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

FORUM POSTING APRIL 2014

PART C: FINDINGS

Contents

C. FINDINGS

Part C of the DWC Guidelines provides the findings from a review of opioid use guidelines available as of December 2013. Part D contains actual excerpts from the guidelines that were reviewed. Where guidelines did not address a particular issue or where consistent recommendations were lacking, a review of recent literature was conducted. The Part C is the basis of the recommendations in Part B of the DWC Guidelines.

1. OPIOIDS FOR ACUTE PAIN (UP TO FOUR WEEKS)

At the time the literature review was conducted for the development of the DWC Guideline, only the Utah and both Washington guidelines directly addressed the use of opioids for acute pain. (Utah 2009; WA AMDG 2010, WA 2013)

The Utah guideline states:

> *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.*
>
> *"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.* (Utah 2009)

The Washington 2010 guideline contains similar language on the use of alternatives as initial therapy:

> *Use opioid medications for acute or chronic pain only after determining that alternative therapies do not deliver adequate pain relief.* (WA AMDG 2010)

And the Washington 2013 guideline states:

> *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).* (WA 2013)

Both the Utah and the Washington 2013 guidelines recommend against use of long-acting opioids in acute pain:

> *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.* (Utah 2009; WA 2013)

And the Washington 2013 guideline states “DO NOT USE long acting or extended release opioids for acute pain or post-operative pain in an opioid naïve worker.” (WA 2013)

Recent high-quality evidence from a population-based prospective study reported that receipt of opioids for more than seven days, or two or more prescriptions, within the first six weeks following acute low back injury was associated with a doubling of risk for long term disability, even after adjustment for baseline reported pain and function, and for medical record documented injury severity. (Naliboff 2011)Additional lower quality observational studies have also documented the association between early opioid use and subsequent disability. (Tao 2012; Webster 2007)

The Washington 2013 guideline states, “evidence does not support the use of opioids as initial treatment for back sprain or other sprains, but if they are prescribed, use should be limited to short term (e.g., <14 days).” (WA 2013) Furthermore, it recommends a link between initial opioid use and expected degree of improvement:

> *Pain intensity and pain interference should decrease during the acute phase (0-6 weeks) 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 (of opioids) 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.* (WA 2013)

It should be noted that opioid use in the presence of a various comorbidities is associated with a considerably elevated risk of death and adverse effects (Cheng 2013; Dean 2004; Deyo 2011; Dunn 2010; Fareed 2009; Goodridge 2010; Grattan 2012; Hadidi 2009; Hall 2008; Mills 2005; MMWR 2005; Nyhlen 2011; Paulozzi 2009; Seal 2012; Shah 2008; Toblin 2010; Webster 2011; Wunsch 2009; Wysowski 2006)

2. OPIOIDS FOR SUBACUTE PAIN (1–3MONTHS)

The literature addressing the subacute period (4–12 weeks or one and three months) of pain is scarce and few guidelines deal with this period separately.

The Utah guidelines state:

> *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.* (Utah 2009)

The Washington 2013 guideline states:

> *With some exceptions, resumption of pre-injury activities such as return to work should be expected during this period.*

It also states:

> *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).* (WA 2013)

3. OPIOIDS FOR CHRONIC PAIN AND CHRONIC OPIOID TREATMENT

The guidelines reviewed are fairly consistent in their recommendations regarding the consideration of chronic opioid treatment. The following excerpts are illustrative.

The ACOEM guidelines state:

> *Routine use of opioids for treatment of chronic non-malignant pain conditions is not recommended, although selected patients may benefit from judicious use.*
>
> *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.* (ACOEM 2011)

The Canadian guidelines state:

> *Before initiating opioid therapy, ensure comprehensive documentation of the patient's pain condition, general medical condition and psychosocial history* (Canada 2010)

3.1. Comprehensive Evaluation and Assessment of Patient

All external guidelines reviewed (See Part D) recommend that prior to initiating opioids for chronic pain or initiating chronic opioid treatment, patients should have a comprehensive evaluation to:

1. Determine the diagnosis for the patient's pain complaint
2. Evaluate how the pain is affecting the patient's quality of life and function
3. Characterize other factors which could affect the choice of therapies
4. Assess prior approaches to pain management and their effectiveness
5. Establish a basis for developing a treatment plan to help reduce the patient's pain and return them to work
6. Initiate a trial of opioids for chronic pain (See Section 3.3.3, Initiation of Chronic Opioid Treatment)

This comprehensive evaluation and assessment will help the clinician in making a decision as to whether or not to initiate opioids for treatment of chronic pain or continue chronic opioid treatment. There is potential for serious harm with chronic use of opioids and a comprehensive evaluation will permit the clinician to best weigh the risks, benefits and alternatives of this treatment decision.

