Burden of Migraine

School/Work/Social Impact, Previous 3 Months

<table>
<thead>
<tr>
<th>Patients With Migraine</th>
<th>25.3%</th>
<th>28.1%</th>
<th>47.7%</th>
<th>34.3%</th>
<th>29.1%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed a Day of Work/School</td>
<td></td>
<td></td>
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<tr>
<td>Work/School Productivity (%)</td>
<td></td>
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</tr>
<tr>
<td>Deliquent Household Work</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Household Productivity (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missed Family or Social Activity</td>
<td></td>
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</tr>
</tbody>
</table>

Practical Considerations for Migraine Diagnosis

PeerView Live

ICHD-3 Diagnostic Criteria for Migraine Without Aura

Migraine (Without Aura)

A. 25 attacks fulfilling B-D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)

C. Headache has ≥2 of the following characteristics:
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe intensity
   4. Aggravation by or causing avoidance of routine physical activity

D. During headache ≥2 of the following:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis

ICHD-3 Diagnostic Criteria for Migraine With Aura

Migraine With Aura

A. 22 attacks fulfilling B-C

B. ≥1 of the following fully reversible aura symptoms:
   1. Visual
   2. Sensory
   3. Speech and/or language

C. ≥2 of the following 4 characteristics:
   1. ≥1 aura symptom spreads gradually over 5-60 minutes
   2. Each individual aura symptom lasts 5-60 minutes

D. Not better accounted for by another ICHD-3 diagnosis and TIA has been excluded

Differentiating Between Episodic and Chronic Migraine

Episodic Migraine

All attacks ≤16 headache days per month

ICHD-3 Diagnostic Criteria for Chronic Migraine

A. Headache ≥15 days/month for ≥8 months fulfilling criteria B and C

B. Headaches fulfill criteria B-D for migraine without aura (≥3 attacks and ≥6 hours in duration)

C. On ≥16 days/month for ≥3 months fulfilling any of the following:
   1. Criteria C and D for migraine without aura
   2. Criteria B and C for migraine with aura
   3. Believed by patient to be migraine at onset and relieved by triptan or ergot derivative

D. Not better accounted for by another ICHD-3 diagnosis

Fluctuations in Episodic and Chronic Migraine Status:
Data From the CaMEO Study

Chronic Migraine Epidemiology and Outcomes (CaMEO) Study

- Longitudinal survey of US adults with EM and CM identified by a web questionnaire
- A validated questionnaire was used to classify respondents with EM (<15 headache days/month) or CM (≥15 headache days/month) every 3 months for a total of five assessments

Headache frequency fluctuated over the course of 15 months

73.4% patients with CM at baseline had at least one 3-month period when they met the frequency criteria for CM

7.6% patients with EM at baseline had at least one 3-month period when they met the frequency criteria for CM

PeerView.com
**Recognizing Migraine in Clinical Practice**

- **P** – Pulsatile quality
- **O** – One day duration (usually 4-72 hours)
- **U** – Unilateral location
- **N** – Nausea or vomiting
- **D** – Disabling intensity

**ID Migraine: A Validated Migraine Screening Tool**

During the last 3 months, did you have the following with your headaches:

- **P** – Photophobia
  - Did the light trouble you (much more than when there is no headache)?
  - Yes ___ No ___

- **I** – Impairment
  - Did your headache ever limit your ability to work, study, or do something you needed to do for 1 day?
  - Yes ___ No ___

- **N** – Nausea
  - Did you ever feel nauseous when you had headache pain?
  - Yes ___ No ___

With 2 of 3 positive:
- Sensitivity = 0.91; specificity = 0.73; positive-predictive value = 91%

**Additional Considerations for Diagnosing Migraine: Red Flags**

1. Stable pattern (6 months) of episodic disabling headache, usually migraine
2. Reserve workup for change in headache pattern, atypical presentations, and examination

**Established and Emerging Options for the Acute Treatment of Migraine**

**General Considerations for Migraine Management**

- Migraine treatment begins with making the diagnosis, discussing it with the patient, and developing a management plan that considers attack frequency, severity, and impact on patient’s QOL, as well as coincidental or comorbid conditions
- Migraine management can be divided into 2 main therapeutic modalities

**Acute Treatment**

- Many patients require both modalities

**Preventive Treatment**

**Acute Treatment of Migraine**

- **Goal**
  - Terminate migraine attack and decrease risk of EM becoming CM
  - Should be a one-and-done response: Pain-free within 2 hours, with minimal AEs and low likelihood of recurrence
  - Should be used no more than 2-3 days a week

**Potential Consequences of Suboptimal Treatment**

- Recent study showed inadequate treatment efficacy associated with increased risk of new-onset CM over course of 1 year
AHS Evidence Assessment of Pharmacotherapies for Acute Treatment of Adults With Migraine: Nonspecific Medications

Effective (Level A)
- Acetaminophen
- NSAIDs
- Aspirin
- Diclofenac, celecoxib, ibuprofen
- Naproxen

Effective (Level B)
- Ketoprofen
- IV and IM ketorolac
- Flurbiprofen
- IV magnesium

Probably Effective (Level B)
- Ergots
  - Diluted nasal spray
  - Combinations
  - Sumatriptan/naproxen

Triptans for the Acute Treatment of Migraines

<table>
<thead>
<tr>
<th>Class</th>
<th>Triptan</th>
<th>Available Routes of Delivery</th>
<th>Headache Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid onset</td>
<td></td>
<td></td>
<td>~50%*</td>
</tr>
<tr>
<td></td>
<td>Sumatriptan</td>
<td>Oral, nasal spray, intranasal powder, subQ injection</td>
<td>~50%*</td>
</tr>
<tr>
<td></td>
<td>Zolmitriptan</td>
<td>Oral, nasal spray</td>
<td>~50%*</td>
</tr>
<tr>
<td></td>
<td>Rizatriptan</td>
<td>Oral</td>
<td>~50%*</td>
</tr>
<tr>
<td></td>
<td>Almotriptan</td>
<td>Oral</td>
<td>~50%*</td>
</tr>
<tr>
<td></td>
<td>Eletriptan</td>
<td>Oral</td>
<td>~45%*</td>
</tr>
<tr>
<td>Slow onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frovatriptan</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Naratriptan</td>
<td>Oral</td>
<td></td>
</tr>
</tbody>
</table>

Vasoconstrictive Properties

- Hemiplegic migraine, brainstem aura
- Amloptipran, naratriptan, sumatriptan, and zolmitriptan are contraindicated in patients taking MAOIs; the FDA issued a warning on triptans and SSRIs or SNRIs and the risk of serotonin syndrome; the AHS reviewed the cases and the risk, and designated classifying the evidence as inconclusive at best

Ergots for the Acute Treatment of Migraines

Dihydroergotamine: Most Widely Available Ergot Alkaloid

Advantages
- Ability to treat late in an attack
- Potential for complete and sustained response

Contraindications
- Vascular disease
- Uncontrolled hypertension
- Renal/retinal failure
- Pregnancy

Lasmidan: An Emerging Therapy for the Acute Treatment of Migraine

Headache Pain-Free at 2 Hours Post-First Dose

- Lasmidan 20 mg
- Lasmidan 40 mg
- Placebo

Most frequently reported AEs with lasmidan after first dose:
- Dizziness, paresthesia, somnolence, fatigue, nausea, and vomiting; most were mild to moderate in severity
Calcitonin Gene-Related Peptide: What Is Its Role in Migraine Pathophysiology?§,

- CGRP is a 37-amino acid neuropeptide that is widely distributed throughout the central and peripheral nervous systems.
- During spontaneous migraine attacks, CGRP concentrations measured from external jugular vein rise.
- IV infusion of CGRP triggers attacks in persons with migraine that are indistinguishable from spontaneous attacks.
- CGRP serum levels decrease after administration of triptans in parallel with symptomatic relief.

Emerging Small Molecule Oral CGRP Receptor Antagonists (GERANTS) for the Acute Treatment of Migraine

Rimegepant
Ubrogepant

Study 301 and Study 302: Phase 3 Studies of Rimegepant Compared to Placebo in the Acute Treatment of Migraine

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo</th>
<th>Rimegepant 75 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-hour pain freedom</td>
<td>14.2%</td>
<td>19.2% (P &lt; .03)</td>
</tr>
<tr>
<td>2-hour MBS freedom</td>
<td>27.7%</td>
<td>36.6% (P &lt; .002)</td>
</tr>
</tbody>
</table>

Study 302: N = 1,072 patients with EM

- CGRP serum levels decrease after administration of triptans in parallel with symptomatic relief.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo</th>
<th>Rimegepant 75 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-hour pain freedom</td>
<td>12%</td>
<td>10.6% (P &lt; .001)</td>
</tr>
<tr>
<td>2-hour MBS freedom</td>
<td>25%</td>
<td>37.6% (P &lt; .001)</td>
</tr>
</tbody>
</table>

Common AEs included nausea and UTI.

ACHIEVE 1: Phase 3 Clinical Trial Comparing Ubrogepant to Placebo for the Acute Treatment of Migraine

- Most common AEs within 60 hours of dosing: Nausea, somnolence, and dry mouth, all with an incidence < 5%.
- In addition, the phase 3 ACHIEVE 2 showed, compared to placebo:
  - Significantly greater proportions of patients treated with 25 mg or 50 mg ubrogepant achieved pain freedom at 2 hours.
  - At 2 hours, the absence of MBS was significantly greater for the 50 mg dose group.

Preventive Treatment of Migraine

- Goal:
  - Reduce attack frequency
  - It may also:
    - Decrease attack duration or severity
    - Enhance the benefit of acute treatment

Conventional and Novel Therapies for Migraine Prevention
Indications for Preventive Treatment in Patients With Migraine

- Patient preference
- Recurring migraine that significantly interferes with patient's QOL and daily routine despite acute treatment
- Failure of, contraindication to, or troublesome AEs from acute medications
- Acute medication overuse
- Very frequent headaches (>1 per week)
- Special circumstances (eg, hemiplegic migraine, brainstem aura, frequent or prolonged aura)

AAN/AHS Evidence-Based Guideline for Episodic Migraine Prevention: Conventional Oral Therapies

<table>
<thead>
<tr>
<th>Level A</th>
<th>Medications with established efficacy (≥2 Class I trials) and should be offered for migraine prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topiramate</td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td></td>
</tr>
<tr>
<td>Timolol</td>
<td></td>
</tr>
<tr>
<td>Divalproex sodium</td>
<td></td>
</tr>
<tr>
<td>Sodium valproate</td>
<td></td>
</tr>
<tr>
<td>Frovatriptan</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level B</th>
<th>Medications are probably effective (1 Class I or ≥2 Class II trials) and should be considered for migraine prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td></td>
</tr>
<tr>
<td>Atenolol</td>
<td></td>
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<tr>
<td>Naloxol</td>
<td></td>
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<tr>
<td>Nasalidipine</td>
<td></td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level C</th>
<th>Medications are possibly effective (1 Class II trial) and may be considered for migraine prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril</td>
<td></td>
</tr>
<tr>
<td>Candesartan</td>
<td></td>
</tr>
<tr>
<td>Clonidine</td>
<td></td>
</tr>
<tr>
<td>Guanfacine</td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td></td>
</tr>
<tr>
<td>Nebivolol</td>
<td></td>
</tr>
<tr>
<td>Pindolol</td>
<td></td>
</tr>
</tbody>
</table>

Conventional Therapies for Chronic Migraine Prevention

Approved Prior to 2018
- Ondansetron
- Recommended total dose 155 units, as 11 injections of 1.6 mL (5 units) for each site divided across 7 headache muscles

Agent With Randomized Controlled Trial Efficacy in Chronic Migraine Prevention:
- Topiramate

Issues With Conventional Therapies for Migraine Prevention

Although a wide array of medications have been used for migraine prevention, there are number of issues associated with these conventional therapies:
- Until very recently, none of the available therapies had been developed specifically for migraine prevention
- A substantial proportion of patients experienced efficacy, safety, adherence, and drug–drug interactions
- Most (80%) suspend oral prophylactic treatment due to AEs and intolerance issues

Anti-CGRP monoclonal antibodies have also shown to be efficacious in the prevention of CM

Monoclonal Antibodies Targeting the CGRP Pathway for Migraine Prevention

- All data analyzed to date for EM and CM show a reduction in mean MMDs with a magnitude of 1-3 days drop over placebo, similar to the registration studies for ondansetron
- Using MMDs is necessary from a regulatory standpoint
- However, MMDs are not a useful clinical endpoint for estimating value, as the clinical effect is underestimated due to inclusion of placebo
- More useful is the drop from baseline and the secondary endpoints such as responder rates
- The MAB studies are uniform in showing efficacy on primary and secondary endpoints and excellent safety and tolerability

Effect of Anti-CGRP MABs on Monthly Migraine Days

- MMDs are unity?
- MMDs are days
- MMDs are
- MMDs are
- MMDs are
Anti-CGRP Monoclonal Antibodies for Episodic Migraine Prevention: Responder Rates From Phase 3 Trials\textsuperscript{1,6} 

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erenumab</td>
<td>70 mg</td>
<td>70 mg</td>
<td>26%</td>
</tr>
<tr>
<td>Fremanezumab</td>
<td>225 mg</td>
<td>225 mg</td>
<td>29%</td>
</tr>
<tr>
<td>Galcanezumab</td>
<td>120/420 mg</td>
<td>120/420 mg</td>
<td>37%</td>
</tr>
<tr>
<td>Eptinezumab</td>
<td>100/900 mg</td>
<td>100/900 mg</td>
<td>37%</td>
</tr>
</tbody>
</table>

\textsuperscript{1}From Naughton B, Smith D, et al. / J Headache Pain 2020

Anti-CGRP Monoclonal Antibodies for Chronic Migraine Prevention: Responder Rates From Pivotal Trials\textsuperscript{1,4} 

<table>
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<td>37%</td>
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<tr>
<td>Eptinezumab</td>
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<td>100/900 mg</td>
<td>37%</td>
</tr>
</tbody>
</table>

\textsuperscript{1}From Naughton B, Smith D, et al. / J Headache Pain 2020

Anti-CGRP Monoclonal Antibodies: Safety and Tolerability\textsuperscript{1} 

In general, the tolerability and AE profiles of anti-CGRP monoclonal antibodies were comparable to placebo across clinical trials.

