STATE OF CALIFORNIA

DIVISION OF WORKERS' COMPENSATION GUIDELINE FOR THE USE OF OPIOIDS TO TREAT WORK-RELATED INJURIES

FORUM POSTING APRIL 2014

Part D: COMPARISON OF RECOMMENDATIONS FROM EXISTING OPIOID GUIDELINES

Part D: Table of Contents

D. Existing Guideline Review

Part D of the DWC Guideline summarizes in tabular format excerpts of recommendations from a review of opioid guidelines for noncancer pain available as of December 2013. This review forms the basis of most findings in Part C and recommendations in Part B.

Note to users of these charts:
Text within quotations is exact language from the guidelines. *DWC comments are italicized.*
The number in parentheses after quoted text indicates the page number in the original guideline. **Please note:** Page numbers were not provided for the ODG (Official Disability Guidelines), because the guidelines are online in html and have no page numbers. In lieu of page numbers, the title of the section from which each quote came in bracketed text introduces each quote.

Opioids for Acute Pain [*If acute phase not defined here, then it was not defined in the guideline*.]	
ACOEM-2011	*No specific recommendation. [Guidelines on opioids are only for chronic pain: "Guidelines for the Chronic Use of Opioids"]* "[Opioids] are potent analgesics widely viewed as helpful in managing moderate to severe acute pain and cancer pain." (1)
APS/AAPM-2009	*No specific recommendation* "Management of cancer pain, pain at end of life, acute pain, postsurgical pain, labor pain, or CNCP in children and adolescents is outside the scope of this guideline." (115)
ASIPP - 2012	*No specific recommendation*
Canadian Guideline-April 2010	*No specific recommendation [Guidelines on opioids are only for chronic pain: "Canadian Guideline for Safe and Effective Use of Opioids for CNCP"]* *[This guideline does have a recommendation for acute or urgent health care facilities for who deal with chronic pain patients asking for prescriptions*: "**R24:** Acute or urgent health care facilities should develop policies to provide guidance on prescribing opioids for chronic pain to avoid contributing to opioid misuse or diversion. (Grade C)." (64)] *Almost no specific recommendations* [*ODG Opioid Guidelines are in the chapter on chronic pain*] [Medications for acute pain (analgesics)]

Opioids for Acute Pain (cont'd)	
ODG *(no page numbers provided because it is an html document)*	"*Opioids* are appropriate analgesics for somatic, neuropathic and visceral pain. [. . .] This study found a negative association between receipt of early opioids for acute LBP and outcomes (disability duration, medical costs, subsequent surgery), but severity was also a strong predictor (confounding variable) of all the outcomes and may explain the early opioid use. (Webster, 2007).[1] *Tramadol* is not recommended as a first-line oral analgesic because of its inferior efficacy to a combination of Hydrocodone/ acetaminophen. There is also no evidence that it has a safer adverse event profile. (Turturro, 1998).[2]"
Utah-2009	**"Opioid Treatment for Acute Pain** **1)** Opioid medications should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies will not provide adequate pain relief. **2)** When opioid medications are prescribed for treatment of acute pain, the number dispensed should be no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition. **3)** When opioid medications are prescribed for treatment of acute pain, the patient should be counseled to store the medications securely, to not share with others, and to dispose of medications properly when the pain has resolved in order to prevent non-medical use of the medications. **4)** Long duration-of-action opioids should not be used for treatment of acute pain, including post-operative pain, except in situations where monitoring and assessment for adverse effects can be conducted. Methadone is rarely if ever indicated for treatment of acute pain." (3)
Veteran's Admin guidelines-May 2010	**Supplementary Therapy** 12. Avoid use of long-acting agents for acute pain or on an as-needed basis in an outpatient setting."

[1] Webster BS, Verma SK, Gatchel RJ. Relationship between early opioid prescribing for acute occupational low back pain and disability duration, medical costs, subsequent surgery and late opioid use. Spine. 2007 Sep 1;32(19):2127-32. "Given the negative association between receipt of early opioids for acute LBP and outcomes, it is suggested that the use of opioids for the management of acute LBP may be counterproductive to recovery."

[2] Turturro MA, Paris PM, Larkin GL. Tramadol versus hydrocodone-acetaminophen in acute musculoskeletal pain: a randomized, double-blind clinical trial. Ann Emerg Med. 1998 Aug;32(2):139-43. Tramadol provides inferior analgesia to hydrocodone-acetaminophen in ED patients with acute musculoskeletal pain.

Opioids for Acute Pain (cont'd)	
	"Availability of Companion Documents: Opioids in the management of acute and chronic pain: independent study. Veteran's Admin opioid web course. Washington (DC): Department of Veterans Affairs (U.S.). Employee education system. Available from the Department of Veterans Affairs Web site." [*I couldn't locate the course on the website.*]
WA Interagency Guidelines (AMD)-2010 Update	"Do not prescribe long-acting or controlled-release opioids (e.g., OxyContin®, fentanyl patches, and methadone) for acute pain." (1) "Use opioid medications for acute or chronic pain only after determining that alternative therapies do not deliver adequate pain relief. The lowest effective dose of opioids should be used." (1)
WA Worker's Comp Guidelines - 2013	"DO NOT USE: Long-acting or extended-release opioids (e.g. Oxycontin®) for acute pain or post-operative pain in an opioid-naive worker." (6) [*boldface in original text*] **"**In general, opioid use for acute pain should be reserved for post-surgery, for the most severe pain (e.g. pain scores ≥ 7), or when alternative treatments such as NSAIDs and non-pharmacological therapies are ineffective**. Evidence does not support the use of opioids as initial treatment for back sprain or other strains, but if they are prescribed, use should be limited to short-term (e.g. ≤ 14 days).** Pain intensity and pain interference should decrease during the acute phase as part of the natural course of recovery following surgery or most injuries. Resumption of pre-injury activities, such as return to work, should be expected during this period. **If use in the acute phase (0-6 weeks) does not lead to improvements in pain and function of at least 30%, or to pain interference levels of 4 or less, continued opioid use is not warranted." (8)**

Opioids for Subacute Pain [*If subacute phase not defined here, then it was not defined in the guideline*.]	
ACOEM-2011	*No specific recommendations [Guidelines are for chronic pain only]*
APS/AAPM-2009	*No specific recommendations* "Management of cancer pain, pain at end of life, acute pain, postsurgical pain, labor pain, or CNCP in children and adolescents is outside the scope of this guideline." (115)
ASIPP – 2012	*No specific recommendations*
Canadian Guideline-April 2010	*No specific recommendations [Guidelines are for chronic pain only]*
ODG	*No specific recommendations [Guidelines are for chronic pain only]*
Utah-2009	**"**The use of opioids should be reevaluated carefully, including assessing the potential for abuse, if persistence of pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition." (3)
Veteran's Admin guidelines-May 2010	*No specific recommendations [Guidelines are for chronic pain only]*
WA Interagency Guidelines (AMD)-2010 Update	*No specific recommendations [Guidelines are for chronic pain only]*
WA Worker's Comp Guidelines - 2013	**"Opioids in the Subacute Phrase (between 6 and 12 weeks):** With some exceptions, resumption of pre-injury activities such as return to work 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 [13, 29]. If the injury is a sprain or strain, opioid use beyond the acute phase is rarely indicated. If opioids are to be prescribed for longer than 6 weeks, the provider must seek authorization. With the exception of catastrophic injuries, the provider must perform the following best practices before L&I or insurer can authorize payment for opioids beyond the acute phase." (9) [*See charts for screening high-risk patients with comorbidities, Prescription monitoring, and tracking pain and function*]."

Opioids for Subacute Pain (cont'd)	
	"During the subacute phase, providers should review the effects of opioid therapy on pain and function to determine whether opioid therapy should continue. Opioids should be discontinued during this phase if: • There is no clinically meaningful improvement in function when compared to function measured during the acute phase. • Treatment resulted in a severe adverse outcome. • Worker has a current substance use disorder (excluding nicotine). • Worker has a history of opioid use disorder (with rare exceptions)." (9)

General Guidelines Regarding Initiation of Chronic Opioid Therapy (COT)			
	Use opioids only after alternative treatments (pharma and non- pharma) have failed?	**Counsels for or against opioid treatment for specific conditions?**	**Exact language**
ACOEM-2011	*Yes.* *Specifies alternative treatments. (2)*	*Yes.* *For select patients with chronic persistent pain, neuropathic pain, or CRPS. (2)*	"Routine use of opioids for treatment of chronic non-malignant pain conditions is not recommended, although selected patients may benefit from judicious use." (2) "Opioids are recommended for select patients with chronic persistent pain, neuropathic pain, or CRPS. Select patients with chronic persistent pain that is not well-controlled (manifested by decreased function attributable to their pain) with non-opioid treatment approaches may be tried on opioids. Other approaches that should have been first utilized include physical restorative approaches, behavioral interventions, self-applied modalities, non-opioid medications (including topical agents) and functional restoration." (2) "Patients with prior psychological disorders, depression, histories of drug abuse/dependence, and/or a personality disorder are often more at risk for a poor outcome and should be cautiously treated with opioids." (2) "High-dose opioids (e.g., morphine, oxycodone) should generally be avoided, as these agents have higher adverse effect profiles. Use of agents such as meperidine, propoxyphene, combination agonists, and mixed agonists/antagonists (butorphanol, nalbuphine, and pentazocine) for management of chronic pain is not recommended." (7)
APS/AAPM-2009	*Yes, but only in the discussion, not in the recs.*	*Yes, but only in the discussion.* *Counsels against opioid treatment for conditions with high psychosocial contributors.*	**"Patient Selection and Risk Stratification Recommendations** 1.1 Before initiating COT, clinicians should conduct a history, physical examination and appropriate testing, including an assessment of risk of substance abuse, misuse, or addiction (strong recommendation, low-quality, low-quality evidence). 1.2 Clinicians may consider a trial of COT as an option if CNCP is moderate or severe, pain is having an adverse impact on function or quality of life,

General Guidelines Regarding Initiation of Chronic Opioid Therapy (COT) (con't)			
			and potential therapeutic benefits outweigh or are likely to outweigh potential harms (strong recommendation, low-quality evidence). 1.3 A benefit to harm evaluation including a history, physical examination, and appropriate diagnostic testing, should be performed and documented before and on an ongoing basis during COT (strong recommendation, low-quality evidence)."(115) ***Discussion.*** [*from first full paragraph*] *"[R]andomized trials that demonstrate the benefits of CIT are most applicable to patients with moderate or more severe pain who have not responded to nonopioid therapies.* [. . .] [E]vidence that demonstrates the efficacy of COT for conditions with strong psychosocial contributors such as some types of chronic low back pain,[74] daily headache,[119] and fibromyalgia[48] is sparse." (116)
ASIPP - 2012			*No specific recommendation*
Canadian Guideline-April 2010	*Not specified*.	*Yes.* *Discusses opioid efficacy in treating a variety of specific conditions (gives high level of detail).* (16-17)	**"Physician considers opioid therapy** (R01-R04): • Comprehensive assessment • Risk of misuse • UDS an option • Opioid efficacy for diagnosis" [fig. 1, p. 8] "R01: Before initiating opioid therapy, ensure comprehensive documentation of the patient's pain condition, general medical condition and psychosocial history (Grade C), psychiatric status, and substance use history. (Grade B). **Comprehensive assessment**" (9) "R04: Before initiating opioid therapy, consider the evidence related to effectiveness in patients with chronic non-cancer pain. (Grade A). **Opioid Efficacy**" (16) *See guideline for more detail about level of efficacy with different strengths and doses of opioids for musculoskeletal pain, neuropathic pain, migraines, GI problems, and fibromyalgia.* (16-17)

General Guidelines Regarding Initiation of Chronic Opioid Therapy (COT) (cont'd)			
			[*see subsequent charts for the other two recommendations, R02, Addiction-risk screening and R03, Urine drug screening*]
ODG (*no page numbers provided because it is an html document)*	*Yes (only non-opioid medications, not non-pharma treatments)*	*Yes. Lists specific conditions that opioids do not treat successfully. Not recommended for headaches or longterm back pain. Not recommended as first-line treatment for some conditions (neuropathic pain osteoarthritis).*	*ODG is unique in distinguishing between the decision to initiate long-term opioid treatment with a trial and the decision to continue opioid treatment 6 months later.* ["Opioids, criteria for use"] **"2) Steps to Take Before a Therapeutic Trial of Opioids:** (a) Attempt to determine if the pain is nociceptive or neuropathic. Also attempt to determine if there are underlying contributing psychological issues. Neuropathic pain may require higher doses of opioids, and opioids are not generally recommended as a first-line therapy for some neuropathic pain. (b) A therapeutic trial of opioids should not be employed until the patient has failed a trial of non-opioid analgesics. (g) The patient should have at least one physical and psychosocial assessment by the treating doctor (and a possible second opinion by a specialist) to assess whether a trial of opioids should occur. When subjective complaints do not correlate with imaging studies and/or physical findings and/or when psychosocial issue concerns exist, a second opinion with a pain specialist and a psychological assessment should be obtained. (Sullivan, 2006) (Sullivan, 2005) (Wilsey, 2008) (Savage, 2008) (Ballyantyne, 2007)"[i] **"1) Establish a Treatment Plan:** d) Ask about Red Flags indicating that opioids may not be helpful in the chronic phase: (The patient has been given a diagnosis in one of the particular diagnostic categories that have not been shown to have good success with opioid therapy: conversion disorder; somatization disorder; pain disorder associated with psychological factors (such as anxiety or depression, or a previous history of substance abuse). Patients may misuse opioids prescribed for pain to obtain relief from depressed feelings, anxiety, insomnia, or discomforting memories. There are better treatments for this type of pathology. (Sullivan, 2006) (Sullivan, 2005) (Wilsey, 2008) (Savage, 2008)

General Guidelines Regarding Initiation of Chronic Opioid Therapy (COT)(cont'd)			
			["Opioids for chronic pain"] "Extreme caution is required for any opioid use in patients with the following: (1) Individuals with a high risk for misuse or diversion; (2) Individuals with evidence of substance abuse issues; (3) Individuals with a family history of substance abuse; (4) Individuals with underlying psychiatric disease. [. . .] - *Chronic back pain*: Opioids appear to be efficacious but should be limited for short-term pain relief in patients with acute low back pain. Long-term efficacy is unclear (>16 weeks), and there is also limited evidence for the use of opioids for chronic low back pain. (Martell-*Annals*, 2007) (White, 2011) (Franklin, 2009) [. . .] Headaches: Not recommended, in particular, due to the risk of medication overuse headache. (Lake, 2008) (Olesen, 2006) See Medication overuse headache." ["Opioids, long-term assessment"] **"Long-term Users of Opioids (6-months or more)"** 1) "Re-assess" [a-f: includes measuring functional improvement, assessing need for psychological consultation and abuse/addiction screening] 2) "Strategy for maintenance" (a) Do not attempt to lower the dose if it is working (b) Supplemental doses of break through medication may be required for incidental pain, end of dose pain, and pain that occurs with predictable situations. This can be determined by information that the patient provides from a pain diary or evaluation of additional need for supplemental medication. (c) The standard increase in dose is 25 to 50% for mild pain and 50 to 100% for severe pain (Wisconsin)" 3) "Visit Frequency" [a: as needed, between 1 and 6 month intervals]
Utah-2009	*Yes.* *Does not specify alternatives; they should be tried or*	*No specific recommendations.*	**"Before prescribing opioid treatment for chronic pain:** 1.1 Recommendation: A comprehensive evaluation should be performed. […]The evaluation should specifically address these issues:

	documented.		• Assess pain and prior treatment of pain.

General Guidelines Regarding Initiation of Chronic Opioid Therapy (COT)(cont'd)			
		No specific recommendations.	• Assess presence of social factors, and medical or mental health conditions that might influence treatment especially those that might interfere with appropriate and safe use of opioid therapy (Department of Veterans Affairs & Department of Defense [Veteran's Admin/DOD], 2003)" (8) "2.1 Recommendation: Alternatives to opioid treatment should be tried (or an adequate trial of such treatments by a previous provider documented) before initiating opioid treatment." (9) [*see subsequent charts for recommendations to use screening tools to identify risk of addiction or abuse and to use the Prescription Monitoring System*]
Veteran's Admin guidelines-May 2010	*Yes. Alternatives referred to in broad terms.*	**"Relative contraindications (Initiate Trial with Caution)** Chronic or recurrent headache" (26)	"A trial of opioid therapy (OT) is indicated for a patient with chronic pain who meets all of the following criteria: a. Moderate to severe pain that has failed to adequately respond to indicated non-opioid and non-drug therapeutic interventions b. The potential benefits of OT are likely to outweigh the risks (i.e., no absolute contraindications) c. The patient is fully informed and consents to the therapy d. Clear and measurable treatment goals are established " (15) "Information from the pain history and physical exam should be reviewed to ensure that the patient has had an adequate therapeutic trial of non-opioid medication therapies." (17)
WA Interagency Guidelines (AMD)-2010 Update	*Yes. Specifies alternative treatments.*	*No specific recommendations.*	**"BEFORE you decide to prescribe opioids for chronic pain** Consider opioid therapy when: • Other physical, behavioral and non-opioid measures have failed (e.g. physical therapy, cognitive behavioral therapy, NSAIDs, antidepressants, antiepileptics), and • The patient has demonstrated sustained improvement in function and pain levels in previous opioid trial, and

General Guidelines Regarding Initiation of Chronic Opioid Therapy (COT) (cont'd)			
			• The patient has no relative contraindication to the use of opioids (e.g. current or past alcohol or other substance abuse, including)." (5)
WA Worker's Comp Guidelines - 2013	*Yes.* *To get <u>prior authorization,</u> doctor must document that alternative treatments failed.*	*No specific recommendations.*	"If opioids are to be prescribed beyond 12 weeks post-injury or post-surgery, the provider **must** have received prior authorization from the department. With the exception of catastrophic injuries, the provider must document the following before L&I or insurer can authorize payment for opioids during the chronic phase: • Clinically meaningful improvement in function (≥ 30%) has been established with opioid use in the acute or subacute phase. • Failure of trials of reasonable alternatives to opioids. • Signed treatment agreement (pain contract). • A time-limited treatment plan, addressing whether chronic opioid therapy is likely to improve the worker's vocational recovery (e.g. work hardening, vocational services). • Consultation with a pain management specialist if the worker's dose is above 120mg/d morphine equivalent dose (MED) and there is no CMIF. Additional appropriate consultations are recommended if the worker has a co-morbid substance use or poorly controlled mental health disorder. • Worker has no contraindication to the use of opioids. • No evidence or likelihood of having serious adverse outcomes from opioid use." (10)