3.2. Consideration of Alternative Treatments for Chronic Pain and Chronic Opioid Treatment

Opioids are not considered the first line of therapy for most patients with chronic pain due to the adverse effects outlined previously in this Guideline and to limited data on their effectiveness in improving both pain and function. (ACOEM 2011; ODG 2013; US VA 2010; Utah 2009; WA AMDG 2010, WA 2013) The majority of guidelines reviewed instruct that chronic opioid treatment may be considered when other more effective and potentially safer therapies have proven inadequate.

3.3. INITIATING AND MONITORING CHRONIC OPIOID TREATMENT

3.3.1 Screening for Risk of Addiction to Opioids or Adverse Events Prior to Chronic Opioid Treatment

Every major guideline reviewed (See Part D) recommends using validated tools to assess the risk of addiction or adverse events in patients who are candidates for chronic opioid therapy. Most of these recommendations are based on expert consensus, since research on use of these tools is relatively sparse.

Systematic reviews and other studies indicate that these tools may accurately predict later misuse of opioids. (Chou 2009b; Nuckols 2012; Turk 2008;) A personal history of illicit drug and alcohol abuse is the strongest predictor of later opioid misuse or abuse. (Turk 2008) Most current guidelines recommend the following brief tools (many of which are publicly available):

- **Tools to screen for past and current substance abuse** (ACOEM 2011, Canada 2010, Chou 2009, Utah 2009, WA AMDG 2010):
    - Opioid Risk Tool (ORT) (See Appendix A1a)
    - Pain Medication Questionnaire (PMQ) (Adams 2004; Buelow 2009; Dowling 2007; Hojsted 2011; Holmes 2006; Jones 2012; Moore 2009; Morasco 2013; Park 2010)
    - Screener and Opioid Assessment for Patients with Pain-Revised SOAPP-R (Butler 2008)
- **Tools to screen for alcohol misuse/abuse in order to identify high-risk patients prior to chronic opioid treatment** (Canada 2010; WA AMDG 2010):
    - Cut down, Annoyed, Guilty, Eye-opener-Adapted to Include Drugs (CAGE-AID) (See Appendix A1b**)**
    - Two-item conjoint screen (TICS[1]) (See Appendix A1c) (Brown 2001)

- **Tools to screen for psychosocial factors in order to identify high-risk patients prior to chronic opioid treatment:**
    - Patient Health Questionnaire-9 (See Appendix A1d) (WA AMDG 2010)
- **Tools to screen for current misuse/abuse of opioids during opioid treatment:**
    - Current Opioid Misuse Measure (COMM) (Butler 2007)
    - Prescription Opioid Misuse Index (POMI) (Knisely 2008)

The following recommendations are found in several of the guidelines reviewed. The ACOEM 2011 guideline states:

> *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.* (ACOEM 2011)

According to the APS/AAPM guideline:

> *Before initiating [chronic opioid therapy], 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).* (APS/AAPM 2009)

Metabolism of opiates is largely genetically determined. (Yee 2013) Genotyping has been used to identify patients at high risk of adverse effects, for example, children at risk of respiratory arrest after using codeine post-tonsillectomy. (Carroll 2012; Racoosin 2013) There is currently inadequate evidence to recommend the routine use of such

genomic information in the current clinical environment to predict the likelihood of addiction or abuse. (Matthews 2012)

Taking a complete history is of utmost importance as this is the primary source for assessing patients for the presence of relevant psychosocial factors affecting prognosis (or risk/benefit ratio) during opioid treatment.

The following cognitive behavioral factors ('yellow flags') show a correlation to increased risk of chronic pain and delayed recovery (Chou 2010; Nicholas 2011; Turner 2008):

- Catastrophic thinking/somatization
- Fear avoidance ('guarding') behavior
- Sense of perceived injustice and anger over the inciting event
- History of childhood abuse/trauma
- History of depression and anxiety

The following cognitive behavioral factors are not 'generative' of chronic pain, but are barriers to successful management of the chronic pain condition are:

- Misplaced health locus of control
- Counterproductive work attitudes
- Limited family support and stress
- Lifestyle issues of obesity, tobacco use, alcohol and drug use

The presence of important co-morbid mental health conditions, such as depression, is a strong risk factor for misuse/abuse and overdose events among patients on chronic opioid treatment. (Grattan 2012; Johnson 2013; Martins 2012; Outcalt 2013; Wassan 2007)The ACOEM 2011 guideline also addresses this issue:

> *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.* (ACOEM 2011)

Use of the PHQ-9 is recommended for assessing the presence of depression prior to initiating chronic opioid treatment. (WA AMDG 2010) A diagnosis of depression can only be made by a qualified licensed medical professional; the use of screening tools is not a substitute to such an evaluation.

Intravenous, intramuscular, submucosal, and transdermal (except buprenorphine) administration of opioids for chronic pain are discouraged if the patient is able to tolerate oral medication.