Slightly increased incidence of:

- Injection-site reactions (erenumab-soe, fremanezumab-vfim, galcanezumab-gmnl)
- Constipation (seen clinically with higher dose of erenumab-soe)
- Respiratory symptoms with some of the monoclonal antibodies in some of the trials.

To date, no apparent safety signals have been observed, including immunogenicity.

- As such, patients will need to be monitored for unusual AEs.

\textsuperscript{1}From Naughton B, Smith D, et al. / J Headache Pain 2020

Anti-CGRP Monoclonal Antibody Treatment

- Consider prescribing:
  - Patients with lack of response, inadequate response, or intolerance to 3 conventional therapies
  - Conventional preventives contraindicated because of co-existing medical conditions
  - No contraindications to their use
  - Effect during pregnancy unknown
  - Recommend using effective birth control methods
  - Discontinue antibody therapy 6 months prior to conception
  - No drug interactions
  - Long-term safety and tolerability still uncertain

Conclusions

- Migraine treatment begins with establishing a diagnosis, discussing it with the patient, and developing a treatment plan that considers attack frequency, severity, and impact on the patient's QOL, as well as co-existing medical conditions.
- There are several challenges associated with conventional therapies for acute and preventive treatment.
- This prompted research investigating therapeutic interventions that are not only effective in reducing headache intensity, duration, and frequency, but are also well tolerated so as to improve patient adherence and long-term outcomes.
- In this respect, therapies directed against CGRP and its receptor represent a major breakthrough in migraine treatment and prevention.
- Identifying appropriate candidates for these new and emerging therapies will be crucial for optimizing outcomes.
Please remember to complete and submit your Post-Test and Evaluation for CME credit.

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• Join the conversation on Twitter @PeerView

Thank you and have a good day.

PeerView
Case Studies in the Practical Evaluation and Management of Irritable Bowel Syndrome with Diarrhea

Michael Cobble, MD, FNLA
Director
Canyon Medical Center, Sandy, Utah
Adjunct Faculty
University of Utah, Salt Lake City, Utah

Statement of Sponsorship and Support

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CME Information

This live activity, Case Studies in the Practical Evaluation and Management of Irritable Bowel Syndrome with Diarrhea, from 06/24/2018 - 06/23/2019, has been reviewed and is acceptable for up to 1.00 prescribed credit by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Disclosures

Michael Cobble, MD, FNLA, has disclosed that he is a consultant to Kowa; as well as on the speaker’s bureau for Amarin, Amgen, Astra Zeneca, Kowa, and Sanofi.

Angela Cimino, PharmD, and Gregory Scott, PharmD, RPh, Editorial Support, disclosed they have no real or apparent conflicts of interest to report.

Learning Objectives

• Identify patients who are appropriately diagnosed based on history and symptoms
• Describe the role of Rome-IV criteria, colonoscopy, and other tests in diagnosis
• Differentiate subtypes of IBS
• Characterize the benefits and limitations of currently available prescription medications for IBS
• Individualize treatment for IBS based on current evidence-based guidelines

Case Study

• A 32-year-old science teacher is referred for further management of abdominal symptoms which started after a trip to Mexico one year ago where he and his wife both developed severe food poisoning.
• Since then he has had daily loose, watery, non-bloody, urgent bowel movements and feels somewhat bloated and distended.
• He reports daily pain in his lower abdomen that worsens just before a bowel movement and improves after having urgent diarrhea.
• His wife’s symptoms have completely resolved.
Case Study (cont.)

- His weight has remained stable. He does not report fevers, chills, rashes, oral ulcers, myalgias or arthralgias.
- He does not take any medications or use alternative therapies. Past medical and surgical history are unremarkable.
- He does not have a family history of irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), celiac disease, or colorectal cancer.

Case Study (cont.)

- He went to an urgent care clinic 3 months after the onset of symptoms.
- A complete blood count, complete metabolic panel, and stool studies were all normal.
- A 2-week trial of a lactose-free diet did not help.
- Loperamide taken as needed has not helped his abdominal pain, bloating, or diarrhea.
- The patient has done some research and brings several questions to the visit.
- The discussion in response to his questions serves as the basis for this presentation.

What is my diagnosis?

IBS Overview

- IBS is a common functional bowel disorder characterized by recurrent abdominal pain associated with altered bowel habits1.
- Abdominal bloating and distension are also often present, but neither is required to make the diagnosis of IBS1.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Type of bowel habit alteration1</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS-D</td>
<td>Diarrhea-predominant</td>
</tr>
<tr>
<td>IBS-C</td>
<td>Constipation-predominant</td>
</tr>
<tr>
<td>IBS-M</td>
<td>Mixed-type with alternating periods of diarrhea and constipation</td>
</tr>
</tbody>
</table>

1Based on new FBRF criteria on days with at least one abdominal symptom
2Most common subtype, affecting approximately 40% of patients

Rome IV Criteria for IBS

Recurrent abdominal pain at least 1 day/week (on average) in the last 3 months associated with 2 or more of the following:

- Relief with defecation
- Onset with alteration in frequency of stool
- Associated with a change in form of stool

IBS is NOT a diagnosis of exclusion.

According to Rome IV criteria,
Is there anything worrisome in my history?

Conditions That Mimic IBS
- Lactose intolerance
- Fructose intolerance
- Small intestine bacterial overgrowth (SIBO)
- Celiac disease
- Inflammatory bowel disease
- Microscopic colitis
- Functional diarrhea
- Functional constipation

Role of Diagnostic Testing
- Diagnosis is based on a thoughtful history and limited physical examination to assess the presence of the distinguishing symptom of IBS
- New to Rome IV criteria is the use of limited testing to consider in patients without alarm symptoms
  - Complete blood count to ensure the absence of anemia
  - C-reactive protein or fecal calprotectin to lower suspicion for IBS and prevent indiscriminate use of colonoscopy
  - Celiac serologic testing

Alarm signs & symptoms warranting further investigation
- Age over 50 years without prior colon cancer screening
- Presence of overt GI bleeding
- Nocturnal passage of stool
- Unintentional weight loss
- Family history of inflammatory bowel disease or colorectal cancer
- Recent changes in bowel habits
- Presence of a palpable abdominal mass or lymphadenopathy

Which one of the following is true regarding the diagnosis of diarrhea-predominant irritable bowel syndrome?

1. The history and physical examination and colonoscopy are essential
2. A C reactive protein or fecal calprotectin level is recommended for patients without alarm symptoms
3. It is a diagnosis of exclusion
4. According to Rome IV, IBS-D is recurrent abdominal pain at least 1 day/week for a minimum of 30 days

Which one of the following is true regarding the diagnosis of diarrhea-predominant irritable bowel syndrome?

1. The history and physical examination and colonoscopy are essential
2. A C reactive protein or fecal calprotectin level is recommended for patients without alarm symptoms
3. It is not a diagnosis of exclusion
4. According to Rome IV, IBS-D is recurrent abdominal pain at least 1 day/week for a minimum of 30 days
Why did my symptoms develop?

...and a gut-brain disorder

IBS may be a brain-gut disorder

IBS as a gut-brain disorder

Which one of the following is true about irritable bowel syndrome?

Which one of the following is true about irritable bowel syndrome?
Will my symptoms go away?

Natural History of IBS

- ~50% of patients have persistent symptoms 3-5 years following diagnosis
- No therapy has been proven to alter the natural history of IBS in the long term
- Uncertain if newer medications have altered natural history

Treatment Overview

- Treatment of IBS-D is directed at decreasing symptoms of abdominal pain, bloating, and diarrhea
- Treatment should be individualized in a stepwise manner according to symptoms and severity
- Moderate symptoms affecting home, social, and work life will likely require scheduled pharmacologic treatment with one or more of a range of options
- For patients with severe symptoms, consider referral to a gastroenterologist for specialty care, combination therapy, and possibly psychological or behavioral intervention (eg, cognitive behavioral therapy, hypnosis, and various relaxation methods)

Severity-based Treatment

Mild
- Education: reassurance
- Diet, lifestyle advice
- Loperamide as needed

Moderate
- Manage stress
- Pharmacologic therapy

Severe
- Pharmacologic therapy
- Psychological treatment
- Goal is improved function vs. complete resolution of symptoms

Therapies for IBS-D by Symptom

<table>
<thead>
<tr>
<th>Abdominal pain/Discomfort</th>
<th>Diarrhea</th>
<th>Bloody/Diarrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Alprazolam</td>
<td>- Alprazolam</td>
<td>- Alprazolam</td>
</tr>
<tr>
<td>- Rifaximin</td>
<td>- Rifaximin</td>
<td>- Rifaximin</td>
</tr>
<tr>
<td>- Antidepressants* (SSRI, TCAs)</td>
<td>- Antidepressants* (SSRI, TCAs)</td>
<td>- Antidepressants* (SSRI, TCAs)</td>
</tr>
<tr>
<td>- Smooth muscle antispasmodics (dicyclomine, hyoscyamine*)</td>
<td>- Smooth muscle antispasmodics (dicyclomine, hyoscyamine*)</td>
<td>- Smooth muscle antispasmodics (dicyclomine, hyoscyamine*)</td>
</tr>
<tr>
<td>- Low FODMAP diet</td>
<td>- Low FODMAP diet</td>
<td>- Low FODMAP diet</td>
</tr>
<tr>
<td>- Probabio*</td>
<td>- Probabio*</td>
<td>- Probabio*</td>
</tr>
<tr>
<td>- Diet*</td>
<td>- Diet*</td>
<td>- Loperamide*</td>
</tr>
</tbody>
</table>

*Not approved for IBS-D by the US FDA

Do diet interventions or exercise help?
First-line lifestyle and dietary modifications may provide adequate symptom relief:

- Exercise
- Stress reduction (e.g., meditation, counseling)
- Attention to impaired sleep
- Limit intake of potential dietary triggers (e.g., alcohol, caffeine, spicy foods, fat, gas-producing foods)
- Soluble fibers with a low rate of fermentation (e.g., psyllium) may have some benefit in addressing diarrhea
- Gluten-free diet may help reduce symptoms, but data do not support additive effect over a low-FODMAP diet alone

Low FODMAP Diet

- Restricts short-chain carbohydrates known collectively as fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs)
- Found in such foods as wheat, broccoli, legumes, dairy, apples, and stone fruits
- Approximately 70% response rate in reducing abdominal pain, bloating, diarrhea, abdominal distention, and flatulence
- Should be guided by a dietitian due to complexity and potential risks for inadequate nutritional intake
- May have durable efficacy even with reintroduction of FODMAPs

Will probiotics help?

- ACG 2014 Guidelines concluded:
  - "Taken as a whole, probiotics improve global symptoms, bloating, and flatulence in IBS"
  - Recommendation: weak
  - Quality of evidence: low
  - The most convincing data for efficacy are derived from multi-strain probiotics containing both Lactobacillus and Bifidobacteria with a concentration of 10 billion CFU/day or less

Will an antibiotic help?

- Neomycin
  - Symptom improvement but rapid bacterial resistance
- Rifaximin
  - Oral, non-systemic antibiotic associated with a low bacterial resistance profile and a favorable side-effect profile
  - FDA-approved for the treatment of adults with non-constipation IBS, including IBS-D
Rifaximin TARGET 1 and TARGET 2 Trials

- Two phase 3 randomized controlled trials; N=1260
- Rifaximin 550 mg TID vs placebo for 14 days
- 40.7% vs. 31.7% with adequate relief of global symptoms at 4 weeks after treatment (P<0.001)
- Incidence of adverse effects (headache, upper respiratory infection, nausea, and diarrhea) was comparable to placebo

Rifaximin: Durability of Effect

Adequate relief was defined as self-reported relief from symptoms for at least 1 week of every 2-week period.