Screening For High Risk Patients (Tools and General Assessment)		
	Risk assessment recommendations prior to COT (part of decision-making process)	**General recommendations if assessment finds high risk** *(For current substance use, see the chart on comorbidities following this one.)*
Exact language in quotes		
ACOEM-2011	*The SOAPP questionnaire is provided in the guideline's appendix (19) and its use is recommended in combination with other questions the doctor should ask the patient directly as part of the initial assessment.* "Screening of patients by asking about prior substance abuse with simple tools and using currently available screening tools designed for use in populations on or considering opioid therapy is recommended as there is evidence that patients with a prior history of drug or alcohol abuse or psychological problems are at increased risk of developing opioid related use/abuse problems. A psychological evaluation would also be indicated in most cases." *Strength of Evidence* – **Recommended, Insufficient Evidence (I)** [*I = consensus based*] (3) "**Screening for Risk of Addiction or Abuse**. "In addition, the Screener and Opioid Assessment for Patients with Pain (SOAPP), a validated, self-administered questionnaire consisting of 24, 14, or 5 questions (see Figure 1c) can be used. This questionnaire does not replace the need for formal professional assessment of abuse or addiction potential for any patient considered for maintenance therapy. Screening for addiction should be done as part of the initial patient evaluation and can be simply performed by asking questions to ascertain whether any of the	"Patients with prior psychological disorders, depression, histories of drug abuse/dependence, and/or a personality disorder are often more at risk for a poor outcome and should be cautiously treated with opioids." (2) "Opioids should be avoided in patients who have prior psychopathology or risk factors for abuse and addiction. If the benefits are felt to substantially outweigh the risks, it may be reasonable to trial opioid therapy. However, these patients are thought to require especially explicit rules of acceptable conduct (i.e., written agreement), careful follow-up by the prescribing physician, and regular follow-up by an appropriate mental health professional prior to, or in conjunction with, the opioid trial unless the treating practitioner has prior experience in the management of patients with chronic pain and opioid use in particular in this population of patients, and is consequently capable of managing the complex psychosocial issues that often impact on outcomes in these patients. The practitioner providing the physical or psychological intervention should be informed of his or her responsibility for both monitoring objective parameters representing patient progress and communicating information regarding progress, or lack of progress, to

Screening For High Risk Patients (Tools and General Assessment)(cont'd)		
	initial patient evaluation and can be simply performed by asking questions to ascertain whether any of the following are present: a. history of alcohol, opioid, or other substance abuse, or a history of chronic, benzodiazepine or other sedative use; b. active alcohol, tobacco, or other substance abuse; c. borderline personality disorders; d. mood disorders (e.g., depression) or psychotic disorders; e. other disorders that are primarily depressive in nature; f. off work for more than 6 months; and g. poor response to opioids in the past. (6)	the physician managing the opioids." (6)
APS/AAPM-2009	*Summary of recommended tools*, p. 116: 1. SOAAP,[ii] Version 1 and the SOAPP-R (the revised version)[iii] 2. Opioid Risk Tool[iv] 3. DIRE instrument[v] "Before initiating COT, clinicians should conduct a history, physical examination and appropriate testing, including an assessment of risk of substance abuse, misuse, or addiction (strong recommendation, low-quality evidence)." (115) "DIRE is clinician-administered and is designed to assess potential efficacy as well as harms. The SOAPP Version 1, SOAPP-R and ORT are patient self-report questionnaires that assess risk of aberrant drug-related behaviors." (116) [*All tools are provided in the Appendices of this guideline*.]	"**High-Risk Patients** **Recommendations** 6.1 Clinicians may consider COT for patients with CNCP and history of drug abuse, psychiatric issues, or serious aberrant drug-related behaviors only if they are able to implement more frequent and stringent monitoring parameters. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist (strong recommendation, low-quality evidence)." (119)

Screening For High Risk Patients (Tools and General Assessment) (cont'd)		
ASIPP - 2012	1. There is limited evidence for reliability and accuracy of available instruments in screening for opioid abuse or illicit drug use due to lack of high quality studies. 2. There is limited evidence that screening for opioid abuse by any of the instruments will reduce the abuse, with lack of long-term published quality literature. 3. There is good evidence that PMPs provide data on patterns of prescription usage. 4. There is fair evidence that prescription drug monitoring programs may reduce prescription drug abuse or doctor shopping. 5. There is limited evidence that prescription drug monitoring programs reduce emergency room visits, drug overdoses, or deaths, due to lack of high quality literature.	1. The evidence of effectiveness and safety of chronic opioid therapy in the elderly for chronic non-cancer pain is fair for short-term and limited for longterm due to lack of high quality studies. 2. The evidence of effectiveness and safety in children and adolescents is limited due to lack of quality studies. 3. The evidence of effectiveness and safety in pregnancy is poor; however, the evidence is good with regards to adverse effects. 4. Effectiveness and safety of opioids in patients with generalized anxiety disorder and depression is limited due to lack of high quality studies with fair evidence of increased risk. 5. The evidence of prevalence of high use of opioids in depression is fair. 6. The evidence of effectiveness and safety in high risk psychological disorder patients with personality disorders and addiction disorders is limited due to lack of high quality studies, with good evidence of increased risk and adverse effects.
Canadian Guideline-2010	*Summary of tools recommended (2-4 are only in the appendix, not mentioned by name in the recommendation)* 1. Opioid Risk Tool 2. Interview guide for alcohol – CAMH 2004 3. Interview guide for substance use 4. CAGE questionnaire "R02: Before initiating opioid therapy, consider using a screening tool to determine the patient's risk for opioid addiction. (Grade B). Addiction-risk screening." (11)	"R11: When initiating a trial of opioid therapy for patients at higher risk for misuse, prescribe only for well-defined somatic or neuropathic pain conditions (Grade A), start with lower doses and titrate in small-dose increments (Grade B), and monitor closely for signs of aberrant drug-related behaviors. (Grade C). **Risk: Opioid misuse**" (40) "The following factors could indicate patients at higher risk of opioid misuse:

Screening For High Risk Patients (Tools and General Assessment) (cont'd)		
	"Most of the screening tools have not been studied in depth, validated, or been compared to each other but the Opioid Risk Tool (ORT) is widely used (see Appendix B-2: ORT). See Appendix B-1 for examples of interview guides and assessment tools that may be used to supplement a comprehensive history of alcohol and substance use." (11) **"Summary of Peer-Reviewed Evidence:** A systematic review of predictors for opioid misuse concluded that none of the screening tools can be recommended with confidence, because the samples were small and unrepresentative (Turk 2008). A personal history of abuse of illicit drugs or alcohol remains the strongest predictor of opioid misuse and abuse." (11)	1) history of alcohol or substance abuse (patient and/or family) 2) uncertain security in the home (e.g., living in a boarding home with minimal protection for possessions), and 3) past aberrant drug-related behaviors" (40)
ODG *(no page numbers provided because it is an html document)*	"[Opioids, screening tests for risk of addiction & misuse] Recommend screening tests for the risk of misuse of prescription opioids and/or aberrant drug behavior (defined as behavior that suggests the presence of substance abuse or addiction), prior to initiating opioid therapy and with ongoing therapy (though frequency of testing is not well defined). [. . .] Results of screening tests should be used in the context of other sources in order to stratify risk and identify those individuals who are not good candidates for opioid therapy, or who require more careful monitoring with use. [. . .] There is minimal literature available to recommend any	["Opioids, criteria for use"] **"4) On-Going Management**. Actions Should Include: (e) Use of drug screening or inpatient treatment with issues of abuse, addiction, or poor pain control. (Webster, 2008)" ["Opioids, screening tests for risk of addiction & misuse"] "It is important to note that being at risk does not necessarily indicate that a patient will develop an addiction disorder, or is addicted. A history of an addiction disorder does not preclude a patient from being treated with opioids. (Savage 1999) (Portenoy, 1996) (Chou, 2009b) (Bohn, 2011) (Turk, 2008) (Moore, 2009) (Jones 2013) (Jones, 2011) (Jamion, 2011) (Atluri,

	one tool over another, and a recent study which compared	2013) (Sehgal, 2012)

Screening For High Risk Patients (Tools and General Assessment) (cont'd)		
	several screening instruments to a risk rating performed by a psychologist found the clinical assessment was the most sensitive predictor of discharge status, with the SOAPP-R being the most sensitive of the self-report measures. (Jones, 2012) Another recent study recommended the use of DIRE Score, ABC Checklist, Screening Tool by Atluri & Sudarshan, SOAPP, PDUQP, or PMQ. (Atluri, 2012)" *Gives detailed objective description of eleven screening tests, labled as "subjective screening tools" and including the SOAPP, SOAPP-R, ORT, COMM, and CAGE tests.* *Global judgment introducing the list*: "The risk of use of a subjective tool is that abusers may not be truthful." *Directly below this list is another list of three screening tests "containing objective measures": ABC (Addiction Behaviors Checklist), DIRE (Diagnosis, Intractability, Risk, Efficacy) and Atluri.*	
Utah-2009	"1. SOAPP-R 2. Opioid Risk Tool 3. Urine Drug Tests* 4. Signs of Substance Misuse†" (55) **weaker recommendation*, *see UDT chart later in this matrix* †*A list of signs to look for* **"3.1 Recommendation:** Use a screening tool to assess the patient's risk of misuse prior to prescribing an opioid medication long term for chronic pain. [. . .] **3.2 Recommendation:** Consider performing drug screening before initiating long term opioid treatment for	**"12. Consultation and management of complex patients"** **"12.2 Recommendation** Patients with a history of addiction or substance use disorder or who have positive drug screens indicative of a problem should be considered for referral to an addiction specialist for evaluation of recurrence risk and for assistance with treatment." (19) "The main goal of a consultation is for the prescribing clinician to receive recommendations for ongoing treatment." (19) **"12.4 Recommendation** Patients with coexisting psychiatric disorder should receive ongoing mental

	chronic pain." (9)	health support and treatment while receiving opioid

Screening For High Risk Patients (Tools and General Assessment) (cont'd)		
		medication for pain control." (19) "Tools to accompany Recommendation 12: • Strategies for Tapering and Weaning • Directory of Resources" (19)
Veteran's Admin guidelines	*Does not name any screening tools, but lists topics of interest for identifying high-risk patients:* "The comprehensive assessment should include: • Past Psychiatric history (including depression, anxiety, other emotional disorders, risk of suicide including family history and previous suicidal attempts) • Medications (including current and past analgesics, their effectiveness, side effects, and tolerability, as well as drugs that may interact with opioid therapy) • Substance use history (personal, family, peer group) • Family history • Social history (including employment, cultural background, social network, marital history, and legal history, other behavioral patterns (i.e. impulse behaviors)) • Abuse (sexual, physical and mental)" (17) "A urine drug test (UDT) should be used to screen for the presence of illegal drugs, unreported prescribed medication, or unreported alcohol use prior to starting therapy. [B]" (17)	**"Absolute contraindications:** a. Acute psychiatric instability. [. . .] c. True Allergy to opioid agents" (25) *(the others involve medications and adverse effects. See the VA guideline.)* **"Determine appropriate setting for opioid therapy** **Recommendation:** For patients with history of drug abuse, psychiatric issues, or serious aberrant drug-related behaviors, initiation of a trial of OT in the primary care setting should only be considered if more frequent and stringent monitoring can be provided. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist." (28) [*makes same recommendation for patients with current disorders*] "**Psychiatric History—Include the following:** […] Patients being treated for depression with MAOIs should not be treated with opioid therapy." (18) **"Substance Use History—** Current substance use disorder (SUD) is not a contraindication to OT. […] Physicians should be especially cautious about prescribing controlled substances to these patients. […]

Screening For High Risk Patients (Tools and General Assessment) (cont'd)		
		Consultation with an addiction specialist for evaluation or co-management may be useful, as well as involvement of the patient's family. An alternative would be the provision of opioids in a structured setting (i.e., Opioid Pain Clinic) that can provide support and evaluation needed for this group of patients (Wiedemer, 2007)." (19)
WA Interagency Guidelines (AMDG-2010 Update)	"1. The Opioid Risk Tool (ORT) 2.The CAGE-AID to screen for alcohol or drug problems 3. The PHQ-9 to screen for depression severity 4. A baseline urine drug test 5. A baseline assessment of function and pain with the 2 item Graded Chronic Pain Scale (provided in appendix)" (5)	"If substantial risk is identified through screening, extreme caution should be used and a specialty consultation (e.g. addiction or mental health specialist) is strongly encouraged. In such cases, a baseline risk assessment using the following tools should be performed and documented in the record: [see list in column the left]" (5) "High risk does not necessarily contraindicate the use of opioids but additional monitoring is indicated whenever risk is increased for any reason. Additional monitoring may include increased frequency of reassessment of pain, function, and aberrant behaviors, decreased number of doses prescribed, and increased frequency of UDT." (6)
WA Worker's Comp Guidelines-2013	*Tools not specified* (*this guideline supplements the WA Interagency guideline)*	"Chronic opioid therapy (COT) should not be prescribed in the presence of current substance use disorder (excluding nicotine) and cautiously if there is past substance use disorder." (3)

Impact of Co-Morbid Conditions[3] On The Decision Of Whether To Initiate Opioid Treatment			
	Is active substance abuse a contra-indication for opioid treatment?	**Are any other prescribed medications contraindications for opioid treatment?**	**Exact language (indicated by quotes)**
ACOEM-2011	*Not specified*	*Use with caution: tramadol with tricyclic, SSRI, or SNRI anti-depressants*	"Patients with prior psychological disorders, depression, histories of drug abuse/dependence, and/or a personality disorder are often more at risk for a poor outcome and should be cautiously treated with opioids." (2) "**Criteria for Initiation:** [. . .] **4. Contra-indications** – There is no evidence of significant psychopathology or an elevated risk of abuse, addiction, or adverse outcome (see Figure 1c for a screening tool). These are relative rather than absolute contraindications to opioid therapy. However, their presence requires the practitioner to take added precautions by increasing patient education and the degree to which opioid use is both monitored and controlled. **5. Expert Consultation** – Patients with a "chronic pain syndrome" or "pain disorder" characterized by behavioral and emotional issues, poor coping, dysfunctional pain behaviors, life disruption, and delayed recovery with symptoms inconsistent with objective findings both clinically and on diagnostic testing should not be considered for opioid therapy until they have had a psychological evaluation and, if warranted, referred for appropriate psychological, behavioral, and/or rehabilitative interventions." (4) "Tramadol should be used cautiously in patients taking tricyclic, SSRI, or SNRI anti-depressants because of the increased risk of central nervous system depression, psychomotor impairment, seizures, and serotonin syndrome. If

[3] For instance: current substance use disorder (including cannabis), concomitant use of sedative/hypnotics and benzodiazepines, as well as other pre-existing medical conditions such as renal disorder, upper respiratory problems, sleep apnea, and constipation.

			tramadol is contraindicated or ineffective, other short-acting opioids such as

Impact of Co-Morbid Conditions[4] On The Decision Of Whether To Initiate Opioid Treatment (cont'd)			
			5mg oxycodone or 5mg hydrocodone every 4 to 6 hours may be used as needed for pain relief." (7)
APS/AAPM-2009	*No, but must be done with extreme care in consultation with specialists.*		**"Recommendation 6.1** Clinicians may consider COT for patients with CNCP and history of drug abuse, psychiatric issues, or serious aberrant drug-related behaviors only if they are able to implement more frequent and stringent monitoring parameters. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist (strong recommendation, low-quality evidence)." (119) *Comorbidities mentioned in the discussion:* "Preexisting constipation, nausea, pulmonary disease, and cognitive impairment probably predict risk for opioid-related adverse effects, though no studies have adequately evaluated the utility of these factors for use in risk stratification." (116)
ASIPP - 2012	*Not specified.*	*Not specified.*	1. There is good evidence that the increased supply of opioids, use of high dose opioids, doctor shoppers, and patients with multiple comorbid factors contribute to the majority of fatalities
Canadian Guideline-April 2010	*Not specified.*	*Makes nuanced rec regarding patients taking benzodiazepines (and driving)*	"**Benzodiazepine tapering** R06: For patients taking benzodiazepines, particularly for elderly patients, consider a trial of tapering (Grade B). If a trial of tapering is not indicated or is unsuccessful, opioids should be titrated more slowly and at lower doses. (Grade C). " (25) Discussion: "A successful trial of benzodiazepine tapering can mean either a dose reduction or elimination of benzodiazepines." (25) **"LTOT and Driving** R14: When assessing safety to drive in patients on long-term opioid therapy [LTOT], consider factors that could impair cognition and psychomotor ability, such as a consistently severe pain rating, disordered sleep, and concomitant medications that increase

[4] For instance: current substance use disorder (including cannabis), concomitant use of sedative/hypnotics and benzodiazepines, as well as other pre-existing medical conditions such as renal disorder, upper respiratory problems, sleep apnea, and constipation.

			sedation [such as benzodiazepines and anticholinergics, tricyclic

Impact of Co-Morbid Conditions on the Decision of Whether to Initiate Opioid Treatment (cont'd)			
			antidepressants, anticonvulsants, antihistamines, breakthrough pain medication]. (Grade C)." (45) "**Co-morbid psychiatric diagnoses** R20: Patients with a psychiatric diagnosis are at greater risk for adverse effects from opioid treatment. Usually in these patients, opioids should be reserved for well-defined somatic or neuropathic pain conditions. Titrate more slowly and monitor closely; seek consultation where feasible. (Grade B)." (55) "Prescribing Cautions for Co-morbid Psychiatric Conditions [includes the two recs in R20 and three others]: 3. Use structured opioid therapy (see Recommendation 21), with a specific treatment agreement, conservative dosing, frequent dispensing, and monitoring for aberrant drug-related behaviours. 4. Closely monitor the patient's mood and functioning. 5. Consider tapering if opioid effectiveness is inadequate (opioid effectiveness = improved function or at least 30% reduction in pain intensity)." (55) *Recs for other comorbidities:* "Patients at higher risk of opioid overdose are those with: 1. **Renal or hepatic impairment:** Caution is advised, because opioids are metabolized in the liver and excreted through the renal system (Tegeder 1999, Foral 2007). Morphine is contraindicated in renal insufficiency. 2. **Chronic obstructive pulmonary disease (COPD) and sleep apnea**: Opioid use may be a risk factor for central sleep apnea (Mogri 2008). Tolerance to the respiratory depressant effects of opioids develops slowly and incompletely, putting COPD patients at risk for respiratory depression with a higher dose increase. 3. **Sleep disorders:** Sleep disorders, including insomnia and daytime sleepiness, are common among opioid users (Zgierska 2007). They may reflect the effects of pain, or the sedating effects of opioids, or

			concurrent depression.

