an unmonitored setting or in the absence of resuscitative equipment, known or suspected paralytic ileus or hypersensitivity (e.g. anaphylaxis)

- b. Current substance use disorder as defined by DSM 5 (except tobacco) or past opioid use disorder
 - c. History of prior opioid overdose
 - d. Pattern of aberrant behaviors ([Table 9](#))
2. Use great caution at any dose, monitor more frequently and consider prescribing take-home naloxone if the patient has one or more of the following risk factors:
 - a. Mental health disorder per DSM 5
 - b. Family or personal history of substance use disorder
 - c. Medical condition that could increase sensitivity to opioid-related side effects (e.g. impaired respiratory function, sleep apnea, high fall risk, altered drug metabolism related to advanced age or impaired renal, hepatic and/or cardiac function)
 - d. Current use of benzodiazepines
 - e. Tobacco use
3. **Do not escalate** COAT to more than 120 mg/day MED without first obtaining a consultation from a trained pain specialistⁱⁱⁱ who agrees that a high dose is indicated and appropriate. Providers must routinely monitor and document sustained improvement in function and quality of life and an absence of the risk factors listed in recommendations 1 and 2.

Evidence

A review of RCTs of opioids for chronic non-cancer pain concluded that the overall effectiveness of opioids for pain was only modest, and that the effect on function was small.¹⁶ Recent published systematic reviews examining the effectiveness of opioids for chronic pain found insufficient data to support the wide prescribing of COAT.^{17,18,49} However, epidemiological studies have shown that patients on COAT who are receiving > 100 mg/day MED have up to nine times the risk of overdosing compared to those on 20 mg/day MED, and for every seven overdoses, one was fatal.⁵⁰⁻⁵³ These studies further showed that even at doses between 50 and 100 mg/day MED, the risk was 2.2 to 4.6 times higher compared to doses < 20 mg/day MED.^{50,51,53} While the majority of overdose deaths occur in higher dose patients, recent studies in WA workers' compensation and Medicaid have shown that nearly half of all overdose hospitalizations occur in patients who are on intermittent or lower dose opioids.^{7,54,55}

Studies have also shown dose-dependent increases in other serious adverse outcomes such as falls, fractures, and motor vehicle accidents.⁵⁶ At high doses, patients are at higher risk for poor functional status, increased pain sensitivity, and continuation of chronic opioids for a prolonged period.^{1,6,26} While a cause and effect relationship is unclear, patients on high dose opioids are more likely to have high risk characteristics, such as mental health disorder, substance use disorder, and/or opioid misuse.¹

ⁱⁱⁱ DOH Prescribing Rules defining [Pain Specialist](#) are listed in five separate rules according to each license type; all are in the Washington Administrative Code Chapter 246, subsections 919 (MDs); 853 (DOs); 922 (DPMs); 817 (Dentists); 840 (ARNPs); and 854 and 918 (PAs – working with DOs or MDs, respectively).

Chronic opioid analgesic therapy is also associated with the development of tolerance to its analgesic effects.^{26,57} Evidence is accumulating that opioid therapy may also paradoxically induce abnormal pain sensitivity, including hyperalgesia and allodynia.⁵⁸⁻⁶⁰ In addition, higher strength opioids may be associated with poorer functional outcomes than lower strength opioids.¹⁹ Thus, increasing opioid doses may not improve function and pain control, but will expose the patients to the risk of dose-dependent adverse outcomes.

The amount of opioids prescribed for patients and their potential availability for diversion has been identified as one of seventeen determinants of opioid-related mortality.⁶¹ Communities with higher rates of prescribing experience higher overall overdose rates, even amongst individuals without prescriptions.

Non-opioid Options for Pain Management

Non-pharmacological Interventions

Pain is a multidimensional experience; so therefore, pain management is most effective when a multimodal approach is utilized ([Table 1](#)). In addition to medication, therapies should include physical activation and behavioral health interventions (such as cognitive behavioral therapy, mindfulness, coaching, patient education, and self-management).

Table 1. Cognitive Behavioral and Non-pharmacological Therapies for Chronic Pain

| | |
|--|---|
| Cognitive | Address distressing negative cognitions and beliefs, catastrophizing (pain coping characterized by excessively negative thoughts and statements about the future) |
| Behavioral approaches | Mindfulness, meditation, yoga, relaxation, biofeedback |
| Physical | Activity coaching, graded exercise |
| Spiritual | Identify existential distress, seek meaning and purpose in life |
| Education (patient and caregivers): | Promote patient efforts aimed at increased functional capabilities |

Adapted from Argoff, 2009 & Tauben, 2015

Clinical Recommendations

1. Perform a thorough history and physical examination at initial visit for pain management.
2. Do not pursue diagnostic tests unless risk factors or “red flags” indicate the need for further evaluation ([Table 2](#)), especially getting an MRI in the first 6 weeks following low back injury <http://www.choosingwisely.org/american-society-of-anesthesiologists-asa-releases-choosing-wisely-list-for-pain-medicine/>.
3. Re-evaluate the patient for other diagnoses if pain persists beyond a few weeks, or if “red flags” develop ([Table 2](#)).
4. Identify functional goals that are important to the patient, as this increases the likelihood that treatment will improve quality of life, even if the pain intensity rating itself does not change.

5. Engage patients in behavior change counseling that promotes self-care and consider emphasizing evidence-based principles of motivational interviewing ([Appendix H: Clinical Tools and Resources](#)).
6. Use powerful interventions such as listening, providing reassurance, and involving the patient in his or her care.
7. Do not prescribe analgesics or perform interventions (e.g. injections) without also tracking pain and function over time using validated instruments.
8. Use validated instruments to assess predictors of suboptimal recovery such as depression, fear avoidance, and catastrophizing, which can lead to persistent pain and functional limitation ([Appendix B: Validated Tools for Screening and Assessment](#)).
9. Consider behavioral interventions to improve patient self-efficacy and address psychosocial barriers to recovery, such as cognitive behavioral therapy, Mindfulness-based Stress Reduction (MBSR), yoga, various forms of meditation and chronic pain self-management.
10. Recommend graded exercise unless contraindicated. Group exercise may have significant benefit and is available to most patients. Use of an activity diary may assist the patient and physician in monitoring progress.
11. Consider spinal manipulation in patients with low back pain.
12. Encourage and facilitate those who have work-related injuries to participate in programs that coordinate efforts to help them get back to work. Do this early in their recovery.
13. Address sleep disturbances by encouraging sleep hygiene ([Table 3](#)) or effective pharmacological therapy (clinical recommendation #6 under Non-opioid Analgesics). Achieving a minimum of 6 hours of restful sleep per night is a reasonable goal.
14. Refer patient to a multidisciplinary rehabilitation program if s/he has significant, persistent functional impairment due to complex chronic pain.

Table 2. "Red Flags" Indicating Need for Further Patient Evaluation

| |
|---|
| Presence of neurological deficit(s) |
| History of malignancy |
| New signs and symptoms of underlying disease |
| Sudden increase in severity or nature of previous pain complaint |
| Unexpected results from urine drug tests (e.g. positive for cocaine, amphetamines, alcohol, etc.) |
| Wounds that don't heal within normal time expectations |
| Evidence of adverse side effects from current treatment regimen |

Adapted from Tauben 2015

Table 3. Recommended Sleep Hygiene Habits

| |
|---|
| Maintain a regular wake/sleep schedule: fixed bed and wake-up times, regardless of weekday or weekend |
| Establish a relaxing routine before bedtime |
| Refrain from taking naps |
| Make the bedroom “device-free”: no TV, computer, or handheld devices |
| Use the bedroom only for sleep, intimacy, and dressing routines |
| Set environment (light, noise, temperature) at comfortable levels |
| No caffeine after noon; some may need to avoid caffeine altogether |
| No exposure to TV or computer screens 2 hours prior to bedtime |
| Exercise - but not within 3 hours of bedtime |
| Avoid alcohol close to bedtime |

Adapted from Tauben 2015

Evidence

Overtreatment, excess attention, or labeling a patient during the acute pain phase can precipitate or increase “sickness behavior,” and avoidance of activity.⁶² For example, in the absence of “red flags” that indicate the need for further evaluation ([Table 2](#)), obtaining an MRI in the first 6 weeks following low back injury may lead to a cascade of further unnecessary treatments and escalating costs.⁶³ Further, there is value in having patients with work-related injuries participate in programs that help them return to work, as these appear to have a small but significant impact on reducing disability among those who have missed at least four weeks of work due to acute or subacute musculoskeletal pain.⁶⁴

Importance of Activity: Unless contraindicated, advice to remain active and engaged in usual activity seems to be the most effective intervention early in the course of a pain episode. A well-studied example is low back pain with or without sciatica. For this condition, advice to remain active has been repeatedly shown to predict better pain and functional outcomes than advice to take bed rest, and is as effective as specific exercises.^{65,66} Aerobic and strengthening exercises have also been shown to reduce pain and disability in osteoarthritis of the knee,⁶⁷ but passive PT interventions have not demonstrated sustained benefit.⁶⁸ In subacute or chronic low back pain there is good evidence of moderate efficacy for exercise interventions.¹⁴ In a recent Cochrane review of interventions for subacute or chronic LBP, exercise obtained the best outcomes when done as part of an individualized regimen with supervision during strengthening and stretching.⁶⁹ Resistance exercise training and aerobic exercise in women with fibromyalgia may improve pain and multidimensional function.⁷⁰ Patient adherence to home exercise programs may be specifically important in evaluating the success of these interventions.⁷¹ This is where keeping an activity diary can be especially helpful.

Psychosocial Factors: Psychosocial factors, such as fear of normal activity (fear avoidance), catastrophizing, and low expectations of healing are strong predictors of the development of persistent pain in patient populations.⁷²⁻⁷⁴ Practitioners’ beliefs and attitudes can impact clinical decision making and subsequent treatment outcomes.⁷⁵

There is good evidence that cognitive behavioral therapy is effective in reducing subacute or chronic low back pain and other chronic pain conditions, including chronic orofacial pain, chronic pain in children, fibromyalgia, persistent pain in the elderly, and inflammatory bowel disease.^{14,76-85} The treatment of depression was shown to have significant benefits in terms of pain reduction, improved functional status and quality of life in a group of older individuals with depression and arthritis.⁸⁶ Other psychological therapies, such as progressive relaxation and biofeedback aimed at muscle relaxation, have not been shown to be superior to active exercise therapies in large cohorts for most outcomes, in systematic reviews of low back pain treatment¹⁴ although both do provide benefit.

Group Support Activities: While patients with acute pain may not require medically supervised rehabilitation interventions, there is evidence to support their benefits in groups of individuals with atypical recovery or with chronic musculoskeletal pathology such as arthritis. Among the benefits that group interventions provide, chronic pain self-management programs are having increasing success at reducing the physical and psychosocial burden of chronic pain while reducing healthcare costs.⁸⁷ These evidence based programs teach strategies for understanding chronic pain and provide a support network with both clinician and lay led (by fellow chronic pain sufferers) workshops, 2.5 hours once a week for 6 weeks. These offer a free or low-cost community based model that has demonstrated short term improvements in pain and multiple quality of life variables.⁸⁸ Modeled after a national study of chronic disease self-management programs, these are being heralded as an effective way to meet the “triple aim goals” of better health, better health care, and better value while reducing health care utilization.⁸⁹ For resources and workshop information, go to <http://livingwell.doh.wa.gov/workshops>.

Spinal Manipulation, Acupuncture, and Yoga: Chou et. al found good evidence of moderate efficacy for spinal manipulation for chronic or subacute low back pain. Acupuncture was associated with moderate short-term improvement in both pain and function, and yoga was associated with moderately superior outcomes in pain and decreased medication use at 26 weeks when compared to self-directed exercise and a self-care education book.¹⁴ In comparative studies, exercise and spinal manipulation, but not acupuncture, appear to have a beneficial impact on improving both pain and function in chronic low back pain.⁹⁰ Acupuncture does not appear to be effective when compared to sham acupuncture.⁹¹

Physical Therapies: Although widely practiced, the application of heat and cold therapies for acute musculoskeletal pain has had a mixed evidence basis. The use of superficial heat has a stronger basis in evidence than the application of cryotherapy, or ice.^{14,92} There is insufficient evidence to make conclusive statements about the benefits of massage therapy. There is no evidence that traction, lumbar supports, interferential therapy, diathermy or ultrasound are effective for chronic low back pain. There is good evidence that transcutaneous nerve stimulation (TENS) is ineffective.⁹³

Structured Intensive Multidisciplinary Pain Programs: Evidence clearly supports the value of multimodal therapies in improving pain and function and reducing disability.^{94,95} In chronic back pain and in other pain conditions, multidisciplinary, intensive rehabilitation involving physical, psychosocial and behavioral interventions has good evidence of moderate effectiveness for pain reduction and improvement of function.⁹⁶ Various tools such as the STarTBack questionnaire⁹⁷ for low back pain or

the Functional Recovery Questionnaire (FRQ)⁹⁸ can be used to stratify patients into groups that might require increased attention and rehabilitative interventions and to plan treatment.³⁶

Sleep Hygiene: There is evidence to suggest that restorative sleep can help predict reduction in pain.⁹⁹ Although sleep treatment is not typically considered “analgesic”, poor sleep and lack of REM sleep in particular, are acutely hyperalgesic.¹⁰⁰ Further, the DSM 5 has reclassified insomnia as ‘sleep-wake’ disorders and acknowledges that, if occurring concomitantly with medical conditions and mental disorders, they are interactive and bi-directional.¹⁰¹ Cognitive behavioral therapy has been shown to be a very effective non-drug strategy for insomnia.¹⁰² Hence, having a sleep management plan is likely to help improve a patient’s pain experience. Morin and Benca have published an excellent review of chronic insomnia management in Lancet 2012.¹⁰³

Mindfulness and Stress Reduction: Mindfulness-based therapy techniques such as meditation and Mindfulness-based Stress Reduction (MBSR) and/or yoga, may be reasonable alternative therapies for chronic pain as they have been successful in helping patients learn to self-manage their pain sensations. Recent systematic reviews have shown these approaches may be as effective as cognitive behavioral therapy, which has consistently been demonstrated in randomized trials to improve chronic pain outcomes.¹⁰⁴⁻¹⁰⁷ In addition, the specific neural mechanisms activated by these treatments have been reported.¹⁰⁷

Non-opioid Analgesics

For most pain conditions, non-opioid analgesics (e.g. acetaminophen and NSAIDs) and adjuvant analgesics (e.g. antidepressants and anticonvulsants) are equally or more effective with less risk for harm than opioids. Providers should consider these medications during acute and subacute pain episodes and/or before initiating or transitioning patients to COAT. Selection of appropriate non-opioid or adjuvant analgesics requires a thorough history and physical exam, and will depend on the patient’s diagnosis, symptoms, pain type, comorbid conditions, and overall risk for adverse drug events ([Appendix F: Diagnosis-based Pharmacotherapy for Pain and Associated Conditions](#)). The use of medical marijuana for pain is beyond the scope of this guideline.

Clinical Recommendations

1. Start with acetaminophen for mild to moderate pain. Acetaminophen may be dosed up to 4 grams for acute use, but <2-3 grams per day may be safer for prolonged use. Assess for all acetaminophen containing products to avoid inadvertent overdose. Use acetaminophen with caution, and at doses of <2 grams daily in those at risk for hepatotoxicity, including those with advanced age and liver disease (e.g. alcohol abuse, hepatitis B and C).
2. Use non-steroidal anti-inflammatory drugs (NSAIDs) for inflammatory, nociceptive pain. Monitor patients for potential renal, gastrointestinal (GI), and cardiac side effects. Consider concurrent H-2 blockers (e.g. famotidine, ranitidine) or proton pump inhibitors (e.g. omeprazole, pantoprazole) to help protect against GI effects. Avoid NSAIDs in patients with a calculated glomerular filtration rate (cGFR) < 60 ml/min/1.73 m².

3. Consider tricyclic antidepressants (TCAs) or serotonin-norepinephrine reuptake inhibitors (SNRIs) and anticonvulsants (e.g. gabapentin, pregabalin) for neuropathic pain, other centralized pain syndromes, or fibromyalgia. Watch for potential cognitive impairment or sedation with anticonvulsants and TCAs.
4. Reserve baclofen or tizanidine for pain associated with spasticity from spinal cord injury or disease of the CNS (e.g. multiple sclerosis). Avoid abrupt discontinuation of baclofen because of the risk of precipitating withdrawal.
5. Do not prescribe muscle relaxants (e.g. methocarbamol, cyclobenzaprine) beyond a few weeks as they offer little long-term benefit. Avoid carisoprodol (Soma) due to the risk of misuse and abuse. Cyclobenzaprine, though not classified as a TCA, is structurally similar, so precautions are the same, and risk of adverse side effects are potentiated when used in combination with TCAs.
6. Prescribe trazodone, tricyclic antidepressants, melatonin, or other non-controlled substances if the patient requires pharmacologic treatment for insomnia.

Evidence

Sleep Medications: If non-pharmacologic options to aid sleep are not effective, treatment with OTC melatonin (1-5 mg) can help, especially since endogenous levels decrease with age.¹⁰¹ This naturally occurring hormone plays a pivotal role in the physiological regulation of sleep by reinforcing circadian and seasonal rhythms; side effects can include drowsiness, dizziness, headache, nausea, and nightmares.¹⁰³ Tricyclic antidepressants (TCAs) are sedating and may assist with sleep initiation and maintenance.¹⁰⁸ Trazodone, another antidepressant, is widely used for sleep but does not have any analgesic properties; and caution is advised if the patient is taking selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), triptans, or tramadol.¹⁰⁹ SNRIs are much less sedating and may disturb sleep by provoking periodic leg movement disorders; and SSRIs decrease REM sleep, increase REM latency, and fragment sleep so they are not good options for insomnia.^{110,111}

Benzodiazepines: Use of benzodiazepines for sleep is not recommended in chronic pain patients because they do not improve patients' reported pain scores,¹¹¹ and they increase the risk of rebound insomnia, overdose (especially when combined with opioids), reduced REM sleep, and the development of tolerance, dependency, and addiction.¹⁰⁹ Although benzodiazepine receptor agonists, (e.g. the Z-drugs: zolpidem, zaleplon, zopiclone, and eszopiclone) are FDA-approved to treat insomnia, they can potentially impair cognitive and psychomotor skills that can increase the risk of falls, sleep-walking, sleep-eating, and driving unaware, or dependence and abuse.^{101,109} For these reasons, these drugs should not be used with patients who have Alzheimer's disease and other comorbid disorders.^{101,112,113}

Acetaminophen (APAP): APAP is the most widely used nonprescription pain medication. Although a recent systematic review concluded that the mean changes in pain relief by acetaminophen did not reach minimal clinically important difference as compared to placebo for acute low back and knee osteoarthritis¹¹⁴ it is still an effective drug for mild to moderate pain.^{115,116} When combined with ibuprofen 200 mg, the combination has been demonstrated to be more effective than opioids.¹¹⁷ Hepatotoxicity can result from prolonged APAP use or doses in excess of recommended maximum total

daily dose including combined-acetaminophen OTC products. Although the FDA's current maximum daily dose is 4 grams, some manufacturers have voluntarily revised their label to recommend a lower maximum of 3 grams daily. The risk of hepatotoxicity increases significantly with age, concomitant alcohol use, comorbid liver disease or dose.¹¹⁸

Non-steroidal anti-inflammatory drugs (NSAIDs): NSAIDs are recommended for nociceptive pain such as traumatic musculoskeletal pain syndromes from traumatic, infectious or degenerative conditions (e.g. muscle, ligament, and or tendon injuries) with evidence to support effectiveness for spinal pain from disc, facet, or spinal ligament injuries¹¹⁹ and neuritis related to connective tissue disorders.¹²⁰ In patients with non-specific low back pain, NSAIDs are equivalent to opioids in relief of pain.¹²¹ The number needed to treat (NNT) for oxycodone 15 mg is approximately 4.6, (95% confidence Interval (CI), 2.9-11) while the NNT for oxycodone 10 mg + acetaminophen 650 mg is only 2.7, (95% CI, 2.4-3.1). The NNT for naproxen 500 mg or naproxen sodium 550 mg is also 2.7, and the NNT for ibuprofen 200 mg + acetaminophen 500 mg is 1.6. Hence, NSAIDs alone or in combinations can be as or more effective than opioids.¹²²⁻¹²⁴ However, their use may be associated with serious cardiovascular (e.g. thrombotic events, myocardial infarction or stroke) and gastrointestinal (e.g. bleeding, ulceration or perforation of the stomach or small intestine) side effects. While cardiovascular risk may increase with duration of use, gastrointestinal events can occur any time during use.

