PAMI learning module content will sometimes overlap due to similar topics. The PAMI website offers access to learning module handouts, pain tools, resources, websites, and recent pain news.

We welcome your feedback on all PAMI materials and are interested in how you use them to improve patient safety and clinical care. Please email emresearch@jax.ufl.edu.

For more information please visit http://pami.emergency.med.jax.ufl.edu/

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Presentation Overview

- Presentation of two patient cases
- Patient assessment, physical exam, and medication history
- Choosing pharmacologic treatment while considering patient factors
- Review safety concerns: Patient factors, allergies, side effects, and adverse drug events
- Special considerations when prescribing pain medications
- Discharge planning and transitions of care
Learning Objectives

• Know the essential components of performing a patient assessment and medication history

• Understand what patient factors should be considered when selecting pharmacological treatment options

• Understand the safety concerns that should be addressed during discharge planning and medication reconciliation
Case Scenario
Case 1 Scenario

• 80 year old female with a history of:
  • Myocardial infarction (MI)
  • Hypertension
  • Osteoarthritis (OA) of right knee

• Patient complains of OA pain frequently interfering with her ability to perform daily activities. There is no history of recent trauma

• Patient reports using naproxen 500 mg in the past for pain relief, but reports it is no longer working

• Pain level is reported as a 6/10

• Patient recently moved in with her daughter and has not found a new primary care doctor

- What patient factors should be considered prior to initiating pharmacologic treatment?
- What would be an appropriate therapeutic option to prescribe for her pain?
Case 1 Scenario Explanation

Chronic NSAID use in this patient is not ideal due to the patient’s age, history of hypertension, and history of MI as NSAIDS can **raise blood pressure**, lead to **GI bleeding and ulcer formation**, and **increase cardiovascular risk**.

**Acetaminophen** is the preferred first line agent for the treatment of osteoarthritis.

- Increased age and a history of HTN suggests a potential risk for renal impairment, therefore NSAIDS should be avoided. Additionally, the American Heart Association and FDA discourage use of NSAIDs in patients with prior MI and stroke due to an increased risk of recurrence.

- Because of their minimal absorption topical NSAIDs, lidocaine patches, or capsaicin cream may also be appropriate options.
Case 2 Scenario

It is a busy Friday night in the emergency department (ED) and the ED and hospital are at full capacity. A 25 year-old female with a history of depression and substance abuse presents with complaints of right facial pain and left leg pain after an altercation. She admits to recent cocaine and alcohol use, but denies other substance abuse.

Home medications include:
- Sertraline 100 mg 1 po BID
- Mirtazapine 30 mg 1 po HS

Exam Findings:
- Right maxillary fracture
- Left ankle sprain
- Multiple contusions
- ETOH level = 215 mg/dL

- How would you treat her pain?
- What potential issues could arise from your treatment selection?

The ED provider decides to admit the patient to the ED observation unit as she is intoxicated and does not have a safe means of going home. During her stay, the patient repeatedly asks for pain medication.
Case 2 Scenario continued

- Patient was initially given **morphine 4 mg IV**, but continues to report her pain as 10/10
- Patient was then given **fentanyl 50 mcg IV**, reducing her pain to 5/10
- Observation admission orders include **oxycodone/acetaminophen 10/325 mg po Q 6 hours prn**
- The ED providers undergo shift change, the patient continues to request more pain medication
- Three hours after admission to the Observation Unit, the nurse calls the newly arrived ED physician who authorizes **hydromorphone 1mg IV x 1 dose**
- Nurse rechecks the patient at 30 minutes and 2 hours post administration of hydromorphone and finds the patient is asleep
- Several hours later at nursing shift change, the patient is **confused and febrile**
Case 2 Scenario **Explanation**

- Special monitoring should be used in this patient due to her history of substance abuse and current intoxication.
- Over sedation, respiratory depression, or even death can occur in patients receiving multiple narcotic agents that are not communicated within the medical team.
- **Serotonin syndrome** may be the causative factor of confusion and fever in this patient.
  - *Serotonin syndrome*, a potentially life-threatening drug reaction, develops when serotonin levels in the body become excessively elevated from medications that either increase serotonin release or decrease its reuptake.
  - This condition typically occurs when two medications that affect serotonin levels are taken together. An example would be a patient who is taking a triptan for migraines and also a SSRI for depression. Symptoms develop on a spectrum and can range from fever and agitation to confusion and loss of muscle coordination.
Case 2 Scenario  **Explanation**

Certain opioids including meperidine, tramadol, methadone, pentazocine, propoxyphene, and fentanyl possess serotonergic activity which can be a factor contributing to serotonin syndrome. Additionally, dextromethorphan also possesses serotonergic activity. Although oxycodone is not thought to contribute to serotonin syndrome, there have been a few case reports of this occurring and further investigation of the mechanism behind this is needed. Patients taking oxycodone along with a SSRI should be monitored carefully.

In addition to pain medications there are numerous other medications that have the potential to cause serotonin syndrome.  *For a comprehensive list visit*  
http://www.uspharmacist.com/content/d/feature/c/23707/

*It is essential that practitioners be aware of potentially serious drug-drug interactions that can occur from use of multiple medications, especially analgesics.*
Background Information
Pharmacologic Treatment of Pain in the Emergency Department

• Pain is a common reason for seeking care in the ED. As a result pain medications are frequently administered.

• Adverse drug events (ADEs) impact more than 800,000 ED patients annually.

• Analgesics account for 8.4% of all ED visits for ADE of which 23.6% required hospitalization.
  • 6.8% were from opioid analgesics.

• While brief opioid use is generally safe for most patients, opioid analgesics may be associated with serious adverse effects like respiratory sedation and potentially death.

• Contributory factors identified for opioid ADEs include:
  • Lack of knowledge regarding potency differences among different opioids
  • Prescribing multiple opioids and administering them in various formulations (i.e., oral, parenteral and transdermal patches)
  • Inadequate monitoring
  • Inadequate patient instructions
  • Decreased health literacy
Pharmacologic Treatment of Pain in the Emergency Department

• There are several pharmacologic treatment options to choose from when managing a patient with pain.

• Patient parameters must be considered when choosing a pain regimen.

• It is important to know trade and generic names of pain medications
  • Click here for a list of common pain medications visit http://pami.emergency.med.jax.ufl.edu/resources/educational-materials/pharmacological-treatment-of-pain/

Factors to consider prior to therapy selection:

• Type of pain
• Comorbidities
• Current and past pain medications
• Allergies
• History of alcohol or drug abuse

• Side effects
• Drug - Drug Interactions
• Past adverse events
• Patient safety
The PAMI Pain Management and Dosing Guide is a free tool for use by health care providers in hospital, EMS or acute care settings and should be used as general guide when managing pain in pediatric and adult populations.

The guide provides treatment options for opioids, non-opioids, procedural sedation, nerve blocks, and IV/IM/IN/topical administration. It includes a step-wise approach to pain, patient safety considerations as well as nonpharmacologic interventions. To take a tour of the dosing guide, click here!