Impact of Co-Morbid Conditions on the Decision of Whether to Initiate Opioid Treatment (cont'd)			
			4. **Cognitive impairment:** Opioids should be avoided in cognitively impaired patients who live alone, unless ongoing medication supervision can be arranged." (21, from table 5-5.2 and footnote to table)
ODG *(no page numbers provided because it is an html document)*	*No, not stated specifically.*	*No, but strongly recommends against concomitant opioid treatment and benzodiazepines or other sedative drugs*	[Opioids for chronic pain] "Benzodiazepines are commonly implicated in opioid overdose deaths and they lower the lethal opioid dose. Consideration of tapering the use of sedative hypnotics and benzodiazepines before starting opioid use if possible is strongly recommended. (Mirakbari, 2003) (Kahan, 2011) (Gomes, 2011) (Toblin 2010)"
Utah-2009	*No, can be done in consultation with specialists.*		**"Consultation and management of complex patients"** (19) "12.1 Recommendation: Clinicians should consider consultation for patients with complex pain conditions, patients with serious co-morbidities including mental illness, patients who have a history or evidence of current drug addiction or abuse, or when the provider is not confident of his or her abilities to manage the treatment." (19) "12.2 Recommendation: Patients with a history of addiction or substance use disorder or who have positive drug screens indicative of a problem should be considered for referral to an addiction specialist for evaluation of recurrence risk and for assistance with treatment." (19) "12.3 Recommendation: Pain patients who are addicted to medications/drugs should be referred to a pain management, mental health or substance use disorder specialist if available, for recommendations on the treatment plan and possibly for assistance in management. "(19) "12.4 Recommendation: Patients with coexisting psychiatric disorder should receive ongoing mental health support and treatment while receiving opioid medication for pain control." (19)

Impact of Co-Morbid Conditions on the Decision of Whether to Initiate Opioid Treatment (cont'd)			
Veteran's Admin guidelines-May 2010	*Yes, excluding nicotine.*	*Yes.* "Providers should carefully evaluate potential drug interactions prior to initiating opioid therapy, (such as MAOI with concurrent meperidine use, methadone with benzodiazepines, fentanyl with CYP3A4 inhibitors, or propoxyphene and alcohol and other CNS depressants" (25)	**"Are There Contraindications to Opioid Therapy that Cannot be Resolved?** **Recommendation"** (24) "1. Opioid therapy trial should NOT be initiated in the following situations (absolute contraindications): • Severe respiratory instability • Acute psychiatric instability or uncontrolled suicide risk • Diagnosed non-nicotine Substance Use Disorder (DSM-IV criteria) not in remission and not in treatment • True allergy to opioid agents (cannot be resolved by switching agents) • Co-administration of drug capable of inducing life-limiting drug-drug interaction • QTc interval > 500 millisecond for using methadone • Active diversion of controlled substances (providing the medication to someone for whom it was not intended) • Prior adequate trials of specific opioids that were discontinued due to intolerance, serious adverse effects that cannot be treated, or lack of efficacy." (24) "2. Opioid therapy trial can be initiated with caution in the following situations. Consider consultation with appropriate specialty care to evaluate if potential benefits outweigh the risks of therapy. a. Patient receiving treatment for diagnosed Substance Use Disorder (DSM-IV criteria). (See Annotation P1) b. Medical condition in which OT may cause harm: • Patient with obstructive sleep apnea not on CPAP • Patients with central sleep apnea (See Annotation P2)

			• Chronic pulmonary disease (mild-moderate asthma, COPD)

Impact of Co-Morbid Conditions on the Decision of Whether to Initiate Opioid Treatment (cont'd)			
			• Cardiac condition (QTc interval 450-500 milliseconds) that may increase risk of using methadone • Known or suspected paralytic ileus • Respiratory depression in unmonitored setting c. Risk for suicide or unstable psychiatric disorder d. Complicated pain • Headache not responsive to other pain treatment modalities" (24)
WA Interagency Guidelines (AMD)-2010	*Yes (no specs regarding nicotine)*	*sedative-hypnotics, benzodiazepines, barbiturates*	"Opioid prescribing should be *avoided* in patients with active alcohol or other substance abuse. Extreme caution should be used, and a consultation with an addiction specialist is strongly encouraged, prior to prescribing opioids for patients with a history of alcohol or other substance abuse." (8) "Do not combine opioids with sedative-hypnotics, benzodiazepines or barbiturates for chronic non-cancer pain unless there is a specific medical and/or psychiatric indication for the combination and increased monitoring is initiated." (5)
WA Worker's Comp Guidelines - 2013	*Yes, excluding nicotine*	*NOT RECOMMENDED: opioids with Carisoprodol, benzodiazepines, sedative-hypnotics or barbiturates (with caveat for spasticity, see exact language column)* *Use with CAUTION : opioids with acetaminophen with acetaminophen combination opioids (such as Vicodin and others*	"Chronic opioid therapy (COT) should not be prescribed in the presence of current substance use disorder (excluding nicotine) and cautiously if there is past substance use disorder." (3) "Because of the increased risk for adverse outcomes from the use of COT in patients with mental health disorders, such as borderline personality disorder, mood disorders (e.g. depression, bipolar disorder, anxiety, post-traumatic stress disorder or PTSD) or psychotic disorders, providers should be cautious when prescribing COT for workers with these co-morbid conditions. Furthermore, workers with current substance use disorders as defined by DSM (excluding nicotine) should not receive COT. Workers with a history of opioid use disorder should only receive COT under exceptional circumstances." (6)

Impact of Co-Morbid Conditions on the Decision of Whether to Initiate Opioid Treatment (cont'd)			
WA Worker's Comp Guidelines - 2013	*Yes, excluding nicotine*	*NOT RECOMMENDED: opioids with Carisoprodol, benzodiazepines, sedative-hypnotics or barbiturates (with caveat for spasticity, see exact language column)* *Use with CAUTION : opioids with acetaminophen with acetaminophen combination opioids (such as Vicodin and others*	"*There may be specific indications for such combinations, such as the co-existence of spasticity. In such cases, a pain specialist consultation is strongly recommended. Consider alternatives such as tricyclic antidepressants or antihistamines to manage insomnia." (7, italics in original)*

Urine Drug Testing				
	Required for all patients before initiating opioid treatment?	**Who to test after COT started?**	**UDTs in monitoring phase frequency? Random or planned?**	**Specific tests explained or recommended**
ACOEM-2011	*No, only high-risk patients.* "While the initial evaluation and treatment plan will not necessarily require urine drug monitoring to ascertain that the prescribed medication is being used and other substances avoided (since opioids use should generally be short-term), this may be warranted if the patient's past history suggests that there is a risk of substance abuse, misuse, or diversion." (6)	*All patients on COT*	*1-4 times a year, randomly, and also "for cause" [synthesis of the two passages quoted below]* "Randomly, at least twice and up to 4 times a year and at termination. Screening should also be performed "for cause" (e.g., provider suspicion of substance misuse including over-sedating, drug intoxication, motor vehicle crash, other accidents and injuries, driving while intoxicated, premature prescription renewals, self-directed dose changes, lost or stolen prescriptions, using more than one provider for prescriptions, non-pain use of medication, using alcohol for pain treatment or excessive alcohol use, missed appointments, hoarding of medications and selling medications). *Strength of Evidence* – **Recommended, Evidence (C)**" (3) "Patients on opioids should be regularly screened on a random basis via urine testing, with frequency of testing being at least yearly or more often as needed.[4]" (10) [4]Jamison and Pham 2007	*No.*
APS/AAPM-2009		*Strong recommendation to test high-risk patients, softer rec to test all patients*	*Periodically, for all types of patients, weak rec for weekly testing of very high-risk patients*	*No.*

Urine Drug Testing (cont'd)				
			"Monitoring Recommendations: [. . .] 5.2 In patients on COT who are at high risk or who have engaged in aberrant drug-related behaviors, clinicians should periodically obtain urine drug screens or other information to confirm adherence to the COT plan of care (strong recommendation, low-quality evidence). 5.3 In patients on COT not at high risk and not known to have engaged in aberrant drug-related behaviors, clinicians should consider periodically obtaining urine drug screens or other information to confirm adherence to the COT plan of care (weak recommendation, low-quality evidence)." (118) **Discussion:** **"**For patients at very high risk for adverse outcomes, monitoring on a weekly basis may be a reasonable strategy." (118) "Random urine drug screens may be more informative than scheduled or routine testing, as patients may change behaviors when they expect to be tested, though there are no studies comparing these approaches." (119)	
ASIPP - 2012	1.There is fair evidence for the diagnostic accuracy of UDT. 2. There is fair evidence to identify patients who are non-compliant or abusing prescription drugs or illicit drugs. 3. There is fair evidence that UDT may decrease prescription drug abuse or illicit drug use when patients are in chronic pain management therapy.			

Urine Drug Testing (cont'd)				
Canadian Guideline-April 2010	*No specifications recommendations address this rubric's questions, but they have a recommendation on UDTs:* "**R03** When using urine drug screening (UDS) to establish a baseline measure of risk or to monitor compliance, be aware of benefits and limitations, appropriate test ordering and interpretation, and have a plan to use results. (Grade C). *Urine drug screening"* (12) *The discussion of UDTs addresses other issues <u>in depth</u>, including a detailed comparison in the appendix of the two types of UDTs, immonoassays and chromatography. (68)*			*Immunoassays vs. chromatagraphy*
ODG *(no page numbers provided because it is an html document)*	*Yes.* [Urine drug testing (UDT)] "A point-of-contact (POC) immunoassay test is recommended prior to initiating chronic opioid therapy." "*At the onset of treatment*: (1) UDT is recommended at the onset of treatment of a new patient who is already receiving a controlled substance or when chronic opioid management is considered." BUT elsewhere, they make a	*With high-risk patients and patients for whom opioid treatment is not lowering pain and increasing function.* *[Urine drug testing (UDT)]* "<u>Ongoing monitoring</u>: (1) If a patient has evidence of a "high risk" of addiction (including evidence of a comorbid psychiatric disorder (such as depression, anxiety, attention-deficit disorder, obsessive-compulsive disorder, bipolar disorder, and/or schizophrenia), has a history of aberrant behavior,	*Frequency depends on risk level of patient. Random screens are recommended.* [Urine drug testing] "Random screens are recommended as patients may change their behavior when expected to be tested. (Chou, 2009b)[5]" " **Cost of Testing:** The Centers for Medicare and Medicaid Services (CMS) recently changed codes for UDT from 80101 to G0431 due to excessive use of UDT and abuse. The new G-code is defined as "drug screen, qualitative; single drug class method (e.g. Immunoassay, enzyme assay) each drug class" and excludes chromatography. An example of reimbursement by CMS for CPT code G0431 at POC is $160. This may vary for	

[5] Chou R, Fanciullo GJ, Fine PG, Miaskowski C, Passik SD, Portenoy RK. Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors: a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. J Pain. 2009; 10:131-46.

	much softer	personal or family history of	State fee guidelines and/or geographic	

Urine Drug Testing (cont'd)				
	recommendation to do so: [Opioids, criteria for use] "**Steps to Take Before a Therapeutic Trial of Opioids:** (j) Consider the use of a urine drug screen to assess for the use or the presence of illegal drugs."	substance dependence (addiction), or a personal history of sexual or physical trauma, ongoing urine drug testing is indicated as an adjunct to monitoring along with clinical exams and pill counts. (2) If dose increases are not decreasing pain and increasing function, consideration of UDT should be made to aid in evaluating medication compliance and adherence." "**On-Going Management**. Actions Should Include: e) Use of drug screening or inpatient treatment with issues of abuse, addiction, or poor pain control. (Webster, 2008)"	location. Cost effectiveness analysis is currently not available for use of monitoring including urine drug testing." Limitations to UDT: There is currently no way to tell from a urine drug test the exact amount of drug ingested or taken, when the last dose was taken, or the source of the drug. A recent systematic review of the use of drug treatment agreements and urine drug testing to discourage misuse when opioids are prescribed for chronic noncancer pain, found weak, heterogeneous evidence that these strategies were associated with less misuse. Limited research did find that UDT was a valuable tool to detect use of nonprescribed drugs and confirm adherence to prescribed medications beyond that identified by patient self-report or impression of the treating physician. (Katz, 2002) (Katz, 2003) (Brahm, 2010) (Compton, 2007) (Gourlay, 2010) (Gourlay 2009) (Heit, 2010) (Heit, 2004) (Jaffee, 2008) (Moeller, 2008) (Nafziger, 2009) (Schneider, 2008) (Starrels, 2010) (Chou, 2009b) (McCarberg, 2011) (Owen, 2012)[6]	

[6] Owen GT, Burton AW, Schade CM, Passik S. Urine drug testing: current recommendations and best practices. Pain Physician. 2012 ;15:ES119-33. "UDT must be done routinely as part of an overall best practice program in order to prescribe chronic opioid therapy. This program may include risk stratification; baseline and periodic UDT; behavioral monitoring; and prescription monitoring programs as the best available tools to monitor chronic opioid compliance."

Urine Drug Testing (cont'd)				
			(Owen, 2012)[7] (Christo, 2011)[8] (Melanson, 2009) (Peppin, 2012) (Atluri, 2012)[9] (Standridge, 2010)[10] **"Criteria for Use of Urine Drug Testing"** 2. "Frequency of urine drug testing should be based on documented evidence of risk stratification including use of a testing instrument." *3. Low risk patients: test within 6 months of beginning COT and yearly after that. "*There is no reason to perform confirmatory testing unless the test is inappropriate or there are unexpected results. If required, confirmatory testing should be for the questioned drugs only."	

[7] Owen GT, Burton AW, Schade CM, Passik S. Urine drug testing: current recommendations and best practices. Pain Physician. 2012 ;15:ES119-33. "UDT must be done routinely as part of an overall best practice program in order to prescribe chronic opioid therapy. This program may include risk stratification; baseline and periodic UDT; behavioral monitoring; and prescription monitoring programs as the best available tools to monitor chronic opioid compliance."

[8] Christo PJ, Manchikanti L, Ruan X, Bottros M, Hansen H, Solanki DR, Jordan AE, Colson J. Urine drug testing in chronic pain. Pain Physician. 2011;14:123-43. "UDT is associated with multiple limitations secondary to potential pitfalls related to drug metabolism, reliability of the tests, and the knowledge of the pain physician."

[9] Atluri S, Akbik H, Sudarshan G. Prevention of opioid abuse in chronic non-cancer pain: an algorithmic, evidence based approach. Pain Physician. 2012; 15:ES177-89. "The pillars of prevention are the screening of patients into high, medium, and low risk categories using screening tools; monitoring patients using UDS, PMP, and pill counts, and lastly, dose limitations."

[10] Standridge JB, Adams SM, Zotos AP. Urine drug screening: a valuable office procedure. Am Fam Physician. 2010 Mar 1;81(5):635-40. "Unexpected positive test results should be confirmed with gas chromatography/mass spectrometry or high-performance liquid chromatography."

Urine Drug Testing (cont'd)				
			4. Moderate risk patients: test 2-3 times a year "with confirmatory testing for inappropriate or unexplained results. This includes patients undergoing prescribed opioid changes without success, patients with a stable addiction disorder, those patients in unstable and/or dysfunction social situations, and for those patients with comorbid psychiatric pathology." *5. High risk patients (especially those with active substance abuse disorders): as often as once a month* *This list of recs on UDTs has 19 recs total, many of which are about what to do given different results of UDTs.*	
Utah-2009	*Yes, a soft recommendation to test <u>all</u> patients, but with reservations about UDTs explained in the discussion* **Recommendation 3.2:** Consider performing drug screening [=*drug tests*] before initiating long term opioid treatment for chronic pain." (9) "It is recommended that this be considered for all patients. When screening is limited to situations	*Nearly all.* "**Recommendation 8.2** Providers should consider performing drug screening on randomly selected visits and any time aberrant behavior is suspected." (15) "It may not be appropriate or necessary for all patients, but should be strongly considered by providers and may provide an opportunity to discuss the risks and problems that can occur with opioid treatment." (15)	*Frequency should match the risk level.* "Base the frequency of random drug screening on the assessed degree of risk of aberrant behavior for the individual patient. Pill counts may also be useful in some circumstances." (15)	*Urine drug screen or other lab test that can detect illegal drugs, other meds or alcohol use. (9)* *Explains immonoassays' strengths and weaknesses. (10)*

Urine Drug Testing (cont'd)				
	when there is suspicion of substance misuse, some misuse may be missed."(9)			
Veteran's Admin guidelines-May 2010	*Yes, with patient consent.* [*Recommendations on UDTs*] "3. With patient consent, obtain a UDT in all patients prior to initiation of OT. [B]" (59)	*All patients, with patient consent.*	*Periodic and random.* "Recommendations: 1. Inform patients that drug testing is a routine procedure for all patients starting or on opioid therapy, and is an important tool for monitoring the safety of their treatment." (59) "2. With patient consent monitor all patients on OT with periodic random UDTs to confirm adherence to the treatment plan. Increase the frequency of UDTs based on risk level for aberrant drug-related behaviors and following each dose increase. [B]" (59)	"6. Understanding of lab methods for drug testing and reporting are necessary to interpret UDT results (i.e., screen versus confirmatory test, substances tested, cut-off levels for tests)." (59)
WA Interagency Guidelines (AMD)-2010 Update	*Yes.* *"*This baseline UDT should be performed on all transferring patients who are already using opioids and for those patients who you are considering for chronic opioid therapy (e.g. 3rd opioid prescription or >6 weeks after an acute injury)." (8)	*All patients on COT (see quote in column to the left)*	*Frequency should match the risk level.* *[exact language from table 2, page 8]* • "Low Risk by ORT =Periodic (e.g. up to 1/year)" • "Moderate Risk by ORT = Regular (e.g. up to 2/year)" "High Risk by ORT or opioid doses >120 mg MED/d = Frequent (e.g. up to 3–4/year)" • "Aberrant Behavior [. . .] = At time of visit (Address aberrant behaviors in person, not by telephone)"	*Description of immonoassays and chromatography tests. Recommends the latter to* "confirm unexpected immunoassay results." (9) "It may be more useful to order an expanded urine

				drug panel to

Urine Drug Testing (cont'd)				
				include any of the drugs listed below in addition to drugs you are prescribing: " (9) *[See guideline for list.]*
WA Worker's Comp Guidelines - 2013* **See row just below for recs added by this guideline that don't fit this chart's rubric.*	*This guideline supplements the Washington Interagency Guidelines.*	*All patients on COT.* **"Executive Summary"** [*of all recs*] "Use of chronic opioid therapy requires regular monitoring and documentation, such as [. . .] administering random urine drug tests." (3)	*Randomly.*	*This guideline supplements the Washington Interagency Guidelines.*
WA Worker's Comp Guidelines - 2013*	*Recs on UDTs for acute and subacute phases.* **"Opioids in the Acute Phase (0 to 6 weeks after injury or surgery)"** "Use urine drug tests, the state's PMP and other screening tools in the AMDG Guideline to ensure controlled substances history is consistent with prescribing record and worker's report." (8) **"Opioids in the Subacute Phase (between 6 and 12 weeks)"** "Administer a baseline urine drug test (UDT). If results reveal "red flags" such as the confirmed presence of cocaine, amphetamines or alcohol, opioid use beyond the acute phase is not indicated [. . .]. Unless cannabis use disorder is diagnosed, the presence of cannabis on a UDT does not preclude the use of opioids." (9)			