Antidepressants (TCAs/SNRIs): TCAs have been studied in many clinical trials with positive results in the treatment of various neuropathic pain conditions and are a good first line option.¹²⁵⁻¹²⁹ Among the drugs reviewed in three different neuropathic pain conditions, low-dose TCAs have the lowest NNT with an average 2.6 (range 2.0 to 5.0). In addition to pain relief, TCAs can offer added benefit to patients who also have depression or whose pain is interfering with sleep. However, caution should be used when prescribing TCAs to elderly patients or those with cardiovascular disorders due to risk of sinus tachycardia, changes in cardiac conduction time or arrhythmias. Besides TCAs, the serotonin norepinephrine reuptake inhibitor (SNRI) duloxetine has been shown to be effective in diabetic peripheral neuropathy, fibromyalgia and chronic musculoskeletal pain.¹³⁰ A systematic review found that there were no differences between venlafaxine and either gabapentin, pregabalin or duloxetine on average pain scores or the likelihood of achieving significant pain relief.¹³¹ Serotonin syndrome has been reported with SNRIs alone and concurrently with other serotonergic agents (e.g. tramadol, fentanyl, triptans, TCAs, lithium, buspirone, St. John's Wort).

Anticonvulsant drugs (ACDs): Gabapentinoids (*gabapentin* and *pregabalin*) have been found to be moderately superior to other ACDs for achieving pain relief.¹³¹ They have robust evidence in treating diabetic peripheral neuropathy, other neuropathies and fibromyalgia.^{132,133} Gabapentin was found to be effective in painful polyneuropathy with an average NNT of 6.4.¹³⁴ In another systematic review of antiepileptic drugs used to treat neuropathic pain, gabapentin was found to be effective at doses of 1800 mg and 2400 mg, although side effects such as dizziness and drowsiness were reported at these doses.¹³¹ Pregabalin has been studied in neuropathic pain conditions such as diabetic neuropathy and spinal cord injury and is FDA-approved to treat those neuropathies as well as fibromyalgia. The efficacy of pregabalin was found to be comparable to duloxetine, amitriptyline and gabapentin, however, pregabalin is classified as a controlled substance (Schedule V) with the potential for misuse or abuse, so

it argues for a more cautious approach to the use of this agent.¹³¹ Other anticonvulsants such as carbamazepine, oxcarbazepine, and lamotrigine have limited or conflicting evidence of efficacy in spontaneous shooting pain of trigeminal neuropathy, diabetic peripheral neuropathy, HIV-related peripheral neuropathy, and multiple sclerosis.^{126,135} All non-gabapentinoid ACDs are associated with risk of hepatotoxicity, hyponatremia, neutropenia, rash (including Stevens-Johnson Syndrome), sedation, and suicidality.

Muscle relaxants and antispasticity drugs: Muscle relaxants have limited evidence for effectiveness for chronic pain and are predominantly sedative.¹³⁶ Carisoprodol (Soma) should never be used due to lack of long-term efficacy, a high risk for abuse and misuse, and serious withdrawal symptoms.¹⁰⁹ When true painful spasticity is present, for instance in spinal cord injury and multiple sclerosis, antispasticity agents (e.g. baclofen and tizanidine) are good treatment options; however, serious and life threatening reactions can occur with abrupt discontinuation.

Part II. Prescribing Opioids in the Acute and Subacute Phase

Opioids in the Acute Phase (0-6 weeks post episode of pain or surgery)

In general, reserve opioids for acute pain resulting from severe injuries or medical conditions, surgical procedures, or when alternatives ([Non-opioid Options](#)) are ineffective or contraindicated. If opioids are prescribed, it should be at the lowest necessary dose and for the shortest duration (usually less than 14 days). The use of opioids for non-specific low back pain, headaches, and fibromyalgia is not supported by evidence.

Receiving a one week supply or ≥ 2 opioid prescriptions after an acute back sprain is associated with a doubling of the patient's risk for long-term disability.^{6,7}

Clinical Recommendations

1. Explore non-opioid alternatives for treating pain and restoring function, including early activation.
2. Prescribe opioids for dental pain only after complex dental procedures and at the lowest dose and duration.
3. Help the patient set reasonable expectations about his or her recovery, and educate the patient about the potential risks and side effects. Provide patient education on safekeeping of opioids, benzodiazepines, and other controlled substances.
4. Expect patients to improve in function and pain and resume their normal activities in a matter of days to weeks after an acute pain episode. Strongly consider re-evaluation for those who do not follow the normal course of recovery.
5. Check the state's Prescription Monitoring Program (PMP) to ensure that the patient's controlled substance history is consistent with the prescribing record. Prescribers may delegate the ability to query the PMP database to any licensed health care professional ([Appendix C: How to use the Prescription Monitoring Program](#)).
6. Assess function and pain at baseline and with each follow-up visit when opioids are prescribed. Document clinically meaningful improvement in function and pain using validated tools.
7. Strongly consider tapering the patient off opioids as the acute pain episode resolves. Taper opioids by 6 weeks if clinically meaningful improvement in function and pain has not occurred.

Opioids in the Subacute Phase (6 -12 weeks post episode of pain or surgery)

With some exceptions, resumption of normal activities should be expected during this period. Use of **activity diaries** is encouraged as a means of improving patient participation and investment in recovery. Non-pharmacological treatments such as cognitive behavioral therapy, activity coaching, and graded exercise are also encouraged ([Recommendations for All Pain Phases](#) and [Non-opioid Options](#)). With the exception of severe injuries, such as multiple trauma, opioid use beyond the acute phase (longer than 6 weeks) is rarely indicated. If opioids are to be prescribed for longer than 6 weeks, the following clinical recommendations should be followed.

Patients with substance use and/or psychiatric disorders are more likely to have complications from opioid use, such as misuse, abuse or overdose.¹

Clinical Recommendations

1. Do not continue to prescribe opioids if use during the acute phase does not lead to clinically meaningful improvement in function or to a pain interference with function level of ≤ 4 ([Figure B](#)).
2. Prescribe opioids in multiples of a 7-day supply to reduce the chance of them running out on a weekend.
3. Have a plan for how and when to discontinue opioids if treatment has not resulted in clinically meaningful improvement in function and pain or the patient has had a severe adverse outcome.
4. Check the state's [Prescription Monitoring Program](#) (PMP) to ensure that the patient's controlled substance history is consistent with the prescribing record. Prescribers may delegate the ability to query the PMP database to a licensed health care professional ([Appendix C: How to use the Prescription Monitoring Program](#)).
5. Screen for depression using PHQ-9 and for anxiety using GAD-7 or other validated tools. If comorbid mental health conditions exist in the presence of pain, they need to be treated or the patient's pain will not improve regardless of opioid therapy.
6. Administer the 4-item [PC-PTSD](#) screen or other validated tools if the patient's history suggests PTSD, or if PHQ-9 or GAD-7 remains elevated after treatment.
7. Screen for opioid misuse risk using the Opioid Risk Tool, SOAPP-R, DIRE, CAGE-AID or other validated tools. Review the patient's medical records and include the patient's support system (e.g. family, friends, etc.) to verify the risk assessment results.
8. Do not prescribe opioids if results of a baseline UDT reveal "red flags" such as the *confirmed* presence of cocaine, amphetamines, non-prescribed benzodiazepines, alcohol, or any other drugs you did not prescribe or have knowledge of ([Appendix D: Urine Drug Testing for Monitoring Opioid Therapy](#)). If cannabis is present on a UDT, the patient should be screened for cannabis use

disorder, as defined by DSM 5. In addition, it would be prudent to have a policy regarding the concomitant use of cannabis and opioids.

9. Avoid new prescriptions of benzodiazepines and sedative-hypnotics. Consider tapering or discontinuing benzodiazepines and/or sedative-hypnotics.
10. Discontinue opioids during this phase if:
 - a. There is no clinically meaningful improvement in function and pain.
 - b. Treatment resulted in a severe adverse outcome (e.g. overdose, bowel obstruction, central sleep apnea).
 - c. The patient has current or history of substance use disorder (excluding tobacco).

Evidence

Short term use of opioids for severe acute injury (e.g. severe trauma, fracture, crush injury, postoperative) is unquestioned and is a standard of care. However, the overall data on effectiveness of opioids for longer term use, especially for improved function, and for routine conditions such as non-specific low back pain, headaches, and fibromyalgia is weak, and the evidence of potential harm is strong. Systematic reviews of efficacy of opioids for low back pain demonstrate modest improvement in pain but little improvement in function and no clear evidence that pain relief will be sustained.^{15,49} For headaches and fibromyalgia, there is a paucity of evidence on effectiveness. Both the European Federation of Neurological Societies and the American Academy of Neurology recommend against the use of opioids for headache.¹³⁷⁻¹³⁹ There is no evidence from randomized trials to support the use of opioids for fibromyalgia, despite some observational studies showing that strong opioids are used in fibromyalgia patients with significant risk factors that would normally mitigate against such use.^{81,140-144}

In addition to these data, evidence from a population-based, prospective study of a low back pain cohort in WA workers' compensation reported that even minimal use of opioids in the first six weeks following an acute low back injury was associated with a doubling of the risk of disability one year later, after adjusting for baseline pain, function, and injury severity.⁶

Evidence on the use of opioids for subacute pain is limited; thus, most of the recommendations for this period represent a consensus of expert opinion of the advisory group. A systematic review of RCTs on conservative treatments for subacute low back pain (6 weeks-3 months), revealed that only advice on staying active was found to be effective.¹⁴⁵

The use of screening tests prior to starting COAT is important in patients with certain comorbid medical conditions. Managing pain in patients with complex medical conditions such as substance use disorder or a mental health condition can be a challenge. Research has shown that patients with substance use or psychiatric disorders (e.g. depression), or both, are actually more likely than patients without these disorders to receive COAT.^{146,147} They are also more likely to have complications such as misuse, abuse or overdose.^{148,149} Adults with a history of depression, alcohol or other non-opioid substance use disorders are three to five times more likely to receive COAT.¹⁵⁰

High-risk COAT prescribing practices (high opioid dose, extended COAT duration, concurrent use of sedatives/hypnotics) are associated with increased risks of opioid overdose and serious fractures.^{22,50} Unfortunately, patients who receive high-risk COAT are also more likely to have high-risk characteristics, including younger age, history of substance use disorder, mental disorders, and presence of opioid misuse.¹ Because of the increased risk for adverse outcomes from the use of COAT in patients with mental health disorders, such as borderline personality disorder, depression, bipolar disorder, anxiety, post-traumatic stress disorder (PTSD) or psychotic disorders, providers should be extra cautious when prescribing COAT when one of these co-morbid conditions is present.

Part III. Opioids for Perioperative Pain

Opioids serve as the cornerstone for severe acute postoperative pain management with proven efficacy for this indication. Nevertheless, patients must be counseled on the limited effectiveness of any analgesic in eliminating pain entirely. A balanced, rational multimodal analgesic approach is most effective in controlling pain while at the same time, minimizing analgesic doses and their resultant side effects that interfere with rehabilitation. Patients on COAT who are undergoing elective surgeries present challenges for perioperative pain management. For this reason, it is important to assess patients' risks for both severe postoperative pain and side effects of opioids. The following recommendations are intended to help manage patients' pain and minimize risk associated with perioperative opioid use.

The goal of opioid therapy is to prescribe the briefest, least invasive and lowest dose regimen that minimizes pain and avoids dangerous side effects.²⁻⁵

Preoperative Period

Clinical Recommendations

1. Conduct a thorough preoperative evaluation, including history and physical:
 - a. Ask about past and current use of, response to and preferences for analgesics.
 - b. Check the Prescription Monitoring Program (PMP), especially for patients with a history of COAT or benzodiazepine or sedative-hypnotic use.
 - c. Assess risk for potential postoperative opioid over-sedation and/or respiratory depression ([Table 4](#)) and difficult postoperative pain control ([Table 5](#)). Inform the entire perioperative team of the results of the risk assessment.
 - d. Consider consultation with a specialist (e.g. pain management, addiction medicine, behavioral health), particularly in patients at risk for both over-sedation ([Table 4](#)) and difficult postoperative pain control ([Table 5](#)).
2. Develop a coordinated treatment plan, including a timeline for tapering perioperative opioids. Identify which provider will be responsible for managing postoperative pain and prescribing opioids:
 - a. Generally, in opioid naïve patients, any opioids prescribed during the first 6 weeks postoperatively should be managed solely by the surgeon.
 - b. If a patient was previously using chronic opioids for the condition being addressed by surgery, the surgeon should consult with the outpatient prescriber as to whether or not the patient is likely to need continued COAT after surgery. If so, develop a plan for transition of pain care back to the outpatient prescriber.

- c. In the immediate postoperative period, during the hospital stay, the surgeon (or a specialist consultant) should manage all pain medication, including chronic methadone, buprenorphine/naloxone, or other COAT, as well as any additional opioids added for acute postoperative pain. These acute post-surgical opioids should be tapered off during the first few weeks after surgery. Continuation of previous COAT upon hospital discharge should be the responsibility of the outpatient prescriber.
3. Inform patient and family of the perioperative pain plan. Set expectations with them about realistic pain management goals, including functional recovery activities, need for multimodal treatment, limits of therapy, timely return to preoperative baseline opioid dose (if any) or lower, and the analgesic tapering timeline.
4. Avoid new prescriptions of benzodiazepines, sedative-hypnotics, anxiolytics, or other central nervous system (CNS) depressants.
5. Avoid escalating the opioid dose before surgery. The lowest effective dose should always be sought, but there is insufficient evidence to recommend routinely lowering chronic opioid doses or discontinuing opioids prior to surgery.

Intraoperative Period

Clinical Recommendations

1. Provide balanced multimodal analgesia, including adjuvant analgesics, when possible (e.g. acetaminophen, NSAIDs, gabapentin and local anesthetic infiltration). Under specialist direction, ketamine, lidocaine, and regional local anesthetic techniques can also help minimize perioperative opioids and their side effects.
2. Provide sufficient intraoperative opioid doses to avoid acute withdrawal in patients who are on high doses of preoperative opioids.

Immediate Postoperative Period

Clinical Recommendations

1. Reserve the use of opioids for moderate to severe acute pain. If used, utilize the lowest possible dose as part of a multimodal regimen, including NSAIDs, acetaminophen, and non-pharmacologic therapies, unless contraindicated.
2. Monitor sedation and respiratory status in patients receiving systemic opioids for postoperative analgesia (e.g. [Richmond Agitation Sedation Scale](#), [Ramsey Sedation Scale](#), or [Comfort Scale](#)). Due to the risk of excessive sedation and respiratory depression, patients should be monitored closely in the initial hours following surgery and with subsequent dose escalations. Monitoring should include assessments of alertness and signs or symptoms of hypoventilation or hypoxia:
 - a. The use of routine oxygen is discouraged as hypoxia is a late sign of respiratory compromise and this sign will be delayed still further by supplemental oxygen.
 - b. There is insufficient evidence to recommend the routine use of more sophisticated noninvasive methods (such as capnography) for monitoring hypoventilation postoperatively.

- c. Providers should be prepared to change or reduce opioids or administer opioid antagonists in patients who develop excess sedation or respiratory depression ([Table 4](#)).
3. Use oral opioids for managing postoperative pain in patients who can tolerate oral medications, particularly following the first or second postoperative day, as pain levels at rest and during activity become less variable.
 - a. Consider the use of patient controlled analgesia (PCA) initially in cases where repeated doses of parenteral opioids are anticipated or required. Providers should be aware of the doses being self-administered by their patients via PCA to guide adjustments. Routine use of continuous opioid infusions (basal rates with PCA) is NOT recommended:
 - b. Consider consultation with specialists for patients receiving high dose PCA, and when opioids, benzodiazepines or sedative-hypnotics are being used in combination with the PCA.
4. Use short-acting “as needed” (PRN) opioids as the foundation for acute severe postoperative pain in the opioid naïve patient. For the opioid tolerant patient, do not add or increase extended release or long-acting opioids for the immediate postoperative period.
 - a. Avoid therapeutic duplication of opioids consisting of more than one type of PRN short-acting opioid (e.g. oxycodone and morphine). Avoid co-administration of parenteral and oral PRN opioids for ongoing pain. If PRN opioids from different routes are needed, provide a clear indication for use (e.g. for a brief, severely painful, closely monitored procedure such as a dressing change).
 - b. Consider scheduling non-opioids for more steady analgesia and to avoid multiple PRNs for pain.
5. Resume chronic regimen as soon as possible if patients were previously on chronic opioids and are expected to continue these postoperatively.
6. Avoid new prescriptions of benzodiazepines, sedative-hypnotics, anxiolytics or CNS depressants. If patients were previously on chronic sedatives, restart these at lower doses in the setting of postoperative opioids to avoid synergies between CNS depressant and opioid side effects.
7. Initiate a bowel regimen as soon as possible postoperatively to minimize opioid-induced bowel dysfunction (constipation). This side effect may still require opioid dose reductions if unresponsive to stool softeners, laxatives or enemas.

Do not discharge the patient with more than a two week supply of opioids, and many surgeries may require less. Continued opioid therapy will require appropriate re-evaluation by the surgeon.

At Time of Hospital Discharge

Clinical Recommendations

1. Avoid continuing or adding new prescriptions of benzodiazepines, sedative-hypnotics, anxiolytics or CNS depressants. Counsel patients and families about risks of using alcohol and other CNS depressants with opioids.
2. Inform the patient and family which provider will be responsible for managing postoperative pain, including who will be prescribing any opioids. Instruct the patient and family on the planned taper of postoperative opioids, including a timeline for return to preoperative or lower opioid dosing for those on chronic opioids.
3. Remind the patient of the dangers of prescription opioid diversion and the importance of secure storage of their medications. Sharing medications with others is never appropriate and is illegal. Instruct the patient and family on prompt disposal of controlled substances either through a [DEA-approved take-back program](#) or FDA guideline for [safe disposal of medicine](#).
4. Follow through with the agreed upon preoperative plan to taper off opioids added for surgery as surgical healing takes place. The goal is always the shortest duration and lowest effective dose:
 - a. Most patients with major surgeries should be able to be tapered to preoperative doses or lower within 6 weeks (approximately 20% of dose per week although tapering may be slower in the 1st week or 10 days and then become much more rapid as healing progresses).
 - b. It is important to remember that for some minor surgeries, it may be appropriate to discharge patients on acetaminophen or NSAIDs only or with only a very limited supply of short-acting opioids (e.g. 2-3 days) - even if they were taking opioids preoperatively.
 - c. For patients who were not taking opioids prior to surgery, but who are still on them after 6 weeks, follow the recommendations in the [Subacute Phase](#).

Table 4. Risks for Over-sedation and/or Respiratory Depression from Postoperative Opioids ¹⁵¹⁻¹⁶⁰

| |
|--|
| Sleep apnea or high risk sleep disorder (morbid obesity/history of snoring/positive STOP Bang score ≥4) |
| Age (<1 and >65 years old) |
| History of over-sedation with opioids |
| Opioid analgesic tolerance or increased opioid dose requirement |
| Concurrent use of other sedating drugs (e.g. benzodiazepines, antihistamines, sedative/anxiolytics or other CNS depressants) |
| History of difficult to control postoperative pain |
| Long (>6 hours) duration of general anesthesia |
| Surgery location and/or type (e.g. airway, upper abdominal, thoracic, scoliosis repair in children) |
| Medical comorbidities (e.g. pulmonary disease/smoker, cardiac disease, other major organ failures) |

Table 5. Risks for Difficult-to-control Postoperative Pain ¹⁶¹⁻¹⁶⁹

| |
|--|
| History of severe postoperative pain |
| Opioid analgesic tolerance (daily use for months) |
| Current mixed opioid agonist/antagonist treatment (e.g. buprenorphine, naltrexone) |
| Chronic pain (either related or unrelated to the surgical site) |
| Psychological comorbidities (e.g. depression, anxiety, catastrophizing) |
| History of substance use disorder |
| History of “all over body pain” |
| History of significant opioid sensitivities (e.g. nausea, sedation) |
| History of intrathecal pump use or nerve stimulator implanted for pain control |

Evidence

A number of reviews of the literature on perioperative pain treatment have been undertaken and published in the last few years, including those from the American Pain Society, the American Society of Anesthesiologists, the Department of Defense, the Veterans Administration, and the Washington State Department of Labor and Industries. These guidelines as well as a PubMed search for additional reviews of this topic in the last 5 years (560, excluding 32 reviews concerning a single surgical procedure) were used and combined with consensus opinions from the experts in the AMDG advisory group to formulate our final recommendations.