A free downloadable pdf of the dosing guide can be accessed on the PAMI website. http://pami.emergency.med.jax.ufl.edu/resources/dosing-guide/
Patient Assessment
Patient Assessment

• When approaching a patient with pain it is essential to perform a thorough assessment including:
  • Evaluation of presenting complaint with focused physical exam
  • Past medical history
  • Current and past medications

• There are several methods for assessing pain, many find the (O)PQRST mnemonic to be a useful assessment tool.

• Refer to the Basics of Pain module for more detailed information regarding patient assessment and OPQRST

PAMI Pain Assessments
http://pami.emergency.med.jax.ufl.edu/resources/educational-materials/pain-assessment-scales/

The following slides will discuss patient assessment.
Physical Exam

• The physical exam can provide information regarding:
  • Location of pain
  • Severity of pain
  • Functionality

• Identifying the type of pain is essential to selecting appropriate therapy (see next slide for types of pain)

• Pain often alters vital signs (increased HR and BP)
  • Monitor vital signs to determine treatment efficacy and safety

• Refer to the Basics of Pain module for further information
Table: Types of pain, mechanism, and clinical examples

<table>
<thead>
<tr>
<th>TYPES OF PAIN</th>
<th>MECHANISM</th>
<th>CLINICAL EXAMPLES</th>
<th>PHARMACOLOGICAL TREATMENT OPTIONS*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UNDERLYING ETIOLOGY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nociceptive</td>
<td>The result of direct tissue injury from a noxious stimuli.</td>
<td>Bone fracture, fresh surgical incision, and fresh burn injury.</td>
<td>May include both opiate and non-opiate medications depending on injury.</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>The result of released inflammatory mediators that control nociceptive input.</td>
<td>Late stages of burn healing, neuritis, and arthritis</td>
<td>Anti-inflammatory agents</td>
</tr>
<tr>
<td>Neuropathic</td>
<td>The result of direct injury to nerves leading to an alteration in sensory transmission.</td>
<td>Diabetic neuropathy, peripheral neuropathic pain, and post-herpetic neuralgia.</td>
<td>Tricyclic, selective norepinephrine reuptake inhibitors, gabapentinoids, or antidepressants</td>
</tr>
<tr>
<td>Psychogenic</td>
<td>Somatic manifestation of psychiatric illness or exacerbation of pain severity due to previous experience, poor coping mechanisms, social history, etc.</td>
<td></td>
<td>Treating the psychiatric illness may help in certain cases where pain is truly a somatic symptom of depression.</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Unknown</td>
<td>Chronic back pain without preceding trauma or obvious inciting event.</td>
<td>May be difficult to adequately address pain since underlying etiology is unknown</td>
</tr>
<tr>
<td><strong>ANATOMIC LOCATION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic</td>
<td>A-delta-fiber activity located in peripheral tissues</td>
<td>Superficial lacerations, superficial burns, superficial abscess</td>
<td>Topical and/or local anesthetics, opiates, non- opiates</td>
</tr>
<tr>
<td>Visceral</td>
<td>C fiber activity located in deeper tissues such as organs</td>
<td>Uterine fibroid pain, pyelonephritis, biliary colic</td>
<td>opiates</td>
</tr>
<tr>
<td><strong>TEMPORAL NATURE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>A neurophysiological response to noxious injury that should resolve with normal wound healing.</td>
<td>Acute fracture, acute knee sprain</td>
<td>Opiate, non-opiates</td>
</tr>
<tr>
<td>Chronic</td>
<td>Pain that extends beyond the time for normal wound healing with resultant development of multiple neurophysiological changes</td>
<td>Chronic low back pain, fibromyalgia, arthritis</td>
<td>Depends on the nature of the pain. Please refer to the module on chronic pain for more detailed information.</td>
</tr>
<tr>
<td>Acute-on-chronic</td>
<td>An acute exacerbation of a chronic pain syndrome</td>
<td>Sickle cell disease, cancer, rheumatoid arthritis, acute injury in chronic pain patient</td>
<td></td>
</tr>
</tbody>
</table>

*Nonpharmacological treatments can be considered at any time for any type of pain.
Medication History

Patients are often **unaware** of their prescribed medications and doses.

It may be difficult to obtain this information from elderly, medicated, confused or demented patients, non-English speakers, the hearing impaired, and those incapacitated due to their presenting medical illness.

Avoid yes and no questions, instead **ask open-ended** questions about medications and medical conditions.

Ask about recent medication usage including herbal and over-the-counter (OTC) medications, dose, frequency, strength, formulation, and last consumption and compare to the medical record if available.

**For example:** Instead of asking if the patient takes any medications, ask what medical problems or conditions they have and the medications they take for that condition.
Medication History

It is essential to use a multi-factorial approach when evaluating a patient’s medication history.

- Patients may not consider OTC, herbals, or PRN medications when reporting their medication history.
- Patients may be using multiple agents for the same indication.
- Check Prescription Drug Monitoring Programs (PDMP) in your state to help gather a complete medication history. PDMPs will be discussed in further detail later in this module.

**Review**
- Past medical records
- Interview family members/caregivers who can obtain medications from home
- Consult with the patient’s primary care physician and pharmacist

**Consider**
- Herbals
- Vitamins and supplements
- Sleep aids
- Samples
- Patches or topical agents
  - Drops

**Inquire**
- Distinguish between scheduled maintenance medications versus as needed or breakthrough pain therapy.
- If taking multiple therapies for breakthrough pain, how does the patient choose which one to utilize?

**Discuss**
Use open ended questions to obtain the most information from the patient.

*Note: If the pain is severe, it may be necessary to treat first.*
Medication History: Prescriptions

*Important questions* to ask regarding *prescriptions* include:

• What pharmacy/pharmacies do you use?

• What other medications prescribed by other healthcare professionals like your dentist, ophthalmologist, or chiropractor are you taking?

• What medications do you take every day? In the past week? When do you take them?

• What medications do you take only as needed? What are they? When do you take them?

• When have you used patches in the past?

• What injections have you had at the doctor’s office or anywhere else?

• What sample medications has your doctor given you to take?
Medication History: OTC and Herbals

**Important questions** to ask regarding non-prescription medications include:

**Over the Counter Medications (OTC)**

- What medications do you take that do not require a doctor’s prescription to purchase?

- What do you take when you get constipation or diarrhea, heartburn, cough/cold, or headache? How often? How much?

- What do you take when you get sick? How often? How much?