3.3.2. Patient Treatment Agreement and Informed Consent

The evidence on effectiveness of a patient treatment agreement is weak. (Alford 2013; Starrels 2010) Despite the paucity of evidence of their effectiveness in reducing adverse effects, most guidelines reviewed recommend using such a treatment agreement if a decision to initiate chronic opioid treatment is made following the screening assessment. (ACOEM 2011; ODG 2013; US VA 2010; Utah 2009; WA AMDG 2010; WA 2013)

The use of a treatment agreement is recommended to document patient understanding of and agreement with what will be expected of them during opioid treatment. Although patients may not adhere to prescribed treatment (and may not do so even with an agreement), these agreements are tools to improve patient knowledge and compliance; they should be coupled with a urine drug screening program. (Starrels 2010) The agreement should clearly describe responsible use of opioids and how to interact with their physician and pharmacy in obtaining medication. If literacy or comprehension is a concern, the ACOEM 2011 guideline recommends that the physician should read the agreement to the patient and ascertain that they understand it or revise the agreement so they can read and understand its content. (ACOEM 2011) Regarding treatment agreements, the APS/AAPM guideline states the following:

> *Informed consent should be obtained prior to starting chronic opioid treatment. A continuing discussion with the patient should include goals, expectations, potential risks, and alternatives to chronic opioid treatment.* (APS/AAPM 2009)

The same guideline also states:

> *Clinicians should consider using a written management plan for chronic opioid treatment to document patient and clinician responsibilities and expectations and to assist in patient education (weak recommendation, low quality evidence).* (APS/AAPM 2009)

The ODG gives very detailed recommendations on this topic:

> *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 limited 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 they are aware of potential adverse effects of the use of opioids including addiction; (11) Information about opioid 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.* (ODG 2013)

3.3.3. Initiation of Chronic Opioid Treatment

Several guidelines (APS, ODG, and US VA) recommend a trial or initiation period prior to committing to long-term treatment with opioids. The initial use of opioids for the treatment of chronic noncancer pain should be considered as a trial, and not a commitment to long-term therapy. Further, it should be communicated to the patient that treatment with opioids will stop if the trial is considered unsuccessful. The patient

should be informed that success will be determined based on a balance between the benefits (e.g. improvements in function, pain, quality of life, return to work) and adverse effects. This communication should be documented as part of the written treatment plan. (See Section 3.3.2, Patient Treatment Agreement and Informed Consent)

There is inadequate evidence that intravenous, intramuscular, submucosal, and transdermal (except buprenorphine) administration of opioids for chronic pain is safe and effective. (Karlsson 2014; Naing 2013) Likewise, there is insufficient evidence to recommend intrathecal opioid delivery for the treatment of noncancer pain. (Hayek 2011)

3.3.4. Use of CURES to Ensure Safe and Effective Opioid Use

Prescription Drug Monitoring Programs such as the Controlled Substance Utilization Review and Evaluation System (CURES) in California are present in most states and collect data in near real time on all dispensed opioids and most other controlled substances. These programs allow a prescriber to check on all sources of dispensed controlled substances (if obtained legally), even if the prescription is self-paid. Most guidelines recommend consulting such programs as part of opioid treatment. (Juurlink 2013; Neven 2012)

The following guidelines offer specific language recommending use of state PDMPs.

The Canadian guideline states: “If available, physicians and pharmacists should access electronic prescription databases that provide information about patient prescription history.” (Canada 2010)

The Washington 2013 guideline states:

> *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.* (WA 2013)

The Utah guideline recommends that the PDMP be checked: 1) before initiating treatment; 2) at least quarterly during titration; 3) at least annually during maintenance; and 4) more often for high-risk patients). (Utah 2009)

3.3.5. Use of Tools to Monitor Patients on Chronic Opioid Treatment

The vast majority of guidelines recommend monitoring patients receiving chronic opioid treatment. The use of screening tools or instruments may be considered to periodically monitor risk during chronic opioid treatment to assess whether patients may be exhibiting aberrant behaviors associated with the misuse of opioid medications. (ODG 2013)

3.3.6. Use of Urine Drug Testing (UDT)

Urine drug testing (UDT) is used to determine whether 1) the patient is taking the medication(s) being prescribed, 2) the patient is taking medications not being prescribed by the primary prescriber, and 3) if the patient is taking illicit substances. A recent systematic review found relatively weak evidence that supports the effectiveness of urine drug testing and opioid treatment agreements in reducing opioid misuse. (Starrels 2010) However, nearly every guideline recommends some use of UDT. Several guidelines recommend UDT as part of the evaluation to determine whether chronic opioid treatment should be embarked upon following a trial of opioids. (ODG 2013; US VA 2010; WA AMDG 2010; WA 2013)

Guidelines recommend a UDT at the onset of treatment for a new patient who is already receiving a controlled substance or when chronic opioid management is considered. (ODG 2013) Many consider UDT a crucial compliance monitoring tool for managing opioid therapy. (ASIPP 2012) UDT is recommended periodically and randomly throughout chronic opioid treatment, with its frequency guided by level of risk of misuse. (ACOEM 2011; APS/AAPM 2009; ODG 2013; Utah 2009)

