STATE OF CALIFORNIA

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

FORUM POSTING APRIL 2014

PART A: EXECUTIVE SUMMARY AND INTRODUCTION

Table of Contents

A1. Executive Summary and Abbreviated Treatment Protocols 1

A1.1 Executive Summary of Proposed "Division of Workers' Compensation Guideline for the Use of Opioids to Treat Work-Related Injuries" for Inclusion in the Medical Treatment Utilization Schedule .. 1

A1.2 Abbreviated Treatment Protocols 6

A2. Background 10

A2.1 Burden of Pain 10

A2.2 Workers' Compensation Context 11

A2.3 Evidence of Effectiveness of Opioid Use in the Acute Period 12

A2.4 Evidence of Effectiveness of Long-Term Opioid Use 12

A2.5 Opioid Safety: Overdose, Serious Adverse Events, and Substance Misuse/Abuse 14

A3. Scope and Target Audience for Opioid Guideline 18

A4. Core Concepts 19

A4.1 Goals and Objectives 21

A5. Evidence-Based Methods 21

A5.1 Guidelines Evaluated 22

References 24

A1. Executive Summary and Abbreviated Treatment Protocols

A1.1 Executive Summary of Proposed "Division of Workers' Compensation Guideline for the Use of Opioids to Treat Work-Related Injuries" for Inclusion in the Medical Treatment Utilization Schedule

Opioid misuse remains a national concern due to adverse health impacts and other unintended consequences. Yet, opioids may be useful as an adjunct in the treatment of pain. The Division of Workers' Compensation Guideline for the Use of Opioids to Treat Work-Related Injuries (Guideline) provides a balance between appropriate treatment of pain among injured workers and safety in the use of opioids for that purpose.

A key difference between occupational and non-occupational guidelines is that a main goal of the former is the restoration of function to ensure early return to work. This Guideline is based on the best available medical evidence and has three main goals: to (1) provide a set of best practices and universal precautions for safe and effective prescribing of opioids for acute (lasting up to four weeks), subacute (lasting four to 12 weeks), and chronic (lasting three or more months) pain due to a work-related injury; (2) prevent and reduce opioid-related long-term disability, morbidity, mortality, and substance misuse and abuse; and (3) recommend opioid prescribing practices that promote functional restoration. The intended audience is primary care and specialty clinicians, providers of utilization review and independent medical review, and insurers. This Guideline does not address pediatric pain, labor pain, pain immediately following catastrophic injuries, or cancer/end of life pain.

The Guideline is divided into four parts: Part A consists of a summary, abbreviated treatment protocols, and an introduction; Part B contains complete recommendations for patient management and appendices with helpful tools for clinicians; Part C presents findings to support the recommendations; and Part D compiles recommendations from a review of existing opioid use guidelines.

The following are key recommended practices:

- Opioid medications are not the first line of treatment for pain and should not in general be used for mild injuries. Other therapies, such as non-opioid medication, appropriate physical activity, and complimentary/alternative modalities should be used first.
- 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 other therapies will not provide adequate pain relief or are contraindicated for medical reasons. They should only be prescribed at the lowest dose that provides pain relief, for a limited time, and with no refill, prior to re-assessment.
    - Opioids for acute pain treatment should be tapered to zero within two weeks whenever possible.
- If opioids are prescribed, the Controlled Substance Utilization Review and Evaluation System (CURES), California's Prescription Drug Monitoring Program should be accessed. If CURES indicates the simultaneous use of other narcotic medication, opioid use may be contraindicated.
- Central nervous system depressants, including anti-histamines, benzodiazepines, and alcohol, should not be used simultaneously with opioids and should be discontinued before prescribing opioid medication.
- Patients should be cautioned about the potential adverse effects of opioids, including impacts on alertness. Driving and operation of heavy equipment should be discouraged while on these medications.

- At the time of initial prescription, and at every visit, patients should be advised regarding responsible storage and disposal of opioid medications.
- In order for opioids to be prescribed beyond the acute phase, there should be no contraindicated comorbidities, non-opioid treatments should be continued, urine drug testing should be performed and reveal no aberrant results, and patients should be carefully monitored, both for improvement in pain and function, as well as indications for discontinuing opioids.
- Short-acting opioids may be indicated for a limited duration to manage moderate to severe post-operative pain and to obtain sleep, especially in the immediate post-operative period.
- Patients with chronic pain may be candidates for treatment with opioids if pain management and functional improvement have not been achieved with other treatment modalities and the following conditions are met:
    - A comprehensive evaluation is performed.
    - Alternative treatments are considered.
    - Screening identifies patients with high risk of addiction or serious adverse events, substance misuse, and psychosocial factors that may contribute to misuse. Such patients are not good candidates for chronic opioid treatment.
    - Patients are informed about risks, benefits, and alternatives for opioids and a treatment agreement/informed consent is completed.
    - Patients undergo urine drug testing prior to initiating an opioid trial.
    - A trial is conducted prior to committing to chronic opioid treatment.
    - CURES is queried and the results documented; aberrant results are a contraindication to chronic opioid treatment.