**Herbal Supplements**

- What vitamins do you take?
- What herbal medications do you take?
- What natural supplements do you take?
- What dietary supplements do you take?
Medication Allergies and Intolerances

• Inquire about the patients **allergies** to medications
  • Document reaction type
  • When the reaction occurred
  • Similar medications taken without a reaction

• Inquire about **intolerances** to medications
  • Patients often confuse allergies with an intolerance
  • Gastritis, nausea, and constipation are considered intolerances not allergies
  • For example: “aspirin upsets my stomach”
Pharmacologic Therapy
Pharmacotherapeutic Principles

Patient Factors to Consider

• Previous effective/failed treatments
• Non-pharmacological therapies
  • Distraction
  • Watching television
  • Reading
  • Guided imagery/Meditation
  • Exercise
  • Relaxation techniques

Patient Education

• Educating patients about pain is an important component to treatment
• Set realistic expectations and establish a mutually agreed upon “tolerable” pain goal
• Discuss with the patient that total elimination of pain may not be possible
Opioid Therapy

There are three classic opioid receptors which are named based on Greek letters:

- **Mu** (all opioid agonists stimulate Mu receptors)
- **Kappa**
- **Delta**

<table>
<thead>
<tr>
<th>RECEPTOR</th>
<th>CLINICAL RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mu</td>
<td><strong>Mu-1:</strong> Analgesia</td>
</tr>
<tr>
<td></td>
<td><strong>Mu-2:</strong> Respiratory depression, sedation, miosis, euphoria, cardiovascular effects, pruritus, nausea, vomiting, decreased GI motility</td>
</tr>
<tr>
<td>Kappa</td>
<td>Spinal analgesia, dysphoria, miosis, respiratory depression, dyspnea, sedation</td>
</tr>
<tr>
<td>Delta</td>
<td>Analgesia, euphoria, dysphoria</td>
</tr>
</tbody>
</table>
Opioid Therapy

Opioids are classified based on mu receptor activity

**Full Agonists:**
Bind and activate the mu receptor producing a biological effect

- Morphine
- Oxycodone
- Hydrocodone
- Fentanyl
- Oxymorphone
- Hydromorphone

Preferred for acute pain

**Partial Agonists:**
Bind and activate the mu receptor with only partial efficacy at the receptor compared to a full agonist

- Buprenorphine

Not typically used for acute pain
Opioid Therapy

Opioids are classified based on mu receptor activity

Mixed Agonists – Antagonists:*
- Pentazocine
- Butorphanol
- Nalbuphine

Antagonists:
- Naloxone
- Naltrexone

*Patients on mixed agonist-antagonist therapy may require a higher doses for pain relief, however these agents display a ceiling effect in which increasing the dose over a given threshold does not lead to additional efficacy

Not typically used in the acute setting

Often used in the emergency setting for reversal of opioid overdose
# Commonly Used Opioids and Dosing

## OPIOID PRESCRIBING CHART

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>Recommended start dose+</th>
<th>Duration of action (Hours)</th>
<th>Recommended start dose</th>
<th>Common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>ADULTS</strong></td>
<td></td>
<td><strong>CHILDREN</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>Parenteral</td>
<td></td>
<td>Oral</td>
</tr>
<tr>
<td><strong>Morphine IR (MSIR®)</strong></td>
<td>15 - 30 mg</td>
<td>2 - 4 mg</td>
<td>IV: 3 - 4</td>
<td>0.3 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Q 4 - 6H</td>
<td>Q 4 - 6H</td>
<td>PO: 3 - 6</td>
<td>Q 4 - 6H</td>
</tr>
<tr>
<td><strong>Hydromorphone (Dilaudid®)</strong></td>
<td>2 - 4 mg</td>
<td>0.5 - 2 mg</td>
<td>IV: 3 - 4</td>
<td>0.03 - 0.06 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Q 4 - 6H</td>
<td>Q 4 - 6H</td>
<td>PO: 3 - 6</td>
<td>Q 4 - 6H</td>
</tr>
<tr>
<td><strong>Hydrocodone/Acetaminophen (Norco®)</strong></td>
<td>5 - 10 mg</td>
<td>-</td>
<td>PO: 4 - 8</td>
<td>0.2 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Q 4 - 6H</td>
<td></td>
<td>Q 4 - 6H</td>
<td>Q 4 - 6H</td>
</tr>
<tr>
<td>**Oxycodone IR (OxylIR®) *</td>
<td>5 - 10 mg</td>
<td>-</td>
<td>PO: 3 - 6</td>
<td>0.2 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Q 4 - 6H</td>
<td></td>
<td>Q 4 - 6H</td>
<td>Q 4 - 6H</td>
</tr>
<tr>
<td><strong>Tramadol (Ultram®)</strong></td>
<td>50 - 100 mg</td>
<td>-</td>
<td>PO: 3 - 6</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Q 6H</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*With or without 325 mg acetaminophen (Max: 4g/day of acetaminophen)
+Consider patient’s weight, prior history, and degree of pain when selecting starting dose
Opioid Prescribing Considerations

When switching between opioids

- Begin with a 30% lower dose than the equi-analgesic dose when switching medications
- Titrate to a safe/effective dose to achieve adequate response

Special populations

- Use caution in:
  - Debilitated patients
  - Renal or Hepatic impairment
  - Elderly (lower starting dose due to sensitivity)
  - Neonates and infants

- Morphine has a renally eliminated active metabolite; avoid or use morphine with extreme caution when using this medication in the above patient populations
- Hydromorphone may be a better choice in the setting of renal insufficiency due to its short half-life and lack of active metabolites
- Avoid meperidine as safer opioids that are equally efficacious are available. Meperidine can cause neurotoxicity and serotonin syndrome.

Tips

Avoid or limit acetaminophen content of medications when treating patients with hepatic impairment.
Equianalgesic Dosing
Equianalgesic or Equipotent Dosing

Providers often are unsure how to convert one opioid agent to an equivalent dose of another agent, or how to change the administration route.

This concept is important for all healthcare providers to be aware of especially in chronically ill or oncology patients.

For example, converting a patient’s home oral morphine dose to an appropriate intravenous inpatient dose. Equianalgesic dosing charts allow providers to switch safely between different opioid medications while still achieving adequate pain control.
Equianalgesic Dosing

There are **two goals** when using the equipotent dosing chart:

1. The calculated starting dose must be **safe** to avoid overdose
2. The dose must be sufficiently efficacious to prevent **worsening** of the pain or withdrawal
Equianalgesic Dosing

It is important to know that equianalgesic dosing charts do NOT account for patient factors.

**Pharmacogenomics**
- CYP enzyme up/down regulation
- Ethnic variability

**Organ system dysfunction**
- Hepatic: avoid acetaminophen products
- Renal: avoid morphine

**Opiate naïve vs. opiate tolerant**
- Long acting preparations may be equivalent in morphine equivalents, but may accumulate in opiate naïve patient

**Patient preference based on medication history**
- Side effect profiles may vary within the same drug class

**Drug Interactions**
- Combining opioids with other medications may increase or decrease opioid levels

**Contraindications due to co-morbidities**
- Tramadol in seizure patients
- Meperidine in renal failure
- Morphine accumulation in renal dysfunction

**Adverse effects**
- Long-acting opiates may suppress respiratory drive in patients with sleep apnea
Equianalgesic Dosing

• Charts represent broad indicators of relative analgesic potency (ranges), variability exists between charts

• When switching between chemical classes of opiates:
  • MUST reduce calculated dose by ~ 30% to account for incomplete cross tolerance
  • Avoid dosing charts when prescribing methadone due to its variability