Urine drug testing can be divided into two categories: immunoassays, which may be performed either in a laboratory or in an office or point of care (POC) setting and laboratory-based gas chromatography/mass spectroscopy (GC/MS) or liquid

chromatography tandem mass spectroscopy (LC/MS/MS). If conducted and interpreted properly, POC screening may be an effective use of resources. (Manchikanti 2011a, 2011b) However, it cannot be used to detect alcohol and some prescribed opioids (e.g., Fentanyl, oxycodone). In addition, POC does not detect the presence of benzodiazepines with much accuracy (only about 70% of the time). (OR 2013) POC testing is also subject to false positive and negative results. (Passik 2013) Thus, POC urine drug testing should be considered an initial screen. Detailed algorithms for UDT and clinical vignettes are available to help guide use. (Heltsley 2010; Moeller 2008; WA AMDG 2010)

Current guidelines contain specific language regarding UDT when the decision is being made as to whether to embark on chronic opioid treatment. The ACOEM 2011 guideline states:

> *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.* (ACOEM 2011)

The Utah guideline states:

> *A positive drug screen indicates the need for caution, but does not preclude opioid use for treatment of pain. Consideration should be given to referral to substance abuse counseling and/or to a pain management specialist. If opioid medication is subsequently prescribed, the patient should be more carefully monitored and conditions under which opioids are being prescribed should be well documented in the treatment plan.* (Utah 2009)

ODG makes the following statement:

> *At the onset of treatment: 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.* (ODG 2013)

The Washington 2010 guideline includes this statement:

> *It is extremely important to keep in mind that immunoassays have both false positive and false negative results. Over-the-counter medication, for example, can cause a positive result.* (WA AMDG 2010)

The ACOEM 2011 guideline also states:

> *All patients on chronic opioid treatment should undergo UDT:*
>
> *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).*
>
> *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.* (ACOEM 2011)

The above two passages may be synthesized to a recommendation to perform UDT from two to four times a year, randomly, and also "for cause."

The APS /AAPM guideline observes:

> *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.* (APS/AAPM 2009)

The guidelines reviewed also recommend that the frequency of UDT should match the risk level:

ODG's guideline makes this recommendation:

> *Frequency of urine drug testing should be based on documented evidence of risk stratification including use of a testing instrument.* (ODG 2013)

The Utah guideline recommends:

> *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.* (Utah 2009)

The Washington 2010 guideline recommends the following frequency of monitoring during chronic opioid treatment (WA AMDG 2010):

Recommended Frequency of Monitoring

Risk of Misuse	**Frequency of UDT**
Low	Once a year
Moderate	Up to twice a year
High or opioid dose > 120 **mg/day morphine equivalent dose**	Up to four times a year

3.3.7. Monitoring Effectiveness of Chronic Opioid Treatment: Tracking Pain and Function and Determining Clinically Meaningful Improvement

3.3.7.1 Tracking Pain and Function to Monitor Effectiveness of Chronic Opioid Treatment

Every guideline reviewed recommends documentation of pain and function specifically as the principal method to determine effectiveness (See Part D).

Excerpts from selected guidelines are provided below.

The Canadian guideline states:

> *When conducting a trial of opioid therapy, start with a low dosage, increase dosage gradually and monitor opioid effectiveness until optimal dose is attained*

When monitoring a patient on long-term therapy, ask about and observe for opioid effectiveness, adverse effects or medical complications, and aberrant drug-related behaviours:

-Evaluate change in pain intensity

-Ask about progress in reaching agreed-on goals, an important indicator of function change. Self-report can be prompted by asking about work, household activity, mood, walking ability, sleep, and social activities." (Canada 2010)

The APS/AAPM guideline states:

Thus, the two most crucial periods during which effectiveness should be determined and documented would be with an initial trial of opioids, usually during the acute phase (1st 6 weeks) and subacute phase (6 weeks—3 months) following injury, and during chronic opioid analgesic therapy (> 3 months) if the documentation during the acute/subacute phase shows meaningful improvement in pain and function. (APS/AAPM 2009)

The recommendations for the frequency of monitoring pain and function vary among guidelines.

The VA/DoD guideline recommends the following:

Evaluate pain intensity at each visit. Intensity of pain should be measured in the following manner using a Numeric Rating Scale (NRS) (0 to 10)

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 phase and every six months after the patient is on stable opioids." (US VA 2010)

However, other guidelines recommend early and frequent assessment of injured workers, which is crucial to the delivery of best practices sufficient to prevent long term disability in this population, including the assessment of the need for an opioid trial, and

its effectiveness. (Cheadle 1994; Frank 1998)

The Washington 2013 guideline emphasizes the need for improvement in both pain and function as a marker of effectiveness during the earlier, pilot phase of an opioid trial. During chronic opioid therapy, this same guideline emphasizes the importance of seeing improved function over improved pain; this shift is not surprising, since this guideline's focus is on the injured worker, and the goal of the workers' compensation system is to return workers to productivity. (WA 2013)

Thus, the existing guidelines and evidence suggest that during chronic opioid analgesic therapy many patients may report modest improvements in pain, but no improvement in function.