- Patients on chronic opioid treatment should be carefully managed, after the following have been documented:
    - Results of questionnaire tools assessing for aberrant behavior, which may indicate the need for discontinuing opioids
    - Results of periodic urine drug testing (at point of care initially and verified by a federally certified laboratory) performed on a random basis during chronic treatment, and if the provider is concerned about misuse, abuse, or diversion
    - Clinically meaningful reduction in pain and functional improvement.
- When titrating the dose of opioids used for treatment of chronic pain to achieve maximal improvement in pain and function, decisions to increase opioids should be made jointly by both the provider and the patient. It is the responsibility of the provider to inform the patient that current evidence shows a dose-related increase in adverse events.
- Although all doses of opioids carry risks, providers should be increasingly vigilant for doses above 80 mg/day morphine equivalent dose (MED), as the known risk of adverse events rises while the evidence for increased benefit remains weak.
- Clinicians should conduct semiannual attempts to wean workers whose dose is above 80 mg/day MED, and who have been on that dose or higher for at least six months, to lower than 80 mg/day MED.
- Clinicians may consult with or refer to a pain specialist based on clinical need:
    - To assess the risk-benefit ratio of using opioids to treat pain in complex patients or those at high risk of adverse effects
    - At the time of a trial of chronic opioid treatment
    - To assist with management of a patient with significant co-morbidities

  - When significant tolerance to opioids is suspected
  - To assist with the management of aberrant behavior or patients who have opioid use disorder
  - To assist with tapering or weaning regimens
  - To assist with management of complex issues not listed above.

- Methadone may be indicated for specific types of patients and should be initiated, titrated, and monitored cautiously by providers who have substantial experience with its use and risks.

A1.2 Abbreviated Treatment Protocols

- **Opioids for Acute Pain (pain lasting up to 4 weeks from onset)**
- **Opioids for Subacute Pain (1–3 Months)**
- **Opioids for Chronic Pain and Chronic Opioid Treatment (3 Months or More)**

Opioids for Acute Pain (Up to 4 Weeks From Onset)

In general, opioids are not indicated for mild injuries, such as

- Acute strains, sprains, tendonitis, myofascial pain, repetitive strain injuries

Opioids may be indicated for moderate to severe injuries and post-operative pain.

First use non-opioid treatments

- Pain medications (e.g., acetaminophen, NSAIDS) unless contraindicated, physical activity including rest, range of motion, exercise, physical therapy, and treatments such as acupuncture

Consider and document relative contraindications

- Depression, anxiety, personality disorder, untreated sleep disorders, past substance abuse, drug seeking behavior, other psychotropic medications, PTSD, and cognitive impairment
- COPD, severe obesity, balance problems/fall risk, osteoporosis, and renal failure

<u>If considering opioids</u>:

- Document nature and extent of injury
- Consult CURES (Controlled Substances Utilization Review and Evaluation System)

Prescribe limited supply of opioids without refills

- Start with weaker opioids at the lowest dose producing analgesia and improving function
- Best prescribed at night or when patient is not at work
- Advise not to take sedative-hypnotic medications (e.g., benzodiazepines) or drink alcohol
- Advise about the potential adverse effects of opioid medications

Track and document levels of pain and function at every visit

Monitor for indications for discontinuing opioids (any one of the following)

- No pain reduction or functional improvement
- Intolerance or severe adverse effects
- Non-compliance

Complete opioid treatment course within 2 weeks whenever possible

- Use tapering rather abrupt cessation if patient has received opioid treatment for more than two weeks

For detailed recommendations, see Part B of the
Division of Workers' Compensation Guideline for the Use of Opioids to Treat Work-Related Injuries

Opioids for Subacute Pain (1–3 Months)

With rare exceptions, resolution of pain and resumption of regular function is anticipated 4 weeks after the initial injury, regardless of whether opioids have been used throughout this time period.

Prior to continuing opioid use beyond 4 weeks, providers should:

Consider and document relative contraindications

- Depression, anxiety, personality disorder, untreated sleep disorders, past substance abuse, drug seeking behavior, other psychotropic medications, PTSD, and cognitive impairment
- COPD, severe obesity, balance problems/fall risk, osteoporosis, and renal failure

Use non-opioid treatments

- Pain medications (e.g., acetaminophen, NSAIDS) unless contraindicated, cognitive-behavioral therapy, activity coaching, graded exercise, and treatments such as acupuncture

If considering opioids beyond 4 weeks:

- Consult CURES (Controlled Substances Utilization Review and Evaluation System)
- Perform urine drug testing (UDT)
- Prescribe lowest dose producing analgesia and improving function

Advise patients on opioids

- Not to take sedative-hypnotic medications (e.g., benzodiazepines) or drink alcohol
- About the potential adverse effects of opioid medications
- Regarding responsible storage and disposal of opioid medications

Track and document levels of pain and function at every visit

Monitor for indications for discontinuing opioids (any one of the following)

- No pain reduction or functional improvement
- Intolerance or severe adverse effects
- Non-compliance revealed by UDT or otherwise evident

When discontinuing opioids, use tapering rather abrupt cessation

For detailed recommendations, see Part B of the
Division of Workers' Compensation Guideline for the Use of Opioids to Treat Work-Related Injuries

Opioids for Chronic Pain and Chronic Opioid Treatment (3 Months or More)

Patients with chronic pain (lasting more than 3 months) may be candidates for treatment with opioids if pain management and functional improvement have not been achieved with other treatments.