<table>
<thead>
<tr>
<th>Phenanthrenes</th>
<th>Phenylpiperdines</th>
<th>Diphenylheptanes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Morphine</td>
<td>• Fentanyl</td>
<td>• Methadone</td>
</tr>
<tr>
<td>• Codeine</td>
<td>• Meperidine</td>
<td></td>
</tr>
<tr>
<td>• Oxycodone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Oxymorphone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hydrocodone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hydromorphone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## APPROXIMATE EQUIANALGESIC DOSING CONVERSION TABLE

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>Oral</th>
<th>Parenteral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine IR (MSIR&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>30 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>4 mg</td>
<td>1 mg</td>
</tr>
<tr>
<td>Hydrocodone/Acetaminophen (Norco&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>30 mg</td>
<td>-</td>
</tr>
<tr>
<td>Oxycodone IR (OxyIR&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>20 mg</td>
<td>-</td>
</tr>
</tbody>
</table>
Resources for Equianalgesic Dosing

• Your hospital pharmacy or pain service

• Websites and tools
  • https://bedsidepainmanager.com/

• Mobile phone apps
  • http://clincalc.com/Opioids/
  • http://www.globalrph.com/narcoticonv.htm
  • http://opioidcalculator.practicalpainmanagement.com/
Opioid Risk Assessment Tool
Opioid Risk Assessment Tools

• There are numerous assessment tools available to help providers determine risk for misuse when prescribing opioid medications to patients suffering from chronic pain. However these tools were all developed for use in primary care settings.

• Examples of these assessment tools include:
  • Opioid Risk Tool (ORT)
  • The Diagnosis, Intractability, Risk, Efficacy (DIRE)
  • The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)
  • The Screening Instrument for Substance Abuse Potential (SISAP)

• Research is ongoing to develop ED screening tools

• The next slide explains the Opioid Risk Tool.
What is the Opioid Risk Tool (ORT)?

The Opioid Risk Tool (ORT)

• Developed in 2005 to assess the risk of abnormal behaviors of patients prescribed opioids
• Patient reported assessment tool that can be administered and scored in less than one minute
• Identifies patients who are at high risk of abusive drug behaviors
• Limited use for patients due to being subjectively based on patient report
• Intended for use in the primary care setting and has not been validated in non-pain populations

Pharmacologic Therapy
Non-Opioids
# Non-Opioids: NSAIDs

## Non-Opioid Prescribing Guidelines

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>Recommended start dose+ Adults</th>
<th>Max daily dose Adults</th>
<th>Recommended start dose Children (age &lt;12)</th>
<th>Max daily dose Children</th>
<th>Common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>325 - 650 mg PO Q 4 - 6H PRN</td>
<td>4,000 mg/day</td>
<td>10 - 15 mg/kg PO Q 4H PRN</td>
<td>2,600 mg/day</td>
<td>Hepatotoxicity</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Rash</td>
</tr>
<tr>
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<td></td>
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<td></td>
<td>Abdominal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nausea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td>Ibuprofen*</td>
<td>400 - 800 mg PO Q 4 - 6H PRN</td>
<td>3,200 mg/day</td>
<td>4 - 10 mg/kg PO Q 6 - 8H PRN</td>
<td>40 mg/kg/day or 2,400 mg/day</td>
<td>GI hemorrhage</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dyspepsia</td>
</tr>
<tr>
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<td></td>
<td>Rash</td>
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<tr>
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<td></td>
<td>Edema</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Abdominal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Renal dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Headache</td>
</tr>
<tr>
<td>Ketorolac*</td>
<td>15 - 30 mg IV Q 6H PRN</td>
<td>60-120 mg/day × 3 days</td>
<td>0.5 mg/kg/dose IM/IV Q 6H PRN</td>
<td>30 mg Q 6H x 5 days</td>
<td>Headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Abdominal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dyspepsia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Edema</td>
</tr>
<tr>
<td>Naproxen*</td>
<td>250 - 500 mg PO Q 8 - 12H PRN</td>
<td>1,500 mg/day</td>
<td>5 mg/kg PO Q 12H</td>
<td>1,000 mg/day</td>
<td>Headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Abdominal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dyspepsia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Edema</td>
</tr>
<tr>
<td>Meloxicam*</td>
<td>7.5 - 15 mg PO daily</td>
<td>15 mg/day</td>
<td>-</td>
<td>-</td>
<td>GI hemorrhage</td>
</tr>
</tbody>
</table>

+Consider patient’s weight, prior history, and degree of pain when selecting starting dose
# Non-Opioids: Neuropathic Agents

Dosing may vary based on new literature, patient response, and comorbidities

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>Recommended start dose</th>
<th>Max daily dose</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (Elavil®)</td>
<td>25 mg QHS 25 mg QHS</td>
<td>200 mg 150 mg</td>
<td>Suicidal ideation in young patients with concomitant MDD or psychiatric disorder.</td>
</tr>
<tr>
<td>Nortriptyline (Pamelor®)</td>
<td></td>
<td></td>
<td>Anticholinergic effects, Sedation, Orthostasis</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta®)</td>
<td>30 mg daily 37.5 mg daily</td>
<td>60 mg/day 225 mg/day</td>
<td>Headache, Somnolence, Fatigue, Orthostatic hypotension, Nausea, Insomnia, Xerostomia</td>
</tr>
<tr>
<td>Venlafaxine (Effexor XR®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin (Neurontin®)</td>
<td>300 mg daily to TID</td>
<td>3,600 mg/day</td>
<td>Somnolence, Seizure risk with abrupt withdrawal, Ataxia</td>
</tr>
<tr>
<td>Pregabalin (Lyrica®)</td>
<td>50 mg TID</td>
<td>450 mg/day</td>
<td>Fatigue, Dizziness, Peripheral edema, Emotional distress and hostility – especially in children</td>
</tr>
</tbody>
</table>
## Non-opioids: Skeletal Muscle Relaxants

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>Recommended start dose ADULTS</th>
<th>Max daily dose ADULTS</th>
<th>Recommended start dose CHILDREN</th>
<th>Max daily dose CHILDREN</th>
<th>Common Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclobenzaprine</td>
<td>5 mg Q 8H PRN</td>
<td>30 mg/day</td>
<td>Not Recommended Age &lt; 15</td>
<td>30 mg/day</td>
<td>Drowsiness, dizziness, fatigue, Dry mouth (anticholinergic effects), GI upset, Headache</td>
</tr>
<tr>
<td>(Flexeril®)</td>
<td></td>
<td></td>
<td>Age ≥ 15: 5 mg Q 8H PRN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methocarbamol</td>
<td>1 g IV/IM once or 1.5 g PO Q 6H for 48 - 72H</td>
<td>3 g/day IV/IM or 8 g/day PO</td>
<td>Not Recommended Age &lt; 16</td>
<td>8 g/day</td>
<td>Drowsiness, dizziness, vertigo, confusion, Amnesia</td>
</tr>
<tr>
<td>(Robaxin®)</td>
<td></td>
<td></td>
<td>Age ≥ 16: 1.5 g PO Q 6H for 48 - 72H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>5 - 10 mg IV/IM 2 - 10 mg PO Q 6 - 8H PRN</td>
<td>40 mg/day</td>
<td>Not Recommended Age &lt; 12</td>
<td>40 mg/day</td>
<td>Dependence, Headache, Drowsiness, dizziness, confusion, Ataxia, Children can experience paradoxical hyperactivity or aggression</td>
</tr>
<tr>
<td>(Valium®)</td>
<td></td>
<td></td>
<td>Age ≥ 12: IV/IM: 0.04 - 0.2 mg/kg Q 2 – 4H PRN PO: 0.12 – 0.8 mg/kg/day divided Q6 – 8H PRN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carisoprodol*</td>
<td>250 mg Q 8H</td>
<td>1,400 mg/day PO</td>
<td>Not Recommended Age &lt; 16</td>
<td>1,400 mg/day</td>
<td>Drowsiness, vertigo, dizziness, Active metabolite, which can add to sedation (meprobamate), Use should be limited (2-3 weeks)</td>
</tr>
<tr>
<td>(Soma®)</td>
<td></td>
<td></td>
<td>Age ≥ 16: 250 - 350 mg PO TID and QHS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Addiction potential with carisoprodol usage
Tips for Selecting Pharmacological Treatments

