Health Care Guideline:

Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management Care for Adults

September 2019

ALERT: The following change has been made to this document.

The recommendation to avoid opioids to treat chronic pain remains unchanged.

However, the work group has changed the recommendation regarding opioid prescriptions for patients on chronic opioids. The updated recommendation recommends that every effort should be made to keep patients who are on chronic opioids below 90 morphine milligram equivalents (MME) per day.

The previous recommendation was to keep patients on chronic opioids below 100 MME per day.

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Pain Assessment Algorithm

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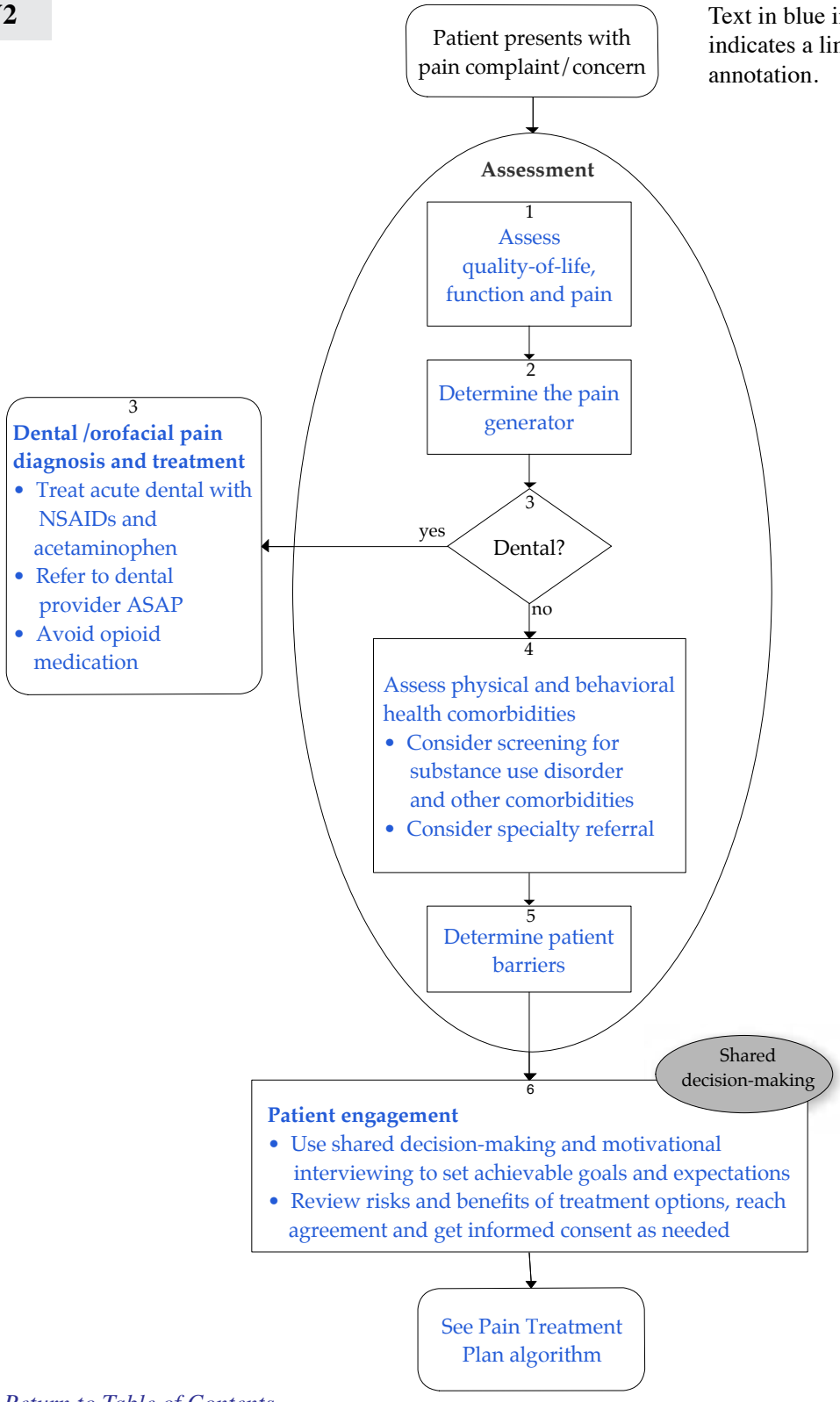

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Pain Treatment Plan Algorithm

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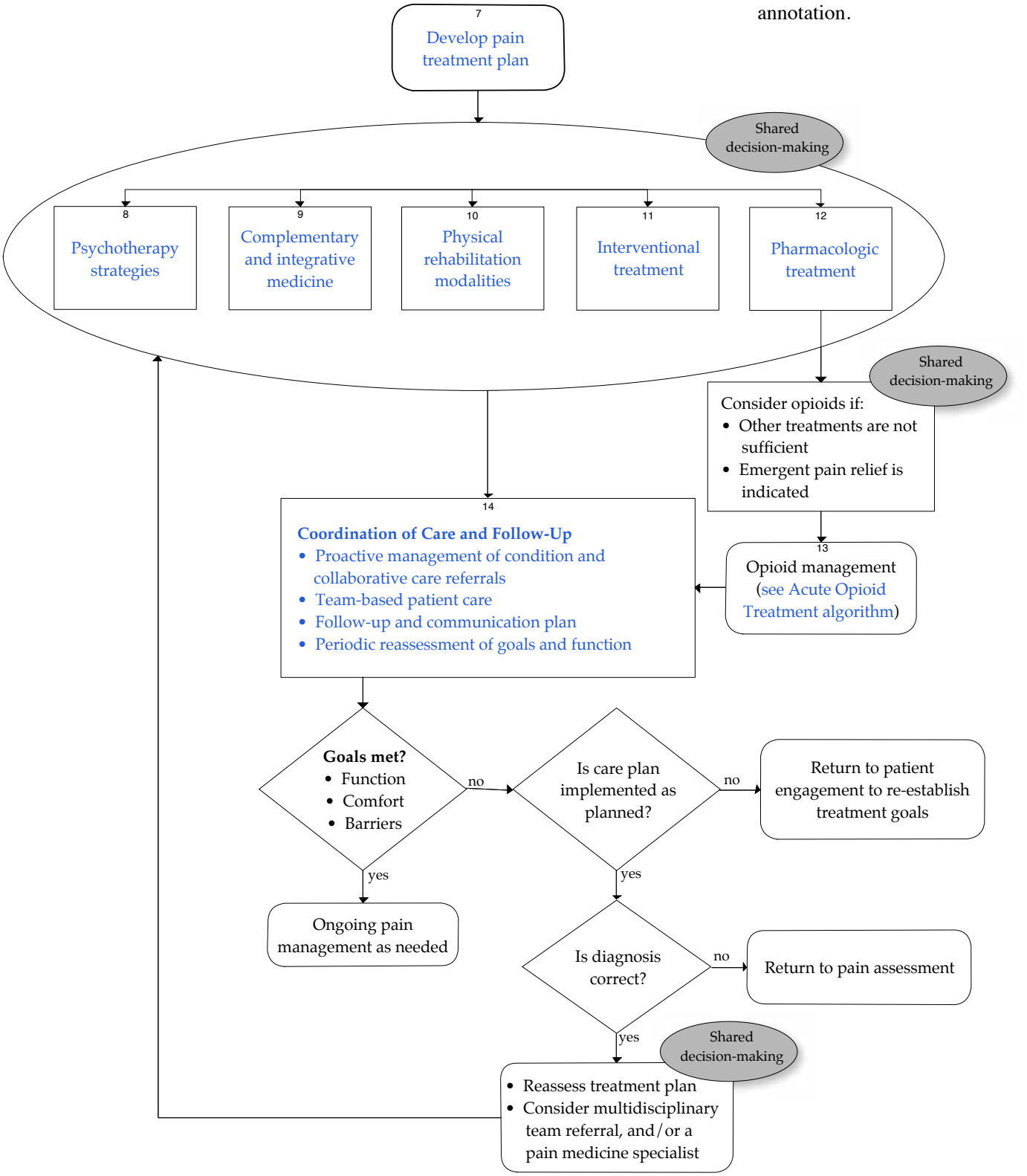

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Acute Opioid Treatment Algorithm

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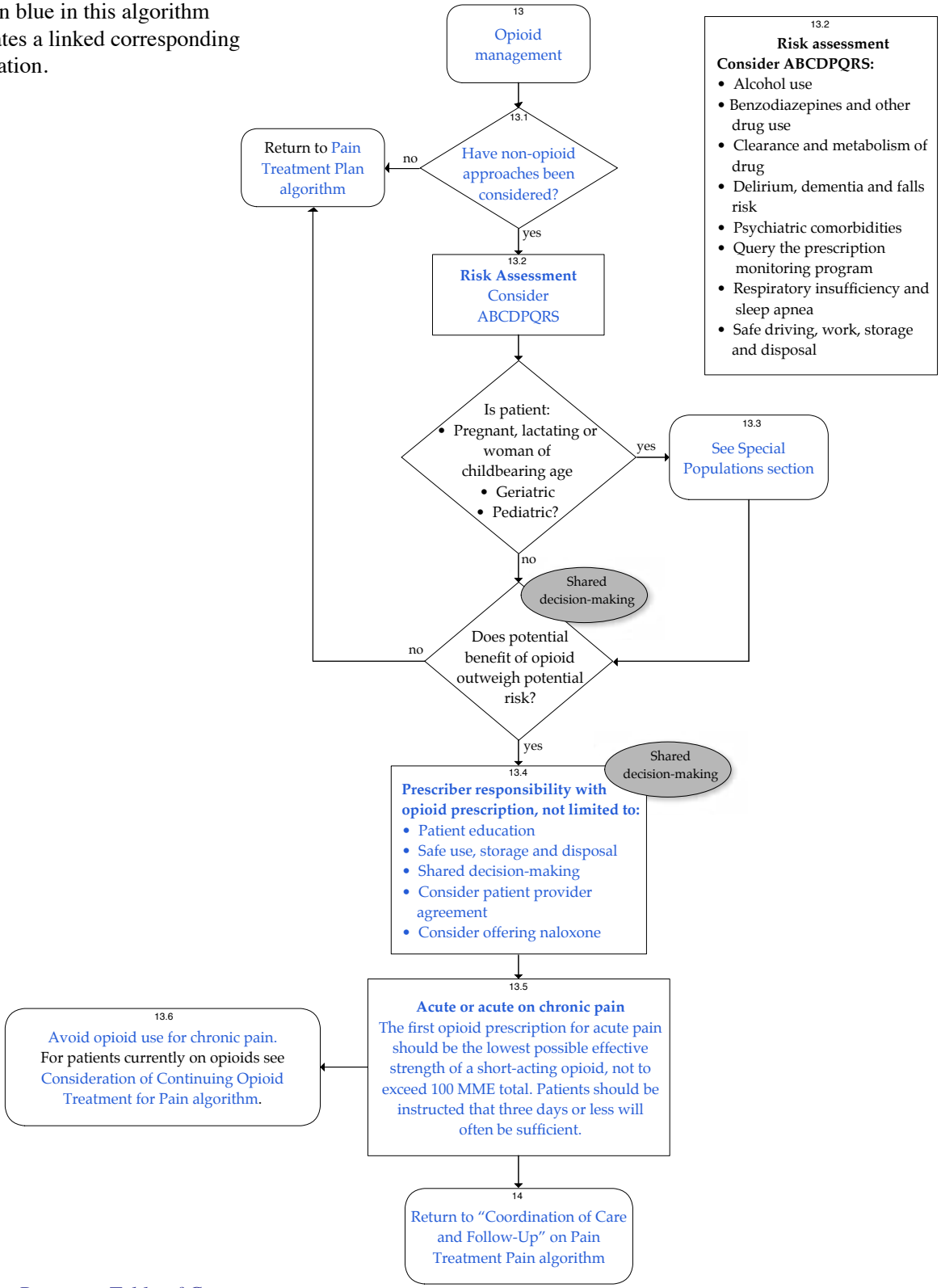

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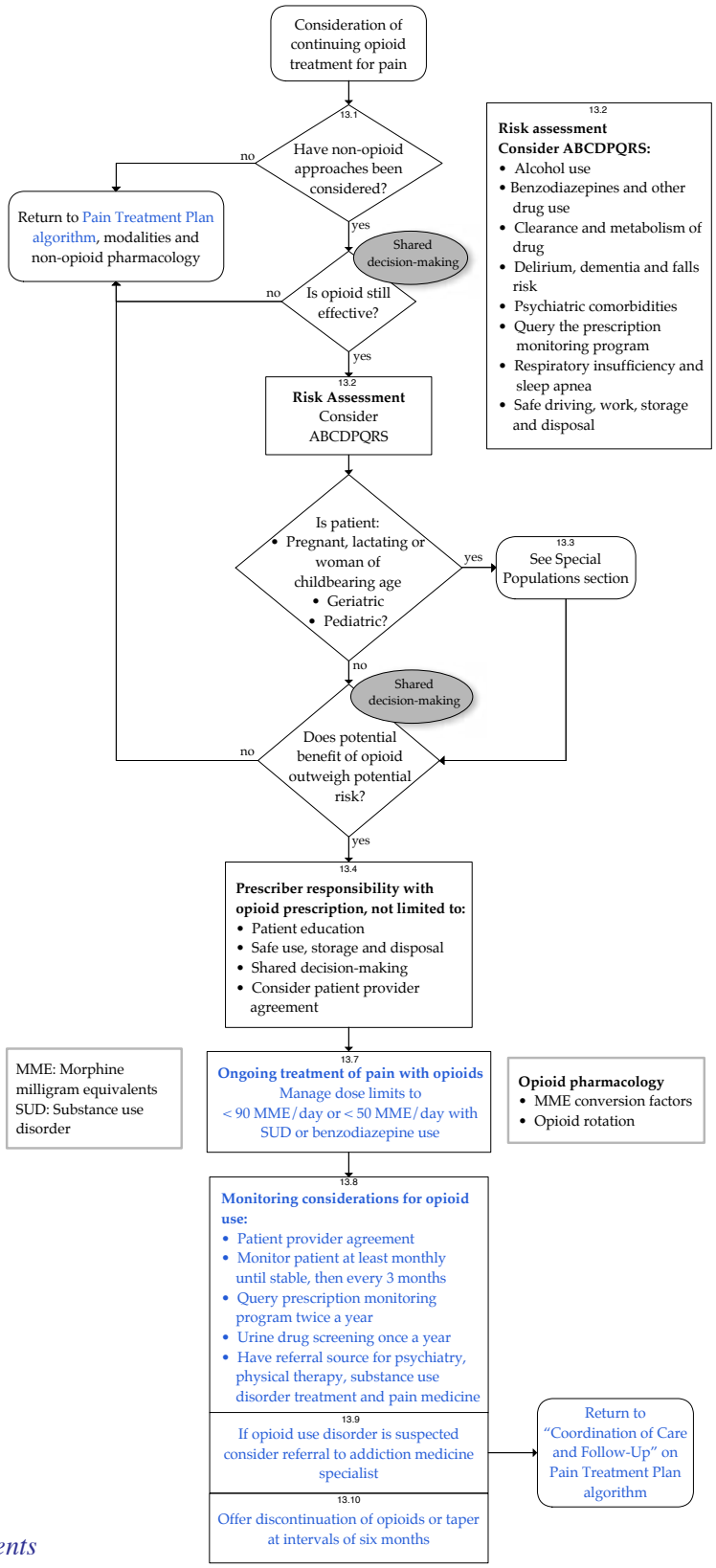
Consideration for Continuing Opioid Treatment Algorithm



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Evidence Grading

Literature Search

This guideline is based on a systematic evidence review evaluating literature published on Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management. The literature search included systematic reviews, randomized control trials, meta-analysis, observational studies, and protocols and/or guidelines for pain and/or opioids. The search included literature from January 1, 2010, through February 8, 2016.

The databases searched include PubMed and Cochrane. The search was limited to only studies in the English language and using human subjects. Other exclusions included cancer pain, migraine pain, palliative and end-of-life. The search included assessment, treatment and management of specific types of pain, specific modalities and specific medication classes (see below). General categories are assessment of, treatment of and management of pain.

In addition to the literature searches, work group members and ICSI staff obtained articles through individual searches. Those reviewed by the work group were included in the guideline where appropriate.

Literature Search Terms

Pain Types	Modality or Topic	Drug or Drug Class
• Axial neck • Axial back • Dental • Arthritis • Musculoskeletal • Joint • Temporal mandibular joint • Facial • Inflammatory • Fibromyalgia • Myofascial • Neuropathic • Neuralgia • Visceral • Whiplash	• Urine drug screen and opioids • Urine toxicology and opioids • Physician drug monitoring program and opioids • Discontinuing opioids • Tapering opioids • Opioid withdrawal • Indications for opioids • Massage therapy • Exercise therapy • Physical therapy • Manual therapy • Spinal manipulation • Manipulative therapy • Aquatic therapy • Topical therapies (ice, heat, ultrasound, infrared) • Passive therapies (ice, heat, ultrasound, infrared) • Psychosocial management • Behavioral health management • Functional assessment and pain • Measuring functional outcomes in chronic pain • Depression • Cognitive behavioral therapy (CBT) • Relaxation therapies • Biofeedback • Mindfulness-based stress reduction (MBSR) • Imagery • Diaphragmatic breathing • Autogenic training • Progressive muscle relaxation training • Hypnosis • Cognitive techniques • Cognitive restructuring • Problem-solving • Complimentary alternative medicine • Tactile stimulation • Intra-spinal local anesthetic • Graded aerobic exercise • Yoga • Acupuncture • Neural blockade • Graded strengthening exercises • Occupational factors • Local injections • Botulin toxin injections • Invasive procedures • Sacroiliac joint injection • Transforaminal epidural injection • Discography • Facet joint injection • Epidural corticosteroid injections • Percutaneous radiofrequency neurotomy	• Acetaminophen (Tylenol) • Muscle relaxants • Antispasmodics • Topical agents • Capsacin • Lidocaine patches and ointment • Diclofenac gel and patch • Topical NSAIDs • Glucosamine • Chondroitin sulfate • Herbal supplements • Butterbur • Feverfew • Magnesium • Riboflavin • Coenzyme Q10 • Anticonvulsants • Antidepressants • NSAIDs • Opioids • Codeine • Morphine • Hydrocodone • Hydromorphone • Meperidine • Oxycodone • Oxymorphone • Buprenorphine transdermal patch • Butrans • Fentanyl • Methadone • Tramadol • Tapentadol

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GRADE Methodology

In recent years, ICSI has transitioned to using a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology as a way to systematically review the evidence and develop recommendations. After gathering the evidence through our literature searches (detailed above), we found a paucity of systematic reviews and randomized controlled trials (RCTs), making the application of GRADE methodology challenging. As an evolving field, there is still much about pain treatment, particularly use of opioids, that remains unstudied or understudied. Given this, GRADE methodology could not be applied to this document. Instead, the work group used the best available evidence to reach consensus recommendations. For each recommendation, the relevant resources used to support that recommendation are noted.

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Recommendations Table

The work group recommendations are a consensus of our expert work group based on the best evidence available. For each recommendation, the relevant resource used to support that recommendation is noted.

Pain Management Recommendations			
Annotation Number	**Topic**	**Recommendation**	**Relevant References**
1	Assessment	Use validated tools to assess and document the patient's functional status, quality of life and pain intensity.	*Keller, 2004 (Observational Study)*
2	Pain generator: opioid-induced pain	• Patients presenting with an indeterminate pain generator should be assessed for exposure to opioids in the past and current opioid use. • Providers should consider checking the Prescription Monitoring Program for patients presenting with pain if his or her opioid exposure is uncertain.	*Nuckols, 2014 (Systematic Review of Guidelines); Cicero, 2014 (Observational Study); Chu, 2006 (Observational Study)*
3	Pain generator: acute dental	• Prescribe ibuprofen and acetaminophen combination as first-line treatment for dental pain. • The referring medical clinician for acute dental pain should not routinely prescribe opioid medications.	*Moore, 2013 (Systematic Review)*
4	Comorbidities: behavioral assessment	Assess for behavioral health comorbidities in patients with chronic pain.	*Hooten, 2016 (Summary Article); Janssens, 2015 (Observational Study); Asmundson, 2009 (Report)*
4	Comorbidities: screen for substance use disorders	Consider screening patients for substance use disorders when there is an unclear etiology of pain.	*Han, 2015 (Observational Study); Hooten, 2015b (Observational Study); Jones, 2013a (Observational Study); Juurlink, 2012 (Review); Sehgal, 2012 (Review); Bohnert, 2011 (Observational Study); Liebschutz, 2010 (Observational Study); Chou, 2009c (Evidence Review); Martell, 2007 (Systematic Review)*

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Annotation Number	Topic	Recommendation	Relevant References
7	Treatment plan	When feasible, a multidisciplinary approach is recommended for treating the patient with pain, especially chronic pain.	*International Association for the Study of Pain, 2014 (Guideline); Gatchel, 2006 (Review)*
8	Treatment: psychotherapy strategies	Psychotherapy such as cognitive-behavioral therapy or mindfulness-based stress reduction is recommended for patients with a chronic pain diagnosis.	*International Association for the Study of Pain, 2014 (Guideline); Kamper, 2014 (Systematic Review); Castro, 2012; (Randomized Control Trial); Grossman, 2007 (Textbook); Gillis, 2006 (Randomized Control Trial); Turner, 2006 (Randomized Control Trial); Broderick, 2005 (Randomized Control Trial); Smyth, 2003 (Review)*
10	Treatment: physical rehabilitation modalities	Exercise should be a component of the treatment for a patient with chronic pain.	*Falla, 2013 (Randomized Control Trial); Cuesta-Vargas, 2011 (Randomized Control Trial); Standaert, 2011 (Systematic Review); Dufour, 2010 (Randomized Control Trial); Hall, 2008 Systematic Review/Meta-analysis); Hurwitz, 2008 Evidence Synthesis); Hayden, 2005 (Systematic Review)*
10	Treatment: passive physical modalities	Passive modalities should only be performed as an adjunct to a concomitant active physical therapy or exercise program.	*Vincent, 2013 (Systematic Review); Standaert, 2011 (Systematic Review)*
10	Treatment: active physical modalities	Extending physical therapy beyond 12 weeks for chronic pain patients should be based on objective clinical improvement.	*Cuesta-Vargas, 2015 (Randomized Control Trial); Cramer, 2013 (Randomized Control Trial); Falla, 2013 (Randomized Control Trial); Standaert, 2011 (Systematic Review); Dundar, 2009 (Randomized Control Trial); Koumantakis, 2005 (Randomized Control Trial); Rainville, 2002 (Observational Study)*

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Opioid Recommendations			
Annotation Number	**Topic**	**Recommendation**	**Relevant References**
11	Treatment: Non-opioid pharmacology: Non-sedative and sedative hypnotics and muscle relaxants	• Sedative hypnotics including benzodiazepines and carisoprodol should be rarely used and if so for short-term (< 1 week) treatment of muscle spasms related to acute pain. • Use of non-sedative hypnotic muscle relaxants are of low benefit, but if used, limit to less than four weeks. Do not use carisoprodol for pain.	*American Geriatric Society 2015 Beers Criteria Update Expert Panel, 2015 (Guideline); Gray, 2015 (Observational Study); Petrov, 2014 (Observational Study); Chou, 2007 (Guideline); Richards, 2012 (Systematic Review); Liu, 2010 (Observational Study); van Tulder, 2003 (Systematic Review)*
13.2	Opioid risk assessment tools	Opioid risk assessment tools and knowledge of opioid-related risks should be used in combination with the overall clinical picture to guide care, including the decision to prescribe as well as how closely to monitor.	*Volkow, 2016b (Summary Article); Wasan, 2015 (Observational Study); Argoff, 2014 (Systematic Review); Jones, 2014 (Observational Study); Atluri, 2012 (Review); Jones, 2012 (Observational Study); Moore, 2009 (Observational Study)*
13.3	Special populations: opioids in pregnancy/women of child-bearing age	Prior to prescribing opioids, women of childbearing age should be counseled on the risks of opioids in pregnancy, including risks to the fetus, counseled on contraception and offered pregnancy testing.	*Desai, 2015 (Observational Study); Han, 2015 (Observational Study); Desai, 2014 (Observational Study); Maeda, 2014 (Observational Study); Whiteman, 2014 (Observational Study); Yazdy, 2013 (Observational Study); Broussard, 2011 (Observational Study)*
13.3	Special populations: opioids in geriatrics	• Geriatric patients should be assessed for risk of falls, cognitive decline, respiratory malfunction and renal malfunction before receiving opioids. • If impairment or risk is detected in a geriatric patient, consider reducing the initial opioid dose by at least 50%.	*Han, 2015 (Observational Study); Makris, 2014 (Review); Rubin, 2014 (Report); Rolita, 2013 (Observational Study); Saunders, 2010 (Observational Study); Solomon, 2010 (Observational Study); Spector, 2007 (Observational Study); Vestergaard, 2006 (Observational Study)*

Annotation Number	Topic	Recommendation	Relevant References
13.4	Patient education and shared decision-making	The first opioid prescription should include patient education, shared decision-making and assessment for related risks.	*Hooten, 2015a (Observational Study)*
13.4	Opioid safe use, public safety	• Patients newly on opioids, or having recently had their opioid dose increased, should be advised not to operate heavy machinery, including driving a car, or participate in other work or home activity that may be affected by the sedating effect of opioids. • An individualized approach that weighs the risks and benefits of driving and other activities should be taken with patients chronically on stable opioids who have tolerance and do not show evidence of sedation.	*National Highway Traffic Safety Administration, 2016 (Fact Sheet); Schisler, 2012 (Expert Opinion)*
13.4	Opioid safe storage and disposal	Clinicians should discuss storage and opioid disposal options with patients at the first opioid prescription and in follow-up visits as needed.	*Centers for Disease Control and Prevention, 2016 (Guideline); Centers for Disease Control and Prevention, 2010 (Summary Article)*
13.4	Opioid formulation	• Long-acting opioids should be reserved for patients with established opioid tolerance and in whom the prescriber is confident of medication adherence. • Long-acting tamper-proof formulation for opioids is preferred.	*Hwang, 2015 (Observational Study); Argoff, 2014 (systematic review); Cassidy, 2014 (Observational Study); Havens, 2014 (Observational Study); Sessler, 2014 (Observational Study); Butler, 2013 (Observational Study); Coplan, 2013 (Observational Study); Severtson, 2013 (Observational Study); Manchikanti, 2012a (Guideline); Severtson, 2012 (Observational Study); Dhalla, 2009 (Observational Study)*

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Annotation Number	Topic	Recommendation	Relevant References
13.4	Patient provider agreement	Initiate a patient provider agreement (PPA) at the time an opioid is prescribed for: • High-risk patients • Daily use of opioids > 30 days • Patient transfers to a new clinic already on opioids • Episodic use up to 90 days over the course of a year • If none of the above, initiate a PPA after 90 days of opioids is prescribed.	*Centers for Disease Control and Prevention, 2016 (Guideline); Hooten, 2015a (Observational Study); Noble, 2010 (Systematic Review/meta-analysis); Starrels, 2010 (Systematic Review); Arnold, 2006 (Review)*
13.4	Monitoring: naloxone	Clinicians should consider offering the patient or close contacts a naloxone kit.	*Coffin, 2013 (Cost-Effectiveness Analysis); Centers for Disease Control and Prevention, 2012a (Report); Albert, 2011 (Observational Study); Yokell, 2011 (Report); Strang, 2008 (Observational Study)*
13.5	Initiating opioids for acute pain	• The first opioid prescription for acute pain should be the lowest possible effective strength of a short-acting opioid, not to exceed 100 MME total. Patients should be instructed that three days or less will often be sufficient. • For patients presenting in acute pain, already on chronic opioids, opioid tolerant or on methadone, consider prescribing an additional 100 MME maximum for this acute episode, with a plan to return to their baseline dose as soon as possible.	*Shah, 2017 (Observational Cohort Prospective Study); Bohnert, 2016 (Observational Study); Centers for Disease Control and Prevention, 2016 (Guideline); Liang, 2015 (Observational Study); Miller, 2015 (Cohort Study)*
13.6	Opioids use for chronic pain	Avoid using opioids to treat patients with chronic pain.	*Chou, 2015 (Systematic Review); Chaparro, 2014 (Systematic Review/Meta-analysis); Manchikanti, 2006 (Observational Study)*

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Annotation Number	Topic	Recommendation	Relevant References
13.7	Ongoing treatment of pain with opioids: morphine milligram equivalents dose limits	• Every effort should be made to keep chronic opioid using patients under 90 morphine milligram equivalents (MME)/day. Prescribers should consider seeking pain medicine consultation if greater than 90 MME is reached.	*Han, 2015 (Observational Study); Turner, 2015 (Observational Study); Franklin, 2012 (Observational Study); Gomes, 2011 (Observational Study); Dunn, 2010 (Observational Study)*
13.7	Ongoing treatment of pain with opioids and benzodiazepines or substance use disorder.	• Opioids should be avoided for patients with substance use disorder or concomitant benzodiazepines use. • If a patient with substance use disorder is prescribed opioids, the opioid dose should be less than 50 MME/day. • If patient requires both opioids and benzodiazepines, opioids should be less than 50 MME/day, taking into careful consideration the benzodiazepine dose. There should be good communication among providers regarding dosing.	*Han, 2015 (Observational Study); Turner, 2015 (Observational Study)*
13.7	Opioid rotation and conversion	• Opioid conversion tables should be used only as guidance when changing opioids. • Doses of the new opioid should be reduced by 50% of the previous daily MME dose and titrated to achieve analgesia.	*Pasternak, 2014 (Summary Article); Vissers, 2010 (Review); Fine, 2009 (Consensus); Pasternak, 2005 (Report)*
13.7	Methadone	• Initiating an opioid-tolerant patient on methadone for chronic pain should be reserved for experienced clinicians who are familiar with its use because its long half-life is associated with overdose and death.	*Wong, 2013 (Summary Article);* *Chou, 2009b (Guideline)*

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Annotation Number	Topic	Recommendation	Relevant References
13.7	Medication management: fentanyl for pain	• Initiating transdermal fentanyl should be done only for patients with chronic opioid use greater than 60 MME daily, adequate subcutaneous adipose tissue and the cognitive ability to apply, remove and dispose of the patches safely. • Patches should be removed after 72 hours, folded upon themselves sticky side inward and promptly flushed down the toilet. • Sublingual fentanyl should be reserved for only those in need of palliative care for extreme pain and unable to take any alternatives.	*U.S. Food and Drug Administration, 2013 (Report); U.S. Food and Drug Administration, 2012 (Report)*
13.8	Opioid monitoring: prescription monitoring program	The prescription monitoring program (PMP) should be queried in the following situations: • If opioids are prescribed in dental, emergency department and urgent care settings, and when doses are changed. • In every instance where there are concerns of substance use disorder, overdose, diversion, indeterminate pain disorder, or polypharmacy. • For those patients with an established stable dose of opioids for a chronically painful condition and a history of compliance with the prescriber, PMP checks should be at least twice per year. • Consider querying the PMP when initiating opioid therapy.	*Han, 2015 (Observational Study); Rutkow, 2015 (Observational Study); Johnson, 2014 (Report); Albert, 2011 (Observational Study)*
13.8	Opioid monitoring: urine drug screen	• Routine random urine drug screens (UDS) for all patients on chronic opioid therapy for pain should be at least once per year. • UDS should be done if there is concern of aberrant behavior based on a prescriber's assessments and clinical judgment.	*Centers for Disease Control and Prevention, 2016 (Guideline); Starrels, 2012 (Observational Study); Reisfield, 2009 (Review); Michna, 2007 (Observational Study); Heit, 2004 (Review)*

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Annotation Number	Topic	Recommendation	Relevant References
13.8	Opioid monitoring: visit frequency	• When initiating an opioid prescription, patients should be monitored within a month to evaluate harms and benefits and assess treatment goals. • Patients on stable opioid doses should be seen every three months.	*Centers for Disease Control and Prevention, 2016 (Guideline)*
13.8	Opioid monitoring: referral for high-risk patients	Opioid prescribers should have a referral source for psychiatric treatment, substance use disorder treatment, physical therapy and pain medicine available if needed.	*Gaither, 2016 (Observational Study); Reuben, 2015 (Report)*
13.9	Opioid use disorder	• Opioid prescribers should recognize the symptoms of opioid use disorder. • Opioid prescribers should understand the treatment options for opioid use disorder and have a referral source available.	*Cousins, 2016 (Observational Study); Gaither, 2016 (Observational Study); Fullerton, 2014 (Review); Thomas, 2014 (Review); Carrieri, 2006 (Report)*
13.10	Discontinuing opioids: tapering	• Once the patient and clinician agree to taper opioids, it should be individualized to the patient circumstances, and a referral source should be available. • While tapering opioids, patients should be offered additional treatment options and frequent follow-up. • Opioid tapering should be discussed and offered at intervals of six months for all patients on chronic opioids.	*Accurso, 2016 (Observational Study); Centers for Disease Control and Prevention, 2016 (Guideline); Berna, 2015 (Review)*

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Foreword

Introduction

Pain affects hundreds of millions of Americans every year; in fact pain is a normal part of life. The 2012 National Health Interview Study showed that 11.2% of adults report having daily pain *(Nahin, 2015)*. Pain care involves all fields of medicine; it is the most frequent presenting concern to a medical and dental clinician. An estimated 20% of patients presenting with a non-cancer pain-related diagnosis receive an opioid prescription *(Daubresse, 2013)*. The experience of pain exists on a spectrum from severely disabling to manageable without any intervention. Pain can be acute and self-limited or chronic and incurable.

Pain care should focus primarily on addressing the underlying cause of pain and optimizing the functional status of the patient in pain. Maximizing patient comfort may be a primary goal in end-of-life care, but the goal of a practitioner should not be to have all patients live a pain-free existence. While a new pain should prompt an evaluation to exclude dangerous pathology, pain in and of itself does not represent a disease state.

There is no biomarker for pain. While objective findings to confirm the type and severity of pain are useful when present, they are often absent. The interpretation of a patient's pain relies on the communication skills of both patient and the clinician. Many factors influence the experience of pain: the type of tissue damaged, the extent of tissue damaged, the nervous system and opioid receptor system of the patient, and the psycho-social context in which the pain is experienced. Pain is most often complex, combining multiple pain generators and amplifiers simultaneously in a given patient. Addressing pain, diagnosing its causes and restoring function to a patient in pain are therefore equally complex. While much of the research has been done using pain scores, the clinician's objective assessment and patient's subjective assessment should correspond to the scores. The barometer of clinical progress and treatment success should be how well the patient is able to re-engage in all the myriad activities that comprise life, especially the ability to work and have healthy social relationships.

There is no such thing as legitimate or illegitimate pain. Pain is an emotional experience as defined by the International Association for the Study of Pain *(International Association for the Study of Pain, 2014)*. As such, it is misguided for a clinician to try to distinguish whether emotional experiences are legitimate or not. All pain is legitimate, but not all pain should be treated in the same way.

For those with function-limiting pain, a wide range of medications, interventions and therapies is available. Unfortunately for many of these interventions, the medical evidence is limited and the outcomes are variable. Many treatments of pain have serious adverse effects that need to be weighed against the indication for which they are used. Chronic pain is best understood as a disorder of suffering and coping, not a disorder of pathoanatomy. The problem is usually not a discrete lesion amenable to correction. Rather, chronic pain often emerges from the entire context of a patient's life, and plans for remedy need to have that same context in order to achieve success.

It is important to remember that healing takes time. Imposing arbitrary end dates can result in testing and interventions that may cause more harm than benefit, particularly when the pain is likely to be self-limited. Treatment plans should focus on long-term health rather than a short-term resolution.

Whatever else the clinician does to manage pain, clear communication, expectation setting and follow-up are paramount. It is increasingly clear that to manage pain adequately and safely, the clinician must dedicate substantial time and energy to the patient, and the patient needs to be actively engaged. Recent public attention and the medical literature have focused on the use of opioids for pain and the opioid epidemic resulting from liberal opioid prescribing. Prescribing opioids is not and should not be simple; intense monitoring, informed consent and patient education are required. This is necessary for all patients, even those thought to be at lowest risk. No indication for opioids lowers the high bar of caution and monitoring required of

those who prescribe opioids. Clinicians should not be less cautious treating one type of pain with opioids than with another type. The decision to start opioids should include a plan to discontinue them, although there may be patients with medical conditions for which chronic opioid use is unavoidable. This work group recommends providers start shared decision-making, education and monitoring with the first prescription of opioids. In addition, the timeline for reevaluation should occur much earlier than currently practiced.

We recognize these more restrictive recommendations around opioids may have unintended consequences; therefore, it is critical that the medical community continue to closely study and monitor the effects of prescribing habits.

However, we firmly believe that a paradigm shift in practice regarding not just opioids but pain treatment in general can be instrumental in improving the health of our individual patients and the population.

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Scope and Target Population

Scope: Assessment, diagnosis and treatment of acute, subacute and chronic pain in ambulatory settings.

Target Population: Adults age 18 years and older with non-cancer pain.