Eluxadoline for IBS-D

- Mixed mu (μ) and kappa (κ) opioid receptor agonist / delta (δ) opioid receptor antagonist
- Low systemic absorption and bioavailability
- Low potential for drug-drug interactions

Eluxadoline primary endpoint: composite responders - pooled data

Safety of Eluxadoline in Patients with IBS with Diarrhea

- 2,814 IBS-D patients (Rome III criteria)
  - 1 phase 2 study (12 wks)
  - 2 phase 3 studies (26 and 52 wks)
- Placebo vs. eluxadoline (75 or 100 mg BID)
- Most frequent AEs:
  - Constipation (2.5% vs. 7.4% vs. 8.1%)
  - Nausea (5.0% vs. 8.1% vs. 7.1%)
- 10 Patients had Sphincter of Oddi Spasm (0.5%); all with prior cholecystectomy
Alosetron for IBS-D

- A 5-HT₂ antagonist
- Reduces stool frequency and abdominal pain; improves urgency
- Treatment population
  - Women with chronic, severe IBS-D who have failed other treatments
  - Dosage: 0.5-1.0 mg PO to BID
- Patient education regarding possible serious adverse effects of severe constipation or ischemic colitis
  - 0.96 cases of ischemic colitis/1000 patient-years
  - 0.36 cases of severe constipation/1000 patient-years
- If ischemic colitis occurs, it is usually within the first month of therapy

Alosetron: Therapeutic Gain for IBS-D

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Female, %</th>
<th>Response: Alosetron, %</th>
<th>Response: Placebo, %</th>
<th>Therapeutic Gain, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camilleri¹</td>
<td>370</td>
<td>53</td>
<td>60</td>
<td>33</td>
<td>27</td>
</tr>
<tr>
<td>Camilleri²</td>
<td>647</td>
<td>100</td>
<td>41</td>
<td>29</td>
<td>12</td>
</tr>
<tr>
<td>Camilleri³</td>
<td>626</td>
<td>100</td>
<td>43</td>
<td>26</td>
<td>17</td>
</tr>
<tr>
<td>Lembach⁴</td>
<td>801</td>
<td>100</td>
<td>73</td>
<td>57</td>
<td>16</td>
</tr>
<tr>
<td>Jones⁵</td>
<td>623</td>
<td>100</td>
<td>58</td>
<td>48</td>
<td>10</td>
</tr>
</tbody>
</table>

¹ Camilleri et al. Am J Gastroenterol 2000;95:1519-1525
² Camilleri et al. Gastroenterology 2000;119:976-982
³ Lembach et al. Am J Gastroenterol 2000;95:1519-1525
⁴ Lembach et al. Am J Gastroenterol 2000;95:1519-1525
⁵ Jones et al. Am J Gastroenterol 2000;95:1519-1525

Selected Pharmacologic Therapies for IBS-D That Do Not Affect the Gut Microbiome*

<table>
<thead>
<tr>
<th>Therapy, Mechanism of Action</th>
<th>Efficacy by Symptom</th>
<th>Dose Regimen</th>
<th>Side effects/ Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loperamide*¹ ²</td>
<td>Improves stool frequency, tenesmus, and urgency; non-constipating</td>
<td>2 to 6 mg daily in divided doses</td>
<td>Abdominal cramps, nausea</td>
</tr>
<tr>
<td>Antidepressants*³ ⁴</td>
<td>May improve abdominal pain and diarrhea</td>
<td>10 to 25 mg at bedtime, then titrate gradually based on symptom response and tolerability to 55-70 mg once daily</td>
<td>Drowsiness, dry mouth, dry eyes, orthostatic hypotension</td>
</tr>
</tbody>
</table>

¹ Not approved for IBS-D in the United States
² Available in some countries
³ Available in some countries
⁴ Not available in the United States

Selected Pharmacologic Therapies for IBS-D That Do Not Affect the Gut Microbiome* (cont.)

<table>
<thead>
<tr>
<th>Therapy, Mechanism of Action</th>
<th>Efficacy by Symptom</th>
<th>Dose Regimen</th>
<th>Side effects/ Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisacodyl</td>
<td>Diarrhea - may be considered after other therapies targeting diarrhea have been unsuccessful</td>
<td>5 to 10 mg 1 to 2 times daily</td>
<td>Constipation, nausea</td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>Cholestyramine 9 grams 2 to 3 times daily, colestipol 2 g once or twice daily, or colesvelam 850 mg once or twice daily</td>
<td>None observed</td>
<td></td>
</tr>
</tbody>
</table>

¹ Not approved for IBS-D in the United States
² Available in some countries
³ Available in some countries
⁴ Not available in the United States

Which one of the following is true regarding the treatment of diarrhea-predominant irritable bowel syndrome?

1. Initial treatment typically consists of lifestyle modification that includes increased exercise, a gluten-free diet, and stress reduction
2. A low FODMAP diet is of little benefit in reducing symptoms such as bloating and abdominal pain
3. Significant improvement in symptoms typically takes 6-8 weeks following initiation of rifaximin
4. Alosetron reduces stool frequency and abdominal pain, but is indicated only for women with IBS-D who have failed other treatments

Which one of the following is true regarding the treatment of diarrhea-predominant irritable bowel syndrome?

1. Initial treatment typically consists of lifestyle modification that includes increased exercise, a gluten-free diet, and stress reduction
2. A low FODMAP diet is of little benefit in reducing symptoms such as bloating and abdominal pain
3. Significant improvement in symptoms typically takes 6-8 weeks following initiation of rifaximin
4. Alosetron reduces stool frequency and abdominal pain, but is indicated only for women with chronic, severe IBS-D who have failed other treatments
Summary

- An individualized approach to the management of patients with IBS-D begins with reassurance, explanation, and a positive diagnosis that includes limited testing to rule out disorders that may mimic IBS-D (e.g., IBD or celiac disease).
- Treatment options should be considered in the context of symptoms, possible etiologic factors, and benefits vs risks.
- Treatment typically begins with dietary modifications, increased exercise, and stress reduction.

Summary (cont)

- A probiotic may be considered, particularly for bloating, and a tricyclic antidepressant for pain.
- Diarrhea may be ameliorated with loperamide or a bile acid sequestrant.
- For persistent and/or more severe symptoms, rifaximin, eluxadoline, or alosetron may be considered, with the specific choice guided by patient-specific factors.

Case Studies in the Practical Evaluation and Management of Irritable Bowel Syndrome with Diarrhea

Thank you!
CHAPTER 1
WELCOME

FACULTY INFORMATION

BIO:
Kirk Mokdad, MD, PhD, PASAP, FACPM
Dr. Mokdad is the Co-director, Medical Director of the
Dartmouth Institute for addiction Recovery. He graduated
from the University of Miss. College of Medicine and
is certified by the American Board in Internal Medicine, Preventive and Addiction Medicine. He serves on Clinical Programs at
the Dartmouth, Cardiovascular and Psychiatry of the University of Miss. College of Medicine. Dr. Mokdad is also certified as a
Methadone Counselor.

DISCLOSURE:
Dr. Mokdad and all staff involved in the development of content declare that neither they nor members of their immediate families have had financial relationships with the
manufacturer of goods or services discussed, or corporate supporters of this symposium.

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interdisciplinary organizations working together to improve pain management and prevent adverse outcomes.

This educational activity is supported by an independent educational grant from the Extentional-RelatedLong-Acting (ER/LA) Opioid Analgesic REMIS Program Companies. Please see the
acknowledgment for a list of the member companies. This activity is intended to be fully compliant with the Opioid Analgesics: REMIS education requirements issued by the US Food and Drug Administration.
PRODUCTS COVERED BY THIS REMS

BRAND NAME PRODUCTS
- Aprovel ® (culosartan / valsartan)
- Aricept ® (donepezil HCl)
- Ariett® (loratadine)
- Aveo ® (celecoxib)
- Bendex ® (bendroflumethiazide / hydrochlorothiazide)
- Bimat ® (bimatoprost)
- Cardura ® (doxazosin)
- Carisil ® (carisoprodol)
- Cefaly ® (sumatriptan)
- Cormax ® (candesartan / hydrochlorothiazide)
- Darvocet (propoxyphene / acetaminophen)
- Decadron (dexamethasone)
- Debist ® (diltiazem / hydrochlorothiazide)
- Desitin ® (hydrocortisone)
- Detrol (tolterodine)
- Diovan ® (valsartan)
- Doxil (liposomal doxorubicin)
- Dripsey ® (cisapride)
- Elavil ® (amitriptyline)
- Epitrop ® (melatonin)
**OPIOID PRESCRIBING - THE PENDULUM SWINGS**

**PRESCRIBING BEHAVIORS**
- Under-Prescribing
- Over-Prescribing
- Appropriate Prescribing

**RESULTING OUTCOMES**
- Unresolved Pain
- Adverse Outcomes
- Adequate Analgesia

---

**REMS: RISK EVALUATION AND MITIGATION STRATEGY**
- On July 2, 2012, the Food and Drug Administration (FDA) approved a Risk Evaluation and Mitigation Strategy (REMS) for extended-release (ER) and long-acting (LA) opioid medications.
- First time FDA has ever mandated a REMS as part of a REMS.

---

**SOURCE OF MOST RECENT RX OPIOIDS AMONG PAST-YEAR MISUSERS 2015**

![Pie chart showing the source of opioids among past-year misusers in 2015]

- 56% - Prescription
- 18% - Over-the-counter
- 12% - Pain Reliever
- 6% - Benzodiazepines

---

**CORE STATEMENT**

Misperceptions, misconceptions, addiction, and overuse of opioids has created a serious public health epidemic in the U.S.

When prescribed well and used as prescribed, opioids can be valuable tools to effectively treat pain.

This course does not advocate for or against the use of Immediate Release (IR) or Extended-Release Long-Acting (ER/LA) opioids. Our purpose is to provide proper education about safe prescribing practices along with effective patient education.

---

**FIRST SPECIFIC DRUG ASSOCIATED WITH INITIATION OF ILLICIT DRUG USE 2013**

2.8 million initiates of illicit drugs

- 73.3% - Medication
- 12.8% - Pain Reliever
- 6.3% - Benzodiazepines
- 6.2% - Transcendants
- 2.7% - Stimulants
- 2.6% - Hallucinogens
- 0.3% - Relaxants and Cocaine

---

**LEARNING OBJECTIVES**

1. Accurately assess patients with pain for consideration of an opioid trial.
2. Establish realistic goals for pain management and restoration of function.
3. Initiate opioid treatment (IR and ER/LA) safely and judiciously, maximizing efficacy while minimizing risks.
4. Monitor and re-evaluate treatment continuously, discontinuing safely when appropriate.
5. Counsel patients and caregivers about use, misuse, abuse, diversion, and overdose.
6. Educate patients about safe storage and disposal of opioids.
7. Demonstrate working knowledge and ability to access general and specific information about opioids, especially those used in your practice.
Summary of 2016 CDC guidelines

- **Non-pharmacologic and non-opioid treatments preferred.**
- Establish treatment goals
- Immediate release first
- Lowest dose preferable; caution when exceeding 50 Morphine Milligram Equivalents
- Avoid exceeding 90 MME
- For acute pain only prescribe what is expected
- Evaluate response to opioids one 1-4 weeks after initiation for chronic pain
- If benefits do not outweigh harms taper and discontinue

---

**Mitigate Risk**


---

**PAIN ASSESSMENT**

**DESCRIPTION OF PAIN**

- **Location**
- **Intensity**
- **Quality**
- **Great/Duration**
- Variations/Patterns/Rhythms

**WHAT RELIEVES THE PAIN?**

**WHAT CAUSES OR INCREASES PAIN?**

**EFFECT OF PAIN ON PHYSICAL, EMOTIONAL, AND PSYCHOLOGICAL FUNCTION**

**PATIENT'S CURRENT PAIN AND FUNCTION**

---

**CHAPTER 3 - PEARLS FOR PRACTICE**

- Explain neurophysiology of pain processing to patients
- When patients understand their concerns are validated
- Pain has biological, psychological, social, and spiritual components

---

**TREATMENT HISTORY**

**NON-PHARMACOLOGIC STRATEGIES AND EFFECTIVENESS**

**PHARMACOLOGIC STRATEGIES AND EFFECTIVENESS**

**CURRENT USE**

- Query state Prescription Drug Monitoring Program (PDMP) to confirm patient report

**DOSEAGE**

- For opioids currently prescribed: opioid, dose, regimen, and duration
  - Important to determine if patient is opioid tolerant

**GENERAL EFFECTIVENESS**

---
INFORMED CONSENT

When initiating a trial of opioid analgesic therapy, confirm patient understanding of informed consent to establish:

- How to manage:
  - Common Adverse Events (AEs) (e.g., constipation, nausea, itching)
  - Deaths (e.g., overdose, addiction, respiratory depression, convulsions)
  - AFx with long-term therapy or if hypoxia, low blood pressure, negative mental status, or sexual dysfunction.

PATIENT-PRESCRIBER AGREEMENT (PPA)

Document signed by both patient and prescriber at time an opioid is prescribed.

- Clarify treatment plan and goals of treatment with patient, patient's family, and other clinicians involved in patient's care.
- Assist in patient education.
- Discuss medication safe-handling, storage, and disposal.
- Document patient and prescriber responsibilities.

PATIENT PROVIDER AGREEMENT (PPA)

- Reinforce expectations for appropriate and safe opioid use:
  - One prescriber
  - Consider one pharmacy
  - Safeguard:
    - Do not store in medicine cabinet
    - Keep locked (medication safe)
    - Do not share or sell
    - Instructions for disposal when no longer needed
    - Prescriber notification for any event resulting in a pain medication prescription
  - Follow-up:
    - Monitoring
      - Random UDT and pill counts
      - Refills
      - Identity behaviors for discontinuation
      - Exit strategy

ADDRESS ABERANT DRUG-RELATED BEHAVIOR

Behavior outside the boundaries of agreed-on treatment plan:

- Unanticipated dose escalations or other noncompliance with therapy on 1 or 2 occasions
- Unapproved use of the drug to treat another symptom
- Openly acquiring similar drugs from other medical sources
- Obtaining prescription drugs from nonmedical sources

Any of these behaviors merit investigation, proceed with caution.