For mild-moderate somatic-nociceptive pain consider non-opioids (acetaminophen or NSAIDs) unless contraindicated.

For intermittent or continuous moderate to severe pain not managed by non-pharmacological and/or non-opioid therapy, addition of an opioid might be indicated after weighing risks and benefits.

For neuropathic pain consider gabapentin/pregabalin, tricyclic antidepressants or serotonin-norepinephrine reuptake inhibitors. For localized pain like non-radicular sciatic pain consider topical anesthetics (EMLA cream or lidocaine patches).
Monitoring

Monitoring **before** and **after** treatment of pain is important in determining efficacy and to rule out side effects/adverse events.

Patients should be re-assessed 15 minutes following IV administration and 30 minutes following oral administration.

**Frequent** monitoring and reassessment should be conducted during procedural sedation and analgesia, as well as prior to discharge or transfer.

**Tips**

If assessed too early the medication may not have had enough time to exert its therapeutic effect.

Refer to the module on **Procedural Sedation & Analgesia** for more information.
Special Population Considerations
Medication Safety in the Elderly

Decreased Renal Function

- Renal function may be reduced 50% or greater leading to increased risk of accumulation

- Changes in renal function may not be evident in the patients serum creatinine level due to the loss of muscle mass accompanied by aging

- Use special caution in opioid naïve patients

Medication Considerations

- Pregabalin/gabapentin
  - Reduce dose to avoid sedation

- Anti-cholinergic
  - Avoid due to concerns of delirium

- Muscle relaxers (i.e., cyclobenzaprine)
  - Should be avoided

- Long acting benzodiazepines (i.e., diazepam)
  - Undergo hepatic oxidation which reduces with aging potentially leading to oversedation and increased fall risk.
## Inappropriate Medications in the Elderly

Table: Adapted from 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>RECOMMENDATION AND RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meperidine</td>
<td>Avoid Not an effective oral analgesic in dosages commonly used; may cause neurotoxicity; safer alternatives available</td>
</tr>
<tr>
<td>Non-COX-selective NSAIDS (oral)</td>
<td>Avoid Avoid Chronic use unless other alternatives are not effective and patient care can take gastroprotective agent (PPI or misoprostol). Increase risk of GI bleeding/PU in high-risk groups, including those &gt;/=75 years old or taking oral or IV steroids, anticoagulants, or antiplatelet agents. PPIs or misoprostol reduces but does not eliminate risk</td>
</tr>
<tr>
<td>Indomethacin, ketorolac (Including IV)</td>
<td>Avoid Increases risk of GI bleeding/PUD in high risk groups (see above), Indomethacin has the most adverse effects</td>
</tr>
<tr>
<td>Pentazocine</td>
<td>Avoid Higher risk for CNS adverse effects such as confusion and hallucinations compared to other opioids</td>
</tr>
<tr>
<td><strong>Skeletal muscle relaxants</strong></td>
<td>Avoid Most muscle relaxants are poorly tolerated by older adults Risk of anticholinergic adverse effects and sedation</td>
</tr>
</tbody>
</table>

| Carisoprodol                              |                                                                                                                     |
| Chlorzoxazone                             |                                                                                                                     |
| Cyclobenzaprine                           |                                                                                                                     |
| Metaxalone                                |                                                                                                                     |
| Methocarbamol                             |                                                                                                                     |
| Orphenadrine                              |                                                                                                                     |
Medication Safety in Pediatric Patients

• Many medications are metabolized in the liver via cytochrome P450 subtypes which are not fully developed in newborns
  • Hepatic enzymes reach full maturity at varying rates but generally over months 1 through 6 of age
• Newborns have a higher percentage of body water compared to adults resulting in a higher volume of distribution for water soluble drugs.

• Newborns also have reduced albumin which may alter drug binding in the plasma, or increased drug levels
• Glomerular filtration rates typically do not reach normal clearance rates until 2 weeks old leading to decreased elimination of medication
• Due to immature respiratory symptoms infants may develop apnea or periodic breathing when given even small opioid doses, monitor frequently
• Several health organizations including the FDA, the European Medicines Agency, Health Canada, and the American Academy of Pediatrics have recommended against the use of codeine in patients younger than 12, those with respiratory insufficiency between ages 12-18, and in nursing mothers due to genetic variations in its metabolism.

Refer to the module on Pediatric Pain Management for more information
Medication Safety in Patients with Chronic Disease and Co-Morbidities

• Certain disease states that may affect drug selection include:
  • Renal or hepatic dysfunction
  • Diabetes
  • HIV therapies
  • Mental health disorders
  • Cardiac conditions
  • Disease states requiring anticoagulant use
  • History of aberrant behavior or substance abuse
  • Gastrointestinal dysfunction (peptic ulcer disease, chronic constipation)
Medication Safety Considerations

THE FIVE RIGHTS OF MEDICATION SAFETY
1. Right Medication
2. Right Route
3. Right Time & Frequency
4. Right Patient
5. Right Dose
## Allergic Reactions

### FOUR TYPES OF HYPERSENSITIVITIES

<table>
<thead>
<tr>
<th>Classification</th>
<th>Immune reactants</th>
<th>Onset/Description</th>
<th>Example of Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type I (Anaphylactic)</strong></td>
<td>IgE</td>
<td><em>Immediate</em>: Severe and rapid occurring within seconds to 30 minutes after exposure</td>
<td>Anaphylactic or anaphylactoid reactions: Erythema, Urticaria, Bronchospasms, CV collapse, Angioedema</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Late-phase</em>: 2-4 hours post exposure and after immediate reaction, peaks at 12 hours and subsides by 24 hours</td>
<td></td>
</tr>
<tr>
<td><strong>Type II (Cytotoxic)</strong></td>
<td>IgG and IgM</td>
<td>Hours</td>
<td>Drug-induced hemolytic anemia, thrombocytopenia, and granulocytopenia</td>
</tr>
<tr>
<td><strong>Type III (Immune complex)</strong></td>
<td>Mostly IgG sometimes IgM</td>
<td>3 - 10 hours</td>
<td>Serum sickness-like reaction, Drug-induced vasculitis</td>
</tr>
<tr>
<td><strong>Type IV (T cell mediated)</strong></td>
<td>Th1, Th2, Th17 cells cytotoxic lymphocytes</td>
<td>Delayed 24 to 72 hours after antigen exposure</td>
<td>Allergic contact dermatitis, Psoriasis, DRESS, SJS, TEN</td>
</tr>
</tbody>
</table>
Allergies Across Structural Classifications

Phenanthrenes
- Morphine
- Codeine
- Oxycodone
- Oxymorphone
- Hydrocodone
- Hydromorphone

Phenylpiperdines
- Fentanyl
- Meperidine

Diphenylheptanines
- Methadone

Type 1 Hypersensitivity Reactions
- Use opioids with caution
- Selection of a structurally different medication may result in decreased risk of cross-sensitivity

Histamine Reactions
- Selecting an agent with a lower histamine release potential may help to reduce symptoms
Adverse Drug Events

Opioid analgesics are among the top medications associated with adverse drug events.