Exclusion: This guideline will not cover patients with migraines, active cancer, and/or those receiving palliative or hospice care. In addition, management of visceral pain is out of the scope of this guideline. Although much of the literature is overlapping with low back pain, this is not a primary focus of this guideline.

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Aims

1. Increase the percentage of patients with clinic visits for pain who have documentation of pain status and functional assessments at the visits. *(Annotation #1)*
2. Increase the percentage of patients with a chronic pain diagnosis who are undergoing physical therapy and have a reassessment of their functional status within 12 weeks of initiating physical therapy. *(Annotation #10)*
3. Increase the percentage of chronic pain patients with an opioid prescription who receive appropriate care. *(Annotation #13.8)*
4. Increase the percentage of patients with a new opioid prescription who are prescribed opioids appropriately. *(Annotation #13.5)*
5. Increase the percentage of chronic pain patients with a long-acting opioid prescription formulation where criteria for prescribing were met. *(Annotation #13.4)*
6. Increase the percentage of patients with new opioid prescriptions in dental, ED and urgent care setting where PMP is checked prior to prescribing. *(Annotation #13.8)*

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Clinical Highlights

- Conduct a comprehensive medical assessment initially, periodically and whenever there is a lack of improvement. This assessment should include:
  - Use of validated tools to assess quality-of-life, function and pain
  - Determination of the pain generator
  - Assessment for comorbidities
  - Discussion of patient barriers
- Active patient engagement in the creation and execution of the biopsychosocial treatment plan is a critical factor of success.
- Develop a treatment plan for pain that uses all available modalities and avoids making medications, especially opioids, the sole focus of treatment.
- Treatment should focus on restoration of function, not elimination of pain.
- Improved documentation of the assessment and plan will reduce duplication and guide other clinicians involved as part of the treatment team.

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Implementation Recommendation Highlights

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

- Communicate a clear and consistent message that clarifies:
  - Pain is a normal part of life, all pain is legitimate, and the goals are to improve quality-of-life, function and comfort.
  - Opioids are to be used cautiously, and the benefits must outweigh the risk for each patient.
- Chronic pain should be managed proactively like any other chronic condition.
  - Develop a process to allow the patient to see a dedicated care team that has interest or expertise in chronic pain.
  - Develop relationships in the community and appropriate referral sources to create an interdisciplinary pain management team.
  - Develop protocols/work flows that guide clinicians to ensure consistent management of pain.

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Related ICSI Scientific Documents

Guidelines

- Adult Acute and Subacute Low Back Pain
- Adult Depression in Primary Care
- Diagnosis and Treatment of Headache

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Definitions

Clinician – All health care professionals whose practice is based on interaction with and/or treatment of a patient.

MME – Morphine milligrams equivalent

Pain

According to the International Association for the Study of Pain, pain is defined as "an unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage" *(International Association for the Study of Pain, 2014)*. The experience of pain is inherently subjective and can only be described accurately by the person experiencing pain.

Types of pain are frequently subdivided according to duration of experience. While the literature demonstrates variability in terms of the specific length of that experience, in general:

- Acute pain lasts for days to a month after a physiologic insult or injury.
- Subacute pain lasts from one to three months after an injury.
- Chronic pain is pain that persists longer than three months.

This categorization can provide helpful information to the clinician about the types of intervention likely to have the best impact on patient outcomes for these different types of pain.

Acute Pain

Acute pain is the normal, predicted physiologic response to an adverse chemical, thermal or mechanical insult associated with surgery, trauma or acute illness/injury. Acute pain results from the activation of the pain receptors (nociceptors) at the site of tissue damage. Acute pain plays a vital survival role for the individual as it provides a warning that something is wrong and prompts remedial action. Acute pain is thus referred to as having "biologic utility" *(Weiner, 2001)*. This is a self-limited process usually lasting one month or less.

Acute pain is usually associated with the time it takes for normal healing to occur and often responds well to treatments designed to interrupt or decrease the intensity of the painful stimulus, such as local anesthetics or splinting, depending on the injury. It is often associated with the increased activity of the sympathetic nervous system, which can produce responses such as hypertension, tachycardia, diaphoresis and restlessness. Examples of injuries producing acute pain are thermal or chemical burns, bone fractures, ischemic tissue damage (myocardial infarction) and inflammatory conditions such as pancreatitis.

Recurrent Acute Pain

Recurrent acute pain represents a special type of chronic pain syndrome in that it reflects acute damage to peripheral tissue, but from a chronic process. Finding the best treatment modalities for these syndromes can represent a significant challenge to the clinician as some of the effective treatments for acute pain, such as opioid medications, when used recurrently can lead to dependence and addiction. Frequently these patients will benefit from the input of a pain medicine specialist. Examples of a recurrent acute pain syndrome include sickle cell disease and migraine/vascular headaches, which are out of the scope of this guideline. (See the ICSI Diagnosis and Treatment of Headache guideline.)

Subacute Pain

According to the American Academy of Pain Management, subacute pain occupies the transitional phase from acute to chronic and is generally associated with the time period of one to three months after the initial injury/insult. These time frames cannot be thought of as definitive. There are different periods of "normal

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healing" for different injuries, reflecting the degree of tissue disruption and the healing capacity of that tissue *(Weiner, 2001)*.

The key distinction with subacute pain is the prognosis for complete recovery to pre-injury functionality *(Weiner, 2001)*. Most patients who experience subacute pain can experience complete recovery and normal functioning within three months of initial injury. Techniques to relieve pain by decreasing the nociceptive stimulus (e.g., immobilization of affected area) are most effective early in the subacute phase. As time progresses, rehabilitative techniques produce the most favorable results. Very often, for patients whose experience of daily pain is longer than three months, a full recovery does not happen.

Chronic Pain

Chronic pain is pain that persists beyond the normal time expected for healing and is associated with the onset of pathophysiologic changes in the central nervous system that adversely affect the individual's emotional and physical well-being. While duration of pain required to meet this definition varies, most professional associations involved in pain management accept pain that persists for longer than three months as chronic.

Chronic pain has no biologic utility and offers the individual little protection from further injury *(Weiner, 2001)*. The experience of chronic pain reflects a complex interplay of emotional, psychological and social factors that contribute to an individual's worsening ability to function. Patients suffering from chronic pain can have mood disorders, sleep disturbances and impaired social interactions. Interventions that act primarily on nociceptors, such as local anesthetic, are unlikely to be successful in managing chronic pain. Rather, the best results are obtained through multimodal and rehabilitative techniques, with the goal of improving function rather than interrupting a painful stimulus *(Weiner, 2001)*.

Chronic pain is best understood as a complex interaction of initial peripheral pain generation followed by central neuroplastic changes in the brain and spinal cord *(Ray, 2012)*. It should also be understood that chronic pain does not exist as a state of pain that is ever-present and unchanging. Rather, the natural course for chronic pain is persistent, underlying discomfort punctuated with acute "flare-ups" *(Suri, 2012)*. These flare-ups may last minutes to hours to several days and lead to impaired functioning. These episodes do not reflect new tissue injury and are almost always self-limiting. A practitioner who specializes in pain medicine can be very helpful achieving the best outcome. Some very common examples of chronic pain include musculoskeletal low back pain, fibromyalgia and joint pain/arthritis.

Acute on Chronic Pain

Patients with chronic pain who experience an acute pain episode often represent a significant clinical challenge to the medical or dental clinician. Critical to appropriate treatment of these patients is determining if the immediate antecedent of the painful event represents a new injury, unrelated to their chronic pain syndrome or if the acute episode is part of the natural disease course of chronic pain. Over half of patients with non-specific chronic low back pain will experience pain "flare-ups" over a two-year period, that can last hours or days *(Suri, 2012)*. Such acute "flares" are very common and can represent a diagnostic challenge, especially to an acute care setting clinician, who is unfamiliar with the patient.

Acute injuries not related to chronic pain conditions can be obvious, such as a patient with a new surgery, or may require further investigation as in the case of a patient with chronic back pain who experiences a kidney stone. If a new injury is identified, these patients deserve all of the appropriate treatment modalities available to alleviate suffering.

Surgery on a non-opioid naïve, chronic pain patient represents a special management challenge, as their pain needs are complex. Often in these instances, the best outcome is achieved through a team approach involving the surgical staff, anesthesiologist and palliative specialist with a specific plan in place ahead of the actual procedure *(Lewis, 2005; Wu, 2002)*. Appropriate perioperative analgesia can be critical to avoiding prolonged escalation of opioid dosing, and facilitate expeditious surgical recovery and return to pre-procedure functioning.

Algorithm Annotations

1. Assess Quality-of-Life, Function and Pain

Work Group Recommendation
Use validated tools to assess and document the patient's functional status, quality-of-life and pain intensity.
Benefit: Standardized assessment tools offer consistency for the documentation of pain intensity and physical function. **Harm:** Clinicians may rely too much on tools, which are only one component of the clinical evaluation. **Benefit-Harms Assessment:** Validated tools provide accurate information for the creation and the ultimate success of progress with a treatment plan. If no tools are utilized, the assessment of the patient becomes subjective.
Relevant Resources: *Keller, 2004 (Observational Study)*

Patients often present to their clinician with differing levels of pain and function. The use of pain scales has been part of pain treatment for many years and has become standard practice. Pain scales should be posted for the patient to understand what the scale means. Clinicians can reassure patients by explaining that two people may have a different score for the same type of pain.

While much of the research has been done using pain scores, the clinicians objective assessment, and the patient's subjective description of his or her pain should correspond to the scores. If not, a more indepth assessment is needed as the reported pain intensifies.

The assessment of the patient's function is now considered as important as the reported pain intensity. Multiple tools are available to evaluate function to establish a baseline and then to reevaluate after treatment has been initiated.

Selected tools will be identified in this document near their respective topic, and a list of tools and resources is located in the Quality Improvement Support section.

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2. Determine the Pain Generator

The most important factor in treating pain is making the correct diagnosis for the origin of the pain. All treatment flows from here. After taking a comprehensive history and completing a detailed physical, the clinician needs to feel confident that the correct diagnosis has been determined. If there continue to be questions in this regard, further consultation should be sought sooner rather than later to avoid unnecessary burden or harm to the patient.

Pain Generators

The worldwide-recognized definition of pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" *(International Association for the Study of Pain, 2014)*. Despite the wide acceptance of the definition of pain, the taxonomy of pain syndromes is underdeveloped, and no widely recognized single classification system currently exists *(Fillingim, 2014; Henriques, 2014)*.

The classification of pain based on a combination of pathophysiological mechanisms and predominately involved organ systems is particularly relevant to clinical practice because the putative mechanisms and involved organ systems are often the corollary of an underlying disease state. This simple classification

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scheme, which reflects the core diagnostic criteria supported by the American Pain Society Pain Taxonomy work group *(Cohen, 2010),* provides a clinically focused framework for organizing the key clinical factors that drive the diagnostic and therapeutic decision-making processes related to the care of adults with pain. The categories in this classification scheme include:

- Neuropathic pain
- Musculoskeletal pain
- Inflammatory pain
- Visceral pain

While not a part of the original classification scheme, this work group recommends a fifth pain generator be considered as part of the differential:

- Opioid-induced pain

Neuropathic Pain

Pain caused by a lesion or disease of the central or peripheral somatosensory nervous system *(International Association for the Study of Pain, 2014)*.

Examples of conditions: Diabetic peripheral neuropathy, post-herpetic neuralgia.

Historical features: Pain characterized as burning, stinging or "pins and needles" sensation.

Physical exam findings: Allodynia (pain due to a stimulus that does not provoke pain), hyperalgesia (increased sensitivity to pain) with or without sensory or motor deficits.

Screening and assessment tools: Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Neuropathic Pain Questionnaire (NPQ) and painDETECT.

Musculoskeletal Pain

Pain caused by a lesion or disease of the musculoskeletal system including muscles, ligaments, tendons, cartilaginous structures and joints *(International Association for the Study of Pain, 2014)*.

Examples of conditions: Axial or radicular spine pain, degenerative joint disease (e.g., knee, hip).

Historical features: Anatomically localized or more diffuse pain characterized as aching, dull with or without sharp exacerbations with movement or weight-bearing activities (e.g., walking).

Physical exam: Localized tenderness, joint deformity with or without weakness attributed to pain.

Screening and assessment tools: Oswestry Disability Scale, Roland-Morris Disability Scale.

Inflammatory Pain

Pain caused by an inflammatory process (e.g., infection, autoimmune), which is generally associated with the infiltration of immune cells and tissue damage *(International Association for the Study of Pain, 2014)*.

Examples of conditions: Rheumatoid arthritis, infected joint.

Historical features: Progressive pain characterized as sharp, lancinating with or without increased pain with movement of the involved anatomical region or signs and symptoms of an infectious process.

Physical exam: Tenderness, erythema, swelling, increased warmth of the involved anatomical region with or without signs and symptoms of an infectious process.

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Screening and assessment tools: Arthritis Impact Measurement Scales (Aims/Aims2), Measure of Intermittent and Constant Osteoartiritis Pain (ICOAP).

Visceral Pain

Pain caused by a lesion or disease involving the thoracic, abdominal or pelvic viscera. This is a heterogeneous category of disease processes that have been judged to be out of the scope of this guideline.

Examples of conditions: Dyspepsia, irritable bowel syndrome, endometriosis, non-cardiac chest pain, chronic angina.

Historical features, physical exam, and screening and assessment tools for visceral pain are beyond the scope of this guideline.

Opioid-Related Alterations in Pain Processing and Acute Opioid Withdrawal

Work Group Recommendation
• **Patients presenting with an indeterminate pain generator should be assessed for exposure to opioids in the past and current opioid use.** • **Providers should consider checking the prescription monitoring program for patients presenting with pain if his or her past opioid exposure is uncertain.**
Benefit: Patients with past exposure to opioids have a different set of expectation and risks, and may suffer from a different set of pain generators than those who are opioid naïve. Patients with past exposure to opioids may have known drug interactions or adverse effects that would affect management decisions. **Harm:** It will take additional time to discuss opioid status during the patient encounter. **Benefit-Harms Assessment:** As the proportion of Americans being exposed to opioids grows, the assessment of opioid exposure becomes increasingly important in patients presenting with pain. Knowing if the patient has been exposed to opioids at the time of his or her pain presentation provides both diagnostic and management information. The prevalence of opioid use is great enough to now justify the burden of assessing opioid use routinely in patients who present with an indeterminate pain generator.
Relevant Resources: *Nuckols, 2014 (Systematic Review of Guidelines); Cicero, 2014 (Observational Study); Chu, 2006 (Observational Study)*

Opioid-induced pain is caused by adaptation of the opioid receptors to chronic exposure to opioids, physiologic reaction to withdrawal of opioids or as a side effect of opioids.

Examples of conditions: Opioid withdrawal, opioid-induced hyperalgesia and opioid tolerance: inadequate benefit of acute opioids in a person chronically exposed to opioids.

Historical features

- Opioid withdrawal: Occurs following abrupt cessation or acute opioid dose reduction. Clinical symptoms of withdrawal may occur within 24 hours of the dose change, and latent symptoms may persist for up to six to eight weeks. Complete resolution of discomfort with administration of opioids also suggests withdrawal. Asking patients if they have opioids remaining at home provides valuable information. Opioid-tolerant patients without any opioids are more likely to be in withdrawal.
- Opioid-induced hyperalgesia: Refers to a pronociceptive process that develops in response to longer-term opioid exposure and is manifested clinically by:
  - a change in the characteristics of preexisting pain (e.g., burning, diffuse pain),

- extension of pain beyond the dermatomal distribution of preexisting pain,
- worsening of pain with opioid dose escalation, and
- improved analgesia with opioid dose reduction *(Hooten, 2015b; Mao, 2015)*.

- Opioid tolerance: Refers to a desensitization process manifested clinically as:
  - reduced analgesia to previously therapeutic dosages of opioids,
  - no change in the characteristics or dermatomal distribution of preexisting pain,
  - improved analgesia with dose escalation, and
  - reduced analgesia with opioid dose reduction.

Physical exam:

- Opioid withdrawal: Withdrawal is characterized by myalgias, arthalagias, anxiety, gastrointestinal complaints (diarrhea, emesis), chills, diaphoresis, opioid craving, piloerection, dilated pupils, rhinorrhea, yawning, tachycardia, hypertension and sleep disruption.
- Opioid hyperalgesia: The physical exam is non-localizing.
- Opioid tolerance: Patients who are chronically exposed to opioids may have an unremarkable exam despite being on opioids. If anything, they demonstrate miosis and mild psychomotor slowing, including slowed speech.

Screening: The prescription-monitoring program is useful to uncover past exposure to prescribed opioids, which is the primary risk factor for both opioid withdrawal and opioid-induced hyperalgesia.

Assessment tools: Clinical opioid withdrawal scale (COWS) is useful for assessing opioid withdrawal https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf.

Other considerations

A great number of acute pain presentations occur in patients already on chronic opioid therapy. This poses a diagnostic riddle: is the acute pain caused by a new pain generator, a flare of the chronic pain generator, an unmasking of the chronic pain after opioid cessation, or opioid withdrawal? Re-emergence of the patient's chronic pain is expected after cessation of opioids, even without opioid withdrawal. With opioid withdrawal, the experience of pain is intensified. Many patients who present in pain due to opioid withdrawal are unaware that this is the cause. If a new tissue injury prompts the patient to use additional (unsanctioned) opioids, the patient may present after his or her opioids are exhausted, with both a new injury and opioid withdrawal. In addition to causing pain when stopped, opioids can cause pain when used, such as in opioid hyperalgesia. Thus, knowledge of the patient's past exposure to opioids can help untangle complicated clinical presentations.

Knowledge of past opioid use is also important for management decisions. Over 56% of all patients receiving a new opioid prescription for acute pain received another opioid prescription from a different provider within the last 30 days *(Bohnert, 2011)*. Patients with a history of opioid exposure may have a higher opioid tolerance than an opioid-naïve patent. The total morphine equivalents of their multiple prescriptions may put them at risk of overdose death. In some cases, the patient may have already had multiple therapeutic trials and respond better to certain pharmaceuticals than others. Most importantly, the patient may have a care plan with another prescriber who should be involved in the management decisions.

For all these reasons, patients presenting with indeterminate pain should be asked if they have taken opioids in the past, and if they still take opioids routinely. Querying the prescription monitoring program (PMP) may reveal the date of the patient's last prescription and may suggest that the patient is chronically taking

opioids. The PMP is an imperfect tool, however, as it does not report methadone for opioid use disorder, or opioids through illicit channels, and there are limitations to accessing controlled substances prescribed outside of the state.

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3. Dental/Orofacial Pain Diagnosis and Treatment

Dental/orofacial pain is a common complaint in both primary and emergency care settings. This section focuses on important diagnostic and treatment considerations to help the medical and dental clinician provide safe and effective care. Generally, dental/orofacial pain can develop from any of the following pain generators: neuropathic (herpes), inflammatory (abscess), musculoskeletal (temporomandibular joint disorder) and visceral (cardiac).

Diagnosis

Historical features

- Patient presents with pain in tooth, soft or hard tissue (intra-oral)
- Patient presents with pain in face or jaw (extra-oral)
- Symptoms can include, but are not limited to hot/cold sensitivity in tooth or teeth, pressure, sensitivity to chewing, nerve pain in jaw and radiated pain to other areas of face.

Physical exam

- Visible clinical features can include disruption or discoloration to the enamel of tooth, gum tissue bleeding, exudate, localized or generalized swelling, intra- or extra-oral sores, broken tooth/ teeth or jaw bone due to traumatic injury, intra- or extra-oral lacerations.

Examples of conditions presenting as dental/orofacial pain include, but are not limited to:

- Maxillary sinusitis presenting as maxillary molar or premolar pain
- Otitis media presenting as temporomandibular joint pain
- Coronary artery disease presenting as left jaw pain
- Herpes zoster presenting as facial/jaw/teeth pain or shingles with oral manifestation
- Trigeminal neuralgia presenting as facial pain
- Neoplasms such as gingival overgrowth or ulcerative gingivitis in patients with leukemia
- Bisphosphonate-related jaw osteonecrosis presenting as jaw pain
- Traumatic injury
- Primary herpes presenting as single or multiple oral lesions
- Substance use disorder presenting with severe rampant decay ("meth-mouth"), drug-seeking behavior and hyperalgesia
- Parafunction (misuse of teeth or mouth) presenting as visible damage to the dental/oral/facial structures caused by self-inflicted destructive obsessive/compulsive behavior

Acute tooth pain may present singularly and localized in an otherwise healthy oral environment, or with several affected teeth and generalized throughout an unhealthy oral environment (chronic pathology).

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Assessment: acute tooth pain

Acute tooth pain in a visibly healthy mouth usually allows location and verification by using several simple procedures:

- Have patient identify the location of pain
- Have patient identify any incident that initiated the onset of the pain (e.g., accident, fall, biting on hard object)
- Visual inspection of the suspected tooth, teeth and hard or soft tissue
- Assess the area for swelling, fistula or presence of exudate
- Utilize light percussion – tap all teeth lightly with a small metal instrument near the painful site
- Have the patient apply biting pressure to individual teeth with a cotton tip applicator, toothpick or the like
- Findings should be communicated to the patient and, when possible, the patient's dentist
- In the situation of an unidentifiable lesion, the treating clinician should consider referral to an oral surgeon for biopsy of the lesion

Assessment: chronic tooth pain

Acute tooth pain in a mouth with obvious chronic pathology – such as decay, fractured teeth, abscess and fistulation affecting one single tooth or several teeth – may be very difficult to assess without dental diagnostic tools and should be referred to a dentist for evaluation, diagnosis and treatment. Testing of the teeth beyond visual evaluation is not necessary before the referral is made to a dental clinician. Carious disease (tooth decay) and periodontal disease are chronic conditions that often affect the entire dentition. If left unchecked and untreated, patients may continue to present with acute painful events until the patient loses an individual tooth or several teeth. Both medical and dental clinicians should use the acute incidents of tooth pain as teachable moments to increase oral health literacy and understanding of oral disease. This will strongly reinforce the importance of comprehensive dental care and patient commitment to dental health to help prevent future pain episodes, tooth loss and compromised overall health related to dental disease.

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Treatment

Work Group Recommendation
• **Prescribe ibuprofen and acetaminophen combination as first-line treatment for dental pain.** • **The referring medical clinician for acute dental pain should not routinely prescribe opioid medications.**
Benefit: Public and patient safety. The combination of ibuprofen and acetaminophen is more effective and has fewer side effects than opioids. **Harm:** None known because it gives the clinician an effective non-opioid option for pain relief. **Benefit-Harms Assessment:** Compassionate, non-opioid oral/facial pain relief before and after the treatment of the underlying cause of the pain can almost always be accomplished and avoids the serious risk that accompanies every dose of an opioid mediation prescribed.
Relevant Resources: *Moore, 2013 (Systematic Review)*

There are several non-opioid recommendations for symptomatic pain relief for medical clinicians to utilize in patients presenting with oral/facial pain. The work group does not recommend the use of opioids for acute dental pain prior to a diagnosis and treatment plan being made by a dental clinician or oral/facial pain specialist.

Treatment options for acute and post-acute pain

- Long-acting local anesthetic (e.g., Bupivacaine for up to eight hours).
- Analgesics – non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen.
- Combination analgesics – ibuprofen in combination with acetaminophen.
- Topical anesthetic rinse when indicated or upon presence of stomatitis, mucositis or mouth ulcers.
- Chlorhexidine antimicrobial mouth rinse when indicated, to help with localized gum inflammation and infection, as well as soothe gum tissue.
- Antibiotics when indicated as a post-operative adjunct to the required dento-surgical therapeutic intervention.

Implementation

It is critical for patients to connect with a dental clinician; the medical practitioner can help direct them. Many state dental associations have directories of low-cost dental clinics and member dentists available online or by calling, that can assist the medical clinician in locating referrals.

The Minnesota Dental Association has developed a protocol for treatment of oral/facial pain for dental professionals. The Minnesota Dental Association protocol recognizes pain as an unpleasant, but essential functional indicator and diagnostic aid. It can provide motivation for patients to seek treatment to address the underlying cause.

See http://mndental.org/files/MDA-Protocol-1.pdf (Minnesota Dental Association Protocol for Assessment and Treatment of Oral/Facial Pain).

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4. Assess Physical and Behavioral Health Comorbidities

The presence of other chronic diseases may also complicate the diagnosis and treatment of pain. Multiple comorbidities place a heavy burden on patients and their families, who often lack the capacity or resources to adequately manage all of them *(Leppin, 2015)*.

Physical Assessment

It is critical that the clinician diagnoses and manages physical comorbidities that may contribute to pain. For example, patients with COPD can have varying levels of pain depending on the severity of their disease *(van Dam van Isselt, 2014)*. Undiagnosed or poorly treated diabetes may lead to the failure to treat peripheral neuropathies.

It is imperative that the treatment team has expertise in deciphering nonverbal pain symptoms for patients with cognitive impairments. Pain is a particularly difficult problem for people suffering from dementia. People with dementia report pain less often, less spontaneously and at a lower intensity than those without a cognitive impairment do *(Zwakhalen, 2006)*. Generally, the more severe the dementia, the less capable patients become of being able to verbally express their pain or discomfort *(McAuliffe, 2012)*. It has been shown consistently in the literature that patients with dementia are undertreated for pain *(Tait, 2008; Achterberg, 2007; Nygaard, 2005; Scherder, 2005; Frampton, 2003)*.

There are a multitude of other physical comorbidities that may be associated with pain. An exhaustive discussion of each is beyond the scope of this guideline. However, diagnosing and treating these physical comorbidities are an essential component of pain treatment.

Behavioral Health Assessment

Work Group Recommendation
Assess for behavioral health comorbidities in patients with chronic pain.
Benefit: Could reveal key barriers in patient's underlying suffering and improve treatment outcome. **Harm:** Could re-expose patient to sense of being traumatized and thereby contribute to flashbacks, nightmares, emotional numbing or outburst. **Benefit-Harms Assessment:** Correct identification of potential underlying behavioral conditions allows for more efficient treatment and the resolution of important contributing factors that could otherwise complicate chronic pain conditions.
Relevant Resources: *Hooten, 2016 (Summary Article); Janssens, 2015 (Observational Study); Asmundson, 2009 (Report)*

Behavioral health comorbidities may influence the experience, report and display of pain. Identification and management of comorbid behavioral disorders are critical to effective pain management. Unmanaged disorders may interfere with the patient's ability to meaningfully participate in a collaborative plan of care.

Depression

The coexistence of pain and depression is a prominent problem in primary care clinics. In 2004, the World Health Organization examined data from primary care centers worldwide. They found that 22% of all primary care patients suffer from chronic debilitating pain. Further, they found that patients with chronic pain were four times more likely to have comorbid depressive disorder than pain-free primary care patients *(Lépine, 2004)*. The findings also showed that the more diffuse the pain complaints, the greater the risk of depression and the bigger the impact on quality of life.

In addition, high baseline pain is a risk factor for a poorer response to depression therapy *(Kroenke, 2008)*.

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The clinician should engage a behavioral health team (psychiatrist, advance practice behavioral health nurses, therapists, etc.) early in the treatment course. Tools such as the PHQ-9 should be utilized to help with the diagnosis of depression and to monitor treatment.

If comorbidity is found between chronic pain and mild-to-moderate major depression, treating both conditions is integral for optimal outcomes *(Bair, 2003)*. If comorbid severe major depressive disorder is diagnosed concurrently with chronic pain, depressive symptoms should be the primary focus of treatment *(Kroenke, 2009a)*.

Some symptoms of depression including feelings of helplessness, dysphoria and frustration are generally expected in patients suffering from chronic pain, because pain often affects the ability to function and enjoy life. If targeted intervention can improve the level of physical functioning and quality of life, mild depressive symptoms may improve without specific intervention.

Optimized antidepressant therapy coupled with pain self-management in patients with comorbid pain and depression can produce substantial improvements in both depression and pain. At the same time, additional interventions may be needed to produce larger improvements in pain, and higher depression response and remission rates *(Kroenke, 2009a)*.

If a severe depressive disorder is present in a patient with chronic pain, it is important to note that such patients are at increased risk of suicide *(Magni, 1998; Breslau, 1991)*. Specifically assess if patient has considered harming him/herself or made plans to kill him/herself. If suicidal thoughts are present, assess whether the patient has a concrete plan for self-harm, assess the patient's means to carry out the plan, and assess lethality of the plan. Suicidal risk is higher in individuals who are struggling with substance use/abuse because judgment can be impaired. Careful inquiry about past suicide attempts is an essential part of risk assessment in psychiatric patients. If suicidality and/or severe depressive disorder is present in the context of chronic pain, consult a psychiatrist immediately. Also, the management of chronic pain and progression toward rehabilitation goals are not possible when severe depression is present.

For more extensive discussion on depression, please refer to the ICSI Adult Depression in Primary Care guideline.

Anxiety disorder

Chronic pain and anxiety disorders – particularly panic disorder, generalized anxiety disorder, social anxiety disorder and post-traumatic stress disorder (PTSD) – frequently co-occur *(Asmundson, 2009)*. Across all chronic pain groups, the prevalence of generalized anxiety disorders (GAD) ranges from 1 to 10%, and the prevalence of panic disorder ranges from 1 to 28% *(Hooten, 2016)*. Untreated anxiety disorders can exacerbate the pain response *(Buhrman, 2015)*. Proper treatment will lead to greater pain control through better coping by the patient. The behavioral health team can assist the clinician with proper diagnosis and treatment. The GAD-7 is a commonly used tool to facilitate diagnosis.

History of trauma/abuse

When evaluating patients with pain, it is important to determine whether there is a history of trauma/abuse. A meta-analysis by Afari, et al. (2014) found that individuals who reported exposure to trauma (psychological, emotional, sexual, physical, combat) were 2.7 times more likely to have a functional somatic syndrome. Sexual abuse and rape victims have been shown to be 2.4 to 4 times more likely to develop functional gastrointestinal disorders and chronic pelvic pain. In addition, sexual abuse is associated with non-specific chronic pain and psychogenic seizures, while rape is associated with fibromyalgia *(Paras, 2009)*.

Adverse childhood experiences (ACEs) are a strong predictor for multiple chronic illnesses in adulthood. These include both depression and substance abuse, conditions that exacerbate the pain response and impede treatment response. A review of the literature shows that abuse in childhood is a strong predictor of depression and physical complaints, both expanded and unexplained, in adulthood *(Arnow, 2004)*.

Because many patients will not volunteer this information, it is critical that clinicians screen patients for trauma/abuse when indicated *(Hooten, 2016)*. If a patient presents with chronic pain and a history of abuse that has not been previously treated, referral for appropriate psychotherapy should be considered.

Post traumatic stress disorder (PTSD)

PTSD profoundly impacts an individual's life and health and has been associated with a number of adverse somatic outcomes *(McFarlane, 2010)* including chronic pain *(Asmundson, 2009; Hoge, 2007; Asmundson, 2002; Sharp, 2001; McFarlane, 1994)*. Afari, et al. found combat exposure and PTSD had the largest association with functional somatic syndromes compared to sexual or physical abuse *(Afari, 2014)*. Soldiers diagnosed with PTSD have shown increased vulnerability to pain-related problems *(Moeller-Bertram, 2014)*.

PTSD psychodiagnostic criteria *(American Psychiatric Association, 2013)*

1. Exposure to actual or threatened death, serious injury or sexual violence.
2. Flashbacks and/or nightmares.
3. Persistent avoidance of reminders of traumatic event.
4. Negative alterations in mood and cognitions.
5. Alterations in arousal and reactivity – reckless/self-destructive behaviors, dissociation, irritability, sleep/concentration problems.

The Primary Care PTSD Screen Tool (PC-PTSD) (http://www.integration.samhsa.gov/clinical-practice/pc-ptsd.pdf) is a commonly used tool to screen for PTSD.

Personality disorders

According to data from the 2001-2002 National Epidemic Survey on Alcohol and Related Conditions, approximately 15% of U.S. adults have at least one personality disorder (DSM-5).

While the prevalence of personality disorder in the general population is estimated at from 4 to 6%, the prevalence in health care settings is much higher, ranging from 25 to 50% *(Hooten, 2016)*.

In individuals with chronic pain, the prevalence of borderline personality disorder ranges from 1 to 28%; narcissistic personality disorder ranges from 2 to 23%; histrionic personality disorder ranges from 6 to 23%; dependent personality disorder ranges from 2 to 17%; and obsessive compulsive personality disorder ranges from 7 to 16% *(Hooten, 2016)*.

Individuals with borderline personality disorder report higher levels of pain than those without this personality dysfunction; older, rather than younger, patients with borderline personality disorder are more likely to have higher pain levels; patients with borderline personality disorder in remission use significantly fewer pain medications; and medical disability status in chronic pain does not necessarily differ between those with and those without borderline personality disorder *(Sansone, 2012)*.

Patients diagnosed with borderline personality disorder experience intense and unstable emotions that are unpredictable in their emergence. Such personality traits are adaptive in some situations and maladaptive in others *(Kalira, 2013)*. Catastrophic thinking is a common maladaptive cognitive distortion that is seen in those with chronic pain *(Hasenbring, 2001)* as well as those diagnosed with borderline personality disorder. It is characterized by an overwhelming amplification of negative feelings and worries that undermine the capacity to function with discomfort. Catastrophizing during pain leads to a more intense and distressing symptom experience *(Severeijns, 2001; Sullivan, 2001)*. Both pharmacotherapies and psychotherapies offer the hope of improvement, but integrated treatment plans are generally needed to achieve improved function.

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Substance Abuse, Dependence, and Addiction

Work Group Recommendation
Consider screening patients for substance use disorders when there is an unclear etiology of pain.
Benefit: Many sources of pain are caused directly or indirectly by the use of addictive substances. Pain treatment decisions are greatly affected by the presence of a substance use disorder (SUD). Screening, brief intervention and referral to treatment (SBIRT) is a routine recommendation for doctors in primary care and emergency care settings, and a pain presentation should trigger an SBIRT. **Harm:** Patients may feel that they are treated with suspicion. Performing a substance use disorder screening for patients in pain will consume provider time. **Benefit-Harms Assessment:** Substance use disorder informs the diagnosis and complicates the treatment of pain in many patients and many settings. There will be numerous patients screening negative for whom the screening was not necessary. But for those who screen positive, the benefit is more appropriate care.
Relevant Resources: *Han, 2015 (Observational Study); Hooten, 2015b (Observational Study); Jones, 2013a (Observational Study); Juurlink, 2012 (Review); Sehgal, 2012 (Review); Bohnert, 2011; Liebschutz, 2010 (Observational Study); Chou, 2009c (Evidence Review); Martell, 2007 (Systematic Review)*

It is important to consider screening patients in pain for SUDs before diagnostic and management decisions are made. Simple screening tools for alcohol and other drugs are easy to apply and useful. If the patient screens negative, he or she likely does not have a SUD. If he or she screens positive, the provider should do a structured interview using the DSM-5 SUD criteria.

There are many compelling reasons to screen patients in pain for a history of SUD. SUDs are over-represented among chronic pain patients *(Chou, 2015; Chou, 2009c; Martell, 2007)*. A few recognized pain syndromes can be indirectly associated with SUDs, such as pain from active hepatitis C *(Spiegel, 2005)*. Some patients with opioid use disorder may misrepresent their pain in order to obtain opioids or these patients may simply not know that their distress is related to opioid craving or withdrawal and not related to pain.

SUD and its consequences affect medication choice for both non-opioids and opioid analgesics. For example, the use and dosing of acetaminophen dosing for patients with alcohol use disorder must be thoughtfully considered. A SUD (to any substance, but particularly to opioids) is the greatest risk for misuse of prescribed opioid analgesics *(Juurlink, 2012; Sehgal, 2012; Liebschutz, 2010; Chou, 2009c; Lanier, 2009)*. Cocaine use has been linked to opioid diversion. Those with a SUD are at the greatest risk of harms from opioid analgesics, including overdose death *(Han, 2015; Jones, 2013a; Bohnert, 2011)*.

There are evidence-based and FDA-approved medications for SUDs *(Volkow, 2016b)*. These medications (notably methadone, buprenorphine and naltrexone) affect medication choice when treating pain *(Alford, 2006)*. Due to heightened privacy laws protecting SUDs, these medications may be absent from the patient's medication list and, in the case of methadone, from the prescription-monitoring program *(Substance Abuse and Mental Health Services Administration, The, 2016)*. Patients may also withhold the status of their SUD, wishing to avoid being stigmatized.

Finally, screening a patient in pain for SUDs sheds light on the patient's overall health status. SUDs are chronic diseases that affect many aspects of the patient's life, especially the patient's ability to adhere to a comprehensive treatment regimen *(Volkow, 2016b)*.

The National Institute on Drug Abuse has a simple four-question screen for drug use in general medical settings: https://www.drugabuse.gov/nmassist/?q=qm_json&pageId=questions_1&pageName=QuickScreen&token_id=136912#.

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5. Determine Patient Barriers

Patient resources

Treatment failure can be the result of the patient lacking the resources to actively and consistently participate in a treatment plan. Not all patients have the resources needed to address pain at their disposal. Access to these resources plays a large role in a patient's ability to utilize health care, engage in healthy lifestyle behaviors and participate in treatment plans. This is true not only for pain management but all health conditions. Socioeconomic factors clinicians need to consider include, but are not limited to:

- Geographic location
- Housing
- Employment
- Transportation
- Social support
- Education

There is a level of burden placed upon the patient to carry out the treatment plan, and that capacity must be addressed to ensure success *(Leppin, 2015)*. Whenever possible, a social worker should be included in the health care team to help patients address resource/socioeconomic barriers that may hinder patient engagement.