Prior to initiating chronic opioid treatment, document the following in the medical record:

Perform a comprehensive evaluation and assessment, including UDT

Prescribe alternative treatments

- Non-opioid pain medications unless contraindicated, cognitive-behavioral therapy, activity coaching, graded exercise, and treatments such as acupuncture

Screen for risk of addiction, adverse events using validated tools

- Drug misuse/abuse (e.g., SOAPP-R, ORT)
- Alcohol misuse/abuse (e.g., CAGE-AID, TICS)
- Additional psychosocial factors contributing to substance misuse/abuse (e.g., PHQ-9)

Perform urine drug testing (UDT)

Complete patient treatment agreement/informed consent
Initiate a trial period of opioid treatment to assess efficacy and side effects (typically 90 d**ays or less)**
Check the Controlled Substance Utilization Review and Evaluation System (CURES)

Once chronic opioid treatment is underway:

Titrate to an effective stable dose

- Use weaker opioids and the lowest effective dose
- Increase vigilance and frequency of monitoring for adverse effects if dose is above 80 mg/day MED

Perform UDT

- Randomly at least 2 times a year for all patients
- 4 times a year for patients on doses greater than 80 mg/day MED for more than 6 months

Track and document levels of pain and function at every visit

Monitor patients on chronic opioid treatment

- With use of questionnaires and other validated screening tools (e.g., COMM, POMI)
- By using valid methods to track pain and function, and determining clinically meaningful improvement
- With regular face-to-face visits during the maintenance period

Indications to discontinue opioid treatment or reduce dose

- Patient desire to discontinue
- Resolution of pain
- Severe adverse effects or overdose events
- Lack of documented improvement in pain and function
- Non-adherence to treatment plan
- Consumption of medication or substances advised not to take
- Dose above 80 mg/day MED (semiannual attempts to reduce dose)

For detailed recommendations, see Part B of the
Division of Workers' Compensation Guideline for the Use of Opioids to Treat Work-Related Injuries

A2. Background

The rapid rise in the use of prescription opioids has been associated with a parallel increase in the number of cases of opioid misuse/abuse and opioid-associated deaths. Coinciding with the rise in opioid use has been an increased awareness of chronic pain as a societal problem. The Division of Workers' Compensation (DWC) Guideline for the Use of Opioids to Treat Work-Related Injuries is an evidence-based guide for using opioids to treat adults with work-related acute, subacute, perioperative, and chronic noncancer pain. A key goal of the DWC Guideline is to provide a balance between appropriate treatment of pain and safety in the use of opioids for those purposes.

Opioid analgesics are widely used to treat severe acute and perioperative pain as well as pain due to cancer and at end of life. However, the use of chronic opioid therapy for noncancer chronic pain remains controversial. (Cheadle 1994; IOM 2011; Noble 2010) While a small number of workers experience "delayed recovery" (persistent debilitation/disability, drug dependence, depression, deconditioning), they account for the majority of total disability burden and costs. Some injured workers may require opioids for the management of their acute or chronic pain. It is not the intention of the DWC Guideline to restrict proper medical use of opioids. However safe and responsible prescribing is necessary to avoid unintended consequences, including prolonged disability and iatrogenic morbidity and mortality.

A2.1 Burden of Pain

Pain that persists for weeks to years is a public health problem that affects more than 100 million adults in the US and reduces their quality of life. (IOM 2011) The resulting costs to society are at least $560–$635 billion per year in direct medical expenses and lost work productivity.

A2.2 Workers' Compensation Context

Reducing preventable disability is of the highest priority for society in general, as well as medical practitioners, employers, and workers' compensation professionals. While the vast majority of injured workers heal quickly and return to work, a relatively non-catastrophic injury may lead to the loss of a productive life. (Cheadle 1994; Frank 1998; IOM 2011) While a small number of workers develop "delayed recovery" (persistent debilitation/disability, drug dependence, depression, deconditioning), they account for the majority of total disability burden and costs.

Failure to return to work early following an injury is a predictor for long-term and entrenched disability. (Cheadle 1994) Using best practices to heal injury and illness, improve function, and encourage return to work immediately following injury is the most effective way to prevent and reduce prolonged disability. (Wickizer 2011; Bernacki 2003) Preventing the transition from acute and subacute pain to chronic pain in a workers' compensation context should be considered parallel to the goal of preventing long-term disability.

For purposes of the DWC Guideline, acute pain is of sudden onset and is expected to last up to four (4) weeks; in the occupational context, acute pain is linked clearly to a specific event, injury, or illness. Subacute pain is pain that lasts between four (4) and 12 weeks (or one and three months). Chronic pain is defined as pain that lasts more than three (3) months. (IOM 2011) Thus, the actions taken immediately following injury and in the ensuing two to three months are crucial in limiting both preventable disability and chronic pain.

This Guideline has therefore focused on use of opioids in the acute, subacute, and chronic periods as critical decision points. It is important to carefully consider whether and how opioids may be used in the acute and subacute periods, since available evidence does not always warrant their use. If the evidence-based decision is to

prescribe opioids, the following steps must be followed as they are crucial to worker outcomes:

1. Weigh the risks and benefits of treatment at all times
2. Follow documentation, treatment, monitoring, and dosage recommendations described in the DWC Guideline for all pain phases.
3. Using extreme caution, make a transparent and planned decision with the patient's consent whether to proceed from treating acute pain with opioids to treatment of subacute and especially chronic pain with opioids.

A2.3 Evidence of Effectiveness of Opioid Use in the Acute Period

While there are no high-quality trials to suggest that opioids are superior to other active treatments for the treatment of mild to moderate acute pain, there is evidence that short course treatment may be effective in alleviating severe acute pain. (Franceschi 2008; Gaskell 2009; Kelley 2012; Moore 2011; Toms 2009) However, non-opioid medications such as non-steroidal anti-inflammatory medications are at least equivalent if not superior for mild to moderate pain and may have fewer unwanted side effects than opioids. (Brown 1986; Clark 2007; Ekman 2006; Innes 1998; Li 2008; Lovell 2004; Veenema 2000) However, non-opioid medications also may cause adverse health effects and may not be tolerated by some patients. (Blondell 2013)

A2.4 Evidence of Effectiveness of Long-Term Opioid Use

Despite the lack of consistent, strong evidence for efficacy, the use of opioids for chronic noncancer pain has greatly increased over the past decade. At the time the DWC Guideline was written, the question as to the long-term effectiveness and safety of opioids for the treatment of chronic noncancer pain remained unanswered. The evidence as summarized by systematic reviews as well as noted by more contemporary

randomized controlled trials (RCTs) is complicated by varying conclusions. These disparate conclusions are sometimes based on the integration of new findings and at other times, on different interpretations of the same data.

