

# Transforming the Treatment of Chronic Pain Moving Beyond Opioids



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A VA Clinician's Guide



# VA PBM Academic Detailing Service Real Provider Resources Real Patient Results

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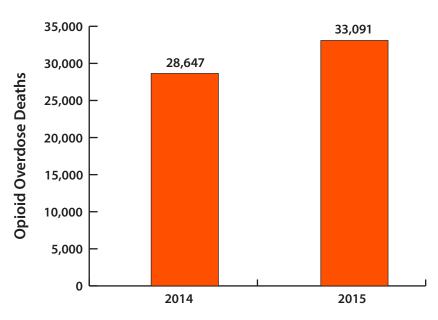
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### Transforming the Treatment of Chronic Pain

Major changes have occurred in the treatment of pain with the focus now on a biopsychosocial model of pain care using multimodal treatments. In 2011, drug overdoses became the leading cause of injury-related death in the United States rising above motor vehicle accidents.<sup>1</sup> Due to the risks of using opioids, new guidelines recommend using non-pharmacologic and non-opioid treatments for chronic pain and recommend against using opioids.

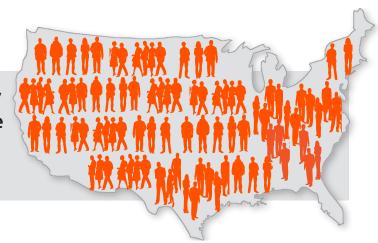
Figure 1. Opioid Overdose Deaths Continue to Increase in the United States 2014–2015<sup>1</sup>



Among 47,055 drug overdose deaths that occurred in 2014 in the United States, 28,647 (60.9%) involved an opioid. Centers for Disease Control (CDC) examined overall drug overdose death rates during 2010–2015 and opioid overdose death rates during 2014–2015 by subcategories (natural/semisynthetic opioids, methadone, heroin, and synthetic opioids other than methadone). Overdose death rates are continuing to increase with data from 2015, showing drug overdoses accounted for 52,404 U.S. deaths, including 33,091 (63.1%) that involved an opioid.

#### What Does This Really Mean?

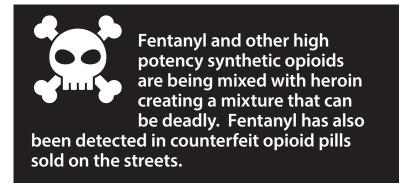
Americans die every day from an opioid overdose (includes prescription opioids and heroin).1



It is not just prescription opioids; heroin use is on the rise. Three out of four new heroin users report abusing prescription opioids before using heroin.<sup>2</sup>

Why are more people using heroin?

- ✓ Low cost
- ✓ Easily available
- ✓ Increased purity
- ✓ Increased potency

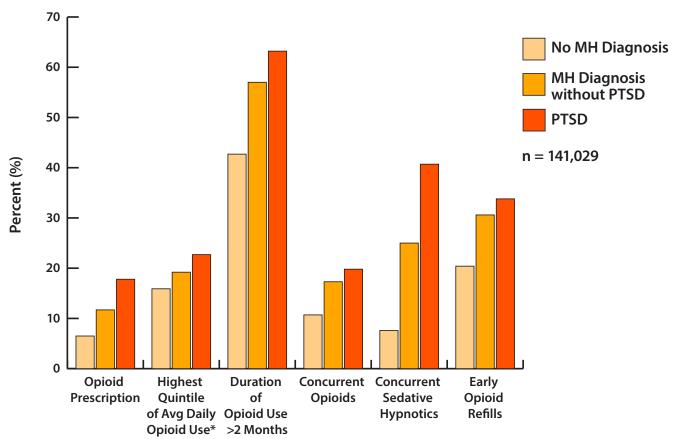


#### **Veteran Specific Considerations**

We, as a healthcare system, need to be vigilant about providing safe and effective pain care to Veterans with pain and identify those who may be seeking relief from psychological pain.<sup>3</sup>

Psychological distress may lead to inappropriate use of opioid medications.

Figure 2: Opioid Prescribing is More Common in Veterans with a Mental Health Diagnosis<sup>4</sup>



Iraq and Afghanistan Veterans who received a new non-cancer-pain diagnosis within 1 year of VA entry were followed for 1 year to evaluate whether an opioid was prescribed for ≥20 consecutive days. Veterans with post-traumatic stress disorder (PTSD) were more likely to be prescribed an opioid at higher doses, take opioids for longer than 2 months, and receive opioids and sedatives concurrently than patients without a mental health diagnosis. \*Opioid use >33 mg MEDD.

#### What Has the Department of Veterans Affairs (DVA) Done in Response?

In 2013, the VA launched the Opioid Safety Initiative (OSI) to reduce the use of opioid medications, improve the safety of opioid prescribing, and expand alternative pain therapies.

By 2016, measurable improvements were observed in metrics involving potentially unsafe opioid use.

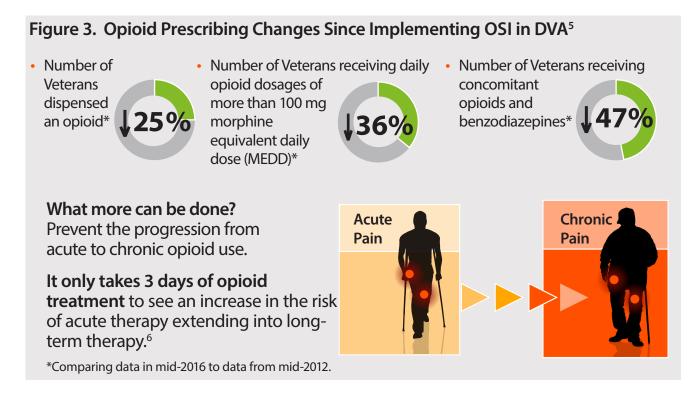
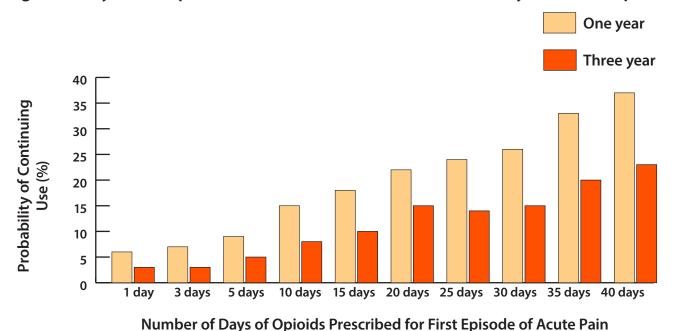


Figure 4: Any Use of Opioids for Acute Pain Increases the Probability of Chronic Opioid Use<sup>6</sup>



Records reviewed of patients  $\ge$ 18 years of age who had at least one opioid prescription during June 1, 2006–September 1, 2015 and  $\ge$ 6 months of continuous enrollment without an opioid prescription before their first opioid prescription. A total of 1,294,247 patients met inclusion criteria, including 33,548 (2.6%) who continued opioid therapy for more than 1 year.