Adequately DOCUMENT all patient interactions, assessments, test results, and treatment plans.
CHAPTER 4 – PEARLS FOR PRACTICE

- Conduct a comprehensive and pain-focused history and physical
- Assess for risk of abuse and for mental health issues
- Determine if a therapeutic trial is appropriate
- Establish realistic goals for pain management and function
- Document EVERYTHING

CHAPTER 5
MANAGEMENT
MONITORING AND DISCONTINUING

PART 1
MONITORING

OPIOID SIDE EFFECTS

- Respiratory depression – most serious
- Opioid-induced Constipation (OIC) – most common
- Sedation, cognitive impairment
- Falls and fractures
- Sweating, miosis, urinary retention
- Hyponatremia
- Tolerance, physical dependence, hyperalgesia
- Addiction in vulnerable patients

Prescribers should report serious AEs to the FDA:
www.fda.gov/medicaldevices/devicereporting/reportaproblem
or 1-800-FDA-1088

OPIOID-INDUCED RESPIRATORY DEPRESSION

Clinichourd of opioid agonists, including
ER/IR opioids
- Fnd immediately recognized and treated unless lead to respiratory arrest and death
- Severe risk
- Initiate therapy or step up therapy
- Monitor by reduced range of breathing and respiratory rate
- Shallow breathing
- CO2 retention can exacerbate opioid withdrawal effects
- Intubated patient must be intubated
- Communicate with other health care providers
- Notify patient and family members to call 911
- Managed with
- High ventilation
- Supportive measures
- Opioid antagonists
- Depending on patient's clinical status

Prescriber Status and Education Requirements

<table>
<thead>
<tr>
<th>Prescriber Status</th>
<th>Education Requirements</th>
<th>Physician</th>
<th>Physician Assistant</th>
<th>Advanced Practice Nurse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensed</td>
<td>3 hrs./2 yrs.</td>
<td>3 hrs./2 yrs.</td>
<td>3 hrs. initially, then 1 hr. annually</td>
<td></td>
</tr>
<tr>
<td>Schedule III-V</td>
<td></td>
<td>Schedule III-V</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prescriber Status and Education Requirements

Initial prescribing limits for acute pain: None

http://medicos.org/0613366130 (June 2016)

http://www.medicash.com/CounterPoint/vol1issue2 (June 2016)

http://www.medicash.com/CounterPoint/vol1issue2 (June 2016)
**OPIOD-INDUCED RESPIRATORY DEPRESSION**

**MORE LIKELY TO OCCUR**
- In elderly, cachectic, or dehydrated patients
- Contraindicated in patients with respiratory depression or conditions that increase risk
- If given concurrently with other drugs that depress respiration
- Patients who are opioid-naive or have just had a dose increase

**REDUCE RISK**
- Proper dosing and titration are essential
- Do not overestimate dose when converting dosage from another opioid product
- Can result in fatal overdose with first dose
- Instruct patients to swallow tablets/capsules whole
- Dose from old, crushed, crushed, or chewed tablets/capsules may be fatal, particularly in opioid-naive individuals

**EQUIANALGESIC DOSE TABLES (EDT)**

Many different versions:
- PUBLISHED
- ONLINE
- ONLINE INTERACTIVE
- SMART-PHONE/APPs

Vary in terms of:
- EQUIANALGESIC VALUES
- WHETHER RANGES ARE USED

Which opioids are included: May or may not include transdermal oxycodone, rapid-onset fentanyl, ER/LA opioids, or opioid agonist-antagonists

---

**OPIOID TOLERANCE**

If opioid tolerant caution should still be used at higher doses

Patients considered opioid tolerant are taking at least:
- 60 mg oral morphine/day
- 250 mcg transdermal fentanyl/day
- 30 mg oral oxycodone/day
- 8 mg oral hydrocodone/day
- 25 mg oral oxymorphone/day

An equianalgesic dose of another opioid

Still requires caution when rotating a patient on an IR opioid to a different ER/LA opioid

**EXAMPLE OF AN EDT FOR ADULTS**

<table>
<thead>
<tr>
<th>Equianalgesic Dose</th>
<th>Usual Starting Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DRUG</strong></td>
<td><strong>SCG/F</strong></td>
</tr>
<tr>
<td>Morphine</td>
<td>10 mg</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>NA</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>NA</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5 mg</td>
</tr>
</tbody>
</table>

**OPIOID ROTATION**

**DEFINITION**
Change from an existing opioid regimen to another opioid with the goal of improving therapeutic outcomes or to avoid AEs attributed to the existing drug (e.g., mycosis)

**RATIONALS**
Differences in pharmacologic or other effects make it likely that a switch will improve outcomes
- Effectiveness and AEs of different mu opioids vary among patients
- Patients show incomplete cross-tolerance to new opioid
- Patient tolerant to first opioid can have improved analgesia from second opioid at a dose lower than calculated from an equianalgesic dosing Table (EDT)

**GUIDELINES FOR OPIOID ROTATION**

- Receiving a relatively high dose of current opioid regimen
- Elderly or medically frail

Does not have these characteristics
- Is changing route of administration

*75%-90% reduction for methadone*
GUIDELINES FOR OPIOID ROTATION

**REPLACEMENT CALCULATED EQUIVALENT OF ERIAA (ERLA) 25-50%**

SELECT % REDUCTION BASED ON CLINICAL JUDGMENT

CLOSE TO 50% REDUCTION IN PATIENTS

CLOSE TO 75% REDUCTION IN PATIENTS

- Receiving a relatively high dose of current opioid regimen
- Elderly or medically frail
- Does not have these characteristics
- Is changing route of administration

*75%-90% reduction for methadone

GUIDELINES FOR OPIOID ROTATION (continued)

**IF SWITCHING TO METHADONE**

- Standard ERAs are less helpful in opioid rotation to methadone
- In opioid tolerant patients, methadone doses should not exceed 30-60 mg/day upon rotation
- Consider inpatient monitoring, including venous blood monitoring
- In opioid-naive patients, methadone should not be given as an initial drug

**IF SWITCHING TO TRANSDERMAL**

- Fantasy, calculate dose conversion based on equianalgesic dose ratio included in the PI
- Buprenorphine, follow instructions in the PI

CONSIDERATIONS FOR CHANGE FROM IR TO ERLA OPIOIDS

**ERIA A/A/D/D SELECTION IS CRITICAL**

- Monitor patients exploit for respiratory depression
- Especially within 2-4 hours of initiating therapy and increasing dosage

**INDIVIDUALIZE DOSAGE BY**

- Starting ERA opiate or changing formula as clinically indicated
- PATIENT, taking into consideration:
  - Age
  - History of adverse reactions to opioids
  - History of tolerance to opioids
  - Concurrent use of other CNS depressants

**BREAKTHROUGH PAIN (BTP)**

PATIENTS ON STABLE ATRA OPIOIDS MAY EXPERIENCE BTP

- Disease progression or a new or unrelated pain
- Target, chronic or progressive factors
- Dose for BTP, starting on ER 25%-50% of total daily opioid dose, administered as appropriate interval
- Never add ER LA for BTP

CONSIDER ADDING

- PER 24-36 hours based on analysis of benefit versus risk
- Risk for abuse or drug-related behaviors
- High risk, only in conjunction with frequent monitoring & follow-up
- Non-opioid drug therapies
- Non-pharmacological treatments

WHEN TO MOVE FROM IR TO ERLA OPIOIDS

**PRIMARY REASONS**

- Maintain stable blood levels (steady state plasma)
- Longer duration of action
- Multiple IR doses needed to achieve effective analgesia
- Poor analgesic efficacy despite dose titration
- Less steep duration

**OTHER POTENTIAL REASONS**

- Patient desire or need to try a new formulation
- Cost or insurance issues
- Adherence issues
- Change in clinical status requires an opioid with different pharmacodynamics
- Problematic drug-drug interactions

PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

INDIVIDUAL STATE LAWS DETERMINE

- Who has access to PDMP information
- Which drugs are monitored
- Whether prescribers are required to report to the PDMP
- Whether prescribers are required to access PDMP information in certain circumstances
- Whether unlinked PDMP reports are sent to prescribers
- Whether prescribers may be excused
- Designated surrogates may have access

NOT ALL FEDERALLY LICENSED FACILITIES REPORT TO PDMPs

Link to state PDMP sites
**PDMP BENEFITS**

Provides full accounting of prescriptions filled by patient

- Some are available online 24/7
- Opportunity to discuss with patient
- Existing prescriptions not reported by patient
- Multiple prescribers/pharmacies
- Drugs that increase overdose risk when taken together
- Patient pays with cash (vs insurance) for controlled meds

---

**TYPES OF UDT METHODS**

Be aware of what you are testing and not testing

- IMMUNOASSAY (AI) DRUG PANELS
  - Either free or bound to protein
  - Identify substances as present or absent according to cutoff
  - Many do not identify individual drugs within a class
  - Suspect to cause accuracy and sensitivity

- GCMS OR LCMS
  - Identify the presence and quantity of substance(s)
  - Identify drugs not included in IA tests
  - When results are contested

---

**PDMP: Prescription Drug Monitoring Program**

- CDSMP (Controlled Substance Monitoring Program)
  - http://www.cdsmp.com
- Administered by the Board of Pharmacy
- Schedule II-IV are monitored
- Dispensers and prescribers are required to register and input data
- Before prescribing, there is an obligation to review under certain circumstances
- Prescriptions can authorize a reported quantity

- Must be reported to PDMP within 24 hours after dispensing
- Unsolicited reports/alerts are sent to prescribers, dispensers, law enforcement and licensing boards
- West Virginia shares data with other state PDMPs
- Out-of-state pharmacies are required to report to the patient’s home state
- Patient will be notified if their record has been accessed

---

**SPECIFIC WINDOWS OF DRUG DETECTION**

How long a person excretes drug and/or metabolite(s) at a concentration above a cutoff

**DETECTION TIME OF DRUGS IN URINE**

- Governed by various factors, e.g. dose, route of administration, metabolism, lab variability, tissue volume and pH
  - For most drugs 1-3 days
  - Chronic use of opioid/opioid drugs increases detection time, e.g., marijuana, barbiturates, benzodiazepines

---

**RATIONALE FOR URINE DRUG TESTING (UDT)**

- Urine testing is done FOR the patient not TO the patient
- Help to identify drug misuse/addiction
- Assist in assessing and documenting adherence

**UDT FREQUENCY IS BASED ON CLINICAL JUDGMENT AND STATE REGULATIONS**

---

**URINE SPECIMEN INTEGRITY**

**SPECIMEN COLOR RELATED TO CONCENTRATION**

- Concentrated samples more reliable than disk samples
- Temp within 4 minutes of voiding is 80-100°F
- pH fluctuates within range of 4.5-9.0
- Creatinine varies with hydration
  - Normal urine
    - >25 mg/dl
  - Dilute: creatinine <20 mg/dl and specific gravity <1.005
  - Concentrated: Creatinine >2 mg/dL and specific gravity >1.020
  - Consistent with human urine
### Interpretation of UDT Results

**Positive Result**
- Demonstrates recent use
  - Most drugs in urine have detection times of 1-3 days
  - Chronic use of a drug may result in a positive for 1 week
- Does not diagnose
  - Drug use or dependence by laboratory
- Does not provide enough information to determine cause
  - Expected time, dose, or frequency of use

**Negative Result**
- Does not disprove drug use
  - May result from factors other than drug use
- May be due to medication, drug taking behavior
  - Drug interactions, medication, misuse of medication

### Kratom
*Mitragyna speciosa*

![Kratom Plant Image]

### Examples of Metabolism of Opioids

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Metabolite</th>
<th>Time to Peak</th>
<th>Metabolite</th>
<th>Time to Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>CODINE</td>
<td>MORPHINE</td>
<td>2-5 min</td>
<td>E-MAMP</td>
<td>1-2 min</td>
</tr>
<tr>
<td></td>
<td>HYDROCODONE</td>
<td></td>
<td>HYDROCODONE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OXYCODONE</td>
<td></td>
<td>OXYMORPHONE</td>
<td></td>
</tr>
</tbody>
</table>

### Abuse-Deterrent Formulation/Tamper Resistant (AD/FR) Opioids
- Response to growing non-medical use problem
- An ER/FR opioid with physical barrier to deter extraction
  - Likely to be crushed, popped, or snorted
  - Consider as one part of an overall strategy
  - Mixed evidence on the impact of AD/FR on misuse
  - Remember overdose is still possible if taken orally in excessive amounts

### Abuse Deterrent Opioids
- Oxycodeone/naloxone ER
  - Targin ER®
  - Buprenorphine/naloxone
  - Generic
  - Suboxone®
  - Zubsolv®
  - Bunavail®
- Morphine sulfate/naltrexone ER
  - Embeda®
- Oxycodeone/naltrexone ER
  - Truvada ER®

*Thank et al. Urinary Concentrations of Morphine and Codeine
Abuse Deterrent Opioids

- Hydrocodone ER
- Hyfiling ER®
- Zohydro ER®
- Vanirela ER®
- Hydromorphone ER
- Embeda®
- Oxycodeine ER* and IR**
  - *Oxycodone®
  - **Zyprexa®
- **Oxynovo®
- **Roxanol® (4/20/2017)
- Morphine sulfate ER
- Arpylo ER®

Naloxone

- Also Available
- Consider offering a naloxone prescription to all patients prescribed IR and ER opioid

Naloxone Regulation

- Effective Date: June 2018
- G2 Limited Immunity
  - Prescribers: Yes
  - Dispensers: Yes
  - Lay People: Yes
- Also Available
  - Without Prescription: Yes
  - To 3rd Party: Yes
  - By Standing Order: Yes
- Carried by First Responders: Yes


Benzhydrocodone

Hydrocodone

Apadaz Approved for the Short-Term Treatment of Acute Pain, MPR, February 23, 2018.

Benzhydrocodone

Hydrocodone

BE READY TO REFER

SUBSTANCE USE DISORDER

SAMHSA substance abuse treatment facility locator

https://treatment.samhsa.govlocator/home

HIGH RISK COMPLEX PATIENTS

High risk patients - check state regulations for requirements

SAMHSA = Substance Abuse and Mental Health Service Administration
PART 2
DISCONTINUING

REASONS FOR DISCONTINUING OPIOIDS

- Pain level decreased in stable patients
- Intolerable and unmanageable AEs
- No progress toward therapeutic goals
- Misuse
  - 1 or 2 episodes of increasing dose without prescriber knowledge
  - Sharing medications
  - Unapproved opioid use to treat another symptom (e.g., insomnia)
- Aberrant behaviors
  - Use of illicit drugs or prescribed opioids
  - Repeatedly obtaining opioids from multiple sources outside
  - Prescription forgeries
  - Multiple episodes of prescription loss
  - Diversion

CHAPTER 5 – PEARLS FOR PRACTICE

- Establish informed consent and PPA at the beginning
- Educate the whole team: patients, families, caregivers
- Refer if necessary
- Anticipate opioid-induced respiratory depression and concomitant
  - Follow patients closely during times of dose adjustments
  - Periodically evaluate functional outcomes
  - Discontinue opioids slowly and safely

TAPER DOSE WHEN DISCONTINUING

- Measure withdrawal symptoms and avoid overdosage
- Patient, family, and healthcare provider must agree with decision
- Develop a tapering schedule based on the patient’s needs
- Increase tapering over time to avoid withdrawal symptoms
- Reassess the patient’s tapering plan to ensure appropriate
- Counseling and education strategies needed

CHAPTER 6
SPECIAL POPULATIONS
OLDER ADULTS

RISK FOR RESPIRATORY DEPRESSION
- Age-related changes in distributor, metabolizer, excretor; absorption less affected

MONITOR
- Initiation and titration
- Concomitant medications (polypharmacy)
- Falls risk, cognitive change, psychosocial status
- Reduce starting dose to 0.5 to 1.25 the usual dosage in debilitated, non-ambulatory patients
- Start low, go slow, but GO
- Patient and caregiver reliability/risk of diversion

ROUTINELY INITIATE A BOWEL REGIMEN.