Some systematic reviews report that oral opioids are significantly more effective than placebo in treating chronic pain, with declines in pain of 30–50% and significant improvements in measures of functional status. (Furlan 2006; Noble 2010; Kalso 2004; Papaleontiou 2010) A recent systematic review of randomized controlled trials of chronic opioid treatment found modest effects for improved pain, and small, inconsistent effects for improved function. (Furlan 2011) Additionally, a systematic review of pharmacological treatments for chronic low back pain found that "opioids are more effective than placebo with respect to pain and disability, with a much greater effect size for pain than disability."(White 2011) Most randomized trials are not longer than four weeks, with the longest trials less than three months in duration.

Evidence of effectiveness for a longer time period has only been assessed in observational studies. A systematic review of longer duration observational studies of chronic opioid treatment came to the following conclusion:

> […] *proper management of a type of strong painkiller (opioids) in well-selected patients with no history of substance addiction or abuse can lead to long-term pain relief for some patients with a very small (though not zero) risk of developing addiction, abuse, or other serious side effects. However, the evidence supporting these conclusions is weak, and longer-term studies are needed to identify the patients who are most likely to benefit from treatment*. (Noble 2010)

Furthermore, a recent report offered the following opinion:

> *Opioids can be an appropriate means of treating patients with chronic pain, particularly those with moderate to severe pain. Four of the systematic reviews we identified found that oral opioids are significantly more effective than placebo in*

> *treating chronic pain, with declines in pain in the range of 30–50%. Use of opioids for chronic pain has also been associated with significant improvements in measures of functional status (such as on SF-36). According to two of these studies, opioids are also more effective at improving pain and functional status than NSAIDs. Nevertheless, the increasing use of opioids has been accompanied by real risks of substance misuse, addiction, diversion, overdose, and death. The Institute of Medicine Report, Relieving Pain in America, summarizes the ongoing challenges involved in balancing effective treatment of pain against the known risks associated with opioid therapy and provides specific recommendations for national and other policy audiences.* (Nuckols 2012)

The overall finding of greater effects of chronic opioid treatment on pain, rather than function or disability, is also true of many other treatments for chronic pain, in that reduction in pain is not always associated with improvement in function and reduced disability. (Chou 2010) This highlights the importance of combining pain treatments with efforts aimed at improving function. The DWC Guideline emphasizes the need to balance the use of opioids to treat pain with measures of effectiveness, by monitoring pain, function, and progress towards reduced disability.

Effective treatment of pain involves using multiple modalities and a multidisciplinary approach. For guidance on the effectiveness of treatment for chronic pain with non-opioid therapies, see the DWC Chronic Pain Medical Treatment Guideline. (DWC 2009)

A2.5 Opioid Safety: Overdose, Serious Adverse Events, and Substance Misuse/Abuse

Overdose: Opiate overdose, whether intentional or unintentional, is a risk of opioid prescribing, and is mainly manifested by depressed mental status, decreased respiratory rate and tidal volume, decreased bowel sounds, and pupillary constriction. Hypotension may also accompany opioid intoxication. Patients may exhibit ataxia and

audible snoring prior to more severe consequences, including collapse and death. If untreated, opioid overdose can lead to hypothermia, coma, seizure, head trauma, aspiration pneumonia, and rhabdomyolysis. Suppression of respiratory drive is one of the most serious complications, as it is most likely to lead to death.

At pharmacological doses, opioids decrease the ventilatory response to carbon dioxide (CO_2). In combination with other central nervous system depressants, opioids can induce acute respiratory failure as defined by a decrease in the partial pressure of oxygen in arterial blood (P_aO_2). However, different opioids vary in their tendency to induce respiratory failure. For instance, methadone causes a dose-dependent decrease in P_aO_2 before hypercapnia is evident. It is believed that the different effects of various opioids is dependent on their relative affinity for discrete opioid receptors in the central nervous system (CNS) as well as pharmacokinetic interactions between the opioid and other co-administered drugs.

In addition to suppressing central respiratory drive and response to CO_2, morphine and related drugs slow respiration by prolonging inspiration and by postponing the spontaneous termination of inspiration ("inspiratory off-switching"). Morphine suppression of phrenic nerve activity can be reversed by cholinergic agents such as physostigmine. It can be proposed that addition of anticholinergic agents in an opioid regimen may lower the toxic threshold of morphine on such mechanisms and potentially increase morbidity and mortality associated with opioid overdose. (Niwa 2011)

The pharmacokinetics of opioid clearance can vary between patients, and can also be influenced by agents that affect opioid metabolism, such as concomitant medications, herbals and dietary supplements. Genetics, age, gender and other dietary influences can also modify opioid clearance through hepatic metabolism. In overdose, the observed half-life of opioids may increase due to changes in absorption and gastric transit. (Boyer 2012)

Serious Adverse Events: According to the US Centers for Disease Control and Prevention (CDC), deaths associated with prescription opioids rose from 4,000 in 1999 to over 14,000 in 2008. (CDC 2011) Moreover, these deaths peaked in the age group of 25–55 years, conferring on this cause of unintentional poisoning death a large burden of premature loss of productive life. (Warner 2011) Additionally, an increasing number of emergency department visits and hospitalizations have been associated with prescription opioids. (Fulton 2013)