Although opioids are effective for short-term pain relief following surgery, side effects may limit their use.¹⁷⁰ The use of a multimodal approach including non-pharmacologic interventions to manage pain can improve treatment and limit side effects from any one class of analgesics.¹⁷¹⁻¹⁸⁴ Preparation for surgery such as training in relaxation, counseling and education can reduce anxiety, postoperative opioids use and physical therapy needs.¹⁸⁵⁻¹⁸⁹ In addition, adjuvant treatments such as acetaminophen, NSAIDs and gabapentin have been demonstrated to be opioid-sparing and help minimize opioid-related side effects.^{184,190-192} The intraoperative use of techniques such as local anesthetic blocks, ketamine and intravenous lidocaine can also reduce opioid requirements.¹⁹³⁻¹⁹⁵

It is important to assess patients’ risk factors for over-sedation and/or respiratory depression and for difficult-to-control postoperative pain. Predictors of postoperative opioid over-sedation and/or respiratory depression include, but are not limited to, sleep apnea, concurrent use of benzodiazepines or other CNS depressant agents, other medical conditions that affect respiratory function and prolonged anesthesia.^{151,156,157,159,160} Risk factors for difficult to control postoperative pain include chronic pain, mental health comorbidities (e.g. anxiety, depression, catastrophizing) and history of substance use disorder.^{161-165,167}

Patients on COAT who are undergoing surgery are at increased risk for both of these complications. These patients have higher pain rating, manifest more anxiety and have frequent and more severe respiratory depressive episodes than opioid naïve patients.^{162-165,196}

The Prescription Monitoring Program provides an accurate picture of the patient's history of opioid, benzodiazepine, and other controlled substance use, which is especially helpful for planning perioperative pain management.^{197,198} It is important to collaborate across the care team (surgeon, anesthesiologist, pain management specialist, bedside nurses, treating provider and the patient) to formulate a postoperative pain management plan including risk factors and a timeline for weaning analgesics. Communication of this treatment plan, as well as realistic expectations concerning postoperative pain, is important for the patient, his or her family and the entire care team to help ensure appropriate treatment and avoid dangerous side effects.¹⁹⁹

The first 24 hours of opioid therapy is a significant period of risk for excess sedation and respiratory depression.¹⁵⁹ Assessment of sedation level and monitoring for adequate ventilation and oxygenation allow for early response and intervention.^{158,159,200-204} When the parenteral route is needed beyond the first few hours after surgery, patient-controlled analgesia (PCA) is recommended and can add an element of safety as the sedated patient is less likely to continue to give themselves opioid doses.²⁰⁵⁻²⁰⁷ However, routine use of PCA is not recommended, as patients can usually resume oral analgesia within hours of the surgery. Analgesic effects of oral and intravenous opioids are comparable, so patients can be transitioned to oral opioids as soon as oral intake is tolerated.²⁰⁸ Concurrent, as needed use of intravenous and oral opioids increases the risk of side effects.²⁰⁹ Constipation is a common adverse effect of opioids and, if left untreated, could lead to bowel impaction. Initiate a bowel regimen as soon as possible postoperatively in those taking opioids to minimize opioid-induced bowel dysfunction.^{210,211}

Part IV. Prescribing Opioids for Chronic Non-cancer Pain

Opioids in the Chronic Phase (>12 weeks after an episode of pain or surgery)

Managing chronic pain and providing appropriate opioid therapy is a challenging aspect of both primary care and specialty care practices. This is why it is critical for providers to be very conscious of the risks and intentional about the treatment plan when prescribing these drugs. The key to effective COAT is sustained improvement in physical function and pain with frequent monitoring to adjust therapy as necessary. Best practice treatment requires ongoing attention to identify adverse outcomes. Providers must balance the need for scientific evidence and skillful clinical decision making in these complex cases.

1 in 5 patients on chronic opioid analgesic therapy will develop opioid use disorder as defined by DSM 5. If tolerance and withdrawal are considered, the prevalence rises to nearly 1 in 3.¹⁰

Clinical Recommendations

1. Prescribe COAT only if there is sustained clinically meaningful improvement in function and no serious adverse outcomes or contraindications.
2. Use extreme caution and consider consultation before prescribing COAT in patients with comorbid mental health disorders (especially PTSD and major depressive disorder), family or personal history of substance use disorder, concurrent use of benzodiazepines or sedative-hypnotics, or medical conditions that could increase sensitivity to opioid-related side effects (e.g. COPD, CHF, sleep apnea, advanced age, or renal or hepatic dysfunction).
3. Reassess the need for COAT in transferred patients who are already using opioids. If current treatment is not benefiting the patient, a dose reduction or discontinuation is warranted. Consider non-opioid options for pain treatment ([Recommendations for All Pain Phases](#) and [Non-opioid Options](#)).
4. Discuss the potential benefits and risks associated with COAT including addiction and overdose. Have a signed opioid treatment agreement to document this discussion and set behavioral expectations including the use of a single prescriber and pharmacy.
5. Prescribe opioids at the lowest possible effective dose. If the dose is increased but does not result in CMIF, then significant tolerance or adverse effects to opioids may be developing and opioids should be tapered back to the previous dose or possibly discontinued.
6. Prescribe opioids in multiples of a 7-day supply to reduce the incidence of the supply ending on a weekend.
7. Initiate a bowel regimen to prevent opioid-induced constipation, especially in older adults. Prescribe regularly scheduled laxatives, such as senna, polyethylene glycol, lactulose, sorbitol, milk of magnesia or magnesium citrate (caution in patients with kidney failure).

8. Use the following best practices to ensure effective treatment and minimize potential adverse outcomes:
 - a. Assess and document function and pain status using validated tools at each visit where opioids are prescribed ([Recommendations for All Pain Phases](#) and [CMIF](#)). This is critical in determining the patient’s ongoing response to opioids and to measure effects from any dose changes.
 - b. Check the state’s PMP at the frequency determined by the patient’s risk category ([Table 18](#)) to ensure controlled substance history is consistent with prescribing record. Prescribers may delegate the ability to query the PMP database to any licensed health care professional ([Appendix C: How to use the Prescription Monitoring Program](#)).
 - c. Repeat random UDTs at the frequency determined by the patient’s risk category to identify aberrant behavior, undisclosed drug use and/or abuse and verify compliance with treatment ([Appendix D: Urine Drug Testing for Monitoring Opioid Therapy](#)).
 - d. Monitor for opioid-related adverse outcomes such as central sleep apnea, endocrine dysfunction, opioid-induced hyperalgesia, opioid use disorder or signs of acute toxicity. Be especially cautious with comorbid conditions that may increase risk for adverse outcomes (including COPD, CHF, obstructive sleep apnea, history of alcohol or substance use disorder, advanced age, or renal or hepatic dysfunction). See [Table 6](#) for recommended monitoring frequency.
 - e. Monitor for medication misuse, aberrant drug-related behaviors or diversion ([Table 9](#)).
 - f. Consult with a pain management specialist before exceeding 120 mg/day MED. If the pain management specialist endorses high dose COAT, consider prescribing naloxone as a preventive rescue medication. Counsel family member or other personal contacts in a position to assist the patient at risk of opioid-related overdose.
9. Do not combine opioids with benzodiazepines, sedative-hypnotics or barbiturates.
10. Do not prescribe methadone for chronic pain unless you are knowledgeable of methadone’s non-linear pharmacokinetics, unpredictable clearance, multiple drug-to-drug interactions and additional monitoring requirements. Free mentoring services are available for prescribing methadone using the [Providers’ Clinical Support System](#).
11. Increase the frequency of monitoring for high risk patients on opioids. Monthly visits are often needed.
12. Discontinue opioids during this phase based on the criteria listed on [Table 8](#).

Table 6. How Often to Monitor Patients on COAT

| Level of Risk | Recommended Frequency |
|--|-----------------------|
| Low risk (no risk factors) | Every 6 months |
| Moderate risk | Every 3 months |
| High risk or opioid doses >120 mg/day MED | Every month |

Table 7. Prescribing Methadone for Pain Management

Prescribing methadone is complex. To prevent serious complications from methadone, prescribers should read and carefully follow the methadone (Dolophine®) prescribing information at www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. The American Pain Society's [clinical practice guideline](#) for safe methadone use is also a valuable resource.

Deaths, cardiac and respiratory, have been reported during initiation and conversion of pain patients to methadone treatment from treatment with other opioid agonists. It is critical to understand the pharmacokinetics of methadone when converting patients from other opioids.

Respiratory depression is the chief hazard associated with methadone or other opioid administration. Methadone's peak respiratory depressant effects typically occur later, and persist longer than its peak analgesic effects, particularly in the early dosing period. These characteristics can contribute to cases of iatrogenic overdose, particularly during treatment initiation and dose titration.

In addition, cases of QT interval prolongation and serious arrhythmia (torsades de pointes) have been observed during treatment with methadone. Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction.

Evidence

The efficacy of long-term opioid use for chronic non-cancer pain has not been established. However, many primary care providers have patients—in some cases inherited from other providers—who have already been placed on COAT after failing other pain management options.

While this guideline continues to identify 120 mg/day MED as the boundary beyond which specialty consultation is warranted, there is no completely safe opioid dose level. There appears to be a steady increase in overdose risk as the opioid dose rises above 20 mg/day MED.⁵⁰⁻⁵³ The cause and effect relationship is unclear, but patients on high dose opioids are more than likely to have high risk characteristics, such as mental health disorder, a substance use disorder, and/or opioid misuse.¹ Recent evidence also shows that the increased risk from escalating the opioid dose is not balanced by an increased benefit in either functional status or average pain level.²¹²

In addition to dose-associated risks, duration of opioid action (long-acting vs. short-acting) has been linked to unintentional overdose.²¹³ Patients receiving long-acting opioids had a 2.5-fold increased risk of overdose as compared to those receiving short-acting opioids after adjusting for age, sex, opioid dose and other characteristics. The risk was significantly higher during the first two weeks after initiation of long-acting opioids.

Chronic opioid analgesic therapy is also associated with the development of physical dependence and addiction (DSM 5 "opioid use disorder"). The true incidence of these serious complications is unknown but is likely to affect more patients than was previously reported.^{18,31,32} In addition, the lack of a useful case definition for any of these dependent states makes it challenging for a primary care provider to identify and intervene appropriately.²⁶ Even with acute low dose opioids, patients are at increased risk for developing opioid use disorder. This risk ranges from an odds ratio of 3.03 for acute low dose opioids (1 – 36 mg/day MED), to 122.45 for patients on chronic high dose opioids (\geq 120 mg/day

MED).³² A recently published large scale study of patients on chronic opioid revealed that the lifetime prevalence of DSM 5 prescription opioid use disorder is 21% (12% mild, 9% moderate to severe).¹⁰ These rates do not consider tolerance or withdrawal. If these physiologic responses are considered, the prevalence is 29%.

Other adverse events most commonly reported in randomized trials include constipation, nausea and vomiting, dizziness, and drowsiness.¹⁹ Much more serious long-term consequences of opioids have only been identified from observational and epidemiological investigations; these include higher risk for poor functional status,⁶ inhibition of endogenous sex hormone production with resulting hypogonadism and infertility,²¹⁴ immunosuppression,²¹ falls and fractures in older adults,²² neonatal abstinence syndrome,²³ cardiac arrhythmia related to methadone,²⁴ central sleep apnea,²⁵ opioid-induced hyperalgesia,⁶⁰ nonfatal overdose hospitalizations,²⁷ emergency department visits,²⁸ and death from unintentional poisoning.²⁹

Part V. Reducing or Discontinuing Chronic Opioid Analgesic Therapy (COAT)

Reasons to Discontinue COAT and Considerations Prior to Taper

Not all patients benefit from opioids, and a prescriber frequently faces the challenge of reducing the opioid dose or discontinuing opioids altogether. Patients on COAT can be reluctant to change, and many who agree to try will have difficulty as the dose is reduced. Such reluctance and difficulty in tapering often reflect anxiety. There may be apprehension about worsening of pain and withdrawal symptoms or, if there is opioid use disorder, about reduced access to the drug. Exploring each of these possibilities in a non-judgmental manner helps the provider understand the patient’s perspective and helps the patient have realistic expectations. This, in turn, strengthens the therapeutic relationship and supports future strategies.

Table 8. When to Reduce, Taper, or Discontinue COAT

| |
|---|
| Patient requests opioid taper. |
| Patient is maintained on opioids for at least 3 months, and there is no sustained clinically meaningful improvement in function (CMIF), as measured by validated instruments (Appendix B: Validated Tools for Screening and Assessment) |
| Patient’s risk from continued treatment outweighs the benefit (e.g. decreased function and increased risk for opioid-related toxicity from concurrent drug therapy or comorbid medical conditions) |
| Patient has experienced a severe adverse outcome or overdose event |
| Patient has a substance use disorder (except tobacco) |
| Use of opioids is not in compliance with DOH’s pain management rules or consistent with the AMDG Guideline |
| Patient exhibits aberrant behaviors (Table 9) |

Clinical Recommendations

1. Help the patient understand that chronic pain is a complex disease, and opioids alone cannot adequately address all of the patient’s pain-related needs. Exploring the patient’s resistance to discontinuing opioids will guide taper strategy. Motivational interviewing skills may be useful when having this conversation.
2. Consider tapering patients in an outpatient setting if they are not on high dose opioids or do not have comorbid substance use disorder or an active mental health disorder, as this can be done safely and they are at low risk for failing to complete the taper.
3. Seek consultation from a pain management specialist or Structured Intensive Multidisciplinary Pain Program (SIMP; described in [Non-opioid Options](#)) for patients who have failed taper in an outpatient setting or who are at greater risk for failure due to high dose opioids, concurrent benzodiazepine use, comorbid substance use disorder or any active mental health disorder. If SIMP is not available, engage patients in activities that emulate the biopsychosocial approach of such a program. Rarely, inpatient management of withdrawal may be necessary.
4. Refer patients with aberrant behaviors ([Table 9](#)) for evaluation and treatment.

How to Discontinue Opioids

Selecting the optimal timing and approach to tapering depends on multiple factors. The rate of opioid taper should be based primarily on safety considerations, and special attention is needed for patients on high dose opioids, as too rapid a taper may precipitate withdrawal symptoms or drug-seeking behavior. In addition, behavioral issues or physical withdrawal symptoms can be a major obstacle during an opioid taper. Patients who feel overwhelmed or desperate may try to convince the provider to abandon the taper. Although there are no methods for preventing behavioral issues during taper, strategies implemented at the beginning of COAT such as setting clear expectations and development of an exit strategy are most likely to prevent later behavioral problems if a taper becomes necessary.

Clinical Recommendations

1. Consider sequential tapers for patients who are on chronic benzodiazepines and opioids. Coordinate care with other prescribers (e.g. psychiatrist) as necessary. In general, taper off opioids first, then the benzodiazepines.
2. Do not use ultra-rapid detoxification or antagonist-induced withdrawal under heavy sedation or anesthesia (e.g. naloxone or naltrexone with propofol, methohexital, ketamine or midazolam).
3. Establish the rate of taper based on safety considerations:
 - a. Immediate discontinuation if there is diversion or non-medical use,
 - b. Rapid taper (over a 2 to 3 week period) if the patient has had a severe adverse outcome such as overdose or substance use disorder, or
 - c. Slow taper for patients with no acute safety concerns. Start with a taper of $\leq 10\%$ of the original dose per week and assess the patient's functional and pain status at each visit.
4. Adjust the rate, intensity, and duration of the taper according to the patient's response (e.g. emergence of opioid withdrawal symptoms ([Table 10](#))).
5. Watch for signs of unmasked mental health disorders (e.g. depression, PTSD, panic disorder) during taper, especially in patients on prolonged or high dose opioids. Consult with specialists to facilitate a safe and effective taper. Use validated tools to assess conditions ([Appendix B: Validated Tools for Screening and Assessment](#)).
6. Consider the following factors when making a decision to continue, pause or discontinue the taper plan:
 - a. Assess the patient behaviors that may be suggestive of a substance use disorder
 - b. Address increased pain with use of non-opioid options.
 - c. Evaluate patient for mental health disorders.
 - d. If the dose was tapered due to safety risk, once the dose has been lowered to an acceptable level of risk with no addiction behavior(s) present, consider maintaining at the established lower dose if there is CMIF, reduced pain and no serious adverse outcomes.
7. Do not reverse the taper; it must be unidirectional. The rate may be slowed or paused while monitoring for and managing withdrawal symptoms.
8. Increase the taper rate when opioid doses reach a low level (e.g. <15 mg/day MED), since formulations of opioids may not be available to allow smaller decreases.

9. Use non-benzodiazepine adjunctive agents to treat opioid abstinence syndrome (withdrawal) if needed. Unlike benzodiazepine withdrawal, opioid withdrawal symptoms are rarely medically serious, although they may be extremely unpleasant. Symptoms of mild opioid withdrawal may persist for six months after opioids have been discontinued ([Table 10](#)).
10. Refer to a crisis intervention system if a patient expresses serious suicidal ideation with plan or intent, or transfer to an emergency room where the patient can be closely monitored.
11. Do not start or resume opioids or benzodiazepines once they have been discontinued, as they may trigger drug cravings and a return to use.
12. Consider inpatient withdrawal management if the taper is poorly tolerated.

Table 9. Aberrant Behaviors

| Less suggestive for addiction but are increased in depressed patients | More suggestive of addiction and are more prevalent in patients with substance use disorder |
|--|---|
| <ul style="list-style-type: none"> • Frequent requests for early refills; claiming lost or stolen prescriptions • Opioid(s) used more frequently, or at higher doses than prescribed • Using opioids to treat non-pain symptoms • Borrowing or hoarding opioids • Using alcohol or tobacco to relieve pain • Requesting more or specific opioids • Recurring emergency room visits for pain • Concerns expressed by family member(s) • Unexpected drug test results • Inconsistencies in the patient’s history | <ul style="list-style-type: none"> • Buying opioids on the street; stealing or selling drugs • Multiple prescribers (“doctor shopping”) • Trading sex for opioids • Using illicit drugs, +UDT for illicit drugs • Forging prescriptions • Aggressive demand for opioids • Injecting oral/topical opioids • Signs of intoxication (ETOH odor, sedation, slurred speech, motor instability, etc.) |

Adapted from Passik, S. 2006

Table 10. Symptoms and Treatment of Opioid Abstinence Syndrome (withdrawal)

| | |
|---|---|
| Restlessness, sweating or tremors | Clonidine 0.1-0.2 mg orally every 6 hours or transdermal patch 0.1-0.2 mg weekly (If using the patch, oral medication may be needed for the first 72 hours) during taper. Monitor for significant hypotension and anticholinergic side effects. |
| Nausea | Anti-emetics such as ondansetron or prochlorperazine |
| Diarrhea | Loperamide or anti-spasmodics such as dicyclomine |
| Muscle pain, neuropathic pain or myoclonus | NSAIDs, gabapentin or muscle relaxants such as cyclobenzaprine, tizanidine or methocarbamol |
| Insomnia | Sedating antidepressants (e.g. nortriptyline 25 mg at bedtime or mirtazapine 15 mg at bedtime or trazodone 50 mg at bedtime). Do not use benzodiazepines or sedative-hypnotics. |

Evidence

Some patients on COAT have adverse effects or the prescriber feels that current treatment is not benefiting the patient, and the patient may do better with tapering of the dose or discontinuing opioid therapy.²¹⁵⁻²¹⁷ Dose reduction, discontinuation of opioids, or transition to medication-assisted treatment for opioid use disorder frequently improves function, quality of life, and even pain control.²¹⁸ Because the experience of pain and the symptoms of withdrawal that accompany an opioid taper vary from one person to the next, there is not a one size fits all approach. The approach to and rate of taper in patients on COAT is based on the individual patient's needs and comorbidities. Expert opinion, rather than systematic reviews or RCTs have informed these "best practice" recommendations.

Many pharmacologic therapies have been studied for use as adjunctive agents during opioid taper to palliate opioid abstinence syndrome (withdrawal) as well as emergent insomnia and anxiety.²¹⁹⁻²²⁴

A multidisciplinary approach to pain, including psychotherapy (behavioral activation, problem solving therapy, etc.), physical therapy, chiropractic, social work, and occupational therapy have been proven to improve function. Multidisciplinary pain programs have strong clinical efficacy and empirical data supporting their cost-efficiency.^{94,95,225-228} These programs, while neither widely available nor well reimbursed, provide significant benefit to many patients. In addition, a multidisciplinary approach may be considered to address the psychosocial and cognitive aspects of chronic pain together with patients' physical rehabilitation.²²⁹

High quality evidence of safety and comparative efficacy is lacking for ultra-rapid detoxification, or for the use of antagonist drugs, with or without sedation.²³⁰

Extremely challenging behavioral issues may emerge during an opioid taper.²³¹ Special care must be taken by the prescriber to preserve the therapeutic relationship during opioid tapering. Otherwise, the taper can precipitate doctor-shopping, illicit drug use, or other behaviors that pose a risk to patient safety. Although there are no fool-proof methods for preventing behavioral issues during an opioid taper, strategies implemented at the beginning of the opioid therapy are most likely to prevent later behavioral problems if an opioid taper becomes necessary. Patients who exhibit aberrant behaviors during the taper may have ([Opioid Use Disorder](#)).²³² Also, serious suicidal ideation (with plan or intent) should prompt engagement of the crisis system or, if available, urgent psychiatric consultation.²³³

If the patient doesn't have substance use or any other active mental health disorder and is not on chronic high dose opioids, taper can usually be done safely in an outpatient setting.

Surprisingly, opioid tapers rarely cause significant and long term increases in pain. If these occur, they tend to be during and immediately following completion of the opioid taper. In addition to antidepressant medications, anti-inflammatories and anticonvulsants can be used to address increased pain in patients who have no contraindications.

