

# Patients on Chronic Opioid Therapy for Chronic Non-Cancer Pain Safety Guideline

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Last guideline approval: May 2020

**Guidelines** are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

## Interim Update July 2020

- **All patients being prescribed long-term opioids are now required to have a safety review of their care plan every 3 months at a COT monitoring visit.** Previously, visit frequency requirements were based on risk stratification (every 3 months for patients in the high-intensity monitoring group, every 6 months for moderate-intensity, and annually for low-intensity). We have updated this guideline to align closely with guidance from the Centers for Disease Control and Prevention and the standards of other Kaiser Permanente regions.
- **All monitoring visits must be done in person or by video, with at least one in-person visit per year.** Telephone and secure messaging conversations no longer count as COT monitoring visits.
- **Urine drug screening (UDS) is based on risk stratification, and is no longer required at every monitoring visit except for patients in the high-intensity monitoring group.** UDS is required at least annually for patients in the low-intensity group, at least every 6 months for the moderate-intensity group, and at least every 3 months for the high-intensity group.

## Major Changes as of May 2020

- The criteria for high-risk opioid use were expanded. Recently added risk factors include mental health conditions (depression, anxiety, PTSD), medical conditions (e.g., obesity, sleep apnea), alcohol and illicit substance use, and advanced age (65 years or older).
- The previous tool for assessing a patient's risk of opioid use disorder (OUD), the Opioid Risk Tool (ORT), was replaced by the updated ORT-OUD tool, which has higher sensitivity and specificity for predicting OUD and easier scoring.
- Screening for sleep apnea using the Epworth Sleepiness Scale is now recommended as part of the initial COT monitoring visit.
- The DSM-5 criteria have replaced the Substance Use Disorder Symptom Checklist as the preferred tool for diagnosing OUD.
- Recommendations against using buprenorphine, Suboxone, cannabinoids (THC and CBDs) for the treatment of chronic pain have been added.
- The guidance on tapering opioids has been expanded to incorporate the BRAVO protocol and recommendations for the speed of taper based on risk stratification.
- Criteria for when to refer to a pain specialist, Mental Health and Wellness, and Addiction Medicine were updated.

## Washington State Law

This guideline is in compliance with the State of Washington regulations [WAC 246-919-850-985](#) on the use of opioids in the treatment of patients with chronic non-cancer pain.

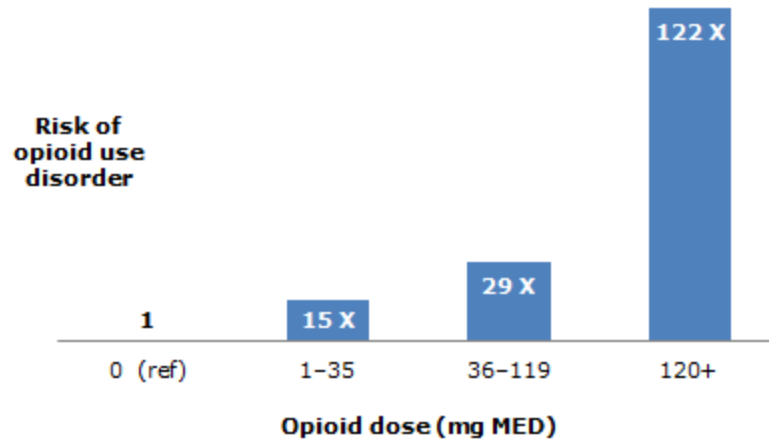
## Introduction: Relationship Between Opioid Dose and Risk Levels

The use of chronic opioid therapy for chronic pain is not an evidence-based practice and is without established benefits that outweigh the considerable risks on a population level; therefore, it should occur only in very rare circumstances.

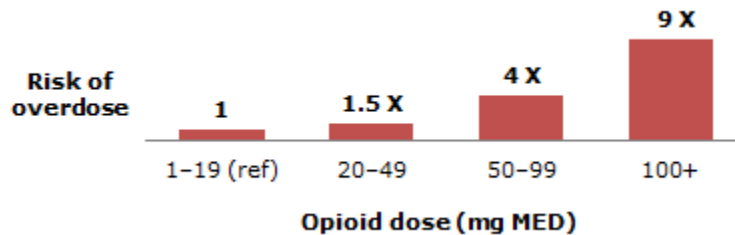
Best practice is to defer use of opioids by employing non-pharmacologic and non-opioid therapies first.

Serious opioid-related risks increase sharply with higher doses.

**Opioid use disorder:** A person taking a relatively low dose of prescribed opioids is **15 times** as likely to develop opioid use disorder as a person who has not been prescribed opioids. The risk continues to rise with escalating doses; at high doses ( $\geq 120$  mg MEDD) of opioids, the person's risk of developing OUD is **122 times** that of a person who has not been prescribed opioids. (Edlund 2014)



**Opioid overdose:** Similarly, a person taking  $\geq 100$  mg MEDD will be **9 times** as likely to overdose as a person taking  $< 20$  mg MEDD. (Dunn 2010) Note that approximately 1 overdose in 7 is fatal.



## Guideline Scope

Kaiser Foundation Health Plan of Washington has adopted the recommendations of the [2015 Agency Medical Directors' Group \(AMDG\) Interagency Guideline on Prescribing Opioids for Pain](#). The guideline is also in alignment with the National Permanente Medical Group 2019 Practice Recommendations for Improving Appropriate Opioid Prescribing and Reducing Potential for Harm.

**This is a safety guideline.** The recommendations in this guideline apply to adult patients who are **already on chronic opioid therapy (COT)** for the treatment of **chronic non-cancer pain**.

**Chronic opioid therapy (COT)** is daily or near-daily use of opioids for at least 90 days, often indefinitely. (Chou 2009. Additionally, COT is defined as a minimum 70-day supply of opioids dispensed in the previous 3 calendar months.

**Chronic non-cancer pain** means a state in which non-cancer pain persists beyond the usual course of an acute disease or healing of an injury, or that may or may not be associated with an acute or chronic pathologic process that causes continuous or intermittent pain over months or years (WAC 246-919-850–985).

The Centers for Disease Control and Prevention has found insufficient evidence to determine the long-term benefits of opioid therapy for chronic pain, and has found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. (CDC 2016)

### Outside the scope of this guideline are:

- Indications for opioid prescribing
- Initiation of opioid prescribing
- General recommendations for the treatment of chronic non-cancer pain

For these areas, Kaiser Foundation Health Plan of Washington has adopted the recommendations of the [2015 AMDG Interagency Guideline on Prescribing Opioids for Pain](#).

This guideline does **not** apply to patients receiving palliative, hospice, or other end-of-life care.

## Expectations for Kaiser Foundation Health Plan of Washington Providers

Using protocols and standard documentation, Kaiser Foundation Health Plan of Washington aims to minimize practice variation in the management of patients on chronic opioid therapy for chronic non-cancer pain, which will improve patient safety, ensure compliance with Washington State law, and ultimately increase both patient and provider satisfaction.

- ✓ Patients on COT shall be **risk-stratified** to the highest appropriate category by the prescribing clinician.
- ✓ Patients on COT shall have **regular COT monitoring visits** that:
  - Occur at a **3-month frequency**, and
  - Include **standard components**.
- ✓ Patients on COT shall **receive all chronic pain management prescriptions from one physician and one pharmacy** wherever possible. Clinicians treating a patient on COT are expected to clarify—both among themselves and with the patient—which clinician holds primary prescribing responsibility. See “Opioid prescribing procedures,” p. 15.
- ✓ Physicians prescribing opioids for chronic non-cancer pain shall have a one-time completion of at least 4 hours of **continuing medical education** relating to this topic. The State of Washington offers an [online CME](#) to help physicians comply with statewide rules.