Opioid Treatment Agreement (Exact language in quotes)					
	Counsels a written agreement?	**Who should have a written agreement?**	**How frequently should written agreement be reviewed and updated?**	**What should written agreement include?**	**Exact Language**
ACOEM-2011	*Yes.*	*All patients*	"Every month initially, then approximately every 3 months in patients stable on treatment for at least 6 months, then every 6 months in well established, stable patients." (8)	*Appendix includes an example of a treatment agreement from the Washington State Treatment Guidelines. (20)* "[P]atients with prior psychopathology or risk factors for abuse and addition [. . .] are thought to require especially explicit rules of acceptable conduct (i.e., written agreement)" (6)	***"Recommendation: Opioid Treatment Agreement ("Opioid Contract") for Patients with Chronic Pain*** The use of a treatment agreement to document patient understanding and agreement with the expectations of opioid use is recommended. There is evidence that many patients do not adhere to prescribed treatment (including with an agreement);3 however, these agreements are felt to be needed and coupled with a urine drug screening program.3,4 Patients should be informed about what is responsible use of opioids and how to interact with their physician and pharmacy in obtaining medication. If literacy is a problem, the physician should read the agreement to the patient and ascertain that they understand it or revise the agreement so they can read and

Opioid Treatment Agreement (Exact language in quotes) (cont'd)					
					understand its content. *Strength of Evidence* – Recommended, Insufficient Evidence (I)" (3)
APS/AAPM-2009* *Recommends getting "informed consent" in discussion. (116)*	*Weak rec. for **written** agreement.*	*For high-risk patients a written agreement* "may be particularly helpful". *(117)*	*No specific recommendation.*	*No specific recommendations, but does give a list of possible content, followed by this disclaimer:* "[T]here is insufficient evidence to guide specific recommendations on which provisions to include. A sample COT management plan is shown in Appendix 7." (117) *It is from the American Academy of Pain Medicine.*	"2.1 When starting COT, informed consent should be obtained. A continuing discussion with the patient regarding COT should include goals, expectations, potential risks, and alternatives to COT (strong recommendation, low-quality evidence). 2.2 Clinicians may consider using a written COT management plan to document patient and clinician responsibilities and expectations and assist in patient education (weak recommendation, low quality evidence)." (116)
ASIPP - 2012					*Not specified*
Canadian Guideline-April 2010	*Weak rec. for **written** agreement*	*High-risk patients or patients that the physician doesn't know well.*	*No specific recommendations.*	*No specific recommendations (only describes what agreements typically include). (22) [See guideline for list.]*	"**R05** Before initiating opioid therapy, ensure informed consent by explaining potential benefits, adverse effects, complications and risks (Grade B). A treatment agreement may be helpful, particularly for patients not well known to the physician or at higher risk for opioid misuse. (Grade C). Risks, adverse effects,

					complications." (18)*I(*

Opioid Treatment Agreement (Exact language in quotes) (cont'd)					
ODG *(no page numbers provided because it is an html document)*	*Yes.*	*All patients.*	*No specific recommendation*	[Opioids, pain treatment agreement] "This plan should be signed and dated and placed in the patient's chart, and include the following: ((1) Goals of therapy, (2) Only one provider gives prescriptions, (3) Only one pharmacy dispenses prescriptions, (4) There will be a limit of number of medications, and dose of specific medications, (5) Medications are not to be altered without the prescribing doctor's permission, (6) Heavy machinery and automobile driving is not to occur until drug-induced sedation/drowsiness has cleared, (7) Refills are limited, and will only occur at appointments, (8) Treatment compliance must occur for all other modalities enlisted, (9) Urine drug screens may be required, (10) The patient must acknowledge that	[Opioids, pain treatment agreement] "Recommended. A written consent or pain agreement for chronic use is not required but may make it easier for the physician and surgeon to document patient education, the treatment plan, and the informed consent."

				they are aware of	

Opioid Treatment Agreement (Exact language in quotes) (cont'd)					
				potential adverse effects of the use of opioids including addiction, (11). Information about opiod management can be shared with family members and other providers as necessary, (12) If opioid use is not effective, the option of discontinuing this therapy may occur, (13) The consequence of non-adherence to the treatment agreement is outlined." *Includes a sample treatment plan from the Utah guidelines.*	
Utah-2009	*Yes.*	*All patients.*	*No specific recommendations.*	*Summary of points (See exact language of recs in column to the right.)* • *Risks and benefits of opioid treatment (including details on possible adverse effects)* • *Responsibilities of patient and clinician*	"5.1 Recommendation: The patient should be informed of the risks and benefits and any conditions for continuation of opioid treatment, ideally using a written and signed treatment agreement." (12) "5.3 Recommendation: The treatment plan, which defines the responsibilities of both patient and clinician, should be documented." (13)

Opioid Treatment Agreement (Exact language in quotes) (cont'd)					
				• *Goals of treatment* • *Guidelines for prescription refills* • *Consent to submit to UDTs* • *Reasons for tapering* *Also lists other optional points to include in agreement. (13)*	"5.4 Recommendation: The treatment plan should contain goals of treatment, guidelines for prescription refills, agreement to submit to urine or serum medication
Veteran's Admin guidelines-May 2010	*Yes.*	*All patients.*	*No specific recommendation.*	*Gives a long list of 16 points that should be part of the informed consent discussion. It includes all the points recommended by other guidelines for the written agreement, and then some. No explicit recommendation that these topics should be included in the written agreement. All the points in the list appear in the sample agreement, as well as several others not in this list.* (*See guideline for list, page 32.)*	"Discuss treatment agreement with patient and family. Request a written opioid treatment agreement." (11) "Discuss a trial of opioid therapy with the patient, and obtain the patient's informed consent in a shared decision-making discussion. Document the informed consent discussion. 2. Review and discuss a written Opioid Pain Care Agreement (OPCA) with the patient who is expected to receive daily opioid therapy for the treatment of chronic pain. The signed agreement can serve as documentation of an informed consent discussion. (For a sample

					agreement, see Appendix C)." (32)

Opioid Treatment Agreement (Exact language in quotes) (cont'd)					
WA Interagency Guidelines (AMD)-2010	*Yes.*	*All patients.*	*No specific recommendation.*	• "Treatment goals, which must include improvements in both function and pain while monitoring for and minimizing adverse effects • Expectation for routine urine drug testing A follow-up plan with specific time intervals to monitor treatment" (5)	"When instituting chronic opioid therapy, both prescriber and patient should discuss and agree on all of the following: • Risks and benefits of opioid therapy supported by an opioid agreement (sample agreements can be found in Appendix G)" (5)
WA Worker's Comp Guidelines - 2013	*Yes.*	*All patients, except for victims of catastrophic injuries.*	*No specific recommendsation.*	*No specific recommendation. This guide supplements the Interagency guidelines.*	"With the exception of catastrophic injuries, the provider must document the following before L&I or insurer can authorize payment for opioids during the chronic phase: [. . .] • Signed treatment agreement (pain contract)." (10) "Continued coverage of COT will depend on the prescriber documenting the following: [. . .] • A current signed treatment agreement." (10)

Prescription Drug Monitoring System (Exact language in quotes)	
ACOEM-2011	*No specific recommendation.*
APS/AAPM-2009	*Soft recommendation*. "Clinicians should also be aware of and use prescription monitoring programs if they are available in their area of practice, as they can help identify patients who obtain drugs from multiple sources." (119)
ASIPP - 2012	There is limited evidence to recommend a routine monitoring of asymptomatic patients on chronic opioid therapy for chronic non-cancer pain for hormonal deficiencies, due to only preliminary evidence and lack of high quality long-term follow-up. There is fair evidence that prescription drug monitoring programs can reduce prescription drug abuse or doctor shopping. There is limited evidence that prescription drug monitoring programs reduce emergency room visits, drug overdoses, or deaths, due to lack of high quality literature.
Canadian Guideline-April 2010	"R22: To reduce prescription fraud, physicians should take precautions when issuing prescriptions and work collaboratively with pharmacists. (Grade C). **Prescription Fraud**" 62 "If available, physicians and pharmacists should access electronic prescription databases that provide information about patient prescription history." (62) *Recommendations for preventing prescription fraud if there is no effective drug monitoring system:* **"Taking Precautions.** In issuing prescriptions, physicians should take the following precautions, which are considered to reduce opioid misuse: 1. Fax prescriptions directly to the pharmacy. 2. If using a paper prescription pad: • Use carbon copies or numbered prescription pads. • Write the prescription in words and numbers. • Draw lines through unused portions of the prescription. • Keep blank prescription pads secure. 3. If using desk-top prescription printing, it is especially important to write a clear signature

	and not use a scribbled initial.

Prescription Drug Monitoring System (cont'd) (Exact language in quotes)	
	4. If using fax or electronic transmission of the prescription (in jurisdictions that permit it) ensure confidentiality, confirm destination, and retain copies. 5. Promote patient's use of a single dispensing pharmacy." (62)**R22**
ODG *(no page numbers provided because it is an html document)*	*Soft recommendation*. [Opioids, screening tests for risk of addiction & misuse] "Results of screening tests should be used in the context of other sources in order to stratify risk and identify those individuals who are not good candidates for opioid therapy, or who require more careful monitoring with use. These include history and physical examination, clinical interview, discussions with family members, urine drug testing results, other monitoring findings (including prescription monitoring program reports and pill counts) and review of medical records."
Utah-2009	*Summary: recommends consulting the prescription drug monitoring system 1) before initiating treatment, 2) at least quarterly during titration and 3) at least annually during maintenance (more often for high-risk patients).* "**Screening for risk of addiction or abuse**" (9)"**3.3 Recommendation:** The prescriber should check Utah's Controlled Substance Database before prescribing opioids for chronic pain." (10) **"Titration phase"** (14) "**7.3 Recommendation:** During the titration phase, until the patient is clinically stable and is judged to be compliant with therapy, it is recommended that the clinician check the Controlled Substances Database at least quarterly." (15) _____ *Also mentioned in context of what can be included in the opioid agreement:* "Specific grounds for immediate termination of the agreement and cessation of prescribing may also be specified, such as forgery or selling of prescriptions or medications (VA/DOD, 2003; Trescot et al., 2008) or obtaining them from multiple providers as documented by Utah's Controlled Substance Database Program." (13) "**Maintenance – Periodic monitoring and dose adjustments**" (15) "**8.2 Recommendation**: During maintenance phase, Controlled Substances Database should be checked at least annually." (16) "The Controlled Substances Database should be checked more often for high risk patients and patients exhibiting aberrant behavior." (16)

Prescription Drug Monitoring System (cont'd) (Exact language in quotes)	
	_____ *In sample treatment plan for prescribing opioids, provided in Appendix:* "___ I agree to obtain prescription medication from one designated licensed pharmacist. I understand that my doctor may check the Utah Controlled Substance Database at any time to check my compliance." (33) _____ *Page in Appendix entitled Opioid Risk Tool (which isn't ORT) specifies how frequently to consult database depending on the risk level of the patient.* • *Low-risk patients*: "Communicate with pharmacies or obtain initial reports from prescription-monitoring programs (where available) and prior medical providers." (52) • *Moderate-risk patients*: "Conduct regular checks (every 6-12 months) of your state's prescription monitoring database, if available, or consult with the patient's pharmacist." (52) • *High-risk patients:* "Consult a prescription database (if available) more frequently." (52)
Veteran's Admin guidelines-May 2010	"No reliable evidence was found on the diagnostic accuracy of urine toxicology testing, pill counts, or prescription drug monitoring programs, or on clinical outcomes associated with implementation of different monitoring approaches (APS/AAPM, 2009)." (20) *Mentioned in sample opioid agreement*: "My providers may obtain information from State controlled substances databases and other prescription monitoring programs." (103)
WA Interagency Guidelines (AMD)-2010	*No specific recommendation.*
WA Worker's Comp Guidelines -2013	*In Executive Summary of recommendations:* "Use of chronic opioid therapy requires regular monitoring and documentation, such as screening for risk of co-morbid conditions with validated tools, checking the Prescription Monitoring Program database, assessing clinically meaningful improvement in function and administering random urine drug tests." (3) *Consultation of database at different phases of pain:* *Acute phase (0 to 6 weeks after onset of pain):* **"**Preliminary data from the Prescription Monitoring Program (PMP) has suggested that substantial numbers of newly injured workers received opioids or other controlled substances in the

	60 days prior to injury. For this reason, providers should check the PMP prior to prescribing opioids for new injuries or

Prescription Drug Monitoring System (cont'd) (Exact language in quotes)	
	occupational diseases." (8) *Subacute phase:* "Access the state's PMP to ensure that the controlled substance history is consistent with the prescribing record and worker's report." (9) *Chronic phase: "*Prescribers should also continue to check the PMP and administer UDTs based on risk, in accordance with AMDG recommendations and DOH regulations." (10) *Pre-operative pain:* The evaluator should also check the opioid prescribing history in the PMP." (11)

Dosing Threshold		
	Numerical threshold or range recommended	**Exact Language indicated in quotes**
ACOEM-2011	*No specific recommendations.*	"If the patient has improved on opioids but still states that his or her activities are limited by pain, a judicious increase in opioid dose can be considered but must be followed by evidence of appropriate pain reduction and/or increased function." (p. 7) Provides a link to the WA opioid dosing calculator, which includes a threshold: "(An opioid-dosing calculator developed by the Washington State Agency Medical Directors' Group is available on-line at www.agencymeddirectors.wa.gov/Files/DosingCalc.xls.)" (p. 7) Provides recommended dosage for tramadol: "Based on the literature, the lower dose combination medication of 37.5mg tramadol/325mg acetaminophen has the best safety profile, although there have been reports of problems with addiction especially among health care workers, along with reports of seizures associated with withdrawal." (7)
APS/AAPM-2009	*Yes (threshold)*	"When opioid doses reach **200 mg** daily of morphine (or equivalent), more frequent and intense monitoring is often appropriate, to sufficiently inform the decision to continue therapy or consider additional dose escalations." (p. 120)
ASIPP - 2012		1. There is good evidence that the increased supply of opioids, use of high dose opioids, doctor shoppers, and patients with multiple comorbid factors contribute to the majority of fatalities. 2. There is good evidence that approximately 60% of fatalities originate from opioids prescribed within the guidelines. 3. There is good evidence that approximately 40% of fatalities occur in 10% of drug abusers. 4. There is fair evidence that long-acting opioids and a combination of long-acting and short-acting opioids contribute to increasing fatalities. 5. There is fair evidence that even low doses of 40 mg or 50 mg daily of morphine equivalent doses are responsible for emergency room admissions with overdoses and deaths.
Canadian Guideline-April 2010	*Yes (threshold)*	"Chronic non-cancer pain can be managed effectively in most patients with dosages at or below **200 mg/day** of morphine or equivalent (Grade A). Consideration of a higher dosage requires careful reassessment of the pain and of risk for misuse, and frequent monitoring with evidence of improved patient outcomes." (p. 5)

Dosing Threshold (cont'd)		
ODG *(no page numbers provided because it is an html document)*	*Yes.*	[Opioids, dosing] "Recommend that dosing not exceed 120 mg oral morphine equivalents per day [. . .] Escalation of doses greater than 120 mg (MED) should be done with caution, and generally under the care of pain specialists, and in certain cases, addiction specialists, with the understanding that many patients who progress to chronic opioid therapy have underlying psychiatric disease and substance abuse issues."
Utah-2009	*Yes (range, with thresholds for specific opioid medications)*	"No clear threshold for high dose has been established based on evidence. The Washington State guideline (WSAMDG, 2007) suggested a threshold of 120 mg of morphine equivalent per day, but has been criticized for that decision. It seems reasonable to increase clinical vigilance at daily doses that exceed 120-200 mg of morphine equivalent per day." (p. 15) [*taken from table in Dosing Guidelines Tool in appendix of guideline*) **Recommended dose threshold for pain consult (not Equianalgesic):** Codeine: 800mg per 24 hours Fentanyl, Transdermal: 50mcg/hour (q 72 hr) Hydrocodone: 30 mg per 24 hours Hydromophone: 30mg per 24 hours (page 73)
Veteran's Admin guidelines-May 2010	*Yes (threshold)*	*21.* If a medication provides less than satisfactory pain reduction despite increasing the dose as tolerated to **a reasonable level (less than 200 mg/day** morphine equivalent), evaluate for potential causes such as non-adherence and drug interactions (see Appendix E, Table E6 in the original guideline document [Drug Interactions]), and consider changing to an alternate opioid medication. *22.* Medication may be increased until limited by adverse effects or clear evidence of lack of efficacy. If a **high dose of medication (greater than 200 mg**/day morphine equivalent) provides no further improvement in function, consider consultation rather than further increasing the dose. (HTML format, no pagination)
WA Interagency Guidelines	*Yes (threshold)*	"The hallmark of this guideline is a recommendation to *not* prescribe more than an **average daily MED of 120mg** without *either* the patient demonstrating improvement in function and

(AMDG)-2010		pain *or* first obtaining a consultation from a pain management expert." (p. 3)

Doing Threshold (cont'd)		
WA Worker's Comp Guidelines - 2013	*This guideline supplements the WA Interagency Guidelines*	The guideline warns strongly against high-dose opioids: "High-dose opioids (e.g., morphine, oxycodone) should generally be avoided, as these agents have higher adverse effect profiles. Use of agents such as meperidine, propoxyphene, combination agonists, and mixed agonists/antagonists (butorphanol, nalbuphine, and pentazocine) for management of chronic pain is not recommended."