Adverse drug events have been linked to:
- Drug-drug interactions
- Inadequate monitoring
- Knowledge deficits of patient and/or prescriber
- Inappropriate prescribing and administration

Considerations to decrease risk of adverse events:
- Avoid rapid dose increases
- Consider safety concerns prior to discharge (falls, driving, etc.)
- Screening for respiratory depression risk factors
- Identify opioid tolerance/intolerance based on patient history
- Ensure the patient is not wearing a pain patch or infusion pump
- Consult pharmacy/pain management when changing the route or type of opioid
Side Effects

Side effects attributed to pain medications may include:

- Constipation
- Bowel ileus
- Central nervous system sedation
- Respiratory depression
- Dizziness
- Drowsiness (continues for the duration of medication)
- Nausea
- Urinary retention
- Itching (may be treated with cetirizine/loratadine)

- Over-sedation (CNS depression) and respiratory sedation can be serious side effects and may require the reversal agent naloxone.
Adverse Drug Events

Characteristics of patients who are at higher risk for oversedation and respiratory depression

- Sleep apnea or sleep disorder diagnosis
- Morbid obesity with high risk of sleep apnea
- Snoring
- Older age; risk is
  - 2.8 times higher for individuals aged 61-70
  - 5.4 times higher for age 71-80
  - 8.7 times higher for those over age 80
- No recent opioid use
- Post-surgery, particularly if upper abdominal or thoracic surgery
- Increased opioid dose requirement or opioid habituation
- Longer length of time receiving general anesthesia during surgery
- Receiving other sedating drugs, such as benzodiazepines, antihistamines, diphenhydramine, sedatives, or other central nervous system depressants
- Preexisting pulmonary or cardiac disease or dysfunction or major organ failure
- Thoracic or other surgical incisions that may impair breathing
- Smoker
- Congenital airway abnormalities
Opioid Induced Constipation
Opioid Induced Constipation

- A recent study reported the number of constipation-related ED visits in the U.S. **increased** by nearly **42%** (from 2006 to 2011).
- In 2011, $1.6 billion was spent on ED care for constipation.
  - One causative factor for constipation are opioids.

- A 2015 ED study found that laxatives were not routinely prescribed to adults discharged with prescriptions for opioid pain medications and concluded that routine prescribing of laxatives may improve the safety and effectiveness of outpatient opioid pain management.

- Opioid induced **constipation** (OIC) is the **most common side effect** of opioids impacting **15-90% of patients**. OIC has been associated with:
  - higher healthcare costs
  - hospital admissions and readmissions
  - longer inpatient stays

**Tips**

Providers must assess, treat, and educate all patients for the possible development of OIC to prevent complications.
Opioid Induced Constipation

- Mu, kappa, and delta receptors are found in the gastrointestinal tract
  - Mu and delta receptors are on the gut smooth muscle
  - Mu specifically affects the myenteric plexus

- Endogenous and exogenous opioids bind these receptors resulting in:
  - Delayed gastric emptying
  - Disturbance of the migrating myoelectric complex
  - Increased anal sphincter pressure
  - Increased fluid reabsorption
  - Impaired defecation response
  - Formation of dry hard stools

Patient Complaints

- Pain
- Bloating
- Cramping
- Gastro-esophageal reflux
- Nausea and vomiting
Assessment of Opioid Induced Constipation

• Assessment of constipation is important in patients who are currently taking/will be prescribed opioids
  • Determine how the patient defines constipation
  • Frequency of defecation is not as important as comfortable evacuation
  • Document past and current laxatives (dose, frequency and efficacy)

• Clinicians can assess functional constipation using the standard Rome III criteria:
  • Straining
  • Passage of hard stools/ Need to manually remove stools
  • Sensation of incomplete evacuation
  • Anorectal obstruction
  • Passing fewer than three stools per week

<table>
<thead>
<tr>
<th>PHYSICAL EXAM</th>
<th>ALARM SYMPTOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital rectal exam</td>
<td>Unexplained weight loss</td>
</tr>
<tr>
<td>Assessment of anal sphincter</td>
<td>Blood in the stool</td>
</tr>
<tr>
<td>Pelvic floor relaxation on</td>
<td>Family history of colon cancer</td>
</tr>
<tr>
<td>straining</td>
<td>Prolonged constipation despite treatment</td>
</tr>
</tbody>
</table>

Treatment of Opioid Induced Constipation

• The first step to managing opioid induced constipation is **Prevention**
  • Prophylactic treatment can be used in any patient regardless of opioid regimen
  • The most common prophylactic regimen consists of a stool softener and a stimulant
  • Addition of an osmotic laxative such as polyethylene glycol may be considered for patients who do not get relief with a stool softener and stimulant alone

• Non-pharmacological options include:
  • Increased exercise
  • Fluids
  • Dietary soluble fiber
  • Encourage defecation promptly after feeling the urge

The following table provides treatment options for OIC
<table>
<thead>
<tr>
<th>CLASS</th>
<th>DRUG</th>
<th>DOSE</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulk Laxatives</td>
<td>Psyllium, Methylcellulose</td>
<td>Not recommended for</td>
<td>Not recommended for OIC due to increased risk of bowel obstruction with impaired GI motility</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment of OIC</td>
<td></td>
</tr>
<tr>
<td>Stimulant</td>
<td>Senna (Senokot-s)</td>
<td>8.6 mg tablets; 2-4 tablets daily</td>
<td>Induces peristalsis by directly irritating the smooth muscle of the intestine</td>
</tr>
<tr>
<td>Laxatives</td>
<td>Bisacodyl (Dulcolax)</td>
<td>5-15 mg daily</td>
<td>Cramping is a common side effect of these agents</td>
</tr>
<tr>
<td>Osmotics/</td>
<td><strong>Sugar Alcohols</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperosmotics</td>
<td>Lactulose</td>
<td>15-60 mL daily</td>
<td>Orally these laxatives are not absorbed and will hold fluids in intestinal tract during transit</td>
</tr>
<tr>
<td></td>
<td>Sorbitol</td>
<td>30-45 mL daily</td>
<td>Lactulose: Use with caution in diabetics</td>
</tr>
<tr>
<td></td>
<td><strong>Macrocol</strong></td>
<td>17 grams mixed with 8oz liquid daily</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>Polyethylene Glycol</td>
<td></td>
<td>Saline laxatives: Avoid in patients with edema, congestive heart failure, chronic renal disease, heart disease or dehydration since saline laxatives can cause electrolyte abnormalities, dehydration, and fluid loss</td>
</tr>
<tr>
<td></td>
<td><strong>Saline</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnesium hydroxide (Milk of Magnesia)</td>
<td>15-60 mL once daily</td>
<td></td>
</tr>
</tbody>
</table>
## Table. Commonly used laxatives for the initial treatment of OIC (continued)