# Managing Chronic Opioid Therapy (COT)

## Risk stratification, intensity of monitoring, and frequency of visits

The intensity of monitoring is determined by the “patient attributes” in Table 1. Patients should be placed in the **highest-intensity group for which they meet at least one of the criteria**. For example, patients taking benzodiazepines should be in the high-intensity monitoring group even if they are on a relatively low dose of opioids (< 40 mg MEDD).

All patients on COT shall have a monitoring visit every 3 months either **in person or by video**, including at least one in-person visit annually. (Telephone and secure messaging conversations are no longer considered monitoring visits.)

Table 1. Chronic opioid therapy patient monitoring groups		
Monitoring group	Patient attributes	Monitoring visit and urine drug screening (UDS) frequency
<b>High-intensity</b> <sup>1</sup>	<ul style="list-style-type: none"> <li>• Taking ≥ 90 mg morphine equivalent daily dose (MEDD) <i>Note:</i> For patients taking ≥ 120 mg MEDD, referral to a <a href="#">pain specialist</a> is required.</li> <li>• Taking methadone or fentanyl</li> <li>• Taking sedative-hypnotic drugs (benzodiazepines, Z-drugs),<sup>2</sup> gabapentin, carisoprodol, or muscle relaxers concurrently</li> <li>• Using alcohol or marijuana concurrently<sup>3</sup></li> <li>• Age 25 years or younger</li> <li>• Age 65 years or older</li> <li>• History of overdose</li> <li>• Legal issues related to substances (e.g., DUI)</li> <li>• ORT score ≥ 8 or ORT-OD score ≥ 3</li> <li>• Mental health conditions: depression, anxiety, substance use disorder, PTSD</li> <li>• Medical conditions: sleep apnea, cardiac disease, pulmonary disease, severe obesity, renal insufficiency, hepatic insufficiency, osteoporosis, pregnancy, history of falls</li> <li>• Illicit substance use: other opioids, other people’s opioid prescriptions, heroin, illicit use of prescription drugs</li> <li>• Repeated aberrant behaviors, such as:               <ul style="list-style-type: none"> <li>○ Frequent early refill requests</li> <li>○ Escalating dose without consulting with physician</li> <li>○ Multiple emergency room/urgent care presentations for opioid treatment</li> <li>○ Getting opioids from multiple prescribers</li> <li>○ Lost or stolen medications</li> <li>○ Sharing medications with others</li> <li>○ Disruptive behavior</li> <li>○ Not taking as prescribed</li> </ul> </li> </ul>	<p>Office or video visit required at least every 3 months.</p> <p>UDS required at least every 3 months.</p>
<b>Moderate-intensity</b> <sup>1</sup>	<ul style="list-style-type: none"> <li>• Taking between 40 mg and 89 mg MEDD</li> <li>• Moderate score (4–7) on the ORT or ORT-OD score ≤ 2</li> <li>• Compliant with pain treatment plan</li> </ul>	<p>Office or video visit required at least every 3 months.</p> <p>UDS required at least every 6 months.</p>
<b>Low-intensity</b>	<ul style="list-style-type: none"> <li>• Taking &lt; 40 mg MEDD</li> <li>• Low score (0–3) on the ORT or ORT-OD score ≤ 2</li> <li>• Compliant with pain treatment plan</li> </ul>	<p>Office or video visit required at least every 3 months.</p> <p>UDS required at least annually.</p>
<p><sup>1</sup> Patients in the moderate- and high-intensity monitoring groups are at increased risk of opioid overdose and death from respiratory depression. Offer <b>naloxone</b> as preventive rescue medication for these patients. See “Prescribing naloxone,” p. 15.</p> <p><sup>2</sup> See the <a href="#">Benzodiazepine and Z-Drug Safety Guideline</a> and this 2016 <a href="#">FDA Safety Warning</a> on the risks of combining benzodiazepines with opioids.</p> <p><sup>3</sup> Per National Permanente Medical Group 2019 Clinician Practice Recommendations for Opioid Prescribing, use of marijuana and/or alcohol is contraindicated while taking opioids. COT should not be initiated in patients currently using alcohol or marijuana, and tapering should be considered in patients using COT concurrently with either of these substances.</p>		

## The chronic opioid therapy monitoring visit: standard components

Steps listed apply to every COT monitoring visit, except *where noted*.

Every monitoring visit is an opportunity to improve safety for patients on COT and to consider adjusting the Opioid Care Plan—including tapering or discontinuation of opioid therapy—based on changes in the patient’s conditions or comorbidities.

For a patient’s **initial** COT monitoring visit (ongoing or new start), use SmartPhrase **.opioidvisit**, which includes all steps required at the initial visit.

For a patient’s **follow-up** COT monitoring visits, use either **.opioidvisit** or **.opioidfollowup** (synonym **.opioidmini**), which includes just the steps that are required at all visits.

Consider using the CHRONICPAIN SmartSet, which incorporates all aspects of the visit, including screening, documentation, care plan, and referral orders.

### 1

**Screening for contradictions and conditions affecting opioid risk**

**History**

*Physical exam – initial visit*

### 1. Medical screening, history, and physical exam

Use of opioid medications is **contraindicated** in patients with

- Known opioid use disorder (see “Recognizing opioid use disorder,” p. 9)
- History of opioid overdose

**Screen for medical issues** that affect opioid risk (e.g., pulmonary, cardiac, renal or hepatic disease; obstructive sleep apnea [using the Epworth Sleepiness Scale]; pregnancy risk; severe obesity; history of falls). See “Tapering or discontinuing opioid therapy,” p. 10.

Obtain/review **patient history**.

*At the patient’s initial COT monitoring visit, conduct a **physical exam**.*

### 2

**Pain and function assessment**

PEG Tool  
and

Oswestry Disability Index  
(optional)

### 2. Pain and function assessment

Continuation of COT should be considered only when the benefits outweigh the risks. AMDG defines clinically meaningful improvement in function 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.

To assess patients’ ongoing response to COT, use the **PEG (Pain/Enjoyment/General function) Tool**, available as the SmartPhrase **.pegscore**. The PEG Tool is also available as a KP HealthConnect documentation flowsheet, review flowsheet, and secure message.

For longitudinal tracking of a patient’s progress towards functional goals, consider using the **Oswestry Disability Index** (available in KP HealthConnect).

### 3

**Prescription monitoring**

PDMP database

### 3. Prescription monitoring

Check the patient’s record in the Washington State Prescription Drug Monitoring Program database every time controlled substances are prescribed to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk.

#### 4

##### Opioid risk assessment – initial visit

Opioid Risk Tool (ORT-OD)

#### 4. Opioid risk assessment (initial visit only)

At the patient's initial COT monitoring visit, use the updated Opioid Risk Tool (ORT-OD) to assess the risk of developing opioid use disorder (OUD) when taking long-term opioids. The ORT is a validated tool recommended by the Washington State AMDG. A score of **3 or higher** indicates a high risk of developing OUD.

#### 5

##### Psychological comorbidity screening

Annual Mental Health  
Questionnaire

#### 5. Psychological comorbidity screening

Screen the patient for depression, suicidal ideation, alcohol use, drug use, PTSD, and anxiety using the [Annual Mental Health Questionnaire](#). Both sides of the questionnaire—including the additional questions on the second page—are **required** for patients on COT, regardless of whether the PHQ-2 screen is positive. Screening for mental health issues is part of adult standard care.