Work and disability issues

A job can serve a strongly positive role in the life of an individual living with chronic pain. Benefits include improved self-esteem, ongoing income, health insurance coverage, a social support system, a sense of normalcy and a place in useful society.

However, chronic pain may limit the ability to perform some normal job activities. Clinicians can assist the working patient by accurately assessing physical limitations, including need for time away from the workplace for medical treatments. Physical restrictions and recommendations should be clearly and simply written in order to provide the employer with supportive guidance. In most conditions associated with chronic pain, complete and permanent disability is not necessary. Due to the cascade of consequences that may occur, it is important, whenever possible, to help patients continue their work pattern.

Risk factors that increase the likelihood of developing chronic pain and disability are generally consistent across all pain generators. Healing from most types of injuries occurs within the acute phase (fewer than 30 days). If pain is not improving during this time, risk factors, diagnosis and the treatment plan should be reevaluated *(de Rooij, 2013)*. In the last 20 years, numerous studies have been performed to identify risk factors for developing chronic pain and disability, most of which were conducted in the low back pain population. Individual risk factors with stronger predictive ability include the following *(Heymans, 2010; Hayden, 2009; Chou, 2009b; Steenstra, 2005; Pincus, 2002)*:

- Fear avoidance beliefs
- Catastrophizing
- Somatization
- Depressed mood
- Distress and anxiety
- Early disability or decreased function

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- High initial pain levels
- Increased age
- Poor general health status
- Non-organic signs
- Compensation dependency

It is important to use a biopsychosocial model that involves an actively engaged patient early in the pain process to understand pre-existing or current factors that may delay recovery. At this early stage, central neuroplastic factors begin to contribute or dominate pain perception and outcome, making adherence to self-management strategies an increasingly important predictor of outcome *(Nicholas, 2012)*.

Secondary gain is considered a significant risk factor for chronic pain and disability. This may manifest itself as social, occupational, family and financial gain. A variety of conditions, including pain, lend themselves to reporting symptoms to achieve secondary gain. This should be considered when evaluating an individual for disability on certain treatment approaches including opioids.

There are alternative approaches to identifying risk, including the international The Flags Group and risk tools such as the STarT Back originating in England. Please see the ICSI Adult Acute and Subacute Low Back Pain guideline for further discussion.

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6. Patient Engagement

The patient has the most important role within the care team. His or her engagement in creating a care plan is essential. A plan given to the patient without his or her active participation is likely to fail. The care team should allocate appropriate time for understanding the patient's preferences and to develop a mutually accepted plan of care. Ideally this care plan should then be available to all of the members of the collaborative care team.

Setting Realistic Goals and Expectations

Understanding the expectations of the patient in regard to his or her treatment plan is critical. Complete elimination of pain is often unrealistic, but setting functional goals regardless of pain level is reasonable and prudent. These goals should be determined by the patient within a shared decision-making process. Unrealistic goals jeopardize the patient's participation in the care plan and could lead to disengagement.

Shared Decision-Making (SDM) (see full ICSI SDM document in Appendix D)

Shared decision-making is a process by which patients and clinicians consider outcome probabilities and patient preferences, and reach a health care decision based on mutual agreement. This is best done where there is medical uncertainty. However, in this guideline we are encouraging regular conversations with the patient to allow shared decision-making around all choices. The many variables that are present in the management of pain (type of pain, behavioral considerations, treatment choices, etc.) make this process necessary.

The patient's beliefs and values are explored and taken into consideration during the discussion. The medical or dental clinician also shares his or her expertise and offers recommendations based on the most up-to-date medical and dental knowledge. The patient's age, gender, culture and spirituality will influence the ultimate plan that is developed.

Specific, measurable goals regarding the patient's pain management are created and must be realistic and obtainable. Potential barriers need to be addressed during the SDM process, and the care plan should reflect strategies to overcome them. Once mutual agreement is made regarding the plan of care, the plan must be documented and distributed to the patient and the care team. With time and potential changes in the patient's experience with pain, revisions to the plan and new goals can be considered.

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Motivational Interviewing Techniques

Motivational interviewing is a form of collaborative, directional conversation for strengthening a person's own motivation for and commitment to change. It is a person-centered counseling style for addressing the common problem of ambivalence about change by paying particular attention to the language of change. It is designed to strengthen an individual's motivation for and movement toward a specific goal by eliciting and exploring the person's own reasons for change within an atmosphere of acceptance and compassion. While initially developed for and tested in the addictions field, motivational interviewing has been widely studied and adopted in health behavior change as an effective strategy in working with patients.

Additional information is available at www.motivationalinterviewing.org.

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7. Develop Pain Treatment Plan

Work Group Recommendation
When feasible, a multidisciplinary approach is recommended for treating the patient with pain, especially chronic pain.
Benefit: The complexities of chronic pain require a complex biopsychosocial approach using a multidisciplinary care team. **Harm:** Not all clinicians have access to psychologists, addiction treatment, physical therapy, or interventional specialists. **Benefit-Harms Assessment:** The chronic pain patient will benefit from multidisciplinary care, even if it is done in a virtual setting and managed by the primary clinician.
Relevant Resources: *International Association for the Study of Pain, 2014 (Guideline); Gatchel, 2006 (Review)*

These recommendations apply to all patients with pain; however, a chronic pain patient may require more support.

Many treatment options are available to patients with pain. The patient should be an active member of the care team in determining which therapies should be initiated. Often, there will be multiple interventions at the same time, especially when there are multiple comorbidities present. This is why a multidisciplinary approach is recommended for pain management.

The biopsychosocial approach views pain as a complex and dynamic interaction among physiologic, psychological and social factors that can perpetuate or worsen the clinical presentation. In contrast, the biomedical approach focuses on specific physical causes and attempts to eliminate that cause. The most common pain is musculoskeletal pain with no cure, so using a biopsychosocial approach focused on rehabilitation rather than cure is an appropriate therapeutic approach *(Gatchel, 2006)*.

Larger emphasis should be placed on utilizing non-pharmacological pain management strategies that enhance healing and improve outcomes. While medication may play a role in pain treatment, the risks of polypharmacy, addiction and other adverse events must be considered and weighed against the potential benefits.

In order to determine which treatment choices are most appropriate for a patient with pain, the clinician and patient need to consider the following questions when creating a treatment plan:

1. **What is the severity of pain, and how does it affect quality of life and functional status?**
2. **What is the diagnosis and mechanism of the pain?**
3. **Are there physical and/or behavioral comorbidities?**

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4. **What are the goals of treatment as determined by the patient?**
5. **What therapy options are available to the patient?**
6. **What is the patient's capacity to follow a treatment plan, and what will be the burden to the patient to follow that plan?**
7. **What are other barriers (financial, housing, employment, lifestyle, transportation, support network and other social determinants) that might interfere with successful treatment?**

By addressing these questions, a comprehensive treatment plan can be created with the patient's participation. Depending on the complexity of the treatment plan, a multidisciplinary team can be formed, with its members recruited to address the patient's unique needs.

There are a number of general strategies that primary care clinicians can utilize to help their patients manage chronic pain.

- Let the patient know you believe that the pain is real and is not in his or her head.
- Ask the patient to take an active role in the management of his or her pain. Research shows that patients who take an active role in their treatment experience less pain-related disability *(French, 2000)*.
- Avoid telling patients to "let pain be their guide," whether it is stopping activity because of pain, taking medications or resting.
- Schedule return visits on a regular schedule, and don't let the appointments be driven by increasing levels of pain. Clinicians are powerful reinforcers, too.
- Reinforce wellness behaviors such as increased activity or participation in an exercise program.
- Enlist the family and other supports to reinforce gains made toward improved functioning.
- Assist the patient in returning to work. Do this in a stepwise fashion that is not dependent on level of pain.
- For the patient with chronic pain, acknowledge that it is a complicated problem, and for successful rehabilitation, a team of health care clinicians is needed. Chronic pain can affect sleep, mood, levels of strength and fitness, ability to work, family members and many other aspects of a person's life.

Treatment sections include:

1. Mechanism-Based Treatment Options Index
2. Psychotherapy Strategies
3. Complementary and Integrative Medicine
4. Physical Rehabilitation and Modalities
5. Interventional Treatment
6. Pharmacologic Non-Opioid Medications
7. Opioid Management

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Mechanism-Based Treatment Options Index

The following tables have been created to assist the reader in locating treatment modalities. It is not in any priority order, and it is meant to summarize treatment options (non-pharmacologic and pharmacologic) specific to each pain generator. This index links to the section in the document that expands upon the treatments.

Neuropathic Pain

Neuropathic Pain	Modality	Medication
Diabetic neuropathy		• Anticonvulsants • Antidepressants • Topical agents
Trigeminal neuralgia	• Soft diet • Cold packs alternating with moist heat	• Anticonvulsants • Antidepressants • NSAIDs
Nerve compression/ radicular pain	• Physical rehabilitation • Cognitive behavioral therapy • Corsets and braces • Therapeutic injections • Interventional procedures	• Anticonvulsants • Antidepressants • Topical agents
Chronic neuropathy	• TENS	• Antidepressants • Anticonvulsants • Topical agents
Post herpetic neuralgia	• Soft diet • Cold packs alternating with moist heat	• Topical agents • NSAIDs • Antidepressants • Anticonvulsants

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Muscle Pain

Musculoskeletal Pain	Modality	Medication
Diffuse non-specific myalgias **Complex regional pain syndrome**	• Biopsychosocial interdisciplinary team approach • Cognitive behavioral therapy • Graded exercise • Massage	• Topical agents • Acetaminophen • Antidepressants • Anticonvulsant
Chronic musculoskeletal pain	• Mindfulness-based stress reduction • Cognitive behavioral therapy • Hypnosis • Yoga/Tai-chi • Acupuncture • Healing touch • Aquatic therapy • Exercise • Manual therapies (neck & back pain) • TENS • Ultrasound	• Acetaminophen • NSAIDs • Topical agents
Acute musculoskeletal pain	• Exercise/movement • Physical therapy	• NSAIDs • Acetaminophen • Topical agents • Muscle relaxants (limited)
Fibromyalgia	• Graded aerobic exercise • Heated aquatic therapy • Relaxation • Interdisciplinary management • Cognitive behavioral therapy • Hypnosis • Healing touch/Qi-gong massage	• Anticonvulsants • Antidepressants

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Inflammatory Pain

Inflammatory Pain	Modality	Medication
Arthritis	• Exercise • Aquatic therapy • Hypnosis • Intra-articular injection	• Acetaminophen • NSAIDs • Glucocorticosteroids • Topical agents
Tendonitis	• Physical therapy • Iontophoresis • Intra-articular injection	• NSAIDs • Glucocorticosteroids • Topical agents
Dental/Orofacial (link)	• Alternate moist heat and cold therapies • Dental consultation	• NSAIDs and acetaminophen • Topical anesthetic rinse • Chlorhexidine antimicrobial rinse • Bupivacaine injection
Temporomandibular disorder	• Soft diet • Cold packs alternating with moist heat • Physical therapy • Phonophoresis • Dental appliances • Manual therapy • Cognitive behavioral therapy • Biofeedback • Hypnosis	• NSAIDs • Anticonvulsants

Opioid-Induced Pain

Opioid-Induced Pain	Modality	Medication
Withdrawal	• Develop opioid taper schedule	• Opioid • Buprenorphine analgesic or methadone with appropriate license
Hyperalgesia	• Opioid reduction • Opioid rotation • Adjuvant medication • Hypnosis	• Anticonvulsants • Antidepressants
Tolerance	• Assess appropriateness of opioid medication • Adjuvant medication • Opioid rotation	• Anticonvulsants • Antidepressants • Muscle relaxant for flare-up

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8. Psychotherapy Strategies

Work Group Recommendation
Psychotherapy, such as cognitive behavioral therapy or mindfulness-based stress reduction, is recommended for patients with a chronic pain diagnosis.
Benefit: Builds patient adherence to a treatment plan. Helps patients replace maladaptive cognitions and behaviors with more adaptive ones. **Harm:** Minimal (if any) adverse side effects of psychotherapy. **Benefit-Harms Assessment:** This could help bring a more complete sense of healing for the patient. Studies show decreased pain, more active and better quality of life, and better general health. Lack of clinicians with expertise or training could pose an access problem.
Relevant Resources: *International Association for the Study of Pain, 2014 (Guideline); Kamper, 2014 (Systematic Review); Castro, 2012 (Randomized Control Trial); Grossman, 2007 (Textbook); Gillis, 2006 (Randomized Control Trial); Turner, 2006 (Randomized Control Trial); Broderick, 2005 (Randomized Control Trial); Smyth, 2003 (Review)*

Pain is a subjective, private experience, but it is invariably described in terms of sensory and affective properties *(Turk, 2002)*. The treatment of individuals diagnosed with chronic pain must emerge from the appreciation of the individual as a whole, including the type of pain, the circumstances of the patient, comorbid psychiatric conditions such as depression, as well as the issue of personality *(Kalira, 2013)*.

In general, the agreed-upon outcome measures and subsequent treatment options need to be discussed before the treatment plan is initiated. Specifically, consider three main categories:

1. Are they doing more?
2. Are they feeling better?
3. Is there less focus on the pain? *(Jensen, 1991)*

It is important to note an important goal is not necessarily the alleviation of the pain, but more so the associated suffering manifested in increased disability and decreased social engagement *(Kalira, 2013)*. By doing more and cultivating a positive self-image, the individual tends to naturally report less burden and increased resilience *(Büchi, 2002)*.

Chronic pain is frequently associated with psychological difficulty and comorbid psychiatric diagnoses. The presence of psychological difficulties should in no way invalidate a patient's complaint of pain, nor should it eliminate the possibility that a general medical condition may also be present and causing the pain. Individuals with persistent pain often experience feelings of helplessness, hopelessness, anxiety, anger and depression. In light of this, it is important to develop treatment plans that go beyond sole reliance on physical modalities to treat the individual reporting chronic pain. The psychotherapy must be tailored to take into account the patient's individual traits and life stressors *(Kalira, 2013)*.

Fear of movement or fear of pain due to movement is a significant concern for many patients with chronic pain. Inactivity or avoidance of movement leads to physical deconditioning and disability. Try not to rely on sedative or hypnotic medications to treat the fear many chronic patients show of activity or fear of increased pain. When patients with chronic pain expose themselves to the activities that they fear, which simply means when they do the things they have been afraid of and avoiding, significant reductions are observed in fear, anxiety and even pain level *(Vlaeyen, 2002)*. If patient's fears are excessive, relaxation strategies may be helpful, or referral for more formal and intensive cognitive-behavioral therapy may be necessary.

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Cognitive-Behavior Therapy (CBT)

A person's cognitions or how one thinks about oneself, others and the future can have a major impact on his or her mood, behavior and physiology. Cognitive restructuring involves several steps that help to modify the way in which a patient views pain and his or her ability to cope with pain. The identification of automatic thoughts that lead to negative emotions is targeted in this approach. The negative thoughts are challenged and coping strategies are substituted. Catastrophic thinking is one of the classic cognitive distortions (e.g., my pain is going to kill me).

Problem-solving assists patients with chronic pain in seeing alternative solutions to their life difficulties. Identification of the problem, generation of possible solutions to the problem, prioritizing the solutions, and implementing a single strategy that can be evaluated for effectiveness are the steps in a problem-solving approach. Having patients experiment with different ways of tackling problems can be an effective way of changing habits or beliefs.

Cognitive-behavioral therapy (CBT) has been used in the treatment of chronic pain for over 30 years. A specific technique is rarely used in isolation; rather, cognitive-behavioral components are most often combined in an interdisciplinary structure. The goals of cognitive-behavioral strategies in the management of chronic pain are to improve physical functioning, assist patients in returning to work, reduce disability, reduce pain-related fear/avoidance, and reduce psychological distress and depression *(Eccleston, 2003)*.

Significant literature exists that supports positive outcomes for cognitive-behavioral approaches, and these strategies are considered to be among the most effective for the treatment of chronic pain. Specific outcomes have been noted in randomized controlled trials and other treatment evaluation studies. These studies demonstrate the efficacy of cognitive-behavioral treatment in improving function and mood, and in reducing pain and disability-related behavior, particularly in low back pain *(Kamper, 2014)*. Studies have demonstrated that CBT can reduce the intensity of pain in patients with chronic temporomandibular disorder pain *(Turner, 2006)*, and chronic musculoskeletal pain *(Castro, 2012)*. In addition, there is evidence demonstrating the beneficial effects of writing about stressful experiences and mindfulness meditation in fibromyalgia *(Grossman, 2007; Gillis, 2006; Broderick, 2005; Smyth, 2003)*.

Patients may be referred to a cognitive-behavioral therapist, counselor, social worker or psychologist for treatment.

Dialectical Behavioral Therapy (DBT)

The central premise of DBT, which is a type of CBT, is for the individual to accept his or her frustration in the moment and change the maladaptive behavior associated with that frustration. Strong emotions are acknowledged and validated, with an emphasis on altering behaviors to improve overall functioning *(Stoffers, 2012)*.

Acceptance and Commitment Therapy (ACT)

ACT is a more recent type of CBT. The ACT clinical model has six core processes:

1. Accepting things as they come.
2. Perceiving things as they are.
3. Being in the present moment.
4. Observing yourself in context.
5. Identifying your values.
6. Committing to actions towards your goals *(Hayes, 1999)*.

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A greater acceptance of the pain is associated with decreases in pain intensity, depression, anxiety and level of disability *(McCracken, 1998)*.

Relaxation Therapy

Relaxation therapies include a number of strategies aimed toward lowering general arousal and promoting a state of relaxation. Types of relaxation therapies include:

- Biofeedback
- Imagery
- Diaphragmatic breathing
- Autogenic training
- Progressive muscle relaxation training

It is believed that relaxation reduces levels of anxiety in patients with chronic pain, which enhances pain tolerance and decreases reports of pain. Relaxation techniques also place greater responsibility on patients to expand their repertoire of coping strategies for managing their pain.

Biofeedback is a process in which a person learns to reliably influence two kinds of physiological responses: responses that are not ordinarily under voluntary control (e.g., respiratory rate, muscle tension) and responses that ordinarily are easily regulated (e.g., heart rate) but for which regulation has broken down due to trauma or disease. Biofeedback-assisted relaxation is commonly used in the treatment of various pain conditions. Biofeedback has been found to be effective in headache management *(Haddock, 1997)* and temporomandibular disorders *(Crider, 1999)*.

Imagery is a simple procedure designed to promote general relaxation. This technique involves imagining a pleasant or relaxing scene such as lying in the sun listening to the waves on a beach. With practice, imagery can be used to reduce autonomic arousal and as an effective attention diversion strategy. For most patients, imagery decreases pain intensity, increases pain tolerance, and improves the associated psychosocial factors (e.g., relationships, depression, confidence) in their lives. The pain will not suddenly and completely be imagined away for good, especially if the patient is dealing with a clear-cut physical injury, but the pain will become far less intense, and distressing, and less of an obstacle in day-to-day functioning *(Pincus, 2009)*.

Diaphragmatic breathing or breathing retraining, is a simple strategy that is easily under the patient's control. The goal is to teach patients correct diaphragmatic breathing, which incorporates both slowed (five to eight breaths per minute) and even breathing, with the same rate for exhaling and inhaling.

Autogenic training focuses attention on desired somatic responses such as sensations of warmth and heaviness in the extremities. These responses are believed to facilitate increased blood flow to the extremities, promoting peripheral warming and a reduction in sympathetic nervous system arousal.

Progressive muscle relaxation training involves focusing attention on 14 different muscle groups throughout the body. With this strategy, patients learn to discriminate various forms of muscle tension and, with practice are able to achieve a state of deep relaxation.

Mindfulness-Based Stress Reduction (MBSR)

Mindfulness-based stress reduction (MBSR) has benefits for those with chronic pain *(Ussher, 2014)*. Mind-body treatments such as MBSR and CBT may provide patients with long-lasting skills effective for managing pain *(Cherkin, 2016)*. The goal is to use mindfulness meditation to challenge habitual patterns of cognitive reactivity, that increase distress and exacerbate pain *(Grossman, 2004)*. Mindfulness aims to empower patients to engage in active coping by encouraging them to be aware of the present, where difficult thoughts, feelings and sensations are acknowledged and accepted without judgment *(Shapiro, 2000)*.

Body scans are a key component of mindfulness meditation. They involve directing patients to focus their attention on the present moment by observing their breath, and bodily sensations, while becoming aware of, and accepting without judgment, any thoughts and feelings that arise. MGSR routinely employs brief body scans *(Kabat-Zinn, 2009)* lasting from 5 to 30 minutes. In the general population, brief mindfulness meditation (20-minute duration) has been shown to reduce sensitivity to experimentally induced pain *(Zeidan, 2010)*.

Hypnosis

Hypnosis is believed to involve a combination of focused attention, dissociation and heightened suggestibility. In the last 50 years, hypnosis has been used for many different purposes in the management of pain, including creating a calm, relaxed and comfortable state; altering perception of unpleasant sensory experiences, enhancing motivation for self-care; improving the tolerability and outcome from procedures; and improving performance with rehabilitation exercises. Hypnosis is safe, without significant side effects when used by trained professionals practicing within the area of their training.

In the last two decades, there has been a dramatic increase in the number of published experimental studies and controlled clinical trials on pain control, postoperative pain management, hypnotic analgesia and headache *(Jensen, 2014)*.

Recent brain research from functional MRI scanning showed the reversal of brain changes associated with chronic pain, with regular hypnotic practice. Neurophysiologic studies reveal hypnotic analgesia has clear and measurable effects on brain and spinal cord functioning related to specific hypnotic suggestions *(Dillworth, 2012; Jensen, 2008)*.

Hypnosis has been studied for a variety of chronic pain conditions including cancer pain, low back pain, arthritis, sickle cell disease, temporomandibular disorder, fibromyalgia, disability-related pain and mixed chronic pain conditions. As reviewed by Elkins, 13 controlled prospective trials indicate hypnotic interventions consistently produce significant decreases in pain and were generally more effective than attention, physical therapy and education *(Elkins, 2007)*. Meta-analysis of clinic hypnosis for chronic pain *(Adachi, 2014; Hawkins, 2001)* showed moderate effect when compared to standard care or other psychological interventions.

Systematic review of hypnosis/relaxation therapy for temporomandibular disorder provided three low quality RCTs supporting evidence for pain reduction and maximum jaw opening *(Zhang, 2015)*.

Taken together, these results indicate that clinical hypnosis is efficacious in a broad range of painful conditions across age groups and well tolerated, without significant risks or complications. Hypnosis can be used alone or in combination with other medical or psychological treatment.

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9. Complementary and Integrative Medicine

While often used interchangeably, the terms complementary, alternative and integrative medicine are different, though interrelated, concepts.

Complementary medicine is a non-mainstream practice used together with conventional medicine.

Alternative medicine is a non-mainstream practice used in place of conventional medicine.

Integrative medicine is a therapeutic modality that combines complementary treatments with conventional medicine in a coordinated way.

https://nccih.nih.gov

https://nccih.nih.gov/health/integrative-health

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More evidence has emerged in recent years evaluating some of these practices, but more research is warranted. Below is a brief description of a few common cultural practices and herbal supplements that have been explored for the treatment of pain. For more information, see the National Institute of Health National Center for Complementary and Integrative Medicine at https://nccih.nih.gov/.

Modality	Description	Indication
Acupuncture	A procedure developed in China involving the stimulation of points on the body using thin solid metallic needles manipulated by hands, electrical stimulation or low-level laser that releases chi or qi, causing reduction in pain or dysfunction.	Musculoskeletal pain *(Lam, 2013; Lee, 2013; Furlan, 2012)*
Qi-gong and healing touch therapy	A gentle energy field therapy that facilitates a deep sense of calm and relaxation in the body-mind-spirit.	Fibromyalgia *(Liu, 2012)* Chronic neck pain in older women *(Holmberg, 2014)* Persistent pain in older adults *(Wardell, 2012)*
Tai-chi and yoga	Mind and body practices that combine physical posturing with breathing, meditation and relaxation, improving the perception of pain.	Chronic low back pain *(Tilbrook, 2014; Tekur, 2012)*
Ayurvedic medicine	Developed in India 5,000 years ago using a variety of components including herbs, minerals, metals and mind-body-spirit to prevent disease.	Use of some combinations have been shown to have anti-inflammatory effects *(U.S. Department of Health and Human Services, 2013)* May be harmful if used without direction of a trained practitioner

Herbal Supplements

Herbal supplements are widely used, and it is important to question patients about their use when taking a medication history. Many herbal supplements are not standardized, and the content of the ingredients can vary substantially from the label and between lots of the same product *(Gurley, 2000)*. Patients are often misinformed and believe that since herbals are natural products, they are safer than prescription medications. Patients who use herbal supplements should be cautioned about adverse effects, drug interactions and the potential impurities of these products *(Miller, 1998; Winslow, 1998)*.

There is limited evidence of efficacy for many of these supplements. Some have known toxicities and significant drug interactions, and their use should be discouraged. While there are many herbal supplements used for pain, the following have little supporting data for use in the treatment of pain but may still have significant potential for drug interactions and adverse effects.

Harpagophytum

Devil's Claw has conflicting evidence about efficacy as an anti-inflammatory or analgesic agent. There are wide variations in chemical components of products. It may have benefits for the treatment of lower back pain. Devil's Claw may increase gastric acid secretion, antagonize the effects of H-2 antagonists, and has anticoagulant effects *(Gagnier, 2007)*.

Arnica is a natural product that is available in a topical cream or gel, and is often used for inflammatory or muscle pain. Oral use is toxic and should be avoided but topical use is generally safe. Arnica has been shown to have anti-inflammatory properties and has benefits for the treatment of osteoarthritis *(Ross, 2008)*. Arnica has also been used for musculoskeletal pain but the evidence for this indication is lacking.

Glucosamine and Chondroitin is commonly used for osteoarthritis, but evidence for efficacy is lacking. Even though some patients get symptomatic relief it does not have disease-modifying effects; nor does it treat or slow the progression of osteoarthritis *(McAlindon, 2014; Hochberg, 2012; Stanton, 2012)*.

Willow bark contains the active ingredient salicia, the precursor of aspirin. Products should be standardized to 60-120 mg salicia per day. Patients allergic to aspirin or NSAIDs may be allergic to Willow Bark and the adverse effect profile is similar to that of aspirin. Willow bark may be useful in the treatment of low back pain *(Gagnier, 2007)*.

Cayenne (C. frutescens) is a topical preparations show improvement over placebo for neuropathic pain *(Pittler, 2008)*.

Lavender essential oils (S. Alba, S. officinale L, S. chilinesis) were shown to reduce low back pain in the short-term compared to placebo *(Oltean, 2014)*.

Medical Cannabis

Cannabis is classified by the DEA as a Schedule I substance and under federal law cannot be disposed for medical treatment. The state of Minnesota has a medical cannabis statue, allowed for use in certain conditions. Intractable pain is an approved certifying condition for medical cannabis in Minnesota. For more information on state regulations, please visit the Minnesota Department of Health website: https://www.health.state.mn.us/people/cannabis/index.html.

A systematic review of medical cannabis for non-cancer pain was completed by the Minnesota Evidence-based Practice Center. This review searched multiple databases from inception to July, 2015 and found only 19 eligible articles representing 21 studies. The most commonly studied form of medical cannabis was nabiximols a botanical-based mouth spray not currently FDA approved. The review found low-strength evidence favoring nabiximols over placebo among adults with peripheral neuropathic pain. No difference between nabiximols and placebo was found for patients with MS and central neuropathic pain. All other evidence was deemed to be insufficient strength *(Butler, 2015)*.

The ICSI work group conducted a literature search to review evidence published after July 2015. The only study found was by Wallace et al (2015). This small, randomized study (n=16) looked at the effect of inhaled cannabis on diabetic peripheral neuropathy.

After reviewing the literature, the work group concludes that further research is needed to assess both the short and long-term benefits and harms. Therefore, the group makes no recommendation regarding medical cannabis for non-cancer pain.

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10. Physical Rehabilitation Modalities

Work Group Recommendation
Exercise should be a component of the treatment for a patient with chronic pain.
Benefit: Exercise improves chronic pain symptoms and functional status, and bolsters overall health and sense of well-being. **Harm:** There may be potential exacerbation of underlying, or undiagnosed, musculoskeletal injury, cardiovascular or neurologic disease. **Benefit-Harms Assessment:** There is not one particular exercise that is superior, and the optimal frequency has not been demonstrated. The current evidence suggests at least 2-3 exercise sessions per week are necessary for clinical benefit.
Relevant Resources: *Falla, 2013 (Randomized Control Trial); Cuesta-Vargas, 2011 (Randomized Control Trial); Hayden, 2011 (Systematic Review); Standaert, 2011 (Systematic Review); Dufour, 2010 (Randomized Control Trial); Hall, 2008 (Systematic Review/Meta-Analysis); Hurwitz, 2008 (Evidence Synthesis)*

Work Group Recommendation
Passive modalities should be performed only as an adjunct to a concomitant active physical therapy or exercise program.
Benefit: Passive physical treatments provide short-term pain relief and potential medium-term benefit. **Harm:** There is minimal risk of harm when applied by trained practitioners. **Benefit-Harms Assessment:** Recommend passive treatments only as a complement to an active therapy or exercise program.
Relevant Resources: *Vincent, 2013 (Systematic Review); Standaert, 2011 (Systematic Review)*

Work Group Recommendation
Extending physical therapy beyond 8-12 weeks for chronic pain patients should be based on objective clinical improvement.
Benefit: Physical therapy facilitates rehabilitation and optimizes functional performance in chronic pain patients when used appropriately. **Harm:** There may be additional resources and cost for patients and service providers without evidence of improved outcomes. **Benefit-Harms Assessment:** An active physical therapy program is recommended. Deconditioned pain patients should begin with a graded or progressive physical therapy program to minimize risk of exercise associated injury, and improve patient engagement and compliance.
Relevant Resources: *Cuesta-Vargas, 2015 (Randomized Control Trial); Cramer, 2013 (Randomized Control Trial); Falla, 2013 (Randomized Control Trial); Standaert, 2011 (Systematic Review); Dundar, 2009 (Randomized Control Trial); Koumantakis, 2005 (Randomized Control Trial); Rainville, 2002 (Observational Study)*

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Exercise and Active Physical Therapy

Exercise as a therapeutic intervention is defined as a structured, repetitive, physical activity aimed to improve or maintain physical fitness *(Caspersen, 1985)*. Clinicians should consider the effectiveness, appropriate dose and potential adverse events when prescribing exercise or physical therapy. A patient-centered approach encourages the patient to be an active participant in the treatment program, which improves clinical outcomes *(Jordan, 2010)*.

Active therapy is defined as strength training and/or conditioning exercise performed by patients under the direction of a licensed practitioner such as a physician, physical therapist or athletic trainer.

Indications/considerations

- All patients with chronic pain should participate in an exercise program to improve function and fitness *(Malmivaara, 2006)*. Formal physical therapy and recreational or self-directed exercise are both beneficial for chronic pain rehabilitation.
- Exercise under expert direction of a physical therapist has demonstrable efficacy in the medical literature in improving pain symptoms and functional performance in chronic pain patients *(Falla, 2013; Cuesta-Vargas, 2011; Hayden, 2011; Standaert, 2011; van Middelkoop, 2011; Hall, 2008; Hurwitz, 2008; Malmivaara, 2006)*.
- Since most patients with chronic pain are physically deconditioned from inactivity, graded or progressive physical therapy is recommended. This approach is better tolerated in this population, which improves patient participation and compliance. Progressive therapy focuses on motor learning principles where specific muscular contractions are first learned and mastered before moving on to a sequence of muscular movements with increasing load *(Falla, 2013; Jull, 2009; Lindström, 1992)*.
- One type of exercise has not been shown to be definitively more effective than another. Studies have shown benefit of flexion exercises, extension exercises, isokinetic intensive machine muscle strengthening, and group aerobic low-impact exercises. Group aerobic exercise and stretching can be as beneficial as structured land-based physical therapy, suggesting this is a reasonable, low-cost alternative for patients *(Mannion, 1999)*.
- Aquatic physical therapy, usually performed in warm water (30-35ºC/86-95ºF), is well tolerated by patients with painful chronic musculoskeletal or neurologic disease. The buoyancy and thermal comfort of warm water exercise decreases nociception via multiple physiologic mechanisms and increases ease of movement *(Hall, 2008)*. Appropriate indications for aquatic therapy are gait instability, neuromuscular disease, inflammatory or degenerative joint disease, morbid obesity, or deconditioning secondary to acute/subacute medical illness *(Dundar, 2009)*. Two sessions of aquatic therapy per week is equally efficacious as three sessions per week *(Cuesta-Vargas, 2015)*.
- Active physical therapy for chronic spinal pain conditions should show clinical improvement in pain and function within 8-12 weeks of initiation. Typical physical therapy sessions are 30-90 minutes, occurring two to three times per week, often with an additional daily home exercise program of 10 minutes.
- If no clinical benefit occurs within this time frame, the appropriateness and efficacy for the prescribed physical therapy should be reconsidered *(Cuesta-Vargas, 2015; Cramer, 2013; Falla, 2013; Standaert, 2011)*.
- Geriatric patients can benefit from a physical rehabilitation program. The American Geriatric Society Panel of Exercise and Osteoarthritis encourages light- to moderate-intensity physical activity for both prevention and possibly restoration of health and functional capacity in patients with chronic disease *(American Geriatrics Society Panel on Exercise and Osteoarthritis, 2001)*.

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Passive Physical Treatments

Passive therapies are defined as the external application of manual and physical treatments to the patient by a clinician. As part of the Choosing Wisely® campaign, the American Physical Therapy Association recommends that clinicians don't employ passive physical agents except when necessary to facilitate participation in an active treatment program. The definitions and indications for conventional passive physical modalities are detailed below.

Spinal manipulation therapy

This is a specific type of manual therapy performed directly on patients by specially trained physicians (DO, MD), chiropractors and physical therapists. It usually involves applying high-velocity low amplitude thrust movements, or slow passive muscle relaxation techniques to increase range of motion and reduce spinal pain.

Indications/considerations

- Manual therapies treating chronic non-specific axial neck pain have been demonstrated, in a systematic review of high-quality RCT's, to have moderate short-term efficacy and minimal long-term efficacy. Manual therapies included in this review were typical chiropractic or osteopathic technical procedures: manipulation, passive mobilization and myofascial relaxation techniques. There was not one particular manual therapy superior to the others. A key finding was that concurrent exercise therapy improved the efficacy of all manual therapies *(Vincent, 2013)*.
- Spinal manipulation therapy for chronic low back pain has similar clinical improvements relative to structured exercise after two months. This was based on a rigorous systematic review, though the evidence for this conclusion is low *(Standaert, 2011)*.
- Spinal manipulative therapy has been shown to be effective in the early intervention of low back pain *(Dagenais, 2010; Walker, 2010; Jüni, 2009; Santilli, 2006; Assendelft, 2004)*.

Traction

Traction therapy is an applied external force to physically distract spinal facet joints and intervertebral foramina. It can be applied manually or with mechanical devices such as a home cervical traction unit.

Indication/considerations

- Cervical spine traction for radiculopathy and axial neck pain is a common practice, though high quality RCTs have not shown any significant clinical benefit over standard physical therapy *(Young, 2009; Borman, 2008)*.
- There is a paucity of recent prospective trials for lumbar spinal traction therapy, and currently there is not any high-quality evidence showing clinical efficacy.
- It is contraindicated in patients with cervical spine instability or craniocervical junction anatomical derangement as seen in rheumatoid arthritis or advanced cervical spondylosis.

Massage therapy

Massage therapy is the manual manipulation of musculoskeletal and connective tissue to improve relaxation and enhance physical rehabilitation.

Indications/considerations:

- Massage therapy has been shown to reduce pain scores for patients with low back pain *(Hsieh, 2006; Cherkin, 2001)*, osteoarthritis of the knee *(Perlman, 2006)*, juvenile rheumatoid arthritis *(Field, 1997)*, chronic neck pain *(Bakar, 2014)* and fibromyalgia *(Brattberg, 1999)*.
- Yet to be determined are the optimal number, duration and frequency of sessions for treating pain.

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Transcutaneous electrical nerve stimulation (TENS)

TENS therapy is the application of low-voltage electrical stimulation to the skin with contact electrodes. Conventional technique uses four electrodes placed around the painful region, delivering 10-30 mA electrical intensity at high frequency (40-150Hz) for 30-60 minutes duration once or twice daily. The proposed pain control mechanisms involve sensory modulation of the central nervous system via the Gate and Endorphin Theories *(Cifu, 2016)*.

Indications/considerations

- Most chronic neuropathic and musculoskeletal pain syndromes can be safely treated with TENS therapy *(Cifu, 2016)*.
- Application near or over a pacemaker/implanted defibrillator, anterior neck, anterior chest, gravid abdomen or insensate skin is contraindicated due to the potential risks *(Cifu, 2016)*.