Office-based buprenorphine treatment is an effective **evidence-based** option which should be considered for patients with both chronic pain and opioid use disorder.²³⁴ Buprenorphine may be the only practical option for patients in rural areas where methadone treatment programs and structured pain programs are difficult to access.

Part VI. Recognition and Treatment of Opioid Use Disorder

Opioid therapy can lead to the development of opioid use disorder. Although the true incidence is unknown, this risk ranges from 3-fold for acute low dose opioids to 122-fold for chronic high dose opioids. As outlined in the DSM 5, substance use disorders including [Opioid Use Disorder](#) are now described as existing across a continuum of severity, from mild to severe. The need for or type of treatment depend on the severity of the condition. According to the broad definition in DSM 5, only two criteria must be met to make a diagnosis of a mild disorder. Two of these criteria, tolerance and withdrawal, are normal physiological consequences of COAT. However, these two criteria do not count toward the DSM 5 diagnosis of opioid use disorder *if the medication is taken appropriately under ongoing medical treatment*. Excluding tolerance and withdrawal, a recently published large scale study found a 21% lifetime prevalence of DSM 5 prescription opioid use disorder (12% mild, 9% moderate to severe) among patients on chronic opioids.¹⁰

The remaining DSM 5 criteria for opioid use disorder pertain to maladaptive behavior patterns. Examples include taking opioids in larger amounts than intended, spending a great deal of time trying to obtain opioids, strong craving for opioids, recurrent opioid use in situations where it is physically hazardous, social impairment such as withdrawal from family and friends, and conflict with medical providers over opioid use. Such behaviors are not unusual in COAT patients, and differentiating between physiologic dependence and opioid use disorder can be difficult.²³⁵

Often, patients will readily acknowledge difficulty due to some of these maladaptive behaviors. These patients may experience an improvement in their quality of life if a transition can be made to medication-assisted treatment for opioid use disorder. However, it is important to recognize the stigma attached to the word “addiction,” and it is generally best to avoid use of that term. “Opioid Use Disorder” may be a more acceptable term to patients who perceive their primary problem to be pain. The term “opioid dependence,” while often acceptable to patients, is best avoided due to possible confusion with its outdated formal definition in DSM-IV.

As efforts to address the prescription opioid overdose epidemic have decreased the supply of prescription opioids, some patients have transitioned to heroin as a cheaper alternative. The numbers of people starting to use heroin have been steadily rising since 2007 with a corresponding increase in heroin overdose.²³⁶ It is important to recognize the potential for this transition and refer high risk patients for appropriate evaluation and treatment.

Clinical Recommendations

1. Assess for opioid use disorder using DSM 5 criteria or refer for a consultation with an addiction specialist if a patient demonstrates aberrant behaviors suggestive of substance use disorder ([Table 9](#) and [Appendix H: Clinical Tools and Resources](#)).

2. Patients diagnosed with opioid use disorder should receive a combination of medication-assisted treatment and behavioral therapies.
3. Contact the Substance Abuse and Mental Health Services Administration (SAMHSA)'s [Providers' Clinical Support System for Opioids \(PCSS-O\)](#) and [Providers' Clinical Support System for Medication Assisted Treatment \(PCSS-MAT\)](#) for treatment issues. Expert physician mentors are available to assist with questions or concerns about opioid tapering and assessment and treatment of substance use disorders.
4. Consider prescribing naloxone as a preventive rescue medication for patients with opioid use disorder, especially if heroin use is suspected. Counsel family member or other personal contacts in a position to assist the patient at risk of opioid-related overdose. For more detail on opioid prevention education, visit www.stopoverdose.org.
5. Check the state's PMP to ensure controlled substance history is consistent with prescribing record. Prescribers may delegate the ability to query the PMP database to any licensed health care professional ([Appendix C: How to use the Prescription Monitoring Program](#)).
6. Be knowledgeable about treatment options:
 - a. Medication-assisted treatment with either sublingual buprenorphine products or methadone is common in patients who have co-occurring chronic pain and opioid use disorder.
 - b. A [DATA 2000 waiver](#) is needed to prescribe sublingual buprenorphine products for opioid use disorder in an office-based setting. Providers without a waiver should consider getting one or refer the patient to a provider with a waiver to prescribe buprenorphine. This treatment may be the only practical option for patients in rural areas where methadone and other treatment programs are difficult to access.
 - c. Patients who require methadone maintenance must be referred to a federally licensed opioid treatment program.

Evidence

There is very little evidence that outpatient non-medication treatment for opioid use disorder is effective.^{237,238} In these programs, patients are tapered off opioids and are expected to attend a treatment program one or more days per week to learn skills necessary to manage symptoms (e.g. pain, mood and anxiety problems, substance craving) without resorting to substance use.

Once a moderate to severe opioid use disorder has been diagnosed, there is strong evidence for efficacy of methadone or buprenorphine maintenance combined with behavioral therapies compared to non-medication treatment.²³⁷⁻²³⁹ Maintenance treatment leads to lower rates of illicit opioid use and likely reduces health care utilization and criminal justice involvement.²⁴⁰⁻²⁴³

There is very little evidence that antagonist therapy with oral naltrexone is effective for patients with opioid use disorder, and there is no evidence in patients with chronic pain. However, it might be considered in selected, highly motivated patients (e.g. impaired professionals).²⁴⁴

Part VII. Chronic Pain Management in Special Populations

In this section, five guest authors who are recognized leaders and clinicians in their fields, provide their views and clinical recommendations for pain management during pregnancy (including neonatal abstinence syndrome (NAS)), in children and adolescents, older adults, and cancer survivors. This section serves as an overview to orient primary care providers to special needs of these populations in regards to opioid use and does not include all modalities for pain management.

Managing Chronic Pain during Pregnancy; and Neonatal Abstinence Syndrome

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Opioid use during pregnancy complicates the clinical management of an already vulnerable group. Opioid use in pregnancy is increasing at an alarming rate, an estimated 3 to 4-fold increase between 2000 and 2009.²⁴⁵ Studies of opioid exposure during pregnancy suggest increased fetal, obstetrical and neonatal risks, including NAS. Many pregnancies are unplanned, and women of reproductive age may be using opioids prior to a clinically recognized pregnancy. These factors make management of opioid use during pregnancy particularly challenging for healthcare providers.

Women who use opioids and could become pregnant require counseling regarding maternal, fetal and neonatal risks.

Clinical recommendations

1. Recommend counseling before (preconception) and during pregnancy for women on COAT to assess and educate about potential maternal, fetal, and neonatal risks.
2. Address underlying contributors to pain syndromes such as stress and anxiety and use non-pharmacologic therapies as appropriate, including stress reduction, exercise, mechanical therapies, activity modification, and complementary and alternative medicine approaches. If appropriate, refer for mental health services ([Non-opioid Options](#)).
3. Use acetaminophen during pregnancy for treatment of pain. Consider NSAIDs in consultation with an obstetrical provider for short duration of therapy (<48 hours) prior to the third trimester.
4. Use caution when initiating short-acting opioids for treatment of pain during pregnancy and limit it to women with severe pain for whom other medical treatments have failed.
5. Assess pregnant women taking opioids for opioid use disorder. If present, refer to a qualified specialist for methadone or buprenorphine treatment for pregnant women. Buprenorphine may have improved neonatal outcomes, but availability may be limited due to provider or geographic access ([Appendix H: Clinical Tools and Resources](#)).
6. Monitor fetal growth for women on opioids, using fundal height or ultrasound surveillance, given the risk of intrauterine growth restriction.

7. Consider a perinatal pediatric consultation for pregnant women on opioids to better prepare them for risks of NAS and possible increased hospital stay for the newborn.
8. Use the Finnegan score to assess neonates during the immediate postnatal period if they were exposed to opioids in utero.
9. Weigh carefully the risks/benefits of opioid detoxification during pregnancy, when making the decision to go forward with treatment; and closely monitor the treatment plan for symptoms of withdrawal and risk of relapse.
10. Assess availability of social and community support for women with opioid use disorder or escalating pain symptoms during pregnancy to help meet any needs for education and services.

Evidence

Ideally, pharmacologic agents would not be needed during pregnancy. However, pain in pregnancy is common and may include musculoskeletal symptoms, exacerbation of previous injuries, headaches and abdominal pain. Some women will require ongoing or episodic opioid treatment for medical conditions, which may be exacerbated by pregnancy. Safety and efficacy data for non-opioid treatments for pain symptoms in pregnancy is limited. Analgesics such as acetaminophen are generally considered safe, while NSAIDs may cause oligohydramnios and premature closure of the ductus arteriosus when used for prolonged periods or during the third trimester.^{246,247} Mechanical therapies, exercise, complementary or alternative medicine, and psychiatric treatment have been beneficial, but each may have risks to a woman's pregnancy based on her history.²⁴⁸

A 2015 CDC study showed that 39% of women age 15-44 on Medicaid between 2008-2012 had filled an opioid prescription each year, compared with 28% of women with private insurance.²⁴⁹ Of pregnant women enrolled in Medicaid between 2000-2007, 21.6% filled an opioid prescription from an outpatient pharmacy during pregnancy²⁵⁰ as compared to 14.4% of pregnant women with private insurance during 2005-2011.²⁵¹ These studies do not provide insight on the indications for opioid prescriptions but illustrate remarkably high rates in both the privately and publicly insured populations.

Fetal and Obstetrical Risks

Opioids are known to cross the placenta and can be detected in fetal umbilical cord blood and meconium.²⁵² The window for teratogenicity is from 4 to 10 weeks after the last menstrual period, which is often before a clinically recognized pregnancy. Research on teratogenicity of opioids is limited and heterogeneous as there is a relatively high 2-3% incidence of major congenital malformations in the general population. Studies have shown that opioid exposed fetuses may be at increased risk for neural tube, cardiac and gastrointestinal defects.^{253,254}

Opioid use during pregnancy is associated with adverse pregnancy outcomes such as preterm delivery, poor fetal growth, and stillbirth.²⁵⁵ Additionally, pregnant women who use opioids have higher rates of depression, anxiety, and chronic medical conditions, with increased health care costs.²⁵⁵ There are, however, numerous confounders that challenge the causal relationship between opioids and adverse obstetrical events, such as co-morbid medical conditions, obesity, poor nutritional status, socioeconomic background, and poly-substance abuse (alcohol, tobacco, illegal drugs).

Risks Associated with Medically Supervised Withdrawal from Opioids

The safety of medically supervised withdrawal from opioids during pregnancy is not well studied, although there are historical reports of embryonic or fetal loss, preterm labor, and fetal distress during maternal opioid withdrawal.²⁵⁶⁻²⁵⁸ Several recent studies have reported successful inpatient medically supervised withdrawal from opioids during pregnancy with no increased risk of adverse obstetrical outcomes.²⁵⁹⁻²⁶¹ Ideally, women should discontinue or minimize opioid dose *prior* to pregnancy to decrease the risk of birth defects, obstetrical complications and neonatal abstinence syndrome. The decision to proceed with opioid discontinuation or medically supervised withdrawal during pregnancy is complex and must be individualized.

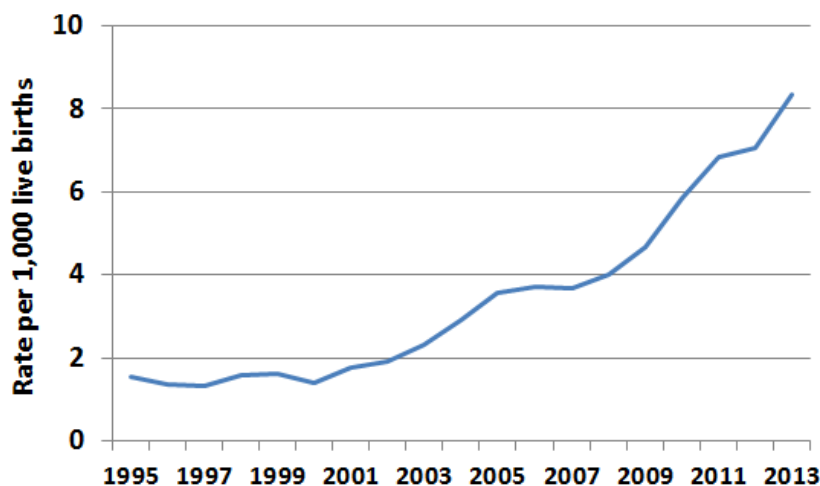
Treatment of Opioid Use Disorder

For pregnant women with opioid use disorder (as defined by DSM 5), use of methadone or buprenorphine reduces illicit drug use, criminal activity and infectious complications (including sexually transmitted diseases, HIV, hepatitis B and C), while improving adherence to prenatal care.²⁶² The American Academy of Pediatrics supports use of methadone (without limitation) and other opioids during breastfeeding. Active use of illegal drugs, however, is a contraindication to breastfeeding.²⁶³

Neonatal Abstinence Syndrome

Long-term opioid therapy during pregnancy can lead to NAS.²⁴⁵ It typically occurs in the first 24 hours to 14 days of neonatal life and is characterized by the Finnegan score, which grades the degree of psychomotor irritability, vasomotor and gastrointestinal disturbances.^{264,265} NAS may occur in up to 60-80% of opioid exposed infants²⁴⁵ and has been increasing at an alarming rate (Figure D). Maternal methadone dose at delivery does not correlate directly with risk of NAS.²⁶⁶ Buprenorphine is associated with a lower incidence and shorter duration of NAS, higher birth weights and longer gestation.²⁶²

Figure D. Infant Hospitalizations for Neonatal Abstinence Syndrome in WA State 1990-2013



Source: Inpatient Hospital Discharge & Birth Certificate Data,
NAS= ICD diagnosis code of 779.5

Managing Chronic Non-cancer Pain in Children and Adolescents

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The use of opioids to treat pain in infants and children presents challenges for a few key reasons. First, with very rare exception, opioids have not been labeled for use in individuals less than 18 years of age, indicating a dearth of quality studies on pharmacokinetics, pharmacodynamics, safety, and, in the youngest children, clinical effectiveness. Second, although acute pain problems in pediatrics have many characteristics in common with adult presentations, persistent, recurrent, and chronic pain in infants, children, and adolescents are often qualitatively different than chronic pain problems in adults. It is a corollary that treatment approaches may vary accordingly. Finally, it is often said that "children are not little adults," meaning one cannot simply extrapolate from adult medicine to pediatrics; however, "adults are big children" and there is mounting evidence to show that poorly treated pain in childhood and adolescence is strongly associated with chronic pain and other difficulties in the adult years.

Clinical Recommendations

1. Prescribe opioids for acute pain in infants and children only if knowledgeable in pediatric medicine, developmental elements of pain systems, and differences in pharmacokinetics and pharmacodynamics in young children.
2. Avoid opioids in the vast majority of chronic non-cancer pain problems in children and adolescents (e.g. abdominal pain, headache, pervasive musculoskeletal pain), as evidence of safety and efficacy is lacking.
3. Opioids are indicated for a small number of persistent painful conditions, including those with clear pathophysiology and when an endpoint to usage may be defined, such as pain associated with most surgical procedures, trauma (including burns), and major reconstructive surgery.
4. Opioids may be indicated for some chronic pain conditions in children and adolescents when there is clear pathophysiology and no definable endpoint. This may include treatment at the end of life or for certain ongoing nociceptive mediated painful conditions, such as osteogenesis imperfecta or epidermolysis bullosa.
5. Put safety first when prescribing opioids to younger patients: limit the total dispensed and educate parents about dosing, administration, storage and disposal to minimize risks of diversion or accidental ingestion. Adolescents should undergo similar screening for risk of substance use disorder that one would conduct with adults.
6. Consult or refer to a pediatric pain specialist when chronic pain problems in children and adolescents are complicated or persistent, given the developmental complexities and potential for ongoing pain problems in the future. These problems are best treated by those with specialty training in the area.

Evidence

Labeling of Opioids for Use in Pediatrics

Approximately 80 percent of drugs prescribed for children in the United States are done so “off label,” as they have not been approved by the FDA for use in the younger age groups.^{267,268} Clinicians, therefore, are faced with a difficult dilemma: do we withhold potentially beneficial medications from young patients because they are not labeled for that age group? In the case of analgesics, this means unnecessary suffering. Or do we give the drugs based on extrapolation from adult studies (with some dosage modifications for body mass or surface area) without direct data on safety and effectiveness?

Even with innovations to improve the study of pediatric medications, such as the Best Pharmaceuticals for Children Act^{iv} and the Pediatric Research Equity Act^v, analgesic medications remain quite under-represented. No analgesic medications have been labeled for children less than 6 months of age and only ibuprofen has been labeled for those 6 to 24 months. Based on expert consensus, the effectiveness of opioids may be extrapolated from studies on adults and older children down to those 2 years of age and older. Still lacking, however, are sufficient data on drug metabolism, dose response, and toxicity.^{269,270}

Although the benefits have been deemed to outweigh the risks for using opioids for acute pain in children, such is not the case for chronic pain and, thus, opioid treatment in this context is generally discouraged.²⁷¹ For example, the American Pain Society (2012) states, “Opioids are rarely indicated in the long-term treatment of chronic non-cancer pain in children, although they may be beneficial in certain painful conditions with clearly defined etiologies.” The Japanese Pediatric Society guidelines state, “The use of opiates for non-cancer chronic pain is debatable; they are generally reserved for treatment of painful syndromes related to cancer, injury, or other acute types of pain. The use of opiates is not recommended for the types of chronic pain described in the present guidelines.”²⁷² The indications are clearly for those conditions with clear underlying pathophysiology and when some endpoint is defined prior to initiation.

Chronic Pain in Pediatrics

The most common presentations of chronic pain in children and adolescents include abdominal pain, headache, and musculoskeletal pain.²⁷³ The most common pain problems in adults are rarely seen in pediatric populations, as they are frequently neuropathic in nature and often are related to degenerative aging processes.²⁷⁴ As a consequence, treatment modalities are often quite different, i.e. biopsychosocial models are emphasized in children, and opioids rarely have a role. The possible exceptions are chronic, non-cancer conditions with known pathophysiology and a defined endpoint (e.g. a patient with avascular necrosis awaiting joint replacement), or conditions with persistent pain with an expected endpoint (e.g. post-trauma or extended post-operative pain).²⁷⁵

^{iv}<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticAct/FDCA/SignificantAmendmentstotheFDCA/ucm148011.htm> and <http://bpca.nichd.nih.gov/Pages/Index.aspx>

^v<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM077853.pdf>

Developmental Trajectories: Adults are Big Children

A comprehensive review of longitudinal studies focused on the continuity or contiguity of pediatric and adolescent chronic pain problems into adulthood is beyond the scope of this guideline. Certainly, adults with chronic pain often recall having had difficulties in their earlier years. More substantial, however, are the prospective longitudinal or cross-sequential studies demonstrating these trajectories. Multiple studies have shown that children with functional abdominal pain are at risk for difficulties as adults that include anxiety or depressive disorders, functional gastrointestinal disorders, and other non-abdominal chronic pain.²⁷⁶⁻²⁸⁰ Similar data have been generated for headaches^{281,282} and back pain²⁸³⁻²⁸⁵ Although no specific studies on prevention have been reported, it seems clear that by addressing pain complaints in the young, morbidity in the subsequent years will be reduced.

Managing Chronic Pain in Older Adults

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Aging is associated with unique biological, psychological and social factors that all play an important role in pain management. As in all age groups, evidence of long-term effectiveness of opioid therapy is lacking. However, in carefully selected and monitored patients, opioids may provide effective pain relief if used as part of a comprehensive multimodal pain management strategy.²⁸⁶ A combination of pharmacologic, non-pharmacologic, and rehabilitative approaches in addition to a strong therapeutic alliance between the older patient and physician is essential to achieve desired treatment outcomes.⁸³

Clinical Recommendations

1. Use opioids with short half-lives, as they are usually the best choices for older adults. Drugs with a long half-life can readily accumulate in older adults and result in toxicity (e.g. respiratory depression, sedation).
2. Weigh the individual patient's needs and clinical presentation with known risk factors when deciding whether short or long acting opioids are best.
3. Avoid the use of agonist-antagonist opioids in older adults as their psychomimetic side effects can be pronounced.
4. Be vigilant when treating patients over 65 to adequately relieve pain while minimizing the risk of delirium and other opioid-related adverse drug events.
5. Use the least invasive method of drug administration (e.g. oral).
6. Initiate opioid therapy at a 25% to 50% lower dose than that recommended for younger adults, and slowly and carefully titrate dosage by 25% increments on an individual basis, balancing pain relief, physical function, and side effects.
7. Have a plan for addressing constipation from the start of opioid therapy. Prophylaxis and/or treatment can include hydration, bulk fiber (only if hydration is maintained), activity, senna, and sorbitol (20 ml of 70% taken twice daily for 3 days per week).
8. Recognize and manage all potential causes of side effects, taking into consideration medications that potentiate opioid side effects:

- a. Sedatives, tranquilizers, and anti-emetics can cause sedation.
 - b. Antihypertensives and tricyclics can cause postural hypotension.
 - c. Antihistamines, phenothiazines, tricyclics, and anticholinergics can cause confusion and urinary retention.
9. Avoid using more than one opioid at the same time. This makes it is easier to identify the cause of an adverse effect or toxic reaction. The incidence of delirium and other adverse reactions increases with the number of prescription drugs taken.
10. **Avoid** the following drugs:
- a. Codeine: the doses required for effective pain relief in older adults are associated with an increased incidence of side effects (e.g. constipation, nausea and sedation).
 - b. Meperidine: the metabolite, normeperidine, is toxic to the CNS and can cause seizures, mood alterations and confusion; more so in older patients, especially if the patient has renal impairment.
 - c. Methadone: has a high drug-drug interaction potential and is associated with prolongation of the QT interval and a potential risk of accumulation due to a long elimination half-life. In addition, methadone is difficult to titrate because of its large inter-individual variability in pharmacokinetics, particularly in the frail elderly.