#### 6

##### Urine drug screening

High-intensity monitoring  
requires UDS at least every  
3 months (every visit)

Moderate-intensity monitoring  
requires UDS at least every  
6 months (every other visit)

Low-intensity monitoring  
requires UDS at least  
annually (one visit per year)

#### 6. Urine drug screening (UDS)

UDS provides objective data regarding patients who are managing chronic pain and can be used to directly improve patient safety. For their safety, it is important that patients take opioids as prescribed, and this test helps assess whether they are doing that. UDS should also be ordered when seeing patients already on COT who are new to the health plan and have no record of recent UDS.

UDS is legally required, and its routine use helps to ensure that all patients on COT are treated equitably.

UDS is for medical purposes only. KPWA does not collect samples for use in a court of law or for workplace testing.

Clinicians should have a discussion with the patient before the UDS that includes:

- The purpose of testing
- What will be screened for
- What results the patient expects
- Prescriptions or any other drugs the patient has taken
- Time and dose of last dose of opioids
- Actions that may be taken based on the results of the screen
- Possibility of cost to the patient

Patients should be notified that the results will become part of their permanent medical record. Unexpected UDS results must be discussed with the patient; the care plan should be reevaluated **only** after unexpected positive and negative results have been confirmed by laboratory testing and after the patient has had the opportunity to discuss the results with the prescribing clinician.

For more detailed information on urine drug screening, see Drug Screening Ordering & Interpretation (staff intranet).

#### 7

##### Care plan

.avsopioidcareplan  
Care Plan AVS

#### 7. Care plan

Use **.avsopioidcareplan** at every visit to:

- Ensure the patient's treatment plan includes all components required by Washington State opioid legislation (<https://app.leg.wa.gov/wac/default.aspx?cite=246-919-850>). **The physician shall use a written agreement that outlines the patient's responsibilities for opioid therapy.** (Note: The legislation does not specify that a paper copy or patient signature is needed.)
- Serve as informed consent and documentation for chronic opioid therapy.

## 8

### Documentation and coding

.opioidvisit  
(initial and follow-up visits)

.opioidfollowup  
(follow-up visits only)

## 8. Documentation and coding

For a patient's **initial** COT monitoring visit (ongoing or new start), use SmartPhrase **.opioidvisit**, which includes all steps required at the initial visit.

For a patient's **follow-up** COT monitoring visits, use either **.opioidvisit** or **.opioidfollowup** (synonym **.opioidmini**), which includes just the steps that are required at all visits.

When documenting an encounter with a patient on COT, providers should include diagnosis codes for **both** the condition being treated with opioid medications **and** the long-term opioid treatment itself:

- **Diagnosis code for underlying condition, and**
- **Z79.891 Long-term (current) use of opioid analgesic**

When COT monitoring is the main reason for the visit, **Z79.891** should be used as the primary diagnosis, with the underlying condition as a secondary diagnosis. Conversely, when managing the underlying condition is the main reason for the visit—for example, when ordering physical therapy for a patient with chronic back pain—providers should document the **underlying condition** (chronic back pain) as the primary diagnosis, and Z79.891 as a secondary diagnosis.

In the rare instances that providers are treating a patient with both a health problem requiring opioid therapy and a concurrent opioid use disorder, documentation should be clear that the opioids are being used to treat the indicated health problem and not as a treatment for the opioid use disorder. (For patients with an existing or suspected opioid use disorder, see “Recognizing opioid use disorder.”)



## Recognizing opioid use disorder

It is not uncommon for patients on COT to develop opioid use disorder (OUD) during their treatment. Whenever OUD is suspected, use the DSM-5 criteria (below) during a conversation with the patient that ideally includes a family member or other observer, or contact the Mental Health and Wellness Mind Phone (1-888-844-4662) for a consultation if unsure how to proceed.

**It is *illegal* for providers to treat opioid use disorders or opioid withdrawal with opioid medications except under very specific circumstances.** In outpatient settings, specific opioid medications may only be used by physicians with a special DEA waiver or by specially regulated opioid treatment programs to treat opioid use disorders. See Pharmacy Suboxone Prescribing on the staff intranet for more information.

### DSM-5: Opioid Use Disorder

For patients who are prescribed opioid medications, there is an expectation that they will have therapeutically induced physical dependence. As a result, the criteria for opioid use disorder are amended here to exclude counting tolerance and withdrawal criteria.

Opioid use disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least 2 criteria occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain, use, or recover from the effects of opioids.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.

If a patient is not being prescribed opioid medications, these are two additional criteria for diagnosis of opioid use disorder:

10. Tolerance, as defined by either of the following:
  - A need for markedly increased amounts of opioids to achieve intoxication or desired effect, or
  - Markedly diminished effect with continued use of the same amount of an opioid.
11. Withdrawal, as manifested by either of the following:
  - The characteristic opioid withdrawal syndrome, or
  - Opioids (or a closely related) substance is taken to relieve or avoid withdrawal symptoms.

Mild: Presence of 2–3 symptoms

Moderate: Presence of 4–5 symptoms

Severe: Presence of 6 or more symptoms

# Tapering and Discontinuing Opioids

## General principles

1. Any time the risks of continued opioid therapy are found to outweigh its benefits, opioid medications should be tapered and possibly discontinued. The decision to taper is the provider's; however, developing the care plan is an opportunity for shared decision-making with the patient and family.
2. Taper planning must be individualized based on the patient's clinical needs, indication for taper, readiness for taper, and ability to comply with care team's tapering instructions, and on the provider's clinical judgement.
  - Determine initial step of taper and document rationale in medical record.
  - Consider referral to Clinical Pharmacist Opioid Taper Program (COMET) for help with dosing complicated tapers.
  - **Do not reverse** a taper. A temporary pause in tapering may be indicated to mitigate side effects.
  - Taper planning should be collaborative to the extent possible between provider and patient/family. Areas for shared decision-making can include tapering rate, choice of which medication to taper first, and any other aspects of planning where patient input is appropriate.
  - Consider using the BRAVO protocol (see below) to support conversations about tapering.
3. Assess the patient's response to the initial dose reduction in the first 1 to 4 weeks.
4. Reassess taper weekly to monthly based on patient's response, and prior to each subsequent dose reduction.
5. Prescribe naloxone for any patient at risk for overdose.
6. Some special populations, such as pregnant women or patients with mental health comorbidities, may require alternative approaches to opioid tapers.
7. For questions before initiating or during an opioid taper, please see the Referral Criteria, p. 19.