3.3.7.2 Clinically Meaningful Improvement in Pain and Function

At the time the literature review was conducted for the development of the DWC Guideline, the Washington 2013 was the only guideline to specifically address the degree to which any improvement in pain and function related to opioid treatment would be considered "clinically meaningful." (WA 2013) Based on the published literature, improvement of pain and function on the order of 30% is considered clinically meaningful. (Dworkin 2008; Ostelo 2008) Before considering chronic opioid therapy, providers should be able to document improvements of this magnitude during both the acute (up to 4 weeks) and subacute (4—12 weeks) phases of opioid treatment.

3.3.8 Opioid Titration and Dosing

Most major guidelines recognize the potential importance of dosing and the occurrence of unintentional overdose. (APS/AAPM 2009; US VA 2010; Utah 2009) At the time the DWC Guideline was being developed, no clear evidence on the relationship between specific doses and overdose events was available. However, it is important to note that three high-quality population-based epidemiological studies of risk of mortality and/or overdose morbidity have been published (and are summarized below) since the literature reviews were conducted for most of the guidelines reviewed (Part D).

The first of these high-quality studies is a cohort study in a large patient population. (Dunn 2010)This study was the first to report a relationship between prescribed opioid dose and overdose events, with a 8.9-fold increased risk of overdose at doses exceeding 100 mg/day MED, a 3.7-fold increased risk at 50–100 mg/day MED, and a 1.4-fold risk for doses 20–50 mg/day MED, compared to doses below 20 mg/day MED in patients with chronic, noncancer pain. For each fatal overdose in the study, more than seven non-fatal overdoses were observed. The study also found that patients receiving sedative-hypnotics concurrently with opioids were at an increased risk. Furthermore, patients in the highest opioid dosing group were often current smokers, had a history of depression treatment, and had a history of substance abuse treatment. The authors state that they controlled for these morbidity risks in their analysis. These data emphasize the importance of appropriate risk screening, as mentioned in Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events Prior to Initiation of Chronic Opioid Treatment.

The second high-quality study that was published recently was a large case-control study of participants from the Veterans Health Administration. This study found that the relative risk of mortality was 1.9 for opioid doses 20-50mg/day MED, 4.6 between 50 and 100 mg/day MED, and over 7 at doses above 100 mg/day MED, compared to those receiving doses less than 20 mg/day MED. The study drew the following conclusions:

> The present study found large hazard ratios in the association of maximum daily dose with risk of death by opioid overdose. However, the estimated overall risk of opioid overdose among individuals treated with opioids (0.04%) and the approximated absolute risk increases for significant associations, which ranged between 0.072% and 0.45%, were small. Opioid overdose death represents a particularly important outcome, but a rare one, and the findings should be interpreted accordingly. (Bohnert 2011)

The third high-quality study of the effects of increasing opioid doses on risk of adverse impacts also demonstrated increased risk with increasing dose, although the risk it revealed was not as high as that shown by the first two studies summarized above. The

odds ratio (OR) for overdose related mortality for 20─49 mg/day MED was 1.3; OR for 50─99mg/day MED was 1.9; and OR for 100─199mg/day MED was 2.04, demonstrating an "attenuated but significant risk" for doses 50─199mg/day. (Gomes 2011)

The evidence in high quality epidemiological studies across three very different health care systems is fairly consistent and is summarized in Appendix E (Opioid Dose and Risk of Morbidity and Mortality). These three studies show that increases in dose clearly correlate with increases in risk of overdose. Of note, the available data shows that no completely safe opioid dose level exists. Additionally, while there is no established "threshold" dose above which opioids are found to be unsafe, and below which they are safe, a pattern of increasing risk of adverse events with increasing doses undeniably emerges from the three most recent studies. The following passage from the Utah guideline provides a good summary of the recent research findings:

> *Evidence and other guidelines are not in agreement regarding the risks and benefits of high daily doses of opioid measured in morphine equivalents. It is likely that the risk-benefit ratio is less favorable at higher doses. Clinical vigilance is needed at all dosage levels of opioids but is even more important at higher doses. Clinicians who are not experienced in prescribing high doses of opioids should consider either referring the patient or obtaining a consultation from a qualified provider for patients receiving high dosages. 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. The Utah guideline spoke to increased clinical vigilance at daily doses exceeding 120-200 mg of morphine equivalent per day.* (Utah 2009)

Both of the Washington guidelines and the Utah guideline recommend that caution be exercised with all dosing of opioids, with the practitioner and patient working together to weigh the relative benefits and risk of not only starting opioids, but of any dose escalation. (Utah 2009; WA AMDG 2010, WA 2013).