Evidence

Approximately 60% of Americans over age 65 have persistent pain, most commonly from musculoskeletal disorders such as arthritis and degenerative spine conditions²⁸⁷ but painful conditions related to neuropathies, advanced heart, kidney, or lung disease are also reported.^{288,289} Older adults are also more likely to undergo surgeries associated with a high incidence of persistent pain.²⁹⁰ Persistent pain or inadequate treatment in older adults is associated with reduced physical performance, falls, decreased sleep and self-rated health, mood, and cognition.²⁸⁶

Due to the frequency of chronic disease and potential for polypharmacy among older adults, drug-disease and drug-drug interactions should also be considered when prescribing. Nutritional alterations (e.g. protein deficiency), age-related changes (e.g. reduced hepatic and renal function, reduced body water, altered ratio of lean body mass to total body weight) and altered pharmacokinetics impact treatment options, necessitating careful evaluation and monitoring.¹⁵³ These age-related changes all make older adults especially vulnerable to opioid side effects and reduce the therapeutic window between beneficial doses and doses that are toxic or lethal.

Though evidence shows that older adults are less likely to misuse and abuse opioids²⁹¹ they are also likely to have higher levels of pain severity and depressive symptoms and more physical disability. These can increase misuse and abuse,²⁹² so an individual approach weighing risks and benefits is best.²⁸⁶

There is insufficient evidence to recommend short-acting versus long-acting opioids, or as-needed versus around-the-clock dosing of opioids. In general, short-acting opioids using as-needed dosing is

suggested. However, one large longitudinal nursing home study showed that extended-release opioids improved functional status and social engagement when compared to short acting opioids.²⁹³ An individual's condition and need for proper pain management must be weighed against the risks of developing adverse effects of COAT.

The potential for side effects is high in older adults due to altered ability to distribute and excrete drugs, resulting in greater peak and longer duration of action. Common opioid side effects include nausea, vomiting, delirium, respiratory depression, sedation, pruritus, hypotension, and urinary retention (especially if there is coexisting benign prostatic hypertrophy). Older adults are particularly prone to constipation and even ileus, making prevention measures particularly important. Opioids have also been linked to an increased risk for falls and non-spine fractures in community living older adults.^{294,295}

Patients over 65 who receive opioids for postoperative pain have a higher risk for opioid-related adverse drug events.²⁹⁶ Delirium has a significant impact on the medical, functional, and cognitive outcomes of older patients, and the risk of delirium increases with inadequate pain control and the use of meperidine.^{297,298} In fact, use of meperidine is listed in the 2012 American Geriatrics Society Beers Criteria as potentially inappropriate for older adults.²⁹⁹

Managing Chronic Pain in Cancer Survivors

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Management of chronic pain in cancer survivors involves unique issues that require a careful and thoughtful approach from the clinician. Although the term cancer survivor has a variety of definitions, for this guideline, a survivor is someone who has completed cancer treatment, is cured or in full clinical remission with no current evidence of disease, and is under cancer surveillance only.^{8,300,301} For these patients, the foremost issues to keep in mind are:

1. Cancer survivors are at risk of recurrent disease, so development of new or worsening pain in the survivor requires a thorough evaluation to explain the pain.
2. The chronic pain experienced by cancer survivors is most often due to their earlier treatment for active cancer (e.g., chemotherapy-induced peripheral neuropathy, radiation treatment effects, persistent post-surgical pain) or residual effects from the previous tumor (e.g., compression fractures) and can persist for many years after that treatment has been completed. This is termed "chronic cancer-related pain" (CCRP), and for the purpose of this guideline, should not be confused with treatment for pain in the setting of active cancer.

In the absence of "red flags" for malignancy, simple exacerbations of chronic pain in the survivor may be treated in a manner similar to chronic non-cancer pain (CNCP). Hence, the best pain management strategy combines diligent monitoring for cancer recurrence with standard chronic pain management therapies, including multimodal and interdisciplinary approaches.

Cancer survivors tend to be older, 45% are over the age of 70, and only 5% younger than age 40.^{8,302} The most common cancer types in survivors are female breast, prostate, colorectal, melanoma, and gynecologic. With this survival benefit comes the burden of long-term and late effects of cancer and cancer therapy. The most common issues are pain, depression, and fatigue. Other chronic problems include cognitive decline, sexual dysfunction, anxiety, and sleep disorders.³⁰³⁻³⁰⁵

Primary care providers will see more patients who are cancer survivors, as their numbers are increasing significantly due to earlier detection and improved cancer therapies.⁸

Clinical Recommendations

1. Make a medical diagnosis for the cause of pain and accurately define its location. Promptly address new and worsening complaints and determine the cause. Always consider cancer recurrence or secondary malignancy in the differential diagnosis. See [Table 13](#) for signs and symptoms of spinal cord compression.
2. Follow the recommendations for treating chronic non-cancer pain once cancer recurrence has been ruled out as the source of pain. This includes using multimodal and interdisciplinary approaches and reducing the opioid dose (if indicated) to the lowest effective levels for pain complaints that remain stable ([Reducing or Discontinuing COAT](#)).
3. Educate survivors about the cause of their pain and the role of opioids in managing chronic cancer-related pain, and discuss the risks and benefits of COAT.
4. Encourage the use of non-pharmacologic therapies with a focus on rehabilitation and pain management. This may include a graduated exercise program, physical therapy, thermal therapy, complementary and alternative measures, and counseling to help with anxiety, depression, and coping ([Non-opioid Options](#)).
5. Use an individualized approach to pain management, paying special attention to those who are hypervigilant about their body sensations and may present with frequent reports of new symptoms. Careful assessment of complaints and review of surveillance testing may help alleviate the survivors' concerns.
6. Be alert to survivors' fear of cancer recurrence, as this commonly underlies pain behaviors. Reassure and redirect them after a thorough evaluation of the pain complaint, and consultation with the oncologist as appropriate.
7. Encourage survivors to actively engage in their pain management plan and to explore options to participate in support groups. An essential component to this is for the clinician to provide a detailed explanation to the patient on the cause or causes of the pain complaint.

During active cancer treatment, patients may have been accustomed to frequently changing and/or escalating opioid doses with any complaint of worsening pain intensity. The survivor with CCRP may be surprised when their provider not only declines to escalate an opioid dose, but instead initiates a slow taper once remission and functional goals have been achieved. Significant education is needed to assist the patient and caregiver to understand this new approach.⁹

Evidence

Chronic cancer-related pain (CCRP) is common in cancer survivors, with an overall incidence of 33% to 40%.^{8,306,307} One study found that 16-73% of breast cancer survivors experience pain, as well as a significant symptom burden of psychological distress and insomnia.³⁰⁸ Survivors younger than 50 years of age report more pain than older patients.³⁰⁹ CCRP typically is more common and more severe in the first few years after completing treatment, then declines in intensity as time passes.³⁰⁷ The Childhood Cancer Survivor Study reported 11% of adult survivors (mean interval from diagnosis 17 years) experienced medium or higher pain intensity;³¹⁰ and 6% of Australian adult cancer survivors at 5-6 years post treatment reported moderate to severe pain.³¹¹ However, certain *late effects* of therapy may emerge or persist for years, or even decades, after completing therapy, such as radiation related plexopathies or fibrosis, producing discomfort, pain, reduced range of motion (ROM) and impacting quality of life.³¹²

Unlike CNCP, identifiable tissue damage caused by the tumor or, more commonly, the cancer treatment, is typically the basis of the pain complaint.³⁰⁷ Examples include painful chemotherapy-induced peripheral neuropathy (CIPN) or post radiation therapy fibrosis, scarring of somatic structures, or tumor-related vertebral compression fractures (e.g. from treated myelomatous lesions). Certain pharmacological therapies can cause lasting pain problems during use, for instance, aromatase inhibitors such as anastrozole, exemestane, and letrozole that are used to prevent recurrence of breast cancer and are taken for variable periods (2-10 years) after completing initial therapy. Nearly half of women using these agents may experience myalgias and arthralgias,³¹³ which may be of enough severity that 21-38% of patients abandon this potentially life-saving therapy³¹⁴ ([Table 11](#)).

Table 11. Common Pain Syndromes Resulting from Cancer Treatment*

| |
|--|
| Chemotherapy-induced peripheral neuropathy (CIPN) |
| Myalgias and arthralgias from aromatase inhibitors in breast cancer survivors |
| Generalized myofascial pain from deconditioning or sleep disorders |
| Post-operative neuropathic pain syndromes such as post-mastectomy, post-amputation, post-radical neck pain |
| Chronic pain from radiation therapy such as muscle fibrosis, plexopathies, lymphedema, and chronic proctitis, cystitis, enteritis, or tenesmus from pelvic radiation |

*For a more extensive description of chronic pain syndromes, the types of cancers they are associated with, along with causes and treatment options, ([Appendix E: Chronic Pain Syndromes in Cancer Survivors](#)).

Chronic cancer-related pain in the survivor can improve significantly with a variety of pharmacological and non-pharmacological therapies. Pain treatments in the survivor should be modeled after chronic non-cancer pain strategies, rather than palliative therapies. In most patients, the primary goal of therapy is functional improvement rather than exclusively a reduction in pain intensity.³¹⁵

Opioids are the foundation for pain management when cancer is an active disease. Although it may often be appropriate to continue opioids in survivors, use of COAT should generally follow the guidelines for CNCP that focus on accurate diagnosis of the components of the pain complaint, and establishing patient-specific functional goals. In cancer survivors, as in CNCP, neuromodulators for neuropathic pain, such as serotonin-norepinephrine reuptake inhibitors (SNRIs), show evidence of benefit, particularly for CIPN caused by taxanes and platinum derivatives.³¹⁶ Tricyclic antidepressants and anticonvulsants continue to be recommended on the basis of efficacy data in other neuropathic pain conditions that are well established for various CNCP complaints.^{317 8} However, it should be noted that efficacy of these agents has not been established in cancer survivors.

Topical agents, such as lidocaine 5% patch, capsaicin cream, or diclofenac gel may be helpful for some post-surgical pain syndromes of cutaneous or myofascial origin. Persistent severe CIPN or radiation-induced fibrosis affecting range of motion, particularly in the head, neck, and shoulder regions, may merit ongoing opioid therapy, and in such situations may be the primary agent of choice.

Non-pharmacological therapies are important strategies in the management of CCRP. Physical therapy, rehabilitation, and graded exercise programs will help reverse deconditioning and functional loss commonly experienced during cancer treatment. Specialized therapy such as manual lymphatic drainage for lymphedema will improve discomfort from swelling. Counseling for anxiety, depression, and pervasive fear of cancer recurrence is beneficial; as is mindfulness training and other cognitive behavioral strategies to reduce pain. Sleep hygiene education is essential for pain management, as sleep disruption is common in this population.³¹³ Traditional sleep-inducing agents such as zolpidem are not recommended for long-term use.

All new or worsening pain in the cancer survivor must be promptly evaluated to eliminate the possibility of cancer recurrence as the source of pain. Consultation with the patient's oncologist is recommended to provide guidance as needed.

Recurrent or Secondary Malignancy

Most survivors struggle with a fear of cancer recurrence, and are well aware that pain may be an initial symptom.³¹³ The clinician should provide reassurance that all new or worsening pain problems will be assessed and appropriately investigated to eliminate cancer as the cause. Extensive emotional support may be needed, and formal counseling with supportive services may be required to assist with anxiety related to the potential for cancer recurrence.^{300,318}

The oncologist will direct surveillance screening, either through his/her office, or guide the primary care provider through the Cancer Treatment Summary and Survivorship Care Plan.³¹⁹⁻³²¹ However, it is

essential that all providers involved in the care of cancer survivors know the signs and symptoms associated with cancer, whether from recurrence or secondary malignancy ([Table 12](#)). In many situations, pain may be the only presenting symptom of recurrence, and it is essential that clinicians closely monitor and assess this complaint.

Table 12. Signs and Symptoms Associated with Recurrence of Malignancy ^{313 300 322}

| |
|--|
| New or worsening pain |
| Unexplained and unintentional weight loss of 10 pounds (4.5 kg) |
| Night sweats |
| Fever and chills |
| Enlarging masses |
| Unusual fatigue |
| Excessive bruising or bleeding |
| Change in moles or skin lesions |
| Altered bowel function |
| Persistent cough or hoarseness |
| Signs of breast cancer recurrence include: new lumps or skin changes in breast or axilla; new dyspnea; persistent headache; new bone, chest, or abdominal pain |

Cancer may occasionally present as metastatic disease with spread to the vertebrae, and in advanced cases, cause spinal cord compression. The most common disease types where this may occur are lung, breast and prostate cancer. Symptoms include: ([Table 13](#)).

Table 13. Signs and Symptoms of Spinal Cord Compression ^{300,322-324}

| | |
|---|--|
| New onset of severe back pain | <ul style="list-style-type: none"> • Thoracic spine is most common site • Pain may be localized to 1-2 vertebrae or be diffuse • Worse at night and with recumbency • Worse with Valsalva maneuver such as occurs with bowel movements • May present as a “band” of pain or numbness around the torso |
| New weakness in the limbs | May be described as “clumsiness” or “heaviness” of the limbs |
| New sensory changes in the limbs | Paresthesias, dysesthesias, lancinating pain |
| Loss of bowel or bladder control | Urinary retention causing overflow incontinence, or fecal incontinence from loss of anal sphincter tone |
| Saddle anesthesia | Numbness in perineum, lower buttocks, posterior proximal thighs |

Part VIII. Appendices

| | |
|--|----|
| Appendix A: Opioid Dose Calculations | 55 |
| Appendix B: Validated Tools for Screening and Assessment | 59 |
| Appendix C: How to use the Prescription Monitoring Program | 60 |
| Appendix D: Urine Drug Testing for Monitoring Opioid Therapy | 62 |
| Appendix E: Chronic Pain Syndromes in Cancer Survivors | 72 |
| Appendix F: Diagnosis-based Pharmacotherapy for Pain and Associated Conditions | 74 |
| Appendix G: Patient Education Resources | 76 |
| Appendix H: Clinical Tools and Resources | 78 |
| Appendix I: Guideline Development and AGREE II Criteria | 81 |

Appendix A: Opioid Dose Calculations

Table 14. Dosing Threshold for Selected Opioids

| Opioid | Recommended dose threshold for pain consult | Recommended starting dose | Considerations |
|----------------------------------|---|--|---|
| Buprenorphine Transdermal | Threshold is beyond maximum daily dose | 5 mcg/hr q 7 days | Maximum dose: 20 mcg/hr due to risk of QTc prolongation |
| Codeine | 800 mg per 24 hours | 30 mg q 4–6 hours | See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. |
| Fentanyl Transdermal | 50 mcg/hour q 72 hours | 12.5 mcg/hour q 72 hours | Use only in opioid-tolerant patients who have been taking ≥60 mg MED daily for a week or longer. |
| Hydrocodone | 120 mg per 24 hours | Immediate Release 5-10 mg q 4–6 hours | See individual product labeling for maximum dosing of combination products. Avoid concurrent use of any OTC products containing same ingredient. |
| | | Sustained Release 10 mg q 12 hours | Use ER formulation with extreme caution due to potentially fatal interaction with alcohol or medications containing alcohol. |
| Hydromorphone | 30 mg per 24 hours | Immediate Release 2 mg q 4–6 hours | Because of its short half-life, hydromorphone is a good choice in older adults with renal impairment. |
| | | Sustained Release 8 mg q 24 hours | |
| Morphine | 120 mg per 24 hours | Immediate Release: 10 mg q 4 hours | Metabolites may accumulate in patients with impaired renal or hepatic function resulting in prolonged effects and toxicity. |
| | | Sustained Release: 15 mg q 12 hours | Use Avinza with extreme caution due to potentially fatal interaction with alcohol or medications containing alcohol. |
| Oxycodone | 80 mg per 24 hours | Immediate Release: 5 mg q 4–6 hours | See individual product labeling for maximum dosing of acetaminophen combination products. Avoid concurrent use of any OTC acetaminophen products. |
| | | Sustained Release: 10 mg q 12 hours | |

| Opioid | Recommended dose threshold for pain consult | Recommended starting dose | Considerations |
|-------------|---|---|--|
| Oxymorphone | 40 mg per 24 hours | Immediate Release: 5–10 mg q 4–6 hours | Use ER formulation with extreme caution due to potentially fatal interaction with alcohol or medications containing alcohol. |
| | | Sustained Release: 10 mg q 12 hours | |
| Tapentadol | 300 mg per 24 hours | Immediate Release 50 mg q 4-6 hours | Dual mechanism of action - binds to mu-opioid receptors and inhibits reuptake of norepinephrine. Use caution when combining with other medications that affect serotonin as it may increase risk of seizures and serotonin syndrome. Do not exceed 600 mg/day for immediate release and 500 mg/day for sustained release formulation. |
| | | Sustained Release 50 mg q 12 hours | |
| Tramadol | Threshold is beyond maximum daily dose | Immediate Release 50 mg q 4-6 hours | Dual mechanism of action - binds to mu-opioid receptors and inhibits reuptake of serotonin and norepinephrine. Use caution when combining with other medications that affect serotonin as it may increase risk of seizures and serotonin syndrome. Do not exceed 400 mg/day for immediate release and 300 mg/day for sustained release formulation. |
| | | Sustained Release 100 mg q 24 hours | |

*Meperidine should not be prescribed for chronic pain.

**Methadone should only be prescribed for chronic pain if the provider is knowledgeable of methadone’s non-linear pharmacokinetics, unpredictable clearance, multiple drug-to-drug interactions and additional monitoring requirements.

***Long-acting formulations should only be prescribed for opioid-tolerant patients who have been taking ≥60 mg MED daily for a week or longer

Morphine Equivalent Dose Table

All conversions between opioids are estimates generally based on equianalgesic dose. Patient variability in response to different opioids can be large, due primarily to genetic factors and incomplete cross-tolerance. **It is recommended that, after calculating the appropriate conversion dose, it be reduced by 25–50% to assure patient safety.**

Table 15. MED for Selected Opioids

| Opioid | Approximate Equianalgesic Dose (oral & transdermal) * |
|-----------------------------|---|
| Morphine (reference) | 30 mg |
| Codeine | 200 mg |
| Fentanyl transdermal | 12.5 mcg/hr |
| Hydrocodone | 30 mg |
| Hydromorphone | 7.5 mg |
| Oxycodone | 20 mg |
| Oxymorphone | 10 mg |
| Tapentadol | 75 mg |
| Tramadol | 300 mg |

*Adapted from Von Korff 2008 & FDA labeling

Table 16. MED for Methadone

| Chronic Methadone Dose | Approximate Conversion Factors to Morphine Equivalent* |
|------------------------|--|
| Up to 20 mg per day | 4 |
| 21 to 40 mg per day | 8 |
| 41 to 60 mg per day | 10 |
| >60 mg per day | 12 |

*Adapted from Ayonrinde 2000. Equianalgesic dose ratios between methadone and other opioids are complex. Methadone exhibits a non-linear relationship due to the long half-life and accumulation with chronic dosing. Because methadone pharmacokinetics are variable across patient populations, these conversion factors are approximate and doses around the cutoff can have huge differences in calculated MED.

Calculating Morphine Equivalent Dose

This guideline provides an electronic [morphine equivalent dose \(MED\) calculator](#) for determining a patient's daily morphine equivalent dose when patients are on one or more opioids. Table 17 below shows samples of morphine equivalents that can be computed using the calculator.

Table 17. Morphine Equivalent Dose Calculation

For patients taking more than one opioid, the morphine equivalent doses of the different opioids must be added together to determine the cumulative dose ([Table 15](#)). For example, if a patient takes six hydrocodone 5 mg / acetaminophen 500 mg and two 20 mg oxycodone extended release tablets per day, the cumulative dose may be calculated as follows:

1. Hydrocodone 5 mg x 6 tablets per day = 30 mg per day.
2. Using the Equianalgesic Dose table in Appendix A, 30 mg Hydrocodone = 30 mg morphine equivalents.
3. Oxycodone 20 mg x 2 tablets per day = 40 mg per day.
4. Per Equianalgesic Dose table, 20 mg oxycodone = 30 mg morphine so 40 mg oxycodone = 60 mg morphine equivalents.
5. Cumulative dose is 30 mg + 60 mg = 90 mg morphine equivalents per day.