## Clinical indications for opioid tapering

Table 2. Clinical indications and methods for individualized tapering of opioid therapy	
Examples of indications	Taper methods
<ul style="list-style-type: none"> <li>Consider for patients taking high-dose, long-acting opioids for many years, with no aberrant behaviors, <b>who do not have other indications as below.</b></li> </ul>	<p><b>SLOWEST</b> 2-5% every 4-8 weeks</p>
<ul style="list-style-type: none"> <li>Function and pain are not improved, or</li> <li>Tolerance has developed with long-term opioid prescription, or</li> <li>Comorbid conditions or other factors increase risk of complications), or</li> <li>Patient requests taper.</li> </ul>	<p><b>SLOW: Most common method</b> 5-10% every 4-8 weeks</p>
<ul style="list-style-type: none"> <li>Medication adverse effects indicate risks are greater than benefits, or</li> <li>Morphine equivalent daily dose exceeds recommended threshold of 90 MEDD, or</li> <li>Comorbid conditions increase risk of complications, or</li> <li>Pain is resolved.</li> </ul>	<p><b>MODERATE</b> 10% per week</p>
<ul style="list-style-type: none"> <li>Urine drug screen is consistent with substance abuse concerns, or UDS does not show presence of opioids, or</li> <li>Patient's behavior suggests possible misuse or diversion of medication. Such behaviors might include:               <ul style="list-style-type: none"> <li>Selling prescription drugs</li> <li>Forging prescriptions</li> <li>Stealing or borrowing drugs</li> <li>Frequently losing prescriptions</li> <li>Aggressive demand for opioids</li> <li>Injecting oral/topical opioids</li> <li>Unsanctioned use of opioids</li> <li>Unsanctioned dose escalation</li> <li>Concurrent use of illicit drugs</li> <li>Getting opioids from multiple prescribers</li> <li>Recurring emergency department visits for chronic pain management</li> <li>Non-adherence to opioid treatment plan</li> <li>Overdose event</li> </ul> </li> </ul>	<p><b>RAPID</b> 20-50% first dose, then 10-20% per day</p> <p>Refer patient for chemical dependency or addiction counseling. (See Referral Criteria, p. 19.)</p> <p>See Treating opioid withdrawal symptoms, p. 14.</p>
<ul style="list-style-type: none"> <li>If patient is not at risk of withdrawal and is not currently taking an opioid (e.g., negative UDS, patient states no longer taking), no taper is needed.</li> <li>Do not resume previous opioid medication.</li> </ul>	<p><b>TAPER NOT NEEDED</b> Consider mental health support. Provide withdrawal medication if indicated. See Treating opioid withdrawal symptoms, p. 14.</p>

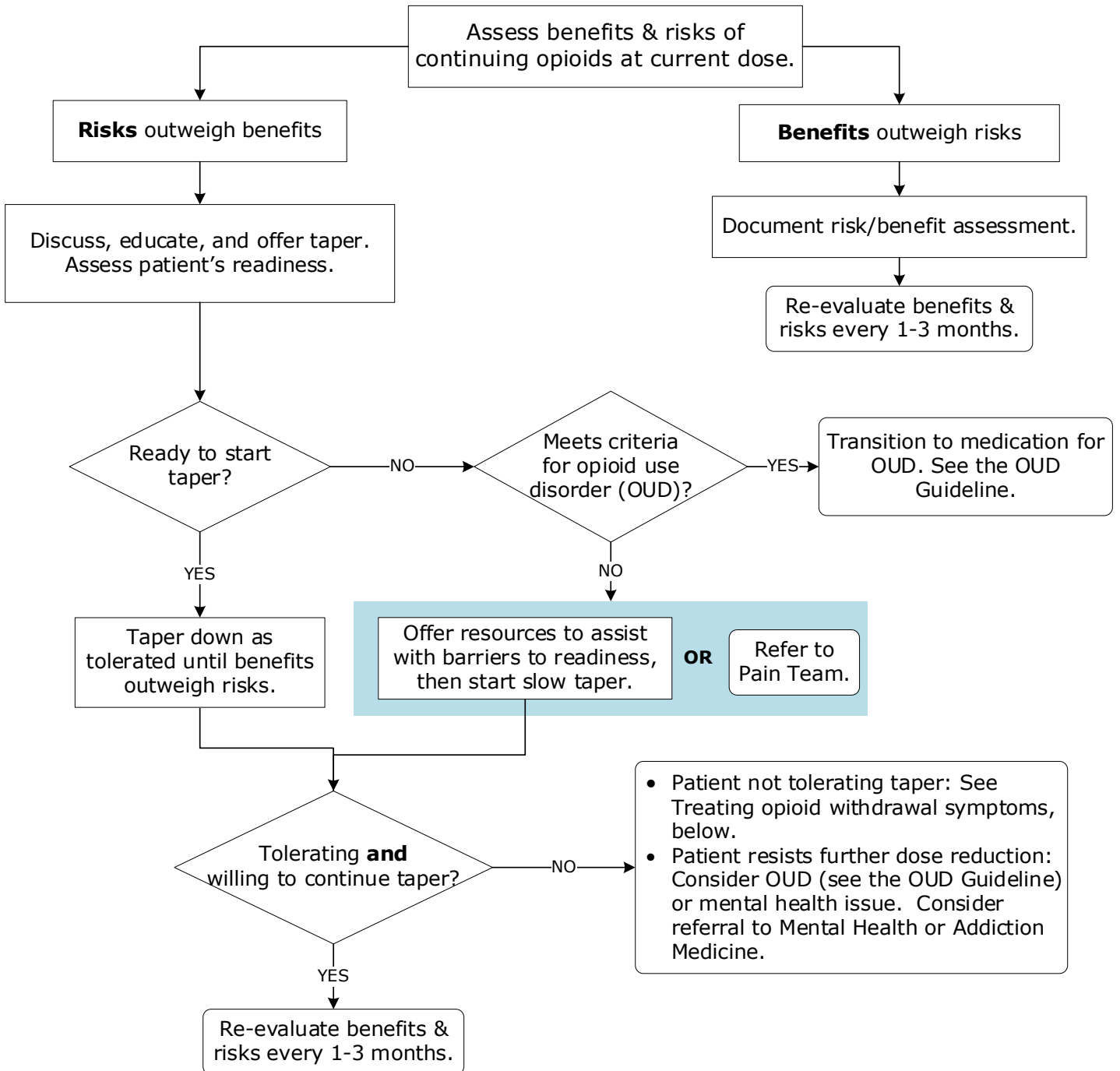
## BRAVO Protocol: how to taper patients off of chronic opioid therapy

The BRAVO protocol was developed to help providers implement a compassionate approach to opioid tapering while also maintaining a therapeutic alliance. It is a helpful approach when tapering opioids, especially with complex chronic pain patients.

[https://content.tts.org/content/Refresher2018/files/G-09\\_Lembke.pdf](https://content.tts.org/content/Refresher2018/files/G-09_Lembke.pdf)

<b>B</b>	<b>Broaching the Subject</b> <ul style="list-style-type: none"><li>• Schedule enough time with your patient to have a discussion on this difficult topic.</li><li>• Anticipate the patient's strong emotional reaction.</li><li>• Identify the feelings normalize those feelings and express empathy with the concerns that patient may have.</li></ul>
<b>R</b>	<b>Risk-Benefit Calculator</b> <ul style="list-style-type: none"><li>• When assessing benefits, weigh the patient's pain relief against their functionality.</li><li>• Involve family members for more objective views on a patient's opioid use.</li><li>• Track common risks such as tolerance and opioid-induced hyperalgesia.</li><li>• Include all of these factors when discussing reasons for tapering off opioids.</li></ul>
<b>A</b>	<b>Addiction Happens</b> <ul style="list-style-type: none"><li>• Addiction is defined by the "Four C's": out of Control use, Compulsive use, Craving and Continued use.</li><li>• Dependence happens when the body relies on a drug to function normally.</li><li>• Dependence and addiction are not equivalent.</li></ul>
<b>V</b>	<b>Velocity Matters – and so Does Validation</b> <ul style="list-style-type: none"><li>• Go slowly, take the necessary time to ease your patients down on their doses.</li><li>• Let the patient be involved when deciding how much to decrease and at what time.</li><li>• It is OK to take breaks in lowering the dosage.</li><li>• Never go backwards, your patient's tolerance will increase and progress will be lost.</li></ul>
<b>O</b>	<b>Other Strategies for Coping with Pain – teach patients these 3 Dialectical Behavioral Therapy (DBT) practices</b> <ul style="list-style-type: none"><li>• STOP: Stop. Take a breath. Observe internal and external experiences and proceed mindfully.</li><li>• Opposite Action Skills: acting opposite to a negative emotional urge in the service or pursuing values goals.</li><li>• Radical Acceptance: accepting reality as it is and not as we wish it to be.</li></ul>

## Opioid Tapering Flowchart



Adapted from Health and Human Services. Available at [https://content.tts.org/content/Refresher2018/files/G-09\\_Lembke.pdf](https://content.tts.org/content/Refresher2018/files/G-09_Lembke.pdf)

## Treating opioid withdrawal symptoms

When opioids are rapidly discontinued (see Table 2, above) or stopped immediately, withdrawal symptoms can occur. The typical time course for symptom development depends on the particular opioid used by the patient.