Using Methadone to Treat Pain *(for recommendations on methadone's role in tapering, see the tapering chart)*		
	Dosing	**Advisability of treating with methadone**
ACOEM-2011	*No specific dose recommendations either for equianalgesic parenteral or oral drug admin or for starting doses:* "The conversion ratio of methadone is highly variable depending on factors such as patient tolerance, morphine dose, and length of dosing (short term versus chronic dosing). Because the analgesic duration of action is shorter than the half-life, toxicity due to drug accumulation can occur within 3 to 5 days." (22)	*No specific recommendations.* "Magnitudes of risk reportedly exceed automobile crashes and methadone has been found to be the most hazardous amongst medications reported." (1) "Methadone has different pharmacokinetics and while the analgesic half-life is 6 to 12 hours, the pharmacological half-life of more than 100 hours for some patients is associated with significant risks of toxicity from accumulation. Methadone is also a more difficult opioid analgesic to use in clinical practice and has frequently been thought to be responsible for elevated mortality rates." (8)
APS/AAPM-2009	"Methadone should therefore be started at low doses and titrated slowly. Based on panel consensus, a safe starting dose in most opioid-naıve patients is 2.5 mg every 8 hours, with dose increases occurring no more frequently than weekly. In older patients or those with renal or hepatic comorbidities, less frequent dosing and more cautious dose titration are recommended." (118)	"4.1 Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be initiated and titrated cautiously, by clinicians familiar with its use and risks (strong recommendation, moderate-quality evidence)." (118)
ASIPP - 2012		The evidence for methadone is limited due to lack of quality studies. There were no adequate clinical studies available for methadone or for other opioids such as hydrocodone. The authors concluded that there is growing evidence that opioids are efficacious in non-cancer pain, but require individual dose titration and consideration of respective tolerability profiles.

Using Methadone to Treat Pain (cont'd)		
Canadian Guideline-April 2010	*No specific recommendations, aside from high vigilance.*[11]	*For treating severe pain, methadone should be considered a third-line treatment (after morphine, oxycodone, hydromorphone [first-line] and fentanyl [second-line]. (27)* "Use methadone to treat pain only if holding a written Health Canada exemption. Titration is hazardous due to its very long half life leading to bio-accumulation. (See Supporting Evidence item 5.)[12]" (28)
ODG *(no page numbers provided because it is an html document)*	[Opioids, dosing] Opioid Dosing Calculator, MED factor: "Methadone, >60mg per day – 12" [*no evidence cited*] "Methadone conversion requires careful consideration because of its long half-life and unusual pharmacokinetic profile compared with most other opioids. In addition, converting	[Methadone] "Recommended as a second-line drug for moderate to severe pain, only if the potential benefit outweighs the risk, unless methadone is prescribed by pain specialists with experience in its use and by addiction specialists, where first-line use may be appropriate. Due to the complexity of dosing and potential for adverse effects

[11] "One observational study of chronic pain patients on opioid therapy was designed to assess whether a dose relationship exists between methadone, non-methadone opioids, benzodiazepines and the indices measuring sleep apnea. They included all consecutive (392) patients on around-the-clock opioid therapy for at least 6 months with a stable dose for at least 4 weeks. Available data were analyzed on 140 patients. The apnea-hypopnea index was abnormal (≥5 per hour) in 75% of patients (39% had obstructive sleep apnea, 4% had sleep apnea of indeterminate type, 24% had central sleep apnea, and 8% had both central and obstructive sleep apnea); 25% had no sleep apnea. They found a direct relationship between the apnea-hypopnea index and the daily dosage of methadone (P = 0.002) but not to other around-the-clock opioids. They concluded that sleep-disordered breathing was common in chronic pain patients on opioids. The dose-response relationship of sleep apnea to methadone and benzodiazepines calls for increased vigilance (Webster 2008)." (38)

[12] Supporting Evidence, Item 5 (p. 31): "**5.1 Methadone for pain is more effective than placebo, but has not been shown to be more effective than other opioids.** Sandoval (2005) conducted a systematic review of methadone for CNCP. The review included 21 studies (1 small randomized trial, 13 case reports, and 7 case series) and concluded that pain improvements were meaningful in 59% of the patients in the uncontrolled studies. The randomized trial demonstrated a statistically significant improvement in pain for methadone (20 mg/day) compared to placebo. Side effects were considered minor. One controlled trial found no difference in analgesic efficacy between morphine and methadone in cancer patients with respect to pain management (Bruera 2004). A similar trial found no difference between methadone, oral morphine and transdermal fentanyl 25 ucg/hour, although methadone titration was more difficult (Mercadante 2005**). 5.2 Physicians must hold an exemption from Health Canada before prescribing methadone for pain.** Methadone has been associated with numerous overdose deaths in pain patients. Methadone analgesic use has increased sharply in the US, with a seven-fold rise from 1997 to 2004 (Sims 2007). This has been accompanied by a 17-fold increase in methadone overdose deaths (Shields 2007, Sims, 2007). Federal law requires that a physician hold a written exemption from Health Canada before prescribing methadone for analgesia. The specific process to apply for a methadone exemption varies by jurisdiction, and may include submission of a letter of support from the applicable medical regulatory authority before Health Canada will provide a methadone exemption. A physician may be able to receive an exemption to prescribe methadone under various circumstances, including if "mentored" by an experienced methadone prescriber. Physicians should confirm the methadone prescribing requirements of the jurisdiction where they practice.

	methadone to morphine is not bidirectional. When switching	

Using Methadone to Treat Pain (cont'd)		
	from an established dose of methadone to another opioid, we must consider that measurable methadone serum levels will be around for days, so both drugs are now readily available, increasing the overall risk for opioid toxicity. (Fudin, 2008)"[13]	including respiratory depression and adverse cardiac events, this drug should be reserved for use by experienced practitioners (i.e. pain medicine or addiction specialists).[14] "The drug should be used with caution in opioid-naïve patients due to the risk of life-threatening hypoventilation." [*no evidence cited*] "Patients should be informed of arrhythmia risk when prescribed methadone. An assessment should be made of history of structural heart disease, arrhythmia, and syncope. No firm guides are agreed upon in terms of pre-treatment or interval EKGs, but recommendation for use is particularly made for patients on high dose drug with cardiac history or evidence of syncope or seizures. (Peng, 2008)"[15]
Utah-2009	[Tool: Dosing Guidelines[16]] "Starting Methadone Dose	"**13.1 Recommendation:** Methadone should only be prescribed by clinicians familiar with its risks and use, and who are prepared to conduct the necessary careful monitoring." (20)

[13] Fudin J. What Is the Maximum Safe Dose of Opioids? *Medscape Pharmacists.* 2008; ©2008 Medscape. 02/21/2008 It appears that the recommendation is a verbatim quote from this article. Article rated 9b.

[14] Institute for Clinical Systems Improvement (ICSI). Assessment and management of chronic pain (4nd edition). Bloomington (MN). 2009. See also the FDA 's "Public Health Advisory, Methadone Use for Pain Control May Result in Death and Life-Threatening Changes in Breathing and Heart Beat" and the FDA monograph, "Information for Healthcare Professionals, Methadone Hydrochloride, FDA ALERT [11/2006]: Death, Narcotic Overdose, and Serious Cardiac Arrhythmias."

[15] Peng P, Tumber P, Stafford M, Gourlay D, Wong P, Galonski M, Evans D, Gordon A. Experience of methadone therapy in 100 consecutive chronic pain patients in a multidisciplinary pain center. Pain Med. 2008;9:786-94

[16] Produced by Utah Department of Health, 2009 adapted from Washington State Agency Medical Director's Group, 2007 and Webster, 2005

<table>
<tr><th colspan="3">Using Methadone to Treat Pain (cont'd)</th></tr>
<tr>
<td></td>
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<table>
<tr><th>Morphine Equivalent</th><th>Healthy Adult <70 yrs</th><th>Adult w/ chronic illness or >70 yrs</th></tr>
<tr><td>Opioid naïve</td><td>5 mg tid</td><td>2.5 mg bid</td></tr>
<tr><td>60 mg – 100 mg</td><td>5 mg tid</td><td>5 mg bid</td></tr>
<tr><td>>100 mg</td><td>5 mg qid</td><td>5 mg bid</td></tr>
</table>
*Webster, 2005"

[Dosing Guidelines]. "Methadone is difficult to titrate due to its half-life variability. It may take a long time to reach a stable level in the body. Methadone dose should not be increased more frequently than every 7 days. Do not use as PRN or combine with other long acting (LA) opiods."[17] (74)

[Tool: The Role of Methadone in the Management of Chronic Non-Malignant Pain, *from the College of Physicians and Surgeons of Ontario*] "In opioid-naïve patients or patients taking codeine preparations, methadone 2.5 mg a8h is safe and usually well-tolerated. For patients already on a major opioid analgesic like oxycodone or morphine, a reasonable starting dose of methadone is 5 mgq8h with dose increments of 5 mg q8h every 5-7 days. A general rule is to provide careful dose titration until adequate pain relief is achieved or side effects limit further dose escalation. [. . .] Patients should be seen weekly during the titration phase and every month or two during the maintenance phase." (71-72)

"Additional ECG examinations were recommended if the methadone dose exceeds 100 mg per day or if a patient on methadone has unexplained syncope or seizure. Guidance was
</td>
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"Methadone interacts with several other medications that can alter its metabolism changing the effects of a given dose on pain and on respiratory depression. Potential for interactions should be considered before starting methadone in a patient taking other medications and before starting any medication in a patient taking methadone." (20) [*no evidence provided*]

"Caution should be used in prescribing methadone to any patient at risk for prolonged QTc interval, including those with structural cardiac disease, cardiac arrhythmias or cardiac conduction abnormalities and in patients taking another medication associated with QTc

interval prolongation (Arizona Center for Education and Research on Therapeutics 2008). (20)

"Clinicians should consider obtaining an electrocardiogram (ECG) to evaluate the QTc interval in patients treated with methadone, especially at higher doses. A recently published consensus guideline (Krantz 2009) recommended that an ECG be performed before prescribing methadone, within the first 30 days, and annually. Additional ECG examinations were recommended if the methadone dose exceeds 100 mg per day or if a patient on methadone has unexplained syncope or seizure." (20)
</td>
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[17] [*Dosing Guidelines Tool*] "Produced by Utah Department of Health, 2009 adapted from Washington State Agency Medical Director's Group, 2007 and Webster, 2005" (74)

Using Methadone to Treat Pain (cont'd)		
	provided for actions to be taken at two levels of QTc prolongation (450-500 ms and greater than 500 ms)." (20) [Krantz 2009]	[*from the Tool cited in the column to the left*] "Clinicians should question patients about symptoms and signs of sleep apnea and consider obtaining a sleep study in patients treated with opioids if they develop any signs of sleep-disordered breathing or respiratory depression. This is particularly important for patients receiving higher doses of opioid medications. In one recent study, 92% of patients on opioid doses at or above 200 mg morphine equivalents had developed ataxic or irregular breathing (Walker, 2007)." (20) [*from the Tool cited in the column to the left*] "Patients should be warned about potential side effects (especially drowsiness and respiratory depression) and the possibility that side effects can continue to evolve for five to seven days after each dose adjustment The spouse or significant other should be available at least twice daily to monitor for toxicity. [. . .] Elderly patients (over the age of 65), patients with severe lung disease and patients who cannot be adequately monitored at home should be considered for inpatient initiation of methadone treatment." (72)
Veteran's Admin guidelines-May 2010	*Five-page <u>in-depth</u> appendix, entitled,* "Methadone Dosing Recommendations for Treatment of Chronic Pain." *Provides separate dosing recommendations for opioid-naïve patients and opioid-tolerant patients* *Salient points:* "The equianalgesic dose of methadone in repetitive dosing is much smaller (1/5th to 1/10th) than that suggested by single-dose studies" (135) "**Table F 1: Points to Consider about Equianalgesic Conversion Ratios**	"**Cautions for use of Methadone in Patients with Chronic Pain:** Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be initiated and titrated cautiously by clinicians who are familiar with its use and risks, or who can consult with clinicians experienced in dosing methadone. Only under these requirements should methadone be considered as an alternative first-line drug for OT in the primary care setting.

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There may be large interpatient variability in the equianalgesic conversion ratio; a single ratio may not be applicable to all patients.[18]
The use of high but ineffective doses of previous opioid may result in overestimation of the equivalent dose of methadone."

"The present dosing recommendations are provided to offer guidance on dosing methadone in the treatment of patients with chronic noncancer pain (CNCP) or chronic cancer pain, particularly when converting from another opioid to methadone. If in doubt, a practitioner should consult a pain management specialist, clinical pharmacist, or another practitioner who has the relevant knowledge.
Dosing Strategies
Recommendations for the use of methadone in the management of chronic non-cancer pain are extrapolated from studies involving mostly patients with cancer pain.
Table F 2: Dosing recommendations for patients receiving codeine preparations or no previous opioids
<table>
<tr><th>Dosing strategy</th><th>Initial MET dose</th><th>Increments</th><th>Comments</th></tr>
<tr><td>Gradual titration
(For CNCP and situations</td><td>2.5 mg q 8 h</td><td>2 2.5 mg q 8 h every 5 to 7 d</td><td>As a general rule, start low and go slow.</td></tr>
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<td>
11. When using methadone:
a. Inform patients of the arrhythmia risk
b. Ask patients about heart disease, arrhythmia, and syncope
c. Obtain an electrocardiogram (ECG) to measure the QTc interval before starting methadone and
once the dose is stabilized (maintenance phase). Measure the QTc annually thereafter if the
patient history is positive for risk factors for prolonged QTc interval, or has known prolonged QTc interval. Perform additional electrocardiography if the methadone dosage exceeds 100 mg/day,
or if the patient has unexplained syncope or seizures
d. If the QTc interval is greater than 450ms, but less than 500ms, reevaluate and discuss with the patient the potential risks and benefits of therapy, and the need for monitoring the QTc more frequently
e. If the QTc interval exceeds 500 ms, discontinue or taper the methadone dose and consider using
an alternative therapy. Other contributing factors, such as drugs that cause hypokalemia, or QT
prolongation should be eliminated whenever possible
f. Be aware of interactions between methadone and other drugs that may prolong QTc interval, or slow the
</td>
</tr>
</table>

[18] Bruera E, Neumann CM. Role of methadone in the management of pain in cancer patients. Oncology (Huntingt) 1999;13:1275-82; discussion 1285-8, 1291.

	necessitating				elimination of methadone, and educate patients about drug interaction." (38)[19]

[19] "Methadone causes QTc prolongation, a predecessor to trosade de pointes Krantz et al., 2009 [LE] III [QE] Fair [SR] C" (40)

Using Methadone to Treat Pain (cont'd)

less frequent monitoring		
Faster titration (For cancer pain and situations where frequent monitoring is possible)	2.5 mg q 6 or 8 h	2.5 mg q 6 or 8 h as often as every day over about 4 d

The dosing recommendations for gradual titration were modified with permission from *Evidence-Based Recommendations for Medical Management of Chronic Non-Malignant Pain*, College of Physicians and Surgeons of Ontario, November 2000. **All doses refer to oral administration."** (136)

"Use additional caution with elderly patients (65 years and older),[20] patients with liver, renal,[21] or pulmonary disease, debilitated patients, and patients previously receiving high doses of opioid. Patients who cannot be monitored at home may be considered for inpatient titration of methadone." (138)

"Recommendations: 1. Opioid therapy trial should NOT be initiated in the following situations (absolute contraindications):

f. QTc interval > 500 millisecond for using methadone" (24)

"2. Opioid therapy trial can be initiated with caution in the following situations. Consider consultation

with appropriate specialty care to evaluate if potential benefits outweigh the risks of therapy."

b. Medical condition in which OT may cause harm:

- Cardiac condition (QTc interval 450-500 milliseconds) that may increase risk of using methadone" (24)

"Providers should carefully evaluate potential drug interactions prior to initiating opioid therapy, (such as MAOI with concurrent meperidine use, methadone with benzodiazepines, fentanyl with CYP3A4 inhibitors, or propoxyphene and alcohol and other CNS depressants)."[22] (25)

[ris*k of undetected diversion*]"Routine UDT often does not detect synthetic and semi-synthetic opioids (methadone, oxycodone fentanyl hydrocodone, meperidine or

[20] Plummer JL, Gourlay GK, Cherry DA, Cousins MJ. Estimation of methadone clearance: application in the management of cancer pain. Pain 1988;33:313-22.

[21] Novick DM, Kreek MJ, Fanizza AM, Yancovitz SR, Gelb AM, Stenger RJ. Methadone disposition in patients with chronic liver disease. Clin Pharmacol Ther 1981;30:353-62.

Kreek MJ, Schecter AJ, Gutjahr CL, Hecht M. Methadone use in patients with chronic renal disease. Drug Alcohol Depend 1980;5:197-205.

[22] "Benzodiazepines have been shown to also increase the risk of central sleep apnea with methadone (Webster & Choi, 2008). Benzodiazepines have also been shown to be associated with an increased risk of death due to methadone toxicity. (McCowan et al., 2009; Caplehorn & Drummer, 2002)" (18)

		hydromorphone).” (26)

<table>
<tr><th colspan="3">Using Methadone to Treat Pain (cont'd)</th></tr>
<tr><td></td><td></td><td>"Initiation strategy for continuous, persistent daily pain:
7. For continuous chronic pain, an agent with a long duration of action, such as controlled-release morphine or methadone is recommended." (37)</td></tr>
<tr><td>WA Interagency Guidelines (AMD)-2010</td><td>[verbatim from Table 4. Dosing Threshold for Selected Opioids, Appendix A: Opioid dose calculations]
<table><tr><th>Recommended dose threshold (not equianalgesic)</th><th>Rec'd starting dose for opioid-naïve patients</th><th>Considerations</th></tr><tr><td>40 mg per 24 hrs</td><td>2.5-5mg BID – TID</td><td>Methadone is difficult to titrate due to its half-life variability. It may take a long time to reach a stable level in the body. Methadone dose should not be increased more frequently than every 7 days. Do not use as PRN or combine with other long-acting (LA) opioids.</td></tr></table>(16)
[From Table 5. MED for Selected Opioids, Appendix Opioid dose calculations]</td><td>[Centers for Disease Control and Prevention Control recommendation] "Do not prescribe long-acting or controlled-release opioids (e.g., OxyContin®, fentanyl patches, and methadone) for acute pain."[23] (1)
"Special care should be taken when prescribing methadone for chronic pain. One helpful article for clinicians is: Methadone Treatment for Pain States.[24] Also, free mentoring services are available for prescribing methadone, using the Physician Clinical Support System. See Appendix H, "Additional Resources." (5)
[from Appendix H] "Physician Clinical Support System has mentors available to help you, by phone or email, with 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 you register at http://www.pcssmentor.org/ a mentor will be assigned to you within 2 days." (46)
Recommends getting assistance from a pain management expert for questions about methadone treatment. (10)</td></tr>
</table>

[23] Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. CDC's Issue Brief: Unintentional Drug Poisoning in the United States. Available at: http://www.cdc.gov/HomeandRecreationalSafety/Poisoning/brief.htm. 2010.