#### Change the Conversation

We need to change our conversation to let Veterans know that we still want to address their pain using a whole-health approach to improve quality of life and increase functional status. Over time, this can lead to pain becoming less overwhelming.

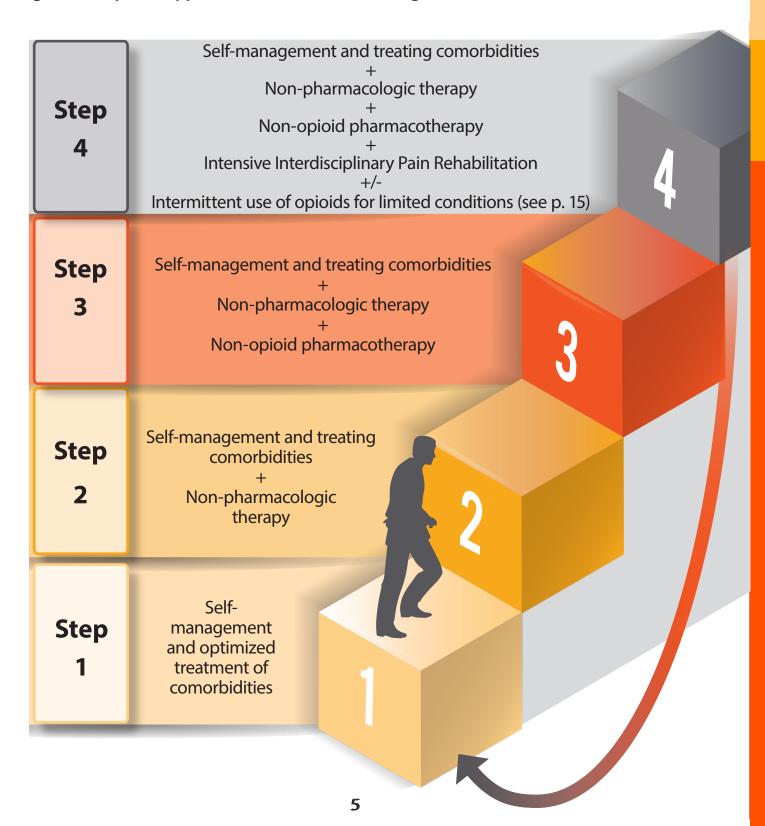
Table 1. Starting the Conversation with Veterans About Opioid Safety

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When the conversation starts like this:	Instead of saying this:	Try saying this:	
Patient requests oxycodone for chronic low back pain	The VA says I cannot prescribe oxycodone any longer.  We will need to use something else.	We have new information showing that opioids like oxycodone are not the best treatment for back pain.  May I talk to you about treatments we have that may work better for you?	
Patient on hydrocodone/ acetaminophen for 3 years: Patient requests a higher dose	I know you have pain, but I cannot give you more hydrocodone and really we should not be using it at all.  I am going to reduce your monthly supply in half this month.	May I talk to you about other treatments that might work better for your pain and are safer in the long run?	
Patient who has been prescribed morphine Sustained Release (SR) for 8 years:  Patient asks at his appointment why he has been prescribed such a dangerous drug after he hears on the news about the high rates of overdose	That morphine was prescribed by the VA provider you had before me.  I never thought it was good for you.  I am not sure how to taper you off of this, so I will send you to the pain clinic.	Yes, this is a concern to me also.  We are realizing that opioids are not the best option for treating pain.  Just as treatments change for diseases like diabetes and heart disease, treatments can change for pain also.  Let's talk about other options for your pain management. How does this sound to you?	

#### **Management of Chronic Pain**

Management of chronic pain should be approached in a stepwise manner, with self-management and non-pharmacologic therapy used first line and tried before starting pharmacologic therapy.<sup>7</sup> In some cases, for patients to start self-management activities, they may need to use a higher treatment step for a period of time. The goal of therapy is to maintain patients on the lowest treatment step.

Figure 5. Stepwise Approach to Chronic Pain Management<sup>7,8</sup>



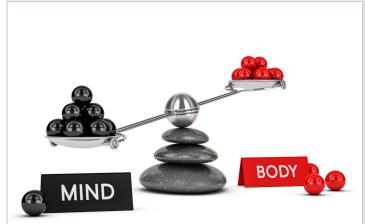
Step 1

#### **Self-management Education**

Self-management education and optimizing treatment of related comorbidities are recommended for all patients with chronic pain.

Figure 6. Self-management Activities and Pain Management Strategies<sup>9–13</sup>

#### **General Health Promoting Activities**



- Practice mindfulness
- Healthy relationships
- Sleep hygiene
- Healthy eating
- Physical fitness/movement
- Tobacco cessation
- Engagement in activities that reflect personal values

#### **Pain Management Strategies**



- Posture
- Weight management
- Anti-inflammatory diet
- Physiologic relaxation strategies
- Self-trigger-point massage
- Education
  - Fear of pain
  - Catastrophizing
- Action oriented support groups

Step 2

#### Non-pharmacologic Therapy<sup>7–26</sup>

For patients who need more help managing their pain, non-pharmacologic therapies are the best place to start. Core therapies are active treatments such as movement therapies and psychological therapies. Complementary and Integrative Health (CIH) therapies such as acupuncture and chiropractic care, can be used widely as short term, bridging therapies with the purpose of transitioning from higher risk passive therapies (such as long-term opioid therapy) to lower risk active therapies (psychological therapies and movement therapies). Use non-pharmacologic treatments based on the type of pain the Veteran is experiencing and the type of treatment the Veteran is willing and able to perform.

Figure 7. Non-pharmacologic Therapies<sup>7–26</sup>

### Psychosocial Interventions

- Cognitive-Behavoiral Therapy (CBT)
- Acceptance and Commitment Therapy (ACT)
- Progressive relaxation therapy
- Mindfulnessbased Therapies
- · Pain School
- Behavior groups

Complementary and Integrative Health (CIH) Therapies



- Acupuncture
- Massage
- Chiropractic therapy
- Ice and heat therapy
- Meditation

Rehabilitation Therapies



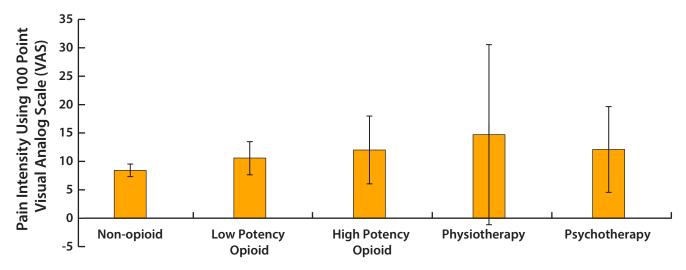
- Physical therapy
- Occupational therapy