Appendix B: Validated Tools for Screening and Assessment

| | Tool Characteristics | | | |
|---|----------------------------------|------------------|----------------------|------------------------------|
| | Administration | Time to Complete | Length | Access Limitations |
| Assessing Function and Pain | | | | |
| Pain, Enjoyment of life, General Activity (PEG) http://mytopcare.org/wp-content/uploads/2013/06/PEG-Pain-Screening-Tool1.pdf | Patient self-report | 1 minute | 3 items | |
| Two Item Chronic Pain Scale | Clinician or patient self-report | 1 minute | 2 items | |
| Risk of Transitioning to Chronic Pain | | | | |
| STarTBack http://www.keele.ac.uk/sbst/startbacktool/ | Patient self-report | <5 minutes | 9 items | |
| Functional Recovery Questionnaire (FRQ) | Clinician or patient self-report | <5 minutes | 6 items | Requires email registration |
| Screening for Risk of Opioid Addiction and Substance Abuse | | | | |
| Opioid Risk Tool (ORT) ³²⁵ | Clinician or patient self-report | 1 minute | 5 (yes/no) questions | |
| CAGE Adapted to Include Drugs (CAGE-AID) ³²⁶⁻³²⁸ | Clinician | <5 minutes | 4 (yes/no) questions | |
| Screener and Opioid Assessment for Patients with Pain - Revised (SOAPP-R) www.painedu.org/soapp.asp | Patient self-report | <10 minutes | 24 items | Requires licensing agreement |
| Current Opioid Misuse Measure (COMM) www.painedu.org/soapp.asp | Patient self-report | <10 minutes | 17 items | Requires licensing agreement |
| DIRE http://integratedcare-nw.org/DIRE_score.pdf | Clinician interview | <2 minutes | 7 items | |
| Alcohol Use Disorders Identification Test (AUDIT) | Clinician or patient self-report | <5 minutes | 10 items | |
| Screening for Mental Health Disorders | | | | |
| Patient Health Questionnaire 9 (PHQ-9) | Patient self-report | <5 minutes | 10 items | |
| GAD-7 http://www.mpho.org/resource/d/34008/GAD708.19.08Cartwright.pdf | Patient self-report | <5 minutes | 7 items | |
| PC-PTSD | Clinician interview | <5 minutes | 4 items | |

*Except for the FRQ, all of the free, publicly available tools listed in this table have demonstrated good content, face, and construct validity in screening for risk of addiction and monitoring opioid therapy. Further validation studies and prospective outcome studies are needed to determine how the use of these tools predicts and affects clinical outcomes.

Appendix C: How to use the Prescription Monitoring Program

Chris Baumgartner, BS, Prescription Drug Monitoring Program Director
Washington State Department of Health

Prescription Drug Monitoring Programs (PDMPs or PMPs) are now operating in 49 states, and have demonstrated their value on many levels.³²⁹⁻³³³ In Washington State, the Prescription Monitoring Program (PMP) is also known as [Prescription Review](#). This database contains the history of all controlled substances dispensed by Washington licensed facilities and providers since implementation in October 2011. The PMP offers key clinical benefits, such as identifying duplicative drug therapy, dangerous drug combinations, other providers involved in the patient’s care, signs of aberrant behaviors and possible misuse, and patient’s medication compliance. Providers or their qualified delegated staff should access the PMP before prescribing and as part of ongoing monitoring of treatment with controlled substances. The PMP is an important tool for providers to improve patient care and prevent opioid misuse when prescribing controlled substances.

How to Access the PMP

Providers can register for access online at www.wapmp.org and the system is available 24/7. For PMP system or program assistance please refer to:

PMP System Help Desk:
Health Information Designs
P.O. Box 529 | Auburn, Alabama 36831
Phone: 877-719-3121
Email: wapmp-info@hidinc.com

Washington State Department of Health
P.O. Box 47852 | Olympia, Washington 98504-7852
Phone: 360-236-4806
Email: prescriptionmonitoring@doh.wa.gov

Additional information, including FAQs, can be found at the [Department of Health’s PMP website](#).

Recommendations for Integrating the PMP into Practice

- Assign someone in your organization the responsibility of ensuring all prescribing and dispensing providers register for access.
- Have all prescribers and dispensers register for master accounts. Prescribers can delegate their authority to licensed staff (e.g. nurses and medical assistants if they register for their own sub-accounts and are linked to the master accounts).
- Request PMP information as appropriate prior to patient visits and place a copy of the report in the patient’s medical chart.
- Consider training someone as a “PMP Champion,” or “Super-User,” who develops system expertise and can help train new staff or assist with questions.

When to Check the PMP

- Prior to prescribing opioids for a new episode of pain or for transferred patients who are already using opioids.
- During the transition from subacute to COAT.
- Routinely for patients for whom you are prescribing chronic opioids and/or other controlled substances ([Table 18](#)).
- Regularly for patients who are being treated for addiction disorder.
- When conducting a preoperative history and medical exam.
- When there is evidence of aberrant behaviors ([Table 9](#)). Address aberrant behaviors in person, not by telephone.

Table 18. Recommended Frequency of PMP Checks during COAT

| Risk Category | Recommended Frequency |
|---|-----------------------|
| Low risk | At least 1/year |
| Moderate risk | At least 2/year |
| High risk or opioid doses >120 mg/day MED | At least 3–4/year |

Interpreting a PMP Report

Providers should access and review the PMP as part of their complete assessment of the patient when prescribing controlled substances, including opioids, for an acute episode or chronic therapy:

- Keep in mind that there could be up to a 2-week lag time for dispensing information, so recently dispensed controlled substances may not be reflected in the PMP report. Also, the PMP database does not contain information from the Department of Defense and Opioid Treatment Programs.
- Compare the PMP report against your medical records. Any discrepancies should be reconciled with the dispensing pharmacy.
- Estimate the patient’s controlled substance consumption with “as needed” or PRN use by reviewing the prescription dispensed dates.
- Coordinate care, which may include requesting medical records, when multiple prescribers are identified on the PMP report.
- Discuss in person with the patient when aberrant behaviors (e.g. early refills) or dangerous combinations of opioids with benzodiazepines, sedative-hypnotics and/or carisoprodol are identified on the PMP report. Provide patient education on the [safe use of controlled substances](#).
- Confirm the patient is taking medication as prescribed.

If the PMP report reveals concerns such as aberrant behaviors, dangerous drug combinations or multiple prescribers, the provider should follow the clinical recommendations in the sections: [Reducing or Discontinuing Opioids](#) or [Opioid Use Disorder](#) and take appropriate actions.

Appendix D: Urine Drug Testing for Monitoring Opioid Therapy

- [i. Using Urine Drug Testing \(UDT\) to Monitor Opioid Therapy for Chronic Non-cancer Pain](#) 63
- [ii. UDT Algorithm for Monitoring Opioid Therapy](#) 67
- [iii. UDT Clinical Vignettes in Chronic Non-cancer Pain](#) 68
- [iv. UDT Frequently Asked Questions \(FAQ\)](#)..... 70

i. Using Urine Drug Testing (UDT) to Monitor Opioid Therapy for Chronic Non-cancer Pain ³³⁴⁻³³⁶

The purpose of drug testing is to identify aberrant behavior, undisclosed drug use and/or abuse and verify compliance with treatment. If a decision has been made to prescribe opioids for chronic non-cancer pain, the prescriber should get a baseline UDT and screen all patients for risk level to develop an appropriate monitoring plan as well as a basis for consultation or referral. Although UDT and other screening tools are helpful in identifying aberrant behavior, it is also important for prescribers to use their clinical judgment in the development of a monitoring plan. The Prescriber should repeat random UDT based on the patient’s risk category. There are several validated screening tools available to assess risk of aberrant behavior. The Opioid Risk Tool (ORT) provides a brief questionnaire that can easily be used in the primary care setting ([Appendix B](#)).

Prior to drug testing, the prescriber should inform the patient of the reason for testing, frequency of testing and consequences of unexpected results. This gives the patient an opportunity to disclose drug use and allows the prescriber to modify the drug screen for the individual circumstances and more accurately interpret the results.

| Risk Category | UDT Frequency | Drugs or Drug Classes to Test | Consideration |
|---|--|--|---|
| Low Risk | 1/year | <ul style="list-style-type: none"> • Drug you are prescribing if not listed • Amphetamines • Opioids • Cocaine • Benzodiazepines • Alcohol | Typically, the initial (screening) drug test uses an immunoassay method to identify the presence of a drug (presumptive positive). Because of cross-reactivity and different sensitivity and specificity between immunoassays, a second confirmatory test is required unless result is expected or the patient has disclosed drug use. Confirmatory drug tests use gas chromatography/mass spectrometry or liquid chromatography/tandem mass spectrometry (GC/MS or LC/MS/MS) to verify a presumptive positive result. |
| Moderate Risk | 2/year | <ul style="list-style-type: none"> • Barbiturates • Oxycodone • Methadone • Fentanyl • Marijuana | |
| High Risk or opioid doses >120 mg MED/d | 3-4/year | | |
| Aberrant Behavior (lost prescriptions, multiple requests for early refills, opioids from multiple providers, unauthorized dose escalation, apparent intoxication, etc.) | At time of visit (Address aberrant behaviors in person, not by telephone) | Testing for all drug classes may not be necessary, depending on clinical situation. | <p>Contact the laboratory director, toxicologist or a certified Medical Review Officer (MRO) in your area for questions about drug testing or result.</p> <p>If a point-of-care (POC) device is used, contact technical support from the manufacturer for questions.</p> |

UDT Results

Interpreting UDT results can be challenging, especially when the parent drug can be metabolized to other commonly prescribed drugs. The table on the next page may aid prescribers when interpreting UDT results. The following UDT results should be viewed as a “red flag”, requiring confirmation and intervention:

- Negative for opioid(s) you prescribed
- Positive for drug (benzodiazepines, opioids, etc.) you did NOT prescribe or have knowledge of
- Positive for amphetamine or methamphetamine
- Positive for alcohol
- Positive for cocaine or metabolites

If a **confirmatory drug test** substantiates a “red flag” result AND is:

- **Positive for prescribed opioid(s)**, prescriber should consider a controlled taper and a referral to an addiction specialist or drug treatment program depending on the circumstances.
 - **Negative for prescribed opioid(s)**, prescriber should stop prescribing opioid(s) and consider a referral to an addiction specialist or drug treatment program depending on the circumstances.
-

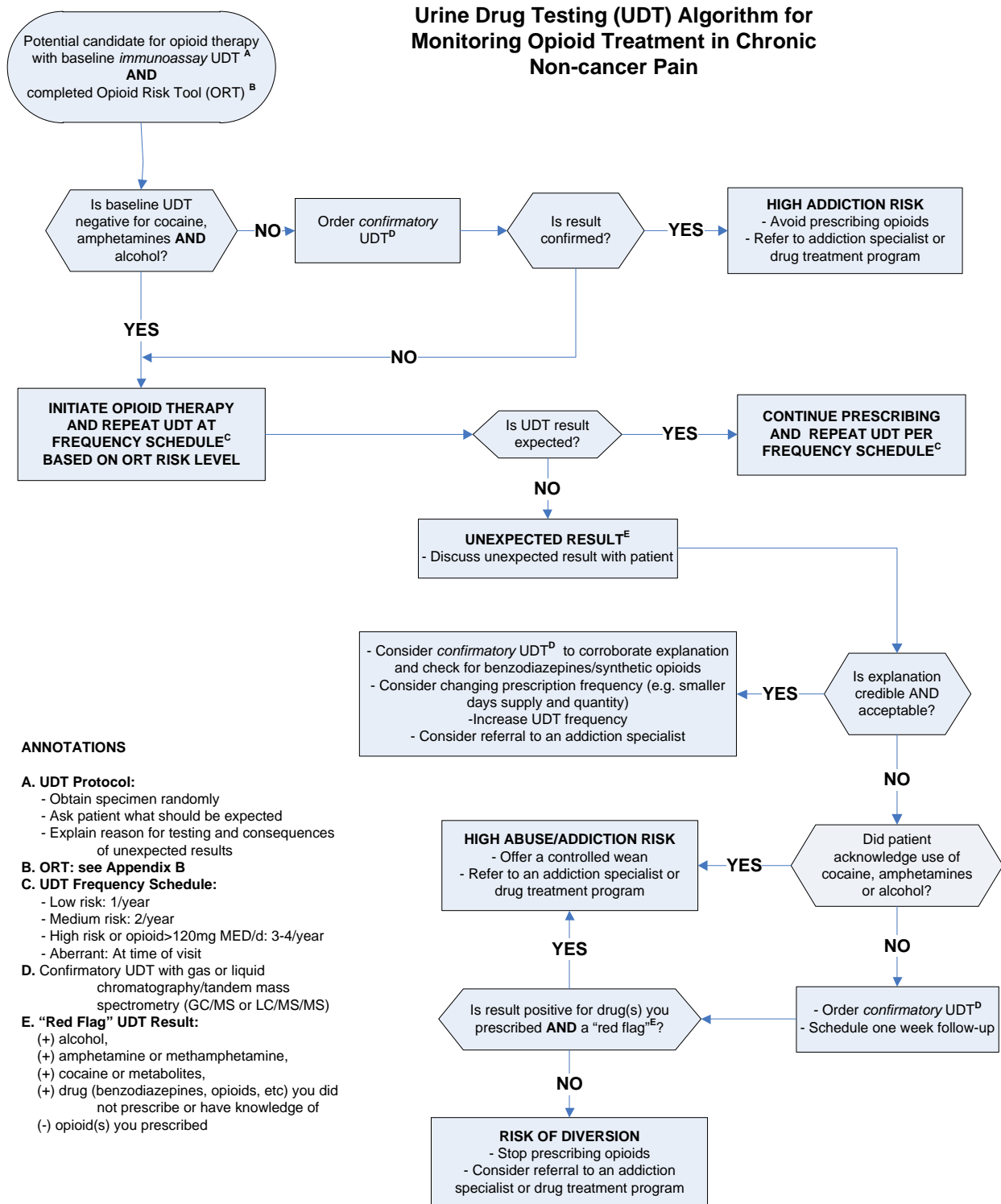
| Drugs or Drug Classes | Detection Time in Urine* | Test to Order | Expected Results | Consideration |
|--|--------------------------|--|--|---|
| Opioids or “opiates” – Natural (from opium) | | | | |
| Codeine (Tylenol #2/3/4) | 1-3 days | Opiates Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates Immunoassay – positive GC/MS or LC/MS/MS – codeine, possibly morphine & hydrocodone | Immunoassays for “opiates” are responsive for morphine and codeine but do not distinguish which is present. Confirmatory testing is required to reliably identify drug(s) present. Since codeine is metabolized to morphine and small quantities to hydrocodone, these drugs may be found in the urine. Also, morphine may metabolize to produce a small amount (<10%) of hydromorphone. |
| Morphine (Avinza, Embeda, MS Contin, Kadian) | 1-3 days | | Opiates Immunoassay – positive GC/MS or LC/MS/MS – morphine, possibly hydromorphone | |
| Opioids – Semisynthetic (derived from opium) | | | | |
| Hydrocodone (Lorcet, Lortab, Norco, Vicodin, Zohydro, Hysingla) | 1-3 days | Opiates Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates Immunoassay – positive GC/MS or LC/MS/MS – hydrocodone, possibly hydromorphone | “Opiates” immunoassays may also detect semisynthetic opioids depending on their cross-reactivity pattern. However, a negative result does not exclude use of semisynthetic opioids. Confirmatory testing (GC/MS or LC/MS/MS) is required to verify compliance with the prescribed semisynthetic opioid(s). |
| Hydromorphone (Dilaudid, Exalgo) | 1-3 days | Opiates Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates Immunoassay – positive GC/MS or LC/MS/MS –hydromorphone | |
| Oxycodone (Roxicet, OxyContin, Percocet, Targiniq) | 1-3 days | Oxycodone Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates Immunoassay – positive GC/MS or LC/MS/MS – oxycodone possibly oxymorphone | Since hydrocodone is metabolized in small amounts to hydromorphone, both may be found in the urine. Likewise, oxycodone is metabolized to oxymorphone, so these may both be present in the urine of oxycodone users. However, the reverse is not true. In other words, hydromorphone and oxymorphone use does not result in positive screens for hydrocodone and oxycodone, respectively. |
| Oxymorphone (Opana) | 1-3 days | Opiates or Oxycodone Immunoassay + GC/MS or LC/MS/MS Opiates | Opiates or Oxycodone Immunoassay – positive GC/MS or LC/MS/MS – oxymorphone | |
| Opioids – Synthetic (man-made) | | | | |
| Fentanyl (Duragesic) | 1-3 days | GC/MS or LC/MS/MS Fentanyl | GC/MS or LC/MS/MS – fentanyl & norfentanyl | Current “opiates” immunoassays do not detect synthetic opioids. Thus confirmatory testing (GC/MS or LC/MS/MS) is needed to identify these drugs. If the purpose is to document compliance with treatment, the laboratory can be instructed to remove the cutoff concentration so that the presence of lower concentrations can be identified. |
| Meperidine (Demerol) | 1-3 days | GC/MS or LC/MS/MS Meperidine | GC/MS or LC/MS/MS – normeperidine, possibly meperidine | |
| Methadone (Methadose) | 3-7 days | Methadone Immunoassay + GC/MS or LC/MS/MS Methadone | Methadone Immunoassay – positive GC/MS or LC/MS/MS – methadone & EDDP | |

| Drugs or Drug Classes | Detection Time in Urine* | Test to Order | Expected Results | Consideration |
|----------------------------|--|---|--|---|
| Others | | | | |
| Alcohol | Up to 8 hours | Alcohol | Alcohol – see Consideration | Additional testing for alcohol metabolites, ethyl glucuronide (EtG) or ethyl sulfate (EtS), can identify alcohol up to 80 hours after consumption. |
| Amphetamines | 2-3 days | Amphetamines, Methamphetamines or MDMA Immunoassay + GC/MS or LC/MS/MS Amphetamines | Amphetamines, methamphetamines or MDMA Immunoassay – see Consideration GC/MS or LC/MS/MS – amphetamine, methamphetamine or MDMA | Amphetamines immunoassays are highly cross-reactive so results should be interpreted cautiously, and may require consultation with the lab. They may detect other sympathomimetic amines, such as ephedrine, pseudoephedrine or selegiline. Confirmatory testing can identify which amphetamine is present. |
| Barbiturates | 1-3 days w/short-acting; up to 30 days w/long acting | Barbiturates Immunoassay | Barbiturates Immunoassay – see Consideration | The clearance half-life of intermediate-acting barbiturates averages 24 hours. It takes about 5 to 7 half-lives to clear 98% of a drug dose. Thus, the presence of an intermediated-acting barbiturate indicates exposure within 5-7 days. |
| Benzodiazepines | 1-3 days w/short-acting; up to 30 days w/long-acting | Benzodiazepines Immunoassay | Benzodiazepines Immunoassay – see Consideration GC/MS or LC/MS/MS – alprazolam, diazepam, clonazepam, lorazepam, etc. | Immunoassays for benzodiazepines have a 28% overall false negative rate and vary in cross-reactivity. Certain benzodiazepines (clonazepam and alprazolam) have limited detectability by most available immunoassays. Confirmatory testing is needed when use is expected or suspected. |
| Cocaine or benzoylecgonine | 2-4 days | Cocaine Metabolites Immunoassay | Cocaine Metabolites Immunoassay – see Consideration | Cocaine immunoassays do not cross-react with other topical anesthetics that end in “caine” (e.g. lidocaine) and are highly specific for cocaine use. |
| Marijuana | 2-4 days; up to 30 days w/chronic heavy use | Cannabinoids (THC) Immunoassay | Cannabinoids Immunoassay – see Consideration GC/MS or LC/MS/MS – THC | THC may be an indicator of the patient’s risk category. Prescribers should have an office policy, discuss with the patients reason for use and adjust monitoring plan accordingly. |