- Short-acting opioids (e.g., heroin or oxycodone): Withdrawal symptoms begin 8–12 hours after last use and peak 48–72 hours after last use.
- Long-acting opioids (e.g., methadone or buprenorphine): Withdrawal symptoms begin more gradually, with a few symptoms in the first 24–48 hours, a peak in symptoms 3–5 days after last use, and some symptoms continuing for up to a few weeks.

While opioid withdrawal is unpleasant, it is not dangerous to patients. Medications for withdrawal symptoms are in Table 3.

<b>Table 3. Medications used to treat symptoms during gradual opioid taper</b>		
<b>Target symptoms</b>	<b>Medication</b>	<b>Dosing</b>
Hypertension, tremors, sweats, anxiety, restlessness	Clonidine <sup>1</sup>	0.1 mg three times daily as needed
Anxiety, restlessness	Hydroxyzine <sup>2</sup> or Diphenhydramine <sup>2</sup>	25 mg every 6 hours as needed
Insomnia	Hydroxyzine <sup>2</sup> or Diphenhydramine <sup>2</sup>	25–50 mg daily at bedtime as needed
Nausea/vomiting	Promethazine <sup>2</sup>	25 mg every 6 hours as needed
	Metoclopramide <sup>2</sup>	10 mg every 6 hours as needed
Dyspepsia	Calcium carbonate	500 mg 1–2 tabs every 8 hours as needed
	Mylanta, Milk of Magnesia	Follow package instructions.
Pain, fever	Acetaminophen (Tylenol)	500 mg every 4 hours (not to exceed 3 g/24 hours)
	Ibuprofen	400 mg every 4 hours as needed
Diarrhea	Loperamide <sup>2</sup>	4 mg initially, then 2 mg every loose stool as needed; maximum 16 mg/day
Muscle spasm	Methocarbamol <sup>2</sup>	1,000 mg every 6 hours as needed
<sup>1</sup> Clonidine is not FDA-approved for this use, although evidence supports use in this setting. This guideline recommends clonidine as the first-line agent, as it is effective in many patients. As a non-opioid treatment option, it is readily available statewide and does not have extra restrictions on prescribing. Monitor blood pressure and pulse. Dosing of clonidine depends on whether patient is acutely withdrawing or gradually being tapered.		
<sup>2</sup> These are high-risk medications for the elderly. Please consider alternatives for patients aged 64 and older.		

# Minimizing Risks When Continuing to Prescribe Opioids

This guideline seeks to balance the appropriate use of opioid therapy in chronic non-cancer pain against its potential harms.

- Opioid therapy is continued only when the expected benefits—such as reduced pain and clinically meaningful improvement in function (as measured with the PEG Tool)—are expected to outweigh the risks of overdose, opioid use disorder, and other opioid-related harms.
- Opioid therapy is prescribed at the lowest necessary dose and for the shortest duration.
- Clinicians who manage patients on COT are skilled and knowledgeable in the principles of opioid prescribing, tapering, and discontinuing opioid medication, and in the assessment and management of risks associated with opioid use, such as the development of opioid use disorder.
- Clinicians who manage patients on COT routinely integrate psychotherapeutic interventions, functional restoration, interdisciplinary treatment as needed and available, and other non-opioid therapies. Pain is a normal sensation. Acceptance of chronic pain and focus on functional goals improves quality of life.
- The Centers for Disease Control and Prevention has found insufficient evidence to determine the long-term benefits of opioid therapy for chronic pain, and has found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. (Dowell 2016)

## Prescribing naloxone as preventive rescue medication

Naloxone is an opioid antagonist that may be used to reverse the symptoms of opioid overdose (including respiratory depression) after a known or suspected opioid overdose. *Naloxone does not replace emergency medical care.*

**Offer to prescribe naloxone as a preventive rescue medication for patients (and their family members) in the moderate- and high-intensity groups**—those who are taking opioid therapy  $\geq 40$  mg MEDD or have other risk factors for opioid overdose as defined in Table 1, p. 5.

The preferred naloxone product at Kaiser Foundation Health Plan of Washington is Narcan nasal spray.

Counsel family members or other personal contacts who are in a position to assist the patient who is at risk of opioid-related overdose.

### Resources

Pharmacy patient handout on naloxone nasal spray (staff intranet). Use SmartPhrase **.avsnaloxone**.

Opioid overdose prevention education: [www.stopoverdose.org](http://www.stopoverdose.org)

## Opioid prescribing procedures

Chronic non-cancer pain patients should receive all chronic pain management prescriptions from one physician and one pharmacy whenever possible. Clinicians involved in treating a patient on COT are expected to clarify—both among themselves and with the patient—which clinician holds primary responsibility for prescribing. Cross-coverage by another Primary Care provider is included as an extension of the primary prescribing clinician.

Before writing a prescription:

- Calculate and document the total morphine equivalent daily dose (MEDD); doing this can help assess the magnitude of seemingly small incremental dosage changes over time. See “Morphine equivalent daily dose,” below.
- Calculate and document the total acetaminophen dose, including prescribed and over-the-counter.

When writing prescriptions, provide explicit directions:

- Provide specific patient instructions (e.g., schedule for taking).
- Avoid range dosing. For example, instead of “1-2 tablets every 4-6 hours,” use “1 tablet every 6 hours.”
- Order medication in multiples of 7 days and include “to last \_\_ days.”
- Consider setting up refills on Tuesday through Thursday so that they don’t fall on a Monday or Friday, when patients and/or providers are more likely to be on vacation.

**Do not** initiate extended-release/long-acting opioid medication in opioid-naïve patients.

**Do not** prescribe extended-release/long-acting opioid medication on an as-needed basis.

- Food and Drug Administration (FDA) labels state that extended-release and long-acting opioid analgesics are indicated “for the management of pain severe enough to require daily, around-the-clock opioid treatment and for which alternative treatments are inadequate.” The labels emphasize first considering potentially less-addictive measures.
- Limitations of use: Due to the greater risks of overdose and death with extended-release formulations, their use should be reserved for patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, are not tolerated, or provide inadequate or insufficient pain management. (FDA news release 2013)
- For patients aged 65 years and older, short-acting opioids are preferable, as metabolism of medications slows with age. (AMDG 2015)

## Morphine equivalent daily dose (MEDD)

An [electronic MEDD calculator](#) is available on the Agency Medical Directors’ Group web site.