Ultrasound

Ultrasound therapy is the application of high-frequency sound waves (> 20,000 Hz) to the skin for deep soft tissue heating using a piezoelectric sound generator, which is also called a transducer. Treatment goal is to increase tissue temperature to 40-45ºC (104-113ºF) for therapeutic effects of increased blood flow, decreased chronic inflammation, increased soft tissue flexibility and reduced pain *(Cifu, 2016)*.

Indications/considerations

- Usual indications are painful musculoskeletal conditions: muscle spasm, contracture, chronic inflammation, and chronic joint and tendon pain *(Cifu, 2016)*.
- Due to the physical properties of ultrasound, prolonged use directly over cortical bone could potentially lead to excessive heating and thermal injury *(Cifu, 2016)*.
- Only competently trained practitioners should apply this modality *(Cifu, 2016)*.

Lumbar spine corsets and braces

There is a multitude of available off-the-shelf (OTS) and custom-fitted (Rx), circumferential lower torso braces typically termed corsets, which are soft, or lumbosacral orthoses, which are semi-rigid or fully rigid, from integrated hard plastic or metal panels. This group of appliances exerts minimal external structural support to the lumbar spine by increasing intra-abdominal pressure and provides increased spinal proprioception to improve posture. Goals of application are to minimize painful or abnormal lumbar spinal motion and improve activity endurance by increasing paraspinal muscle tone *(Rao, 2012)*.

Indications/considerations

- Usual indications are subacute or chronic lumbar spinal disease and injury such as disc herniation, stable vertebral compression fractures, arthritic pain, lumbar scoliosis, paraspinal muscle strain or non-specific chronic low back pain.
- Prescription lumbosacral orthoses are fit by orthotists, who are licensed practitioners with expertise in creating and applying braces.

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11. Interventional Treatment

In general, interventional treatments refer to various percutaneous or minor surgical procedures targeting specific anatomical structures identified as possible sources of pain. Although no specific temporal criteria are available to guide referral, patients who have failed conservative treatment are generally considered to be potential candidates for this form of therapy.

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Diagnostic Injections

Indications: Identify specific anatomical structures contributing to pain symptoms.

Diagnostic injections are often used to confirm a putative diagnosis and to identify patients who may be candidates for further interventional treatments. Blocks targeting nerves innervating the lumbar facet joints (e.g., medial branch blocks) and sacroiliac joints (e.g., both intra- and extra-articular blocks) help distinguish patients with axial low back pain who may be candidates for percutaneous radio frequency denervation procedures *(Cohen, 2010; Cohen, 2008)*.

Provocative discography is often touted as the only means to establish a relationship between disc pathology and symptoms, but it is characterized by a high false-positive rate in some patients (e.g., those with psychopathology and prior surgery) *(Provenzano, 2012)*. Furthermore, the evidence that discography may improve surgical outcomes is limited to one recent subgroup analysis of a randomized study comparing fusion outcomes in those patients who underwent pre-surgical discography screening and those who did not *(Margetic, 2013)*.

Among patients with radicular pain, selective nerve root blocks can be considered when imaging, physical examination or electrodiagnostic studies are inconsistent or non-corroborative *(Yeom, 2008)*.

Therapeutic Injections

The use of injections and other minimally invasive interventions has risen dramatically over the past decade, but increased utilization has not been generally accompanied by a concomitant reduction in disability rates or surgical procedures *(Manchikanti, 2012b; Deyo, 2009)*.

Interlaminar epidural steroid injections

Indications: Radicular spine pain

Epidural steroid injections (ESIs) are the most frequently performed image-guided pain medicine procedures for radicular pain. There are three approaches to the epidural space: interlaminar, transforaminal and caudal techniques.

In well-selected patients, ESIs appear to provide significant benefit compared to sham injections and conservative treatments for approximately six weeks, but not all studies suggest that patients may experience more sustained benefits *(Friedly, 2014; Cohen, 2013a)*. Similar to other treatments, patients with greater disease burden, on opioid therapy; and with coexisting psychosocial dysfunction are less likely to respond to ESIs *(Kirpalani, 2011; Hopwood, 1993; Jamison, 1991)*.

One recent systematic review found that ESIs may possibly reduce the need for surgery in the short term *(Bicket, 2015)*, but the evidence for long-term surgery prevention is mostly anecdotal and based on indirect evidence or small clinical trials *(Riew, 2006)*.

Technical factors that may improve ESI treatment results include the use of transforaminal rather than interlaminar injections, and the use of depo-steroids *(Cohen, 2013a)*. However, the administration of transforaminal depo-steroids may be associated with rare but catastrophic consequences including spinal cord infarction, especially when used in the cervical spine *(Benzon, 2015; Alturi, 2013)*.

Researchers are investigating alternatives to the administration of epidural steroids. One such alternative that has garnered intense interest is the use of inflammatory cytokine inhibitors such as the tumor necrosis factor antagonist etanercept. To date, clinical trials evaluating epidural etanercept have yielded conflicting results *(Freeman, 2013; Cohen, 2012; Ohtori, 2012)*.

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Facet joint injections

Indications: Axial spine pain

Facet joints are an important source of spinal pain in the cervical and lumbar regions. These joints can be reliably anesthetized by way of fluoroscopically guided joint injections. Generally, a depot corticosteroid is administered concomitantly. However, mixed evidence exists regarding the sustained therapeutic benefits of facet joint corticosteroid injections *(Manchikanti, 2015a; Manchikanti, 2015b; Staal, 2009)*.

Indications: Axial spine pain

Sacroiliac joint injections

Indications: Lateral low back or upper gluteal pain

The sacroiliac joint is a widely recognized source of low back and buttock pain but may also include lower extremity pain. Diagnostic blocks using local anesthetic can confirm this structure as a source of low back and leg pain. Corticosteroids are often incorporated into the injection. Currently, there is an evolving clinical practice of using ultrasound as a means to provide imaging for both diagnostic blocks and therapeutic injections *(Wu, 2016)*. Conflicting evidence exists regarding the efficacy of sacroiliac joint injections *(Kennedy, 2015; Scholten, 2015; Simopoulos, 2015)*.

Radio frequency neurotomy

Indications: Axial low back or neck pain

Percutaneous radio frequency (RF) neurotomy is a treatment for facet-related neck and back pain. This procedure has also been used to treat sacroiliac joint pain. Properly selected candidates for this procedure should experience complete or nearly complete relief of their pain following fluoroscopically guided, low-volume local anesthetic blocks of the medial or lateral branch nerves that innervate the targeted joints *(Cohen, 2013b; Hansen, 2012; Cohen, 2007)*. To minimize false-positive results, an equivalent degree of relief of an appropriate pharmacologic duration should be carefully documented on two separate occasions, using two different types of local anesthetic. The RF procedure is performed by placing an insulated needle electrode with an exposed tip adjacent to and in parallel with the medial or lateral branch nerves that supply the target joints. Radio frequency current applied to the electrode then heats the adjacent tissues and coagulates the nerve supply to the joint. Mixed evidence exists regarding the efficacy of RF neurotomy *(Maas, 2015; Manchikanti, 2015a)*.

Intervertebral disc procedures

Indications: Midline low back with or without radiation to the thigh area

A variety of interventions has been developed to treat discogenic pain. Placebo-controlled studies evaluating intradiscal steroids *(Khot, 2004; Simmons, 1992)* and cytokine inhibitors *(Cohen, 2007)* have yielded negative results. Although an initial placebo-controlled study evaluating intradiscal methylene blue injection demonstrated a success rate of over 90% at two-year follow-up *(Peng, 2010)*, the lack of supporting preclinical evidence and the failure to replicate these results in subsequent uncontrolled studies have led to the virtual abandonment of this treatment *(Gupta, 2012; Kim, 2012)*. Several techniques have been developed to treat discogenic low back pain by heating intradiscal elements. Although an early controlled study suggested that some patients may benefit from intradiscal electrothermal therapy (IDET) *(Pauza, 2004)* – a treatment that purportedly acts by coagulating pain receptors, altering collagen architecture in the disc, and sealing annular tears – subsequent studies either failed to replicate these results *(Kvarstein, 2009; Freeman, 2005)* or found only short-term benefits *(Freedman, 2003)*. More recently, a similar procedure known as biacuplasty has emerged that circumvents some of the technical problems associated with performing IDET. Randomized trials suggest that patients who underwent biacuplasty obtained better pain relief and functional improvement compared to controls, with the results persisting through one-year follow-up *(Desai, 2016; Kapural,*

2015a). However, concerns regarding the risk of disc injury after annulus puncture limit the widespread use of this treatment at the current time.

Myofascial trigger point injections

Indications: Localized muscular pain

Myofascial pain is characterized by the presence of trigger points, which are hyperirritable tense bands of skeletal muscles *(Malanga, 2010)*. Patients will typically present with a history of localized or regional pain, and the range of motion may be reduced in the affected muscles. On physical examination, palpation of a trigger point will typically provoke sharp localized pain that may be referred to a contiguous body region, although this can be difficult if not impossible to discern in non-superficial muscles *(Malanga, 2010)*. The efficacy of local anesthetic, steroid, botulinum toxin and dry needle myofascial trigger point injections are mixed *(Liu, 2015; Ong, 2014; Kietrys, 2013; Waseem, 2011; Staal, 2009; Cummings, 2001)*.

Advanced Interventional Therapies

Neurostimulation

Indications: Radicular spine pain not refractory to other conventional pharmacologic and interventional treatments

Neurostimulation – which includes spinal cord, dorsal root ganglion, motor cortex and deep brain stimulation – provides pain relief through modulation of the nervous system. Spinal cord stimulation, the most widely used neurostimulation technique, involves placement of electrodes in the epidural space. Referral to a pain medicine specialist for a neurostimulation evaluation is typically reserved for patients who have failed other pain therapies including medications, injections and physical modalities. Spinal cord stimulation exerts analgesic effects by stimulating large, fast-conducting sensory fibers, thereby inhibiting the slower-conducting A-delta and C nociceptive fibers responsible for pain transmission.

Conventional spinal cord stimulation acts by creating an area of paresthesia within the anatomical distribution of pain, though high-frequency and burst stimulation have been found to be more effective than traditional stimulation for alleviating pain without the accompanying paresthesias *(Pope, 2015; Bartleson, 2009)*. One of the most widely recognized indications for neurostimulation is refractory radicular pain in association with failed back surgery syndrome *(Deer, 2014)*. Although the evidence supporting neurostimulation for axial low back pain is limited, a recent randomized study found high-frequency spinal cord stimulation to be more effective than conventional stimulation *(Kapural, 2015b; Deer, 2014)*. Other indications include neuropathic pain, ischemic pain and refractory angina. However, the evidence supporting use of neurostimulation is mixed *(Grider, 2016; Tsigaridas, 2015; Frey, 2009; Simpson, 2009; Taylor, 2009)*.

Intrathecal drug delivery systems

Indications: Severe pain syndromes refractory to conventional therapies

Intrathecal drug delivery systems, also referred to as pain pumps or morphine pumps, administer medications directly to the intrathecal space *(Prager, 2014)*. A small caliber catheter is placed percutaneously in the intrathecal space and tunneled subcutaneously to a programmable reservoir pump that is typically implanted in the subcutaneous tissues of the lower abdominal region. Medications that are typically used as solo therapy or in combination include opioids (e.g., morphine, hydromorphone, fentanyl), local anesthetics (e.g., bupivacaine), clonidine and ziconotide, which is a novel N-type voltage-gated calcium channel blocker approved only for intrathecal use *(Deer, 2012)*. Although the primary indication for intrathecal drug delivery is intractable cancer-related pain, patients with refractory and possibly inoperable low back pain due to failed back surgery syndrome or, less frequently, spinal stenosis may occasionally be considered for intrathecal drug delivery *(Deer, 2012)*. Intrathecal drug delivery systems have been shown to have favorable

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benefits on pain, functionality and health care expenditures *(Bolash, 2015; Hatheway, 2015; Guillemette, 2013; Patel, 2009; Turner, 2007)*.

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12. Pharmacologic Treatment

Pharmacologic treatment alone should not be relied upon for treatment of chronic pain, but rather used as an adjunct to patient engagement and other modalities. Pharmacologic treatments should be initiated to increase function and restore a patient's overall quality of life, not just pain relief. Medications are not the focus of treatment in managing pain. They should be used when needed to meet overall goals of therapy in conjunction with other treatment modalities, such as psychosocial, rehabilitation and functional management, non-pharmacologic, complementary medicine and interventional management.

General principles for pharmacologic management *(Wisconsin Medical Society Task Force on Pain Management, 2004)*

- A thorough medication history is critical to the development of an effective treatment plan. This should include prescription medications, over-the-counter medications, herbals and supplements.
- Base the initial choice of medication(s) on the severity and type of pain, as well as patient specific factors including age, co-existing diseases, other current medications and medication history.
- Define the goals of therapy before prescribing, and tailor medications to meet the individual goals of each patient by using shared decision-making.
- Look for medication-related fears and misconceptions, as they may lead to poor compliance with a therapeutic regimen.
- Give medications an adequate therapeutic trial. When treating inflammatory or neuropathic pain, benefits may take weeks or longer to appear.
- Patients need to know that whether prescribed or non-prescribed, all medications have risks and benefits. Watch for and manage side effects.
- Rational poly-pharmacy, or multi-nodal analgesia, includes the use of two or more medications with complementary mechanisms of action that may provide greater pain relief with less toxicity by using lower doses of each medication. However, avoid prescribing two medications in the same class at the same time. Use the least invasive route of administration, preferably oral.
- Be alert for additive side effects and possible interactions with other medication the patient is taking. Titrate doses to achieve optimal balance between analgesic benefit, side effects and functional improvement. Some medications require gradual upward titration to achieve optimal analgesia and to minimize adverse effects.
- Taper and discontinue medications that do not produce the desired therapeutic outcome and do not meet the treatment goals. This practice helps to prevent expensive and potentially dangerous poly-pharmacy.

Non-Opioid Medications:

The following non-opioid medication classes may be used for pain treatment.

- Acetaminophen
- Anticonvulsants
- Antidepressants
- Glucocorticosteroids

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- Muscle relaxants and antispasmodics
- Non-steroidal anti-inflammatory drugs (NSAIDs)

See Appendix B, "Non-Opioid Pharmacology," for details about each of these classes, including names of medications, indications, general mechanism, common adverse events, contraindications and monitoring parameters.

The work group does want to highlight one recommendation related to non-sedative and sedative hypnotics benzodiazepines and muscle relaxants.

Work Group Recommendation
• **Sedative hypnotics including benzodiazepines and carisoprodol should be rarely used and if so for short-term (< 1 week) treatment of muscle spasms related to acute pain.** • **Use of non-sedative hypnotic muscle relaxants are of low benefit, but if used, limit to less than four weeks.** • **Do not use carisoprodol for pain.**
Benefit: Skeletal muscle relaxants are better than placebo but not more effective than NSAIDs in the treatment of low back pain. Sedative hypnotics are effective for treating anxiety and muscle spasms in acute pain. **Harm:** Muscle relaxants are central nervous system (CNS) depressants and cause additive sedation and other adverse effects, especially in combination with opioids. Sedative hypnotics have significant side effects, specifically in the geriatric population. Additive side effects when taken with other CNS depressants are potential for dependence and withdrawal symptoms. **Benefit-Harms Assessment:** Muscle relaxants should not be used as the standard first-line treatment but may provide short-term benefit in some patients. Risk of significant side effects and potential for dependence and withdrawal outweigh the benefit for long-term use.
Relevant Resources: *American Geriatrics Society 2015 Beers Criteria Update Expert Panel, 2015 (Guideline); Gray, 2015 (Observational Study); Petrov, 2014 (Observational Study); Richards, 2012 (Systematic Review); Liu, 2010 (Observational Study); Chou, 2007 (Guideline); van Tulder, 2003 (Systematic Review)*

Opioid Medications

For more information on opioid pharmacology, including names of medications, indications, mechanism of action, common adverse effects, contraindications, hepatic/renal dosing, opioid utilization, as well as individual medication details, see Appendix C, "Opioid Pharmacology." The following section provides an in-depth discussion of opioid management.

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13. Opioid Management

Opioid Overview

In 2014, 245 million prescriptions of opioids were dispensed in the United States. Three to four percent of Americans are taking chronic opioids *(Volkow, 2016b)*, and hydrocodone combined with acetaminophen was the most common prescription written in 2010 *(DeNoon, 2011)*. Musculoskeletal complaints occupy three of the five top causes of years lived with disability in America *(Murray, 2013)*.

Opioids encompass a large group of chemicals, that activate the muopioid receptor, reducing pain among other actions. While the potency (or dosing) varies, the efficacy of all opioid agonists is comparable. No opioid is inherently safer, or more efficacious, or more addictive than another. The dose, the route it is administered, the individual differences of the patient and the medication formulation are some variables

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that account for different individual responses to opioids. Opioids are regulated by the Drug Enforcement Agency (DEA) as schedule II medications. One exception is tramadol, a schedule IV medication, which is sometimes overlooked as an opioid because of its mixed receptor action *(Drug Enforcement Administration, 2014a; Drug Enforcement Administration, 2014b)*. Emergency visits due to tramadol-related harms are rising *(Substance Abuse and Mental Health Services Administration, The, 2015)*. Another exception is heroin, chemically called diacetylmorphine, which is a schedule I in the United States but used medicinally in other countries. Heroin is not fundamentally different from the opioids clinicians routinely prescribe, a fact that accounts for the rising use of heroin among pharmaceutical opioid users *(Compton, 2016; Dart, 2015; Cicero, 2014; Thomas, 2014; Kuehn, 2013)*. The heroin epidemic and pharmaceutical opioid epidemic are intertwined.

Starting in the 1990s, because of an increased focus on improving patient pain scores, changing federal and state regulations, and a growing array of pharmaceutical opioids being marketed, opioid prescriptions increased dramatically *(Zgierska, 2012; Dhalla, 2011; Von Korff, 2011)*. Clinicians began prescribing new opioid formulations for a growing list of indications to a wider spectrum of patients, for durations and in dosages not previously used *(Chen, 2016; Kuehn, 2014)*. These changes happened without high-quality medical evidence to support them *(Chou, 2015; Dowell, 2013; Okie, 2010; Chou, 2009a)*. A new standard of practice evolved, embracing the widespread use of opioids for pain *(Von Korff, 2011)*.

At the time, providers were encouraged to titrate opioid doses to a patient's report of pain and not to functional status. Clinicians were reassured that addiction was a rare adverse event when opioids were prescribed for pain *(Porter, 1980)*. Risk assessment tools were developed to screen for patients at high risk of addiction and overdose *(Passik, 2008; Webster, 2005)*. Some prescribers incorrectly concluded that those who do not screen positive were risk-free. Experts advised that very high doses of opioids do not pose a risk to patients, as long as the patient had tolerance. However, increasing evidence disproves these recommendations *(Dhalla, 2011; Von Korff, 2011)*.

It is now clear that many people are hurt and even killed by opioids *(Dhalla, 2011; Centers for Disease Control and Prevention, 2011)*. Families and communities have suffered from what the CDC calls the "opioid epidemic" *(Centers for Disease Control and Prevention, 2015)*. Medical experts, payers, regulatory agencies and members of the public are calling for a change in current opioid prescribing practices: fewer prescriptions, fewer pills, lower dosages, tamper-proof formulations, and increased screening and referrals for opioid addiction. Some of the above reactions to the opioid epidemic have evidence supporting them, but many do not.

Even though the medical/dental community clearly acknowledges that our past prescribing practices created a problem, current opioid prescribing practices are still largely informed by poor-quality medical evidence *(Chou, 2015; Nuckols, 2014; Von Korff, 2011)*. In this vacuum of evidence, the standard of care has begun shifting away from liberal opioid prescribing toward increased demands on patients and prescribers *(Buppert, 2015)*. Some clinicians and patients are concerned about these changes, particularly that pain may be undertreated or that patients will be harmed by abrupt discontinuation of opioids.

Every day patients seek medical care in droves, hoping for relief from painful conditions. Some patients already on opioids continue to experience pain even as they face adverse effects of the opioids. Sometimes the risks are so great that the opioids need to be stopped immediately despite the patients' pain. Clinicians feel that their training and the health care systems employing them do not support the right decisions. Providing meaningful recommendations for opioid prescribers in this charged and changing climate is challenging. In the following section, the work group has highlighted the available evidence to date and relied on expert opinion (of this group and other work groups) in areas lacking evidence to summarize recommended courses of action and the range of acceptable clinical practice. Special attention will be paid to providing other modalities to minimize the harms of opioids.

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Overall, it is clear that the best way to reduce the harms of opioids is to prescribe them only when needed and only in the minimum quantity needed *(Coffin, 2014; Lembke, 2012)*.

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13.1. Have Non-Opioid Approaches Been Considered?

Rarely should the first choice for management of pain be opioids. The first opioid prescription should be given only after other options are tried or carefully considered. Furthermore, even after an initial prescription for opioids, prescribers should consider non-opioid treatment alternatives before prescribing refills. Such alternatives, detailed elsewhere in the guideline, include psychotherapy strategies, complementary alternative medicine, physical modalities and rehabilitation, non-opioid pharmacology and interventional treatment.

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13.2. Risk Assessment

Before initiating opioids for pain, providers should seek a specific diagnostic cause of the pain, and document objective findings on physical exam or other objective tests.

Risk Assessment Tools

Recommendation
Opioid risk assessment tools and knowledge of opioid-related risks should be used in combination with the overall clinical picture to guide care, including the decision to prescribe as well as how closely to monitor.
Benefit: Assessment of opioid-related risks may help physicians weigh risks against benefits when deciding if to prescribe opioids. In addition, knowledge of the risk factors for the various adverse outcomes of opioids helps physicians determine the intensity of monitoring and follow-up for patients. Reviewing the risks also serves as a patient education tool. **Harm:** The use of risk assessment tools does not have an adequate sensitivity or specificity to predict opioid-related harms or to rule them out. Universal precautions should be used for all patients receiving opioids. Using risk assessment tools has not been shown to improve clinical outcomes. Risk assessment tools should not be used to exclude patients with mental health or addictive disorders from proper treatment of pain. **Benefit-Harms Assessment:** Used correctly, knowledge of the risks of opioid related harm, including risk assessment tools, can help providers more carefully monitor those at high risk. In cases where the risk/benefit of opioids is uncertain, risk assessment can tip the provider against use of opioids. These tools can also be used incorrectly; for instance, they cannot be used to assure a patient that he or she has no risk, and they should not be used to exclude mentally ill patients from routine treatment of pain.
Relevant Resources: *Volkow, 2016b (Report); Wasan, 2015 (Observational Study); Argoff, 2014 (Systematic Review); Jones, 2014 (Observational Study); Atluri, 2012 (Review); Jones, 2012 (Observational Study); Moore, 2009 (Observational Study)*

Many risk assessment tools have been developed but unfortunately none of them has the sensitivity or specificity required to reassure a patient that he or she is risk-free from the harms of opioids *(Jones, 2014; Jones, 2012; Moore, 2009)*. There is limited evidence that the use of risk assessment tools in practice decreases adverse effects *(Argoff, 2014; Chou, 2009a)*. Risk assessment tools have been used to exclude patients from receiving opioid analgesia, but this is not their proper use. The risks must be balanced against the benefits. Patients at high risk must be carefully considered, and conditions with low or no benefit should avoid opioid use. (See the following Opioid Prescribing Protocol Risk/Benefit Chart.)

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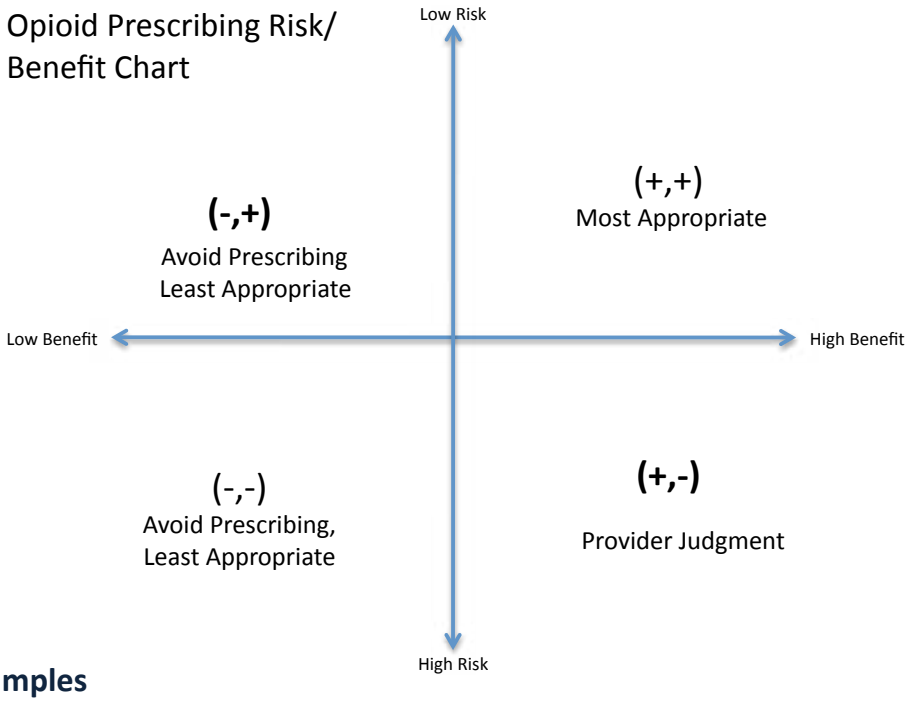

Examples

Condition	Risk Factors	Appropriateness
Pancreatitis	None	(+,+) High Benefit, Low Risk= **Most Appropriate**
Pancreatitis	Alcoholic	(+,-) High Benefit, High Risk= **Provider Judgment**
Fractured Ankle	None	(+,+) High Benefit, Low Risk= **Most Appropriate**
Fractured Ankle	Sleep Apnea	(+,-) High Benefit, High Risk= **Provider Judgment**
Strep Throat	None	(-,+) Low Benefit, Low Risk= **Least Appropriate**
Strep Throat	Severe Depression	(-,-) Low Benefit, High Risk= **Least Appropriate**
Headache	None	(-,+) Low Benefit, Low Risk= **Least Appropriate**
Headache	Drug use disorder	(-,-) Low Benefit, High Risk= **Least Appropriate**

A patient determined to be high risk requires closer monitoring if opioids are prescribed. An algorithmic approach, including risk assessment and monitoring, has shown promise *(Atluri, 2012)*. Two important lessons emerge from the risk assessment tool literature. First, no patient can reliably be determined risk-free. Second, mental health disorders, particularly childhood sexual trauma, and addictive disorders, particularly opioid use disorder, confer increased risk of adverse events in those receiving opioids. Depression and anxiety symptoms correlate to higher opioid doses and less pain relief *(Wasan, 2015)*.

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The ABCDPQRS mnemonic is one useful tool that addresses potential contraindications/risks to opioid use. Please see Appendix A for more detailed information.

A – Alcohol Use
B – Benzodiazepines and Other Drug Use
C – Clearance and Metabolism of Drug
D – Delirium, Dementia and Falls Risk
P – Psychiatric Comorbidities
Q – Query the Prescription Monitoring Program
R – Respiratory Insufficiency and Sleep Apnea
S – Safe Driving, Work, Storage and Disposal

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13.3. Special Populations

Pregnant, Lactating or Women of Childbearing Age

Work Group Recommendation
Prior to prescribing opioids, women of childbearing age should be counseled on the risks of opioids in pregnancy and on contraception, and offered pregnancy testing.
Benefit: There may be teratogenic effects to opioids. Neonatal abstinence syndrome is costly and burdensome on the family and medical system. Opioid withdrawal in pregnancy may compromise obstetrical outcomes. Many opioid prescribers are uncomfortable continuing opioids in pregnancy. **Harm:** There is no harm in counseling the patient. Counseling takes additional time during the patient encounter. **Benefit-Harms Assessment:** The use of opioids in women of childbearing age, and in pregnancy, is widespread. Most pregnancies are unaffected by exposure to low dose or intermittent opioids. Some pregnancies are affected, including a low rate of teratogenicity, rising neonatal abstinence syndrome rates, and challenging the comfort of the opioid prescriber and the obstetrician. A discussion on the risks and benefits of opioids use seems prudent for this population.
Relevant Resources: *Desai, 2015 (Observational Study); Han, 2015 (Observational Study); Desai, 2014 (Observational Study); Maeda, 2014 (Observational Study); Whiteman, 2014 (Observational Study); Yazdy, 2013 (Observational Study), Broussard, 2011 (Observational Study)*

Unlike almost all other addictive drugs, men and women are equally affected by opioids *(Han, 2015; Centers for Disease Control and Prevention, 2011; Voelker, 2013)*. Opioids can be used for pain during pregnancy; 22% of all pregnant women receive opioids during their pregnancy *(Volkow, 2016a; Desai, 2014; Maeda, 2014)*. While earlier studies did not show a link to birth defects *(Viteri, 2015)*, recent studies suggest there may be an association with certain birth defects. A large retrospective cohort study in Ireland found an association between methadone and major congenital anomalies *(Cleary, 2011)*. Broussard et al. evaluated data from the National Birth Defects Prevention Study (a population-based case-control study from 1997-2005) and found that opioid use was significantly associated with conoventricular septal defects, atrioventricular septal defects, hypoplastic left heart syndrome, spina bifida and gastroschisis *(Broussard, 2011)*. Analysis of data from the Slone Epidemiology Center Birth Defects Study spanning 1998-2010 suggests that opioid use in the periconceptual period appears to be associated with increased risk of neural tube defects *(Yazdy, 2013)*. While these studies had limitations and further research is needed, clinicians and patients should be aware of the evolving evidence and the potential association between opioid use and certain birth defects.

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In a cross-sectional analysis of pregnancy-related discharges from 1998-2009 in the United States, Whiteman et al. found opioid use was associated with increased odds of threatened preterm labor, early onset delivery, poor fetal growth and stillbirth *(Whiteman, 2014)*. In their retrospective cohort study, Cleary et al. found that methadone was associated with increased risk of very preterm birth, being small for gestational age, and admission to the neonatal intensive care (NICU) *(Cleary, 2011)*. Heavy exposure to opioids during pregnancy may results in neonatal abstinence syndrome (NAS), which is neonatal opioid withdrawal *(Desai, 2015)*. NAS may require weeks of care in the NICU, during which the neonate is weaned using an opioid (typically morphine or methadone). Children who have NAS meet their normal childhood milestones but long-term complications of NAS are unknown. NAS rates are rising steadily in America *(Tolia, 2015)*. Four percent of NICU beds are occupied by NAS cases *(Tolia, 2015)*.

How to best manage opioids for pain in pregnancy is not known – when or if to wean, whether long or short acting is better, how to minimize the risk of NAS. A pregnant patient on continuous opioids may be referred to high-risk obstetrics. In addition, pregnant women on opioids should be screened for opioid use disorder, and if present should be promptly referred to methadone maintenance clinics or a trained buprenorphine provider *(Park, 2012)*. Prior to prescribing opioids, women who are not pregnant but of child-bearing age should be counseled on the risks of opioids in pregnancy, counseled on contraception and offered pregnancy testing. Women who are not pregnant but of childbearing age and already on chronic opioids should regularly be counseled on birth control. Pregnant women not on opioids should be urged to minimize their exposure to opioids.

This work group recognizes that pain control for pregnant women is a difficult issue as there is a paucity of treatment options. The discussion of opioids is part of a larger conversation on the risk and benefits of all the available options. A full, detailed discussion of pain treatment in pregnancy is beyond the scope of this guideline.

The American Academy of Pediatrics classifies morphine as compatible with breastfeeding. Long-term effects on neurobehavior and development are unknown. Morphine is passed on to infants in breast milk in concentrations ranging from 0.8 to 12% of the maternal dose. Occasional doses of hydrocodone probably represent a minimal risk to a nursing infant, but higher and more frequent maternal doses may case toxicity *(Briggs, 2014)*. In summary, low doses of as needed (prn) opioids used while breastfeeding are a minimal risk, but infants should be observed for changes in breathing and sedation. Breastfeeding is best avoided in infants when the mother is using higher doses or chronic administration of opioids.

In 2007, the FDA issued a warning on codeine for nursing mothers. Please see the FDA Information for Healthcare Professional sheet for more information: https://www.fda.gov/media/104268/download.

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Geriatrics

Work Group Recommendation
Geriatric patients should be assessed for risk of falls, cognitive decline, respiratory malfunction, and renal malfunction before receiving opioids. **If impairment or risk is detected in a geriatric patient, consider reducing the initial opioid dose by at least 50%.**
Benefit: Doing a unique assessment for geriatric patients is important because of this group's unique vulnerabilities. Lowering the dose of opioids may lower the risk of opioid-related harm, such as falls and respiratory suppression, in this population. **Harm:** Geriatric patients are a diverse group of patients, some more fragile and others more robust. They should not be treated as having equal risk of opioids as a group. The most fragile geriatric patients may also have contraindications to the common alternatives to opioids. This may lead to undertreatment of pain. **Benefit-Harms Assessment:** Like many of the high-risk populations, using special precautions and lower doses in the geriatric population lowers the risk of opioid-related harms while also risking undertreating pain.
Relevant Resources: *Makris, 2014 (Review); Rubin, 2014 (Report); Rolita, 2013 (Observational Study); Saunders, 2010 (Observational Study); Solomon, 2010 (Observational Study); Spector, 2007 (Observational Study); Vestergaard, 2006 (Observational Study)*

Geriatric populations are more likely to have vulnerabilities to the adverse effects of opioids: impaired drug clearance, polypharmacy, past response to opioids, increased likelihood of falls and fractures, chronic medical conditions, liver and renal malfunction, respiratory insufficiency and cognitive impairment. Harm to older populations receiving opioids is increasingly recognized *(Han, 2015; Kronick, 2014; Rubin, 2014; Rolita, 2013; Saunders, 2010; Solomon, 2010; Spector, 2007; Vestergaard, 2006)*. Careful consideration of the unique risks and benefits in this population is warranted *(Makris, 2014)*. Our work group emphasizes the need for risk assessment and an individualized approach to the elderly patient based on their functional status and comorbidities.

Pediatrics

To safely prescribe opioids to pediatric patients requires consultation with a pharmacist or clinician trained in age- and weight-appropriate dosing. Codeine has a black box warning against use in pediatric patients due to its incidence of accidental overdose.

Adolescents prescribed opioids require special care. A study by Miech et al. of 6,220 individuals found that adolescents exposed to opioids for traditional indications prior to high school graduation had a 33% increase in future opioid misuse *(Miech, 2015)*. In addition, adolescents may have undiagnosed mental health issues, as well as early substance use disorder, conferring additional risk. DeVries et al. found that despite guideline recommendations against opioid use for adolescents with headaches, 46% of adolescents studied received opioids for this indication *(DeVries, 2014)*. Further, there was a correlation between opioid use for headache and subsequent emergency room visit *(DeVries, 2014)*.

Opioids should be avoided if possible in this population. If opioids are to be prescribed, it is ideal for there to be close parental/caregiver supervision of opioid use whenever possible.

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13.4. Prescriber Responsibility with Opioid Prescription

Patient Education and Shared Decision-Making

Work Group Recommendation
The first opioid prescription should include patient education, shared decision-making and assessment for related risks.
Benefit: Appropriate informed consent and shared decision-making should occur early in the course of prescribing opioids. Much opioid-related harm, including overdose, can happen early in the course of pain treatment. Aberrant behaviors and comorbidities should be identified as early as possible. Patient expectations should be set early in the course of opioid treatment. **Harm:** Patients may feel that they are being treated with suspicion. Very low-risk patients will be asked to spend time and energy to receive opioids. Clinician time and clinical resources will be dedicated early in the course of opioid prescribing. **Benefit-Harms Assessment:** Early patient education, re-education, screening for comorbidities and detecting aberrant behaviors represent a burden to patients and clinicians that is outweighed by the benefit of promptly addressing opioid-related harms and providing the patient with up-to-date and thorough education about the risks of opioids. This approach emphasizes universal precautions.
Relevant Resources: *Hooten, 2015a (Observational Study)*

Shared decision-making should happen at the time of the first opioid prescription and frequently thereafter. Patients are typically not given adequate information about the risks and benefits of opioids, many of which start with the first use. The decision to initiate or continue opioids should involve careful description of the risks and benefits of opioids. Repetition is necessary, as patients in pain may be less able to remember this critical information. All patients, even those deemed low risk, should be given information about the harms of opioids. Patients should have these harms explained free of stigma and judgment, assuming that any patients could experience them. The information should be clearly stated in understandable language. If available, a pharmacist may also provide education.

Clinicians and patients should understand that opioids actually change the chemistry of the brain and its response to pain.

- Homeostatic adaptations within the central nervous system (CNS) to opioid exposure may contribute to the development of tolerance *(Christie, 2008)*.
- Opioids profoundly influence the synaptic plasticity that underlies learning and memory, leading to the potential development of addiction *(Christie, 2008)*.
- Opioids can cause inhibition of LH- and gonadotropin-releasing hormone secretion, resulting in lower steroid hormone levels.
- Opioids can cause inhibition of estradiol and testosterone secretion, resulting in hypogonadism, menstrual irregularities, sexual dysfunction, infertility and osteoporosis.
- Opioids can cause inhibition of insulin secretion, leading to hyperglycemia and worsening diabetes.