Exercise



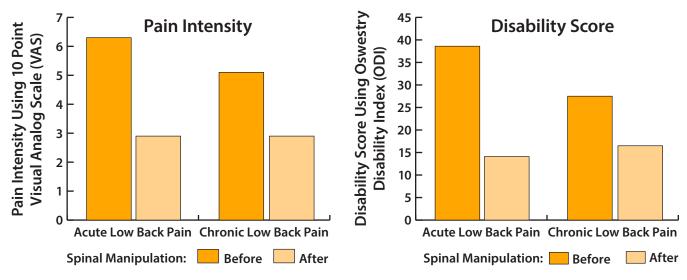
- Stretching
- Tai chi
- Swimming
- Hiking
- Walking
- Yoga
- Chair exercises

Figure 8. Similar Reduction in Pain Intensity Between Non-Pharmacologic Therapy and Non-Opioid, Low Potency Opioid and High Potency Opioid Therapy<sup>27</sup>



Meta-analysis comparing different treatments for chronic pain from arthritis, low back pain, neuropathic pain and fibromyalgia. Weighted mean differences between pain intensities, using a 100 point visual analog scale (VAS), were used. Non-opioid treatments included NSAIDs, acetaminophen or paracetamol, and COX-2 inhibitors. Low potency opioids included codeine and tramadol. High potency opioids included fentanyl, morphine, oxycodone and oxymorphone. Physiotherapy included ultrasound, thermotherapy, and nerve stimulation. Psychotherapy included cognitive behavioral therapies. Medications were compared to placebo and physiotherapy and psychotherapy were compared to wait-list controls.

Figure 9. Effect of Spinal Manipulation for Acute and Chronic Low Back Pain Shows Statistically Significant Improvement in Pain Intensity and Disability After 2 Weeks<sup>28</sup>



Nonrandomized prospective clinical trial evaluating the effect of spinal manipulative therapy using a single high velocity low amplitude thrust (HVLT) to the involved segment of the lumbosacral region as compared to a group receiving no treatments. Six treatments were used on alternate days over a 2 week span. No other treatments were allowed in the study. Pain VAS and disability ODI were used to determine effect.

Recommend non-pharmacologic treatments first line to Veterans with chronic pain.

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#### **Pharmacological Treatment Strategies**

#### Non-opioid Pharmacotherapy<sup>8,29</sup>

Recommend addition of non-opioid pharmacotherapy in patients who continue to have intolerable pain despite using non-pharmacologic approaches. Select non-opioid therapy based on the type of pain and patient specific comorbidities.

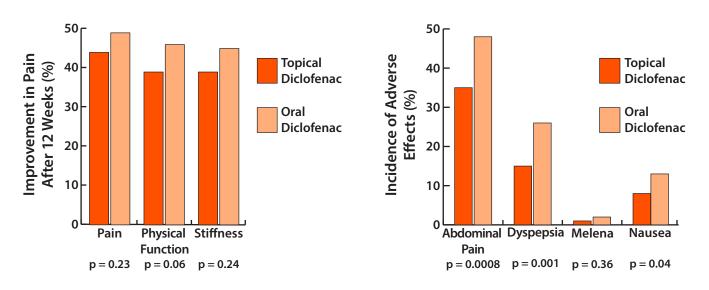
Types of non-opioid pharmacotherapy:

- Topical Therapy
- Oral Therapy

#### **Topical Therapy**

Lowest risks for adverse effects and can provide benefit in reducing pain and improving function.

Figure 10. Topical Diclofenac is as Effective as Oral Diclofenac for Joint Pain with Fewer Side Effects<sup>30</sup>



Randomized, double-blind, double-dummy equivalence trial of topical diclofenac solution compared to oral diclofenac (50 mg three times daily) for 12 weeks in patients with knee osteoarthritis. Pain and physical function were measured by the Western Ontario and McMaster Universities (WOMAC) VA 3.1 OA Index and pain global assessment (PGA).

Figure 11. Topical Therapy<sup>31</sup>

**TOPICALS** • Diclofenac formulations: gel, solution, or patch • Used for localized pain in a joint area like the knee, ankle, shoulder, and wrist Produces localized anti-inflammatory effects **NSAIDs** - Evidence does not support use for low back pain • Less systemic side effects compared to oral NSAIDs due to minimal systemic absorption Safer to use in patients taking oral anticoagulants Lidocaine patch • Used for peripheral neuropathic pain • Blocks abnormal peripheral neuronal conduction Lidocaine - Provides local analgesia to painful skin where the medication is applied Systemic absorption is very low when applied to intact skin • Methyl salicylate formulations: cream, ointment or patch Can be combined with menthol and/or camphor Used for local/regional effect for musculoskeletal pain **Methyl Salicylate**  Counterirritant causing mild inflammation which results in deeper pain relief · Apply to intact skin Capsaicin formulations: cream or ointment · Used for peripheral neuropathic pain and musculoskeletal pain • Depletes substance P with daily use leading to desensitization of Capsaicin sensory nerve fibers and resulting in less pain • Must use multiple times a day every day to maintain effective pain control

Products are listed based on evidenced based recommendations. Not all products listed may be available on VA National Formulary and may require non-formulary request or prior authorization request. To view VA National Formulary: https://www.pbm.va.gov/PBM/NationalFormulary.asp. NSAID = nonsteroidal anti-inflammatory drug.

#### **Oral Therapy**

Selection of non-opioid medications should be made based on individual patient characteristics (e.g., type of pain, other medications, comorbidities).

Figure 12. Oral Therapy<sup>31–43</sup>



#### Acetaminophen

- First line therapy for the treatment of osteoarthritis and musculoskeletal pain
- Not associated with GI ulcer, platelet or anti-inflammatory effect at doses
   <2000 mg/day</li>
- Maximum dosage 2000 mg in patients with liver disease and 4000 mg daily in patients without liver diseases
  - Caution patients about acetaminophen in over-the-counter and combination products
- Not recommended for chronic low back pain due to lack of pain reduction

#### NSAIDs

- First line agents for musculoskeletal pain and acute and chronic low back pain
  - May be more effective than acetaminophen, but are associated with more side effects (e.g., GI ulceration, CV effects including MI and stroke, and renal toxicity)
- Trial more than one NSAID, since there can be variability in patient response
- NSAIDs are contraindicated in the setting of CABG\*
- Adding an NSAID to a pain regimen containing an opioid may have an opioid-sparing effect of approximately 20–35%

#### **Antidepressants**

- Tricyclic antidepressants (TCAs) and serotonin norepinephrine reuptake inhibitors (SNRIs)
- First line agents for neuropathic pain such as from diabetes and for chronic musculoskeletal pain
- Helpful in patients with concurrent chronic pain and depression

#### **Anticonvulsants**

- Gabapentin, pregabalin, carbamazepine, oxcarbazepine
- Gabapentin and pregabalin are first line agents for diabetic nerve pain
- Insufficient evidence to recommend for or against use for treating low back pain, including patients with radiculopathy

<sup>\*</sup>Do not use perioperatively and avoid in the first 10–14 days after CABG surgery. Skeletal muscle relaxants are not recommended to treat chronic pain. CABG = coronary artery bypass graft.