In addition to prescribed opioids, in the majority of opioid-associated deaths cases a postmortem exam reveals other drugs, including multiple opioids, antidepressants, and either sedative/hypnotics or benzodiazepines. A published review of national data reports that in about half of deaths involving opioid analgesics, more than one type of drug contributed to the death. Benzodiazepines were most frequently associated with opioid analgesics deaths; other drugs included cocaine and heroin. (CDC 2009) This finding emphasizes the need to exercise caution in prescribing benzodiazepines and other sedative hypnotics with opioids. (See Section 7, Concurrent Use of Benzodiazepines and Other Sedative Hypnotics)

The most commonly reported adverse effects of opioid use are constipation, nausea, dyspepsia, headache, fatigue, lethargy, and urinary retention. (Noble 2010) Other major adverse effects of opioids include myocardial infarction, allergic reactions, impairment of executive function, sleep apnea, and death. The safety profile of chronic opioid treatment also includes less common adverse effects such as endocrine disorders, neonatal abstinence syndrome, falls and fractures in the elderly, and a potential increased risk of road trauma. (Elliott 2012) The true incidence of these adverse effects is unknown.

Substance Misuse and Abuse: There has been a significant increase in the use of opioids that were not prescribed for a medical reason, with one study estimating that

one in 25 opioid prescriptions is used for such non-medical purposes. (Katz 2010) Based on the 2010 National Survey on Drug Use and Health, more than 35 million Americans age 12 and older used an opioid analgesic for non-medical purposes at some time in their life—an increase from about 30 million in 2002. (US DHS2011) Use of prescription opioids for non-medical purposes now surpasses that of other illicit substances—marijuana, cocaine, methamphetamine, and heroin. (US DHS 2006)

Despite the large numbers of patients misusing and abusing prescription opioids, the overall incidence and prevalence of substance abuse and misuse of opioids in patients treated for chronic pain remains unclear, with systematic reviews and retrospective studies reporting varying results. For instance, a recent systematic review found that the median incidence of opioid dependence syndrome was 0.5% (range 0–24%) and median prevalence was 4.5% (range 0–31%). (Minozzi 2013) The study concluded that the "available evidence suggests that opioid analgesics for chronic pain conditions are not associated with a major risk for developing dependence." However, another review was critical of the methodology of most of the studies attempting to assess substance misuse and abuse rates. (Juurlink 2012) This same review suggests that earlier studies that demonstrated very low rates of substance abuse were particularly flawed. The authors identified a more contemporary study that found that 35% of longer term opioid users met the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria for a current or previous opioid use disorder. (Boscarino 2011) It is clear that higher-quality studies are needed to more accurately characterize the incidence and prevalence of prescription opioid misuse and abuse.

While the overall incidence and prevalence of opioid misuse is not well understood, certain identified factors do predispose patients to persistent opioid use and higher rates of substance misuse and abuse. One of these factors is psychosocial distress (e.g. depression, anxiety, and post-traumatic stress disorder (PTSD)), and this finding reinforces the importance of assessing these co-morbidities in patients with chronic pain

being considered for chronic opioid therapy (See Section 3.3.1, Screening for Risk of Addiction to Opioids or Adverse Events Prior to Initiation of Chronic Opioid Treatment). (Grattan 2012; Martins 2012; Outcalt 2013)

Coinciding with the increases in opioid-associated deaths and opioid misuse and abuse has been a substantial escalation in opioid prescribing and dosage between 2000 and 2010. (Kenan 2012) Opioids are currently the second most widely prescribed class of medications (statins for lowering cholesterol are the first). Indeed, the combination agents containing hydrocodone/acetaminophen (sold under brand names including Vicodin and Norco) are the most prescribed medications in the country at 131 million prescriptions per year. (DEA 2013) This rise in sales of prescription opioids over the past decade has contributed greatly to the observed increases in serious adverse events and opioid substance misuse/abuse. It is a primary goal of the DWC Guideline to significantly reduce the rate of opioid-related adverse events and substance misuse and abuse.

A3. Scope and Target Audience for Opioid Guideline

The target audiences for the DWC Guideline are primary care and medical and surgical specialty physicians, including pain specialists, caring for injured workers in the State of California and medical providers who perform utilization review and independent medical review. Employers and insurers will also find the concepts in the document useful. The Guideline is meant to assist in the decision to initiate trials of opioid therapy for patients with acute, perioperative, and chronic pain, and to assist in safer, more judicious and effective use of opioids if they are prescribed on a chronic basis.

A key focus of this DWC Guideline is to seek a balance between appropriate treatment of pain and safety in the use of opioids for that purpose. As noted in the 2011 White House Office of National Drug Control Policy comprehensive action plan on prescription

drug abuse, "...any policy in this area must strike a balance between our desire to minimize abuse of prescription drugs and the need to ensure access for their legitimate use." (White House Office 2011)

The DWC Guideline does not address pediatric pain, labor pain, or cancer/end of life pain. Caution should also be exercised in extrapolating these recommendations to the non-workers' compensation population. While some of the concepts applied here are common to all patient populations, a significant difference between occupational and non-occupational guidelines is that a key goal of the former is the restoration of function to ensure early return to work.