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Safe Use, Storage and Disposal

Work Group Recommendation
Patients newly on opioids, or having recently had their opioid dose increased, should be advised not to operate heavy machinery, including driving a car, or participate in other work or home activity that may be affected by the sedating effect of opioids. **An individualized approach that weighs the risks and benefits of driving and other activities should be taken with patients chronically on stable opioids who have tolerance and do not show evidence of sedation.**
Benefit: The sedating effect of opioids impairs one's ability to drive a motor vehicle and carry out other tasks similarly sensitive to wakefulness and reaction time. As a safety measure, it is important to clearly warn patients about the risk to themselves and others performing potentially dangerous tasks while on opioids. With the development of opioid tolerance and the absence of sedation, studies have shown that patients can safely drive a motor vehicle. **Harm:** Driving, work and household prohibitions can be burdensome and may prevent timely return to normal life activities. **Benefit-Harms Assessment:** The risk to public safety of patients newly on opioids operating motor vehicles and carrying out similar tasks clearly outweighs the inconvenience to the individual on opioids. Determining when the patient has enough tolerance to safely drive is a subjective judgment call, and prescribers should err on the side of caution and document carefully.
Relevant Resources: *National Highway Traffic Safety Administration (Fact Sheet) (2016); Schisler, 2012 (Expert Opinion)*

Work Group Recommendation
Clinicians should discuss storage and opioid disposal options with patients at the first opioid prescription and in follow-up visits as needed.
Benefit: Proper storage and disposal can reduce opioids involved in diversion and overdose. **Harm:** There are no easy options for disposal of opioids. **Benefit-Harms Assessment:** Considering the great harm of excess opioids to the community, every opioid prescription should be accompanied with storage and disposal information. Disposal information is everchanging and complicated. While communicating the information is not highly burdensome, staying abreast of the latest information may be.
Relevant Resources: *Centers for Disease Control and Prevention, 2016 (Guideline); Centers for Disease Control and Prevention, 2010 (Summary Article)*

According to the National Highway Traffic Administration panel, classification of risk of driving with morphine "depends on tolerance, dose, time of exposure, acute or chronic use, presence or absence of underlying pain, physiological status of the individual and the presence of other drugs" *(National Highway Traffic Safety Administration, 2016)*. Non-tolerant opioid users will likely experience greater impairment. Education about driving safety on opioids can reduce drugged driving *(McCarthy, 2015)*. Local law may vary on what meets the definition of "driving under the influence" of a controlled substance, and prescribers should understand and follow local laws.

All patients should be instructed to store their opioids – ideally locked – in a location unreachable by family members and house guests. Patients should be instructed to dispose of the opioids promptly at the end of the pain episode. In one study of urologic procedures, 67% of patients received excess opioids, and 92% received no disposal instruction *(Bates, 2011)*. Opioid disposal is a problem needing more solutions. The

Food and Drug Agency and the Drug Enforcement Agency allow for schedule II substances (e.g., opioids) to be flushed down the toilet *(Drug Enforcement Administration, 2014a)*. The Environmental Protection Agency does not endorse this method of disposal. Almost all Minnesota counties have a pill take-back site, usually at a law enforcement building *(U.S. Food and Drug Administration, 2015)*. Pharmaceutical disposal bags with activated charcoal are available for safe at-home disposal. Fentanyl patches require special handling. As soon as they are removed, they should be folded sticky side inward and promptly flushed. Every year children die from inadvertent exposure to fentanyl patches *(U.S. Food and Drug Administration, 2015)*. Unused opioids should be disposed of promptly at the end of the pain episode for which they were prescribed. Opioids should not be stored in case of a future pain episode, unless specifically directed by the prescriber.

Opioid Formulation

Work Group Recommendation
Long-acting opioids should be reserved for patients with established opioid tolerance and in whom the prescriber is confident of medication adherence. **Long-acting tamper-proof formulation for opioids is preferred.**
Benefit: Tamper proof formulations of opioids have been linked to decrease diversion, abuse and death, when used for chronic pain. See the FDA site for more information: www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm163647.htm When used for acute pain, or in patients without opioid tolerance, long-acting opioids are associated with inadvertent opioid overdose death. Methadone pharmacology is complicated, and its routine use is associated with overdose death. **Harm:** Tamper-proof formulations may not be covered or may have greater copay. For some situations, such as sleep, the duration of short acting opioids is insufficient to treat pain. **Benefit-Harms Assessment:** While there may be some select circumstances where use of long-acting opioids seems appealing in acute pain, they have failed to show benefit and are associated with overdose death. Using methadone in acute or chronic pain is associated with harm, owing to its unique pharmacology. If long-acting opioids are indicated, using a tamper-proof formulation may improve outcomes.
Relevant Resources: *Hwang, 2015 (Observational Study); Argoff, 2014 (Systematic Review); Cassidy, 2014 (Observational Study); Havens, 2014 (Observational Study); Sessler, 2014 (Observational Study); Butler, 2013 (Observational Study); Coplan, 2013 (Observational Study); Severtson, 2013 (Observational Study); Manchikanti, 2012a (Guideline); Severtson, 2012 (Observational Study); Dhalla, 2009 (Observational Study)*

Many studies have credited tamper-proof opioid formulations of opioids with a decrease in opioid misuse, diversion, death, opioid street value, and in some cases a corresponding increase in heroin use *(Dart, 2015; Hwang, 2015; Argoff, 2014; Cassidy, 2014; Havens, 2014; Sessler, 2014; Butler, 2013; Coplan, 2013; Severtson, 2013; Severtson, 2012; Cicero, 2012)*. The rise in heroin use after initiation of tamper-proof formulations is interpreted to mean that addictions are exposed rather than created by this change in formulation. These formulations are currently on patent and are expensive. That said, when available, tamper-proof formulations are likely to decrease the harms of opioids.

Initially it was hoped that long-acting formulations of opioids would provide better pain control and decrease the adverse effects of immediate-release opioids, or even be less addictive. This has not been borne out in the medical literature *(Manchikanti, 2012a)*. Early initiation of long-acting opioids can harm the patient by causing overdose *(Dhalla, 2009)*. Long-acting opioids should be used only in patients with established opioid tolerance and in whom the prescriber is confident of their medication adherence.

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Patient-Provider Agreement (PPA)

Work Group Recommendation
Initiate a patient-provider agreement (PPA) at the time an opioid is prescribed for: • **High-risk patients** • **Daily use of opioids > 30 days** • **Patient transfers to a new clinic already on opioids** • **Episodic use up to 90 days over the course of a year** • **If none of the above, initiate a PPA after 90 days of opioids is prescribed.**
Benefit: PPAs provide the patient with a clear set of expectations in writing. **Harm:** It has not been demonstrated that PPAs improve clinical outcomes. PPAs may be used as a pretext for dismissing undesirable patients. **Benefit-Harms Assessment:** PPAs have not been proven an effective medical intervention; however, they provide a clear set of expectations for patients and clinicians. Executed and used correctly, a PPA can help prevent patient provider disagreement and allow the clinic to insist on consistent and universal practices for opioid-receiving patients. When done incorrectly, a PPA may cause patients to be dismissed from care without appropriate referrals or follow-up.
Relevant Resources: *Centers for Disease Control and Prevention, 2016 (Guideline); Hooten, 2015a (Observational Study); Noble, 2010 (Systematic Review/Meta-analysis); Starrels, 2010 (Systematic Review); Arnold, 2006 (Review)*

A patient-provider agreement (PPA) should be used for a large proportion of patients receiving opioid prescriptions *(Arnold, 2006)*. PPAs are formal written agreements between patient and clinician, stating the responsibilities of each party. PPAs have not been shown to prevent aberrant drug-related behaviors *(Starrels, 2010)*. PPAs clarify the situations that will result in discontinuation of opioids, among other consequences. PPAs often inadequately describe the clinicians' responsibility to the patient. Most protocols suggest initiating a PPA after 90 days of continuous opioid use *(Reuben, 2015; Noble, 2010)*, but sooner is preferable. Studies show that after a single opioid prescription, the patient's risk of opioid misuse is increased *(DeVries, 2014; Alam, 2012)*.

The work group suggests initiating a PPA any time an opioid is prescribed for high-risk patients, for patients with daily use of opioids > 30 days, for patients already on opioids transferred to a new clinic, and for patients with episodic use up to 90 days over the course of a year. If none of these applies, initiate a PPA after 90 days of opioids have been prescribed. Many health care systems ask the patients to sign an informed consent at the time they sign the PPA *(Cheatle, 2012)*. While the PPA and an informed consent cover much the same information, the informed consent has more medico-legal implications. Some health care systems review and renew their treatment plan, PPA and informed consent yearly.

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Consider Offering Naloxone

Work Group Recommendation
Clinicians should consider offering the patient and close contacts (family/friends/caretaker) a naloxone kit.
Benefit: Community access to naloxone may save lives that would otherwise be lost to opioid overdose death. Many states explicitly support and legally protect this use of naloxone in law. **Harm:** Naloxone is not a treatment of the underlying causes of opioid overdose. Some forms of overdose are not reversed by a single dose of naloxone. Inducing opioid withdrawal may cause discomfort or other adverse effects. Training is required. Emergency services should be called when naloxone is used. Widespread use of naloxone may compromise its supply for those who need it the most. **Benefit-Harms Assessment:** Home use of naloxone can save the life of a person who would otherwise die from an opioid overdose, but it does not correct the underlying cause of the overdose, and it requires training to use appropriately.
Relevant Resources: *Coffin, 2016 (Observational Study); Coffin, 2013 (Cost-Effectiveness Analysis); Centers for Disease Control and Prevention, 2012a, (Report), Albert, 2011 (Observational Study); Yokell, 2011 (Report); Strang, 2008 (Observational Study)*

The CDC credited a recent plateauing of the opioid death curve to the widespread distribution of naloxone rescue kits *(Centers for Disease Control and Prevention, 2012a; Albert, 2011; Yokell, 2011)*. Currently, one state has mandated that naloxone kits be co-prescribed with opioids, and many states have legislation explicitly protecting naloxone use for opioid overdose reversal *(Boyer, 2012)*. Naloxone can be administered intra-nasally, intramuscularly or subcutaneously by a layperson *(Medical Letter, The, 2016)*. Naloxone distribution will likely save health care dollars *(Coffin, 2013)*.

Patients who are prescribed naloxone should be directed to a free online or community training *(Strang, 2008)*. Because the reversal effect of naloxone does not outlast the sedating effect of many opioids, it is necessary to activate emergency services whenever a naloxone kit is used. The work group recommends that prescribers should considering offering a naloxone kit and training to all patients prescribed opioids and their close contacts (family/friends/caretaker). High-risk patients who should definitely be offered naloxone include those with an addiction, respiratory insufficiency, sedative/hypnotic use, dose greater than 100 MME/day, on chronic opioids with an acute injury, and history of opioid overdose. Recent laws allow pharmacists in some states to use standing orders to dispense to all who ask.

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13.5. Acute or Acute on Chronic Pain

Work Group Recommendation
• **The first opioid prescription for acute pain should be the lowest possible effective strength of a short-acting opioid, not to exceed 100 MME total. Patients should be instructed that three days or less will often be sufficient.** • **For patients presenting in acute pain, already on chronic opioids, opioid tolerant or on methadone, consider prescribing an additional 100 MME maximum for this acute episode, with a plan to return to their baseline dose as soon as possible.**
Benefit: This limited dosing would reduce surplus opioid prescriptions as well as reduce potential of opioid abuse, overdose and diversion. It encourages frequent follow-up for pain requiring opioids and facilitates early recognition of aberrant opioid use. **Harm:** This limited dosing has potential to undertreat pain. It may cause inconvenience to patients by making them return to clinic for ongoing opioids and places some burden on providers arranging for early follow-up. In addition, some pain generators typically require more than three days of opioids. The opposite may also be true if providers automatically prescribe the full 100 MME when the patient could find relief with much less. **Benefit-Harms Assessment:** The medical community has typically overprescribed opioids for acute pain to ensure that no patient is ever undertreated, but at the risk of providing surplus opioids to the patient and the community, and specifically harming those with vulnerability to opioids. Lowering the total quantity of opioids prescribed will prevent much of this harm, but in exchange some patients with ongoing pain will receive insufficient opioids, forcing them to return for evaluation from their primary clinician. While this may be a short-term burden to the patient and system, it will, over time, lessen the burden to patients and clinicians by decreasing the harms of opioids. Those already taking opioids chronically have higher tolerance and thus may receive less analgesia from opioids. These patients are also at a higher risk, may have more comorbidity, may already be on opioid doses known to have adverse effects, and are likely to have an opioid patient-provider agreement. Thus, while treating the opioid-tolerant patient with equivalent doses will provide less analgesia, it will also mitigate harms.
Relevant Resources: *Shah, 2017 (Observational Cohort Prospective Study); Bohnert, 2016 (Observational Study); Centers for Disease Control and Prevention, 2016 (Guideline); Liang, 2015 (Observational Study); Miller, 2015 (Cohort Study)*

The first opioid prescription for acute pain should be the lowest possible effective dose of a short acting opioid, not to exceed 100 MME total. Patients should be instructed that three days or less will often be sufficient. For instance 20 hydrocodone 5 mg tablets, or 13 oxycodone 5 mg tablets, would equal 100 MME total, the maximum recommended dose for acute pain. Long-acting opioids should not be prescribed as the initial therapy for acute pain *(Miller, 2015; Dhalla, 2009)*. For patients presenting in acute pain, already on chronic opioids, opioid tolerant or on methadone, consider prescribing an additional 100 MME maximum for this acute episode, with a plan to return to their baseline dose as soon as possible. The benefit to an opioid-tolerant patient is less, but the risks are higher *(Franklin, 2012; Gomes, 2011; Dunn, 2010)*. The chances of chronic opioid use begin to increase after the third day supplied and rise rapidly thereafter *(Shah, 2017)*. At the end of this initial prescription, if the patient believes there would be benefit from continued opioids, a follow-up visit should be scheduled since the likelihood of chronic use also increases with the second prescription *(Shah, 2017)*.

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13.6. Avoid Opioid Use for Chronic Pain

Work Group Recommendation
Avoid using opioids to treat patients with chronic pain.
Benefit: This will lower the total opioid use in the United States and the corresponding harms from opioids. Opioids have no proven efficacy for chronic pain but do have known harms. Preventing chronic exposure to opioids is easier and preferable to detoxing a patient chronically on opioids. **Harm:** A subset of patients with chronic pain may benefit from chronic opioids. Patients already on chronic opioids cannot be easily detoxed from opioids, and this recommendation should not be taken as advice to detox existing chronic pain patients on long-term opioids. **Benefit-Harms Assessment:** Pain that has no easily identifiable pain generator, and no cure, is a daunting problem in medicine and causes great suffering. These patients try many modalities of care and too often end up on chronic opioid therapy. There are no proven benefits of opioids for most patients with chronic pain, but there are proven harms. Until further knowledge emerges, it is prudent to avoid initiating opioids in these patients.
Relevant Resources: *Chou, 2015 (Systematic Review); Chaparro, 2014 (Systematic Review/Meta-analysis); Manchikanti, 2006 (Observational Study)*

Since chronic pain is a complex problem, it requires a multidisciplinary approach. There is no evidence that opioids for chronic pain relieve pain or improve function *(Chou, 2015; Chaparro, 2014; Gaskell, 2014; Loder, 2013; Manchikanti, 2006)*. In the absence of evidence, we urge all providers to avoid treating chronic pain with opioids. Those already taking opioids for chronic pain require careful monitoring and prevention of dose escalation or other adverse events. It is reasonable to suggest a voluntary and slow taper for patients on chronic opioids.

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13.7. Ongoing Treatment of Pain with Opioids

If the use of continued opioids is unavoidable, we urge providers to consider the following issues.

Manage Dose Limits

Work Group Recommendation
• **Every effort should be made to keep chronic opioid using patients under 90 morphine milligram equivalents (MME)/day. Prescribers should consider seeking pain medicine consultation if greater than 90 MME is reached.**
Benefit: Opioid doses greater than 90 MME/day are associated with overdose death; as the dose increases, so do the risk and the strength of the associations. **Harm:** Some patients will have undertreated pain. Patients already on higher dose of opioids may struggle to lower their dose to a safe range. It is impossible to predict who will or will not overdose. Some patients who would not have been harmed by opioids will have their dose limited. **Benefit-Harms Assessment:** Given a fairly clear dose response association between MME and death, patients should be kept under 90 MME/day, even at the cost of potentially undertreating pain in some.
Relevant Resources: *Han, 2015 (Observational Study); CDC, 2016 (Guideline);Turner, 2015 (Observational Study); Franklin, 2012 (Observational Study); Gomes, 2011 (Observational Study); Dunn, 2010 (Observational Study)*

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Work Group Recommendation
• **Opioids should be avoided for patients with substance use disorder or concomitant benzodiazepines use.** • **If a patient with substance use disorder is prescribed opioids, the opioid dose should be less than 50 MME/day.** • **If patient requires both opioids and benzodiazepines, opioids should be less than 50 MME/day, taking into careful consideration the benzodiazepine dose. There should be good communication among providers regarding dosing.**
Benefit: Patients with substance use disorder or benzodiazepine use are at higher risk of overdose if given opioids. Therefore, it is prudent to avoid opioids in these populations. If opioids are prescribed, the work group recommends a dose less than 50 MME/day to minimize adverse events. **Harm:** Some patients will have undertreated pain. **Benefit-Harms Assessment:** The risk of prescribing opioids to these populations outweighs the beneficial pain relief opioids may provide. Alternative pain management strategies should be employed.
Relevant Resources: *Han, 2015 (Observational Study); Turner, 2015 (Observational Study)*

Studies have examined the relationship of the total daily dose of oral opioids, expressed as daily morphine milligram equivalents (MME), and opioid overdose death. In almost all cases a dose-response relationship is found, reaching statistical significance at 100 MME/day, with an increased risk of death thereafter *(Han, 2015; Gomes, 2011; Dunn, 2010)*. The risk of death at 100 MME/day appears to be at least twofold, with some studies finding a higher risk than that. In a study of Washington state, where the maximum dose of opioids was limited, overdose deaths decreased *(Franklin, 2012)*. The goal is to reduce the risk. The Centers for Disease Control and Prevention guideline for prescribing opioids for chronic pain recommends assessing balance of benefits and risks when considering increasing dosage to ≥ 50 MME/day and to avoid increasing dosage to ≥ 90 MME/day *(CDC, 2016)*. This work group agrees that every effort should be made to keep chronic opioid use below 90 MME/day using the lowest dose possible to effectively treat pain.

Opioids incur greater risk of overdose in certain populations, including patients with substance use disorder or benzodiazepine use *(Centers for Disease Control and Prevention, 2016; Han 2015; Turner, 2015)*. Therefore, opioids should be avoided in patients with substance use disorder or benzodiazepine use. Alternative pain management strategies should be employed for these patients. However, the work group recognizes there may be situations where opioids are given to these populations. It is the consensus of this expert work group that if opioids cannot be avoided for patients with substance use disorder or benzodiazepine use, the opioid dose should be less than 50 MME/day. This threshold is intended to provide guidance in the absence of direct evidence. The clinician must also carefully consider the benzodiazepine dose. Communication among providers is critical for patient safety.

For additional information about MME, please see Appendix C, "Opioid Pharmacology."

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Opioid Rotation and Conversion

Work Group Recommendation
Opioid conversion tables should be used only as guidance when changing opioids. **Doses of the new opioid should be reduced by 50% of the previous daily MME dose and titrated to achieve analgesia.**
Benefit: This avoids overestimating opioid needs with a new opioid due to incomplete cross-tolerance and reduces the risk of adverse events and harm with the new opioid. **Harm:** Patients may not experience adequate pain relief if taking opioids chronically and may experience mild withdrawal until the new opioid can be titrated to effective dose. This dose reduction may lead to more frequent dose changes and clinic visits until adequate pain control is achieved. **Benefit-Harms Assessment:** Opioid conversion tables were developed from opioid-naïve patients and do not account for incomplete cross-tolerance in opioid-tolerant patients. Despite the chance of mild withdrawal, it is safer to underestimate the dose titrating as necessary than overestimate the dose causing harm.
Relevant Resources: *Pasternak, 2014 (Report); Vissers, 2010 (Review); Fine, 2009 (Consensus); Pasternak, 2005 (Summary Article)*

Opioid rotation refers to a switch from one opioid to another in order to minimize adverse effects or improve therapeutic response *(Pasternak, 2014)*. The exact mechanism by which opioid rotation improves response is not known, but the theoretical basis relates to individual variation between opioids and their relative potencies *(Knotkova, 2009)*. Equianalgesic tables can be used to estimate the optimal dose of a new opioid, but they provide only an estimate *(Vissers, 2010)*. Most patients will require a lower dose than what is calculated, due to the development of cross-tolerance.

The long-term exposure to any medication, which results in the development of tolerance to the effects of other structurally similar medication, is the phenomenon known as cross-tolerance *(Dumas, 2008)*. The cross-tolerance that develops from long-term exposure to opioids is incomplete and may be due to multiple mechanisms *(Dumas, 2008)*, including genetic differences between individuals that result in reduced receptor densities *(DuPen, 2007)*, altered binding affinities and desensitization of the mu opioid receptors *(Ross, 2005)*.

Due to the incomplete cross-tolerance of opioids and the variability of the equianalgesic tables, the range of dose reductions used by studies for opioid rotation is broad. A dose reduction of 33-75% *(Pasternak, 2014; Vissers, 2010; Pasternak, 2005)* has been identified in the literature. Regardless of the conversion used, it is recommended to initiate the new opioid at the lowest dose and gradually titrate the dose, if necessary, to provide adequate analgesic response *(Vissers, 2010)*. The work group recommends that doses of the new opioid should be reduced by 50% of the previous daily MME dose and titrated to achieve analgesia.

Advances in mobile technology have brought many opportunities to access reference material in a variety of formats *(Haffey, 2013)*. Although the number of available apps continues to increase, there is little data regarding the reliability and effectiveness of these tools *(Wallace, 2014)*. The majority of the applications available for download have no evidence of health care professional (HCP) involvement *(Wallace, 2014; Haffey, 2013)*. Of the 23 applications identified in one study, 11 (48%) provided a direct reference for their opioid conversions and 10 (43%) had a dose reduction tool to account for cross-tolerance *(Haffey, 2013)*.

A statistically significant difference in conversion outputs for hydromorphone was found between mobile applications with and without medical involvement, but the differences for codeine, oxycodone, fentanyl and morphine were not significant *(Haffey, 2013)*. The FDA has recently released guidance for mobile

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medication applications with plans to enforce medical devices applications but does not explicitly list opioid conversion calculators. For additional information, refer to http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf.

This guideline does not endorse the use of one specific application over another, but does recommend using applications with health care provider involvement and transparency about the source of the information used.

Opioid Hyperalgesia

A consequence of high-dose opioids besides overdose is hyperalgesia. Some patients become sensitized to pain as their dose of opioids increases. The prevalence of this condition is not known *(Meldrum, 2003)*. Escalating pain despite escalating opioid doses, in the absence of corresponding tissue damage, suggests this condition. If the patient has opioid-induced hyperalgesia, lowering the dose will produce relief. If opioids are unavoidable and the patient has opioid-induced hyperalgesia, consultation with a pain specialist is warranted.

Methadone

Work Group Recommendation
Initiating an opioid-tolerant patient on methadone for chronic pain should be reserved for experienced clinicians who are familiar with its use because its long half-life is associated with overdose and death.
Benefit: Trained clinicians are more familiar with the pharmacokinetic/pharmacodynamics properties of methadone and are better equipped to dose appropriately and provide the necessary monitoring to avoid adverse events. **Harm:** Clinicians trained in methodone prescribing may not be available to all patients who may benefit from methadone. **Benefit-Harms Assessment:** Methadone has a long and variable half-life that is not consistent between patients. It is highly lipophilic, and the respiratory depressant effect lasts longer than the analgesic effect. Methadone requires close follow-up and should only be initiated by clinicians experienced with its use.
Relevant Resources: *Wong, 2013 (Summary Article); Chou, 2009b (Guideline)*

Of all the opioids, methadone has one of the longest and most variable half-lives, thereby increasing the risk for accumulation of toxic levels *(Paulozzi, 2012)*. In addition, there are many important drug-drug interactions. Consequently, choosing the dose for acute pain management using methadone requires slow, careful titration of the dose. Patients need careful education. Methadone has been associated with a disproportionate number of overdose deaths relative to how often it is prescribed *(Centers for Disease Control and Prevention, 2016)*. Many opioid guidelines, including ours, advise prescribers against using methadone for pain unless they have specific training.

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Fentanyl

Recommendation
• **Initiating transdermal fentanyl should be done only for patients with chronic opioid use greater than 60 MME daily, adequate subcutaneous adipose tissue and the cognitive ability to apply, remove and dispose of the patches safely.** • **Patches should be removed after 72 hours, folded upon themselves sticky side inward and promptly flushed down the toilet.** • **Sublingual fentanyl should be reserved for only those in need of palliative care for extreme pain and unable to take any alternatives.**
Benefit: Fentanyl patches are long-acting, renal-safe synthetic opioids, and as such they occupy a fairly unique niche in the opioid pharmacopeia. There are not many replacement medications. **Harm:** Fentanyl products are associated with accidental overdose deaths, including when an improperly disposed patch sticks to a toddler or household pet. Transdermal fentanyl is unsafe in cachectic patients lacking adipose tissue, given fentanyl's lipophillicity. SL fentanyl is exceedingly potent and apt to cause overdose if overused. **Benefit-Harms Assessment:** Fentanyl is a highly potent, lipophilic synthetic opioid that can be used to good effect treating pain if opioids are indicated. However, due to its high potency, fentanyl has caused accidental overdoses, and the transdermal patches need special handling and disposal instructions. Only patients with established opioid tolerance should receive fentanyl. Fentanyl SL formulations can be very helpful but are best reserved for those in pain in the dying process.
Relevant Resources: *U.S. Food and Drug Administration, 2013; U.S. Food and Drug Administration, 2012*

Every year transdermal patches are responsible for accidental opioid poisoning deaths of children and house pets inadvertently exposed to discarded patches *(U.S. Food and Drug Administration, 2013; U.S. Food and Drug Administration, 2012)*. Therefore, careful disposal information is critical. Inappropriate handling or tampering with fentanyl patches is extremely dangerous and may cause death.

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13.8. Monitoring Considerations for Opioid Use

All recent opioid-related guidelines agree that patients receiving opioid analgesics require monitoring *(Gaither, 2016)*, though the nature of the monitoring is not supported by high-quality evidence.

Risk Assessment Tools

Risk assessment tools may be used in the monitoring of a patient taking opioids. Please see the "Risk Assessment" section in 13.2 for more detail.

Patient-Provider Agreements (PPA)

A patient-provider agreement (PPA) should be initiated at the time an opioid is prescribed for:

- High-risk patients
- Daily use of opioids > 30 days
- Patient already on opioids transfers to a new clinic
- Episodic use up to 90 days over the course of a year

However, if none of the above applies, initiate a PPA after 90 days of opioids is prescribed.

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Please see the "Patient-Provider Agreement" section in 13.4, "Prescriber Responsibility with Opioid Prescripton," for more detail.

Prescription Monitoring Program (PMP)

Work Group Recommendation
The prescription monitoring program (PMP) should be queried in the following situations: • **If opioids are prescribed in dental, emergency department and urgent care settings, and when doses are changed.** • **In every instance where there are concerns of substance use disorder, overdose, diversion, indeterminate pain disorder or polypharmacy.** • **For those patients with an established stable dose of opioids for a chronically painful condition and a history of compliance with the prescriber, PMP checks should be at least twice per year.** **Consider querying the PMP when initiating opioid therapy**
Benefit: Detect clinician shopping, polypharmacy, opioid exposure and tolerance, and estimate the likely home supply of opioids. The PMP may reveal other prescribers whom to contact before prescribing opioids. A PMP query can help verify the patient's story. A PMP query affects clinician decision-making and may lower overall opioids prescribed and overdoses. **Harm:** PMP queries take time and training. Each state has a different program, with different laws governing their use, and incomplete cross-talk between states. Not every source of opioids is captured in a state PMP. **Benefit-Harms Assessment:** To query the PMP is yet another time and energy burden on medical providers, but it provides invaluable knowledge about the patient's exposure to opioids and other controlled substances, as well as other prescribers. Clinicians should know the loopholes and omissions inherent to their state's PMP.
Relevant Resources: *Han, 2015 (Observational Study); Rutkow, 2015 (Observational Study); Johnson, 2014 (Report); Albert, 2011 (Observational Study)*

Most guidelines recommend querying the PMP before prescribing an opioid, in all settings, even before giving a one-time opioid prescription to seemingly low-risk patients. Greater than 50% of the time an opioid is prescribed, the patient has already received an opioid from a different prescriber within the last month *(Gugelmann, 2011)*. Opioid misuse and opioid use disorders do not obey the typical demographics of other drug use disorders *(Han, 2015)*. In a study looking at opioid prescribing behavior before and after a PMP query, a high proportion of prescribing decisions is changed in light of the information the PMP query provided, both decreasing and increasing the total opioid prescribed *(Gugelmann, 2011)*. After mandating PMP queries prior to all opioid prescriptions, deaths from opioid overdoses and total opioids prescribed decreased in New York, Oregon and Florida *(Vowles, 2015; Rutkow, 2015; Johnson, 2014; Oregon Health Authority, 2013; Albert, 2011; Porter, 1980)*. It is helpful to document the results of the PMP in the medical record, both to demonstrate the physician's diligence in decision-making, and to capture outside information in the medical chart for future review.

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Urine Drug Screening

Work Group Recommendation
• **Routine random urine drug screens (UDS) for all patients on chronic opioid therapy for pain should be done at least once per year.** • **UDS should be done if there is concern of aberrant behavior based on a prescriber's assessments and clinical judgment.**
Benefit: UDS can identify other substances being used that were not disclosed by the patient. UDS can identify when the patient is not taking the prescribed substance. **Harm:** UDS are costly. UDS have many false positives and negatives and may be difficult to interpret. Patients may not be prepared to provide a UDS. Use of UDS has not been shown to improve outcomes. UDS does not, in itself, make a diagnosis of substance use disorder or diversion. **Benefit-Harms Assessment:** Despite many complicating factors and lack of evidence that it improves outcomes, it is still standard of care, and universally recommended, that opioid prescribers check UDS on all patients routinely, and in any patient when there is concern of diversion or unsanctioned substance use. The ideal frequency and type of urine drug screen is not known.
Relevant Resources: *Centers for Disease Control and Prevention, 2016 (Guideline); Starrels, 2012 (Observational Study), Reisfield, 2009 (Review); Michna, 2007 (Observational Study); Heit, 2004 (Review)*

Used properly, the UDS helps to identify patients at risk of adverse events and refer them to the appropriate level of care. Referral to mental health or substance use disorder treatment, however, does improve mortality *(Gaither, 2016)*. Most guidelines recommend that a UDS be done before every new controlled substance prescription and routinely for existing prescriptions *(Michna, 2007)*. There is scant evidence demonstrating that this leads to improved outcomes *(Gaither, 2016; Starrels, 2010)*. In addition, a UDS can be costly and difficult to interpret *(Reisfield, 2009; Michna, 2007; Heit, 2004)*. Even if interpreted accurately, a UDS does not diagnose a substance use disorder or confirm opioid diversion. Some clinicians use inappropriate UDS results as grounds for tapering opioids or dismissing the patient from care, but no evidence suggests this benefits the patient. The optimal frequency of UDS is not known, but random testing at least once per year, and as dictated by clinical suspicion, may be appropriate.

Pill Count Callbacks

Patients with higher risk may be asked to randomly come to the clinic or a pharmacy with less than 24 hours notice to count remaining opioid pills.

The medical literature has shown no well-established benefit of callbacks. Patients often express frustration that their life has been interrupted. Callbacks should be done only for patients demonstrating repeated difficulty taking their medicine as prescribed and for patients in whom there is suspicion of diversion. Some patient-provider agreements have a callback provision, so it is wise to warn patients in advance that a random pill count is possible, and confirm their contact information and travel plans.

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Visit Frequency

Work Group Recommendation
When initiating an opioid prescription, patients should be monitored within a month to evaluate harms and benefits, and assess treatment goals. **Patients on stable opioid doses should be seen every three months.**
Benefit: Developing a strong relationship is important for both opioid prescribing and pain treatment. There is an increasing number of recommendations and regulations that apply to opioid prescribing. These can be time consuming and overwhelming to the patient if attempted on a single visit. Therefore, repeated education is necessary. **Harm**: There is not certain evidence that frequency of visits improves outcomes. Increasing frequency of visits may be burdensome to patients. Some patients have maintained stability on opioids with less frequent visits and may expect to continue the current expectations. **Benefit-Harms Assessment**: While there is a lack of definitive evidence, and this will consume health care resources and potentially burden patients, increasing the frequency of visits for those receiving opioids, in particular those early in treatment for their pain, allows for many critical tasks to take place between provider and patient including education, screening and relationship building.
Relevant Resources: *Centers for Disease Control and Prevention, 2016 (Guideline)*

Drug Enforcement Agency (DEA) recommendations are that every month's prescription for a schedule II controlled substance (e.g., most opioids) be accompanied by a doctor's visit and a medical document including physical exam, diagnosis and rationale for prescribing. For patients at a low risk of harm, the DEA allows for three months of opioids to be given at one time, using three separate written prescriptions (DEA Rules for Prescribers). In practice, patients on opioids are seen far less frequently than this, and often the documentation needs are not met. While research has not yet assessed whether more frequent visits improve outcomes, opioid prescribers should be prepared to see their patients frequently to ensure that treatment goals are met. In the highest risk patients, weekly visits may be necessary. The work group recommends that when initiating an opioid prescription, patients should be monitored within a month to evaluate harms and benefits, and assess treatment goals. The frequency of visits for a patient on chronic opioids is every three months, and this should be reserved for the most stable and long-term patients, never new patients.

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Referrals for High-Risk Patients

Work Group Recommendation
Opioid prescribers should have a referral source for psychiatric treatment, substance use disorder treatment, physical therapy and pain medicine available if needed.
Benefit: It is important to provide patients with a multidisciplinary approach to the treatment of pain when necessary. Multidisciplinary care may improve pain outcomes and mitigate the harms caused by mental health and addiction, specifically lowering the risk of inadvertent overdose and death. **Harm:** Access to addiction and psychiatric resource in the community may be sparse. **Benefit-Harms Assessment:** Patients with mental health and/or addictive disorders receiving opioids are at high risk for harm, including death. To safely treat such patients, prescribers perform better and have better outcomes if they have access to referrals for assessment and treatment of these disorders.
Relevant Resources: *Gaither, 2016 (Observational Study); Reuben, 2015 (Report)*

Patients in pain benefit from a team approach. Recent evidence suggests that access to physical rehabilitation services, psychiatric care and substance use disorder treatment confers mortality benefit for patients on chronic opioids *(Gaither, 2016; Reuben, 2015; Coffin, 2014)*. Communication among the many clinicians caring for a patient in pain is essential. Communication among clinicians may require a release of information *(Substance Abuse and Mental Health Services Administration, The, 2016)*. Typically the patient should be expected to receive opioids from only one clinician and allow open communications among all clinicians.

Overdose

Opioid overdose is the most serious adverse effect of opioids. Pharmaceutical opioid overdose deaths rose dramatically in the late 1990s and early 2000s, accounting for more than 18,800 deaths in 2014 *(Centers for Disease Control and Prevention, 2016; Bock, 2015; Jones, 2013b; Centers for Disease Control and Prevention, 2011)*. This was the highest toll yet recorded. One does not need to have an opioid use disorder (OUD) to have an opioid overdose, though OUD is the most important risk factor. Other risks for opioid overdose include total opioid doses greater than 100 MME/day *(Liang, 2015; Gwira, 2014; Paulozzi, 2012; Bohnert, 2011)*, recent initiation of a long-acting opioid formulation *(Dhalla, 2009)*, advancing age, any substance use disorder (excluding tobacco), a mental health disorder, past opioid overdose *(Jones, 2013b)* and concomitant benzodiazepine use *(Dasgupta, 2016; Han, 2015; Turner, 2015; Jones, 2015; Dhalla, 2009)*. Important medical comorbidities that make a patient vulnerable to opioid overdose include renal insufficiency, respiratory insufficiency, sleep apnea and cognitive impairment.

In a patient surviving an opioid overdose, it is crucial to diagnose OUD if present, and to refer for appropriate treatment *(Gaither, 2016; Volkow, 2016b)*. Absent an OUD diagnosis, the clinical intervention should be tailored to the cause of the overdose. In a study of non-fatal opioid overdoses, 91% of patients are maintained on opioids after surviving the overdose. Continuing opioids after surviving an opioid overdose confers risk of repeated overdose and death *(Larochelle, 2016)*. Short of discontinuing the opioid, other actions clinicians may take after opioid overdoses include renal dosing, discontinuing a benzodiazepine and home health services to assist in adherence. Efforts should be made to minimize polypharmacy. A urine drug screen and an evaluation of alcohol use can uncover high-risk behaviors. Whatever the provider does, careful monitoring is required in patients who survive an opioid overdose. Providers should carefully document patients' understanding of the event and their reaction to it.