[24] 21. Toombs JD, Kral LA. Methadone treatment for pain states. Am Fam Physician 2005;71(7):1353-1358.

	"Methadone: Chronic: 4mg*	

Using Methadone to Treat Pain (cont'd)		
	*Equianalgesic dosing ratios between methadone and other opioids are complex, thus requiring slow, cautious conversion (Ayonrinde 2000)"[25] (16)	
WA Worker's Comp Guidelines - 2013	*No specific recommendations. This guideline supplements the Washington Interagency guideline.* "**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" "Methadone for pain (see box warning below). Due to methadone's nonlinear pharmacokinetics, unpredictable clearance and multiple drug-drug interactions, providers should use extreme caution when prescribing this drug for pain. Additional information is available at www.agencymeddirectors.wa.gov/opioiddosing.asp." (7)	"DO NOT USE • methadone for acute or break-through pain" (6) *[first and last sentences of a large shaded box on the possible adverse effects of methadone]* **Prescribing methadone is complex.** [. . .] "Methadone treatment for analgesic therapy in patients with acute or chronic pain should only be initiated if the potential analgesic or palliative care benefit of treatment with methadone is considered and outweighs the risks." (7)

[25] Ayonrinde OT, Bridge DT. The rediscovery of methadone for cancer pain management. Med J Aust 2000;173:538.

Opioid Dosing Calculator	
ACOEM-2011	"(An opioid-dosing calculator developed by the Washington State Agency Medical Directors' Group is available on-line at www.agencymeddirectors.wa.gov/Files/DosingCalc.xls.)" (7) *Appendix 1 of the guideline provides a two-page chart entitled "Equianalgesic Dosing of Opioids for Pain Management"* (22) *An important caveat precedes the chart (I have kept the italics from the original): "Equianalgesic doses contained in this chart are approximate, and should be used only as a guideline. Dosing must be titrated to individual response. There is often incomplete cross-tolerance among these drugs. It is, therefore, typically necessary to begin with a dose lower (e.g., 25% to 50% lower) than the equianalgesic dose when changing drugs and then titrate to an effective response. Dosing adjustments for renal or hepatic insufficiency and other conditions that affect drug metabolism and kinetics may also be necessary.* A *website with an equianalgesic dose calculator is available at http://www.hopweb.org."* *A cautionary caveat also follows the chart: "Users of this document are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and Internet links in this article were current as of the date of publication."*[26] [*See guideline for specific dose recs*]
APS/AAPM-2009	*No specific dosage recommendations.* *"*In patients who are opioid-naive, or have modest previous opioid exposure, opioids should be started at a low dose and titrated slowly, to decrease risk of opioid-related adverse effects. However, there is insufficient evidence to recommend specific optimal starting doses and methods of dose titration. In general, opioid doses should be individualized based on risk for adverse outcomes and responses to therapy. Some patients, such as frail older persons or those with comorbidities, may benefit from more cautious initiation and titration of therapy." (117)
ASIPP - 2012	1. There is good evidence that the increased supply of opioids, use of high dose opioids, doctor shoppers, and patients with multiple comorbid factors contribute to the majority of fatalities. 2. There is good evidence that approximately 60% of fatalities originate from opioids prescribed within the guidelines. 3. There is good evidence that approximately 40% of fatalities occur in 10% of drug abusers. 4. There is fair evidence that long-acting opioids and a combination of long-acting and short-acting opioids contribute to

[26] [Chart] [a]dapted from Therapeutic Research Center. Equianalgesic dosing of opioids for pain management. *Pharmacist's Letter/ Prescriber's Letter*. 2010;26(Number 260712). Reprinted with permission from Therapeutic Research, Jeff M. Jellin, PharmD, Editor-in-Chief; 3120 W. March Lane, P.O. Box 8190, Stockton, CA 95208; Phone: 209-472-2240; www.pharmacistsletter.com or www.prescribersletter.com.

	increasing fatalities.

<table>
<tr><th colspan="2">Opioid Dosing Calculator (cont'd)</th></tr>
<tr><td></td><td>5. There is fair evidence that even low doses of 40 mg or 50 mg daily of morphine equivalent doses are responsible for emergency room admissions with overdoses and deaths.</td></tr>
<tr><td>Canadian Guideline-
April 2010</td><td>"Table B-9.1 Opioid Suggested Initial Dose and Titration, Modified from Weaver 2007 with information from the e-CPS (Canadian Pharmacists Association, 2008)" (35)</td></tr>
<tr><td>ODG (no page numbers provided because it is an html document)</td><td>[Opioids, dosing]
Opioid Dosing Calculator
Morphine Equivalent Dose (MED) factor:
Codeine – 0.15
Fentanyl transdermal (in mcg/hr) – 2.4
Hydrocodone – 1
Hydromorphone – 4
Methadone, 41 to 60 mg per day – 10
Methadone, >60 mg per day – 12
Morphine - 1
Oxycodone – 1.5
Oxymorphone - 3
"The table [above] lists standard conversion factors although there are drawbacks to equivalency tables because they do not consider a recommended dose reduction for opioid cross-tolerance. The Washington State Agency Medical Director's Group guidelines includes a convenient opioid conversion table."</td></tr>
<tr><td>Utah-2009</td><td>
<table>
<tr><th>"MED for Selected Opioids*</th><th>Approximate Equianalgesic Dose (oral & transdermal)*</th></tr>
<tr><td>"Morphine (reference)</td><td>30 mg</td></tr>
<tr><td>Codeine</td><td>200 mg</td></tr>
<tr><td>Fentanyl transdermal</td><td>12.5 mcg/hr</td></tr>
<tr><td>Hydrocodone</td><td>30 mg</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th colspan="2">Opioid Dosing Calculator (cont'd)</th></tr>
<tr><td></td><td>
<table>
<tr><td>Hydromorphone</td><td>7.5 mg</td></tr>
<tr><td>Oxycodone</td><td>20 mg</td></tr>
<tr><td>Oxymorphone</td><td>10 mg</td></tr>
</table>
**Adapted from Washington 2007 Guidlelines" (from Dosing Guidelines Tool, page 73)
</td></tr>
<tr><td>Veteran's Admin guidelines-May 2010</td><td>Appendix E: Drug Tables
Table E 1: Short-acting, Orally Administered Opioids in Adults (106-109)
Table E 2: Use of Long-acting Opioids in Adults (110-113)</td></tr>
<tr><td>WA Interagency Guidelines (AMD)-2010</td><td>Recommends using their online opioid dosing calculator when patients are taking different types of opioids:
http://agencymeddirectors.wa.gov/mobile.html</td></tr>
<tr><td>WA Worker's Comp Guidelines - 2013</td><td>No specific recommendations. This guideline supplements the WA Interagency Guidelines.</td></tr>
</table>

Tracking Pain and Function *(with focus on function)*				
	Is improvement in function an important goal	**Definition of improvement in function (Exact language in quotes)**	**Discontinue opioids if there is no functional improvement with initial trial?**	**Discontinue opioids if there is no functional improvement even on higher levels of opioids?**
ACOEM-2011	*Yes, see column to right. (1)*	"**Functional Improvement:** Functional benefit should be represented by improvement in objective parameters of physical, behavioral, or occupational/vocational performance as a result of opioid use. This requires documentation regarding the pain problem, objective physical findings, and current functional status both at home and at work and at the initiation of treatment, including a clear statement regarding what objective or functional goals are to be achieved through use of the opioids if other than full functional recovery. Examples of documentation supporting functional improvement include increased physical output or performance (with focus on job specific activities), resolution of physical findings (such as improvement in radicular symptoms, or weakness); increased active range of motion, strength or aerobic capacity; and increased social engagement accompanied by decreased emotional distress." (1) *Provides list of relevant factors that a physician should evaluate in the initial examination, presumably to determine baseline for assessing functional improvement later on.* (4) "While opioids are prescribed due to their analgesic effects, the purpose of opioid therapy is to improve function." (7)	*Yes.* (Recommendation 2, *see middle column)*	*Not specified.*

Tracking Pain and Function (cont'd)				
		Recommendations for Opioid Use 2. "*Indications for Discontinuation* – Failure of initial trial to result in objective functional improvement, resolution, improvement to the point of not requiring this intervention, intolerable adverse effects that are not self-limited, non-compliance, and/or surreptitious medication use." (2)		
APS/AAPM-2009	*Soft yes. It is mentioned as a factor to keep track of.* "**5. Monitoring, Recommendations** 5.1 Clinicians should reassess patients on COT periodically and as warranted by changing circumstances. Monitoring should include documentation of pain intensity and level of functioning, assessments of progress toward achieving therapeutic goals, presence of adverse events, and adherence to	*No specific definition.*	*Not specified.*	*Not specified.*

Tracking Pain and Function (cont'd)				
	prescribed therapies (strong recommendation, low quality evidence)." (118)			
ASIPP - 2012		*No specific recommendations.*		
Canadian Guideline-April 2010	*Yes.* *However, if pain is 30% less due to opioids, improved function is not necessary. See R09 in column to the right.*	*Initial evaluation should include an assessment of how pain affects patient's functions.* "Comprehensive knowledge of the patient's pain condition includes […] estimate of the pain intensity and the functional impairment that arises from it (impact of pain on work, school, home and leisure activities)." (9) "The goal of opioid therapy for chronic non-cancer pain is rarely the elimination of pain, but rather an improvement in function or a reduction of pain intensity by at least 30%. Before starting opioids, a discussion with the patient about specific goals related to pain reduction and functional improvement should address any unrealistic expectations. These agreed-on goals should be documented in the patient's record; they are critical in determining that opioids are effective and should be monitored over time." (18) **"R09 Recommendation Statement** When conducting a trial of opioid therapy, start with a low dosage, increase dosage gradually and monitor opioid effectiveness until optimal dose is attained. (Grade C). Optimal dose. [. . .] **Opioid effectiveness = improved function or at least 30% reduction in pain intensity.** [. . .] **2.1 Assessing Function Change**	*Not specified*	"Before prescribing over 200 mg/day, consider: 1. Patient's response to opioids: Has the patient shown appropriate opioid effectiveness (i.e., improved function or at least 30% reduction in pain intensity) in response to the dose increases to date? (Opioids have a graded response with the greatest benefit at the lowest doses.) If response has been insignificant continuing to increase the dose will be futile.

		The patient's progress in reaching agreed-on goals is an		Switching or

Tracking Pain and Function (cont'd)				
		important indicator of function change. Self-report can be prompted by asking about work, household activity, mood, walking ability, sleep, and social activities. For an example of a structured assessment tool frequently use in trials, see Appendix B-9: Brief Pain Inventory©." (33) **Appendix B-9: Brief Pain Inventory** (77-78) *Inventory includes questions on function tool, with questions on how pain has interfered with general activity, mood, walking ability, normal work (including housework and work outside the home), relations with other people, sleep, enjoyment of life, and school work (both class work and homework).*		discontinuing the opioid could be considered." (36)[27]
ODG *(no page numbers provided because it is an html document)*	*Yes.*	*No definition*	*Not specified*	[Opioids, criteria for use] **6) When to Discontinue Opioids:** "lack of significant benefit (persistent pain and lack of improved function despite high doses of opiates- e.g. > 120 mg/day morphine equivalents)".
Utah-2009	*Yes.* *"Goals for*	"When opioids are to be used for treatment of chronic pain, a written treatment plan should be established	*Not necessarily.*	*Implicitly, not explicitly.*

[27] For extensive discussion of evidence of dangers of prescribing over 200 mg/day, see pages 37-39 of Canadian guideline.

	treatment	that includes measurable goals for reduction of pain		

Tracking Pain and Function (cont'd)				
	of chronic pain should include improvement in the tolerability of the pain and in function (College of Physicians and Surgeons of Ontario, 2000)." (11)	and improvement of function."* (3) * "Function" as used here is defined broadly to include physical, emotional, cognitive, psychological and social function." (3) "Assess the effects of pain on the person's life and function. • Assess the severity of pain, functional status of the patient, and the patient's quality of life using a method/instrument that can be used later to evaluate treatment effectiveness. Tools to accompany Recommendation 1: • Sheehan Disability Tool • Pain Management Evaluation Tool" (8) "**4. Establish treatment goals** **4.2 Recommendation:** Goals for treatment of chronic pain should be measurable and should include improved function and quality of life as well as improved control of pain." (10) "Goals for functional improvement and measures to track progress against those goals should be established and documented to serve as a basis of evaluating treatment outcome (VA/DOD, 2003; Hegmann, Feinberg, Genovese, Korevaar, & Mueller, 2008).[28] These include:	**"7.2 Recommendation:** When pain and function have not sufficiently improved on a current opioid dose, a trial of a slightly higher dose could be considered." (14)	**"10. Discontinuing opioid treatment** **10.2 Recommendation:** Discontinuation of opioid therapy is recommended if any of the following occurs: […] Patient claims or exhibits a lack of effectiveness" (17)

[28] Hegmann K. T., Feinberg S. D., Genovese E. , Korevaar W. C., Mueller K. L. (2008). Chapter 6: Chronic pain. In American College of Occupational and Environmental Medicine's Occupation Medicine Practice Guidelines (2nd ed.).

Tracking Pain and Function (cont'd)				
		• Objective physical findings obtained by the examining clinician (e.g., improved strength, range of motion, aerobic capacity); • Functional status at work (e.g., increase in physical output, endurance, or ability to perform job functions); and • Functional status at home (e.g., increased ability to perform instrumental activities of daily living, and frequency and intensity of conditioning)." (11) "Document the patient's progress toward treatment goals, including functional status, at every visit, rather than merely reporting the patient's subjective report of decreased pain." (18)		
Veteran's Admin guidelines-May 2010	*Yes.* "The titration phase involves adjustment of the dosage to achieve the desired clinical outcomes (pain relief, improved function, and patient satisfaction with minimal or tolerable adverse effects)." (36)	"A discussion of patient responsibilities should be patient-centered and address the following issues : • Goals of therapy -- Partial pain relief and improvement in physical, emotional, and/or social functioning."[29] (32) "Evaluate pain-related function using objective documentation whenever possible, such as physical therapy progress notes, employment records, exercise diaries, family reports, clinician observations (e.g., walking distance), or validated instruments or NRS rating scales on a monthly basis during the titration	*Possibly.* "Failure to achieve at least partial analgesia, or improved function, at relatively low initial doses in the nontolerant patient raises questions about the potential efficacy of opioid therapy for the patient's pain	*Possibly*. "During the [titration]] phase, a lack of response despite dose escalation may indicate that the patient has opioid non-responsive pain and opioid therapy should be discontinued." (36)

[29] The improvements in pain and function that are expected and that are critical to the decision to continue to opioid therapy should be made clear at the beginning of therapy. It should be noted that a review of the literature found only a few references of improved function (Turk et al.,
2002) (32)

		phase and every six months after the patient is on	syndrome." (63)	

Tracking Pain and Function (cont'd)				
		stable opioids. Assessment of function may include: • Employment • Enjoyment of life • Emotional distress (depression and anxiety) • Housework, chores, hobbies and other day to day activities • Sleep • Mobility • Self-care behaviors • Sexual function" (64)[30]		
WA Interagency Guidelines (AMD)-2010	*Yes.* "Treatment goals [. . .] must include improvements in both function and pain while monitoring for and minimizing adverse effects." (5)	"The key to effective opioid therapy for chronic non-cancer pain is to achieve sustained improvement in pain and physical function.[31] Tracking function and pain is critical in determining the patient's ongoing response to opioids and whether any improvement is consistent with potential changes in opioid dosing. Critical to this guideline, if function and pain do not substantially improve with opioid dose increases, then significant tolerance to opioids may be developing and consultative assistance is strongly recommended. An assessment of function and pain should consistently measure the same elements to adequately determine the degree of progress. While	*Yes (though stated inversely)* **"BEFORE you decide to prescribe opioids for chronic pain** Consider opioid therapy when: The patient has demonstrated sustained improvement in function and pain levels in previous	*Possibly.* "The total daily dose of opioids should not be increased above 120mg oral MED without either the patient demonstrating improvement in function and pain or first obtaining a consultation from a practitioner

[30] Evidence Table- Evaluate function related to chronic pain after initiation of therapy: Caldwell et al., 1999; Peloso et al., 2000 Roth et al., 2000. For all three references, LE is I, QE is Good and SR is A. (66)

[31] Devulder J, Richard U, Nataraja SH. Impact of long-term use of opioids on quality of life in patients with chronic, nonmalignant pain. Curr Med Res Opin 2005;21(10):1555-1569. 28 *and* Loeser JD, Egan KJ. Managing the chronic pain patient. New York: Raven Press, 1989.

		there is no universally accepted tool to assess opioid	opioid trial, […]" (5)	qualified in chronic

Tracking Pain and Function (cont'd)				
		therapy's impact on function and pain, several are available and listed in Appendix C. In particular, the AMDG recommends using the two item Graded Chronic Pain Scale [...[32] as an ongoing and rapid method to easily track function and pain in the medical record. See Appendix C for instructions on scoring and interpretation." (6) "Other functional assessment tools that may be helpful in monitoring your patient's progress include, but are not limited to: • **SF36 Health Survey*** **www.rand.org/health/surveys_tools/mos/mos_core_36item.html** • Brief Pain Inventory* • **www.ohsu.edu/ahec/pain/paininventory.pdf** • ***Quick*Dash*** for musculoskeletal disorders of the upper extremities • **www.dash.iwh.on.ca/outcome_quick.htm** • Quality of Life Scale* • **www.uic.edu/orgs/qli/questionaires/ questionnairehome.htm** • Oswestry Disability Index* • **www.workcover.com/public/download.aspx?id=794 &str=disability index oswestry** • Neck Disability Index*	"If function and pain do not improve after a sufficient opioid trial, consider discontinuing opioids (see *Tapering or Discontinuing Opioids,* page 10). (7)	pain management." (3)

[32] "There is extensive research on the reliability, validity and responsiveness to change of these pain severity ratings, which is summarized in the following reference: Von Korff M. Chronic Pain Assessment in Epidemiologic and Health Services Research: Empirical Bases and New Directions. Handbook of Pain Assessment: Third Edition. Dennis C. Turk and Ronald Melzack, Editors. Guilford Press, New York., In press." (30)

Tracking Pain and Function (cont'd)				
		• **www.workcover.com/public/download.aspx?id=792&str=disability index neck** • Short Musculoskeletal Function Assessment* See: **www.ejbjs.org/cgi/reprint/81/9/1245** * These instruments have all been independently validated and may be available at websites other than those listed above." (6-7)		
WA Worker's Comp Guidelines - 2013	*Yes.* "Effective use of opioids must result in clinically meaningful improvement in function. Continuing to prescribe opioids in the absence of clinically meaningful improvement in function or after	"**Measuring the Impact of Opioid Use** Beyond the acute phase, effective use of opioids should result in **clinically meaningful improvement in function (CMIF)**. Providers should track function and pain on a regular basis, using the same validated instruments at each visit, to consistently determine the effect of opioid therapy. The department endorses the Two Item Graded Chronic Pain Scale [16][33] as a quick, two-question tool to track both function and pain when opioids are prescribed (see AMDG Guideline, Appendix C at **www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf**). CMIF is defined as an improvement in function of at least 30% as compared to the start of treatment or in response to a dose change [17, 18].[34] **A decrease in pain intensity in the absence of improved function is not considered CMIF.**	*Yes.* [*in boldface in the original]* "**If use in the acute phase (0-6 weeks) does not lead to improvements in pain and function of at least 30%, or to pain interference levels of 4 or less,**	**Executive Summary** [*last recommendation*] "Discontinue opioids if treatment has not resulted in clinically meaningful improvement in function, or the worker has experienced a

[33] 16. Von Korff, M., Ormel, J., Keefe, F.J., and Dworkin, S.F., *Grading the severity of chronic pain.* Pain, 1992. **50**(2): p. 133-49.