#### **Concerns About Adverse Effects from Oral NSAIDS**

Figure 13. Gastrointestinal Toxicity—What are the Risks?<sup>44-46</sup>

<b>25</b> %
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- Approximately 25% of chronic NSAID users will develop GI ulcer disease; 2 to 4% will bleed or perforate
- Consider COX-2 selective NSAIDs like meloxicam and etodolac which have lower GI risks than other NSAIDs
- Celecoxib (COX-2 inhibitor)
  has a lower risk of GI events
  compared to naproxen
  and ibuprofen

## Risk > 1st Few Months

- Risk of GI ulcers reduces after the first few months of NSAID use but not completely
- Patients taking NSAIDs for <1 month had an increased risk for GI bleeding when compared to long-term users
- Gastric ulcers and duodenal ulcers in 1 study were found to be more common in patients who had used NSAIDs for less than 3 months

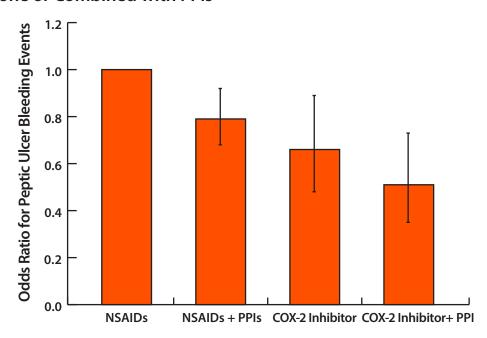
Table 2. Primary Prevention of NSAID Induced GI and CV Toxicity<sup>43,47</sup>

GI Risk Factor Assessment	Patients with GI Risk Factors Only	Patient with GI Risk Factors and High Cardiovascular Risk Requiring Low Dose Aspirin
<ul> <li>High Risk</li> <li>History of previously complicated ulcer, especially recent</li> <li>More than 2 risk factors: <ul> <li>Age &gt;65 years</li> <li>High dose NSAID therapy</li> <li>Previous history of uncomplicated ulcer</li> <li>Concurrent use of aspirin (including low dose), corticosteroids or anticoagulants</li> </ul> </li> </ul>	Alternative therapy or COX-2 inhibitor + PPI* or misoprostol	Avoid NSAIDs or COX-2 inhibitors Use alternative therapy (e.g., acetaminophen)
Moderate Risk  • 1–2 risk factors	NSAID + PPI* or misoprostol	NSAID/COX-2 inhibitor** + PPI* or misoprostol
Low Risk  No risk factors	NSAID alone	NSAID/COX-2 inhibitor** + PPI* or misoprostol

<sup>\*</sup>High dose and long-term use (>1 year) of PPIs has been linked to side effects including: osteoporosis, Clostridium difficile associated diarrhea, pneumonia, and decreased absorption of magnesium and Vitamin B12.

<sup>\*\*</sup>Consider NSAID or COX-2 inhibitor that may have lower CV risks like naproxen, ibuprofen, or moderate dose celecoxib. CV = cardiovascular; PPI = proton pump inhibitor; COX-2 inhibitor = cyclooxygenase 2 inhibitor.

Figure 14. Peptic Ulcer Bleeding Events Were Similar Between Users of Conventional NSAIDs Combined with PPIs Compared with Selective COX-2 Inhibitors
Alone or Combined with PPIs<sup>48</sup>



Case-control study from the Netherlands during the period of January 1998 to December 2012 in subjects who had ever used conventional NSAIDs and/or selective COX-2 inhibitors who were >18 years at first hospital admission with a primary discharge diagnosis of GI toxicity defined as peptic ulcer disease (PUD) in the GI tract. They identified 2,634 PUD cases and 5,074 age-matched controls that were current users of conventional NSAIDs or selective COX-2 inhibitors at the index date.

#### Cardiovascular Risks<sup>38,49,50</sup>

- NSAIDs and COX-2 inhibitors can increase cardiovascular risk
  - Hypertension, stroke, myocardial infarction, and heart failure
  - Avoid use in patients with a history of heart failure or recent myocardial infarction
- Diclofenac and indomethacin appear to have higher risks
- Naproxen, ibuprofen, and moderate dose celecoxib (100 mg twice daily) may have a lower risk<sup>38</sup>

#### Renal Risks<sup>51</sup>

- Both COX-2 selective and nonselective NSAIDs are associated with renal side effects and may result in acute and chronic renal failure
- Risk factors include:
  - Elderly
  - Dehydrated state
  - Other comorbidities like congestive heart failure, diabetes, and cirrhosis

Figure 15. Options for Treating Neuropathic Pain Based on Level of Evidence<sup>39–43</sup>

#### Tricyclic **SNRIs Anticonvulsants Antidepressants** Duloxetine, Gabapentin, Amitriptyline, venlafaxine imipramine pregabalin, despiramine, carbamazepine\* oxcarbazepine\* nortriptyline ■ NNT 3-4 ■ NNT 6-7 ■ NNT 7-8 Efficacy shown More data Most data for for all types of available for postherpetic duloxetine nerve pain neuralgia, diabetic Caution in Consider in neuropathy and patients over patients with spinal cord injury 65 years of age comorbid Gabapentin and depression Most studies pregabalin found ■ Most data have used to lack benefit amitriptyline for diabetic for acute and neuropathy, chronic sciatica Nortriptyline chemotherapypain and desipramine related have less peripheral Combining anticholinergic neuropathy and gabapentin with effects pain in multiple nortriptyline is sclerosis more effective Recommended than either drug for chronic low Duloxetine is alone for diabetic back pain recommended peripheral for chronic neuropathy or musculoskeletal postherpetic pain and chronic neuralgia low back pain

<sup>\*</sup>Carbamazepine and oxcarbazepine have strong evidence for treatment of trigeminal neuralgia, but evidence is weaker for other types of nerve pain. Oxcarbazepine may have fewer side effects than carbamazepine.

NNT = number needed to treat. PTSD = post-traumatic stress disorder. SNRI = serotonin norepinephrine reuptake inhibitors.

#### Considerations when using neuropathic pain treatments: 42-43

- Trial of the medication should last at least 12 weeks to determine effectiveness
- If the patient does not respond or has intolerable side effects
  - Taper off the medication over a few weeks
- If the patient has a partial response
  - Consider adding a second neuropathic pain agent with a different mechanism of action
  - Most evidence supports the combination of gabapentin with nortriptyline or other TCA, particularly for diabetic neuropathies

If non-pharmacologic treatments alone do not reduce a patient's pain, consider adding non-opioid pharmacotherapy.

Step 4

#### Intensive Interdisciplinary Pain Rehabilitation

Intensive Interdisciplinary Pain Rehabilitation (IIPR) is a resource intensive treatment that requires active patient participation and motivation and may result in modest long-term improvements in pain and function.<sup>52</sup> Core elements of IIPR include integrated psychological and movement therapies with medication management. Programs may also include a variety of CIH therapies. The focus of treatment is improving physical, social, and psychological functioning and empowering the patient to implement daily use of self-management strategies.