Although some guidelines recommend prescribing the opioid antagonist naloxone (trade names include Narcan) to patients on chronic opioids who are at risk for overdose, none of the ones reviewed for the DWC Guideline provided this recommendation

3.3.9. Maintenance of Chronic Opioid Treatment

VA/DoD guideline recommends that providers assess patients at least every one to six months based on the following:

> *Individualize and adjust visit frequencies based on patient characteristics, comorbidities, level of risk for potential drug misuse (i.e., diversion, addiction, abuse, and aberrant drug-related behavior), type of pain, and type and dose of opioids.*
>
> *No specific visit frequency applies to all patients. Select a frequency that allows close follow-up of the patient's adverse effects, pain status, and appropriate use of medication.* (US VA 2010)

3.3.10. Treating Break-Through Pain (BTP)

Breakthrough pain, a term derived from the cancer pain literature, is defined as a transient increase in pain to greater than moderate intensity, among patients who have relatively stable, controlled baseline pain. (Hojsted 06; Manchikanti 2011c) A recent systematic review concluded that overall, more than one in two patients with cancer experienced BTP, although there was variability between the reviewed studies. (Deandrea 2014) Some authors also describe the occurrence of BTP in noncancer chronic pain and recommend extended release opioids and morphine for its resolution. (Portenoy 1990, 1999, 2006, 2010a, 2010b)

Most of the guidelines reviewed did not provide specific guidance for treating BTP in injured workers, (ACOEM 2011; ASIPP 2012; Canada 2010; Utah 2009, WA AMDG 2010; WA 2013) while others contained inconsistent recommendations:

The APS/AAPM guideline states:

> *There is insufficient evidence to guide recommendations regarding optimal treatment strategies for breakthrough pain in patients with CNCP. Limited evidence from short-term trials suggest that short-acting or rapid onset, as-needed opioids may be effective in this setting, but more studies are needed to evaluate the long-term benefits and harms of this strategy, and to compare effects of different short-acting or rapid onset opioids.* (APS/AAPM 2009)

ODG states that short-acting opioids are often used to treat intermittent or breakthrough pain and also that NSAIDS may also be used for this purpose. (ODG 2013)

The VA/DoD guideline states:

> *There is insufficient evidence to guide recommendations regarding optimal treatment strategies for breakthrough pain in patients with [chronic non-cancer pain]. Most of the trials evaluating supplemental opioid doses for exacerbation of pain were conducted in patients who were treated for end-of life care.* (US VA 2010)

A systematic review was unable to identify significant evidence of breakthrough pain in chronic noncancer pain patients. (Manchikanti 2011c) The authors of this review recommended that appropriate management of increased pain in chronic noncancer pain patients should be managed by a comprehensive assessment, and that treatment be based on appropriate pain management principles, with modalities other than opioid medication.

4. INDICATIONS AND METHODS FOR TAPERING OPIOIDS

4.1 INDICATIONS FOR TAPERING OPIOIDS

The majority of guidelines (the APS/AAPM, Canadian, Utah, and both Washington

guidelines) address aspects of tapering opioids among patients who have been on opioids on a generally continuous basis for at least 90 days. (APS/AAPM 2009; Canada 2010; Utah 2009; WA AMDG 2010; WA 2013) For the most part, the vast majority of recommendations in these guidelines are consensus-based, since there is a lack of published data on the indications for tapering or on effectiveness of various tapering methods in the patient population receiving chronic opioid treatment.

The guidelines reviewed universally agree that tapering should be considered when opioids have been ineffective, when serious adverse events have occurred, or when aberrant or illegal behaviors have occurred.

Indications for tapering:

Most guidelines describe tapering a patient to either a lower dose of opioids or completely off under the following circumstances:

- Patient expresses a desire to discontinue therapy
- Resolution of pain
- No documented improvement in pain and function, unless there are extenuating circumstances, or patient claims a lack of effectiveness
- Patient is non-adherent to treatment plan and monitoring
- Patient has engaged in illegal or dangerous activity, including: diversion, prescription forgery, suicide attempt, involvement in a motor vehicle accident and/or arrest related to opioids, aggressive or threatening behavior in the clinic.
- Severe adverse effects or overdose events.

4.2. METHODS FOR TAPERING OPIOIDS

In the absence of strong evidence, the guidelines reviewed differ as to the most effective tapering methods.

The APS/AAPM guideline states:

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.

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. (APS/AAPM 2009)

According to the Canadian guideline:

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.

"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. AND 1) Tapers can usually be completed between 2–3 weeks and 3–4 months. (Canada 2010)

The tapering process specified in the Washington 2013 opioid guideline is as follows:

- *Step 1: Discontinuing Opioids in a Community Care Setting: A gradual taper of approximately 10% per week (see AMDG Guideline [WA 2010]) 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][1] 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 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. In these situations, formal inpatient detoxification and/or a 4-week SIMP treatment program may be required.*

Due to the lack of high quality evidence of safety and comparative efficacy, ultra rapid detoxification using IV or IM antagonist drugs, is not recommended.