## Equianalgesic dosing and cross-tolerance

All conversions between opioids are estimates generally based on “equianalgesic dosing” (ED). Patient response to these EDs can vary widely, due primarily to genetic factors and incomplete cross-tolerance. **It is recommended that, after the appropriate conversion dose is calculated, it be reduced by 25–50% to ensure safety.**

- Reduce opioid dose by 30–50% to accommodate for unknown cross-tolerance and titrate to goal.
- The wide variation among individuals is multifactorial and poorly understood.
- Incomplete cross-tolerance can lead to greater than anticipated potency in a new opioid, even in the same class of analgesic.
- Monitor clinical response and adverse effects.

Table 4. Morphine equivalent daily dosing (MEDD) for selected opioids <sup>1</sup>	
Opioid	Approximate equianalgesic dose (oral and transdermal) <sup>2</sup>
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
Tramadol	300 mg

<sup>1</sup> Agency Medical Directors’ Group (AMDG) 2015.  
<sup>2</sup> Adapted from Von Korff 2008 and FDA labeling.



## Methadone

Additionally, methadone has unique characteristics that make it difficult to translate dose to MEDD. Methadone exhibits a non-linear relationship due to its long half-life and accumulates with chronic dosing. You may see a dramatic increase in MEDD depending on the dose. The conversion factors for methadone in the AMDG calculator are based on chronic dosing and as follows:

Table 5. Methadone conversion factors <sup>1</sup>	
Methadone	Factor
≤ 20 mg/day	4
21–40 mg/day	8
41–60 mg/day	10
> 60 mg/day	12
<sup>1</sup> Ayonrinde 2000	

## Approaches that are not recommended

### Buprenorphine

Use of buprenorphine (film or patch) or Suboxone (buprenorphine/naloxone) is not recommended for the treatment of chronic pain due to lack of evidence of safety and efficacy. However, patients who are currently taking Suboxone should not be abruptly stopped. Consult with the Pain Team or Addiction Medicine before tapering.

### Cannabinoids (THC/CBD)

There is insufficient evidence from high-quality studies to determine that any cannabis-based products are effective in reducing pain in patients with chronic non-cancer pain or in increasing the rates of opioid discontinuation. There is limited low-quality evidence suggesting that cannabis-based products may reduce pain in patients with neuropathic pain, however the effect was minimal to moderate.

Adverse effects of cannabis include higher risk of cognitive impairment, headache, nasopharyngitis, nausea, somnolence, and dizziness. KP National 2019 Clinician Practice Recommendations for Opioid Prescribing advises avoiding using opioids in patients who choose to use marijuana.

## Adverse effects of opioids

**Serious** adverse effects may include:

- **Slowed breathing (respiratory depression) that can cause death.** This is more likely for patients who:
  - Have sleep apnea or chronic lung disease,
  - Are on higher opioid doses,
  - Take more medicine than prescribed,
  - Have renal or hepatic impairment, or
  - Use any of the following at any time while taking prescribed opioids: alcohol, other prescription medicines (such as sleep aids, muscle relaxers, and tranquilizers), or street drugs.

See also “Prescribing naloxone as preventive rescue medication,” p. 15.

- **Sedation (sleepiness and sluggishness)** can cloud patients’ judgment and slow their reaction time, putting them at increased risk for falls and accidents while driving, using tools, or operating heavy equipment. Driving while on opioids may be considered driving under the influence (DUI).
- **Babies born to mothers taking opioids will be dependent on opioids at birth.** Women who are trying to get pregnant should not take opioids. Women who become pregnant while taking opioids should consult with their physician to make a plan regarding their medication.

- **Physical dependence, tolerance, or addiction to opioids.** Patients with *physical dependence* will experience withdrawal if they stop suddenly. Patients with *tolerance* need to take more of the medicine to get the same effect. Patients with *addiction* are not able to control their use of opioids even if they want to, which may result in harmful outcomes. See “Recognizing opioid use disorder,” p. 9.

**Common** adverse effects may include:

- Constipation
- Depression
- Fatigue
- Itching (a side effect and not an allergic reaction)
- Nausea or vomiting
- Decreased sex drive (decreased testosterone)
- Low blood pressure
- Difficulty with urination
- Insomnia
- Increased sensitivity to pain (hyperalgesia)
- Impaired immune system

## Referral Criteria

<b>Table 6. Referral recommendations for patients on COT for chronic non-cancer pain</b>	
<b>Specialty</b>	<b>Reason for referral</b>
Integrated Mental Health Specialist	<ul style="list-style-type: none"> <li>• Contact urgently to assess patients with <b>suicidal ideation</b>.</li> <li>• Can provide short-term therapy:               <ul style="list-style-type: none"> <li>○ To help patients develop better coping skills for chronic pain</li> <li>○ For mild to moderate depression</li> </ul> </li> </ul>
Mind Phone Consultation	<ul style="list-style-type: none"> <li>• Always an option for recommendations related to diagnostic assessment or mental health medication treatment.</li> </ul>
Mental Health & Wellness Referral	<ul style="list-style-type: none"> <li>• Primary treatment with psychotherapy (individual or group) for moderate to severe mental health conditions</li> <li>• Severe depressive or anxiety disorders which have not responded to trials of two or more SSRI/SNRIs</li> <li>• Patients with complex presentation and diagnostic uncertainty (e.g., possible bipolar disorder)</li> <li>• Any condition with severe symptoms, elevated suicide risk, and/or psychosis</li> </ul>
Addiction Medicine Referral (may be virtual/telephonic consultation)	<ul style="list-style-type: none"> <li>• Co-occurring non-opioid substance use disorder</li> <li>• Suspected opioid use disorder with diagnostic uncertainty</li> <li>• Urine drug screen positive for alcohol, sedative, cocaine or methamphetamine use</li> <li>• Patient request for help with addiction</li> <li>• Consideration of a new start of medication treatment for OUD, including methadone, naltrexone, or buprenorphine (Suboxone) treatment</li> <li>• Concern about substance use disorder</li> <li>• Difficulty adhering to opioid care plan</li> <li>• Problematic use of medications other than opioids</li> <li>• Taking Suboxone from an outside provider for OUD</li> </ul>
Pain Specialist <sup>1</sup>	<p><b>Pain specialty consultation is <i>required</i> for:</b></p> <ul style="list-style-type: none"> <li>• <b>Taking over 120 MEDD or dose increase to 120 mg MEDD or higher per day</b></li> </ul> <p><b>Consider pain specialty consultation if any of the following:</b></p> <ul style="list-style-type: none"> <li>• Taking &gt; 90 mg MEDD</li> <li>• Taking Suboxone from an outside provider for chronic pain</li> <li>• Help with tapering/discontinuing opioid medication</li> <li>• Taking long-term opioids (more than 1 year)</li> <li>• Previous failed attempt to taper</li> <li>• Patients on fentanyl or methadone (these tapers can be complex)</li> </ul>
<p><sup>1</sup> Pain specialists may include rheumatologists, neurologists, and anesthesiologists. See <a href="http://wac.wa.gov/WAC-246-919-945">WAC-246-919-945</a> for more information.</p>	

# Preventing Conversion from Acute to Chronic Opioid Therapy: General Principles

There is no evidence to support the use of ever-increasing doses of opioids for non-cancer pain. There is now evidence that this leads to harm. (See National Permanente Medical Group 2019 Practice Recommendations.)

The best way to minimize chronic opioid use is to minimize acute opioid prescribing. Sixty percent of patients who take opioids for 3 months are still taking them 5 years later. (AMDG 2015)

Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than that needed for the expected duration of pain severe enough to require opioids. (CDC 2016)

For acute, subacute, and perioperative prescribing, general principles from the AMDG guideline are listed here. Refer to the [full AMDG guideline](#) for more detailed recommendations.