WOMEN WITH CHILDBEARING POTENTIAL

KNOW THE REPRODUCTIVE PLANS AND PREGNANCY STATUS OF YOUR PATIENTS
- 40% of women with childbearing potential are prescribed opioids
- Opioid exposure during pregnancy causes increased risk for fetus
- Most women do not know they are pregnant in first few weeks
- Therefore all women of childbearing age are at risk
- No adequate nor well-controlled studies of opioids for pain in pregnancy

THE PREGNANT PATIENT

Potential risk of opioid therapy to the newborn is neonatal opioid withdrawal syndrome

GIVEN THESE POTENTIAL RISKS, CLINICIANS SHOULD
- Counsel women of childbearing potential about risks and benefits of opioid therapy during pregnancy and after delivery
- Encourage minimization of opioid use during pregnancy, unless potential benefits outweigh risks to fetus
- Refer to a high risk OB/Gyn who will ensure appropriate treatment for the baby

FEDERAL AND STATE REGULATIONS

Comply with federal and state laws and regulations that govern the use of opioid therapy for pain

FEDERAL
- Code of Federal Regulations, Title 21 Section 1308 defines and regulates the DEA registration process for pain management
- United States Code (USC) - Controlled Substances Act, Title 21, Section 829: regulations

STATE
- Database of state statutes, regulations, and policies for pain management

CHAPTER 7

KNOW YOUR FEDERAL STATE LAWS
CHAPTER 8
COUNSELING PATIENTS AND CAREGIVERS

COUNSEL PATIENTS ABOUT PROPER USE

EXPLAIN

- Inform prescriber of ALL meds being taken
- Warn patients not to abruptly discontinue or reduce dose
- Risk of falls
- Caution with operating heavy machinery and when driving
- Sharing or selling opioids can lead to others' deaths and is against the law

OPINDS CAN CAUSE DEATH EVEN WHEN TAKEN PROPERLY

- Signs/symptoms are respiratory depression, gastrointestinal obstruction, allergic reactions

WARN PATIENTS

Never break, chew, crush, or add an oral ER/ELA lozenge or extended-release patch to a drink or paper towel. Proper disposal is important to prevent accidental ingestion by children.

Use of CNS depressants or alcohol with ER/ELA opioids can cause overdose & death
- Use with alcohol may result in rapid reactions and absorption of a potentially fatal dose of CR/ER opioids
- CNS depression includes sedation, hypnosis, and amnesia, illegal drugs

PRODUCT-SPECIFIC INFORMATION

- About the IR or ER/ELA opioid (especially when converting)
- Take opioid as prescribed
- Adhere to dose regimen
- How to handle missed doses
- Notify prescriber if pain not controlled
- Call prescriber for options on side effect management

USE PATIENT COUNSELING DOCUMENT

DOWNLOAD:

ORDER HARD COPIES:
www.cpr4.com/store/category/counseling documents

COUNSEL PATIENTS ABOUT PROPER USE (continued)

EXPLAIN

- Tell patients and caregivers, medications must be kept in a locked container
- Will periodically assess for benefits, side effects, and continued need for IR/ER/ELA opioids
- Need for re-evaluation of underlying medical condition if the clinical presentation changes over time

OPINDS SHOULD BE STORED IN A SAFE AND SECURE PLACE

- Away from children, family members, visitors, and pets
- Safe from theft

COUNSEL PATIENTS ABOUT PROPER USE (continued)

EXPLAIN

- Read the ER/ELA opioid Medication Guide received from pharmacy every time an ER/ELA opioid is dispensed

REMEMBER PATIENT CAREGIVERS TO

- City of Hope, 2016

COUNSEL PATIENTS ABOUT PROPER USE (continued)

EXPLAIN

- City of Hope, 2016
### OVERDOSE POISONING, CALL 911

- Person cannot be aroused or awakened or is unable to talk
- Any trouble with breathing, heavy snoring is warning sign
- Gurgling noises coming from mouth or throat
- Body is limp, seems lifeless; face is pale, clammy
- Fingernails or lips turn blue/purple
- Slow, unusual heartbeat or stopped heartbeat

### REMEMBER...

**STEP 1: MONITOR**
- Note how many pills in each prescription
- Keep track of dosage and refills
- Make sure everyone in the house knows

**STEP 2: SECURE**
- Keep meds in a safe place (lock drawers)
- Encourage parents of your teens friends to secure their prescriptions

**STEP 3: DISPOSE**
- Discard unused or unused meds
- Consult P&L for disposal

### TALK WITH YOUR PATIENTS WHO ARE PARENTS

- Consider the behavior you are modeling
- 49% of parents have taken pain medications without a prescription at some point
- 11% have given their children pain medications without a prescription
- Teens report that their parents do not talk with them about prescription drug rules
- Evidence suggests that pre-college parental conversation helps reduce high-risk substance abuse among college students

### RX OPIOID DISPOSAL

New "Disposal Act" expands ways for patients to dispose of unwanted/expired opioids

**DECREASE AMOUNT OF OPIOIDS INTRODUCED INTO THE ENVIRONMENT, PARTICULARLY INTO WATER**

**Collection receptacles**
Call DEA Registration Call Center at 1-800-882-5639 to find a local collection receptacle

**Mail-in postage**
Obtained from authorized collectors

Look for local take back programs
- Participating by dropping off prescription medication
- Participating by properly disposing

### OTHER METHODS OF OPIOID DISPOSAL

- Take drugs out of original containers
- Store in existing medicine or other container
- Remove identifying information on label

### SUBSTANCES PARENTS HAVE DISCUSSED WITH TEENS

<table>
<thead>
<tr>
<th>Substance</th>
<th>% of Teens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beer alcohol</td>
<td>51%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>27%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>16%</td>
</tr>
<tr>
<td>Opioid prescription</td>
<td>86%</td>
</tr>
<tr>
<td>Any Rx drug used w/o doctors Rx</td>
<td>72%</td>
</tr>
<tr>
<td>Heroin</td>
<td>27%</td>
</tr>
<tr>
<td>Methadone</td>
<td>27%</td>
</tr>
<tr>
<td>Rxs with markings</td>
<td>10%</td>
</tr>
<tr>
<td>Steroids w/o doctors Rx</td>
<td>70%</td>
</tr>
<tr>
<td>Inhalers</td>
<td>14%</td>
</tr>
</tbody>
</table>

*% of teens whose parents have discussed*
CHAPTER 9 — PEARLS FOR PRACTICE

- Use formal tools (PHAs, rounding documents) to educate patients and caregivers
- Emphasize safe storage and disposal to patients and caregivers
- Consider co-prescribing naloxone

CHAPTER 9

DRUG CLASS CONSIDERATIONS

- Concurrent use with other CNS depressants can increase risk of respiratory depression, hypotension, profound sedation, or coma
- Reduce initial dose of one or both agents
- May enhance nrem sleep by blocking action of natural sleep-related neuropeptides and increase respiratory depression
- Avoid concurrent use of parabanic agents or modest to moderate dose of full opioid agonist
- May reduce analgesic effect and form precipitate withdrawal
- Concurrent use with antiemetics or medication increases risk of urinary retention and severe constipation
- May lead to paradoxical effects

FDA: PRESCRIPTION DRUG DISPOSAL

- As soon as they are no longer needed
- Includes transdermal adhesive skin patches
- Used patch (3 days) still contains enough opioid to harm/kill a child
- Dispose of used patches immediately after removing from skin
- Fold patch in half so sticky sides meet, then flush down toilet
- Do NOT place used or unneeded patches in household trash
- Buprenorphine (buprenorphine transdermal system) exception: can seal in Patch-Disposal Unit provided and dispose of in trash

FOR SAFER USE: KNOW DRUG INTERACTIONS, PK, AND PD

- CNS depressants can potentiate sedation and respiratory depression
- Use with MAOIs may increase respiratory depression
- Can reduce efficacy of antipsychotics, mood stabilizers
- Multidose use can increase
- Drugs that inhibit or reduce P450 enzymes can increase
- Lower blood levels of some opioids

TRANSDERMAL/TRANSMUCOSAL DOSAGE FORMS

Do not cut, damage, chew, or swallow

- Can impair or delay systemic exposure
- Potentially reduce dose of opioid
- Monitor patients with fever, the signs or symptoms of accidental opioid exposure
- Most fentanyl patches are not safe for use in children

DRUG INTERACTIONS COMMON TO OPIOIDS

- Avoid concomitant use of parabanic agents or modest to moderate dose of full opioid agonist
- May reduce analgesic effect and form precipitate withdrawal

*Dependence: Methadone, buprenorphine/lanclonate
CONSIDERATIONS FOR CLINICIANS

- Use available scientific evidence, advise patients
- Inform about potential effects, AE's mostly mild and well tolerated (cough, anxiety)
- Screen for potential misuse/abuse, diversion
- Set treatment goals, use PPA
- Encourage patients to keep notes, discuss with them
- Document everything
- Regular re-evaluation
- Consider periodic UDTs
- Discontinue if not helpful moving toward goals
- Eddibles are the fastest growing delivery system
- No well controlled studies on the combined use of opioids and cannabis


YOUR PARTICIPATION IS IMPORTANT

Thank you for completing the post-activity assessment for the CDS RE session

Your participation in this assessment allows CDS RE to report de-identified numbers to the FDA

A strong show of engagement will demonstrate that clinicians have voluntarily taken this important education and are committed to patient safety and improved outcomes

THANK YOU!

SUMMARY

Prescription opioid abuse and overdose is a national epidemic, Clinicians must play a role in prevention.

- Anybody, anybody, is at risk for treatment with opioids
- Addicting therapy, and the risks are significant
- Patients and caregivers need to be educated on personal use and diversion
- Be familiar with approved and product specific drug information

THANK YOU!
WWW.CORE-REMS.ORG

Our session stops here, but your review continues...

Refer to Appendix 1 for specific drug information on ER/LA opioid analgesic products

For detailed information, prescribers can refer to prescribing information available online via CDFlabs at www.fda.gov/medwatch or Drugs@FDA at www.fda.gov/medwatch

Appendix 1. Drug Specific Slides
Methadone Hydrochloride Tablets (Dolophine) continued

- For refer to full PI

Product specific safety instructions

- CIQ prolongation & toxicity de poince
- Peak respiratory depression occurs later & persists longer than analgesic effect
- Cautions may increase during pregnancy
- False-positive UDT possible

- Varies depending on patient's prior opioid experience

Fentanyl Transdermal System (Duragesic), continued

Specific contraindications:
- Patients who are not opioid tolerant
- Management of:
  - Acute or exacerbation of patient's chronic pain
  - Patient with painful malignant disease
- Non-opioid pain: use patient for 2 days
- Non-surgical pain: use patient for 4 days
- Med. pain

Drug interactions

- CYP3A4 inhibitors may increase fentanyl exposure
- CYP3A4 inducers may decrease fentanyl exposure
- Discontinuation of concurrent CYP3A4 inhibitors may increase fentanyl plasma concentration

opioid tolerance

- All done indicated by opioid-tolerant patients only

Product specific safety considerations

- Accidental exposure due to secondary exposure to swallowed/diluted application site
- Irritated drug exposure to increased one body temp or liver
- Reactions
- Application site reactions

Relative potency:

- See individual PI for conversion recommendation from prior opioid

Methadone Hydrochloride Tablets (Dolophine)

Dosage interval

- Every 9 to 12 h

- Initial dose in opioid non-tolerant patients 2.5 – 10 mg
- Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose & death. Use low doses according to table in full PI
- Titrate slowly with dose increases no more frequent than every 3-5 d.
- Because of high variability in methadone metabolism, some patients may require substantially longer periods between dose increases (up to 12-d)
- Higher inter-patient variability in absorption, metabolism, & relative analgesic potency
- Opioid denervation or maintenance treatment only provided in a specially certified opioid (opioid) treatment program (e.g., patients only)

Drug interactions

- Pharmacokinetic drug-drug interactions w/ methadone are complex
  - CYP1A2 inhibitors may decrease methadone levels
  - CYP2B6 inhibitors may increase methadone levels
  - Anticonvulsants may decrease methadone levels
- Potentially nephrotoxic agents may increase risk for CIQ prolongation & toxicity de poince
- Benzodiazepines may increase respiratory depression

Morphine Sulfate ER-Naltrexone (Embeda)

Capsules 20 mg 0.9 mg, 30 mg 1.2 mg, 50 mg 2.4 mg, 60 mg 2.4 mg, 80 mg 3.2 mg, 100 mg 4 mg

Dosage interval

- Once a day or every 12 h

- Initial dose 15 to 20 mg/12 mg
- Titrate using a minimum of 12 mg increments
- Swallow capsules whole do not chew, crush, or dissolve
- Crushing or chewing will release morphine, possibly resulting in toxic overdose, & naltrexone, possibly resulting in withdrawal symptoms
- May open capsules & sprinkle on food for patients who can swallow
- AID without choosing, see below

Drug interactions

- Alcohol beverages or medications we should may result in rapid release of absorption of potentially fatal dose
- Naltrexone may decrease the increase absorption/micropoly of morphine by 3-fold