A4. Core Concepts

Although this DWC Guideline is evidence-based, consistent evidence on which to base specific treatment recommendations was lacking on many issues related to opioid prescribing. In such situations, recommendations were based on expert consensus following a critical assessment of the available literature. The DWC Guideline was based on the following core concepts that represent the current state of evidence, professional standards, and societal beliefs:

- Effective pain management is a professional responsibility and the duty of people in the healing professions. (IOM 2011) Providing effective resources for practicing physicians to enable the delivery of best practices in community-based settings is most likely to allow effective, ongoing treatment of pain.
- Pain is influenced by a combination of biological, psychological, and social factors and requires a comprehensive approach to prevention and management. (IOM 2011; DWC 2009)
- The transition from acute to subacute pain to chronic pain and the development of long-term disability are of particular concern in the workers' compensation

system. It is of the highest public health and societal interest to prevent this transition to chronic pain and long-term disability. Psychosocial variables are generally more accurate predictors of the development of chronic pain than biomedical findings.

- Opioids can be an effective treatment for chronic noncancer pain, but their use must be balanced with potential risks.
- Opioids are not indicated in all painful conditions. Furthermore, medications alone in general, and opioids specifically, are often inadequate to manage chronic pain. Other effective pharmacological and non-pharmacological treatments should be considered, alone or in combination. (Chou 2007a; Chou 2007b)
- Given chronic pain's diverse effects, interdisciplinary assessment and treatment produces the best results, especially for those with severe and persistent pain problems. (IOM 2011)
- Patient care is improved with good communication and collaboration between clinicians across disciplines within primary care, between primary and specialty care physicians, and between clinicians and patients.
- The use of opioids for the treatment of pain presents risks and potential harms. Prescribers have an obligation to assess risks and minimize harms.
- Optimal implementation of the best practices described in this Guideline should include education of patients and the general public about the potential benefits and harms of opioids and their role in using opioids safely and effectively.

To reduce the overuse, misuse, and abuse of opioids, the DWC Guideline must be actively implemented in clinical practice; this includes the use of tools, some of which are provided as part of the Guideline. In addition, it is essential to raise public awareness about the need to improve the effectiveness and safety of opioid prescribing.

A lack of quality data on the long-term benefits, risks, and adverse effects of opioid therapy has created a strong need for more research in these areas. The DWC Guideline is not meant to serve as a training manual for opioid prescription. Some clinicians may need to acquire additional skills and knowledge to safely and effectively prescribe opioids for pain.

A4.1 Goals and Objectives

The goals of the recommendations in the DWC Guideline are the following:

- To prevent and reduce opioid-related long-term disability, morbidity, mortality, and substance misuse and abuse.
- To provide a set of best practices and universal precautions for safe and effective prescribing of opioids for acute, subacute, and chronic pain.
- To recommend opioid prescribing practices that promote functional restoration.

A5. Evidence-Based Methods

The DWC Guideline for the safe prescription of opioids for injured workers is based on the best available medical evidence. The methodology used is consistent with the published literature regarding guideline development. (Harber 2008) Based on available resources, relevant existing evidence-based guidelines were accessed, reviewed, and evaluated and the highest level of evidence chosen for this Guideline. As of this writing, the review was restricted to guidelines available as of December 2013. Whenever possible, recommendations that were common to all or most of the guidelines reviewed received priority and were adopted as recommendations, even if they were only based on expert consensus. The guidelines that were evaluated are listed in Section A.5.1 below.

Where common recommendations across guidelines were lacking, the following sequential approach was utilized:

a. High-level evidence from high-quality therapeutic studies (i.e., from RCTs) and prognostic studies (prospective cohort studies) were adopted as recommendations. For example, specific dosing guidance was based on high quality RCTs.

b. If no high-level evidence was available, the recommendations of a major guideline were adopted, even when other guidelines did not replicate these recommendations, as long as they aligned with the goals and objectives identified for this DWC Guideline. For example, this was the case for guidance on tapering.

A5.1 Guidelines Evaluated

- **American College of Occupational and Environmental Medicine (ACOEM)**

  ACOEM's Guidelines for the Chronic Use of Opioids. American College of Occupational and Environmental Medicine. 2011(ACOEM 2011)

- **American Pain Society—American Academy of Pain Medicine (APS/AAPM)**

  Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. 2009 (APS/AAPM 2009)[1]

- **American Society of Interventional Pain Physicians (ASIPP)**

  American Society of Interventional Pain Physicians Guidelines for Responsible Opioid Prescribing in Chronic Noncancer pain. 2012 (ASIPP 2012)[2]

[1] Please note that since this guideline was published as a journal article, "Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain," the guideline appears in the Reference list under the author Chou.

- **Canada**

  Canadian Guideline for Safe and Effective Use of Opioids for Chronic Noncancer Pain. National Opioid Use Guideline Group (NOUGG). April 30 2010 Version 4.5 (Canada 2010)

- **Utah**

  Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain. Utah Department of Health. 2009. (Utah 2009)

- **Veterans Administration/Department of Defense (VA/DoD)**

  US Veterans Affairs AdministrationClinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. Version 2.0 2010. (US VA 2010)

- **Washington State (WA)**

  Interagency Guideline on Opioid Dosing for Chronic Noncancer Pain. Agency Medical Directors' Group (AMDG). 2010. (WA AMDG 2010)

  Guideline for Prescribing Opioids to Treat Pain in Injured Workers. Washington State Department of Labor & Industries. July 1, 2013. (WA 2013)

- **Work Loss Data Institute. Official Disability Guidelines (ODG)**

  ODG Evidence-Based Medical Treatment and Return-to-Work Guidelines (Official Disability Guidelines). 2013 (18th) annual edition). (ODG 2013)

See Part D of the DWC Guideline for a summary of recommendations from the guidelines reviewed.

[2] Please note that since this guideline was published as a journal article, "American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2--guidance," the guideline appears in the Reference list under the author Manchikanti.