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13.9. If Opioid Use Disorder is Suspected, Consider Referral to Addiction Medicine Specialist

Opioid Use Disorder Assessment

Work Group Recommendation
Opioid prescribers should recognize the symptoms of opioid use disorder. **Opioid prescribers should understand the treatment options for opioid use disorder and have a referral source available.**
Benefit: Patients with opioid use disorder (OUD) receiving opioids for pain are at high risk of aberrant behavior and overdose death. Making the diagnosis of OUD and offering the proper referral for treatment may be a lifesaving intervention. Buprenorphine and methadone, given by a certified and trained specialist in their use, confers mortality benefit for patients with OUD. Intramuscular naltrexone decreases illicit use of opioids. **Harm:** Physicians are largely untrained at recognizing, counseling and treating patients with OUD. Referral options for medication-assisted therapy are sparse in many communities. **Benefit-Harms Assessment:** Of all the patients receiving opioids for pain, those with OUD are at the greatest risk of harm. Yet knowledge of diagnosis and treatment of OUD is insufficient among opioid prescribers. It is critical that providers take the time to become versed with this important risk factor of harm from opioids.
Relevant Resources: *Cousins, 2016 (Observational Study); Gaither, 2016 (Observational Study); Fullerton, 2014 (Review); Thomas, 2014 (Review); Carrieri, 2006 (Report)*

A systematic review of 38 studies by Vowles et al. (2015) found that the rates of opioid misuse averaged between 21 and 29% among adult patients with chronic non-cancer pain. Misuse was defined as opioid use contrary to the directed or prescribed pattern of use, regardless of the presence or absence of harm or adverse effects *(Vowles, 2015)*. In 2013, the nationwide 12-month prevalence of nonmedical use of prescription opioids and opioid use disorder (OUD) was 4.9 and 0.9%, respectively *(Han, 2015)*. Adolescents with healthy attitudes about drugs who are exposed to sanctioned opioid pharmaceuticals for pain have a 33% increase in future opioid misuse after high school *(Miech, 2015)*. Opioid-naïve adults who received opioids after a cataract removal had a 62% increased chance of still taking opioids a year later *(Alam, 2012)*. Opioid misuse, and later OUD, should not be viewed as "aberrant behavior" happening in difficult patients. It should be viewed as a potential adverse effect of opioids in all patients *(Volkow, 2016b; Kirschner, 2014; Dowell, 2013)*.

Risk factors for developing opioid misuse include another addiction (including tobacco), mental health disorders, history of childhood sexual trauma, past incarceration, family history of addiction, young age and higher reported pain severity *(Sehgal, 2012; Liebschutz, 2010; Chou, 2009d; Lanier, 2009)*. Twin studies show that the heritability of OUD is 55%, and in some groups even higher *(Sun, 2012)*. Knowledge of risk factors is critical, but no patient is free of risk of developing OUD.

Opioid use disorder, or addiction, is one of the most consequential and feared adverse effects of opioid use *(Volkow, 2016b; Kirschner, 2014)*. The best clinical tool for diagnosing OUD is the recently updated DSM-5 criteria *(American Psychiatric Association, 2013)*. The ASSIST-2 is a validated tool used to screen for substance use disorders. Patients with OUD can be challenging. Some physicians find it hard to address these patients' needs in the current medical system *(Lembke, 2012; Zgierska, 2012)*.

Pain and OUD are not mutually exclusive *(Neumann, 2013; Alford, 2006)*. A patient can suffer from chronic pain and secondarily develop an OUD; patients with OUD commonly develop painful conditions. The prevalence of OUD has been estimated at 10% or higher, by various authors, among patients taking opioids

chronically for pain *(Vowles, 2015; Juurlink, 2012; Boscarino, 2011)*. Some patients on chronic opioids for pain who develop OUD report improved pain control in a medication-assisted treatment setting using methadone or buprenorphine *(Neumann, 2013)*.

Opioid Use Disorder Treatment

OUD is a treatable chronic disease *(Volkow, 2016b; Volkow, 2014)*. Patients taking opioids chronically, who have access to substance use disorder services have a lower rate of overdose death *(Gaither, 2016)*. Treatment of OUD is the same regardless of the primary opioid used. No opioid should be considered inherently less addictive.

All opioid prescribers should understand the diagnostic criteria of OUD and have a referral for appropriate treatment available *(Coffin, 2014)*. FDA approved treatments of OUD include sublingual buprenorphine, oral methadone and intramuscular naltrexone *(Volkow, 2014)*. Methadone and buprenorphine have a well-established record of improving mortality, decreasing incarceration, decreasing IV needle use and improving pregnancy outcomes *(Cousins, 2016; Fullerton, 2014; Thomas, 2014; Volkow, 2014; Schwartz, 2013; Carrieri, 2006)*. Intramuscular naltrexone for OUD maintained sobriety in greater than 50% of patients for the first year *(Krupitsky, 2013)*. Intramuscular naltrexone can be prescribed by doctors and advanced practice providers. Only physicians can prescribe buprenorphine after completing an eight-hour training course *(Volkow, 2014)*. Methadone maintenance therapy for OUD should be provided only by a licensed addiction clinic *(Volkow, 2014)*. If a methadone or buprenorphine patient is admitted to the hospital, his or her maintenance drug can be continued by the inpatient provider if deemed medically suitable *(Alford, 2006)*.

Buprenorphine and naltrexone displace opioid agonists from the opioid receptors, blocking the action of opioid analgesics. Providers treating patients in pain who are taking these opioid blockers should consult with a physician or pharmacist knowledgeable about these medications. Patients on methadone maintenance therapy (MMT) can be given conventional opioid analgesics for pain, in the same quantity and strength. MMT patients will have diminished effect of the opioids and also have a higher risk of overdose and misuse of the opioids *(Alford, 2006)*. Therefore careful consideration of the risks and benefits for these patients is important. The most important step when treating a patient with an OUD on medication-assisted therapy is to communicate with his or her addiction provider. This will require a specific release of information *(Substance Abuse and Mental Health Services Administration, The, 2016)*.

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13.10. Offer Discontinuation of Opioids or Taper at Intervals of Six Months

The following are indications for discontinuation/taper of opioids:

- Patients who have had an opioid overdose require rapid dose reduction or opioid discontinuation, or another appropriate adjustment of medical care. Larochelle (2016) found that of 91% of opioid overdoses requiring hospitalization, the opioid dose is not adequately tapered.
- Patients at very high risk of opioid-related harm need rapid dose reduction or opioid discontinuation in a safe place.
- Patients not at risk of withdrawal (e.g., on low doses) can be discontinued without a taper.
- Patients with repeated infractions of the patient-provider agreement or with known diversion can be discontinued without a taper.
- Every patient on opioids should be offered individualized opioid tapering and additional treatment options at six-month intervals.

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Patients of any risk level who are not at risk of withdrawal can discontinue opioids without adverse effects. Patients at high risk for harm who are in pain may have an increase in pain as their opioids are decreased. Discontinuing opioids usually does not resolve the underlying pain generator; nor does it address the cause of any aberrant opioid-related behaviors. Providers who discontinue opioids incautiously may cause a health care crisis in the patient and create burden in other parts of the medical system.

Providers need to carefully assess when the harm to the patient of continuing opioids outweighs the harm of discontinuing the opioids. Patients are not always willing participants in the discontinuation of their opioids, but in select circumstances there are established benefits.

Immediate Discontinuation of Opioids

In some cases, an ongoing prescription of opioids should be discontinued immediately without a taper. Such cases include life-threatening side effects from the opioid, known diversion or a serious breach of the patient-provider agreement. Immediate discontinuation is also appropriate if the patient's exposure to opioids was minimal to begin with. If the patient has already passed through withdrawal – five or more days from his or her last opioid – the patient does not require a taper.

A past opioid overdose is the most compelling reason to immediately discontinue or drastically lower opioids. One study found that after non-fatal opioid overdoses, 93% of patients remain on opioids, conferring risk of repeat overdose and death *(Larochelle, 2016)*. With or without an overdose, OUD should warrant prompt referral to a medication-assisted addiction program and discontinuation of opioids. Patients with OUD who are tapered off opioids are at risk of self-harm unless referred to treatment *(Compton, 2016; Nagar, 2015)*. Inpatient detoxification programs are available for those who do not want to attend an addiction program but also do not want to experience withdrawal.

Tapering Opioids

Work Group Recommendation
Once the patient and clinician agree to taper opioids, it should be individualized to the patient's circumstances, and a referral source should be available. **While tapering opioids, patients should be offered additional treatment options and frequent follow-up.** **Opioid tapering should be discussed and offered at intervals of six months for all patients on chronic opioids.**
Benefit: Each patient has unique reactions to opioids and exposure to them, making uniform tapering protocols impractical. Patient involvement in their own taper may improve outcomes. Intensified care during an opioid taper may improve patient-doctor communication and identify complications early. **Harm:** No good trial demonstrates how to best taper patients receiving opioids. **Benefit-Harms Assessment:** Guidelines and protocols are encouraging less use of opioids and emphasizing the harms of opioids but no one can say with certainty how to best taper a patient already on opioids. A reasonable recommendation is that providers work closely with patients, monitoring for risks, and individualize an opioid taper.
Relevant Resources: *Accurso, 2016 (Observational Study); Centers for Disease Control and Prevention, 2016 (Guideline); Berna, 2015 (Review)*

Clinicians should routinely ask patients on chronic opioids if they would like to try to discontinue their opioids, even if there are no adverse events. It is the consensus of the work group that opioid tapering

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should be discussed and offered at intervals of six months for all patients on chronic opioids. This discussion should be part of the review of pain, function, quality of life, medications, adverse effects and the risk/benefit analysis for opioid use.

It is impossible to know the correct number of days, or increments of change, to make an outpatient opioid taper successful. Therefore, providers tapering opioids should maintain open communication and close follow-up throughout the process. Factors that complicate outpatient tapers include long duration of opioid therapy, high-dose opioids, past failed tapers, psychiatric comorbidity, substance use disorders and cognitive impairment.

Traditionally opioids are tapered in increments of 10% of the original dose. The fastest taper is 10 days, each day lowering by an equal amount *(Berna, 2015)*. Tapers are often 30, 45 or 60 days, decreasing opioids by 10% at regular intervals throughout *(Centers for Disease Control and Prevention, 2016)*. Exact increments of 10% are often not possible and are not necessary. Patients may tolerate increments as great as 30% early in the taper and prefer increments less than 10% late in the taper (Washington state guideline). What matters most is open communication and steady progress toward the goal of cessation of opioids *(Accurso, 2016)*.

Pregnant women who are at risk of opioids withdrawal should not be tapered off opioids without expert guidance. Opioid withdrawal in pregnancy can cause preterm labor and miscarriage.

A prolonged taper may be preferred for patients on long-term, high-dose opioids without an urgent reason for a taper. Decreasing the opioid dose once a week, or even once every other week, allows the patient to adjust fully to the new, lower dose before the dose changes again. Prolonged tapers allow the patient to take the same number of pills every day for a week or more, simplifying the regimen and helping adherence. If the patient is feeling unwell, a brief pause in the taper is acceptable. Patients may take six months or longer, slowly and steadily lowering the opioid dose, before they discontinue the opioid entirely.

Troubleshooting a Failed Taper

During a taper, patients may experience sweats, chills, gastrointestinal symptoms, poor sleep, restlessness and a variety of types of pain *(Wesson, 2003)*. It is appropriate to reassure the patient that this is an expected part of withdrawal and offer symptomatic support. As the taper progresses, the pain treated with opioids may reemerge. Addressing that pain through other modalities is critical. Patients are less likely to adhere to the taper if they are not provided with other tools to address their pain.

Sometimes a taper fails because it involves too many small doses of opioids. Simplifying the taper by switching to a comparable opioid dose, but consolidating to fewer long-acting pills, may improve outcomes. For example, a patient may fail to taper from 24 five mg oxycodone tablets taken daily but succeed at tapering from two long-acting oxycodone taken daily. This should be done only by an experienced clinician as long-acting opioids are generally not preferable to short-acting opioids and medication adherence is essential. In addition, consulting with a pharmacist may help you design the optimal taper.

As opioids are tapered, anxiety will increase. The more rapid the taper, the more pronounced the effect. If the patient has an underlying mental health disorder he or she is less likely to tolerate the taper, particularly a rapid taper *(Wasan, 2015)*. Pain psychology consults and psychiatry may be necessary if a taper is failing. Giving the patient some control over the speed of the taper may also help.

Patients with underlying substance use disorders may struggle with tapering opioids. They are also at risk of harming themselves after a taper by seeking opioids through other, sometimes illicit, channels *(Dart, 2015; Nagar, 2015)*. Patients with OUD should be referred to a medication-assisted treatment program, which can either maintain or taper the patient on an alternative and safer medication (buprenorphine or methadone) *(Berna, 2015)*. Patients with other substance use disorders need close follow-up and careful monitoring of their substance use as they taper. An alcoholic may compensate for decreased opioid by increasing alcohol intake.

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Patients unable to consistently follow instructions may need an intervention to assist adherence. Patients with cognitive impairments may not be able to execute a taper. Benzodiazepines cause amnesia and disinhibition, both of which may interfere with a taper. Sometimes the very aberrant behavior that prompts the taper (erratic pill taking) is the thing that makes the taper fail. Home health services with automated medicine cabinets help some patients. Some pharmacies are willing to accept multiple short-term prescriptions for the opioid taper, breaking the taper up into a week at a time or less frequently.

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14. Coordination of Care and Follow-Up

The collaborative care model is an approach to health care delivery that includes providing care management and system support *(Katon, 1999)*. It utilizes a team approach including the patient as a team member and specialty consultation support.

Elements of a collaborative care model include:

- Dedicated staff to coordinate, support and educate patients
- Methods for reliable and systematic patient follow-up
- Consistent use of evidence-based treatment practices

The care team may include members outside of the health care system or clinic. The creation of information-sharing protocols among the entities is crucial; the patient's consent for this sharing must be obtained. Primary care clinicians can play an important role in the seamless coordination of care, with the help of nurse care managers and community health workers.

Ongoing shared decision-making

The care team must have the tools and resources needed to engage in close communication with the patient while the care plan is being instituted. Alterations to the plan are common and need to be reflected in the written care plan. Again, mutual agreement between the patient and the care team regarding changes in the plan is vital.

Contracts and patient self-management

Physicians use "medication contracts" to monitor the patient's adherence to the care plan. These contracts are instituted most often when opioids are prescribed but could be used in other instances where the care team deems them necessary. The use of a pain management contract allows for the documentation of understanding between the care team and the patient. This document should be seen as a means to facilitate care and can, if used appropriately, improve communication among the clinicians and patient. Many of the elements within a pain agreement hold the patient accountable for his or her own self-management of the pain medication.

Follow-up and communication plan

A follow-up plan as well the patient's preferred means of communication should be outlined in the care plan. Coordination of appointments is the obligation of the care team. With the many new ways patients communicate with their care team (e.g., text messaging, patient portals) or receive care (e.g., telehealth visits), the ease of communication has been improved when these tools are implemented.

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The Aims and Measures section is intended to provide protocol users with a menu of measures for multiple purposes that may include the following:

- population health improvement measures,
- quality improvement measures for delivery systems,
- measures from regulatory organizations such as Joint Commission,
- measures that are currently required for public reporting,
- measures that are part of Center for Medicare Services Physician Quality Reporting initiative, and
- other measures from local and national organizations aimed at measuring population health and improvement of care delivery.

This section provides resources, strategies and measurement for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.

The subdivisions of this section are:

- Aims and Measures
- Implementation Recommendations
- Implementation Tools and Resources
- Implementation Tools and Resources Table

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Aims and Measures

1. Increase the percentage of patients with clinic visits for pain who have documentation of pain status and functional assessments at the visits. *(Annotation #1)*

   Measure for accomplishing this aim:

   a. Percentage of patients with visits for pain who have documentation of the following at the visits *(all or none measure):*

      - Pain status assessment
      - Functional assessment

2. Increase the percentage of patients with a chronic pain diagnosis who are undergoing physical therapy and have a reassessment of their functional status within 12 weeks of initiating physical therapy. *(Annotation #10)*

   Measure for accomplishing this aim:

   a. Percentage of patients with chronic pain diagnosis who are undergoing physical therapy and have a reassessment of their functional status within 12 weeks of initiating physical therapy.

3. Increase the percentage of chronic pain patients with an opioid prescription who receive appropriate care. *(Annotation #13.8)*

   Measure for accomplishing this aim:

   a. Percentage of patients with chronic pain diagnosis who are prescribed opioids with documentation of the following:

      - Patient-provider agreement
      - Urine drug testing once in the past 12 months
      - Risk assessment
      - Patient education on the risks, side effects and disposal of opioids
      - PMP check twice in the past 12 months since the last visit
      - Follow-up visits at least once a quarter
      - MME dose/day documentation
        - If opioid prescription, < 90 MME/day
        - If concurrent benzodiazepines prescription, < 50 MME/day
      - Taper or discontinuation of opioids at intervals of six months
      - Naloxone prescription offered or on file

4. Increase the percentage of patients with a new opioid prescription who are prescribed opioids appropriately. *(Annotation #13.5)*

   Measure for accomplishing this aim:

   a. Percentage of patients with a new opioid prescription (no opioid prescription for at least 90 days) that is less than 100 MME total of short-acting opioid.

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5. Increase the percentage of chronic pain patients with a long-acting opioid prescription formulation where criteria for prescribing were met. *(Annotation #13.4)*

   Measures for accomplishing this aim:

   a. Percentage of long-acting formulations where following criteria for prescribing were met:

      - History of tolerance is checked
      - Medication adherence is verified

6. Increase the percentage of patients with new opioid prescriptions in dental, ED and urgent care setting where PMP is checked prior to prescribing. *(Annotation #13.8)*

   Measure for accomplishing this aim:

   a. Percentage of new opioid prescriptions in dental, ED and urgent care settings where PMP is checked prior to prescribing.

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Measurement Specifications

Measurement #1a

Percentage of patients with visits for pain who have documentation of the following at the visits (all or none measure):

- Pain status assessment
- Functional assessment

Population Definition

Patients with visits for pain. Excluding migraines, active cancer and those receiving palliative or hospice care.

Data of Interest

$$\frac{\text{\# of patients with the documentation of pain and functional status assessments at the visit}}{\text{\# of patients with visits for pain}}$$

Numerator and Denominator Definitions

Numerator: Number of patients who have documentation of the following at the visits: pain status assessment and functional assessment.

Denominator: Number of patients with visits for pain.

Method/Source of Data Collection

Query the EMR for the number of patients with office visits for pain. Out of that number, determine the number of patients who had documentation that pain status and functional status assessments that were done at the visit.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is an all or none process measure, and improvement is noted as an increase in the rate.

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Measurement #2a

Percentage of patients with a chronic pain diagnosis who are undergoing physical therapy and have a reassessment of their functional status within 12 weeks of initiating physical therapy.

Population Definition

Patients with chronic pain diagnosis, undergoing physical therapy. Excluding migraines, active cancer and those receiving palliative or hospice care.

Data of Interest

$$\frac{\text{\# of patients who have a reassessment of their functional status within 12 weeks of initiating physical therapy}}{\text{\# of patients with chronic pain diagnosis, undergoing physical therapy}}$$

Numerator and Denominator Definitions

Numerator: Number of patients who have a reassessment of their functional status within 12 weeks of initiating physical therapy.

Denominator: Number of patients with chronic pain diagnosis, undergoing physical therapy.

Method/Source of Data Collection

Query the EMR for the number of patients with chronic pain diagnosis who are undergoing physical therapy. Out of that number, determine the number of patients who had a reassessment of their functional status within 12 weeks of initiating physical therapy.

Time Frame Pertaining to Data Collection

Quarterly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

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Measurement #3a

This measure is designed to help a health care system determine whether the policies they have put in place are being followed regarding the management of a patient with chronic pain who is prescribed opioids long term. The health care system may choose to use these components as a bundle of all or none, or select only the components of opioid management that they wish to measure and improve.

Percentage of patients with chronic pain diagnosis who are prescribed opioids with documentation of the following:

- Patient-provider agreement
- Urine drug testing once in the past 12 months
- Risk assessment
- Patient education on the risks, side effects and disposal of opioids
- PMP check twice in the past 12 months since the last visit
- Follow-up visits at least once a quarter
- Opioid MME dose/day documentation
  - If opioid prescription, < 90 MME/day
  - If concurrent benzodiazepines prescription, < 50 MME/day
- Taper or discontinuation of opioids at intervals of six months
- Naloxone prescription offered or on file

Population Definition

Patients with pain diagnosis who are prescribed opioids. Excluding migraines, active cancer and those receiving palliative or hospice care.

Data of Interest

$$\frac{\text{\# of patients with documentation of the following as specified in the numerator}}{\text{\# of patients with chronic pain diagnosis who are prescribed opioids}}$$

Numerator and Denominator Definitions

Numerator: Number of patients with documentation of the following:

- Patient provider agreement
- Urine drug testing once in the past 12 months
- Risk assessment
- Patient education on the risks, side effects, and disposal of opioids
- PMP check twice in the past 12 months since the last visit
- Follow-up visits at least once a quarter
- Opioid MME dose/d documentation
  - If opioid prescription, < 90 MME/d
  - If concurrent benzodiazepines prescription, < 50 MME/d
- Taper or discontinuation of opioids at intervals of six months
- Naloxone prescription offered or on file

Denominator: Number of patients with chronic pain diagnosis who are prescribed opioids.

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Method/Source of Data Collection

Query the EMR for the number of patients with chronic pain diagnosis who are prescribed opioids. Excluding migraines, active cancer and those receiving palliative or hospice care. Out of that number, determine the number of patients who had documentation of the components specified in the numerator.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

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Measurement #4a

Percentage of patients with a new opioid prescription (no opioid prescription from your institution for at least 90 days) that is less than 100 MME total of short-acting opioid.

Population Definition

Patients with pain diagnosis with a new opioid prescription (no opioid prescription for at least 90 days). Excluding migraines, active cancer and those receiving palliative or hospice care.

Data of Interest

$$\frac{\text{\# of patients with new opioid prescriptions that are less than 100 MME total of short-acting opioid (no opioid prescription for at least 90 days), whichever is less}}{\text{\# of patients with chronic pain diagnosis with a new opioid prescription}}$$

Numerator and Denominator Definitions

Numerator: Number of patients with new opioid prescriptions that are less than 100 MME total of short-acting opioid.

Denominator: Number of patients with chronic pain diagnosis with a new opioid prescription (no opioid prescription for at least 90 days). Exclude patients with an opioid prescription for cancer, migraine and end-of-life care.

Method/Source of Data Collection

Query the EMR for the number of patients with chronic pain diagnosis with a new opioid prescription (no opioid prescription for at least 90 days). Exclude patients with an opioid prescription for cancer, migraine, and end-of-life care. Out of that number, determine the number of patients with new opioid prescriptions that are less than 100 MME of total of short-acting opioid.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

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Measurement #5a

Percentage of long-acting formulations where the following criteria for prescribing were met:

- History of tolerance is checked
- Medication adherence is verified

Population Definition

Patients with chronic pain diagnosis with an opioid prescription with a long-acting formulation. Excluding migraines, active cancer and those receiving palliative or hospice care.

Data of Interest

$$\frac{\text{\# of patients with an opioid prescription that is long-acting with the criteria for prescribing met}}{\text{\# of patients with chronic pain diagnosis with an opioid prescription, with a long-acting formulation}}$$

Numerator and Denominator Definitions

Numerator: Number of patients with an opioid prescription that is long-acting where the following criteria for prescribing were met:

- History of tolerance is checked
- Medication adherence is verified

Denominator: Number of patients with chronic pain diagnosis with an opioid prescription with a long-acting formulation. Exclude patients with an opioid prescription for cancer, migraine and end-of-life care.

Method/Source of Data Collection

Query the EMR for the number of patients with chronic pain diagnosis with an opioid prescription with a long-acting formulation. Exclude patients with an opioid prescription for cancer, migraine and end-of-life care. Out of that number, determine the number of patients with an opioid prescription that is long-acting formulation where the following criteria for prescribing were met:

- History of tolerance is checked
- Medication adherence is verified

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

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Measurement #6a

Percentage of new opioid prescriptions in dental, ED and urgent care settings where PMP is checked prior to prescribing.

Population Definition

Patients with new opioid prescriptions in dental, ED and urgent care settings. Excluding migraines, active cancer and those receiving palliative or hospice care.

Data of Interest

$$\frac{\text{\# of patients with new opioid prescriptions where PMP is checked prior to prescribing}}{\text{\# of patients with new opioid prescriptions in dental, ED and urgent care settings}}$$

Numerator and Denominator Definitions

Numerator: Number of patients with new opioid prescriptions where PMP is checked prior to prescribing.

Denominator: Number of patients with new opioid prescriptions in dental, ED and urgent care settings. Exclude patients with an opioid prescription for cancer, migraine and end-of-life care.

Method/Source of Data Collection

This measure requires the use of a structured data field in the EMR to document PMP check. Query the EMR for the number of patients with new opioid prescriptions in dental, ED and urgent care settings. Exclude patients with an opioid prescription for cancer, migraine and end-of-life care. Out of that number, determine the number of patients with new opioid prescriptions where PMP is checked prior to prescribing.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is noted as an increase in the rate.

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Implementation Recommendations

Prior to implementation, it is important to consider current organizational infrastructure that address the following:

- System and process design
- Training and education
- Culture and the need to shift values, beliefs and behaviors of the organization

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline:

- Communicate a clear and consistent message that clarifies:
  - Pain is a normal part of life, all pain is legitimate, and the goals are to improve function, quality of life and comfort.
  - Opioid usage is the last resort, and the benefits must outweigh the risk for each patient.
- Chronic pain should be managed proactively like any other chronic condition:
  - Develop a process to allow the patient to see a dedicated care team that has interest or expertise in chronic pain.
  - Develop relationships in the community and appropriate referral sources to create an interdisciplinary pain management team.
  - Develop protocols/work flows that guide clinicians to ensure consistent management of pain.

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Implementation Tools and Resources

Criteria for Selecting Resources

The following tools and resources specific to the topic of the guideline were selected by the work group. Each item was reviewed thoroughly by at least one work group member. It is expected that users of these tools will establish the proper copyright prior to their use. The types of criteria the work group used are:

- The content supports the clinical and the implementation recommendations.
- Where possible, the content is supported by evidence-based research.
- The author, source and revision dates for the content are included where possible.
- The content is clear about potential biases, and conflicts of interests and/or disclaimers are noted where appropriate.

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Implementation Tools and Resources Table

Author/Organization	Title/Description	Web Sites/Order Information
Resources		
100 Million Healthier Lives, convened by the Institute for Healthcare Improvement	This site has links to numerous tools to help you work in collaboration with your community to fight the opioid epidemic.	http://www.100mlives.org/approach-priorities/#opioid
Institute for Functional Medicine	Information for clinicians about functional medicine.	https://www.functionalmedicine.org
International Association for the Study of Pain	IASP Taxonomy has definitions of pain. The patient resources section has links to numerous resources.	http://www.iasp-pain.org/index.aspx
Minnesota Dental Association Protocol for Assessment and Treatment of Oral/Facial Pain		http://mndental.org/files/MDA-Protocol-1.pdf
National Center for Complementary and Integrative Medicine	Patient and provider education materials.	http://nccih.nih.gov/
Substance Abuse and Mental Health Services Administration	Patient and provider education materials.	http://www.samhsa.gov/
Turn the Tide Rx Campaign	This site is sponsored by the Office of the Surgeon General to help fight the opioid epidemic.	http://turnthetiderx.org/
U.S. Department of Health and Human Services/ National Institutes of Health	Patient education material on prescription drugs: abuse and addiction.	https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiate-WithdrawalScale.pdf
U.S. Department of Justice, Drug Enforcement Administration (DEA)	Information about efforts to prevent diversion of drugs of abuse, drug uses and effects.	https://www.deadiversion.usdoj.gov/ http://www.getsmartaboutdrugs.com
U.S. Food and Drug Administration	FDA has resources related to opioids including provider and patient education such as appropriate disposal.	http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337852.htm
U.S. Food and Drug Administration ER/LA Opioid Analgesics REMS	The Extended-Release and Long-Acting Opioid Analgesics Risk Evaluation and Mitigation Strategy. A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential serious risks associated with a drug product and are required by the Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks.	https://www.fda.gov/drugs/information-drug-class/opioid-analgesic-risk-evaluation-and-mitigation-strategy-rems
Veterans Association Patient Education Materials	Taking Opioids Responsibly for Your Safety and the Safety of Others: Patient Information Guide on Long-term Opioid Therapy for Chronic Pain	https://www.va.gov/PAINMANAGEMENT/Opioid_Safety_Initiative_OSI.asp

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Author/Organization	Title/Description	Web Sites/Order Information
Implementation Tools		
Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST)	Opioid assessment tool/substance use risk.	http://www.who.int/substance_abuse/activities/assist_test/en/
American Psychiatric Association	DSM-5	https://www.psychiatry.org/psychiatrists/practice/dsm
CAGE-AID	Alcohol screening plus substance abuse and mental health.	http://www.integration.samhsa.gov/images/res/CAGEAID.pdf
Centers for Disease Control and Prevention	Calculating total daily dose of opioids for saver dosing.	http://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf
Clinical Opiate Withdrawal Scale (COWS)	Opioid withdrawal signs and symptoms.	https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiate-WithdrawalScale.pdf
DIRE score	Opioid Assessment tool	http://integratedcare-nw.org/DIRE_score.pdf
Faces Pain Scale	For clinical, educational, or research purposes, use of the FPS-R is free of charge, and permission for use is not needed, ***provided that the scale is not modified or altered in any way***. Please download the FPS-R and instructions.	Faces Pain Scale – Revised, © 2001, International Association for the Study of Pain (http://www.iasp-pain.org/FPSR)
GAD-7	Anxiety screen	https://www.integration.samhsa.gov/clinical-practice/GAD708.19.08Cartwright.pdf
National Institute on Drug Abuse	The National Institute on Drug Abuse has a simple 4-question screen for drug use in general medical settings.	https://www.drugabuse.gov/nmassist/?q=qm_json&pageId=questions_1&pageName=QuickScreen&token_id=136912#
Oswestry Low Back Disability Index	Functional/QOL Assessment	http://www.rehab.msu.edu/_files/_docs/Oswestry_Low_Back_Disability.pdf
Pain intensity, Interference with enjoyment of life, and Interference in general activity (PEG)	Multidimensional pain Intensity and interference	See Appendix E
PHQ-9	Depression screen	http://www.phqscreeners.com/sites/g/files/g10016261/f/201412/PHQ-9_English.pdf
Roland-Morris Disability Scale	The original questionnaire and all translations are in the public domain. No permission is required for their use or reproduction.	http://www.rmdq.org

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Author/Organization	Title/Description	Web Sites/Order Information
Implementation Tools (continued)		
The Primary Care PTSD Screen Tool (PC-PTSD)	Commonly used tool to screen for PTSD.	http://www.integration.samhsa.gov/clinical-practice/pc-ptsd.pdf

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The subdivisions of this section are:

- References
- Appendices

References

Links are provided for those new references added to this edition (author name is highlighted in blue).

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Appendix A – ABCDPQRS Mnemonic

This tool was developed by the ICSI Acute Pain Assessment and Opioid Prescribing Protocol work group to assist Minnesota clinicians and should be modified if used in other states.

Alcohol Use

Alcohol affects judgment and memory, and impairs respiration when combined with opioids, all of which place the patient at increased risk of accidental overdose and trauma. There is no known safe dose of alcohol for a patient taking opioids, particularly when the patient is opioid naïve or on a higher dose than previously taken. The safest recommendation for patients on new or higher-than-baseline doses of opioids is to abstain from alcohol completely.

In a patient using opioids for pain, an alcohol use disorder confers particular risk when combining alcohol and opioids in an unsafe manner or using opioids inappropriately even in the absence of alcohol use. Two useful and simple screenings tools are included below. For patients who have a positive screen, a deeper evaluation for an alcohol use disorder is indicated. For those with at-risk alcohol use but not an alcohol use disorder, consider a brief intervention. For those with an alcohol use disorder, treatment in primary care or referral to addiction treatment is indicated *(Bohnert, 2011; Feldman, 2011)*.

Screening tools

One simple screening tool uses two questions to assess for alcohol and drug use disorders in the primary care and emergency settings:

> "How many times in the past year have you had five or more drinks (if male), four or more drinks (if female) in a day?" A response of ≥ 1 is considered positive.
>
> "How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?"

A response of ≥ 1 to either question is considered positive. A positive screen does not diagnose substance use disorder but suggests a problem and warrants caution in prescribing opioids. The link below is a simple pocket guide for this issue.

> http://pubs.niaaa.nih.gov/publications/Practitioner/pocketguide/pocket_guide5.htm

A three-question screening tool for hazardous alcohol use is the AUDIT-C. This tool is also well validated and can be seen at the link below:

> http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2517893/

SBIRT Model for Substance Use

For those patients who have a positive screen for misuse of drugs or alcohol, "Screening, Brief Intervention, Referral to Treatment (SBIRT)" is a comprehensive and integrated approach to the delivery of early intervention and treatment services. SBIRT reduces alcohol consumption and alcohol-related harm when done in the outpatient or emergency department settings. Additional information can be obtained at ICSI SBIRT Model and Implementation and http://www.samhsa.gov/sbirt.

Benzodiazepines and Other Drug Use

Like alcohol, benzodiazepine (BZD) used concurrently with opioids increases the risk of over sedation, overdose and trauma. Patients using BZDs and opioids should be counseled not to combine these medications. The BZD prescriber should be made aware of opioid prescriptions if possible. Patients on opioids

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and BZDs with other risks factors for opioid-related adverse events (e.g., respiratory compromise, risk of falls or substance use disorder) are at a particularly increased risk of harm.

Marijuana use is so pervasive that it is not practical to test every patient in acute pain for marijuana. However, those patients known to consume it regularly warrant more careful monitoring when prescribing opioids for pain *(Pesce, 2010; Reisfield, 2009; Ellickson, 2005)*.

Cocaine use has been associated with increased risk of diversion of opioids, and any patient with a substance use disorder should be educated carefully about the risks of combining drugs and overusing opioids. Clinicians may choose to prescribe fewer pills, use smaller doses and follow up within three to five days *(Gudin, 2012; Liebschutz, 2010; Becker, 2009; Ives, 2006)*.

Further information on substance use issues can be accessed at the link below:

https://www.samhsa.gov/data/

Clearance and Metabolism of the Drug

Many opioids require renal clearance of active metabolites. Morphine and meperidine are toxic in renal insufficiency (GFR < 60). For patients with severely decreased renal function (GFR < 30), hydrocodone and oxycodone will have delayed elimination. Before prescribing opioids, consider whether the patient may be at risk of renal insufficiency, and check the medical record for a recent serum creatinine.

Hepatic impairment, if severe, can affect the metabolism of many opioids. A dosage adjustment or change of dosing interval may be necessary for morphine, hydrocodone and oxycodone. For patients with impaired liver function, consider lowering the dose of acetaminophen or, preferably, avoiding the use of acetaminophen/opioid combination medication altogether. Half of the liver transplants in America are caused by acetaminophen-related liver failure; half of those are caused by combination opioid/acetaminophen product overuse. Before prescribing a combination product, evaluate the patient for possible liver impairment. If acetaminophen is not needed, do not prescribe the combination product *(Johnson, 2007)*.

Delirium, Dementia and Falls Risk

Patients on acute dosing of opioids are at an increased risk from falls and other accidental trauma. This is particularly so for geriatric patients. Opioids should be used cautiously for patients with past falls or at an increased risk of fracture. Some guidelines suggest prescribing half the normal initial dose when treating the elderly. Other CNS depressants such as anticholinergic medications, alpha adrenergic blockers and benzodiazepines will compound the risk of falls and fractures in patients on opioids.

Opioids can precipitate delirium in some patients. Those with significant risk factors for opioid-induced delirium include the elderly patients with cognitive impairments, polypharmacy, advanced liver or kidney disease, and patients with prior episodes of delirium precipitated by opioids. Consider these factors when dosing opioids, and educate the patient and his or her family of the risks *(Manchikanti, 2012a)*.

Psychiatric Comorbidities

World Health Organization data obtained in primary care centers worldwide show that 22% of all primary care patients suffer from persistent debilitating pain and that these patients are four times more likely to have comorbid anxiety or depressive disorder than pain-free primary care patients *(Lépine, 2004)*.

Opioids should be regarded as having powerful anxiolytic properties as well as analgesic properties. Opioids have no indication for mental health disorders, yet this anxiolytic effect is readily recognizable by the distressed patient. Psychic distress may exacerbate nociceptive (physical) pain or be confused for physical pain. The most common reason for illicit opioid use in high school is for relief of anxiety. Many mental health disorders are correlated with increased opioid misuse, opioid-related accidents and accidental opioid

overdose death. Post-traumatic stress disorder and childhood sexual trauma increase the risk of opioid-related adverse events tenfold. Depression and anxiety disorders (including generalized anxiety disorder, social anxiety disorder and obsessive compulsive disorder) are known to increase the risk of opioid misuse and harm, as well. Childhood attention deficit hyperactivity disorder is a risk for later pharmaceutical misuse. Opioid withdrawal can exacerbate psychotic symptoms *(Seal, 2012; Liebschutz, 2010; Fleming, 2008; Wasan, 2007)*.