*detection time for most drugs depends on the drug, dose, frequency of use and individual metabolism

ii. UDT Algorithm for Monitoring Opioid Therapy

Figure E: UDT Algorithm for Monitoring COAT for CNCP



iii. UDT Clinical Vignettes in Chronic Non-cancer Pain

| Case Studies | Discussion |
|---|---|
| <p>New Patient: A 31-year-old female with low back pain from an injury 2 months ago. She wants to establish care. According to the patient, she was initially prescribed naproxen and hydrocodone in the emergency room. She is currently taking naproxen OTC, but no reported opioids. Her other medical conditions include depression for which she takes citalopram. You are considering prescribing opioid(s) and your suspicion for drug abuse is low. What should you do?</p> | <p>IF you have decided to initiate chronic opioid therapy AND prior to prescribing, you should:</p> <ol style="list-style-type: none"> 1. Obtain a baseline UDT; 2. Assess risk of aberrant behavior with ORT; 3. Assess psychiatric status (e.g. PHQ-9); 4. Obtain a signed opioid agreement; 5. Establish treatment goals including improvements in both function and pain; 6. Describe expectations for behavior related to use of opioids (take as prescribed, use one pharmacy, one prescriber, no early refills, no self-escalation, no sharing of drugs, etc.) 7. Develop a follow-up plan to monitor treatment, including the frequency of UDT's based on ORT |
| <p>New Patient on Opioids: A 45-year-old male presents with severe neck pain from a motor vehicle accident 2 years ago. He has been treated with OxyContin 30 mg BID and oxycodone 5 mg 1 tab Q3h PRN (MED = 150 mg/day). He reports no history of substance abuse. Due to "personality differences" with previous provider, he would like you to assume care and continue prescribing OxyContin and oxycodone for his neck pain. You have no medical records to confirm previous treatment. What should you do?</p> | <p>Do not prescribe opioids at initial visit since records are unavailable:</p> <ul style="list-style-type: none"> • Comprehensively evaluate the patient, • Order a baseline UDT, • Inform patient that a signed release of information form is required prior to prescribing opioids. Also request medical records from previous provider(s) or consider contacting the previous prescriber for information on treating this patient and • Schedule a follow-up visit for when UDT results and medical records are available. <p>On follow-up visit, if UDT is consistent and prior medical records show improved pain and function with no history of aberrant behaviors, follow steps 2–7 above before prescribing.</p> |
| <p>Compliance Testing in a patient on < 120 mg MED/day: A 55-year-old male with chronic knee pain comes in for a routine visit. His opioid regimen consists of methadone 5 mg QID and hydrocodone/acetaminophen 5/500 mg 1 tab Q6h PRN (MED = 100 mg/day). He has moderate risk on ORT and last random UDT was a year ago. What should you do?</p> | <p>Assess the risks and benefits of current opioids. Discuss with the patient reason for testing, frequency of testing and consequences of unexpected results, order an immunoassay test for the drug classes below, and follow the UDT algorithm.</p> <ul style="list-style-type: none"> • Amphetamines • Opiates • Cocaine metabolites • Methadone • Benzodiazepines • Alcohol metabolites • Oxycodone |
| <p>Unexpected Results: The immunoassays from the above vignette were positive for methadone, opiates and cocaine metabolites but negative for the remainder of the drug classes tested. Confirmatory testing with GC/MS was done per laboratory protocol. The confirmatory results show methadone, hydrocodone and benzoyllecgonine (cocaine metabolite). What should you do?</p> | <p>Discuss the unexpected results with the patient and offer a controlled taper and referral to an addiction specialist.</p> |

| Case Studies | Discussion |
|--|---|
| <p>Point of Care Testing: A 47-year-old male with rotator cuff tendonitis has chronic shoulder pain managed with morphine SR 30 mg TID and oxycodone/acetaminophen 5/325 mg 1 tab Q4h PRN (MED = 135 mg/day). He reports no other drug therapy. A treatment agreement has been signed by you and the patient recently. You perform a random UDT using a point-of-care testing kit. The immunoassays are positive for opiates but also positive for benzodiazepines. What should you do?</p> | <p>Discuss the unexpected results with the patient:</p> <ul style="list-style-type: none"> • If explanation is credible (e.g. receiving treatment for anxiety from another provider), you may want to send the urine sample to laboratory to confirm his story. You may also want to discuss future expectations with the patient and request records from other treating providers for possible specialty consultation. • If explanation is not accepted (e.g. patient admits benzodiazepine use that is not prescribed for the patient), confirmatory testing is not necessary but offer a controlled taper and/or referral to an addiction specialist depending on the circumstances. • If result cannot be explained, send original urine sample to laboratory for confirmatory testing. |

iv. UDT Frequently Asked Questions (FAQ)

Q **Drug screening implies that I don't trust my patients. How do I get around this?**

A Self-report of drug use has limited validity, and monitoring behavior alone can fail to detect problems revealed by UDTs. Creating a UDT policy in advance and applying it consistently to all patients on opioids may help de-stigmatize the testing. Inform patients that drug testing is a routine procedure for all patients starting or maintained on opioid therapy and it is an important tool for monitoring the safety of opioid therapy. Possible language for explaining to patient includes:

- “Ensures my capacity to provide treatment for your pain while balancing the need for safety.”
- “Provides critical information needed to assess the success of your therapy.”
- “Prescription medications are a common form of treatment for chronic pain. However, each person reacts differently to them. UDT enables us to identify individual risks related to your medications and avoid problems.”
- “Our clinic uses ‘universal precautions’ in opioid prescribing, which includes UDT. This is the same as wearing gloves on all patients when drawing blood.”

Q **Can I tell whether my patient has taken the dose of opioid(s) I prescribed?**

A No. It is very difficult to correlate urine drug concentration with a patient's dose. UDT can detect the parent drug and/or its metabolite(s) and demonstrate recent use of prescribed drugs and illegal substances. However, it CANNOT determine the amount of drug used and when the last dose was taken, nor can it identify the source of the drug.

Q **My patient says he is a “high metabolizer” and that is why the expected drug is not found in the urine. Is this possible?**

A A small percentage of persons are ultrarapid metabolizers. They metabolize specific drugs more rapidly than typical patients. It would be rare to take an opioid as prescribed and have a totally negative UDT. It is important that you use testing that is specific to the medication of interest and with cutoff thresholds that are extremely low.

Q **How do I deal with marijuana?**

A This is a complex issue. Marijuana is currently classified as a Schedule I drug by the DEA. For that reason, many providers will not prescribe opioids to patients using cannabis. Other providers reference State “Medical Marijuana” laws (<http://apps.leg.wa.gov/RCW/default.aspx?cite=69.51A&full=true>) and feel comfortable prescribing opioids to cannabis users. Some providers adopt a “don't ask, don't tell” policy, and request the lab to remove marijuana from the UDT so that positive results are not seen. Do your homework and create an office policy. Then disclose this policy to your patients.

Q **Would short-acting opioids show up in UDT?**

A Urine testing typically has a 1 to 3-day window of detection for most drugs depending on dose and individual differences in drug metabolism. Short-acting opioids can be detected if the lab removes the cutoff concentration so that the presence of lower concentrations is detected. If the laboratory uses LC/MS/MS, then it will have a lower limit of detection (LOD) with less interference.

Q Why confirm results?

A Immunoassays used in drug screening can cross-react with other drugs and vary in sensitivity and specificity. Thus, confirmation with a more accurate method may be required for clinical decision making. Confirmatory drug testing (GC/MS or LC/MS/MS) of the original specimen is recommended for unexpected results, or in cases where patients are known to be high risk. However, on occasion, even confirmatory testing requires expert assistance for interpretation. Consider consultation with the lab before discussing/confronting the patient with unexpected test results and discontinuing opioid therapy.

Q Should I use temperature and adulteration strips?

A It depends. Drug testing for clinical compliance, unlike employment testing, does not require a strict “chain-of-custody”. However, if tampering is a concern, the specimen should be monitored for temperature and/or adulterants. Normal human urine should have a temperature between 90°F – 100°F, pH between 4.5 – 8.5 and creatinine >20mg/dL. Be aware that there are multiple websites and devices devoted to getting a “clean” urine drug screen.

Q Should I perform a drug screen on every visit for patients using opioids for chronic pain?

A No. Random screening based on the frequency recommended in the guideline should suffice for most patients. Those patients who you feel require drug screening on every visit, are perhaps not candidates for chronic opioid therapy.

Appendix E: Chronic Pain Syndromes in Cancer Survivors

Sources: ^{322 337 307 313 338 339 340 8}

| Pain Syndrome | System | Type of Cancer | Cause of Pain | Treatment Options & Notes |
|---|------------------|---|--|---|
| Chemotherapy-induced peripheral neuropathy (CIPN) | Neurological | Breast Ovarian Colorectal Lymphoma Multiple myeloma | Vinca alkaloids (vincristine), platinum compounds (cisplatin), taxanes (paclitaxel), bortezomib | Antidepressant: SNRI: duloxetine TCAs: nortriptyline, desipramine Anticonvulsants: gabapentin, pregabalin Opioids PT/OT/ Rehabilitation CBT |
| Chronic post-operative neuropathic pain syndromes | Neurological | Breast Neck Lung Sarcoma | Post-mastectomy, post-radical neck, post-thoracotomy, post-amputation pain syndromes Neuroma | Antidepressant: SNRI: duloxetine TCAs: nortriptyline, desipramine Anticonvulsants: gabapentin, pregabalin Opioids Topical: lidocaine 5% patch, capsaicin cream PT/OT for ROM CBT |
| Chronic radiation fibrosis | Integumentary | Breast Neck | Long-term and late radiation effects (may develop years after completion of therapy). Fibrosis causes decreased ROM, tightness, discomfort | PT/OT Massage for myofascial release Trigger point injection Opioids |
| Lymphedema | Integumentary | Breast Pelvic tumors | Surgery or radiation may interfere with lymph drainage from affected limb; may be discomfort more than pain. | Compression garments PT for ROM Manual lymphatic drainage Diuretics are not helpful Opioids not likely to be helpful |
| Chronic arthralgias | Musculo-skeletal | Breast | Aromatase inhibitors, used to prevent recurrence of breast cancer, cause symmetrical pain aching or stiffness in shoulders, elbows, wrists, fingers, knees, ankles | Exercise PT/OT/Thermal/Rehabilitation Medicine Massage Acetaminophen NSAIDs Antidepressants: duloxetine, desipramine Anticonvulsants: pregabalin, gabapentin Change to another aromatase inhibitor For severe intensity, consider opioids primarily for functional improvement. |
| Scar pain from surgery or radiation | Integumentary | Breast All | Tissue fibrosis leading to pain and decreased ROM | Massage for scar release |

| Pain Syndrome | System | Type of Cancer | Cause of Pain | Treatment Options & Notes |
|------------------------------------|------------------|---|--|---|
| Myofascial pain | Musculo-skeletal | Hematopoietic cell transplant All cancers may cause myalgias and arthralgias from deconditioning | High dose corticosteroids High dose cyclophosphamide Deconditioning Radiation fibrosis | Exercise, aerobic, stretching and strengthening PT/OT/Rehabilitation Medicine Thermal Massage Acupuncture Acetaminophen NSAIDs Antidepressants: duloxetine, nortriptyline Anticonvulsants: gabapentin, pregabalin Topical: lidocaine 5% patch, capsaicin cream Trigger point injections For severe intensity, consider opioids only for validated and demonstrated functional improvement. |
| Vertebral compression fractures | Skeletal | Ovarian failure from chemotherapy or surgery, prostate, all cancers at risk, especially GYN, prostate, myeloma, hematopoietic cell transplant | Painful vertebral compression fractures | Opioids (acute) NSAIDs PT/Rehabilitation Weight bearing exercise (subacute & chronic) Bisphosphonates |
| Avascular necrosis of major joints | Skeletal | Hematopoietic cell transplant, especially unrelated donor allogeneic transplant Acute lymphoblastic leukemia | High dose steroids can lead to painful (aseptic) degeneration of joint of such severity that joint replacement may be required in young adults | Opioids Exercise, especially swimming PT Thermal Off-weight joint with cane/crutches |
| Dyspareunia | Genital | Breast, ovarian, any cancer treatment causing ovarian failure | Decreased vaginal lubrication, vaginal stricture from pelvic surgery or radiation | Vaginal lubricants PT for Pelvic floor exercises and vaginal dilators Sexual therapy Low-dose vaginal estrogen cream # |

There are no FDA approved medications specifically for chronic pain conditions in cancer survivors.

Recommend contacting the oncologist prior to initiating vaginal estrogen cream, especially if patient had estrogen-receptor positive breast cancer.

- NSAIDs = non-steroidal anti-inflammatory agents (e.g. naproxen, ibuprofen).
- PT/OT = physical therapy or occupational therapy
- ROM = range of motion
- Thermal = hot packs, ice packs
- CBT = cognitive behavioral therapy

Appendix F: Diagnosis-based Pharmacotherapy for Pain and Associated Conditions

| Best Used For... | Adjuvant Drug | Key Points |
|---|--|--|
| Minor arthritis, backache, muscle and joint pain | Topical menthol, methyl salicylate, trolamine salicylate or capsaicin | May experience burning, stinging or itching sensations during and following application but high concentration capsaicin or repeat applications will produce a loss of responsiveness to stimuli. Caution: Wash hands or use gloves when handling capsaicin. |
| Minor to moderate pain | Acetaminophen (APAP) | APAP 325 mg + ibuprofen 200 mg provides better pain relief than oral opioids. Caution: Hepatotoxicity increases with dose, age, use of alcohol, and co-occurring liver disease. Keep to < 2 grams daily if at risk for hepatotoxicity. Some manufacturers have voluntarily revised their label to recommend a lower maximum of 3 grams daily. |
| Pain from spasticity (spinal cord injury or multiple sclerosis) | Tizanidine or baclofen | Caution: Do not abruptly discontinue baclofen due to potential for severe rhabdomyolysis and fever. |
| Neuropathic pain conditions (diabetic peripheral neuropathy, post-herpetic neuralgia, spinal cord injury, cauda equina syndrome, phantom limb pain, HIV neuropathy, chemotherapy-induced peripheral neuropathy, etc.) | Tricyclic antidepressants (amitriptyline, nortriptyline, doxepin, desipramine), serotonin norepinephrine reuptake inhibitors (duloxetine, venlafaxine), anticonvulsants (gabapentin, pregabalin) | Low dose TCAs and gabapentin are good first line therapy options especially helpful with sleep disturbance. Caution: Gabapentin and pregabalin can cause cognitive slowing, weight gain, and edema. Also, pregabalin is a controlled substance. |
| Trigeminal neuralgia | Carbamazepine | Caution: Monitor for hematologic (aplastic anemia, agranulocytosis) and dermatologic (toxic epidermal necrolysis, Stevens-Johnson syndrome) complications. Because there is a strong association between dermatologic complication and the presence of human leukocyte antigen (HLA-B*1502), the FDA and the manufacturers of carbamazepine recommend that patients with ancestry in genetically at-risk populations be screened for the presence of the HLA-B*1502 allele prior to initiating carbamazepine therapy. |
| Neuropathic pain condition + depression or anxiety | Tricyclic antidepressants (amitriptyline, nortriptyline, doxepin, desipramine) or serotonin norepinephrine reuptake inhibitors (duloxetine, venlafaxine) | Caution: Monitor for dose related QTc prolongation (TCAs > SNRIs). Also, SNRIs can provoke leg movement disorders. |
| Non-specific low back or nociceptive pain or pain from traumatic, infectious, or degenerative conditions, or pain from connective tissue disorders | Nonsteroidal anti-inflammatory drugs (naproxen, ibuprofen, meloxicam, diclofenac, etodolac, nabumetone, ketoprofen, piroxicam, sulindac, tolmetin, etc.) | Naproxen 500 mg or naproxen sodium 550 mg alone and ibuprofen 200 mg + acetaminophen 500 mg are as effective, or more effective than opioids. Caution: Monitor patients for potential renal, gastrointestinal (GI), and cardiac side effects. Risk increases with age and dose. |

| Best Used For... | Adjuvant Drug | Key Points |
|---|---|--|
| Fibromyalgia | Duloxetine, gabapentin or pregabalin | Caution: Serotonin syndrome has been reported with SNRIs (e.g. duloxetine) when taken alone or concurrently with other serotonergic agents (e.g. triptans, tramadol, fentanyl, TCAs, etc.) |
| Localized neuropathic pain (HIV polyneuropathy, postherpetic neuralgia) | Topical lidocaine or capsaicin | May experience burning, stinging or itching sensations during and following capsaicin application but high concentration or repeat applications will produce a loss of responsiveness to stimuli. Caution: Wash hands or use gloves when handling capsaicin. |
| Insomnia | <ul style="list-style-type: none"> • Melatonin 1-5mg • Tricyclic antidepressants (TCAs) • Trazodone • Benzodiazepine receptor agonists or Z-drugs (e.g. zolpidem, zaleplon, zopiclone, eszopiclone) | Melatonin side effects include drowsiness, dizziness, headache, nausea, and nightmares. Caution: Trazodone is not advised when patient is taking SSRIs or SNRIs. Caution: Z-drugs can potentially induce unsafe behaviors like sleep-driving or preparing and eating food when not fully awake; have limited value with reducing chronic pain. |

Appendix G: Patient Education Resources

Providing quality treatment for your patients is critical, and so is educating them about the risks of taking opioid medications. Resources that can help you provide this education are listed here.

| Resource | Description |
|--|---|
| <p>Chronic Pain American Chronic Pain Association</p> <p>Chronic Pain Self-Management Program</p> <p>Substance Abuse and Mental Health Services Administration (SAMHSA) Evans Health Lab’s Advice for Patients Taking Opioids</p> | <p>Patients and their families can access plain-language fact sheets, worksheets, communication tools and videos on topics such as medications, pain management programs, and going to the ER. Addresses health literacy with tools for how to read an OTC label, and how to store medications safely.</p> <p>Find a local six-week workshop, developed by the Stanford Patient Education Research Center.</p> <p>Downloadable booklet <i>You Can Manage Your Chronic Pain to Live a Good Life</i></p> <p>Provides advice for people on, or about to start taking opioid medications, related to chronic non-cancer pain.</p> |
| <p>Fibromyalgia Fibromyalgia Information Foundation</p> | <p>Overview of fibromyalgia, diagnosis, treatment, preventive advice and new research discoveries. The site does mention the use of opioids and benzodiazepines for fibromyalgia, which is not supported by this guideline.</p> |
| <p>Headaches National Headache Foundation</p> | <p>Contains topic sheets, educational modules, and videos on all kinds of headaches. Useful for providers also; contains links to research.</p> |
| <p>Medications National Institute of Health’s Daily Med</p> <p>UpToDate</p> | <p>Sponsored by the National Library of Medicine, this site contains information for professionals as well as patients on almost all drugs.</p> <p>This is a paid subscription service, which consumers are not likely to use directly. Providers who have access can download patient information on the basics of: narcotic pain medicines, prescription drug abuse, opioid use disorder, and alcohol and illegal drug use in pregnancy.</p> |
| <p>Stress and Mental Health Anxiety Disorders Association of America</p> <p>National Institute of Mental Health</p> <p>Depression Screening.org</p> | <p>Information for healthcare providers and consumers. Detailed information about anxiety disorders, how to find help, and tips for managing anxiety.</p> <p>Information on mental health topics including signs and symptoms, treatment, locating local services, and research.</p> <p>Confidential online depression screening test, symptoms and treatments, personal stories and sources of help.</p> |
| <p>Sleep National Sleep Foundation</p> | <p>General information about sleep health and safety, and sleep-related problems.</p> |
| <p>Setting Patient Health Goals Swedish’s Structuring Your Own Management of Pain (STOMP) brochure</p> | <p>Brochure is designed to help patient set health goals to alleviate pain and improve quality of life. It includes general information about pain, goal-setting ideas and steps to take to achieve those goals.</p> |

| Resource | Description |
|---|--|
| <p>Opioid Safety Washington State Department of Health's Take as Directed The Addiction Technology Transfer Center Network</p> | <p>Includes possible risks from taking opioids, warning signs of drug abuse or addiction, tips on preventing overdoses and signs of overdose and problematic opioid use.</p> <p>A fact sheet with six tips for preventing others from stealing your prescription medicines; good for printing.</p> |
| Books | |
| <p><i>Treat Your Own Neck and Back</i> (5th Ed.) by R. McKenzie</p> | <p>Patient handbook for common neck pain will help patients learn to relieve their problems and prevent recurrence of their symptoms in the future. It covers a step-by-step system of education, awareness, exercise and prevention.</p> |
| <p><i>Managing Pain Before It Manages You</i> (3^d Ed.) by M Caudill</p> | <p>Simple set of tools to help patients live with their pain more effectively and independently.</p> |
| <p><i>Mind Over Mood: Change How You Feel by Changing the Way You Think</i> by D Greenberger and C Padesky</p> | <p>Step by step worksheets teach specific skills to conquer common mental health issues such as depression, anxiety, and low self-esteem.</p> |
| <p><i>Thoughts and Feelings: Taking Control of Your Moods and Your Life</i> by M. McKay, M.Davis, and P.Fanning</p> | <p>Adapts the powerful techniques of cognitive behavioral therapy into a set of tools readers can use against anxiety, depression, and obsessiveness.</p> |
| <p><i>The War on Pain</i> by S. Fishman & L. Berger</p> | <p>An introduction to interdisciplinary pain management that integrates traditional and alternative techniques.</p> |
| <p><i>Heal Your Headache: The 1-2-3 Program for Taking Charge of Your Pain</i> by D. Buchholz & S.G. Reich</p> | <p>Information on how to avoid triggers and use preventative medications rather than pain relievers which can cause rebound headaches.</p> |
| <p><i>Chronic Pain Solution: Your Personal Path to Pain Relief</i> by J.N. Dillard & L.A. Hirschman</p> | <p>Useful information on how to approach and relieve chronic pain.</p> |
| <p><i>Snoring and Sleep Apnea: Sleep Well, Feel Better</i> by R. Pascualy</p> | <p>This book is for patients and health care professionals and covers causes, diagnosis, treatment, and surgical techniques.</p> |

Appendix H: Clinical Tools and Resources

Consultation Resources

The WA State Department of Health maintains a webpage specifically for pain management^{vi} where the rules for opioid prescribing (including obtaining consultations with pain specialists) are referenced in five separate places, each for the different specialists who can prescribe opioids: MDs, DOs, PAs (within the MD or DO rules), ARNPs, DPMs, and Dentists. They are codified in Washington Administrative Code Chapter 246, and can also be found at the state’s legislative website (www.leg.wa.gov).