- 100 mg qid opiate for use in opioid-tolerant patients only

Fentanyl Transdermal System (Duragesic)

12.5, 25, 37.5, 50, 62.5, 75, 87.5, and 100 mcg/h

("These strengths are available only in generic form"

Patient general

- Use product-specific information for dose conversion from prior opioid
- Hepatic or renal impairment: use 50% of dose if mild/moderate, avoid use if severe
- Application:
  - Apply to intact skin
  - Avoid areas with a lot of hair
  - Avoid body sites that are hairy or have a lot of hair
  - Rotate site of application
  - Titrate in a minimum of 7.5 mg increments between dose adjustments
  - Do not cut
  - Avoid exposure to heat
  - Avoid accidental contact when handling or carrying for children
  - Dispose of unused patches: fold adhesive side together & flush down toilet

Hydromorphone Hydrochloride (Exalgo)

ER Tablets 8 mg, 12 mg, 16 mg, 32 mg

Dosage interval

- Once a day

- Use conversion ratio in individual PI
- Start patients w/ moderate hepatic impairment on 25% dose prescribed for patient at normal function
- Renal impairment, start patients w/ moderate on 50% of patients w/ severe on 75% dose prescribed for patient at normal function
- Titrate in increments of 4-8 mg using a minimum of 3-4 d intervals
- Swallow tablets whole do not chew, crush, or dissolve
- Do not use in patients w/ sulfa allergy (contains sodium metabisulfite)

Drug interactions

- More

- All doses are indicated by opioid-tolerant patients only

Product specific safety considerations

- Allergic manifestations to sulfa component
- + 5 1 prn morphone to hydromorphone oral dose ratio, use conversion recommendations in individual product information

Relative potency:

- See individual PI for conversion recommendations from prior opioid
**Oxycodone (Xtampza ER)**

**ER Capsules 9 mg, 13.5 mg, 18 mg, 27 mg, 36 mg**

**Dosing interval:**
- Every 12 h

**Key instructions:**
- Opioid naive and non-tolerant: initiate with 9 mg every 12 h.
- Titrates using a maximum of 1:2:1 intramix.
- Take with some form of food in order to ensure consistent plasma levels.
- Maximum daily dose: 279 mg (9 mg x 36 mg), safety of excipients not established for higher doses.
- May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without choking, or immediately.
- May also be administered through a NG or G tube feeding tube.
- Hepatic impairment: initiate therapy at 1/3 to 1/2 usual dose.
- Renal impairment: creatinine clearance >40 mL/min, follow conservative approach.

**Drug interactions:**
- CYP3A4 inhibitors may increase hydrocodone exposure.
- CYP3A4 inducers may decrease hydrocodone exposure.

**Opioid tolerant:**
- A single dose >36 mg or a total daily dose >72 mg for opioid-tolerant patients only.

**Product-specific safety concerns:**
- None

**Relative potency oral morphine:**
- There are no established conversion ratios for Xtampza ER, defined by clinician.

---

**Naloxone (Narcan)**

**Dosing interval:**
- 8 mg or 50 mg: onset 2-5 minutes, duration 45 min
- 0.4 mg or 2 mg: onset 1-2 min, duration 45 min
- 1 mg or 5 mg: onset 3-5 min, duration 2 hours

**Key instructions:**
- Monitor respiratory rate.
- Monitor level of consciousness for 3-4 hours after expected peak of blood concentration.
- Note: reversal of anesthesia will occur.
- Lager doses required to reverse effects of hypnotic, sedation, muscle paralysis, or general anesthesia.

**Drug interactions:**
- May antagonize effects of opioids
- May have a synergistic effect with other CNS depressants.

**Opioid tolerant:**
- Assess sign and symptoms of opioid withdrawal, may occur w/ 0.2-2 hr.
- May precipitate seizures, abnoraul movements, increased BP temperature.
- Brevetax, 10% naloxone dose, in opioid resistant & degree of dependence.

**Product-specific safety concerns:**
- Ventricular arrhythmias, hypertension, hypotensive, acute & chronic.
- As naloxone plasma levels decrease, sedation from opioid overdose may increase.

---

**Hydrocodone Bitartrate (Zohydro ER)**

**ER Capsules 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg**

**Dosing interval:**
- Every 12 h

**Key instructions:**
- Initial dose in opioid non-tolerant patient is 10 mg.
- Titrate in increments of 10 mg every 3-7 day intervals.
- Small capsules whole (do not chew, crush, or dissolve).

**Drug interactions:**
- Alcohol/benzodiazepine interaction may result in rapid release & absorption of a potentially fatal dose of hydrocodone.
- CYP3A4 inhibitors may increase hydrocodone exposure.

**Opioid tolerant:**
- Single dose >40 mg total daily dose >60 mg for use in opioid tolerant patients only.

**Product-specific safety concerns:**
- None

**Relative potency oral morphine:**
- Approximately 1.5-1 oral morphine to hydrocodone oral dose ratio.

---

**Appendix 2. Detailed Disclosure Information for CO*RE Staff and Faculty**

The following individuals disclose no relevant financial relationships:

**Faculty Advisory Panel & Reviewer COI**

<table>
<thead>
<tr>
<th>Faculty Advisor Panel</th>
<th>Advisor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steven Levin, MD</td>
<td>Clinical Professor of Family Medicine, University of California San Diego School of Medicine</td>
</tr>
<tr>
<td>John Onder, MD</td>
<td>Associate Professor and Chief Academic Officer, Western Kentucky University College of Medicine</td>
</tr>
<tr>
<td>Cynthia Suber, MD, PhD</td>
<td>Associate Professor and Chair, Department of Anesthesiology, University of Pittsburgh School of Medicine</td>
</tr>
<tr>
<td>Marcus Goldstein, MD, PhD</td>
<td>Professor and Chair, Department of Anesthesiology, University of California San Diego School of Medicine</td>
</tr>
<tr>
<td>Eric W. Brown, MD, PhD</td>
<td>Professor and Chair, Department of Anesthesiology, University of California San Diego School of Medicine</td>
</tr>
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**External/Consulting Relationships:**

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<tbody>
<tr>
<td>Robert Saltzberg, MD, PhD</td>
<td>Assistant Professor, Department of Anesthesiology, University of California San Diego School of Medicine</td>
</tr>
<tr>
<td>Donald B. Cleare, MD, PhD</td>
<td>Professor, Department of Anesthesiology, University of California San Diego School of Medicine</td>
</tr>
</tbody>
</table>

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**The following individuals disclose no relevant financial relationships:**

**CO*RE Partner Staff COI**

<table>
<thead>
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<th>Advisor</th>
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<tbody>
<tr>
<td>Michael A. Friedman, MD</td>
<td>President &amp; Chief Executive Officer, California Pacific Medical Center</td>
</tr>
<tr>
<td>Bruce Brown, MD</td>
<td>President &amp; Chief Executive Officer, Desert Valley Hospital</td>
</tr>
<tr>
<td>David E. Holmes, MD, PhD</td>
<td>President &amp; Chief Executive Officer, Arrowhead Regional Medical Center</td>
</tr>
<tr>
<td>John R. Kato, MD, PhD</td>
<td>President &amp; Chief Executive Officer, Valley Presbyterian Hospital</td>
</tr>
<tr>
<td>Jennifer L. Whitaker, MD</td>
<td>President &amp; Chief Executive Officer, Cone Health</td>
</tr>
<tr>
<td>Susan M. O'connor, MD, PhD</td>
<td>President &amp; Chief Executive Officer, Providence Saint John Hospital</td>
</tr>
</tbody>
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The following individuals disclose no relevant financial relationships:

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<tr>
<td>Optima Health</td>
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<tr>
<td>InterStudy</td>
<td>InterStudy Laboratory Services</td>
</tr>
<tr>
<td>Health Policy</td>
<td>Henry J. Kaiser Family Foundation</td>
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</table>

ER/LA Opioids REMS Knowledge Test

1. A 67-year-old man with chronic back pain (L4/L5) has been taking an opioid for 1 year. His physical examination shows no signs of opioid use. His recent lab work is normal. He has been taking 60 mg of oxycodone ER daily. His doctor wants to switch him to ER/LA.

A. Advise the patient to take one dose of oxycodone ER with food on the first day.
B. Advise the patient to take one dose of oxycodone ER with food on the first night.
C. Advise the patient to take one dose of oxycodone ER with food on the first week.
D. Advise the patient to take one dose of oxycodone ER with food on the first month.

2. The patient is switched to oxycodone ER and is advised to take the first dose with food. The patient returns the next day with breakthrough pain. The patient used to take a 10 mg oxycodone ER before switching to oxycodone ER.

A. Advise the patient to take an additional dose of oxycodone ER as needed.
B. Advise the patient to take another 10 mg oxycodone ER with food.
C. Advise the patient to take another 15 mg oxycodone ER with food.
D. Advise the patient to take another 30 mg oxycodone ER with food.

3. The patient’s pain is still not controlled. The patient is advised to take another 10 mg oxycodone ER with food. The patient returns the next day with breakthrough pain again.

A. Advise the patient to take another 15 mg oxycodone ER with food.
B. Advise the patient to take another 30 mg oxycodone ER with food.
C. Advise the patient to take another 45 mg oxycodone ER with food.
D. Advise the patient to take another 60 mg oxycodone ER with food.

4. The patient is now switching to ER/LA and is started on ER/LA 60 mg.

A. Advise the patient to take one dose of ER/LA 60 mg with food on the first day.
B. Advise the patient to take one dose of ER/LA 60 mg with food on the first night.
C. Advise the patient to take one dose of ER/LA 60 mg with food on the first week.
D. Advise the patient to take one dose of ER/LA 60 mg with food on the first month.

5. The patient’s pain is still not controlled. The patient is advised to take another dose of ER/LA 60 mg.

A. Advise the patient to take another ER/LA 30 mg with food.
B. Advise the patient to take another ER/LA 45 mg with food.
C. Advise the patient to take another ER/LA 60 mg with food.
D. Advise the patient to take another ER/LA 75 mg with food.

ER/LA Opioids REMS Knowledge Test

6. A 51-year-old woman with chronic low back pain (L4/L5) has been taking an opioid for 1 year. Her physical examination shows no signs of opioid use. Her recent lab work is normal. She has been taking 60 mg of oxycodone ER daily. Her doctor wants to switch her to ER/LA.

A. Advise the patient to take one dose of oxycodone ER with food on the first day.
B. Advise the patient to take one dose of oxycodone ER with food on the first night.
C. Advise the patient to take one dose of oxycodone ER with food on the first week.
D. Advise the patient to take one dose of oxycodone ER with food on the first month.

7. The patient is switched to oxycodone ER and is advised to take the first dose with food. The patient returns the next day with breakthrough pain. The patient used to take a 10 mg oxycodone ER before switching to oxycodone ER.

A. Advise the patient to take an additional dose of oxycodone ER as needed.
B. Advise the patient to take another 10 mg oxycodone ER with food.
C. Advise the patient to take another 15 mg oxycodone ER with food.
D. Advise the patient to take another 20 mg oxycodone ER with food.

8. The patient’s pain is still not controlled. The patient is advised to take another 10 mg oxycodone ER with food. The patient returns the next day with breakthrough pain again.

A. Advise the patient to take another 15 mg oxycodone ER with food.
B. Advise the patient to take another 20 mg oxycodone ER with food.
C. Advise the patient to take another 25 mg oxycodone ER with food.
D. Advise the patient to take another 30 mg oxycodone ER with food.

9. The patient is now switching to ER/LA and is started on ER/LA 60 mg.

A. Advise the patient to take one dose of ER/LA 60 mg with food on the first day.
B. Advise the patient to take one dose of ER/LA 60 mg with food on the first night.
C. Advise the patient to take one dose of ER/LA 60 mg with food on the first week.
D. Advise the patient to take one dose of ER/LA 60 mg with food on the first month.