<table>
<thead>
<tr>
<th>CLASS</th>
<th>DRUG</th>
<th>DOSE</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lubricant Laxative</td>
<td>Mineral oil (Fleet)</td>
<td>15-45 mL in 24 hours (max: 45 mL in 24 hours)</td>
<td>Decreases water absorption, lubricates the intestine, and decreases colonic absorption of water. Patients must remain upright during administration of mineral oil and remain upright for 30-60 minutes to decrease risk of aspiration. Note: Prolonged use of mineral oil could lead to decreased absorption of fat soluble vitamins. Beware of drug interactions as well. It is recommended that mineral oil should not be used longer than 1 week</td>
</tr>
<tr>
<td>Stool Softener</td>
<td>Docusate sodium</td>
<td>50-300mg per day in 1 - 4 divided doses</td>
<td>Often combined with a stimulant laxative for OIC. No evidence to show effectiveness in treating OIC with a softener alone Adequate fluid intake is essential for efficacy Contraindicated with mineral oil</td>
</tr>
<tr>
<td>Combination</td>
<td>Docusate/Senna</td>
<td>8.6/100 mg tablets: 2 tablets once daily Max: 2-4 tablets daily</td>
<td>See above</td>
</tr>
</tbody>
</table>
Newer Agents Approved for the Treatment of Opioid Induced Constipation

• There are several new therapies available for OIC
  • Naloxegol (Movantik)- a peripheral acting mu opioid receptor antagonist
  • MethylNaltexone bromide (Relistor)- a peripheral acting mu opioid receptor antagonist
  • Lubiprostone (Amitiza)- a locally acting chloride channel activator.
Special Considerations

Pharmacogenomic (Phase I & II)

Prescription Drug Monitoring Programs
Pharmacogenomic Considerations
Understanding Opioids and the Cytochrome P450 Enzyme System

• It is essential to understand that drug metabolism can be affected by the numerous pharmacogenomic variations in the patient population.

• When considering the metabolism of opioids, it is important to know which opioids undergo Phase I or Phase II metabolism.
  • For example, codeine undergoes Phase 1 metabolism and morphine undergoes Phase 2 metabolism.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Drug metabolism that occurs via CYP 450 enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>Drug metabolism that occurs via conjugation</td>
</tr>
</tbody>
</table>
As the majority of medications undergo Phase 1 metabolism, including opioids, there is a substantial potential for drug-drug interactions. For patients who respond poorly to an agent, consider using an agent that is metabolized differently.
Pharmacogenomic Considerations
Understanding Opioids and the Cytochrome P450 Enzyme System (Phase I)

• The Human Genome Project studies the genetic variations that result in different enzyme activity levels

• Patients typically will not have a pharmacogenomic profile

• Prescribers should consider the genetic variability in CYP450 metabolism across different ethnicities

• The CYP450 2D6 enzyme system has four different activity levels
  • Tramadol is metabolized by CYP2D6 therefore the effects of these variations will be outlined

Tramadol → CYP2D6 → O-desethyltramadol (active metabolite)
## Pharmacogenomic Considerations
Understanding Opioids and the Cytochrome P450 Enzyme System (Phase I)

<table>
<thead>
<tr>
<th>CYP2D6 variations</th>
<th>Effect on enzyme activity</th>
<th>Tramadol effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultra rapid metabolizers</td>
<td>Increase enzyme activity; clear drug quickly</td>
<td>Could lead to overdose due to increased activity of CYP2D6</td>
</tr>
<tr>
<td>Extensive metabolizer</td>
<td>Normal metabolizing enzyme</td>
<td>Expected results from tramadol</td>
</tr>
<tr>
<td>Intermediate metabolizer</td>
<td>Range of effects on metabolizing enzymes</td>
<td>Variable responses</td>
</tr>
<tr>
<td>Poor metabolizers</td>
<td>Lack of effective metabolizing enzyme</td>
<td>No effect from tramadol since it must be converted via 2D6 to the active metabolite for analgesia response</td>
</tr>
</tbody>
</table>
Key Points of Pharmcogenetics

• Realize that some patients may not achieve adequate analgesia from certain pain medications because of insufficient drug metabolism and not because they are drug seekers.

• Still others may develop symptoms of overdose even with therapeutic doses

An understanding of opioid metabolism can guide dose adjustments or the selection of a different opioid when analgesia is insufficient or adverse events are intolerable.
Prescription Monitoring Programs (PMP)

- What is a PMP?
  - A **state specific** electronic database which collects data on controlled substances dispensed
- PMPs currently do not have interstate communication
- PMPs distribute data to individuals who are authorized under state law to receive the information for purposes of their profession
  - Allows for continuity of care through various healthcare settings
  - Increased patient safety
    - Provides awareness of all active controlled substance medications on file for a patient
    - Alerts prescribers to suspected “doctor shopping”
Prescription Monitoring Program (PMP)

- Florida has the Electronic-Florida Online for the Reporting of Controlled Substances Evaluation (E-FORCSE)
  - **E-FORCSE** can be viewed by registered healthcare providers
  - All controlled substances *dispensed* by pharmacies **MUST** be registered in database
    - Veteran’s Affairs is exempt
    - Methadone clinics are exempt
  - Pharmacies are required to submit dispensing information within a short time period. In Florida, pharmacies are required to submit information **within 7 days** of dispense date.

Tips: The PMP is useful in verifying a patient’s current or past controlled medication regimen.
Prescription Monitoring Programs (PMP)

All entries of the PMP are in chronological order and include the following information:

1. Name of medication
2. Strength of medication
3. Prescriber’s name
4. Date medication prescribed and dispensed
5. Quantity and days supply of medication dispensed
6. Name of pharmacy that dispensed the medication
7. Number of refills prescribed
American College of Emergency Physicians policy statement on electronic prescription monitoring

- Protect patient privacy.
- Not discourage a patient with a genuine medical condition from seeking care.
- Support access to legitimate medical use of controlled substances.
- Ensure accuracy and completion of the data.
- Be voluntary.
- Provide liability protection for the practitioner.
- Minimize burdensome requirements on the physician.
- Utilize a robust monitoring system with intra-state linkages, easily accessible and navigable by practitioners seven days a week, twenty-four hours a day.
- Be limited to appropriate individuals and agencies including physicians, pharmacists and law enforcement.
- Not be used to evaluate physician’s practice.
- Allow physicians to monitor their own prescribing patterns and to identify potential unauthorized use.
There are several limitations with Prescription Monitoring Programs

- Not integrated with electronic medical record.
- Requires separate log in process with password.
- Site maintenance.
- Delay in time prescription is filled to when it shows up in system.
- If pharmacy inputs data incorrectly then the filled prescription may not show.
- Multiple records for same patient.
- Doesn’t provide interpretation.
- How many overlapping rx?
- Doesn’t report type of physician writing prescription or their contact information.
- Doesn’t take into account non-medical use.
- Doesn’t tell you abuse history.
- Doesn’t tell you if patient is in a pain contract.
There have been several studies looking at using data from PMPs to predict opioid overdose and high-risk behaviors. 