UW School of Medicine and its academic medical centers offer a toll free consultation and referral service available 24 hours per day 7 days per week. This service links providers with a faculty physician with expertise in any particular area. To access these services visit, call 800.326.5300, email medcon@u.washington.edu or visit, <http://uwmedicine.washington.edu/Patient-Care/Referrals/Pages/MEDCON.aspx>. Click on “Refer a Patient.” The entire process can be done online, including transfer of records and images.

UW TelePain offers a weekly (with few seasonal exceptions) free teleconference where primary care providers can call and present complex pain management cases (with personally identifiable patient information redacted) and receive consultative advice from a multidisciplinary group of pain specialists. There is also a 20-30 minute didactic section on pain related topics before cases are presented. Visit: <http://depts.washington.edu/anesth/care/pain/telepain/index.shtml>.

Mentoring Resources

Physician Clinical Support System has mentors available by phone or email to answer providers’ questions on methadone or buprenorphine. In addition, guidance on specific clinical questions and helpful tools can be downloaded from the website. There is no cost for this service. Once the provider registers at <http://pcssmat.org/mentoring/>, a mentor is assigned within 2 days.

UW offers a free online course called COPE-REMS that is designed to educate healthcare providers on how to better treat and manage patients with chronic pain in order to improve patient outcomes. Its goal is to increase knowledge and confidence among providers about how to best treat chronic pain, including whether and when to start, modify or stop opioid therapy. The course contributes to national health goals of preventing opioid misuse, abuse and overdose. It is aimed at physicians, registered nurses, ARNPs, physician assistants, psychiatrists, and other care managers who treat patients with chronic pain. Visit: <https://trainingexchange.org/our-programs/cope-rems>.

^{vi} <http://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/HealthcareProfessionsandFacilities/PainManagement>

Treatment and Referral Resources

There are several treatment options available for opioid use disorder. A combination of medication and behavioral therapies has been found to be most successful (SAMHSA Medication Assisted Treatment for Opioid Addiction in Opioid Treatment Program

www.kap.samhsa.gov/products/trainingcurriculums/pdfs/tip43_curriculum.pdf).

- Department of Social and Health Services (DSHS) Tool Kit to help address drug and alcohol issues in Medicaid patients <http://maa.dshs.wa.gov/pharmacy/ToolKit.htm>
- DSHS Division of Alcohol and Substance Abuse at 877-301-4557. A referral for treatment may be made to any one of the licensed opioid treatment programs (OTPs) in Washington State: <http://www.dshs.wa.gov/dbhr/dadirectory.shtml>
- A list of treatment centers certified by the Division of Behavioral Health and Recovery is available at www.dshs.wa.gov/dbhr/dadirectory.shtml.
- A partial list of physicians authorized by SAMHSA and the DEA to prescribe buprenorphine for treatment of opioid use disorder and treatment programs that also provide it can be found at: http://buprenorphine.samhsa.gov/pls/bwns_locator/provider_search.process_query?alternative=C&HOICEG&one_state=WA

Sample Doctor-Patient Agreements for Chronic Opioid Use (links only)

L&I's Opioid Treatment Agreement in English <http://www.lni.wa.gov/Forms/pdf/F252-095-000.pdf> and Spanish <http://www.lni.wa.gov/Forms/pdf/F252-095-999.pdf>

HCA's Medicaid Chronic Pain Agreement <http://www.hca.wa.gov/medicaid/pharmacy/pages/toolkit.aspx>

DSM 5 Criteria for Substance Use Disorder, by the American Psychiatric Association:

<http://pcssmat.org/wp-content/uploads/2014/02/5B-DSM-5-Opioid-Use-Disorder-Diagnostic-Criteria.pdf>

Everyday Helpful Resources

- UW Department of Anesthesiology and Pain Medicine keeps a useful [Pain Medicine Provider Toolkit](#) on their website with educational and resource information.
- For tips on motivational interviewing, check out: *Motivational Interviewing in Health Care: Helping Patients Change Behavior* by Stephen Rollnick, William R. Mill, and Christopher C. Butler, Guilford Press 2007, (Review at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2779641/>) .
- Swedish's pain management guide, [STOMP](#) (Structure your Own Management of Pain) is a helpful resource for patients with chronic pain to be more active in their care and improve their pain and function.

Emergency department guidelines help coordinate care with primary care providers

The emergency department (ED) is a significant outpatient source of prescription opioids. Yet there has been little guidance on how to treat pain in the emergency department while minimizing the potential for overdose and abuse. The Washington Chapter of the American College of Emergency Physicians (WA-ACEP) has developed a set of guidelines that outline good prescribing practices for ED providers. The guidelines include a patient information brochure that explains to patients the purpose of the guidelines and the risks associated with prescription opioids. More information can be obtained at <http://www.washingtonacep.org/painmedication.html> and <http://here.doh.wa.gov/materials/pain-medication-guidelines/?searchterm=emergency%20department>.

EDs across the state have collaborated to take advantage of a visit tracking system used by every ED in the state to notify the emergency care provider of a patients ED visit history. A randomized clinical trial of citywide ED care coordination performed by Washington State University and funded by the Centers for Disease Control shows the effectiveness of this approach. The trial demonstrated a statistically significant reduction in ED visits made by frequent users and a large reduction in opioid prescribing to these patients by ED providers. The results of this trial are pending publication. Coordinating ED care for frequent users is a promising approach to address high risk opioid prescribing from the ED.

Appendix I: Guideline Development and AGREE II Criteria

Guideline Development

The Washington State Agency Medical Directors' Group (AMDG), which sponsored this guideline, works to improve the health care purchased by Washington State by making evidence-based decisions that maximize the effectiveness, cost-effectiveness, and safety of the health care delivered to Washington residents, while reducing or preventing harm. The group consists of the medical directors and senior health policy staff from four Washington State agencies: Corrections, Health, Labor and Industries (for workers' compensation), and the Health Care Authority (for Medicaid and public employee benefits).

In April 2014, the AMDG invited state health officials, policy leaders, and health care providers specializing in pain medicine, psychiatry, family medicine, psychology, internal medicine, physiatry, palliative care, and other fields to lend their expertise to the guideline process and content. This advisory committee had diverse interests, experience, and views, which made for robust discussions. Each member signed conflict of interest disclosures, and though some had financial arrangements with various companies, none posed a conflict of interest when contributing to this guideline. A complete list of their names and affiliations can be found in the [Acknowledgment](#) section.

The guideline was posted for public comment for four weeks; the comments were reviewed by agency staff and workgroup leads, and considered before the guideline became final. A list of these comments and responses is available on the AMDG website. Principal funding and resources for the guideline development were provided by state agencies and staff. In addition, contracted committee members received reimbursement for their formal committee time and travel, similar to other statutory evidence-based committees for Washington State.

Research Methods and Decision-Making

The co-chairs of the opioid guideline committee designated several workgroups to review the evidence and make clinical recommendations for each section. The workgroups met at committee meetings or on their own in person or via webinars and exchanged information and views via email. Each workgroup was assigned an agency staff to support scheduling meetings and collating, editing and formatting workgroup product. The entire guideline advisory committee met in person three times to review guideline progress and, as much as possible, reach consensus on the final clinical recommendations.

Each workgroup did its own reviews of the evidence. A large proportion of recommendations are based on consensus of expert opinion due to lack of studies specific enough to guide a recommendation, workgroups did not summarize overall strength of recommendations.

AGREE II Criteria

This guideline meets most of the specific criteria for the “Appraisal of Guidelines for Research and Evaluation,” (AGREE), which is the industry standard for ensuring its development followed a rigorous strategy, appropriate methodology, and high quality systematic development and implementation process. This standard was developed by the Canadian Institute of Health Research and is used by the United States Agency for Healthcare Research and Quality and the National Guideline Clearinghouse.

DOMAIN 1: SCOPE AND PURPOSE

The overall objective(s) of the guideline is (are) specifically described; health question(s) covered by the guideline are specifically described; and population (patients, public etc.) to whom guideline is meant to apply is specifically described.

Opioids during acute/subacute phase, clinically meaningful improvements and alternative treatments

1. When should PMP be accessed?
 - a. At first opioid prescription?
 - b. At point of decision on chronic opioid therapy?
 - c. During monitoring?
 - d. For any emergency department opioid prescription?
2. Excluding trauma and surgery, what are indications and contraindications for acute, subacute, and chronic opioid use?
 - a. How does this relate to the new FDA labeling on ER/LA opioids?
 - b. Should mild-moderate conditions, such as musculoskeletal sprains and strains, fibromyalgia, headaches, etc. be contraindications to opioid use?
3. What is considered clinical meaningful improvement (CMI) in pain and function with opioid use?
 - a. What are the most reliable and valid publicly available brief instruments for tracking pain and function?
 - b. Which instruments, such as the PROMIS, may be best for tracking function, rather than pain interference with function?
 - c. Should the baseline for tracking CMI be measured at the start of opioid therapy, or at some other point?
4. What pharmacologic and non-pharmacologic treatments are effective initial treatments or as alternatives to opioid treatment for acute and subacute pain?
5. What pharmacologic and non-pharmacologic treatments are effective in preventing the transition from acute/subacute to chronic pain?
6. What pharmacologic and non-pharmacologic treatments are effective in treating chronic pain?

Opioids for perioperative pain

1. For patients undergoing elective surgery, what risk factors are there for difficult post-operative pain control?
2. For patients undergoing elective surgery, what pre-operative practices help improve pain control in the post-operative period?
3. For patients who are on COAT, what pre-operative recommendations should be given to improve management of post-operative pain?
 - a. What dose and/or duration of COAT signal post-op opioid tolerance concerns?
 - b. Should patients on high dose COAT be tapered before elective surgery?
 - c. How long would one expect opioid tolerance to persist?
4. What adjuncts are helpful for opioid sparing in the postoperative period in patients with (and, if different, without) opioid tolerance?
5. Is there a recommended dose range for managing post-surgical pain (either doses per se or % of baseline opioid requirement)?

6. Is there evidence to support the use of long-acting opioids for acute post-surgical pain?
7. Are high doses of post-operative opioids associated with adverse outcomes, such as development of refractory pain, tolerance, or overdose events? If so, how high?
8. By how many days after surgery should we expect patients to have returned to their COAT dose (or lower)?
9. If formal weaning is required to return to preoperative opioid doses, how long after surgery should this start and at what rate?

When to discontinue chronic opioid therapy and initiate addiction treatment

1. When should opioids be weaned?
 - a. Rate of taper (how much, how quickly)?
 - b. When adjunctive treatments may be indicated (e.g. behavioral treatment, more formal detox)?
 - c. What if the patient is not interested or willing?
2. In what circumstances should someone be weaned off entirely vs. tapered down to a lower dose?
3. How to proceed if weaning attempt(s) failed?
4. What resources are available in the community to help support providers and patients when tapering opioids?
5. What is the evidence on safety and efficacy for available treatments for addiction?
6. What precautions are necessary for treating chronic pain in patients with current or former substance use disorder?

What resources are available in the community to help support addiction recognition and treatment for providers and patients?

DOMAIN 2: STAKEHOLDER INVOLVEMENT

The guideline development group includes individuals from relevant professional groups; the views and target preferences of the target population (patients, public, etc.) have been sought; and target users of the guideline are clearly defined.

Where found: Title, Introduction, Appendix I and Acknowledgements

The Guidelines were developed in collaboration with a broad advisory group of the state’s academic leaders, pain specialists, and clinicians in both primary care and specialty areas in response to the growing epidemic of opioid-related unintentional overdoses. A list of participating clinicians and their affiliations can found in the Acknowledgements. The opioid guideline committee did not include public member although the public had an opportunity to comment on the guideline during the four-week public comment period. Public comments were reviewed by agency staff and workgroup leads, and responses were considered before the guideline became final. A list of these comments and responses is available on the AMDG website.

The main target population is primary care providers and any provider who treats patients with chronic pain. Primary care providers as well as specialists were included in the guideline advisory group, the names of which are documented in the acknowledgements section. A secondary target population is public and private payers in WA state. The statutory public/private Robert Bree Collaborative, representing all major health care sectors and payers in WA has preliminarily unanimously voted to endorse this guideline.

DOMAIN 3: RIGOR OF DEVELOPMENT

Systematic methods were used to search for evidence; criteria for selecting the evidence are clearly described; strengths and limitations of the body of evidence are clearly described; health benefits, side effects and risk have been considered in formulating the recommendations; an explicit link between the recommendations and the supporting evidence; guideline has been externally reviewed by experts prior to its publication; and procedure for updating guideline is provided.

Where found: Introduction, Uncertain Long-term Efficacy and Clear Evidence of Harm, Evidence for each section and Appendix I

This is the 3rd edition of the AMDG interagency opioid guide. First published in 2007, the guideline is updated every 5 years or when there is substantial new evidence on COAT to warrant an update. Guideline development and all updates were done in collaboration with a broad advisory group of the state's academic leaders, pain experts, and clinicians in both primary care and specialty areas. The updates build upon the previous guideline.

A literature review was done in Medline – PUBMED. Searches began in March of 2014. Search terms included “opioids and chronic pain”, “chronic pain and treatment”, “opioid related adverse events”, “risk and dose and opioids”, “opioids and overdose and deaths”, and “chronic pain management”. The search was limited to English, humans, the last 10 years and in some cases, to systematic reviews and meta-analysis. Additional hand searches of relevant studies in reference lists were done. A search was also performed in the National Guideline Clearinghouse for relevant guidelines. Guidelines selected for review addressed the use of opioids in the treatment of chronic non-cancer pain. In addition, each workgroup did its own reviews of the evidence. A large proportion of recommendations are based on consensus of expert opinion due to lack of studies specific enough to guide a recommendation, workgroups did not summarize overall strength of recommendations. The following is a brief description of the literature search for the main topics:

CMIF

PubMed was searched for relevant studies on methodology and measuring pain and function. Key search terms included “meaningful improvement” and “pain” and “function” or “MCID” and “pain” and “function.” This search yielded 240 abstracts.

Dosing threshold and adverse effects

A literature review was done in Medline/ PUBMED. Searches began in March of 2014. Search terms included “opioids and chronic pain”, “chronic pain and treatment”, “opioid related adverse events”, “risk and dose and opioids”, “opioids and overdose and deaths” and “chronic pain management.”

Alternatives to Opioids

The evidence for this section is derived from systematic reviews of randomized trials published since the Chou et al (2007) review of RCTs for pharmacologic and non-pharmacologic treatments of acute, subacute, and chronic low back pain. Using key terms “chronic pain”, “randomized”, and “systematic review”, we reviewed 976 abstracts, 42 of which were relevant to this review. More recent reviews that incorporated older RCT results took precedence over older systematic reviews. In addition, we used key words “systematic review” and “cognitive behavioral therapy” and “chronic pain” to identify conditions other than chronic low back pain for which cognitive behavioral therapy may have been effective; we reviewed 586 abstracts, and included 8 additional studies.

Acute and subacute phase

PubMed was searched for randomized trials and systematic reviews of randomized trials, in the treatment of low back pain, headaches, and fibromyalgia. Key terms used included “systematic reviews” and “opioids” and either “low back pain” or “headaches” or “fibromyalgia”. The final numbers of articles used were: 7 of 180 for low back pain; 3 of 219 for headache; and 3 of 60 for fibromyalgia. A search of the literature on specific use of opioids during the subacute pain period yielded no randomized trials. In addition, the use of screening tests prior to starting COAT was covered in the 2010 AMDG guideline.

Perioperative period

A number of reviews of the literature on perioperative pain treatment have been undertaken and published in the last few years including those from the American Pain Society, the American Society of Anesthesiologists, the Department of Defense, the Veterans Administration, and the Washington State Department of Labor and Industries. These guidelines as well as a PubMed search for additional reviews of this topic in the last 5 years, which yielded 560 articles, excluding 32 reviews concerning any single surgical procedure.

Chronic non-cancer pain

The literature was reviewed in PubMed for studies since 2010. The committee also reviewed the opioid prescribing guidelines from other government agencies and public and private insurers.

Reducing or discontinuing COAT and treatment of opioid use disorder

A search of the literature on opioid tapering yielded no randomized trials. In addition, treatment for withdrawal symptoms was covered in the 2010 AMDG guideline. A review of recent meta-analyses and systematic reviews and a few well-designed randomized clinical trials provided the basis for recommendations on the treatment of opioid use disorder.

Pregnancy and Neonatal Abstinence Syndrome

A literature search in PubMed was conducting using text terms "pregnancy" and "opioid" and one of the following different terms to identify pertinent studies: "detoxification" or "neonatal abstinence" or "NSAID and oligohydramnios" or "adverse outcomes."

Children and Adolescents

The literature was reviewed using Medline, years 1996 to present. Search terms were "opioid" and "chronic pain". The search returned 48 articles, none of which were used. Searches for "off label drug use in pediatrics" were more relevant and articles already familiar to the author were used.

Opioid Use in Older Adults

A literature search was performed in October 2014, using PubMed and the search terms "opioids and older adults". Of 887 abstracts identified, 31 were examined in detail. Two other relevant guidelines were also included in the review.

Cancer Survivors

PubMed searches limited to 5 years were performed in April 2014 and again in January 2015 using the search terms "cancer survivor" and "pain" revealing over 500 results, which were narrowed by "reviews", "systematic reviews" and "therapy" resulting in approximately 100 abstracts, of which 35 were examined in detail. In addition, the National Comprehensive Cancer Network (NCCN) 2015 Survivorship Guidelines reference list of 621 items was reviewed for additional relevant papers (Pam Davies).

A literature search was performed in April 2015 using PubMed and the search terms "cancer survivors and pain treatments (Dr. Fitzgibbon).

DOMAIN 4: CLARITY OF PRESENTATION

The recommendations are specific and unambiguous; different options for the management of the condition or health issues are clearly presented; and key recommendations are easily identifiable.

Where found: Throughout the guideline

- Recommendations are clearly identified and can be found within each clinical section
- Supporting evidence for recommendations are clearly documented
- Tables and algorithms are used to illustrate processes and decision making
- Appendices are used for more detailed references so key recommendations are not obscured.

DOMAIN 5: APPLICABILITY

The guideline describes facilitators and barriers to its application; provides advice and/or tools on how the recommendations can be put into practice; potential resources implication of applying the recommendations have been considered; and guideline presents monitoring or auditing criteria.

Where found: Within each section of the guideline, appendices, and on the AMDG website

The 2007 and 2010 AMDG opioid guidelines were widely diffused, both in WA state via the [AMDG website](#) and the [National Guideline Clearinghouse](#). All of the tools necessary for successful implementation of the prior guidelines can be accessed on the AMDG website, such as an app for opioid dosing calculation, and brief, validated publicly available screening instruments for risk assessment.

The statutory public/private Bree Collaborative, representing all major health care sectors and payers in WA state, has preliminarily and unanimously voted to endorse this guideline and are planning final endorsement at their July, 2015 quarterly meeting. As such, the guideline would become the standard for all residents in WA state.

The committee explicitly chose not to address in this guideline, issues such as resource limitations (e.g. access to pain specialists), inadequate reimbursement, and medicinal cannabis. Although important topics, the committee felt that these were beyond the scope and capacity of what they could effectively achieve and still have a clinically useful guideline. The authors are aware of potential barriers to the guideline's application, and the state agencies will continue to seek ways of communicating and educating providers about how to improve care through the use of this guideline. All recommendations were written to apply to the general population in Washington State, and are considered to be implementable by most providers.

DOMAIN 6: EDITORIAL INDEPENDENCE

The views of the funding body have not influenced the content of the guideline; and competing interest of the guideline development group members have been recorded and addressed.

Where found: Appendix I

Although funding and resources for the guideline development were supported by state agencies, the guideline was approved by advisory committee via a consensus process. Each committee member signed conflict of interest disclosures, and though some had financial arrangements with various companies, none posed a conflict of interest when contributing to this guideline. A complete list of their names and affiliations can be found in the [Acknowledgment](#) section.

Acknowledgements

The Washington State Agency Medical Directors’ Group wishes to acknowledge the many individuals and groups from both the private and public sectors who provided crucial consultation and input to this guideline. Their clinical, scientific, and technical expertise helped ensure that this guideline would be relevant, accurate, and of practical use to prescribers. Every effort was made to create a guideline as evidence-based as possible. Where scientific evidence was insufficient or unavailable, the best clinical opinions and consensus of the advisory group were used.

We are grateful for the time and efforts made by each of the following persons:

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