A mental health condition does not preclude opioid use for pain, but clinicians prescribing opioids for pain should carefully consider if the pain reported is a surrogate for psychic distress. Patients with mental health disorders should be educated that they will experience psychic relief from the opioids and that this relief is not the intended effect of the pain medication. Patients with untreated or undertreated mental health disorders should be offered safe and appropriate psychiatric care. Before prescribing opioids to mentally ill patients, an assessment of suicide risk is wise. The Safe-T tool is recommended by the American Psychiatric Association practice guidelines and can be found at http://www.integration.samhsa.gov/images/res/SAFE_T.pdf.

Mental Health Screening Tools

The PHQ-2 is a well-validated, two-question screening tool for depression. A score greater than three has 82% sensitivity and 90% specificity for major depressive disorder.

"Over the past two weeks, how often have you been bothered by any of the following?" (on a 0 through 3 scale) *(Gilbody, 2006)*

- Little interest or pleasure in doing things
- Feeling down, depressed or hopeless

The GAD-2 also has high sensitivity and specificity for anxiety disorders *(Kroenke, 2007)*. The GAD-2 has a similar introduction and scoring, but the questions are about:

- feeling nervous, anxious or on edge; and
- not being able to stop or control worrying.

Query the Prescription Monitoring Program

Query a prescription monitoring program (PMP) when prescribing opioids for an acute pain condition. In greater than 50% of acute pain visits, the patient has already received from a different clinician an opioid for that pain within one month. The PMP lists all controlled substances filled in the state in the last 12 months and increasingly includes data from other states, as well. (Prescriptions from methadone maintenance clinics, Indian Health Service, long-term care facilities, and the Veterans Administration pharmacy are currently not included in Minnesota.) Non-prescribers (e.g., administrative help, nurses, interns) can query the PMP as a physician proxy in Minnesota in order to expedite the process *(Volkow, 2011; Gugelmann, 2011; Paulozzi, 2011; Wang, 2009)*.

See the link below to register and/or access the database:

http://pmp.pharmacy.state.mn.us/

For information about monitoring programs within your state or country, contact your pharmacy board.

Respiratory Insufficiency and Sleep Apnea

Patients with hypoxia, hypercapnia, sleep apnea, chronic obstructive pulmonary disease, congestive heart failure and concurrent use of benzodiazepines, alcohol or barbiturates will be at an increased risk of respiratory insufficiency and respiratory arrest from opioids. Sleep apnea is a commonly missed diagnosis, and the

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symptoms of this disease are often not readily apparent to the patient or physician. Opioids likely exacerbate both obstructive and central sleep apnea.

Safe Driving, Work, Storage and Disposal

Minnesota law states that driving under the influence of a controlled substance or having any amount or the metabolites of a Schedule II controlled substance constitutes a DWI. Aside from the legal implications, it is unsafe to drive on new or newly increased doses of opioids, let alone attempting to drive while in acute pain. Similarly, work, parenting or other duties requiring concentration and coordination will be impaired by opioids and by acute severe pain itself. Involve and inform the patient's family and/or caregiver to provide additional support in the areas above.

To access a hard copy of the statute, see the link below:

http://www.house.leg.state.mn.us/hrd/pubs/dwiover.pdf

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Appendix B – Non-Opioid Pharmacology

Acetaminophen

Acetaminophen is an analgesic that may be used initially for the treatment of mild chronic pain or to augment other agents in treating mild to moderate pain. It lacks anti-inflammatory effects but is generally well tolerated at therapeutic doses. It does not damage the gastric mucosa but may have chronic renal- or hepatic-adverse effects *(American Pain Society, 2008)*. Dosage should be restricted to a maximum of 4,000 mg per 24 hours, including acetaminophen contained in combination opioid products such as hydrocodone with acetaminophen. Acetaminophen should be used cautiously or avoided in patients with liver impairment.

Names of medications: Tylenol and various over-the-counter (OTC) products.

Indications

- Acetaminophen is an analgesic that may be used for the treatment of mild to moderate acute or chronic pain or to augment other agents.

Mechanism of action

- Has a central analgesic effect, with unknown mechanism. Possibly through inhibition of prostaglandin synthesis and elevation of the pain threshold.

Common adverse events

- Low incidence of GI effects, possible renal toxicity and liver toxicity associated with high-dose, long-term use.
- FDA recommends a maximum of 4,000 mg in 24 hours, including acetaminophen in combination opioid products.
- Lower dose limits of 2,000-3,000 mg daily for elderly, hepatically impaired patients, alcoholics and patients on other hepatotoxic medications.

Contraindications

- Use cautiously or avoid in patients with liver toxicity.

Anticonvulsants

Anticonvulsants have been used for the treatment of pain for over 50 years. Most of the evidence to support the use of anticonvulsants in pain management is for treatment of neuropathy and fibromyalgia. Mechanisms of action for the anticonvulsants differ and are not fully understood in relation to analgesic effect. In general, the class has a significant risk of side effects and requires frequent monitoring by the prescribing provider. Use in certain populations, such as the geriatric population, should be done with caution and with close follow-up.

Names of medications: Carbamazepine, gabapentin, lamotrigene, oxcarbazepine, sodium valproate, and pregabalin

Indications

- **Trigeminal neuralgia**
  - Carbamazepine *(Vargas-Espinosa, 2012; Goodyear-Smith, 2009)*
  - Oxcarbazepine
  - Lamotrigine *(Goodyear-Smith, 2009)*

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- **Fibromyalgia**
  - Pregabalin *(Wiffen, 2013)*
  - Gabapentin
  - Lacosamide **not beneficial** *(Hearn, 2012)*
  - Phenytoin **not beneficial** *(Birse, 2012)*
- **Diabetic peripheral neuropathy**
  - Pregabalin *(Griebeler, 2014; Wiffen, 2013; Moore, 2011; Goodyear-Smith, 2009)*
  - Gabapentin *(Griebeler, 2014; Wiffen, 2013; Goodyear-Smith, 2009)*
  - Oxcarbazepine
  - Carbamazepine *(Griebeler, 2014; Goodyear-Smith, 2009)*
  - Sodium valproate *(Goodyear-Smith, 2009)*
- **Post-herpetic neuralgia**
  - Pregabalin *(Wiffen, 2013; Goodyear-Smith, 2009)*
  - Gabapentin *(Wiffen, 2013; Vargas-Espinosa, 2012, Goodyear-Smith, 2009)*
  - Carbamazepine *(Goodyear-Smith, 2009)*
  - Sodium valproate *(Goodyear-Smith, 2009)*
- **Painful HIV-associated neuropathy**
  - Lamotrigine *(Goodyear-Smith, 2009)*
  - Gabapentin *(Goodyear-Smith, 2009)*
- **Complex regional pain syndrome type I**
  - Lamotrigine *(McCleane, 2000)*
- **Neuropathic pain associated with spinal cord injuries**
  - Pregabalin *(Snedecor, 2013; Goodyear-Smith, 2009)*
  - Gabapentin *(Goodyear-Smith, 2009; Kroenke, 2009b)*
- **Pain in patients with Guillain-Barre syndrome**
  - Carbamazepine *(Goodyear-Smith, 2009)*
  - Gabapentin *(Goodyear-Smith, 2009)*
- **Acute and chronic pain**
  - Lamotrigine **not beneficial** *(Wiffen, 2007)*
- **Polyneuropathy**
  - Levetiracetam **not beneficial** *(Holbech, 2011)*
  - Phenytoin **not beneficial** *(Birse, 2012)*

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General mechanism

- Pregabalin and gabapentin modulate the alpha2delta subunit of the N-type voltage-gated calcium channels, regulating the influx of calcium into the nerve and reducing the outflow of excitatory neurotransmitters that transmit pain.
- Phenytoin analgesic properties seem to be related to its membrane-stabilizing action.
- Carbamazepine prevents repeated discharges in neurons.
- Sodium valproate and clonazepam are thought to work through enhancement of GABA inhibitory system.

Common adverse events

Nausea, vomiting, diarrhea, hyponatremia (carbamazepine, oxcarbazepine), rash, pruritis, weight gain, edema, dry mouth.

Contraindications

- Bone marrow depression, with or within 14 days of monoamine oxidase (MAO) inhibitor use (carbamazepine).
- Use of NNRTIs (phenytoin).
- Hepatic disease or significant impairment, urea cycle disorders, pregnant women for prevention of migraines, known mitochondrial disorders (valproate).
- Recent alcohol use (within six hours), patient with metabolic acidosis or taking metformin (topiramate).

Monitoring parameters

- Carbamazepine: Complete blood count (CBC) with differential, reticulocytes, serum iron, lipid panel, liver function tests, urinalysis, blood urea nitrogen (BUN), serum carbamazepine levels, thyroid function tests, serum sodium when initiating or changing doses.
- Lamotrigine: Serum levels of concurrent anticonvulsants, liver function tests (LFTs), renal function when initiating or changing doses.
- Oxcarbazepine: Serum sodium, thyroid labs and CBC.

Antidepressants

Tricyclic antidepressants (TCAs), serotonin norepinephrine reuptake inhibitors (SNRIs) and to a lesser extent selective-serotonin reuptake inhibitors (SSRI) have a role in the treatment of pain, especially if the patient has co-existing insomnia, anxiety or depression. Antidepressants may provide pain relief independent from their antidepressant effects, since analgesic effects occur earlier and at lower doses compared to antidepressant effects. TCAs are very effective in the treatment of neuropathic pain; however, side effects including significant anticholinergic properties may limit their use in specific populations. Evidence continues to grow to support the use of SNRIs in neuropathic pain, and now that a few of the agents are available generically, their use in clinical practice for pain management has expanded greatly in the past few years.

Names of medications: Amitriptyline, bupropion, doxepin, imipramine, nortriptyline, despiramine, venlafaxine, desvenlafaxine, duloxetine, milnacipran

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Indications

- **Diabetic peripheral neuropathy**
  - Duloxetine *(Griebeler, 2014; Kroenke, 2009b)*
  - Venlafaxine *(Griebeler, 2014)*
  - Nortriptyline *(Griebeler, 2014)*
  - Amitriptyline *(Griebeler, 2014)*
- **Fibromyalgia**
  - Duloxetine *(Arnold, 2004)*
  - Venlafaxine *(Arnold, 2004)*
  - Milnacipran *(Gendreau, 2005; Vitton, 2004)*
- **Neuropathic pain**
  - Buproprion *(Semenchuk, 2001)*
  - Venlafaxine *(Sindrup, 2003)*
  - Duloxetine *(Arnold, 2004)*
- **Painful physical symptoms**
  - Duloxetine *(Robinson, 2013; Romera, 2012; Gaynor, 2011a; Gaynor, 2011b; Perahia, 2009; Brecht, 2007)*

General mechanism

- Bupropion inhibits reuptake of norepinephrine and dopamine.
- Duloxetine and venlafaxine inhibit serotonin and norepinephrine reuptake, and are a weak inhibitor of dopamine reuptake.
- Milnacipran, amitriptyline, nortriptyline, doxepin, imipramine and despiramine inhibitor of norepinephrine and serotonin reuptake and potentiation of descending inhibitory pathways.

Common adverse events

Elevated blood pressure, nausea, dry mouth, insomnia, drowsiness, constipation, fatigue, dizziness, orthostatic hypotension (TCAs).

Contraindications

- Tricyclic antidepressants are contraindicated in patients with patients with severe cardiac disease (specifically conduction disturbances) and severe gastrointestinal dysfunction.
- Bupropion is contraindicated in patients with seizure disorders and history of anorexia/bulimia.
- Duloxetine is contraindicated in patients with uncontrolled glaucoma.
- Recommend avoiding TCAs in older adults due to the risk of anticholinergic side effects.

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Monitoring parameters

- Blood pressure should be checked prior to initiating therapy and on regular basis.
- BUN/Creatinine.
- LFTS (SNRIs).
- Heart rate, blood pressure and electrocardiogram (ECG) in older adults and patients with preexisting cardiac disease (TCAs).

Glucocorticosteroids

Glucocorticoids are adrenalcortical steroids that have potent anti-inflammatory properties and are used primarily in rheumatic disorders and other acute inflammatory diseases. Glucocorticoids can be administered orally or by injection, including epidural injections, injection into facet joints, the sacroiliac space and intra-articular injections (see the "Interventional Treatment" section). In rheumatoid arthritis, they reduce joint tenderness and pain more than NSAIDs, but benefits must be weighed against significant adverse effects associated with chronic use.

Names of medications: Oral dexamethasone, hydrocortisone, prednisone, and long-acting injectable suspensions, methylprednisolone and Triamcinolone.

Indications: As adjunctive therapy for:

- **Rheumatoid arthritis**
- **Osteoarthritis**
- **Bursitis**
- **Synovitis**
- **Epicondylitis** using Iontophoresis treatment *(Nirschl, 2003)*
- **Lateral epicondylitis** using iontophoresis and phonophoresis of naproxen are equally effective *(Baskurt, 2003)*

General mechanism

- Reduce inflammation by suppression of polymorphonuclear leucocytes.
- Suppression of the immune system by reducing activity and volume of the lymphatic system.

Common adverse events: Are dose dependent and associated with chronic use. Low incidence of adverse effects in doses comparable to prednisone 5 mg daily with increasing incidence in doses of 10-15 mg or higher. Adverse effects include GI bleed, hyperglycemia, increased infections, osteoporosis, and increased skeletal fractures and mood disorders.

Monitoring parameters

- With chronic use monitor blood glucose, white blood cells, and watch for other signs and symptoms associated with adverse effects (GI, CNS changes) (Micromedex).

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Muscle Relaxants and Antispasmodics

Skeletal muscle relaxant may be useful along with analgesics for the short-term management of muscle spasms and pain. There is mixed evidence supporting the use of these medications for long-term use. Some medications including benzodiazepines and carisoprodol are centrally acting and carry the risk of physical dependence. Muscle relaxants are more beneficial for acute short-term use and are not recommended for chronic use.

Names of medications: Baclofen, carisoprodol, chlorzoxazone, cyclobenzaprine, dantrolene, metaxalone, methocarbamol, orphenadrine and tizanidine.

Indications

- **Peripheral musculoskeletal conditions:** Muscle relaxants include antispasmodic agents used to treat spasms.
- **Acute low back pain:** The American Pain Society and the American College of Physicians recommend reserving skeletal muscle relaxants as an optional alternative treatment for acute low back pain, with acetaminophen and NSAIDs as first-line agents. This recommendation is based on available literature, which shows skeletal muscle relaxants are better than placebo but not more effective than NSAIDs in patients with acute back pain *(Chou, 2007)*.
- **Chronic back pain:** A recommendation from the Cochrane review is that skeletal muscle relaxers may provide some benefit, but there is little evidence to support their use as the standard of treatment for chronic back pain. Additionally, these studies demonstrate the efficacy of skeletal muscle relaxers for up to 14 days after symptom onset, and evidence for long-term use is lacking. Other studies suggest treatment with these medications is less than a month *(Chou, 2007)*.
- **Fibromyalgia**
  - A meta-analysis evaluating the use of cyclobenzaprine showed that, although this medication was better than placebo for the treatment of fibromyalgia, it was considered inferior to antidepressants.
  - Tizanidine is a muscle relaxant that may be used for longer periods of time due to its alpha-2 sympathomimetic mechanism of action, but it may cause hypotension. It may provide benefits as an adjunct in the treatment of fibromyalgia.
  - Cyclobenzaprine has shown benefits in the treatment of fibromyalgia at doses of 10 to 40 mg daily *(Tofferi, 2004)*. It is a tricyclic amine and has side effects similar to the tricyclic antidepressants, including drowsiness/dizziness, dry mouth and an increased risk for arrhythmias. Concurrent use of cyclobenzaprine with tricyclic antidepressants is not contraindicated, but patients should be monitored for the potential increase in these related adverse effects.
- **Spasticity including multiple sclerosis, spinal cord injury, traumatic brain injury, cerebral palsy and post-stroke syndrome**
  - Botulinim toxin A in combination with physical and occupational therapy improves functional outcomes in these conditions.
  - Baclofen, dantrolene and tizanidine are FDA approved.
  - Benzodiazepines, dantrolene, and baclofen have been used to treat spasticity in cerebral palsy but are generally less useful than botulinum toxin.
  - Intrathecal baclofen administered via a pump achieves higher cerebrospinal fluid drug levels as compared with oral administration. Intrathecal baclofen may be effective in reducing spasticity in severely affected patients, but its use is also associated with substantial complications.

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- Antispasticity agents used to decrease spasticity (increased tone or contractions of muscles causing stiff or awkward movements as a result of an upper motor neuron damage) in neurological disorders.

- **Muscle spasms:** Evidence for the use of tizanidine comes from a Cochrane review, which showed that the combination of tizanidine plus analgesics provided better pain relief and a decrease in muscle spasms compared to analgesics alone *(Van Tulder, 2003)*.
- **Lancinating, paroxysmal neuropathic pain:** Baclofen may have benefits in the treatment *(Cherkin, 1998; Borenstein, 1990)*.

Mechanism of action

- Cyclobenzaprine is a tricyclic amine with undefined mechanism of action.
- Tizanidine is an alpha adrenergic agonist with undefined mechanism of action.
- Carisoprolol is metabolized to mebrobamate, a central acting depressant.
- Injection of botulinum toxin type A into affected muscles blocks the presynaptic release of acetylcholine from motor endplates of the lower motor neuron at the myo-neural junction and decreases tone by limiting muscle contraction.

Common adverse events

Drowsiness/dizziness, dry mouth and hypotension (more common with tizanidine). Some medications such as benzodiazepines and carisoprodol are centrally acting and carry the risk of physical dependence.

Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs are indicated for the treatment of mild to moderate inflammatory or non-neuropathic pain. In general, NSAIDs should be used for periodic flare-ups rather than for long-term chronic use. NSAIDs have significant opioid dose-sparing properties and in turn may reduce opioid-related side effects. Use of NSAIDs should be monitored closely due to the class risk of cardiovascular, gastrointestinal and renal adverse effects. This is in alignment with the recommendations made by the American Society of Nephrology as part of the Choosing Wisely® campaign, and additional information can be found at http://www.choosingwisely.org/societies/american-society-of-nephrology/.

Names of medications: Aspirin, salsalate, naproxen, ibuprofen, ketoprofen, flurbiprofen, oxaprozin, diclofenac, etodolac, indomethacin, tolmetin, sulindac, meloxicam, piroxicam, meclfenamate, mefenamic acid, nabumetone and celecoxib.

Indications

- **Acute** – Periodic use for mild to moderate inflammatory or non-neuropathic pain **(tendonitis, bursitis, dysmenorrhea, gout, headaches, low back pain)**
  - Ketoprofen *(Wong, 2016; Friedman, 2015; Sarzi-Puttini, 2013)*
  - Diclofenac *(Dietrich, 2014; Daniels, 2012)*
- **Chronic – Osteoarthritis, rheumatoid arthritis** *(Colebatch, 2012; Kroenke, 2009b)*

General mechanism

- Peripheral inhibition of the enzyme cyclooxygenase (COX), which plays a central role in inflammatory conditions, as well as an effect on the central nervous system.

Common adverse events

Platelet inhibition, dyspepsia, gastric ulceration, nephrotoxicity, hepatotoxicity, confusion.

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Contraindications

- Patients with renal insufficiency, GI bleeding, platelet dysfunction, reduced cardiac output, difficult to control hypertension, hypovolemia, hyponatremia, aspirin-sensitive asthma or cirrhosis.
- Recommended to avoid use in older adults. (American Society of Nephrology as part of the Choosing Wisely® campaign)

Monitoring parameters

- CBC
- Periodic liver function tests
- Renal function (urine output, serum BUN/creatinine)

Topical Therapies

Topical NSAIDs can provide acceptable levels of pain relief in knee and hand osteoarthritis, and are available through a diclofenac 0.3% topical patch and 1% topical gel. Topical formulations provide more localized pain relief with efficacy comparable to oral products. They generally have a lower incidence of GI adverse effects compared with oral NSAIDs. Topical NSAID GI adverse effects did not differ from placebo but were less frequent than with oral NSAIDs *(Derry, 2012)*.

Capsaicin, the active ingredient in the herbal product cayenne, is used topically to deplete the pain mediator substance-P from afferent nociceptive neurons. Topical creams and solutions have been used in treating both neuropathic pain and arthritic pain. Capsaicin should be applied for at least six weeks to see full benefits. The side effect of local burning is common, and most patients become tolerant after a few days *(Mason, 2004; Devers, 2000)*.

Names of medications: Capsacin, lidocaine patches and ointment, and diclofenac gel and patch.

Indications

- **Neuropathic and arthritic pain, diabetic neuropathy, post-herpetic neuralgia.**
  - Capsaicin topical creams and solutions have been used *(Fusco, 1997; Treatment of Painful Diabetic Neuroplasty with Topical Capsaicin, 1991)*.
  - Lidocaine in the form of an ointment or a patch *(Rowbotham, 1995)*.
  - Topical lidocaine 5% patches are FDA approved for post-herpetic neuralgia.
  - Topical lidocaine 5% patches are FDA approved for post-herpetic neuralgia and have shown efficacy in other neuropathic pain syndromes. Systemic absorption of lidocaine is minimal, and the patch has a clean safety profile with the correct dosage schedule.
  - Topical NSAIDS are approved for and provide acceptable pain relief in knee and hand osteoarthritis.

Mechanism of action

- Capsaicin, the active ingredient in the herbal product cayenne, is used topically to deplete the pain mediator substance-P from afferent nociceptive neurons. It deactivates local C-polymodal nociceptors at the vanilloid receptor.
- Topical NSAIDs inhibit the enzyme cyclooxygenase resulting in reduce formation of prostaglandins, thromboxanes and prostacyclin.

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Common adverse events

Dermatitis and other local reactions are usually not severe. Topical NSAID GI adverse effects did not differ from placebo but were less frequent than with oral NSAIDs *(Derry, 2012)*. Capsaicin products have local burning.

Contraindications

- NSAIDs should be avoided in patients who have experienced asthma, urticaria or other allergic reactions to aspirin or other NSAIDs.

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Appendix C – Opioid Pharmacology

Names of medications

- **Naturally occurring opioids:** codeine, morphine
- **Semi-synthetic opioids:** hydrocodone, hydromorphone, oxycodone, oxymorphone, buprenorphine
- **Synthetic opioids:** meperidine, fentanyl, methadone, tramadol, tapentadol

(Pathan, 2012; Trescot, 2008)

Indication

Severe acute pain and chronic pain related to cancer *(Chou, 2009a)*.

The FDA has announced class-wide safety labeling changes for immediate release (IR) opioids due to the risks associated with opioid medications. "The updated indication clarifies that because of these risks, IR opioids should be reserved for pain severe enough to require opioid treatment and for which alternative treatment options (e.g., non-opioid analgesics or opioid combination products, as appropriate) are inadequate or not tolerated." For additional information, please refer to http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm491739.htm - Press release.

General mechanism of action

Opioids bind to mu, delta and kappa opioid receptors on the presynaptic terminals of the nociceptive C-fibers and A delta fibers inhibiting the release of pain neurotransmitters *(Trescot, 2008)*. Opioids also activate presynaptic receptors on GABA neurons inhibiting the release of GABA and promoting extra dopamine release *(Trescot, 2008)*. Unlike other modalities, opioids have no ceiling effect on pain relief, but use is limited by the development of adverse effects *(Pasternak, 2014)*.

Common adverse effects

- The most common side effects of opioids are nausea and constipation *(Benyamin, 2008)*.
- Additional side effects include vomiting, pruritus, sedation, physical dependence, tolerance, respiratory depression, euphoria, dysphoria, miosis, urticaria and hypotension *(Benyamin, 2008)*.

The FDA released a safety communication warning requiring changes to be made to the labels of all opioid medications warning about the risks of serotonin syndrome, adrenal gland insufficiency and reduced sex hormone levels. For additional information, please refer to https://www.fda.gov/media/96472/download.

Absolute contraindications

Absolute contraindications to opioids include severe respiratory instability, acute psychiatric instability or uncontrolled suicide risk, diagnosed non-nicotine substance use dismedication drug capable of inducing life-limiting drug-drug interactions, QTc interval longer than 500 milliseconds if prescribed methadone, acute diversion of controlled substances and prior adequate trials of specific opioids that were discontinued due to intolerance, serious adverse effects or lack of efficacy *(U.S. Department of Veterans Affairs, 2010)*.

Hepatic/renal dosing

Opioid pharmacokinetics depends on patient-related factors as well as the chemical properties of each opioid *(Gelot, 2014)*. Hepatic or renal insufficiency may change the pharmacokinetic properties of opioids complicating treatment *(Gelot, 2014)*. Please refer to the following charts for recommendations about using opioids in patients with hepatic or renal insufficiency.

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Recommendations for Opioids in Hepatic Impairment *(Gelot, 2014)*	
Opioid	Recommendations
Codeine	Not recommended. In severe hepatic dysfunction, codeine is not converted to morphine, leading to poor analgesia.
Fentanyl	99% metabolized in the liver. Studies have not demonstrated pharmacokinetic alterations, but careful monitoring is warranted.
Hydrocodone	Use with caution. Monitor for overdose due to parent compound not being converted to metabolites.
Hydromorphone	Undergoes phase II reaction, but use with caution.
Methadone	Use with caution. Risk of accumulation because of increased free drug.
Meperidine	Not recommended. The toxic metabolite normeperidine may accumulate.
Morphine	Use with caution.
Oxycodone	Use with caution. Dose adjustment recommended (½-⅓ of original dose).
Oxymorphone	Contraindicated in moderate-to-severe hepatic impairment.
Tramadol	Not recommended. Significant pharmacokinetic changes in moderate-to-severe hepatic impairment.
Tapentadol	Not recommended with severe hepatic impairment *(Vadivelu, 2013)*.

Recommendations for Opioids in Renal Impairment *(Gelot, 2014)*	
Opioid	Recommended.
Codeine	Not recommended due to accumulation.
Fentanyl	Appears safe, but renal dosage adjustment may be necessary.
Hydrocodone	Use cautiously. Adjust dosage.
Hydromorphone	Use cautiously. Adjust dosage.
Methadone	Appears safe; however, renal dosage adjustment may be necessary.
Meperidine	Not recommended due to metabolites.
Morphine	Not recommended due to metabolites.
Oxycodone	Use cautiously. Adjust dosage.
Tramadol	Not recommended.
Tapentadol	Not recommended with severe renal impairment *(Vadivelu, 2013)*.

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Opioid Utilization

Oral morphine milligrams equivalent (MME) doses are increasingly being used as a metric to represent opioid use *(Nielsen, 2016)*. MMEs are based on the idea that different doses of different opioids may produce a similar analgesic effect *(Nielsen, 2016)*. The following table depicts MMEs for the most commonly used opioids. Of note, methadone has a complicated pharmacokinetic and pharmacodynamic profile with a variable MME ratio *(Chou, 2009a)*. Initiating a patient on methadone should be reserved for experienced clinicians who are familiar with its use *(Chou, 2009b)*.

MME Conversion Factors
(Centers for Disease Control and Prevention, 2016; Washington State – Agency Medical Directors' Group, 2015; Nielsen 2016)

Oral Preparations	**Unit Converted From**	**Recommended MME**
Codeine	mg/day	0.1
Hydrocodone	mg/day	1
Hydromorphone	mg/day	4
Methadone 1-20 21-40 41-60 > 60	mg/day	 4 8 10 12
Morphine	mg/day	1
Oxycodone	mg/day	1.5
Oxymorphone	mg/day	3
Tapentadol	mg/day	0.4
Tramadol	mg/day	0.2
Transdermal Preparations	**Unit Converted From**	**Recommended MME**
Buprenorphine	mcg/hour	2.2
Fentanyl	mcg/hour	2.4
Parenteral Preparations	**Unit Converted From**	**Recommended MME**
Hydromorphone	mg/day	17.5
Fentanyl	mcg/day	0.2
Meperidine	mg/day	0.4
Morphine	mg/day	3
Oxymorphone	mg/day	30

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Whether data is presented at the individual (patient) level or in total, the recommended conversion factors can be used to convert a given dose/amount of an opioid to MMEs using the following formula: strength per unit × (number of units/day (or total)) × MME conversion factor = MME units per day (or total) *(Nielsen, 2016)*.

MME conversion examples

- A patient is taking Oxycontin 30 mg three times a day: 30 mg x 3 doses/day x conversion factor of 1.5 = 135 mg MME/day.
- A patient is using a 25 mcg fentanyl patch every three days: 25 mcg x 1 patch/day x conversion factor of 2.7 = 67.5 mg MME/day.
- A patient received a quantity of fifteen Tramadol 100 mg tablets: 100 mg x 15 tablets x conversion factor of 0.2 = 300 mg MME total.

It should be noted these calculations are only intended to convert an opioid to morphine equivalents *(Nielsen, 2016)*. Different conversion factors may be necessary when converting to an opioid other than morphine *(Nielsen, 2016)*.

Opioid Rotation

Opioid	Equianalgesic Potency*	
	Oral	**Parenteral**
Morphine	30 mg	10 mg
Hydromorphone	7.5 mg	1.5 mg
Oxycodone	20 mg	NA
Methadone	Variable	Variable
Meperidine	300 mg	75 mg
Fentanyl	NA	0.1 mg
Codeine	200 mg	100 mg
Hydrocodone	20-30 mg	NA
Oxymorphone	10 mg	1 mg
Tramadol	300 mg	NA
Tapentadol	150 mg	NA

* http://www.cancer.gov/about-cancer/treatment/side-effects/pain/pain-hp-pdq#link/_63_toc *(Pharmacist's Letter/Prescriber's Letter, 2014; Chou, 2009a)*

Naturally Occurring Opioids

Codeine: (MME = 0.1)

Indication: Mild to moderate pain *(Codeine package insert, 2015)*

Additional Mechanism(s) of Action: None

Specific Adverse Effects: None

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Precautions/contraindications

- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for the CYP2D6 genotype recommend avoiding use in known ultra-rapid metabolizers (1-2% of patients) or poor metabolizers (5-10% of patients) *(Crews, 2014)*.
- Use in renal failure and dialysis is not recommended due to the accumulation of active metabolites *(Dean, 2004)*.
- In 2007, the FDA identified that infants of nursing mothers taking codeine may have an increased risk of morphine overdose if the mother is an ultra-rapid metabolizer of codeine. When prescribing codeine to nursing mothers, physicians should choose their lowest dose for the shortest period of time and should closely monitor mother-infant pairs. For more information, refer to https://www.fda.gov/media/104268/download.
- The FDA added a **black box warning** in 2013 recommending alternative analgesics for children undergoing tonsillectomy and/or adenoidectomy. Respiratory depression and death have occurred in children with evidence of cytochrome P450 2D6 polymorphism. For more information, refer to https://www.fda.gov/media/104268/download. The FDA is currently evaluating the safety of codeine for cough in children under the age of 18 due to potential serious side effects.

Additional information

- Available alone or in combination with acetaminophen. (Micromedex).
- Metabolized to codeine-6-glucuronidide, to the active metabolite morphine by cytochrome P450 2D6 and norcodeine by CYP3A4 *(Codeine package insert, 2015)*.

Morphine: (MME oral = 1, MME IV = 3)

Indication: Moderate to severe pain *(Morphine package insert, 2012)*.

Additional mechanism(s) of action: None

Specific adverse effects

- May cause severe hypotension and elevated intracranial pressure *(Morphine package insert, 2012)*.

Precautions/contraindications

- Use in renal failure and dialysis is not recommended due to the accumulation of active metabolites *(Dean, 2004)*.

Additional information

- Available in injectable, rectal, rapid-acting oral, 12-hour sustain release and 24 hours sustained-release oral formulations (Micromedex).
- Metabolized by glucuronidation to an active metabolite morphine-6-glucuronide and the inactive morphine-3-glucuronide *(Morphine package insert, 2012)*.

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Semi-Synthetic Opioids

Hydrocodone (MME = 1)

Indication: Moderate to moderately severe pain *(Norco package insert, 2014)* or pain severe enough to require around-the-clock opioid treatment when alternative therapies are inadequate *(Zohydro package insert, 2015; Hyslinga package insert, 2014)*.

Additional mechanism(s) of action: None

Specific adverse effects

- QTc prolongation has been observed when daily doses of Hyslinga exceed 160 mg/day *(Hyslinga package insert, 2014)*.

Precautions/contraindications

- Contraindicated in patients with acute or severe bronchial asthma in unmonitored settings or without resuscitative equipment *(Zohydro package insert, 2015; Hyslinga package insert, 2014)*.
- Use Zohydro cautiously in patients with severe hepatic and renal impairment *(Zohydro package insert, 2015)*.
- Norco should be used cautiously during pregnancy only if the potential benefits outweigh the potential risks *(Norco package insert, 2014)*.
- May cause fetal harm or neonatal opioid withdrawal syndrome (NAS) if used during pregnancy *(Zohydro package insert, 2015)*.
- Use during lactation is not recommended *(Zohydro package insert, 2015)*.

Additional information

- Available in combination with acetaminophen *(Norco package insert, 2014)* or alone as a twice-daily extended-release product *(Zohydro package insert, 2015)* or a once-daily extended-release product. *(Hyslinga package insert, 2014)*.
- Hydrocodone is metabolized primarily by CYP2D6 to the active metabolite hydromorphone and by CYP3A4 to inactive metabolize norhydrocone. CYP3A4 inhibitors, or discontinuation of CYP3A4 inducers, may cause elevated hydrocodone concentrations prolonging adverse effects and respiratory depression *(Norco package insert, 2014)*.
- Zohydro and Hyslinga must be swallowed whole *(Zohydro package insert, 2015; Hyslinga package insert, 2014)*.
- Currently there are no recommendations for converting from Zohydro or Hyslinga to an alternative opioid *(Zohydro package insert, 2015; Hyslinga package insert, 2014)*.

Hydromorphone (MME oral = 4, MME IV = 17.5)

Indication: Moderate to severe pain *(Dilaudid package insert, 2015)*.

Additional mechanism(s) of action: None

Specific adverse effects:

- May cause severe hypotension and elevated intracranial pressure *(Dilaudid package insert, 2015)*.

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Precautions/contraindications

- Exalgo is contraindicated in opioid-naïve patients and patients with moderate to severe hepatic impairment *(Exalgo package insert, 2015)*.
- Hydromorphone should be used carefully in renally impaired and dialysis patients *(Dilaudid package insert, 2015)*.
- Exalgo is not recommended for patients with severe renal impairment *(Exalgo package insert, 2015)*.

Additional information

- Available in injectable, rectal and both rapid-release *(Dilaudid package insert, 2015)* and once-a-day extended-release oral dosage forms *(Exalgo package insert, 2015)*.
- Primarily metabolized into inactive metabolite hydromorphone-3-glucornide *(Dilaudid package insert, 2015)*.
- Exalgo must be swallowed whole *(Exalgo package insert, 2015)*.
- Ghost capsules may be visible in stool *(Exalgo package insert, 2015)*.

Oxycodone (MME = 1.5)

Indication: Moderate to moderately severe pain *(Oxycodone package insert, 2014)*.

Additional mechanism(s) of action: None

Specific adverse effects: None

Precautions/contraindications:

- Use cautiously in patients with severe renal impairment *(Dean, 2004)*.
- Concomitant use of CYP3A4 inhibitors, such as macrolide antibiotics (e.g., azithromycin), azole-antifungal agents (e.g., ketoconazole) and protease inhibitors (e.g., ritonavir) may result in increased oxycodone concentrations and subsequent adverse effects. Concurrent use with CYP3A4 inducers, such as phenytoin and carbamazepine, may result in decreased oxycodone concentrations or lack of efficacy. *(Oxycodone package insert, 2014)*.

Additional information:

- Available in combination with acetaminophen or alone as a short-acting or long-acting oral dosage form (Micromedex).
- Metabolized by CYP3A4 to the active metabolite noroxycodone and by CYP2D6 to the active metabolite oxymorphone *(Oxycodone package insert, 2014)*.

Oxymorphone (MME oral = 3, MME IV = 30)

Indication: Moderate to severe pain *(Oxymorphone package insert, 2014)* and for the relief of moderate to severe pain in patients requiring continuous around-the-clock opioid treatment for chronic pain *(Opana ER package insert, 2012)*. Oxymorphone ER is not indicated for acute pain *(Opana ER package insert, 2012)*.

Additional mechanism(s) of action: None

Specific adverse effects:

- May increase intracranial pressure *(Oxymorphone package insert, 2014)*.

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Precautions/contraindications

- Use in patients with moderate to severe hepatic dysfunction is contraindicated *(Oxymorphone package insert, 2014)*.
- Use cautiously in patients with severe renal impairment *(Oxymorphone package insert, 2014)*.