For patients with chronic non-cancer pain who are opioid naïve, long-term opioid therapy should not be started.

It may be reasonable to use intermittent, non-daily, opioid therapy for patients with certain chronic pain conditions associated with recurrent inflammatory, ischemic, or mixed pain such as rheumatoid arthritis or sickle cell anemia. Opioid therapy should not be used in isolation and requires careful monitoring and re-evaluation at least every 3 months.





- Discuss the patient information guide "Taking Opioids Responsibly"
- Set expectations for pain management, develop functional goals, and discuss opioid dosing limits of ≤20 mg MEDD
- Complete the consent for Long-Term Opioid Therapy: VA Form 10-0431
   Consent for Long-Term Opioid Therapy for Pain
- Perform risk mitigation strategies
  - Urine Drug Testing (UDT)
  - Prescription Drug Monitoring Program (PDMP)
- Provide opioid overdose education and offer naloxone distribution (OEND)

#### **Setting Expectations for Pain Management**

It is important to inform the Veteran that the goal is to assist them in returning to a productive and fulfilling life. Complete pain relief is not a realistic goal.

Table 3. Set Realistic Patient Expectations<sup>8</sup>

Goal	Pain Reduction	Improved Function	Minimize Side Effects
Education	<ul> <li>Total pain relief is not realistic</li> <li>Goal is to take the edge off and reduce pain by 20–30%</li> </ul>	<ul> <li>Ultimate goal is to improve quality of life (QOL)</li> <li>Degree of pain that interferes with QOL is highly personal</li> </ul>	Educate on potential side effects and risks associated with the chosen treatment(s)

For patients currently taking long-term opioids for chronic pain:



Close follow up is required (≤3 months) to assess the benefits vs risks, perform risk mitigation strategies, and provide OEND.<sup>8</sup> Patients should be evaluated for tapering and, when risks exceed benefits, opioids should be reduced to a lower dose or discontinued. Continue optimizing whole person pain care and maintain vigilance for symptoms of opioid use and/or psychiatric comorbidities.

Table 4. Follow up for Patients on Long-Term Opioids<sup>8,29</sup>

#### Assess

- Function, risks and benefits of opioid therapy
- Adverse effects
- Pain and functional treatment goals
- Adherence to treatment plan
- Complications or co-occurring conditions (medical, mental health, and/or SUD)

#### **Complete risk mitigation strategies**

- Urine drug testing (UDT)
- Prescription drug monitoring program (PDMP)
- Monitoring for overdose and suicidality
- Opioid overdose education and naloxone distribution (OEND)

#### Discuss expectations and optimize comprehensive pain care plan

- Pain reduction
- Improved function
- Minimizing side effects

#### **Evaluate for opioid taper**

Follow up should be performed at least every 3 months if opioid dose is stable and more frequently if needed based on risk factors

#### Situations Where the Risks of Prescribing Opioids May Be the Highest<sup>8</sup>

- ✓ Using opioids with medications for other conditions that increase the risk of overdose (e.g., benzodiazepines)
- ✓ Concerns about opioid use disorder (OUD), substance use disorder (SUD), or diversion of opioids
- ✓ Patient nonadherence with opioid safety measures and risk mitigation strategies
- ✓ Patient is not participating in comprehensive care plan
- ✓ Use of opioids in Veterans younger than 30 years of age
- ✓ Opioid dose is over the maximal recommended dose (≥90 mg MEDD)
- ✓ Pain condition not effectively improved with opioids or opioids are not providing a clinically meaningful improvement in function
- ✓ Pain conditions which may be worsened by opioids (e.g., fibromyalgia, headache)
- ✓ Unmanageable side effects

#### **Comorbidities**

It is important to address other comorbidities that can complicate pain management. Functioning will not improve without addressing other comorbidities that can worsen pain and/or pain perception or increase the risks of opioid therapy.<sup>8</sup>

Figure 16. Addressing Comorbidities<sup>8</sup> Mental Health Depression • PTSD Medical Anxiety **Substance Use**  Diabetes • Insomnia Disorder (SUD) • COPD Alcohol Sleep Apnea Opioids Obesity Tobacco **PAIN** 

#### **Evaluate Patients for Suicidality<sup>8</sup>**

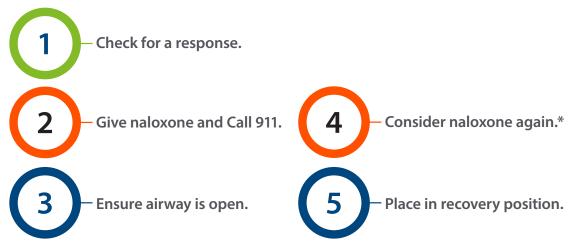
Patients with chronic pain have an increased risk of suicide

- ✓ Assess patient for risk factors including mental health diagnoses, past suicide attempts, intentional self-harm, traumatic brain injury, and psychosocial factors (e.g., recent job loss, legal charges)
- ✓ Ask about suicidal ideation, intent, plan, and past attempts
- ✓ Refer as needed for treatment of depression or other mental health disorders, and provide patients with supportive psychological therapy using safe drug treatments

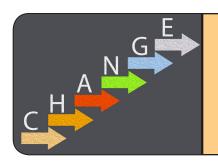
#### Opioid Overdose Education and Naloxone Distribution (OEND)53

- Education and training for patients on how to prevent, recognize, and respond to an opioid overdose
- Provide overdose education and naloxone prescriptions to all patients taking opioids chronically for pain
  - Factors placing patients at a higher risk for overdose
    - □ Concurrent opioid and benzodiazepine use
    - □ Doses of opioids over 50 mg MEDD
    - □ Patients with OUD
    - □ Patients tapering dose of opioids due to lower tolerance
- Naloxone is available for outpatient dispensing

Figure 17. OEND and Basic Steps for Responding to an Opioid Overdose



<sup>\*</sup> If the person doesn't start breathing in 2–3 minutes, give the second dose of naloxone; naloxone wears off quickly so a second dose may also be needed if the person stops breathing again.



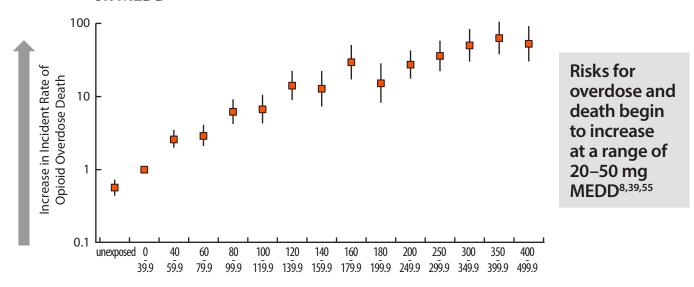
A change in treatment plan must be considered for all Veterans who have an opioid overdose.<sup>54</sup>

Risk mitigation strategies, including UDT, checking state PDMP, providing OEND, should be done at least annually in all Veterans prescribed opioids for pain.