- *If steps 1 and 2 fail, (and the patient meets DSM-V criteria for opioid use disorder)can authorize up to 6 months of addiction treatment through a licensed chemical dependency treatment center.* (WA 2013)

5. DOCUMENTATION OF MORPHINE EQUIVALENTS

The Washington 2010 guideline recommends documentation of dosage as MED/day at each visit so that the primary prescriber knows the exact dosing on a continuous basis. (WA AMDG 2010) This same guideline also recommends that the provider check the state PDMP to ascertain the patient's compliance with the prescribed dose.

[1] Reference in the cited passage to Nielsen, S., Hillhouse, M., Thomas, C., Hasson, A., and Ling, W., *A Comparison of Buprenorphine Taper Outcomes Between Prescription Opioid and Heroin Users.* J Addict Med, 2012.

6. Pain Medicine Consultation

There is consistency among the guidelines reviewed that prescribing providers may find it beneficial to obtain consultation with a pain medicine or other specialist either prior to escalating the dose or at any time the provider deems it necessary during chronic opioid treatment, even when all criteria have been met. (APS/AAPM 2009; Utah 2009; US VA 2010) The purpose of such consultation would be to assist with a range of complex issues (as determined by the requesting physician) related to the care of patients at all stages of pain.

7. Concurrent Use of Benzodiazepines and Other Sedative Hypnotics

Benzodiazepines and other sedatives can increase the risk of problematic side effects or adverse events when combined with opioids, particularly respiratory depression and/or aspiration. Both opioids and benzodiazepines have been implicated in the worsening of obstructive sleep apnea and thus are contraindicated with this condition due to suppression of the gag reflex and reduction of airway protection. Similarly, other illnesses that compromise respiratory function and oxygenation, such as COPD or pneumonia, may pose additional risks for patients taking opioids, especially if they are also taking sedative/hypnotic medications such as benzodiazepines.

It has been estimated that there are at least 100 million prescriptions for benzodiazepines filled in the U.S. annually, and prescriptions for these agents are also rising. Similarly, prescriptions for anxiolytics/sedatives/hypnotics rose from 2.8% to 4.7% of the population during the same sample periods. (NCHS 2013) With these increases, prescription drug overdose death rates have more than tripled since 1990. Increasingly, benzodiazepines have been implicated in fatal drug poisonings in the U.S., and are the most common concomitant medication found in fatal opioid overdoses, emphasizing their potential contribution to deaths from inadvertent overdose. (Warner 2009) Of the 14,800 deaths related to prescription analgesics in 2008, approximately

half involved more than one drug; the most common concomitant drugs included benzodiazepines, cocaine and heroin. (CDC Nov 2011) Benzodiazepines were mentioned in 17% of the deaths as the only additional medication detected and in an additional 3% of deaths involving a prescription analgesic with more than one other drug. (Warner 2009)

Though studies specific to injured workers are lacking, prescription oversight programs have implicated benzodiazepines as a source of increased morbidity and negative outcomes in opioid-maintained patients. Such negative outcomes have included increased risk of overdose and death. (Bramness 2007)

Polypharmacy is a particular challenge for the prescriber, who may not be aware of all other prescription or non-prescription agents a patient is utilizing. Even some over-the-counter products (e.g., kava) can exert effects on the benzodiazepine receptor complex and have additive or synergistic effects with other depressants. (Almeida 1996) Thus, such “natural” complementary medications may pose risks similar to benzodiazepines in patients also maintained on chronic opioids.

8. METHADONE

The main usage of methadone is to treat patients who are addicted to opioids and to manage chronic pain. (Eyler 2013) Because of its special pharmacokinetics, and prolonged half-life, use of methadone for treatment of chronic pain must be undertaken with particular care.

The Utah guidelines state the following:

> *Methadone-related death rates have been increasing in Utah and the U.S. In 2006, methadone was implicated in 30% of non-illicit drug-related deaths in Utah. Methadone was the most common drug identified by the Utah Medical Examiner as causing or contributing to accidental deaths, accounting for a disproportionate number of deaths compared to its frequency of use. Methadone was the single*

drug most often associated with overdose death and had the highest prescription adjusted mortality rate (PAMR) with an average of 150 deaths for every 100,000 prescriptions during 1998–2004. From 1997–2004, population-adjusted methadone prescriptions increased 727%. The increase in the methadone prescription rate was for treatment of pain and not addiction therapy. (Utah 2009)

The FDA has issued a public health advisory to alert patients and their caregivers and health care professionals to the following important safety information on methadone:

- ***Prescribing methadone is complex.*** *Methadone should only be prescribed for patients with moderate to severe pain when their pain is not improved with other non-narcotic pain relievers. Pain relief from a dose of methadone lasts about 4 to 8 hours. However methadone stays in the body much longer—from 8 to 59 hours after it is taken. As a result, patients may feel the need for more pain relief before methadone is gone from the body. Methadone may build up in the body to a toxic level if it is taken too often, if the amount taken is too high, or if it is taken with certain other medicines or supplements.*