## **Acute phase** (0–6 weeks post episode of pain or surgery)

- Check the Washington State Prescription Drug Monitoring Program (PDMP) before prescribing.
- Don't prescribe opioids for non-specific back pain, headaches, or fibromyalgia.
- Prescribe the lowest necessary dose for the shortest duration.
- Three days or less will often be sufficient; more than seven days will rarely be needed. (CDC 2016)
- Opioid use beyond the acute phase is rarely indicated.
- **Required:** Use the SmartPhrase **.acuteopioidtreatment** for documentation when prescribing or offering an acute opioid prescription.

## **Subacute phase** (6–12 weeks post episode of pain or surgery)

- Don't continue opioids without clinically meaningful improvement in function and pain.
- Screen for comorbid mental health conditions and risk for opioid misuse using validated tools.
- Recheck the PDMP and administer a baseline urine drug test if you plan to prescribe opioids beyond 6 weeks.

## **Perioperative** (preoperative through time of hospital discharge)

- Refer to the [2018 AMDG Supplemental Guidance on Prescribing Opioids for Postoperative Pain](#).
- Evaluate thoroughly preoperatively: Check the PDMP and assess for risk for over-sedation and difficult-to-control pain.
- Tapering opioids is not required before surgery, but avoid escalating the dose before surgery. Set appropriate expectations with patients that their pain management needs will be met following surgery, with the understanding that they will return to their preoperative dose (or less) following surgery.
- Discharge with acetaminophen, NSAIDs, or very limited supply (2–3 days) of short-acting opioids for some minor surgeries.
- For patients on chronic opioids, taper to preoperative doses or lower within 6 weeks following major surgery.

## **Special populations**

- Pregnant women: Counsel women before and during pregnancy about maternal, fetal, and neonatal risks.
- Elderly patients: For older adults, initiate opioids at a 25–50% lower dose than for younger adults.
- Adolescents and children: Avoid prescribing opioids for most chronic pain problems.
- Cancer survivors: Rule out recurrence or secondary malignancy for any new or worsening pain.

# Evidence Summary

The Chronic Opioid Therapy Safety Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

As part of our improvement process, the Kaiser Permanente Washington guideline team is working towards developing new clinical guidelines and updating the current guidelines every 2–3 years. To achieve this goal, we are adapting evidence-based recommendations from high-quality national and international external guidelines, if available and appropriate. The external guidelines should meet several quality standards to be considered for adaptation. They must: be developed by a multidisciplinary team with no or minimal conflicts of interest; be evidence-based; address a population that is reasonably similar to our population; and be transparent about the frequency of updates and the date the current version was completed.

In addition to identifying the recently published guidelines that meet the above standards, a literature search was conducted to identify studies relevant to the key questions that are not addressed by the external guidelines.

A supplementary literature search and evidence review was conducted in May 2020; no new studies were published after the October 2019 evidence review that would change the guideline recommendations.

## External guidelines eligible for adapting

- Washington State Agency Medical Directors Group (AMDG). Interagency Guideline on Prescribing Opioids for Pain. Olympia, WA: Washington State Agency Medical Directors' Group; 2015. <http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf>
- Washington State Agency Medical Directors Group (AMDG). Prescribing Opioids for Postoperative Pain – Supplemental Guidance. Olympia, WA: Washington State Agency Medical Directors' Group; 2018. <http://www.agencymeddirectors.wa.gov/Files/FinalSupBreeAMDGPostopPain091318wcover.pdf>
- National Permanente Medical Group 2019 Clinical Practice Recommendations for Opioid Prescribing.
- Dowell D, Haegerich TM, Chou R. Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1-49. DOI: <http://dx.doi.org/10.15585/mmwr.rr6501e1>. <https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm>

## Key questions addressed in the KPWA guideline

### Question 1. What is the clinical effectiveness and safety of buprenorphine buccal film (Belbuca) for the management of non-cancer chronic pain in opioid-experienced and opioid-naïve adults?

- There is a lack of published randomized controlled trials (RCTs) with long-term follow-up that compared the buprenorphine buccal film to an active comparator (e.g., an analgesic, buprenorphine transdermal patch, or other opioid formulations). The published literature consisted only of the two pivotal short-term RCTs (Rauck 2016, Gimbel 2016) and a long-term follow-up observational study (Hale 2017).
- The two short-term RCTs provide moderate-quality evidence that buccal buprenorphine (BBUP) is more effective than placebo in reducing pain over a 12-week duration in selected naïve or opioid-experienced patients with chronic low back pain. The proportions of responders (patients with  $\geq 30\%$  or  $\geq 50\%$  pain reduction) were also higher in the BBUP versus the placebo groups in the two studies. The results also indicate that BBUP had good safety and tolerability in both naïve and experienced patients. However, these results have to be interpreted cautiously, as:
  - The trials included patients with moderate to severe low-back pain and excluded those with pain due to other chronic conditions, which may limit generalization of the results.
  - Patients in the opioid-experienced trial were self-selected, as only those who were on opioid (30-60 MSE) and were willing and able to taper their opioid treatment to  $\leq 30$  mg/d, agreed to participate in the study.
  - BBUP was compared to a placebo and not to an active comparator such as an analgesic or any other buprenorphine preparation.
  - Patients entering the double-blinded randomized phase were those who had successfully achieved an adequate analgesia and good tolerability in the titration phase, which may limit generalization of the results.
  - The 12-week duration of the two trials may be insufficient to determine the long-term efficacy, safety, and tolerability of BBUP.

- There is insufficient evidence to determine the long-term safety and efficacy of BBUP in patients with chronic pain.
- There is insufficient evidence to determine the comparative safety and efficacy of BBPU versus an active comparator.

**Question 2. What is the clinical effectiveness and safety of transdermal buprenorphine (Butrans patch), for the management of non-cancer chronic pain in opioid-experienced and opioid-naïve adults?**

- The available evidence from low- to moderate-quality studies suggests that transdermal buprenorphine is modestly more effective than placebo in reducing chronic, moderate to severe low-back, knee, or hip osteoarthritic pain in both opioid-naïve and opioid-experienced patients.
- Moderate-quality evidence from two published noninferiority trials (Karlsson 2009, Conaghan 2011) that directly compared **buprenorphine** transdermal system (BTDS) versus oral opioid preparations (tramadol in one study and codamol in the other) in patients with osteoarthritis indicates that BTDS is non-inferior to other opioid preparations in reducing pain related to osteoarthritis.
- There is evidence from one equivalence trial (James 2010) that BTDS had similar analgesic efficacy as the sublingual buprenorphine tablets but with fewer side effects (nausea, vomiting and dizziness).
- There is fair evidence from one RCT with an active control (Conaghan 2011) that the use of buprenorphine patch in addition to paracetamol was non-inferior to cocodamol with respect to analgesic efficacy in older patients with hip or knee osteoarthritis.
- Transdermal buprenorphine patches are associated with a high incidence of adverse events that the investigators considered mild to moderate.
- The most frequently reported side effects of BTDS were application site reactions, nausea, vomiting, dizziness, somnolence, and headache in opioid-naïve and opioid-experienced patients.
- Discontinuation rates due to the adverse events ranged between studies from 13-48%.
- No serious BTDS-related adverse events or potential misuse or overdose with BTDS were reported.
- The published trials had an enrichment design, which should be considered when generalizing the results.
- It should be noted that most of the published studies were sponsored by the manufacturers of buprenorphine products and the principal investigators had financial ties to the industry.