Additional information

- Available as an injectable, immediate-release *(Oxymorphone package insert, 2014)* and extended-release oral formulations *(Opana ER package insert, 2012)*.
- Metabolized to active metabolite 6-OH-oxymorphone and an inactive metabolite oxymorphone-3-glucoronide *(Oxymorphone package insert, 2014)*.
- No dosage conversions are available for converting from oxymorphone ER to another opioid *(Opana ER package insert, 2012)*.
- Oxymorphone ER tablets must be swallowed whole *(Opana ER package insert, 2012)*.

Buprenorphine (MME = 2.2)

Indication: Indicated for the management of pain severe enough to require around-the-clock opioid treatment when alternative therapies are inadequate *(Butrans package insert, 2014)*.

Additional mechanism(s) of action: Partial agonist at the mu and ORL-1 receptors, a full agonist at the delta opioid receptor and an antagonist at the kappa opioid receptor *(Butrans package insert, 2014)*.

Specific adverse effects

- QTc prolongation at doses exceeding 20 mcg/hour *(Butrans package insert, 2014)*.

Precautions/contraindications

- Accidental exposure to even one dose, especially in children, may be fatal *(Butrans package insert, 2014)*.
- Butrans 20 mcg/hour may not provide adequate analgesia for patients requiring > 80 MME/day *(Butrans package insert, 2014)*.
- Butrans has not been evaluated in patients with severe hepatic toxicity *(Butrans package insert, 2014)*.
- Avoid use in patients with a history of prolonged QTc *(Butrans package insert, 2014)*.

Additional information

- Patches are changed once weekly and should not be reapplied to the same site within three weeks. *(Butrans package insert, 2014)*.
- Opioid-naïve patients and patients requiring < 30 mg of MME/day should be initiated with a 5 mcg/hour patch. Patients requiring 30-80 MME/day should be initiated with a 10-mcg/hour patch *(Butrans package insert, 2014)*.
- Do not apply heat directly to the patch as an increase in absorption may occur *(Butrans package insert, 2014)*.
- Do not use if patch is cut and do not cut the patch *(Butrans package insert, 2014)*.
- Patch disposal – Place patch in disposal unit or fold the adhesive side on itself and flush down the toilet. *(Butrans package insert, 2014)*.

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Synthetic Opioids

Meperidine (MME 0.4)

Indication: Moderate to severe pain *(Meperidine package insert, 2016)*.

Additional mechanism(s) of action: None

Specific adverse effects

- May increase intracranial pressure and aggravate preexisting convulsions *(Meperidine package insert, 2016)*.

Precautions/contraindications

- Concurrent use of MAOIs, or use within the last 14 days, is contraindicated *(Meperidine package insert, 2016)*.
- Avoid use in severe renally impaired patients *(Meperidine package insert, 2016)*.

Additional information

- Available in oral and injectable formulations (Micromedex).
- Metabolized by N-demethylation to active metabolite normeperidine, which has 2-3 times the CNS effects of meperidine *(Meperidine package insert, 2016)*.
- Use is limited to 48 hours and dose should not exceed 600 mg/24 hours due to the metabolite normeperidine *(Berry, 2001)*.
- The American Pain Society (2008) and ISMP (2007) do not recommend meperidine's use as an analgesic.
- Oral route is not recommended for acute or severe pain *(Berry, 2001)*.
- Meperidine is not recommended for the treatment of chronic pain due to bioaccumulation and adverse effects *(Hegmann, 2014)*.

Fentanyl (MME IV = 0.2, MME transdermal = 2.7)

Indication: Transdermal fentanyl is indicated for the management of pain in opioid-tolerant patients *(Duragesic package insert, 2014)*.

Transmucosal immediate-release fentanyl (TIRF) products (buccal tablets, sublingual tablets, transmucosal lozenges, nasal spray, buccal soluble film and sublingual spray) are indicated for the management of breakthrough cancer pain in those who are already tolerant on regular opioid therapy (TIRF Education Program).

Specific adverse effects: None

Precautions/contraindications

- Avoid use in patients with severe renal and hepatic impairment *(Duragesic package insert, 2014)*.
- CYP3A4 inhibitors, or discontinuation of CYP3A4 inducers, may result in a fatal overdose from the transdermal patch *(Duragesic package insert, 2014)*.

Additional information

- Available as injectable, transdermal and transmucosal immediate-release products (Micromedex).
- Metabolized by CYP3A4 to inactive metabolites *(Duragesic package insert, 2014)*.

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- Patches are applied every 72 hours, although some patients may require patches to be applied every 48 hours *(Duragesic package insert, 2014)*.
- Kinetics – Fentanyl levels increase gradually between 12 and 24 hours after the patch has been applied. Significant amounts of fentanyl continue to be absorbed 24 hours or more after a patch has been removed. Seventeen or more hours are required for a 50% reduction in serum fentanyl concentrations after patch has been removed *(Duragesic package insert, 2014)*.
- Avoid exposure of fentanyl patch to direct heat. Heat increases the release of fentanyl in a temperature dependent manner *(Duragesic package insert, 2014)*.
- Patch disposal – Patches should be disposed immediately after removal by folding stick side on itself and flushing down the toilet. Unused patches should be removed from their liners, folded in half on the adhesive side and flushed down the toilet. Failure of proper disposal of fentanyl transdermal patches has resulted in accidental exposure and deaths *(Duragesic package insert, 2014)*.
- Despite an FDA-issued Public Health Advisory in July 2005 regarding the appropriate and safe use of the transdermal system, death and life-threatening adverse events related to fentanyl overdose have occurred when the fentanyl patch was used to treat pain in opioid-naive patients and when opioid-tolerant patients have applied more patches than prescribed, changed the patch too frequently, and exposed the patch to a heat source.
- Directions for prescribing and using the fentanyl patch must be followed exactly to prevent death or other serious side effects from fentanyl overdose.
- In 2012, the FDA evaluated a series of 26 pediatric accidental exposure to fentanyl patches over 15 years and re-emphasized the importance of appropriate storage, use, application and disposal of fentanyl patches to prevent potentially life-threatening harm from accidental exposure. This is in addition to the previous warnings in 2005 and 2006 following reports of death and life-threatening adverse events related to fentanyl overdose. For additional information, please refer to http://www.fda.gov/Drugs/DrugSafety/ucm300747.htm.

Methadone (MME = 4-12)

Indication: Pain severe enough to requiring daily, around-the-clock, long-term opioid treatment *(Methadone package insert, 2016)*.

Additional mechanism(s) of action: The S isomer is an NMDA antagonist and inhibits the re-uptake of norepinephrine and serotonin *(Trescot, 2008)*.

Specific adverse effects

- QTc prolongation. Cases of serious QT interval prolongation leading to serious arrhythmias have been reported *(Methadone package insert, 2016)*.

Precautions/contraindications

- Contraindicated with MAOIs or use within 14 days of discontinuing MAOIs *(Methadone package insert, 2016)*.

Additional information

- Available in injectable and oral formulations in a variety of concentrations *(Methadone package insert, 2016)*.
- Primarily metabolized by CYP3A4, CYP2B6 and CYP2C19 to inactive metabolize 2-ethylidene-1, 5-dimethyl-3,3-diphenylpyrrolidene *(Methadone package insert, 2016)*.

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- Initiating a patient on methadone requires a cautious and highly individualized approach due to inter-patient differences in the pharmacokinetic properties of the medication. Methadone is highly lipophilic and has a prolonged, but variable, half-life *(Methadone package insert, 2016)*.
- The analgesic effect lasts 4-8 hours, but the peak respiratory depressant effect occurs later and last longer than the analgesic effects *(Methadone package insert, 2016)*.
- Steady-state concentrations are attained 3-5 days after initiating therapy *(Methadone package insert, 2016)*.
- Baseline EKGs are recommended for all patents being initiated on methadone, with follow-up EKGs at 30 days and annually thereafter. More frequent EKG monitoring is recommended for all patients requiring >100 mg/day or those with unexplained syncope and seizures *(Krantz, 2009)*.

Tramadol (MME = 0.2)

Indication: Tramadol immediate release is indicated for the relief of moderate to moderately severe pain *(Tramadol package insert, 2012)*. Tramadol extended-release is indicated for the relief of moderate to moderately severe pain in adults who require around-the-clock treatment for an extended period of time *(Tramadol ER package insert, 2009)*.

Additional mechanism(s) of action: Inhibits the reuptake of norepinephrine and serotonin *(Tramadol package insert, 2012)*.

Specific adverse effects

- Seizures have been reported in patients receiving tramadol within the recommended dose range *(Tramadol package insert, 2012)*.

Precautions/contraindications

- Contraindicated with MAOIs or use within 14 days of discontinuing MAOIs *(Tramadol package insert, 2012)*.
- Concomitant use of tramadol with SSRIs, TCAs and other opioids increases risk of seizure *(Tramadol package insert, 2012)*.
- Development of serotonin syndrome has been seen when tramadol is used concomitantly with SSRIs, TCAs, MAOIs and triptans *(Tramadol package insert, 2012)*.
- Dose adjustments are required for immediate-release products and extended-release are contraindicated in patients with severe renal or hepatic impairment *(Tramadol package insert, 2012)*.

Additional information

- Available in combination with acetaminophen, or alone as a regular-release product (Tramadol package insert) and extended-release product *(Tramadol ER package insert, 2009)*.
- Metabolized by CYP2D6 to the active metabolite O-desmethyl tramadol, which has a higher affinity for the mu opioid receptor than the parent compound *(Tramadol package insert, 2012)*.
- Max daily dose is 400 mg/day *(Tramadol package insert, 2012)*.

Tapentadol (MME = 0.4)

Indication: Tapentadol immediate-release tablets are indicated for the relief of moderate to severe acute pain in patients > 18 years of age *(Nucynta package insert, 2013)*. Tapentadol extended release tablets are indicated for the relief of severe pain and neuropathic pain related to diabetic peripheral neuropathy *(Nucynta ER package insert, 2014)*.

Additional mechanism(s) of action: Inhibits the reuptake of norepinephrine *(Nucynta package insert, 2013)*.

Specific adverse effects: None

Precautions/contraindications

- Contraindicated with MAOIs or use within 14 days of discontinuing MAOIs *(Nucynta package insert, 2013)*.
- Prescribe cautiously in patients with a history of seizure disorder *(Nucynta package insert, 2013)*.
- Development of serotonin syndrome has been seen with concomitant use of SSRIs, SNRIs, TCAs, MAOIs and triptans *(Nucynta package insert, 2013)*.
- Not recommended for use in patients with severe renal or hepatic impairment *(Nucynta package insert, 2013)*.

Additional information

- Available in regular-release *(Nucynta package insert, 2013)* or extended-release *(Nucynta ER package insert, 2014)* oral formulations.
- Primarily metabolized by glucuronidation to inactive metabolites *(Nucynta package insert, 2013)*.
- Max daily dose for tapentadol is 700 mg on day one and 600 mg on subsequent days *(Nucynta package insert, 2013)*.
- Max daily dose for tapentadol ER is 500 mg per day *(Nucynta ER package insert, 2014)*.

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Appendix D – ICSI Shared Decision-Making Model

ICSI Institute for Clinical Systems Improvement

The Collaborative Conversation™ Shared Decision-Making and the Translation of Evidence into Practice

A consistent finding from clinical and health services research is the failure to translate research into practice. The translation of evidence into practice can be advanced through the use of shared decision-making since shared decision-making results in evidence being incorporated into patient and clinician consultations.

Shared decision-making (SDM) is a process in which patient and clinicians collaborate to clarify all acceptable options, ensure that the patient is well-informed and chose a course of care consistent with patient values and preferences and the best available medical evidence. (Minnesota Shared Decision-Making Collaborative [MSDMC], 2011).

Evidence-based guidelines may recommend the use of shared decision-making for decisions in instances where the evidence is equivocal, when patient action or inaction (such as medication adherence or lifestyle changes) can impact the potential outcome, or when the evidence does not indicate a single best recommendation.

SDM is a patient-centered approach that involves a conversation between the patient and the clinician. It is ideal to involve caregivers and family members in these conversations as well. Family members and caregivers can participate in discussions, ask questions, hear content the patient may miss and provide invaluable support in decision follow-through. Although only patients and clinicians are specifically mentioned throughout this document for brevity purposes, this does not diminish the importance of caregivers and families in patient-centered care.

Both the patient and the clinician bring expertise to the shared decision-making conversation. Clinicians' expertise includes disease etiology, prognosis, options for treatment including the burden and benefit to the patient, and outcome probabilities. Patients' expertise lies in their knowledge of their risk tolerance, body, priorities, family and financial issues, as well as their daily experience with the condition (adapted from Making Shared Decision-Making a Reality. No decision about me, without me. Coulter, A., Collins, A., The King's Fund 2011).

Treatment options vary in their burden on a patient. SDM offers an opportunity to help the patient select a treatment to which they can adhere. When conversations discussing options occurs, patients and clinicians are actively engaged while considering the attributes and issues of the available options. This empathic approach results in the clinician and patient co-creating a decision and a plan of care (adapted from Montori, V., the Mayo Clinic KER UNIT, April 2015). Decision aids can be supportive of this conversation when they communicate the best available evidence to inform the patient and clinician discussion.

Without a conversation, clinicians may make assumptions about what the patient prefers. This creates the potential for discrepancies between what clinicians assume and what patients want, resulting in a "preference misdiagnosis" (adapted from Health Policy Publishing, LLC, May 2013).

Difficulty in initiating a conversation is cited by patients and clinicians as one of the barriers to shared decision-making. To address this impediment, ICSI worked with patients, practicing clinicians, and other stakeholders to develop the Collaborative Conversation™ model for use across the care continuum.

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Collaborative Conversation™

A collaborative approach towards decision-making is a fundamental tenet of Shared Decision-Making (SDM). The Collaborative Conversation™ is an interprofessional approach that nurtures relationships; enhances patients' knowledge, skills and confidence as vital participants in their health; and encourages them to manage their health care. Within a Collaborative Conversation™ , the perspective is that the patient, rather than the clinician, knows which course of action is most consistent with the patient's values and preferences.

Use of Collaborative Conversation™ elements and tools is even more necessary to support patient, care clinician and team relationships when patients and families are dealing with high stakes or highly charged issues. A diagnosis of a life-limiting illness is one example of such a circumstance.

The overall objective for the Collaborative Conversation™ approach is to create an environment in which the patient, family and care team work collaboratively to reach and carry out a decision that is consistent with the patient's values and preferences, along with the best available evidence. A rote script, completed form or checklist does not constitute this approach. Rather it is a set of skills employed appropriately for the specific situation. These skills need to be used artfully to address all aspects of the person involved in making a decision: cognitive, affective, social and spiritual.

Key communication skills help build the collaborative conversation approach. These skills include (Adapted from O'Connor, Jacobsen Decisional Conflict: Supporting People Experiencing Uncertainty about Options Affecting their Health [2007], and Bunn H, O'Connor AM, Jacobsen MJ Analyzing decision support and related communication [1998, 2003])

1. **Listening skills**

   Encourage patient to talk by providing prompts to continue such as ***go on, and then? and uh huh*** or by repeating the last thing a person said, ***It's confusing***.

   Paraphrase content of messages shared by patient to promote exploration, clarify content and to communicate that the person's unique perspective has been heard. The clinician should use their own words rather than just parroting what they heard.

   Reflection of feelings usually can be done effectively once trust has been established. Until the clinician feels that trust has been established, short reflections at the same level of intensity expressed by the patient without omitting any of the message's meaning are appropriate. Reflection in this manner communicates that the clinician understands the patient's feelings and may work as a catalyst for further problem solving. For example, the clinician identifies what the person is feeling and responds back in his or her own words like this: "***So, you're unsure which choice is the best for you.***"

   Summarize the person's key comments and reflect them back to the patient. The clinician should condense several key comments made by the patient and provide a summary of the situation. This assists the patient in gaining a broader understanding of the situation rather than getting mired down in the details. The most effective times to do this are midway through and at the end of the conversation. An example of this is "***You and your family have read the information together, discussed the pros and cons, but are having a hard time making a decision because of the risks.***"

   Perception checks ensure that the clinician accurately understands a patient or family member perspective, and may be used as a summary or reflection. They are used to verify that the clinician is interpreting the message correctly. The clinician can say, "***So you are saying that you're not ready to make a decision at this time. Am I understanding you correctly?***"

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2. **Questioning Skills**

   Open and closed questions are both used, with the emphasis on open questions. Open questions ask for clarification or elaboration and cannot have a yes or no answer. An example would be, "***What else would influence you to choose this?***" Closed questions are appropriate if specific information is required, such as "***Does your daughter support your decision?***"

   Other skills such as summarizing, paraphrasing, and reflection of feeling can be used in the questioning process so that the patient doesn't feel pressured by questions.

   Verbal tracking, referring back to a topic the patient mentioned earlier, is an important foundational skill (Ivey & Bradford-Ivey). An example of this is the clinician saying, "***You mentioned earlier…***"

3. **Information-Giving Skills**

   Providing information and **providing feedback** are two methods of information giving. The distinction between providing information and giving advice is important. Information giving allows a clinician to supplement his or her knowledge and helps to keep the conversation patient centered. Giving advice, on the other hand, takes the attention away from the patient's unique goals and values, and places it on those of the clinician.

   Providing information can be sharing facts or responding to questions. An example is "***If we look at the evidence, the risk is…***" **Providing feedback** gives the patient the clinician's view of the patient's reaction. For instance, the clinician can say, "***You seem to understand the facts and value your daughter's advice.***"

When to Initiate a Collaborative Conversation™

Certain seminal events occur along the care continuum, creating especially opportune times for collaborative conversations. More than one of these opportunities may present at a time, and they will occur in no specific order.

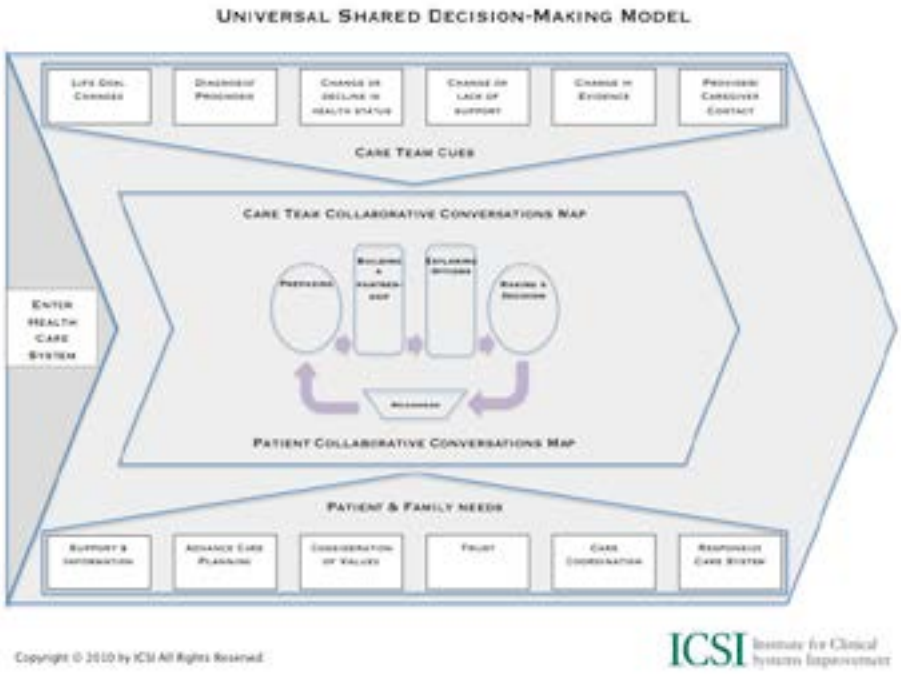

Table 1

Cues for the Care Team to Initiate a Collaborative Conversation™:

- Life goal changes: *Patient's priorities change related to things the patient values such as activities, relationships, possessions, goals and hopes, or things that contribute to the patient's emotional and spiritual well-being.*
- Diagnosis/prognosis changes: *Additional diagnoses, improved or worsening prognosis.*
- Change or decline in health status: *Improving or worsening symptoms, change in performance status or psychological distress.*
- Change or lack of support: *Increase or decrease in caregiver support, change in caregiver, change in caregiver status, change in financial standing, difference between patient and family wishes.*
- Disease progression: *Change in physical or psychological status as a result of the disease progression.*
- Clinician/caregiver contact: *Each contact between the clinician/ caregiver presents an opportunity to reaffirm with the patient that the care plan and the care he or she is receiving are consistent with his or her values.*

Patient and Family Needs within a Collaborative Conversation™

- Request for support and information: *Decisional conflict is indicated by, among other things, the patient verbalizing uncertainty or concern about undesired outcomes, expressing concern about choice consistency with personal values, or exhibiting behavior such as wavering, delay, preoccupation, distress or tension. Support resources may include health care professionals, family, friends, support groups, clergy and social workers. When patient expresses a need for information regarding options and their potential outcomes, the patient should understand the key facts about the options, risks and benefits, and have realistic expectations. The method and pace with which this information is provided to the patient should be appropriate for the patient's capacity at that moment.*
- Advance Care Planning: *With the diagnosis of a life-limiting illness, conversations around advance care planning open up. This is an opportune time to expand the scope of the conversation to other types of decisions that will need to be made as a consequence of the diagnosis of a life-limiting illness.*
- Consideration of Values: *The personal importance a patient assigns potential outcomes must be respected. If the patient is unclear how to prioritize his or her preferences, value clarification can be achieved through the use of decision aids, detailing the benefits and harms of potential outcomes in terms of how they will directly affect the patient, and through collaborative conversations with the clinician.*
- Trust: *The patient must feel confident that his or her preferences will be communicated to and respected by all caregivers.*
- Care Coordination: *Should the patient require care coordination, this is an opportune time to discuss the other types of care-related decisions that need to be made. These decisions will most likely need to be revisited often. Further, the care delivery system must be capable of delivering coordinated care throughout the continuum of care.*
- Responsive Care System: *The care system needs to support the components of patient- and family-centered care so the patient's values and preferences are incorporated into the care he or she receives throughout the care continuum.*

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The Collaborative Conversation™ Map is the heart of this process. The Collaborative Conversation Map™ can be used as a stand-alone tool that is equally applicable to clinicians and patients, as shown in Table 2. Clinicians use the map as a clinical workflow. It helps get the shared decision-making process initiated and provides navigation for the process. Care teams can use the Collaborative Conversation™ to document team best practices and to formalize a common lexicon. Organizations can build fields from the Collaborative Conversation™ Map in electronic medical records to encourage process normalization. Patients use the map to prepare for decision-making, to help guide them through the process and to share critical information with their loved ones.

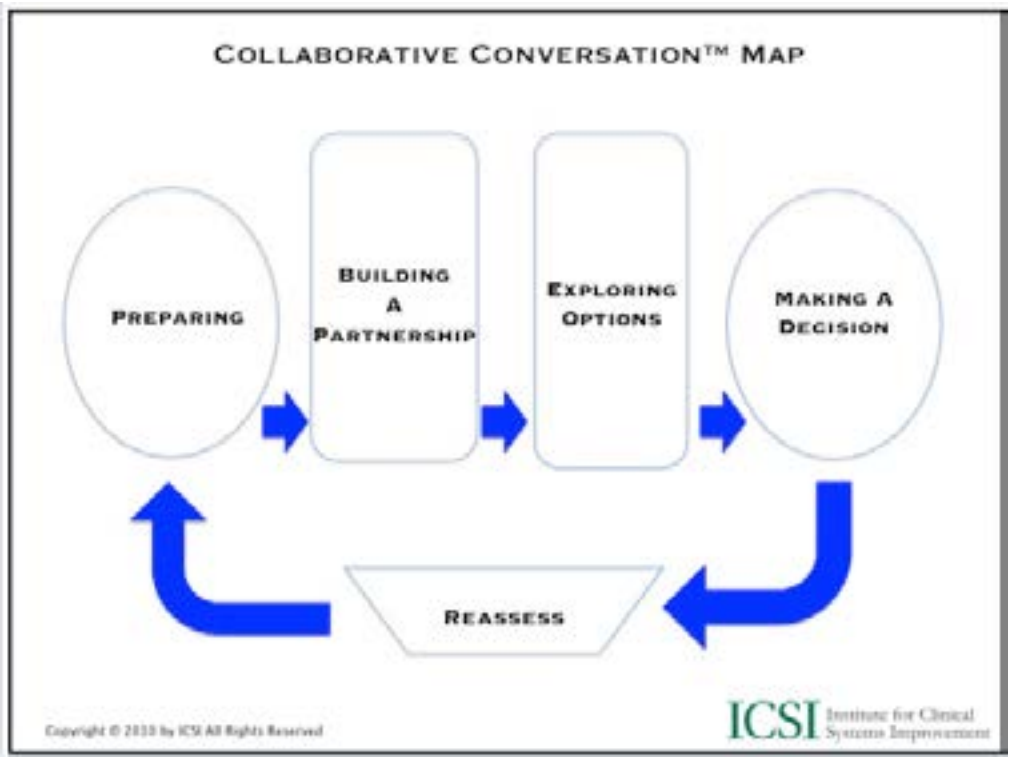

Table 2

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Evaluating Shared Decision-Making

It has proven challenging to assess shared decision-making. Measuring shared decision-making remains important for continued adoption of shared decision-making as a mechanism for translating evidence into practice; promoting patient-centered care; and understanding the impact of shared decision-making on patient experience, outcomes and revenues. Many assessments exist, but they are often proxy measures.

Two suggested methods for measuring shared decision-making are the CollaboRATE tool and the SURE Test. These two tools measure different aspects of shared decision-making, as described below.

The CollaboRATE tool measures the level of shared decision-making in the clinical encounter from the patient's perspective. It is a brief patient-reported measure of shared decision-making. The tools and guidance on their use can be found at http://www.collaboratescore.org/.

The SURE Test is a brief screening questionnaire the patient uses to access his or her readiness and capacity to make a decision or to determine whether he or she is comfortable with the choice that was made. In other words, it provides information on how likely a patient may be experiencing decisional conflict. If the SURE Test indicates decisional conflict may exist, the Decisional Conflict Scale should be completed in order to assess clinically significant decisional conflict.

Shared decision-making is a useful mechanism for translating evidence into practice. While research on the impacts of shared decision-making continues to grow, there is mounting evidence that both patients and clinicians benefit from SDM. Shared decision-making offers the opportunity to bring evidence and the patient's values into the patient/clinician discussion of health choices.

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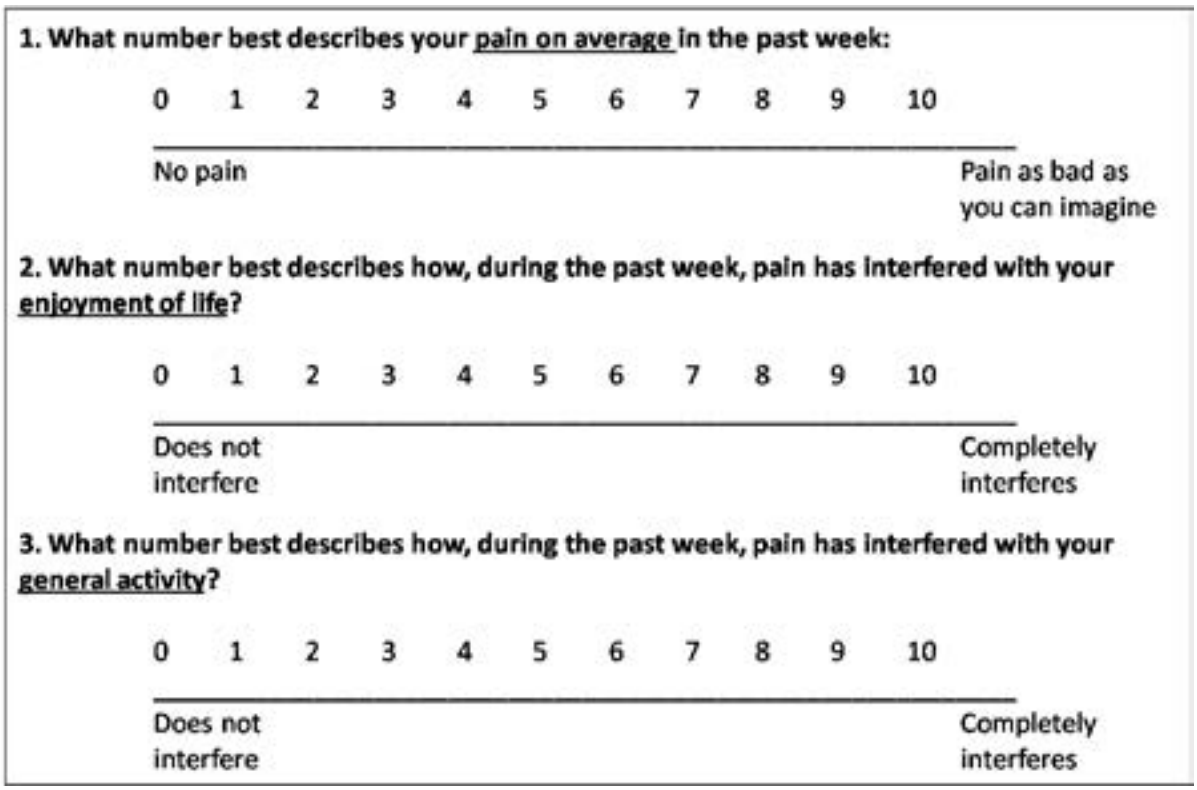
Appendix E – PEG: A Three-Item Scale Assessing Pain Intensity and Interference



1. What number best describes your pain on average in the past week:

0 1 2 3 4 5 6 7 8 9 10

No pain — Pain as bad as you can imagine

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

3. What number best describes how, during the past week, pain has interfered with your general activity?

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

Interview version

1. What number best describes your pain on average in the past week, on a scale from 0 to 10 where 0 is "no pain" and 10 is "pain as bad as you can imagine"? [0 to 10]

   The following two questions ask you to describe how, during the past week, pain has interfered with your life on a "0 to 10" scale, where 0 is "does not interfere at all" and 10 is "completely interferes."

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life? [0 to 10]

3. What number best describes how, during the past week, pain has interfered with your general activity? [0 to 10]

Scoring: The PEG score is the average of the 3 individual item scores. For clinical use, round to the nearest whole number.

The PEG is freely available in the public domain. Publications and reports should cite the original publication: Krebs EE, Lorenz KA, Bair MJ, et al. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. *J Gen Intern Med* 2009;24:733-38.

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ICSI has long had a policy of transparency in declaring potential conflicting and competing interests of all individuals who participate in the development, revision and approval of ICSI guidelines and protocols.

In 2010, the ICSI Conflict of Interest Review Committee was established by the Board of Directors to review all disclosures and make recommendations to the board when steps should be taken to mitigate potential conflicts of interest, including recommendations regarding removal of work group members. This committee has adopted the Institute of Medicine Conflict of Interest standards as outlined in the report, Clinical Practice Guidelines We Can Trust (2011).

Where there are work group members with identified potential conflicts, these are disclosed and discussed at the initial work group meeting. These members are expected to recuse themselves from related discussions or authorship of related recommendations, as directed by the Conflict of Interest committee or requested by the work group.

The complete ICSI policy regarding Conflicts of Interest is available at http://bit.ly/ICSICOI.

Funding Source

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ICSI facilitates and coordinates the guideline development and revision process. ICSI, member medical groups and sponsoring health plans review and provide feedback but do not have editorial control over the work group. All recommendations are based on the work group's independent evaluation of the evidence.

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Disclosure of Potential Conflicts of Interest

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Research Grants: None
Other: None

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Research Grants: None
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Research Grants: None
Other: None

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Other: None

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Guideline Related Activities: None
Research Grants: None
Other: Honorarium from Minnesota Medical Association for Opioids REMS (Risk Evaluation and Mitigation Strategies), and from Mayo and the State of Minnesota for teaching engagements. Dr. Reznikoff states that he donates all honoraria to charity.

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Guideline Related Activities: None
Research Grants: None
Other: None

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Guideline Related Activities: Served on a multidisciplinary group for a longitudinal care program for Low Back Pain for the International Union of Operating Engineers Local Union #49
Research Grants: None
Other: None

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Guideline Related Activities: None
Research Grants: None
Other: Received monies for travel/accommodations from the Minnesota Dental Association.

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ICSI seeks review from members and the public during the revision process.

Member Review

All ICSI documents are available for member review at two points in the ICSI revision process. The ICSI Response Report is sent to members at the beginning of a document revision. The goal of this report is to solicit feedback about the guideline, including but not limited to the algorithm, content, recommendations, and implementation. Members are also welcome to participate in the public comment period.

The work group would like to thank the following organizations for participating in the Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management: Non-Opioid Approaches and Opioid Management pre-revision review:

- *HealthPartners Medical Group, Bloomington, MN*
- *Hudson Physicians, Hudson, WI*
- *Medica Health Plan, Minnetonka, MN*
- *North Memorial Health Care, Minneapolis, MN*
- *Stillwater Medical Group, Stillwater, MN*

Public Comment

ICSI makes a draft of the guideline available to the public on the ICSI website. The public is invited to comment in an effort to get feedback prior to its finalization. All comments will be reviewed by the ICSI facilitator and work group members as needed. ICSI work group may or may not make changes to the guideline based on public comment responses.

The work group would like to thank all those who took time to thoughtfully and thoroughly review our draft and submitted comments for the Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management: Non-Opioid Approaches and Opioid Management guideline.

Invited Reviews

For some guidelines, ICSI will invite experts in the community to comment on a guideline draft prior to finalization. This is done during the public comment period.

The work group would like to thank all those who took time to thoughtfully and thoroughly review our draft and submitted comments for the Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management: Non-Opioid Approaches and Opioid Management guideline.

- *Miles Belgrade, MD, Comprehensive Pain Center; Head and Neck Pain Clinic; VA Health Care System*

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ICSI Patient Advisory Council (PAC)

The ICSI Patient Advisory Council responds to any guideline review requests put forth by ICSI facilitators and work groups. The PAC members may be involved at the beginning, middle, and/or end of the revision process. Patient advisors who serve on the council consistently share their experiences and perspectives in either a comprehensive or partial review of a document.

The PAC members provided thoughtful suggestions on additional places where clinicians could improve patient and family communication during the draft revision process that we were able to incorporate in the final document. We are also pleased to announce that the Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management guideline has received the PAC Seal of Approval.

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Document Drafted Jan – May 2005
Critical Review June 2005
First Edition Dec 2005
Second Edition Apr 2007
Third Edition Aug 2008
Fourth Edition Dec 2009
Fifth Edition Dec 2011
Sixth Edition Dec 2013
Public Comment Jul 2016
Eighth Edition Sep 2016
Eighth Edition Aug 2017

Document History

- Converted to GRADE methodology for reviewing evidence
- Supporting specific initiative
- Added Choosing Wisely
- Combined with Acute Pain Assessment and Opioid Prescribing Protocol
- Combined with Asssessment of Chronic Pain
- Updated acute opioid recommendations based on new literature in coordination with the Opioid Crisis Acute Pain Prescribing working group. This working group of subject matter experts was established as the result of 15 health care organizations and health plans coming together to work on pressing issues to improve the health of Minnesota communities, beginning with opioids and mental health. The Committee on Evidence-Based Practice approved changes on August 18, 2017.

The next revision will be no later than September 2022.

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ICSI Document Development and Revision Process

Overview

Since 1993, the Institute for Clinical Systems Improvement (ICSI) has developed more than 60 evidence-based health care documents that support best practices for the prevention, diagnosis, treatment or management of a given symptom, disease or condition for patients.

Audience and Intended Use

The information contained in this ICSI Health Care Guideline is intended primarily for health professionals and other expert audiences.

This ICSI Health Care Guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients and families are urged to consult a health care professional regarding their own situation and any specific medical questions they may have. In addition, they should seek assistance from a health care professional in interpreting this ICSI Health Care Guideline and applying it in their individual case.

This ICSI Health Care Guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition.

Document Development and Revision Process

The development process is based on a number of long-proven approaches and is continually being revised based on changing community standards. The ICSI staff, in consultation with the work group and a medical librarian, conduct a literature search to identify systematic reviews, randomized clinical trials, meta-analysis, other guidelines, regulatory statements and other pertinent literature. This literature is evaluated based on the GRADE methodology by work group members. When needed, an outside methodologist is consulted.

The work group uses this information to develop or revise clinical flows and algorithms, write recommendations, and identify gaps in the literature. The work group gives consideration to the importance of many issues as they develop the guideline. These considerations include the systems of care in our community and how resources vary, the balance between benefits and harms of interventions, patient and community values, the autonomy of clinicians and patients and more. All decisions made by the work group are done using a consensus process.

ICSI's medical group members and sponsors review each guideline as part of the revision process. They provide comment on the scientific content, recommendations and implementation strategies. This feedback is used by and responded to by the work group as part of their revision work. Final review and approval of the guideline is done by ICSI's Committee on Evidence-Based Practice. This committee is made up of practicing physicians, nurses and other clinicians, drawn from ICSI member medical groups.

Implementation Recommendations and Measures

These are provided to assist medical groups and others to implement the recommendations in the guidelines. Where possible, implementation strategies are included that have been formally evaluated and tested. Measures are included that may be used for quality improvement as well as for outcome reporting. When available, regulatory or publicly reported measures are included.

Document Revision Cycle

Scientific documents are revised as indicated by changes in clinical practice and literature. ICSI staff monitors major peer-reviewed journals for any pertinent evidence that would affect a particular guideline and recommendation.

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