10. The patient’s pain is still not controlled. The patient is advised to take another dose of ER/LA 60 mg.

A. Advise the patient to take another ER/LA 30 mg with food.
B. Advise the patient to take another ER/LA 45 mg with food.
C. Advise the patient to take another ER/LA 60 mg with food.
D. Advise the patient to take another ER/LA 75 mg with food.
**CONFLICT OF INTEREST STATEMENT**

- Dr. Breining and Dr. Young have no conflicts of interest and no financial disclosures

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**OBJECTIVES**

- Discuss 2018 & 2019 West Virginia legislation pertinent to the practice of medicine and delivery of care regarding opioids
- To demonstrate specific statutory requirements including rules and regulations of the West Virginia Board of Pharmacy, West Virginia Board of Medicine and West Virginia Board of Osteopathic Medicine relating to controlled substance prescribers (WV-CSMP)
- To describe recent legislative changes; compliance with controlled substance laws and rules related to substance abuse and prescription drug abuse

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**2018 LEGISLATIVE SESSION**

- SB 273 The Opioid Reduction Act of 2018
- SB 442 Relating to prior authorizations
- HB 4336 Updating the schedule of controlled substances
- SB 401 Requiring specified coverage in health benefit plans for outpatient and inpatient treatment for substance abuse disorders
- SB 272 Relating generally to drug control introduced by request of Governor Justice
- HB 4197 Relating to emergency dispatch

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**SB 273 The Opioid Reduction Act of 2018**

- Limits initial prescriptions of controlled substances to certain patients
- Subsequent prescriptions also limited
- Does not apply to certain patients such as those under cancer treatment, in palliative care, in nursing homes, or established patients prior to January 1, 2018
- Requires narcotics contracts for any prescriptions exceeding 7 days whereby the patient is limited to receiving Schedule II drugs from one physician and pharmacy

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**The Opioid Reduction Act of 2018 (Cont.)**

- A breach of the contract may be a basis for termination of the relationship
- SB 273 strengthens existing law by requiring the Board of Pharmacy, upon consultation with affected professionals
- WVSSMA supported this bill and provided significant direction for policy makers relating to limitations on initial prescriptions for opioids
**SB 442 Relating to Prior Authorizations**

- Purpose of this bill was to establish universal forms and deadlines when a prior authorization is submitted
- Payers must respond to electronic prior authorization requests within 48 hours for urgent and within 7 days for non-urgent matters
- Passed the House and Senate unanimously
- Later vetoed by Governor Justice
- Expect this to be reintroduced and followed through in the upcoming session (see additional slides)

**HB 4336 Updating the Schedule of Controlled Substances**

- Amended certain schedules of controlled substances
- Among other things, added Gabapentin as a Schedule V controlled substance
- WVSMC supported this bill and engaged with lawmakers and their staff in the development of the underlying public policy for this legislation

**SB 401 Requiring Specified Coverage in Health Benefit Plans for Outpatient and Inpatient Treatment for Substance Abuse Disorders**

- Requiring specified coverage in health benefit plans for treatment of substance abuse disorders
- WVSMC supported this bill to promote the improvement in healthcare delivery for substance abuse

**SB 272 Relating to Drug Control Introduced by Request of the Governor**

- Require hospital emergency rooms and departments, as well as certain other law enforcement and medical care providers, to report suspected or confirmed drug overdoses to the Office of Drug Control Policy
- Permits counties experiencing drug overdoses higher than the national average to establish certain community-based recognition and response efforts and seek federal and private funding to implement these programs
- Requires all first responders, regardless of frequency of drug overdoses in their communities, to carry naloxone and be trained in its use

**HB 4197 Relating to Emergency Dispatch**

- Require persons employed to dispatch emergency calls in county emergency dispatch centers to complete a training course in emergency cardiovascular care for telephonic cardiopulmonary resuscitation
- There were disagreements between the two chambers over the extent of training and/or continuing education on CPR techniques that dispatchers were to complete
- Even though the bill passed out of the House and the Senate, the two chambers could not resolve this dispute and, the bill was not enacted

**2019 LEGISLATIVE SESSION**

- HB 2768 Corrections to the Opioid Reduction Act
- HB 3132 Relating to Medication Assisted Treatment
- HB 2351 Relating to Prior Authorizations
- SB 620 Requiring prescriptions to be made by electronic means
HB 2768 CORRECTIONS TO THE OPIOID REDUCTION ACT

- This bill corrects some of the technical errors in the Opioid Reduction Act of 2018. Most notably, it corrects the verbiage in the bill so that opioids are consistently defined as Schedule II opioids.
- Also requires that physical examinations that must be conducted by a physician when maintaining a patient on an opioid may be limited to the condition that the opioid is prescribed for.

HB 2768

- This eliminated some unintended consequences with the prescribing of ADHD medicine. ADHD medicine is not covered with this law.
- Also, the prescribing of benzodiazepines is now clarified as not covered by this law either.
- Later changes in the bill also clarified that the physical exam needs only to concentrate on the areas pertinent to the prescription of the opioid.
- Last year’s bill does not apply to patients admitted in the hospital.

HB 3132 RELATING TO MEDICATION-ASSISTED TREATMENT

- The bill encourages the development of more Medication-Assisted Treatment (MAT) by exempting those practices that have less than 30 patients in a MAT program from the onerous regulatory requirements of the Office of Health Facility Licensure and Certification.
- The bill requires that these small practices attest to OHPAC that they have completed training on addiction treatment.

HB 2331 RELATING TO PRIOR AUTHORIZATIONS (CARRIED OVER FROM 2018)

- The purpose of this bill was to require insurance carriers to develop prior authorization forms and create the capability to submit these forms electronically by July 1, 2020. This bill was actually more stringent than the previous one that the Governor vetoed the prior year.
- The bill mandates the use of NCPDP SCRIPT Standard ePA transactions.
- Requires the insurance provider to respond to a prior authorization request within 7 days.
- Two (2) days if the request is deemed urgent.

SB 620 REQUIRING ELECTRONIC PRESCRIPTIONS (DEAD)

- This bill would have required that all prescriptions be sent in electronically.
- There were some exceptions that allowed for temporary technological or electrical failure.
- There was a provision for a maximum of one year waiver for economical hardship or technological limitations.
- This would have created a great disadvantage and would have been costly for those physicians in rural areas who don't currently have an EMR that is capable of prescribing electronically.
- This bill was introduced on 3/15/19 and single reference to Senate Health. It never made it on the agenda and died a quiet death there.

Controlled Substance Monitoring Program

- CSMP is available at the website: https://www.csmp.wv.gov

- All licensees who dispense Schedule II, III and IV controlled substances to residents of West Virginia must provide the dispensing information to the West Virginia Board of Pharmacy (BOP) each 24 hour period.
Controlled Substance Monitoring Program (Cont.)

CSMP website can be accessed by:
- Physicians
- Pharmacists
- Dentists
- Veterinarians
- Physician Assistants
- Advanced Practice Registered Nurses
- Other Prescribers and Dispensers

Controlled Substance Monitoring Program (Cont.)

- The data is housed in a high security, HIPAA-compliant database within the state of West Virginia
- The data is accessible to Prescribers and Dispensers who have been credentialed and who agree to confidentiality requirements for access to and the use of this information

Controlled Substance Monitoring Program (Cont.)

- Prescribers and pharmacists authorized to access the patient information must certify before each search that they are seeking data solely for the purpose of providing healthcare to current patients
- Authorized users agree that they will not provide access to any other individuals, including members of their staff unless and until they are authorized as designees

CSMP 2018 Annual Report

- The number of Controlled Substances Monitoring Program (CSMP) users has more than quadrupled in the last four years, and utilization of the CSMP continues to grow
- The total number of controlled substance doses West Virginia patients received this year was 31.2 million less than in 2017, reflecting the second consecutive year with over a 31 million dose decrease
- The powerful opioid hydrocodone has shown the sharpest decline, with a 26% reduction from last year and a 62% reduction over the last seven years
- The CSMP recently began collecting data for Schedule V products, which includes drugs like gabapentin (Neurontin) and pregabalin (Lyrica)

CSMP 2018 Annual Report (Cont.)

- Currently sharing prescription data with the border states OH, VA, MD, KY and PA, in addition to 21 other states and DC
- CSMP Advisory and Database Review Committees meet regularly, and continue to monitor and assess PMP data, to proactively address potential drug diversion activities and to find ways to reduce the State's drug overdose problem
- 2017 West Virginia drug overdose deaths were a record high (1232), with heroin and fentanyl continuing to be the most commonly involved drugs in those deaths

CSMP 2018 Annual Report (Cont.)

- CSMP epidemiologists and data analysts are creating and maintaining numerous data maps and analyses to help identify potential issues with controlled substance prescribing and patient activity in West Virginia
- A new version of the CSMP was completed this year, which includes new functionality, easier access and enhanced data analytics
- The Board of Pharmacy has obtained a federal grant to provide CSMP data integrated into the workflow of pharmacists and prescribers through their electronic medical record and pharmacy record systems
Welcome to Pathways in Management
Osteoarthritis and Chronic Low Back Pain

Supported by an educational grant from Pfizer/Orly

Disclosures

Author Faculty: Pat and Sharon
Our Faculty have no relevant financial relationships to disclose.

Pat Cullison, DO
Benjamin Smith, PA-C
Doug Yancey, DO
Wendy Vossible, CHP, FCBP, FFM

Cheri Glass, MD

Curriculum Faculty:
Our clinicians have no relevant financial relationships to disclose.

Mary W. Weis, CHP, FACHBP
Jeff D. Decker, CHP
Christopher Larrson
Maria Michelle Lopez, HHP, BA

Heidi Riner

Dinda Robertson, HHP
Shelby B. Rodriguez, CHP, FACHBP

Pamela Zenzema, NHA, FIPA, FAAN, FAAH

Our Goal Is To Help You...

› Provide successful strategies and resources for the management of OA and CLBP
› Support the art and science of medicine
› Increase your knowledge and confidence in caring for patients with OA and CLBP
› Support a partnership between clinician and patient

Learning Objectives

This activity will improve your ability to:
Develop practical strategies to manage pain and improve function for patients with osteoarthritis (OA) and chronic low back pain (CLBP) by:

› Using appropriate assessment, management, and educational tools and resources to support the care of patients with OA and CLBP
› Assessing and implementing the nationally accepted guidelines and standards of care for OA and CLBP
› Describing pathophysiology so patients understand the etiology of their pain and treatment rationale
› Partnering with patients to establish positive and realistic goals of their care

Organization Abbreviations

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAFP</td>
<td>American Academy of Family Physicians</td>
</tr>
<tr>
<td>AOCP</td>
<td>American Academy of Orthopaedic Surgeons</td>
</tr>
<tr>
<td>ACCA</td>
<td>American College of Occupational and Environmental Medicine</td>
</tr>
<tr>
<td>ACIP</td>
<td>American College of Physicians (Internal Medicine)</td>
</tr>
<tr>
<td>ARS</td>
<td>American College of Radiology</td>
</tr>
<tr>
<td>ARHP</td>
<td>American College of Rheumatology</td>
</tr>
<tr>
<td>AHQ</td>
<td>Agency for Healthcare Research and Quality</td>
</tr>
<tr>
<td>AOA</td>
<td>American Osteopathic Association</td>
</tr>
<tr>
<td>AVS</td>
<td>American Venous Surgery Society</td>
</tr>
<tr>
<td>ACOA</td>
<td>American College of Osteopathic Anesthesiologists</td>
</tr>
<tr>
<td>AMTA</td>
<td>American Medical Technologists Association</td>
</tr>
<tr>
<td>AORTA</td>
<td>American Association of Rheumatology Therapists Association</td>
</tr>
<tr>
<td>ABRM</td>
<td>American Board of Regenerative Medicine</td>
</tr>
</tbody>
</table>

Supported by an educational grant from Pfizer/Orly
Throughout this Education

www.PathwaysInManagement.org

Prevalence in our Patients

Twenty-five most common diagnoses

1. Hypertension
2. Hyperlipidemia
3. Diabetes
4. Back pain
5. Anxiety
6. Obesity
7. Carpal tunnel
8. Reflux esophagitis
9. Respiratory problems
10. Hypertension
11. Visual refractive errors
12. General medical exam
13. Migraines
14. Fibromyalgia
15. Infection and fatigue
16. Pain in joints

2013 Data from Practice Fusion, USA

Patient 1: Sue with Knee Pain

- 62-year-old
- Knee OA >3 years
- BMI = 30
- No prescribed medications
- Tired OTC meds, weight management

Patient 2: Juan with Back Pain

- 53-year-old
- CLBP >3 years
- BMI = 39
- Tried OTC meds, weight management
- Pain is interfering with activities at home and work

Ask Yourself

What do you think when you see patients like Sue and Juan on your schedule?

- How confident are you that you will be able to make a noticeable difference in these patients' pain and function?
- What are your expectations for these patients?
- What do you think the patients' expectations are?

Let's start by reviewing the components of a good assessment ...
**Components of a Good Assessment**

- History
- Physical
- Diagnostics
- Labs
- Imaging
- Red Flags

Be thorough, don't assume.

**History and Physical**

<table>
<thead>
<tr>
<th>Knee Physical Exam</th>
<th>Back Physical Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redness/swelling</td>
<td>Rash</td>
</tr>
<tr>
<td>Palpable site of pain</td>
<td>Asymmetry</td>
</tr>
<tr>
<td>Effusion</td>
<td>Range of motion</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Palpate site of pain, check function</td>
</tr>
<tr>
<td>Identify any significant or abnormal findings</td>
<td>Neurologic</td>
</tr>
<tr>
<td></td>
<td>Identify any significant or abnormal findings</td>
</tr>
</tbody>
</table>

Example:

- Example:
  - Full Stanford Video Clip: https://www.youtube.com/watch?v=/y7dbH5Hb2h8

**Red Flags**

**INFECTION**
- Constitutional symptoms
- Axilla swelling/redness and heat
- Persistent fever for more than 3 weeks
- Night sweats
- New onset headaches

**AUTOIMMUNE/IMMUNE**
- Autoantibodies
- Sera levels
- Significant weight loss
- History of inflammatory bowel disease
- History of infections
- More than one joint involved

**CARCINOMA OF MARROW**
- History of cancer
- Unexplained weight loss
- Immunocompromise
- Unintentional weight loss
- Bone pain not improved with conservative management

**SPINE FRACTURE**
- History of significant trauma
- Fall or injury in elderly or presence of osteoporosis
- Fracture not identified

**CALCIFIED EPIDURAL SYMPTOMS OR SEVERE NEUROLOGIC COMPROMISE**
- Acute onset of severe back pain
- Unexplained weight loss
- Unintentional weight loss
- Significant neurological findings

**RED FLAGS**
- Major weakness in lower limbs

Adapted from A/AHNS Recommendations (2018)

**Functional and Pain Assessment**

**Functional Assessment**
- Becoming standard of care to assess and record a patient's function
- Trackability
- Can assess a wide range of function
- Can be performed by a variety of caregivers

**Pain Assessment**
- Standard of care
- Trackability

Integrated into EHRs

**Assess Function:**

**Brief Pain Inventory (BPI) Questionnaire**

**Pain Enjoyment General Activity (PEG)**

**Screen for Depression and Anxiety**

- Depression
  - Multiple tools available including:
    - PHQ-9
    - SCID
    - HAM-D
    - CES-D
    - Beck Depression Inventory
    - Geriatric Depression Scale
- Anxiety
  - GAD-7
- Somatization

Select the appropriate tools for your EHR and clinic setting.
**Possible Sources of Back Pain**

- Back Strain
- Disc herniation
- Osteoarthritis/spinal stenosis
- Spondylolisthesis
- Ankylosing spondylitis
- Infection
- Cancer
- Fracture
- Nonspinal causes: Including abdominal aortic aneurism, kidney stone, infection, or stomach ulcer.