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#### Does the Dose of Opioid Matter?

Figure 18. Exponential Increase in the Incident Rate of Opioid Overdose Death Based on MEDD<sup>55</sup>



Milligram Morphine Equivalent Daily Dose (MEDD)

Observational cohort study of 2,182,374 patients in North Carolina prescribed opioids for pain. Opioid analgesics were dispensed to 22.8% of residents. Of the 2,182,374 patients prescribed opioids there were 478 overdose deaths. Mortality rates increased over the range of MEDD. In addition, 80% of opioid analgesic patients also received benzodiazepines. Rates of overdose death among patients with concurrent opioid and benzodiazepine use were 10 times higher than those using opioids alone.

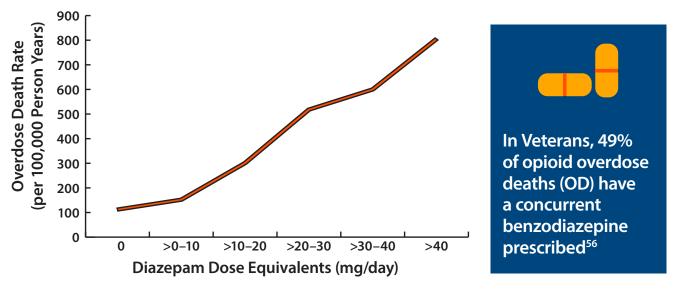
When opioids are prescribed chronically, it is preferable to keep doses below 20–50 mg MEDD. Reassess risks and benefits for all patients on long-term opioid therapy and if functional benefits do not clearly outweigh risks, consider a slow taper to a reduced dose or to discontinuation.

#### Opioid and Benzodiazepine Combinations – These can be lethal!

Opioids when co-administered with substances with sedative properties, like benzodiazepines, can result in unintentional fatal outcomes. 56,57

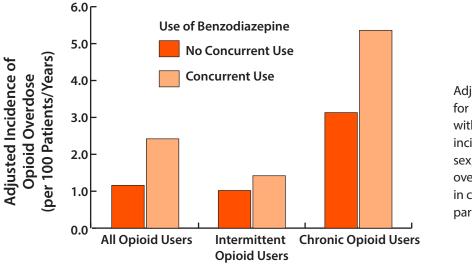
Figure 19. Opioid Overdose with Co-Administered Benzodiazepine:

The Risk Increases with Increasing Doses of the Benzodiazepine<sup>56</sup>



This case-cohort study (2004–2009) found that of the 2,400 Veterans in the study population who died from an opioid overdose death, 1,185 (49%) died during a period in which they had been prescribed concurrent benzodiazepines. Risk of overdose increased as daily benzodiazepine dose increased.

Figure 20. Opioid Overdoses Increase When Patients Use Opioids in Combination with Benzodiazepines<sup>57</sup>



Adjusted incidence of opioid overdose for patients taking opioids with and without benzodiazepines. Adjusted incidence incorporates controls for year, sex, age and characteristics. Incidence of overdose increases when opioids are used in combination with benzodiazepines, particularly with chronic opioid use.

Avoid prescribing opioids and benzodiazepines in combination.

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#### **Opioid Taper**

Consider tapering opioids in Veterans where the risk of continuing the opioid outweighs the benefit of continuing the opioid. When a taper is necessary, the first step is talking with the Veteran about the taper.

- Explain the risks of opioid therapy as they apply to the Veteran and why tapering is necessary.
- Review how the taper will be done and provide support during the taper.
- Pauses in the taper may be necessary for the Veteran to adjust to the new dose before further reductions are made.
- If the Veteran has opioid use disorder (OUD) or shows behaviors consistent with OUD, do not start an opioid taper. First, the provider should:
  - Address OUD and consider prescribing medication assisted treatment (MAT) or
  - Connect the Veteran with a substance use disorder clinic who can provide OUD services

**Table 5. Starting the Conversation with Veterans About Tapering Opioids** 

Conversation	Instead of this:	Consider saying this:
Starting the conversation	The VA wants me to stop your oxycodone. My hands are tied.	I am concerned about your safety with the oxycodone I am prescribing you for pain.  May I talk to you more about this?
Continuing the conversation	I know you have pain, but I cannot give you this medicine anymore. You will have to figure something else out.	Have you heard about the increase in deaths from overdose in people taking opioids like oxycodone?  How do you feel about this?
Introduce other options for pain	You know, acetaminophen would work just as well. How about you go to the drug store and pick up some of that?	There are other treatments and medications we can try for your pain.  They are safer and could be as effective and might be even more effective than the oxycodone.  May I tell you more about this?

Conversation	Instead of this:	Consider saying this:
Talk about tapering the opioid	I am going to give you a prescription for X tablets of oxycodone.  For the first week, cut your dose in half. Then the next week, reduce by another half and keep doing that until you are off.  We should have it all done by the end of the month.	As we start the new treatment, I recommend that we start with a very small reduction in oxycodone which will help move your dose to a safer level. This would involve reducing by X tablets a week/month (5–10% reduction per month). Our experience and studies show that as we reduce the oxycodone gradually and add other more effective treatments, your pain levels will likely stay the same.  In some cases, patients have experienced some discomfort in the first few weeks of the taper but it usually improves with time.  What are your thoughts on reducing the oxycodone?
Provide support and follow up	I will schedule you to follow up in 6 months.	In 2 weeks, the PACT team (nurse, pharmacist, or provider) will give you a call and see how you are doing with the lower dose of oxycodone and the new treatment.
Talk about possible emergence of OUD during an opioid taper		Your brain has been exposed to and has adapted to these medications over the past several years.  As the opioid dose is lowered,  your brain may react by producing a strong desire to take more opioids or  you may find that you cannot take your mind off opioids or are having a difficult time taking the opioids as prescribed  If you notice any of these things, please contact us right away so we can help you.  It is important you know that we have effective treatments in case you notice any of these symptoms.

For more information: See VA PBM Academic Detailing Opioid Taper Tool (http://www.pbm.va.gov/PBM/academicdetailingservice/Pain\_and\_Opioid\_Safety.asp).

#### Some Patients Will Struggle with Tapering

What might this mean?

- The speed of the taper may be too fast
  - Reducing opioid doses 5–20% per month is appropriate for most patients but some may need a slower taper of 2–5% reduction per month
  - Pausing for 2–4 weeks after a dose reduction may be necessary in some patients to allow them to adjust to the new dose
- The Veteran may be anxious and fearful about the taper and may need more counseling and support during the taper
- Co-occurring mental health conditions may be worsening during the taper and should be addressed
- The Veteran may have opioid use disorder (OUD)
  - Screen for OUD
  - If patient has OUD, provide or refer for medication assisted treatment (MAT)
- The Veteran may need other non-pharmacologic and non-opioid treatments
- The Veteran may be diverting medications

If the Veteran has OUD, pain treatments will need to be tailored to ensure safety and reduce overdose risks. Consultation with a pain specialist and a behavior health provider is recommended to determine the most appropriate treatment plan that includes relapse-prevention strategies.<sup>3,58-60</sup>

Assess for OUD and if present, offer or refer for medication assisted treatment and counseling prior to starting or continuing an opioid taper.