**Question 3. What is the clinical effectiveness and safety of the off-label use of buprenorphine/naloxone products for the management non-cancer chronic pain in adults?**

- There is insufficient published evidence from high-quality RCTs to determine the comparative effectiveness and safety of sublingual buprenorphine and other opioid preparations used for the management of non-cancer chronic pain in adults.
- There is insufficient evidence to determine the maximum dose of sublingual buprenorphine that may be allowed for the management of non-cancer chronic pain in adults.
- There is moderate-quality evidence from one RCT (James 2010) showing that sublingual buprenorphine has an equivalent analgesic effect as BTDS in adults with non-cancer chronic pain, but is associated with more side effects and is less tolerated than BTDS.
- There is insufficient published evidence from high-quality RCTs to determine the comparative effectiveness of buprenorphine-naloxone to other opioid preparations in patients with non-cancer chronic pain in the treatment of chronic pain.
- There is low-quality evidence from one small RCT with limitations (Neumann 2013) and retrospective observational studies suggesting that buprenorphine/naloxone therapy may be effective in reducing chronic pain in patients who are dependent on prescription opioids.

**Question 4. What is the association between post-traumatic stress disorder (PTSD), chronic pain, and the risk of developing prescription opioid use disorder?**

- There is fair evidence from several observational studies, systematic reviews, and meta-analyses of published observational studies suggesting that there is an association between PTSD and chronic pain. However, there is insufficient evidence to determine that it is a cause-and-effect association. There is also insufficient evidence to determine the temporal association between the two. (Ecker 2018, Fishbain 2017, Giordano 2018, Ravn 2018, Siqveland 2017)
- The published systematic reviews and meta-analyses also provide fair evidence suggesting that the prevalence of PTSD differs between the types of chronic pain experience and that anxiety and depression are related to both PTSD and chronic pain.
- Observational studies and national surveys (including Bilevicius 2018, Hassan 2017, and Meier 2014, among several others) show that the rates of prescribed opioid use and misuse are significantly higher among patients with PTSD compared to those without PTSD.

**Question 5. Which PTSD screening tools have been validated for patients with chronic pain?**

- There is a lack of published U.S. studies validating the PTSD scales among patients with chronic pain. Only two European studies were identified by the literature search; one small Danish study (Andersen 2018) validated the PTSD-8 scale in chronic pain patients and another study validated the Swedish version of the Posttraumatic Diagnostic Scale (Åkerblom 2017).

**Question 6. Does screening adult patients on chronic opioid use for sleep apnea using STOP-Bang or another sleep apnea questionnaire reduce the risk of developing sleep apnea and/or respiratory depression?**

- The published literature indicates that chronic opioid use may be associated with central sleep apnea and to a lesser degree with obstructive sleep apnea (Jungquist 2012, Correa 2015, Filiatrault 2016).
- There is low- to moderate-quality evidence from earlier observational studies (Walker 2007, Webster 2008) suggesting a dose-response relationship between opioid dose and the severity of sleep apnea, particularly on central sleep apnea.
- There is insufficient evidence to determine whether STOP-Bang or other instruments are appropriate for screening patients on opioid therapy for sleep apnea. The STOP-Bang questionnaire may not be the appropriate tool to identify risk of total sleep apnea in opioid users. (STOP-Bang is useful for obstructive rather than central sleep apnea.)
- The literature search did not identify any sleep apnea screening tool that has been validated for chronic pain patients on opioid therapy.

**Question 7. What is the association between chronic pain and correlates of suicidal ideation in adults with chronic pain and opioid use disorder?**

- There is moderate-quality evidence from a systematic review of observational studies (Tang 2006, Casne 2006), and a narrative review (Racine 2018) that chronic pain itself, regardless of its type, is a risk factor for suicidality.
- The evidence on the association between pain characteristics (including type, severity and duration) and suicidality is conflicting.
- The POINT cohort study on the pharmaceutical opioid use and dependence among people living with chronic pain (Campbell 2015) shows the following:
  - A diagnosis of depression and a past suicide attempt were independent risk factors for suicidal ideation.
  - Depression was not a significant predictor for elevating a suicidal risk to an attempt.
  - Poorer pain-coping skills were associated with a suicide attempt in the past 12 months.
  - Pain-specific factors such as type, severity, and duration were not independently associated with lifetime or past-12-month ideation or lifetime attempt.
  - Pain-specific factors for suicide risk were only more important than other risk factors in the past-12-month ideation to action.
  - All published studies were observational, and the results have to be interpreted with caution.

**Question 8. Is there evidence that the use of Oswestry Disability Index in addition to the PEG (Pain, Enjoyment of life, General activity) screening tool would add incremental benefit in the assessment of function during routine follow-up of patients with chronic pain?**

- The literature search did not identify any study that monitored chronic pain patients with the PEG scale together with the Oswestry Disability Index.

**Question 9. What are the benefits of using CBD (cannabidiol) or THC (tetrahydrocannabinol) for chronic pain (monotherapy or in combination with other medications including opioids)?**

**Question 10. What are the harms of using CBD or THC in combination with opioids in patients with chronic pain?**

- The overall evidence on the effectiveness and safety of cannabis/cannabinoids for non-cancer chronic pain is limited due to several factors, including:
  - The small sizes of published RCTs.
  - Risk of bias in the published trials.
  - The limited duration of the studies, which is insufficient to determine long-term benefits and harms.
  - Insufficient data on the doses and types of cannabinoids used.
  - Most studies used placebo as a comparator and did not provide sufficient data on the other analgesics used in conjunction with the cannabinoids and their doses.
- There is insufficient evidence from high-quality studies to determine that any cannabis-based products are effective in reducing pain in patients with non-cancer chronic pain in general.
- There is limited low-quality evidence suggesting that cannabis-based products may reduce pain in patients with neuropathic pain. The effect observed on pain reduction varied between systematic reviews with or without meta-analyses from minimal to moderate (Kansagara 2017, Nugent 2017, Mücke 2018, Stockings 2018).
- There is moderate-quality evidence showing that cannabinoids may have a statistically significant but modest effect on reducing non-cancer chronic pain related to multiple sclerosis compared to placebo. However, it was associated with higher rates of adverse effects and withdrawal from treatment due to adverse events (Nielsen 2018, Stockings 2018).
- Harms associated with cannabis use may outweigh any observed benefit.
- Patients treated with cannabinoids were more likely to withdraw from the studies due to adverse events.
- The most commonly reported adverse events were headache, nasopharyngitis, nausea, somnolence, and dizziness.
- There is insufficient evidence to determine the efficacy and safety of cannabinoids in patients with fibromyalgia.
- There is insufficient evidence to determine the efficacy and safety of cannabinoids in patients with rheumatoid arthritis.
- There is insufficient evidence to determine the long-term safety and efficacy of cannabis in patients with neuropathic or any other non-cancer chronic pain.
- There is insufficient evidence to show that cannabis use reduces prescribed opioid use or increases the rates of opioid discontinuation.



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# Guideline Development Process and Team

## Development process

This guideline was adapted from externally developed evidence-based guidelines and organizations that establish the community standards for chronic opioid therapy for chronic non-cancer pain. The guideline team reviewed additional evidence using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis. For details, see Evidence and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in May 2020.

## Team

The following specialties were represented on the development and/or update team: chemical dependency, clinical laboratory, family medicine, mental health and wellness, pain team, patient safety, pharmacy, pharmacy informatics, physical therapy, and urgent care.

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## Disclosure of conflict of interest

Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care–related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Chronic Opioid Therapy Safety Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.