Predictors include:
• Number of days receiving more than 100 morphine milligram equivalents
• Number of ‘trinity’ days (opioid, benzodiazepines, muscle relaxer)
• Number of prescriptions
• Multiple drug days
• Early refills

Predictors for high-risk behaviors:
• >/= 4 opioid prescriptions AND
• >/= 4 providers for schedule II-V medications in the past 12 months
Discharge Planning
Discharge Planning

Caregivers and family members should be included in discharge planning as they often are dispensing medications to pediatric and elderly patients. Educate them about the prescribed medication name—both generic and trade names—to avoid confusion and potential duplication of medications.

Pain medications that can cause sedation (such as opioids and benzodiazepines) should be fully explained both verbally and in writing as it may not be appropriate for the patient to drive or do certain tasks.

When discharging or transferring patients recognize that pain medication drug levels may peak during transport times.

Patients treated in the ED should be counseled to follow-up with their out-patient physicians in a timely manner.

Components of Discharge Planning

- Medication education
- Medication interactions and side effects
- Medication reconciliation
- Driving and activity instructions
- Home safety and fall prevention
- Work or school releases when applicable
- Follow-up with appropriate referrals
Access to Medication Post Discharge

• Ensure that the medications prescribed are affordable for the patient

• Consider the addition of the patients diagnosis code for narcotic prescriptions to prevent complications or delays at retail pharmacies

• Some pain medications such as oxycodone or morphine may be kept in limited quantities at retail pharmacies

• Most retail pharmacists are available to communicate with hospital staff regarding medication inventory and pricing
  • Make sure the phone number on patient prescriptions leads to an appropriate person and not a general hospital number
Transition of Care

• Hospital admission
  • A full report on treatments received should be provided to the receiving medical team
    • Timing
    • Dosing
    • Efficacy
    • Side effects experienced

• Long term care discharge
  • Educate caregivers on the patient’s diagnosis and medications
    • Dosing regimen
    • Side effects
    • Drug interactions
    • Follow-up
PAMI ED Discharge Planning Toolkit for Pain

Detailed discharge instructions are a key element of reducing risk and return visits for ED patients with painful conditions and those discharged with pain medication prescriptions.

See PAMI website for more information and to download the Discharge Planning Toolkit for Pain

http://pami.emergency.med.jax.ufl.edu/2016/10/10/introducing-the-pami-ed-discharge-planning-toolkit-for-pain/
Summary
Summary

• Selection of a pain regimen can be complex and requires consideration of patient specific factors

• Opioid medications do not come without risk, patients should be evaluated frequently for drug interactions and adverse events

• Discharge planning requires a collaborative effort to ensure patient safety
The PAMI Pain Management and Dosing Guide is a free tool for use by health care providers in hospital, EMS or acute care settings and should be used as general guide when managing pain in pediatric and adult populations.

The guide provides treatment options for opioids, non-opioids, procedural sedation, nerve blocks, and IV/IM/IN/topical administration. It includes a step-wise approach to pain, patient safety considerations as well as nonpharmacologic interventions. To take a tour of the dosing guide, click here!

A free downloadable pdf of the dosing guide can be accessed on the PAMI website. http://pami.emergency.med.jax.ufl.edu/resources/dosing-guide/
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## Physician Resources and Dosing Cards

<table>
<thead>
<tr>
<th>Resource</th>
<th>Link</th>
</tr>
</thead>
<tbody>
<tr>
<td>How to take a medication history</td>
<td><a href="https://www.youtube.com/watch?v=YeOi_A_6Ug0">https://www.youtube.com/watch?v=YeOi_A_6Ug0</a></td>
</tr>
<tr>
<td>SCOPE (Safe and Competent Opioid Prescribing Education) of Pain</td>
<td><a href="https://www.scopeofpain.com/">https://www.scopeofpain.com/</a></td>
</tr>
<tr>
<td>Assessment Resources and Dosing Card</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------</td>
<td></td>
</tr>
<tr>
<td>PainCAS: Clinical Assessment System</td>
<td><a href="https://www.paincas.com/Welcome/Welcome">https://www.paincas.com/Welcome/Welcome</a></td>
</tr>
<tr>
<td>Opioid Risk Management: Current Opioid Misuse Measure (COMM™)</td>
<td><a href="https://www.paincas.com/Welcome/Welcome">https://www.paincas.com/Welcome/Welcome</a></td>
</tr>
<tr>
<td>Opioid Risk Management: Screener and Opioid Assessment for Patients in Pain (SOAPP®)</td>
<td><a href="https://www.painedu.org/soapp.asp">https://www.painedu.org/soapp.asp</a></td>
</tr>
<tr>
<td>Equianalgesic Dosing</td>
<td><a href="https://bedsidepainmanager.com">https://bedsidepainmanager.com</a></td>
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<tr>
<td>Equianalgesic Dosing Apps</td>
<td><a href="http://clincalc.com/Opioids/">http://clincalc.com/Opioids/</a></td>
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<td></td>
<td><a href="http://www.globalrph.com/narcoticonv.htm">http://www.globalrph.com/narcoticonv.htm</a></td>
</tr>
<tr>
<td></td>
<td><a href="http://opioidcalculator.practicalpainmanagement.com/">http://opioidcalculator.practicalpainmanagement.com/</a></td>
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</table>
## Patient Resources

<table>
<thead>
<tr>
<th>Resource</th>
<th>URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners Against Pain Communication Guides for the Patient</td>
<td><a href="http://www.partnersagainstpain.com/">http://www.partnersagainstpain.com/</a></td>
</tr>
<tr>
<td>The ACPA’s Ten Steps For Moving From Patient To Person</td>
<td><a href="http://theacpa.org/Ten-Steps">http://theacpa.org/Ten-Steps</a></td>
</tr>
<tr>
<td>PAMI Patient &amp; Family Resources</td>
<td><a href="http://pami.emergency.med.jax.ufl.edu/resources/patient-and-family-information/">http://pami.emergency.med.jax.ufl.edu/resources/patient-and-family-information/</a></td>
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PAMI learning module content will sometimes overlap due to similar topics. The PAMI website offers access to learning module handouts, pain tools, resources, websites, and recent pain news.

We welcome your feedback on all PAMI materials and are interested in how you use them to improve patient safety and clinical care. Please email emresearch@jax.ufl.edu.

For more information please visit http://pami.emergency.med.jax.ufl.edu/