#### **Summary**



Opioids are no longer recommended for treatment of chronic pain.



Non-pharmacologic and non-opioid treatments should be used first line for most types of pain.



In patients already prescribed opioids for chronic pain, weigh the risks and benefits of continued use.



Follow up with all patients taking chronic opioids at least every 3 months and use risk mitigation strategies including UDT, PDMP review, and OEND.



If the risks of continuing the opioid are high, discuss slowly tapering the opioid (5–20% per month) and using non-pharmacologic and non-opioid alternatives.



Screen for OUD in patients struggling with tapering opioids and showing high risk behaviors. Medication assisted treatment with buprenorphine/naloxone or methadone might be necessary.

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#### References

- 1. Rudd RA, Seth P, David F, Scholl L. Increases in Drug and Opioid-Involved Overdose Deaths United States, 2010–2015. *MMWR Morb Mortal Wkly Rep*. ePub: 16 December 2016.
- 2. Centers for Disease Control and Prevention. Vital Signs: Today's Heroin Epidemic More People at Risk, Multiple Drugs Abused. *MMWR Morb Mortal Wkly Rep.* 2015.
- 3. Hoge CW. Interventions for war-related posttraumatic stress disorder: meeting Veterans where they are. *JAMA*. 2011;306(5):549–551.
- 4. Seal KH, et al. Association of Mental Health Disorders with Prescription Opioids and High-Risk Opioid Use in US Veterans of Iraq and Afghanistan. *JAMA* 2012; 307:940–7.
- 5. Gellad WF, Good CB, Shulkin DJ. Addressing the opioid epidemic in the United States: Lessons from the Department of Veteran Affairs. *JAMA* 2017;177(5):611–612. doi:10.1001/jamainternmed.2017.0147
- 6. Shah A, Hayes CJ, Martin BC. Characteristics of initial prescription episodes and likelihood of long-term opioid use United States, 2006–2015. *MMWR Morb Mortal Wkly Rep.* 2017;66:265–269.
- 7. Qaseem A, Wilt TJ, McLean RM, Forciea MA, for the Clinical Guidelines Committee of the American College of Physicians. Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med.* 2017;166:514–530. doi: 10.7326/M16–2367
- 8. U.S. Department of Veteran Affairs, Department of Defense. VA/DoD Clinical Practice Guidelines for Opioid Therapy for Chronic Pain. Veterans Health Administration, Office of Quality & Performance, Evidence Review Subgroup; Revised February 2017.
- 9. Peters ML, Smeets E, Feijge M, et al. Happy despite pain: a randomized controlled trial of an 8-week internet-delivered psychology intervention for enhancing well-being in patients with chronic pain. *The Clinical Journal of Pain*. 2017. DOI:10.1097/AJP.000000000000494
- 10. Keefe FJ, Wren AA. Optimism and pain: a positive move forward. *Pain*. 2013;154:7–8.
- 11. Ong AD, Zautra AJ, Reid MC. Chronic pain and the adaptive significance of positive emotions. *Am Psychol.* 2015;70:283–284
- 12. Carson JW, Keefe FJ, Lynch TR, et al. Loving-kindness meditation for chronic low back pain: results from a pilot trial. *J Holist Nurs*. 2005;23:287–304.
- 13. Bolier L, Haverman M, Westerhof GJ, et al. Positive psychology interventions: a meta-analysis of randomized controlled studies. *BMC Pub Health*. 2013;13:119.

- 14. Chou R, Deyo R, Friedly J, et al. Non-pharmacologic therapies for low back pain: a systematic review for an American College of Physicians Clinical Practice Guideline. *Ann Intern Med*. 2017;166(7):493–505.
- 15. Wu Pl, Meleger A, Witkower A, et al. Non-pharmacologic options for treating acute and chronic pain. *PM&R* 2015;7(11):S278–S294. https://doi.org/10.1016/j.pmrj.2015.09.008
- 16. Osteoarthritis: National clinical guideline for care and management in adults 2014. National Institute for Health and Care Excellence. http://www.nice.org.uk/guidance/cg177/chapter/about-this-guideline
- 17. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of non-pharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res*, 2012;64:465–474
- 18. Fritz JM, Brennan GP, Hunter SJ. Physical therapy or advanced imaging as first management strategy following a new consultation for low back pain in primary care: associations with future health care utilization and charges. *HSR: Health Services Research* 2015;50(6 December):1927–1940.
- 19. Turner JA, Jensen MP, Romano JM. Do beliefs, coping, and catastrophizing independently predict functioning in patients with chronic pain. *Pain*. 2000;85(1,2):111–125. **doi.org/10.1016/ 50304-3959(99)00259-6**
- 20. Leeuw M, Goossens MEJB, Linton SJ, et. al. The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. *Journal of Behavioral Medicine*. 2007;30(1):77–94.
- 21. Veehof MM, Oskam MJ, Schreurs KMG, Bohlmeijer ET. Acceptance-based interventions for the treatment of chronic pain: a systematic review and meta-analysis. *Pain*. 2011;152(3):533–542.
- 22. Henschke N, Ostelo RW, van Tulder MW, et al. Behavioural treatment for chronic low-back pain. *Cochrane Database Syst Rev.* 2010:lssue 7. Art No. CD002014. [PMID:20614428] doi:10.1002/14651858. CD002014.pub3
- 23. Cherkin DC, Sherman KJ, Balderson BH, Cook AJ, Anderson ML, Hawkes RJ, et al. Effect of mindfulness-based stress reduction vs cognitive behavioral therapy or usual care on back pain and functional limitations in adults with chronic low back pain: a randomized clinical trial. *JAMA*. 2016;315:1240–9. [PMID: 27002445] doi:10.1001/jama.2016.2323
- 24. Morone NE, Greco CM, Moore CG, et al. A mind-body program for older adults with chronic low back pain: a randomized clinical trial. *JAMA Intern Med*. 2016;176:329–37. [PMID: 26903081] doi:10.1001/jamainternmed.2015.8033
- 25. Morone NE, Rollman BL, Moore CG, Li Q, Weiner DK. A mindbody program for older adults with chronic low back pain: results of a pilot study. *Pain Med.* 2009;10:1395–407. [PMID: 20021599] doi:10.1111/j.1526–4637.2009.00746.x
- 26. Kamper SJ, Apeldoorn AT, Chiarotto A, Smeets RJ, Ostelo RW, Guzman J, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. *Cochrane Database Syst Rev.* 2014:Issue 9. Art No. CD 000963. [PMID: 25180773] doi:10.1002/14651858.CD000963.pub3
- 27. Reinecke H, Weber C, Lange K, *et. al.* Analgesic efficacy of opioids in chronic pain: recent meta-analyses. *B J Pharmacol*. 2015;172(2):324–333.
- 28. Teodorczyk –Injeyan JA, McGregor M, Triano JJ, Injeyan HS. Elevated production of noiciceptive C-chemokines and sE-selectin in patients with low back pain and the effects of spinal manipulation: A non-randomized clinical trial. *Clinical Journal of Pain*. Published ahead of print. April 2017. DOI: **10.1097/AJP.000000000000507**