**Imaging**

- **Knee**
  - Imaging not required to make diagnosis in typical presentations of OA (LoA III-IV).
  - Use conventional radiography prior to either imaging modalities (LoA II-IV).
  - Weight-bearing imaging key

- **Back**
  - Imaging should NOT be performed on early evaluations for acute LBP w/o red flag signs (CW).
  - Ok to x-ray due to chronicity of pain, even without red flags (ACRAd).
  - "Abnormal" findings are so common they are normal by age 40. (A2004).

Art vs. Science
For back pain refer to appropriate use criteria.


**ACR Radiology Appropriateness Criteria**

| Condition | Low Back Pain | Acute, subacute, or chronic unexplained low back pain or radiology.
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Rating</td>
<td>Criteria</td>
<td>Score</td>
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<tr>
<td>1</td>
<td>Hyperextension test (+)</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Hip flexion test (+)</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Tilt test (+)</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Straight leg raise test (+)</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>CT spine w/ and w/o contrast</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>MRI spine w/ and w/o contrast</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>MR spine w/ and w/o contrast</td>
<td>7</td>
</tr>
<tr>
<td>8</td>
<td>CT spine w/ and w/o contrast</td>
<td>8</td>
</tr>
</tbody>
</table>

Rating scale: 1. 1, 2, 3 clinically not appropriate; 4, 5, 6 likely appropriate; 7, 8, 9 likely appropriate.

**Imaging of the Low Back**

- Spine AP view
- Spine Lateral view

All these patients have back pain!

**Degenerative Disc Disease**

Among people over age 60, who do not have back pain, an MRI will find:

- 9 in 10 have disk degeneration
- 9 in 10 have disk signal loss (desiccation)
- 8 in 10 have disk height loss
- 8 in 10 have a bulging disk
- 8 in 10 have an annular fissure
- 8 in 10 have a disk protrusion
- 8 in 10 have facet degeneration
- 8 in 10 have spondylolisthesis

**Differential Diagnosis**

- **History**
  - Nothing remarkable
  - Nothing remarkable

- **Red Flags**
  - No red flags identified

- **Labs**
  - No labs

- **Imaging**
  - No imaging

Record Functional and Pain Assessment; Screen for Depression.
Goals in Setting Expectations

Positive approach
- OA (mild and moderate): Function can be improved, pain can be reduced
- Back: Assume the patient that LBP is common, has an excellent prognosis and, in most cases, is not debilitating on a long-term basis (ACOEM)

Patient-provider journey
- Build a therapeutic alliance, partner with and empower patients, work together—take time and “I’m here for you”, together identify what patients will do for themselves

Use multiple pathways and evidence-based strategies
- Blend science with the “art” of medicine

Focus on Return to Function

Target Improved Function
- At least as important as pain rating
- What is achievable?
- Is patient motivated?

Decreased Pain
- Is it realistic?
- If patients have linked the single goal of decreased pain to the goal of happiness, they may be unhappy while pursuing this goal despite other achievements or experiences

Guideline Considerations

What they tell us:
- Commonalities where authorities all agree
- Levels of evidence in recommendations

What they don’t tell us:
- The evidence is lacking, and more research is desperately needed (AAOS Knee OA)
- Absence of evidence ≠ absence of efficacy
- Controversies (e.g., injections for CLBP: evidence vs practice)
- Influence of reimbursement
OA Guidelines

<table>
<thead>
<tr>
<th>Organization</th>
<th>Year</th>
<th>Guideline</th>
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<tbody>
<tr>
<td>AAOP</td>
<td>2014</td>
<td>Reference AAOS Guideline</td>
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<tr>
<td>AAGS</td>
<td>2013</td>
<td>Knee non-arthroplasty</td>
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<td>ACODEM</td>
<td>2015</td>
<td>Knee arthroplasty</td>
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<tr>
<td>ACHS</td>
<td>2012</td>
<td>Recommendations for OA of hand, hip, knee</td>
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<tr>
<td>AHRQ (DHHS)</td>
<td>2017</td>
<td>OA knee</td>
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<tr>
<td>AHRQ (OMH)</td>
<td>2018</td>
<td>Non-pharmacological Treatment of Chronic Pain</td>
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<tr>
<td>Choosing Wisely</td>
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<td>Selected recommendations</td>
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OA Knee Guideline: AHRQ

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Short Term (≤ 3 mos)</th>
<th>Medium Term (3 - 12 mos)</th>
<th>Long Term (≥ 12 mos)</th>
<th>Function</th>
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<tbody>
<tr>
<td>Low-level Laser Therapy</td>
<td>Low</td>
<td>M</td>
<td>M</td>
<td></td>
</tr>
<tr>
<td>Spinal Manipulation</td>
<td>Low</td>
<td>M</td>
<td>S, M</td>
<td></td>
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<tr>
<td>Massage</td>
<td>Med</td>
<td>S</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Yoga</td>
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<td>S, M</td>
<td>S, M</td>
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<tr>
<td>Multidisciplinary Rehabilitation</td>
<td>Low - Med</td>
<td>S, M</td>
<td>S, M</td>
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<tr>
<td>Acupuncture</td>
<td>Low - Med</td>
<td>S, L</td>
<td>S</td>
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<tr>
<td>Mindfulness-based stress reduction</td>
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<td>S, L</td>
<td>S, M, L</td>
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<tr>
<td>Cognitive Behavioral Therapy</td>
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<td>S, M, L</td>
<td></td>
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<tr>
<td>Exercise</td>
<td>Low - Med</td>
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<td>S, M, L</td>
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CLBP Guidelines

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<tr>
<td>AAOP</td>
<td>2017</td>
<td>Revised ACP guideline</td>
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<td>Low Back Disorders (and algorithms)</td>
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<td>ACHS</td>
<td>2017</td>
<td>Low Back Pain</td>
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<tr>
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<td>2017</td>
<td>Appropriately use Corticosteroids</td>
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<tr>
<td>NPI</td>
<td>2017</td>
<td>Pharmacological Treatment of Chronic Pain</td>
</tr>
<tr>
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<td>Osteopathic Manipulation. LBP</td>
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<tr>
<td>OsteoChristianity</td>
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<td>Selected recommendations</td>
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CLBP Guideline: AHRQ

<table>
<thead>
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<th>Intervention</th>
<th>Short Term (≤ 3 mos)</th>
<th>Medium Term (3 - 12 mos)</th>
<th>Long Term (≥ 12 mos)</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multidisciplinary Therapy</td>
<td>Med</td>
<td>S, M, L</td>
<td>S, M, L</td>
<td></td>
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<tr>
<td>Acupuncture</td>
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<td>S, M, L</td>
<td>S, M, L</td>
<td></td>
</tr>
<tr>
<td>Mindfulness-based stress reduction</td>
<td>Low - Med</td>
<td>S, L</td>
<td>S, M, L</td>
<td></td>
</tr>
<tr>
<td>Cognitive Behavioral Therapy</td>
<td>Med</td>
<td>S, M, L</td>
<td>S, M, L</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>Low - Med</td>
<td>S, M, L</td>
<td>S, M, L</td>
<td></td>
</tr>
</tbody>
</table>

Algorithm Excerpt: Knee OA

ACODEM Recommends:

1. Consider activity modification, weight loss, NSAIDs, acetaminophen
2. Change NSAID
3. Consider viscosupplementation, injections, glucocorticoid injections
4. Consider surgical management, arthroplasty

ACODEM (https://www.acodem.org) is the knee algorithm.

Are there any algorithms we can use to guide us as we develop a treatment plan?

Algorithm (https://www.acodem.org) is the knee algorithm.
Low Back Algorithm

ACOEM Recommends

1. NSAIDs, topiramate, skeletal muscle relaxants, and carefully considered opioids for short term treatment
2. Consider yoga, spinal manipulative techniques, physical therapy
3. Consider duloxetine, cognitive behavioral therapy, and multidisciplinary rehabilitation
4. Keep active!
5. Patient education is key!

Evidence on Movement

Encourage active treatment plan, avoid prolonged bed rest or passive modalities (CW).

Knee

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Back</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients in a walking exercise program (ACOEM)</td>
<td>Nonpharmacologic should be first line therapy and include exercise (ACP)</td>
</tr>
<tr>
<td>Strong recommendation for cardiovascular and/or resistance land-based exercise, aquatic exercise, and weight loss (ACOEM)</td>
<td>Prescribe activity including progressive walking program (ACOEM)</td>
</tr>
<tr>
<td>Evidence supports exercise, including PF (AAOS)</td>
<td>Exercise has beneficial medium/long-term outcomes (AHRQ)</td>
</tr>
</tbody>
</table>

First Line Treatments

Knee

- Consider activity modification, weight loss (ACOEM)
- NSAIDs (ACOEM, ACP)
- Activity: walking program (ACOEM)

First line non-pharmacologic: include exercise, cognitive therapy, acupuncture, yoga, biofeedback, manipulation (ACP)

NSAIDs: acetaminophen

Side effects of NSAIDs including gastrointestinal, renal and cardiovascular toxicity should be considered before prescribing.

The best medication is one the patient will take.

Neuroanatomy of the pain pathway and analgesic targets in OA
**Medications**

<table>
<thead>
<tr>
<th>Knee</th>
<th>Back</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence-based medicine supported NSAIDs, tramadol (AAOS)</td>
<td>If non-pharmacological inadequate, move to pharmacological (NSAIDs first (ACP))</td>
</tr>
<tr>
<td>Little evidence for acetaminophen, aspirin, topical (AAOS)</td>
<td>Tramadol or diclofenac after NSAID (ACP)</td>
</tr>
<tr>
<td>Some recommendation to start with topical to minimize GI toxicity (Cochrane)</td>
<td>Do NOT use opiates first (CH)</td>
</tr>
<tr>
<td>No recommendation regarding opioid analgesics (ACRheum)</td>
<td>No evidence of benefit for acetaminophen, extended-release, TCA (ACP)</td>
</tr>
<tr>
<td>No recommendation regarding diclofenac (ACRheum)</td>
<td></td>
</tr>
</tbody>
</table>

**Knee Injections**

Knee Injections

- Some evidence for steroid injections (AAOS)
- No evidence-based value for viscosupplementation (hyaluronic acid) injections in improvement of function for moderate to severe knee OA (ACOS)
- No recommendation for intra-articular hyaluronic injections (ACRheum)

**Knee Recommendations**

<table>
<thead>
<tr>
<th>Knee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Either ice or heat can be helpful (ACOEM)</td>
</tr>
</tbody>
</table>

No recommendation for:

- Participation in balance exercises (alone or with strengthening exercises)
- Wearing lateral wedged insoles
- Receiving manual therapy alone (ACRheum)

**Adding Pharmacotherapy**

- Exercise only
- Exercise + OTC NSAIDs
- Exercise + Prescription
- Exercise + Other including injection referral

**Osteopathic Manipulative Treatment**

Osteopathic Manipulative Therapy (OMT) is "the therapeutic application of manually guided forces by an osteopathic physician to improve physiologic function and/or support homeostasis that has been altered by somatic dysfunctions." In OMT, a DO moves a patient’s muscles and joints using techniques that include stretching, gentle pressure, and resistance.

AOA consensus recommendations:

1. Evidence points in favor of using OMT to treat LBP
2. Greater benefit appears to be pain control + improvement in functionality

**Knee Bracing**

- Knee sleeves are controversial.
- Off-loader bracing can be helpful for moderate to severe cases (ACOEM).
- No recommendation for wearing knee braces, or using laterally developed patellar taping (ACRheum).
So many options to improve physical function are available. Where should I start?

Personalizing the Plan

Patient
- Move
- Water aerobics
- Heat and ice
- Knee braces
- Muscle movement and habit
- Core strengthening

Clinician
- Coach patient to behavior change
- Prescribe medications (anticoagulants, statins)
- Chronic Disease Management
- Prescribe medication

Community-based activities
- Silver Sneakers
- Walking program
- Insurance education

Clinic
- Use cardiac rehab
- List of community resources
- Health coach and case coordination

What is your Treatment Plan?

Engaging Sue and Juan

Communication approach
- Come alongside
- Motivational interviewing
- Patient education
- Use other professionals in your practice or community

Other Considerations:

Sue (Knee OA)
- QoL is more impacted?
- Has CVD and diabetes?
- Taking care of mom with Alzheimer's?

Juan (Back)
- Has work-related pain?
- Is sleep impaired?
- Lives on farm 30 miles from town?
- Wants to use CBD or medical marijuana?

How can I best manage patients like Sue and Juan in my office?

It's not just about the patients, but also about the clinicians.
Reframe success.
You may not totally fix the problem, but making a difference in some way is success.
"Losing 10% of weight or cutting down on smoking by a quarter."
Summary

- These are common conditions: approx 84% of adults experience low back pain within their lifetime and 60% over age 55 exhibit some OA.
- You can make a difference in your patient’s lives for a condition that may be frustrating!
- It’s not about eliminating disease, it is about the patient being able to achieve life goals.
- Build a therapeutic alliance with your patient through regular check-ins, and good problem solving.
- Imaging should be highly selective and not “routine.”
- Keep patients moving.
- Be creative in your recommendations.
- Art and science of medicine.
- Use medications appropriately.

Key Points

- You can make a difference in your patient’s lives for a condition that may be frustrating (for them AND you!)
- It’s not about eliminating disease, it is about the patient being able to achieve life goals.
- Partner with patients to reframe the conversation to focus on function (not pain) and find what motivates them to MOVE!

Monday in the Office

- Next: 10 patients
- Chart review:
  - Implement FES or another functional assessment
  - Implement exercise prescription
  - Patient education
  - Promote walk or back exercises or yoga program
  - Reduce number of patients receiving imaging for uncomplicated back pain (InCode OW Imaging on a bill)

Visit www.PathwaysInManagement.org

Thank you for attending!