[34] 17. Dworkin, R.H., Turk, D.C., Wyrwich, K.W., Beaton, D., Cleeland, C.S., Farrar, J.T., Haythornthwaite, J.A., Jensen, M.P., Kerns, R.D., Ader, D.N., Brandenburg, N., Burke, L.B., Cella, D., Chandler, J., Cowan, P., Dimitrova, R., Dionne, R., Hertz, S., Jadad, A.R., Katz, N.P., Kehlet, H., Kramer, L.D., Manning, D.C., McCormick, C., McDermott, M.P., McQuay, H.J., Patel, S., Porter, L., Quessy, S., Rappaport, B.A., Rauschkolb, C., Revicki, D.A., Rothman, M., Schmader, K.E., Stacey, B.R., Stauffer, J.W., von Stein, T., White, R.E., Witter, J., and Zavisic, S., *Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations.* J Pain, 2008. **9**(2): p. 105-21.
18. Ostelo, R.W., Deyo, R.A., Stratford, P., Waddell, G., Croft, P., Von Korff, M., Bouter, L.M., and de Vet, H.C., *Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change.* Spine (Phila Pa 1976), 2008. **33**(1): p. 90-4.

Tracking Pain and Function (cont'd)				
	The development of a severe adverse outcome is not proper and necessary care in the Washington State workers' compensation system" (3) [*in boldface in original*] "**Obtain baseline measures of pain and pain interference (function) within 2 weeks of filing a claim."** (8)	Other validated instruments may also be used to measure functional improvement (see AMDG Guideline, Tools for Assessing Function and Pain at **www.agencymeddirectors.wa.gov/Files/OpioidGdline. The** American Chronic Pain Association has created a 10-item Quality of Life Scale for people with pain, which helps correlate the Graded Chronic Pain Scale with actual daily activities [19].[35] Use of the PROMIS web-based tool (**www.nihpromis.org/**) may also be helpful in determining the effectiveness of COT. **Ultimately, effective COT should result in improved work capacity or the ability to progress in vocational retraining.** Evaluation of clinically meaningful improvement should occur at three critical decision-making phases: 1. At the end of the acute phase (about 6 weeks following injury or surgery), to determine whether continued opioid therapy is warranted in the subacute phase. 2. At the end of the subacute phase (3 months following injury), to determine whether to prescribe COT. 3. Periodically during COT, to assess impact on function and risk of therapy." (5) "With the exception of catastrophic injuries, the provider must document the following before L&I or insurer can authorize payment for opioids during the chronic phase: • Clinically meaningful improvement in function (≥ 30%) has been established with opioid use in the acute or subacute phase." (10) "Continued coverage of COT will depend on the prescriber	**continued opioid use is not warranted**." (8) "During the subacute phase [*between 6 and 12 weeks*], providers should review the effects of opioid therapy on pain and function to determine whether opioid therapy should continue. Opioids should be discontinued during this phase if: • There is no clinically meaningful improvement in function when compared to function measured during the acute phase." (9)	Severe adverse outcome or overdose event" (3) "Continuing to prescribe opioids in the absence of clinically meaningful improvement in function or after the development of a severe adverse outcome is not considered proper and necessary care in the Washington State workers' compensation system. In addition, the use of escalating doses to the point of developing opioid use disorder is not proper and necessary care." (6) [*full text of one*

[35] American Chronic Pain Association. Quality of Life Scale: A measure of function for people with pain.

		documenting the following:		*shaded box*]

Tracking Pain and Function (cont'd)				
		• CMIF is maintained, or pain interference with function score is ≤ 4 with stable dosing. If COT dose is increased, CMIF must be demonstrated in response to the dose change." (10)		

Tapering I [*See following chart for two more tapering rubrics: 1) ancillary interventions and 2) what to do if tapering fails*.]				
	When to taper	**How to taper**	**Consult a specialist?**	**Exact language**
ACOEM – 2011	*For opioid-naïve patients, when there is improvement in function and less pain* *Recommended for opioid-tolerant patients:* *1) on high doses,* *2) with hyperalgesia,* *3) with more pain, decreased function.* *If first weaning trial unsuccessful, do yearly trials.*	*Slowly and carefully over several months for all patients who have been on opioids for over a month.*	*Yes, in most cases.* "In most cases, patients being weaned from opioids should be referred to a mental health professional with experience in substance abuse or management of patients on opioids. This is in order for the patient to be counseled regarding any anxiety associated with reduction of opioid dose as anxiety will complicate the weaning process." (8)	*Opioid-naïve patients:* "**Attempts at Weaning** – Once patients have demonstrated improvement in function, concomitant reduction in pain suggests that attempts to decrease the opioid dose may be appropriate. This should be done slowly in conjunction with careful monitoring of the patient's clinical and functional status, with the goal of weaning him or her entirely from opioids after several months. If attempts at weaning are accompanied by increased pain and worsened functional performance, the medication dose can be reinstituted and weaning may be attempted again after the patient has stabilized. If weaning remains problematic, consideration can be given to long-term opioid use. High-dose opioids are never indicated in patients without clear anatomic explanations for their pain." (7-8) *Opioid-tolerant patients:* "Patients on opioids may or may not have been appropriately placed on these agents and may be using excessive doses. A trial of weaning from opioids in conjunction with initiation of treatments and activities aimed at functional restoration is recommended for these patients, although the likelihood of success will be dependent upon the clinical presentation. Even with recognized benefit, opioids are not benign drugs and patients should remain under medical scrutiny

				and undergo weaning trials no less than yearly.

Tapering I (cont'd)				
				It is recognized by many pain specialists that a subset of patients are no worse off if they do not improve upon opioid detoxification." (8) "In general, use of high doses of extended release opioids or the equivalent forms of immediate action drugs (see Appendix 1 for common doses) should prompt efforts at weaning, especially if the patient has not reported any functional gains despite increases in dose. The presence of adverse effects such as opioid-induced hyperalgesia or simply increased pain and decreased function despite opioid use are also grounds for weaning." (8) *Regarding withdrawal symptoms:* "There must be judicious assessment for physiologic signs of withdrawal, and these should be managed with appropriate medical therapies when needed (potentially reinstating opioids prior to resuming a more gradual taper for significant withdrawal symptoms). Such withdrawal signs should be clearly discriminated from the patient's verbal complaints of symptoms, since the latter are often well learned in many patients with chronic pain. It is inappropriate to reduce doses rapidly in patients who have been on opioids for more than a month, as some degree of physical dependence may have already developed." (8)
APS/AAPM-2009	*Aberrant drug behavior, adverse effects, failure to meet treatment*	*No specific recommendation, but lays out various options for how*	*No specific recommendation, but when possible, inpatient setting may be best for patients*	"Clinicians should taper or wean patients off of COT who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress toward meeting

	goals	*quickly to taper.*	*with comorbidities.*	therapeutic goals, or experience intolerable

Tapering I (cont'd)				
				adverse effects (strong recommendation, low-quality evidence)." (120) "Patients should be tapered or weaned off COT when they engage in serious or repeated aberrant drug-related behaviors or diversion, experience intolerable adverse effects, or make no progress toward meeting therapeutic goals." (120) "Although there is insufficient evidence to guide specific recommendations on optimal strategies, a taper or wean can often be achieved in the outpatient setting in patients without severe medical or psychiatric comorbidities. When available, opioid detoxification in a rehabilitation setting (outpatient or inpatient) can be helpful, especially for patients unable to reduce their opioid dose in a less structured setting." (120) "Approaches to weaning range from a slow 10% dose reduction per week to a more rapid 25% to 50% reduction every few days. Evidence to guide specific recommendations on the rate of reduction is lacking, though a slower rate may help reduce the unpleasant symptoms of opioid withdrawal. [22,109,131]" (120)[36]

[36] 22. Chugh SS, Socoteanu C, Reinier K, Waltz J, Jui J, Gunson K: A community-based evaluation of sudden death associated with therapeutic levels of methadone. Am J Med 121:66-71, 2008

109. Ralphs JA, Williams AC, Richardson PH, Pither CE, Nicholas MK: A comparison of patient-controlled reduction and staff controlled cocktail methods. Pain 56:279-288, 1994

Tapering I (cont'd)				
				"Anecdotal clinical experience of panel members suggests that at high doses (eg, over 200 mg/d of morphine or equivalent), the initial wean can be more rapid. The rate of dose reduction often must be slowed when relatively low daily doses, such as 60 to 80 mg daily of morphine (or equivalent), are reached, due to occurrence of more withdrawal symptoms." (120-121)
ASIPP- 2012				*No specific recommendations.*
Canadian Guideline – April 2010	*For patients on <200mg/day who have seen "insignificant effects" from opioids* *Adverse effects or insufficient effectiveness and failed trials of other opioids.* *Pregnant patients*	*Extensive, detailed recommendations (1.3 pages worth).* *Use morphine to taper from oxycodone or hydromophone.* *Weekly visits.* *See last column for more detail.*	*No specific recommendation.*	**"R13 Recommendation statement. Switching or discontinuing opioids.** For patients experiencing unacceptable adverse effects or insufficient opioid effectiveness from one particular opioid, try prescribing a different opioid or discontinuing therapy. (Grade B)." [37] (43) "Opioids should be tapered and discontinued if the patient's pain remains unresponsive after a trial of several different opioids." (43) **"Considerations before Dose Exceeds 200 mg/day** [. . .] If response has been insignificant, continuing to increase the dose will be futile. Switching or discontinuing the opioid could be

130. Tassain V, Attal N, Fletcher D, Brasseur L, Degieux P, Chauvin M, Bouhassira D: Long term effects of oral sustained release morphine on neuropsychological performance in patients with chronic non-cancer pain. Pain 104:389-400, 2003

[37] Baron MJ, McDonald PW. Significant pain reduction in chronic pain patients after detoxification from high-dose opioids. Journal of Opioid Management 2006 Sep;2(5):277-82. (GRADE B, Supports Recommendation 13). *See page 43 of guideline for detailed summary and assessment of this article.*

				considered." (36) **"Recommendation statement. Pregnant patients. R19** Pregnant patients taking long-term opioid therapy should be tapered to the lowest

Tapering I (cont'd)				
				effective dose slowly enough to avoid withdrawal symptoms, and then therapy should be discontinued if possible. (Grade B)." (53) Withdrawal symptoms, and then therapy should be discontinued if possible. (Grade B). " (53) **Appendix B-12: Opioid Tapering** "**Precautions for Outpatient Opioid Tapering** 1) **Pregnancy:** Severe, acute opioid withdrawal has been associated with premature labour and spontaneous abortion. [. . .] 4) **Concurrent medications.** Avoid sedative-hypnotic drugs, especially benzodiazepines, during the taper. [. . .] **2.2 Type of Opioid, Schedule, Dispensing Interval** 1) Use controlled-release morphine if feasible (see 2.3 below). 2) Prescribe scheduled doses (not p.r.n.). 3) Prescribe at frequent dispensing intervals (daily, alternate days, weekly, depending on patient's degree of control over opioid use). Do not refill if patient runs out. 4) Keep daily schedule the same for as long as possible (e.g., t.i.d.). **2.3. Rate of the Taper** 1) The rate of the taper can vary from 10% of the total daily dose every day, to 10% of the total

				daily dose every 1–2 weeks.

Tapering I (cont'd)				
				2) Slower tapers are recommended for patients who are anxious about tapering, may be psychologically dependent on opioids, have co-morbid cardio-respiratory conditions, or express a preference for a slow taper. 3) Once one-third of the original dose is reached, slow the taper to one-half or less of the previous rate. [. . .] **2.4 Switching to Morphine** 1) Consider switching patients to morphine if the patient might be dependent on oxycodone or hydromorphone. 2) Calculate equivalent dose of morphine (see Appendix B-8: Oral Opioid Analgesic Conversion Table). 3) Start patient on one-half this dose (tolerance to one opioid is not fully transferred to another opioid). 4) Adjust dose up or down as necessary to relieve withdrawal symptoms without inducing sedation." (85) **"2.5 Monitoring during the Taper** 1) Schedule frequent visits during the taper (e.g. weekly). [. . .] **2.6 Completing the Taper** 1) Tapers can usually be completed between 2–3 weeks and 3–4 months." (86)

Tapering I (cont'd)				
ODG *(no page numbers provided because it is an html document)*	*No improved function or decreased function, adverse effects, aberrant drug behavior hyperalgesia*[38]	*Slow taper in most cases.* *Immediate discontinuation if illegal activities going on.* [Weaning of medications (opioids, benzodiazepines, carisoprodol)] *Suggested tapering protocols:* Opioid weaning should include the following: (a) Start with a complete evaluation of treatment, comorbidity, and psychological conditions; (b) Clear written instructions should be given to the patient and family; (c) If the	[Weaning of medications (opioids, benzodiazepines, carisoprodol)] "If the patient cannot tolerate the taper, refer to an expert (pain specialist, addiction medicine specialist)"	[Opioids, criteria for use] "Weaning should occur under direct ongoing medical supervision as a slow taper except for the below mentioned possible indications for immediate discontinuation. The patient should not be abandoned. (a) If there is no overall improvement in function, unless there are extenuating circumstances. (b) Continuing pain with the evidence of intolerable adverse effects; lack of significant benefit (persistent pain and lack of improved function despite high doses of opiates – e.g. > 120 mg/day morphine equivalents) (c) Decrease in functioning (d) Resolution of pain (e) If serious non-adherence is occurring (f) The patient requests discontinuing (g) Immediate discontinuation has been suggested for: evidence of illegal activity including diversion, prescription forgery, or stealing; the patient is involved in a motor vehicle accident and/or arrest related to opioids, illicit drugs and/or

[38] Chang G, Chen L, Mao J. Opioid tolerance and hyperalgesia. Med Clin North Am. 2007; 91:199-211.

Lee m, Silverman S, Hansen H, Patel V, Manchikanti L. A Comprehensive Review of Opioid-Induced Hyperalgesia. Pain Physician 2011; 14:145-161 http://www.painphysicianjournal.com/2011/march/2011;14;145-161.pdf

		patient cannot		alcohol; intentional suicide attempt;

Tapering I (cont'd)				
		tolerate the taper, refer to an expert (pain specialist, addiction medicine specialist); (d) Taper by 20 to 50% per week of original dose for patients who are not addicted and are on relatively low doses (the patient needs 20% of the previous day's dose to prevent withdrawal); (e) A slower suggested taper is 10% every 2 to 4 weeks, slowing to a reduction of 5% once a dose of 1/3 of the initial dose is reached; (f) Greater success may occur when the patient is switched to longer-acting opioids and then tapered; (g) Office visits should occur on a weekly basis or more		aggressive or threatening behavior in the clinic. It is suggested that a patient be given a 30-day supply of medications (to facilitate finding other treatment) or be started on a slow weaning schedule if a decision is made by the physician to terminate prescribing of opioids/controlled substances. (h) Many physicians will allow one "slip" from a medication contract without immediate termination of opioids/controlled substances, with the consequences being a re-discussion of the clinic policy on controlled substances, including the consequences of repeat violations. (i) If there are repeated violations from the medication contract or any other evidence of abuse, addiction, or possible diversion it has been suggested that a patient show evidence of a consult with a physician that is trained in addiction to assess the ongoing situation and recommend possible detoxification. (Weaver, 2002) (j) When the patient is requesting opioid medications for their pain and inconsistencies are identified in the history, presentation, behaviors or physical findings, physicians and surgeons who make a clinical decision to

		frequently as needed; (h) Assess		withhold opioid medications should

Tapering I (cont'd)				
		for withdrawal using a scale such as the Subjective Opioid Withdrawal Scale (SOWS), Objective Opioid Withdrawal Scale (OOWS), or Clinical Opiate Withdrawal Scale (COWS); & (i) Recognize that this may take months." *Medications used to manage withdrawal from opioids include methadone, buprenorphine, and clonidine.*		document the basis for their decision." [Opioid hyperalgesia] "*Treatment*: Suggested treatment for patients with increasing pain (assumes that the patient has had improvement with opioids at some point): (1) It is not unreasonable to give a trial of opioid dose escalation to see if pain and function improves. If pain improves, the diagnosis is probable tolerance. If pain does not improve or worsens, this may be evidence of opioid hyperalgesia and the opioid dose should be reduced or weaned."
Utah – 2009	*Opioids not effective, adverse effects, illegal behaviors* (17)	*10% decreased dose per week, slower (monthly decrease) for some patients and even faster for others* (68) *Treat withdrawal symptoms such as insomnia with antidepressants, but not with benzodiazepines*	*Only for patients with complicated withdrawal symptoms* (68) *Refer for counseling if there are significant behavioral issues* (68)	**"10. Discontinuing opioid treatment 10.1 Recommendation:** An opioid treatment trial should be discontinued if the goals are not met and opioid treatment should be discontinued at any point if adverse effects outweigh benefits or if dangerous or illegal behaviors are demonstrated. Reference Guidelines: 5 [. . .*Rec 10.2 doesn't contribute anything really new*] **10.3 Recommendation:** When possible, offer to assist patients in safely discontinuing medications even if they have withdrawn from