- 29. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA*. April 19, 2016; 315(15):1624–1645.
- 30. Tugwell PS, Wells GA, Shainhouse JZ. Equivalence study of a topical diclofenac solution (Pennsaid) compared with oral diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *J Rheumatol*. 2004;31(10):2002–2012.
- 31. Micromedex. Truven Health Analytics. 2017. Accessed March 2017. www.truvenhealth.com/products/micromedex.
- 32. Barkin RL et al. Management of Chronic Noncancer Pain in Depressed Patients. *Postgraduate Medicine*. 2011; 123:143–54.
- 33. Towheed TE, Maxwell L, Judd MG, et al. Acetaminophen for osteoarthritis. *Cochrane Database Syst Rev.* 2006(1):CD000396.
- 34. Munir MA, et al. Nonopioid Analgesics. Med Clin N Am 2007; 91:97–111.
- 35. Roelofs PD, et al. Non-steroidal Anti-inflammatory Drugs for Low Back Pain. *Cochrane Database Syst Rev.* 2008(1):CD000396.
- 36. Antman EM, Bennett JS, Daugherty A, et al. Use of nonsteroidal antiinflammatory drugs an update for clinicians: a scientific statement from the American Heart Association. *Circulation*. 2007;115(12):1634–1642.
- 37. Romsing J, Møiniche S, Mathiesen O, et al. Reduction of opioid-related adverse events using opioid-sparing analgesia with COX-2 inhibitors lacks documentation:a systematic review. *Acta Anaesthesiol Scand* 2005;49:133–42 2.
- 38. Kehlet H, Callesen T. Postoperative opioid analgesia: time for reconsideration? *J Clin Anesth* 1996;3180(96):441–5.
- 39. Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol*. 2015;14:162–73.
- 40. Moulin DE, Boulanger A, Clark AJ, et al. Pharmacological management of chronic neuropathic pain: revised consensus statement by the Canadian Pain Society. *Pain Res Manag.* 2014;19:328–35
- 41. Mathieson S, Chiro M, Maher CG, et al. Trial of pregabalin for acute and chronic sciatica. *NEJM*. 2017;376:1111–1120. DOI: **10.1056/NEJMoa1614292**
- 42. Pop-Busui R, Boulton AJM, Feldman EV, et al. Diabetic neuropathy: a position statement by the American Diabetes Association. *Diabetes Care*. 2017;40:136–154.
- 43. Waldfogel JM, Nesbit SA, Dy SM. Pharmacotherapy for diabetic peripheral neuropathy and quality of life: a systematic review. *Neurology*. 2017;88:1–10.
- 44. Nissen SE, Yeomans ND, Solomon DH, et al. Cardiovascular safety of celecoxib, naproxen, or ibuprofen for arthritis. *N Engl J Med* 2016;375:2519–29. DOI: **10.1056/NEJMoa1611593**
- 45. Griffin MR, Piper JM, Daugherty JR, et al. Nonsteroidal anti-inflammatory drug use and increased risk for peptic ulcer disease in elderly persons. *Ann Intern Med* 1991;114:257–263
- 46. Allison MC, Howatson AG, Torrance CJ, et al. Gastrointestinal damage associated with the use of nonsteroidal anti-inflammatory drugs. *N Engl J Med* 1992;327:749–754.
- 47. Lanza FL, Chan FK, Quigley EM. Guidelines for prevention of NSAID-related ulcer complications. *Am J Gastroenterol*. 2009;104:728–738.

- 48. Bakhriansyah M, Souverein PC, de Boer A, Klungel OH. Gastrointestinal toxicity among patients taking selective COX-2 inhibitors or conventional NSAIDs, alone or in combination with proton pump inhibitors: a case-control study. *Pharmacoepidemiol Drug Saf.* 2017 March 31. doi: 10.1002/pds.4183. [Epub ahead of print]
- 49. McGettigan P, Henry D. Cardiovascular risk and inhibition of cyclooxygenase: a systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2. *JAMA*. 2006;296:1633–1644
- 50. Patrono C, Baigent C. Nonsteroidal anti-inflammatory drugs and the heart. *Circulation*. 2014;129(8):907–916. **doi.org/10.1161/CIRCULATIONAHA.113.004480**
- 51. Harirforoosh S, Jamali F. Renal adverse effects of nonsteroidal anti-inflammatory drugs. *Journal Expert Opinion on Drug Safety.* 2009;8(6):669–681.
- 52. Kamper SJ, Apeldoorn AT, Chiarotto A, Smeets RJ, Ostelo RW, Guzman J, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. *Cochrane Database Syst Rev.* 2014: CD000963. [PMID: 25180773] doi:10.1002/14651858.CD000963.pub3.
- 53. NALOXONE KITS Interim Recommendations for Issuing Naloxone Kits for the VA Overdose Education and Naloxone Distribution (OEND) Program, 2016.
- 54. Larochelle MR, et al. Opioid prescribing after nonfatal overdose and association with repeated overdose. *Ann Intern Med.* 2016;164(1):1–9.
- 55. Dasgupta N, Funk MJ, Proescholdbell S, Hirsch A, Ribisl KM, Marshall S. Cohort study of the impact of high-dose opioid analgesics on overdose mortality. *Pain Med.* Sep 1 2015.
- 56. Park TW, et al. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ*. 2015. 350: p. h2698.
- 57. Sun EC, Dixit A, Humphreys K, et. al. Association between concurrent use of prescription opioids and benzodiazepines and overdose: retrospective analysis. *BMJ*. 2017;356:j760 http://dx.doi.org/10.1136/bmj.j760
- 58. Chang Y-P and Compton P. Management of chronic pain with chronic opioid therapy in patients with substance use disorders. *Addict. Sci. Clin. Pract.*, vol. 8, no. 1, p. 21, 2013.
- 59. Oregon Pain Guidance of Southern Oregon Opioid Prescribing Guidelines: A Provider and Community Resource. 2014.
- 60. Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain: An educational aid to improve care and safety with opioid therapy 2015 Update, Agency Medical Directors Group [Online]. Available: http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf. [Accessed: 8-May 2017].

#### **U.S. Department of Veterans Affairs**

This reference guide was created to be used as a tool for VA providers and is available to use from the Academic Detailing Service SharePoint.

These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

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