References

American College of Occupational and Environmental Medicine. ACOEM's guidelines for the chronic use of opioids. 2011. URL:http://www.acoem.org/uploadedFiles/Knowledge_Centers/Practice_Guidelines/Chronic%20Pain%20Opioid%202011.pdf Accessed 6/18/2013

Bernacki EJ, Tsai SP. Ten years' experience using an integrated workers' compensation management system to control workers' compensation costs. J Occup Environ Med. 2003; 45: 508–16.

Blondell RD, Azadfard M, Wisniewski AM. Pharmacologic Therapy for Acute Pain. Am Fam Physician. June 1, 2013;87(11):766-772.

Boscarino JA, Rukstalis MR, Hoffman SN, et al. Prevalence of prescription opioid-use disorder among chronic pain patients: comparison of the DSM-5 vs DSM-4 diagnostic criteria. J Addict Dis. 2011;30:185–94.

Boyer EW. Management of Opioid Analgesic Overdose. N Engl J Med. July 2012;367(2):146–155.

Brown FL, Jr., Bodison S, Dixon J, Davis W, Nowoslawski J. Comparison of diflunisal and acetaminophen with codeine in the treatment of initial or recurrent acute low back strain. Clin Ther. 1986;9 (Suppl C):52–8.

Canada: National Opioid Use Guideline Group (NOUGG). Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. 2010 [cited 2013 March 21]. Available from: http://nationalpaincentre.mcmaster.ca/opioid/

Centers for Disease Control and Prevention (CDC). Warner M, Chen LH, Makuc DM. Increase in fatal poisonings involving opioid analgesics in the United States, 1999–2006. NCHS Data Brief;22 Sept 2009. URL: http://www.cdc.gov/nchs/data/databriefs/db22.pdf

Cheadle A, Franklin G, Wolfhagen C, et al. Factors influencing the duration of work-related disability: A population-based study of Washington State workers' compensation. Am J Publ Health. 1994;84:190–96.

Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain. 2009a;10:113-30.

Chou R, Huffman LH; American Pain Society; American College of physicians. Medications for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Ann Int Med. 2007b;147:505–14.

Chou R, Huffman LH; American Pain Society; American College of Physicians. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Ann Int Med. 2007a;147:492–504.

Clark E, Plint AC, Correll R, Gaboury I, Passi B. A randomized, controlled trial of acetaminophen, ibuprofen, and codeine for acute pain relief in children with musculoskeletal trauma. Pediatrics. 2007;119(3):460–7.

Drug Enforcement Administration. Hydrocone. April 2013. http://www.deadiversion.usdoj.gov/drug_chem_info/hydrocodone.pdf Accessed 1/20/2014.

DWC Chronic Pain Medical Treatment Guideline. 2009. http://www.dir.ca.gov/dwc/DWCPropRegs/MTUS_Regulations/MTUS_ChronicPainMedicalTreatmentGuidelines.pdf

Ekman EF, Ruoff G, Kuehl K, et al. The COX-2 specific inhibitor valdecoxib versus tramadol in acute ankle sprain: a multicenter randomized, controlled trial. Am J Sports Med. 2006;34(6):945–55.

Elliott JA, Opper SE, Agarwal S, Fibuch EE. Non-analgesic effects of opioids: opioids and the endocrine system. Curr Pharm Des. 2012;18:6070–8.

Franceschi F, Marini M, Ursella S, et al. Use of oxycodone in polytrauma patients: the "Gemelli" experience. Eur Rev Med Pharmacol Sci. 2008;12(2):123–126.

Fulton-Kehoe D, Garg R, Turner JA, et al. Opioid poisonings and opioid adverse events in workers in Washington State. Am J Ind Med. 2013 Oct 10. doi: 10.1002/ajim.22266

Furlan AD, Chaparro LE, Irvin E, Mailis-Gagnon A. A comparison between enriched and nonenriched enrollment randomized withdrawal trial of opioids for chronic noncancer pain. Pain Res Manag. 2011;16:337–51.

Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. CMAJ 2006 May 23;174(11):1589–94.

Gaskell H, Derry S, Moore RA, McQuay HJ. Single dose oral oxycodone and oxycodone plus paracetamol (acetaminophen) for acute postoperative pain in adults. Cochrane Database of Syst Rev. 2009 Jul 8;(3): CD002763 doi: 10.1002/14651858.CD002763.pub2.

Grattan A, Sullivan M, Saunders K, Campbell C, Von Korff M. Depression and prescription opioid misuse among chronic opioid therapy recipients with no history of substance abuse. Annals Fam Med. 2012;10(4):304–11.

Harber P, Wynn BO, Lim YW, et al. Selection of workers' compensation treatment guidelines: California experience. J Occup Environ Med. 2008;50:1282–92.

Innes GD, Croskerry P, Worthington J, Beveridge R, Jones D. Ketorolac versus acetaminophen-codeine in the emergency department treatment of acute low back pain. J Emerg Med. 1998;16(4):549–56.

Institute of Medicine. National Academy of Sciences. Relieving pain in America: A blueprint for transforming prevention, care, education and research. June, 2011.

Juurlink DN, Dhalla IA. Dependence and addiction during chronic opioid therapy. J Med Toxicol. 2012;8:393–9.

Kalso E, Edwards JE, Moore RA, McQuay HJ: Opioids in chronic non-cancer pain: Systematic review of efficacy and safety. Pain. 2004;112:372–380.

Kelley NE, Tepper DE. Rescue therapy for acute migraine, part 3: opioids, NSAIDs, steroids, and post-discharge medications. Headache. 2012 March;52((3):467–82.