		(68)		treatment or been discharged for agreement

Tapering I (cont'd)				
				violations. The goal is to taper all patients off opioid medication safely. "Strategies for Tapering and Weaning" in the Tool Section contains advice on tapering opioid medications (WSAMDG, 2007). If the patient is discharged, the clinician is obliged to offer continued monitoring for 30 days post-discharge. Tools to accompany Recommendation 10: • Strategies for Tapering and Weaning" (17) *This tool is on page 68. Unique to this guideline: recs for recognizing and managing behaviorial issues during opioid weaning.*
Veteran's Admin-Guidelines – May 2010	*Treatment ineffective, adverse effects outweigh benefits, dangerous or illegal behaviors* (83)	*Discontinue immediately with unsafe or illegal patient behaviors* (84) *Various rates of tapering depending on the individual* (86)	*Not necessary if patient is choosing to taper* (86) *Patients with high risk for aberrant behaviors (diversion, suicide, etc.) should see an addiction or pain specialist "with expertise in dealing with difficult cases"* (86) *Complicated withdrawal symptoms-see a pain specialist or a center* (86) *Addicted patients: "referred for SUD treatment " "in a primary care setting"* (86)	*Seven pages devoted to this topic.* "Opioid therapy should be tapered off and discontinued if any of the following situations occur: a. The medication fails to show partial analgesia with incremental dose titration b. Trials with different agents provide inadequate analgesia c. There is other evidence that the pain may not be opioid responsive d. Real or potential harms outweigh real or potential benefits e. Patient request." (83)

Tapering I (cont'd)				
				"2. Clear written and verbal instructions should be given to patients/family to educate them about the slow taper protocol that will minimize abstinence (withdrawal) syndromes. 3. Patients who are unable to tolerate the taper as described should be considered for referral to, or consultation with, a pain specialist, substance use specialist or other expert." (86) "***for Tapering:*** − Taper by 20%-50% per week [of original dose], for patients who are not addicted. The goal is to minimize adverse/withdrawal effects. − The rapid detoxification literature indicates that a patient needs 20% of the previous day's dose to prevent withdrawal symptoms. − Decisions regarding tapering schedule should be made on an individual basis. Sometimes faster or slower tapering may be warranted. − Some experts suggest that the longer the person has been on opioids, the slower the taper should be. − Remain engaged with the patient through the tapering process, and provide psychosocial support as needed. − Consider using adjuvant agents, such as antidepressants to manage irritability, sleep disturbance, or antiepileptics for neuropathic pain. (Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain. (2007) available at: http://www.agencymeddirectors.wa.gov/Files/O

				pioidGdline.pdf)

Tapering I (cont'd)				
				– Do not treat withdrawal symptoms with opioids or benzodiazepines after discontinuing opioids. (Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain (2007) available at: http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf)" (87) "**Follow-up as Indicated** *RECOMMENDATIONS* 1. Do not abandon a patient under any circumstances. 2. Maintain contact with any patient who withdraws from treatment due to a disagreement. 3. Refer patients with comorbid psychiatric disorders to appropriate mental health providers." (89)
WA Inter-agency Guidelines (AMDG)-2010	*No improvement in function and pain, significant adverse effects or high-risk behavior exhibiting drug-seeking behaviors (diversion, forging prescriptions, stealing drugs, frequently losing prescriptions, aggressive demand*	*10% decreased dose per week, slower (monthly decrease) for some patients and even faster for others* (10) *Treat withdrawal symptoms such as insomnia with antidepressants, but not with*	*Yes.* "Examples of when to seek assistance include tapering patients off opioids" (10)	"If function and pain do not improve after a sufficient opioid trial, consider discontinuing opioids." (7) "If the patient tested negative for prescribed opioids and if confirmatory testing substantiates a "red flag" result (see Table 3[39]), the prescriber should consider a controlled taper or stop prescribing opioids immediately." (9) *Tapering protocol (10) is absolutely identical (verbatim) to Utah Guideline (published after the AMDG), with one small exception. The AMDG*

[39] Table 3: Red flags = Positive for cocaine or metabolites; Positive for drug (benzodiazepines, opioids, etc) you did not prescribe or have knowledge of; Positive for alcohol

	for opioids, injecting	*benzodiazepines*		*has the following sentence, which the Utah*

Tapering I (cont'd)				
	opioids, unsanctioned use of opioids or dose escalation, use of illicit drugs, failing a drug screen, getting opioids from multiple prescribers, recurring emergency department visits for chronic pain management (13)	(11) *Use clonidine to treat other withdrawal symptoms, such as nausea.* (10) *[Utah guidelines picked up the AMDG tapering protocol guidelines verbatim, with no alterations.]* *Appendix H (46) includes a description of the Opioid Taper Plan Calculator, developed by Washington State Medicaid in collaboration with the University of Washington pain management experts.* (**http://hrsa.dshs.wa.gov/pharmacy/pdf/TaperSchedule.xlsx**). [*the link appears to be*		*guidelines did not keep:* "Rapid reoccurrence of tolerance can occur for months to years after prior chronic use." (11) *Utah guidelines also picked up the AMDG advice on how to recognize and manage behaviorial issues during opioid tapering. The differences between the two guidelines are minor. Below, I have indicated sentences that were either deleted or reworded (but without changing the meaning significantly) in the Utah Guideline.* **"Recognizing and managing behavioral issues during opioid tapering** Opioid tapers can be done safely and do not pose significant health risks to the patient. ~~Special care needs to be taken by the prescriber to preserve the therapeutic relationship at this time. Otherwise, taper can precipitate doctor-shopping, illicit drug use, or other behaviors that pose a risk to patient safety.~~ Extremely challenging behavioral issues may emerge during an opioid taper38. Behavioral challenges frequently arise when a prescriber is tapering the opioid dose and a patient places great value on the opioid he/she is receiving. In this setting, some patients ~~may feel overwhelmed or desperate and will try to convince the prescriber to abandon the opioid taper.~~ Challenges may include: Focus on right to pain relief ("You don't

		broken]		believe I have real pain”)

Tapering I (cont'd)				
				Arguments about poor quality of pain care with threats to complain to administrators or licensing boards Attributing one's deteriorating psychological state, including suicidal thoughts, to opioid withdrawal.[40] There are no fool-proof methods for preventing behavioral issues during an opioid taper, but strategies implemented at the beginning of the opioid therapy are most likely to prevent later behavioral problems if an opioid taper becomes necessary ~~(see *AFTER you decide with the patient to prescribe chronic opioid therapy*, page 5). Serious suicidal ideation (with plan or intent) should prompt urgent psychiatric consultation39.~~
WA Worker's Comp Guidelines -2013	*Same as AMDG recs, with the following specifications:* *No sustained CMIF over three months of opioid treatment.* *Use of opioids is not in compliance with various rules and guidelines (see last*	*Same as AMDG for step 1, then adds on other protocols if that step is unsuccessful.* See Steps 1-2 in far-right column.	Not for all workers, only those who fail to taper in a community care setting or who are "at high risk for failure due to high dose, concurrent benzodiazepine use, or co-morbid substance use or mental health disorder" (13). In those cases, seek consultative assistance from "a pain management specialist, a structured intensive	"**When to Discontinue COT** • Worker or AP requests opioid taper OR • Worker is maintained on opioids for at least 3 months and there is no sustained CMIF, as measured by validated instruments OR • Worker's risk from continued treatment outweighs benefit OR • Worker has experienced a severe adverse outcome or overdose event OR

[40] Utah guideline rewrite: "Guilt provocation ("You are indifferent to my suffering"); Threats of various kinds; Exaggeration of their actual suffering in order to disrupt the progress of a scheduled taper" (68)

	column for details).			• Evidence of aberrant behavior

Tapering I (cont'd)				
				(inconsistent urine drug test result, lost prescriptions, multiple requests for early refills, multiple prescribers, unauthorized dose escalation, apparent intoxication, etc.) Or • Use of opioids is not in compliance with DOH's pain management rules, L&I's rules, AMDG Guideline or L&I's Guideline for Prescribing Opioids to Treat Pain in Injured Workers." (13) *How to taper:* "**Step 1: Discontinuing Opioids in a Community Care Setting** […] A gradual taper of approximately 10% per week (see AMDG Guideline, Tapering or Discontinuing Opioids and Appendix H at **www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf**) can be carried out by the attending provider. Adjuvant agents like clonidine and psychological support such as cognitive behavioral therapy can be provided to assist with the taper process. The department or insurer may also authorize temporary coverage of buprenorphine or buprenorphine/naloxone to assist with the tapering process (see L&I coverage policy) [33]. The AP may also seek consultative assistance from a pain management specialist. **Step 2: Discontinuing Opioids in an Intensive Setting** For those workers who have failed step 1 or who are at high risk for failure due to high dose, concurrent benzodiazepine use, or co-morbid substance use or mental health disorder, the prescriber should consider seeking consultative assistance from a pain management specialist, a structured intensive multidisciplinary program (SIMP) provider or addiction medicine specialist. Adjuvant agents and

				psychological support can provided to assist with the taper

Tapering I (cont'd)				
				Process. The department or insurer may also authorize temporary coverage of buprenorphine or buprenorphine/naloxone to assist with the tapering process (see L&I coverage policy). In these situations, formal inpatient detoxification and/or a 4-week SIMP treatment program may be required. [*in shaded box*] Due to the lack of high quality evidence of safety and comparative efficacy, ultra rapid detoxification (e.g. within three days), using antagonist drugs with or without sedation, will not be covered." (13) **Additional Services:** *If steps 1 and 2 fail, can authorize up to 6 months of addiction treatment through a licensed chemical dependency treatment center. (14)* **"Treatment Options for Opioid Use Disorder:** – Buprenorphine (Subutex®, Suboxone®) – Methadone – Naltrexone (Depade®, Revia®, Vivitrol®) – Drug-free outpatient treatment" (14)

Tapering II		
	Ancillary Interventions to take during tapering	**If all attempts to taper are unsuccessful**
ACOEM-2011	"A referral to a physical therapist or equivalent for instruction in home exercise and individualized techniques to reduce or prevent muscle pain or stiffness should also be considered. Use of self-applied palliative remedies such as topical analgesics (including lidocaine and capsaicin) or heat (especially heat wraps) may be useful. Judicious participation in aerobic activities that do not exceed patient tolerance is recommended (it is better to build patients up gradually than have exercise lead to increased pain and requests for reinstitution of opioids at previous doses). Selected patients with access to a swimming pool may also benefit from a regular program of aquatic exercise. Use of adjunctive medications such as NSAIDs, acetaminophen, anti-depressants, herbal remedies, anti-convulsants, and any other medications appropriate for the patient's clinical presentation should be considered." (8-9)	"**Maintenance on Opioids** – If the patient is unable to tolerate further dose reduction despite the use of appropriate supportive interventions as described above, and assuming identifiable pathology linked to the chronic pain state, then in some circumstances opioids may be maintained. Such patients should be required to complete a formal opioid agreement and fulfill the other requirements recommended previously as prerequisites for maintaining them on chronic opioids." (9)
Veteran's Admin guidelines-May 2010		"RECOMMENDATIONS 1. Do not abandon a patient under any circumstances. 2. Maintain contact with any patient who withdraws from treatment due to a disagreement. 3. Refer patients with comorbid psychiatric disorders to appropriate mental health providers. DISCUSSION A provider should never abandon a patient. This has both legal and ethical ramifications. Providers should seek both legal and ethical consultations if they fear their actions may be interpreted as patient abandonment. Providers should make

Tapering II (cont'd)		
		every effort to find another treatment option for the patient. Providers should be aware, however, that prescribing opioid medications other than for legitimate medical purposes is against the law. Often, after a patient disagrees with the treatment decision to medically withdraw from opioid therapy, the patient will drop out of treatment. If this occurs, the provider should send a registered letter to the patient. The letter should inform the patient that he has two weeks to return to treatment or his case will be closed and he would have to go through intake again before care is resumed." (89)
	No other guidelines have specific recommendations on this topic.	*A number of the guidelines strongly urge physicians not to abandon patients (such as the Veteran's Administration). AMDG addresses the similar worst-case scenario by recommending treatment in a chemical dependency treatment program for patients with Opioid Use Disorder. (14)*

Perioperative Pain		
	Use of opioids in the perioperative period for opioid-naïve patients	**Use of opioids in the perioperative period for patients on COT (Exact language in quotes)**
ACOEM-2011	*No specific recommendations*	*No specific recommendations* "Management of cancer pain, pain at end of life, acute pain, postsurgical pain, labor pain, or CNCP in children and adolescents is outside the scope of this guideline." (115)
APS/AAPM-2009	*No specific recommendations*	*No recommendations*
ASIPP - 2012		*No specific recommensations.*
Canadian Guideline – April 2010	*No specific recommendations*	*No recommendations*
ODG	*No specific recommendations*	*No recommendations*
UTAH - 2009	*No specific recommendations*	*No recommendations*
Veteran's Admin Guidelines – May 2010	*No specific recommendations*	**"Management of buprenorphine-treated patients transferred from another provider:** […] d. In the event of anticipated pain (i.e., an elective procedure or surgery) SL buprenorphine should be stopped for 48 hours before the scheduled event." (90-91)
WA Interagency Guidelines (AMD)-2010	*No specific recommendations*	*No specific recommensations*
WA Worker's Comp Guidelines -2013	"DO NOT USE: Long-acting or extended-release opioids (e.g. Oxycontin®) for acute pain or post-operative pain in an opioid-naive worker." (6)	*Many, very specific recommendations for each stage of the perioperative period (pre, intra and post). Here are some highlights:* "Based on the lack of evidence, there is no consensus on whether or not to taper chronic opioids before elective surgery." (11) **Before Surgery (pre-operatively), the surgeon and AP should:** • Have a coordinated treatment plan for managing surgical pain,

		including identifying the post-operative opioid prescriber.

Perioperative Pain (cont'd)		
		• Obtain a pre-operative anesthesia consult, as above. Workers on buprenorphine need special anesthesia care and should have a consult at least 2 weeks before surgery. • Access the PMP and review the worker's controlled substance history to get accurate information on opioid dose and concurrent medication use. Provider should discuss any apparent discrepancies with the worker. • Prepare the worker for elective surgery by setting appropriate expectations for pain management. Workers need reassurance that their pain management needs will be met, and they need to know that their opioid use is expected to return to the pre-operative dose, or less, following surgery. • Consider an opioid taper, but this is not required. Avoid escalating opioid dose before surgery. • Avoid prescribing new benzodiazepines or sedative-hypnotics. • Consider a consult with a pain management specialist before surgery for workers on high dose opioids or who have co-morbid mental health or substance use disorder. **Day of Surgery (intra-operatively), the anesthesiologist should:** • Use anti-inflammatories, acetaminophen or both, if not contraindicated. • Continue pre-operative opioids to decrease the risk of withdrawal symptoms and use regional blocks, if appropriate. • Consider the use of other non-opioid analgesic adjuncts (e.g. gabapentin, ketamine or lidocaine) for opioid sparing effects. **After Surgery (post-operatively), the surgeon or hospitalist and AP should:** • Continue pre-operative opioids, with extra analgesia for acute pain via patient-controlled analgesia (PCA) while hospitalized.

Perioperative Pain (cont'd)		
		• Use care when transitioning from PCA to oral opioids. DO NOT perform a "straight" conversion from IV to oral opioid because of a lack of complete cross-tolerance. • Expect the worker to need more time than other patients to stabilize pain control after transitioning to oral opioids. • **Discharge the worker on the same pre-operative opioid regimen and only supplement with short-acting (not extended-release) opioids for post-operative pain.** [*boldface in original doc*] • Do not prescribe long-acting or extended-release opioids for post-operative pain unless the worker was previously maintained on these drugs. • Avoid new sedative-hypnotics and benzodiazepines. • Taper total opioids to pre-operative dose or lower by 6 weeks. • A specialist may be needed for workers on high dose opioids or who have co-morbid mental health or substance use disorder.

[i] Sullivan MD, Edlund MJ, Zhang L, Unützer J, Wells KB. Association between mental health disorders, problem drug use, and regular prescription opioid use. Arch Intern Med. 2006;166:2087-93. CONCLUSIONS: Common mental health disorders and problem drug use are associated with initiation and use of prescribed opioids in the general population. Attention to psychiatric disorders is important when considering opioid therapy.

Sullivan MD, Edlund MJ, Steffick D, Unützer J. Regular use of prescribed opioids: association with common psychiatric disorders. Pain. 2005;119:95-103.Depressive, anxiety and drug abuse disorders are associated with increased use of regular opioids in the general population. Depressive and anxiety disorders are more common and more strongly associated with prescribed opioid use than drug abuse disorders.

Wilsey BL, Fishman SM, Tsodikov A, Ogden C, Symreng I, Ernst A. Psychological Comorbidities Predicting Prescription Opioid Abuse among Patients in Chronic Pain Presenting to the Emergency Department. Pain Med. 2008 Feb 5. Patients in chronic pain should be assessed for psychological and addiction disorders because they are at increased risk for abusing opioids. They should also be referred for psychosocial treatment as part of their care, where appropriate.

Savage SR, Kirsh KL, Passik SD. Challenges in using opioids to treat pain in persons with substance use disorders. Addict Sci Clin Pract. 2008;4:4-25. This article provides practical guidelines for the use of opioids to treat pain in individuals with histories of addiction.

Ballantyne JC, LaForge KS. Opioid dependence and addiction during opioid treatment of chronic pain. Pain. 2007;129:235-55. Erratum in: Pain. 2007;131:350. Considering the potentially serious adverse effects of opioids, the idea that pain relief could diminish over time may have a significant impact on the decision to embark on this therapy, especially in vulnerable individuals.

[ii] 10. Butler SF, Budman SH, Fernandez K, Jamison RN: Validation of a screener and opioid assessment measure for patients with chronic pain. Pain 112:65-75, 2004

[iii] 12. Butler SF, Fernandez K,Benoit C,Budman SH, Jamison RN: Validation of the revised screener and opioid assessment for patients with pain (SOAPP-R). J Pain 9:360-372, 2008

[iv] 138. Webster LR, Webster RM: Predicting aberrant behaviors in opioid-treated patients: Preliminary validation of the Opioid Risk Tool. Pain Med 6:432-442, 2005

[v] 4. Belgrade MJ, Schamber CD, Lindgren BR: The DIRE score: Predicting outcomes of opioid prescribing for chronic pain. J Pain 7:671-681, 2006