- ***Patients should take methadone exactly as prescribed.*** *Taking more methadone than prescribed can cause breathing to slow or stop and can cause death. A patient who does not experience good pain relief with the prescribed dose of methadone, should talk to his or her doctor.*

- ***Patients taking methadone should not start or stop taking other medicines or dietary supplements without talking to their health care provider.*** *Taking other medicines or dietary supplements may cause less pain relief. They may also cause a toxic buildup of methadone in the body leading to dangerous changes in breathing or heart beat that may cause death.*

- ***Health care professionals and patients should be aware of the signs of methadone overdose.*** *Signs of methadone overdose include trouble breathing or shallow breathing; extreme tiredness or sleepiness; blurred vision; inability to*

think, talk or walk normally; and feeling faint, dizzy or confused. If these signs occur, patients should get medical attention right away. (US FDA 2006)

According to the Washington 2013 guideline:

- *Respiratory depression is the chief hazard associated with methadone administration. Methadone's peak respiratory depressant effects typically occur later, and persist longer than its peak analgesic effects, particularly in the early dosing period. These characteristics can contribute to cases of iatrogenic overdose, particularly during treatment initiation and dose titration.*
- *In addition, cases of QT interval prolongation and serious arrhythmia (torsades de pointes) have been observed during treatment with methadone. Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction.*
- *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.* (WA 2013)

9. MANAGING PERIOPERATIVE PAIN IN WORKERS ON CHRONIC OPIOID TREATMENT UNDERGOING ELECTIVE SURGERY

Although it is generally recognized that patients on chronic opioid treatment present a special problem, there is a paucity of data on best management practices for use of peri-operative opioids in these patients in whom elective surgery is planned.

Chronic opioid treatment prior to surgery is a risk factor for prolongation of opioid use post-operatively. (Rapp 1995) In general, patients on chronic opioid treatment will report higher pain scores and manifest more anxiety than other patients. (Carroll 2012; Rapp 1995; Theunissen 2012) They will also likely require higher opioid doses in the intra and post-operative period. Patients receiving chronic opioid treatment undergoing

surgery also have more frequent and more deadly respiratory depressive episodes than opioid-naïve patients. (Rapp 1995)

Managing pain in workers on chronic opioid treatment who are undergoing elective surgeries presents unique challenges and requires a coordinated treatment plan for pain management prior to surgery. This requires a collaborative effort involving the surgeon, anesthesiologist, pain management specialist, attending provider and the worker.

Evidence is lacking regarding the advisability of tapering opioids in patients receiving chronic opioid treatment before elective surgery.

The Washington 2013 guideline recommends the following:

> *A pre-operative evaluation, preferably by an anesthesiologist, one to two weeks prior to surgery. This should consider the worker's current opioid dose (both prescribed and actually taken) and a thorough medical history that includes information about mental health and substance use disorder. Accurate dosage information is especially important for planning peri-operative pain management. The evaluator should also check the opioid prescribing history in CURES. The recommendations below will help manage the workers' pain and minimize their risk associated with surgery.* (WA 2013)

10. Opioid Use in Catastrophic Injuries

Catastrophic injuries such as severe burns, crush or spinal cord injury in which significant recovery of physical function is not expected are exempt from many of the recommendations in this guideline. For example, clinically meaningful functional improvement may not occur following catastrophic injury.

11. RESPONSIBLE STORAGE AND DISPOSAL OF OPIOID MEDICATIONS

Although there are no uniform guidelines regarding the exact method by which opioids should be disposed, there is agreement that unused medications should be rendered unusable. (ACPM 2011)

ACRONYMS

BTP	break-through pain
CAGE-AID	Cut down, Annoyed, Guilty, Eye-opener-Adapted to Include Drugs
CLIA	Clinical Laboratory Improvement Amendments
CNS	central nervous system
COMM	Current Opioid Misuse Measure
COPD	chronic obstructive pulmonary disease
CURES	Controlled Substance Utilization Review and Evaluation System
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
DWC	Division of Workers' Compensation
ECG	electro-cardiogram
GC/MS	gas chromatography mass spectrometry
GCPS	Graded Chronic Pain Scale
LC/MS	liquid chromatography mass spectrometry
MED	morphine equivalent dose
MTUS	Medical Treatment Utilization Schedule
NSAID	nonsteroidal anti-inflammatory drug
ORT	Opioid Risk Tool
PCA	patient-controlled analgesia
PDMP	Prescription Drug Monitoring Program

PEG	Average pain intensity (P), interference with enjoyment of life (E), and interference with general activity (G).
PHQ-9	Patient Health Questionnaire, ninth edition
PMQ	Patient Medication Questionnaire
POC	point of collection
POMI	Prescription Opioid Misuse Index
PTSD	post-traumatic stress disorder
RCT	randomized controlled trial
SIMP	structured intensive multidisciplinary program
SOAPP-R	Screener and Opioid Assessment for Patients with Pain-Revised
TICS	Two-item Conjoint Screen
UDT	urine drug test
WHYMPI	West Haven-Yale Multidimensional Pain Inventory

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