Kenan K, Mack K, Paulozzi L. Trends in prescriptions for oxycodone and other commonly used opioids in the United States, 2000–2010. Open Med. 2012;6(2):e41–7.

Li C, Ni J, Wang Z, et al. Analgesic efficacy and tolerability of flupirtine vs. tramadol in patients with subacute low back pain: a double-blind multicentre trial*. Curr Med Res Opin. 2008;24(12):3523–30.

Lovell SJ, Taira T, Rodriguez E, Wackett A, Gulla J, Singer AJ. Comparison of valdecoxib and an oxycodone-acetaminophen combination for acute musculoskeletal pain in the emergency department: a randomized controlled trial. Acad Emerg Med. 2004;11(12):1278–82.

Manchikanti L, Abdi S, Atluri S, et al. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2--guidance. Pain Physician. 2012;15(3 Suppl):S67–116.

Martins SS, Fenton MC, Keyes KM, et al. Mood and anxiety disorders and their association with non-medical prescription opioid use and prescription opioid-use disorder: longitudinal evidence from the National Epidemiologic Study on Alcohol and Related Conditions. Psychol Med. 2012;42:1261–72.

Minozzi S, Amato L, Davoli M. Development of dependence following treatment with opioid analgesics for pain relief: a systematic review. Addiction. 2013;108:688–98.

Moore RA, Derry S, McQuay HJ, Wiffen PJ. Single dose oral analgesics for acute postoperative pain in adults. Clin Evid (Online). 2011a May 9;2011. pii: 1102.

Niwa Y, Haji A. M3-receptor activation counteracts opioid-mediated apneusis, but the apneusis per se is not necessarily related to an impaired M3 mechanism in rats. Life Sci. 2011;89:685–90.

Noble M, Treadwell JR, Tregear SJ, et al. Long-term opioid management for chronic noncancer pain (Review).Syst Rev. 2010; CD 006605. http://www.update-software.com/BCP/WileyPDF/EN/CD003113.pdf (Accessed 2/21/14)

Nuckols TK, Diamant AL, Popescu I et al. Report to the California Department of Industrial Relations and the California Commission on Health and Safety and Workers' Compensation. Identifying risky opioid prescribing practices. 2012. URL: http://www.dir.ca.gov/chswc/Reports/2012/Identifying%20Risky%20Opioid%20Prescribing%20Practices_2012.pdf, Accessed 6/18/2013.

Outcalt SD, Yu Z, Hoen HM, et al. Health care utilization among veterans with pain and posttraumatic stress symptoms. Pain Med. 2013; Feb 22. doi: 10.1111/pme.12045.

Papaleontiou M, Henderson CR, Turner BJ, et al. Outcomes Associated with Opioid Use in the Treatment of Chronic Non-Cancer Pain Among Older Adults: A Systematic Review and Meta-Analysis.J Am Geriatr Soc. 2010 July; 58(7):1353–1369. doi: 10.1111/j.1532-5415.2010.02920.x (Accessed 2/21/14)

Toms L, Derry S, Moore RA, McQuay HJ. Single dose oral paracetamol (acetaminophen) with codeine for postoperative pain in adults. Cochrane Database of Syst Rev. 2009, Issue 1. doi:: 10.1002/ 14651858.CD001547.pub2

U.S. Dept of Health and Human Services. Substance Abuse and Mental Health Services Administration (SAMHSA). Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. Sept 2011. URL: http://www.samhsa.gov/data/NSDUH/2k10ResultsRev/NSDUHresultsRev2010.pdf

U.S. Dept of Health and Human Services. Substance Abuse and Mental Health Services Administration (SAMHSA). Results From the 2005 National Survey on Drug Use and Health: National Findings. 2006. URL: http://www.oas.samhsa.gov/nsduh/2k5nsduh/2k5Results.pdf

Utah Department of Health. Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain. 2009. URL:http://health.utah.gov/prescription/pdf/Utah_guidelines_pdfs.pdf

Veenema K, Leahey N, S. S. Ketorolac versus meperidine: ED treatment of severe musculoskeletal low back pain. Am J Emerg Med. 2000;18(4):404–7.

U.S. Veterans Affairs Administration. Clinical Practice Guideline: Management of Opioid Therapy for Chronic Pain. URL: http://www.healthquality.va.gov/COT_312_Full-er.pdf. 2010.

Washington State Department of Labor & Industries. Guideline for Prescribing Opioids to Treat Pain in Injured Workers. 2013. URL:http://lni.wa.gov/ClaimsIns/Files/OMD/MedTreat/FINALOpioidGuideline010713.pdf

Washington State Department of Labor & Industries, Washington Agency Medical Directors' Group. Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain: An educational aid to improve care and safety with opioid therapy, 2010 Update. 2010. URL:http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf

White AP, Arnold PM, Norvell DC, et al. Pharmacologic management of chronic low back pain: synthesis of the evidence. Spine. 2011;36 (Supp):S131–43.

White House Office of National Drug Control Policy. Epidemic: Responding to America's Prescription Drug Abuse Crisis. 2011. URL: http://www.whitehouse.gov/sites/default/files/ondcp/issues-content/prescription-drugs/rx_abuse_plan.pdf Accessed 6/17/2013.

Wickizer TM, Franklin G, Fulton-Kehoe D, et al. Improving quality, preventing disability and reducing costs in workers' compensation healthcare. A population-based intervention study. Med Care. 2011;49:1105–1111.

Work Loss Data Institute. ODG Evidence-Based Medical Treatment and Return-to-Work Guidelines (Official Disability Guidelines). 2013 (18th annual edition). Chronic Pain Chapter (updated 2/18/13). Accessed 3/8/13 at http://www.odg-twc.com/.