Opioid Analgesics
Risk Evaluation and Mitigation Strategy (REMS)

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Educational Objectives

At the conclusion of this activity, participants should be able to:

• Identify risk factors and vulnerabilities associated with addiction to opioid analgesics and provide patient/caregiver counselling when necessary
• Discuss the components of an effective treatment plan, including patient interactions, treatment goals, and collaboration within the healthcare team
• Analyze the specific benefits and risks to initiating non-medication therapies before utilizing long-term medications
• Recognize patients who are candidates for treatment with nonopioid pharmacologic analgesics
• Explain the decision to initiate long-term opioid analgesics, including ER/LA opioids, with consideration to providing in-home naloxone
• Determine when referral to a pain specialist is appropriate for a patient with chronic pain
The Prevalence of Chronic Pain in the US Is High

- Approximately 100 million US adults experience chronic pain (33%)
- Consider appropriate nonpharmacologic, nonopioid options before starting opioids
- If an opioid is chosen consider benefit vs risk

Ensure availability of opioids for patients with pain

Establish systems of control to prevent abuse

Adapted


Treatment of Chronic Pain Is a Low Priority

Incidence of chronic pain in US is greater than diabetes, heart disease and cancer combined

PCP Perceptions of Chronic Conditions

Chronic Pain Affects Many Dimensions of Patient Life

Physical
• Function
• Activities of daily living
• Sleep/rest

Psychological
• Anxiety/Depression

Social
• Relationships
• Ability to show affection/sexual function
• Isolation


Chronic Noncancer Pain Prevalence Due to Age vs Cancer Pain

• Chronic noncancer pain in all adults over age 18 years
  – 15-20% prevalence
• Noncancer pain in 60 to 69 year olds (aging)
  – 78% prevalence
• Cancer pain
  – 65-85% prevalence in advanced cancer

Chronic Pain Landscape and Challenges

• Partial efficacy of all therapies
• Bothersome and dangerous adverse event profile
• Lack of potential cure
• Treatment focuses on palliative care, not prevention or coping
• Similar to approach taken with other chronic conditions (e.g. diabetes)
• Overriding goal is to help patients learn how to live with pain and improve quality of life

Barriers to Effective Pain Management

• Political
  – Attitudes, behaviors, expectations
  – Prescribing guidelines
• Insurance
  – Step therapy
  – Denials
• Legal
  – Fear of sanctions
• Lack of access to interdisciplinary pain management
Opioid Morbidity and Mortality
2017/2016 By the Numbers

2017
• 72,300 drug overdose deaths
• 49,000 opioid overdose deaths
• 29,400 fentanyl overdose deaths
• 15,900 heroin overdose deaths

20162,3
• 19,300 prescription opioid overdose deaths
• 3,280 methadone overdose deaths
• 52 million non-medical use all drugs
• 2.2 million non-medical use prescription opioids
• 1-8% become addicted
• 4% advance to heroin


The Need for Comprehensive Pain Education

• Two competing public health concerns
  1. The large number of Americans with acute and chronic pain
  2. The epidemic of prescription opioid abuse
• Healthcare providers need to understand
  1. All options to treat pain – nonpharmacologic, nonopioids
  2. Only use opioids when other treatments fail and benefits exceed risks
• With better understanding of treatment options, healthcare providers can counsel patients about options and provide strategies to reduce risk
Definitions and Mechanisms of Pain

IASP Definition of Pain

“An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”
Does Pain Have a Purpose?

- **Adaptive**
  - Protective to prevent further injury so reparation can begin
- **Maladaptive**
  - Sensitization of the nervous system may facilitate pain
  - Pain becomes the pathology generating spontaneous and exaggerated pain without a protective role
  - Chronic pain is not just acute pain which lasts a long time

Long-Term Consequences of Acute Pain

**Potential for Progression to Chronic Pain**

- Surgery or injury causes inflammation
- Peripheral Nociceptive Fibers
  - Transient Activation
  - Sustained Currents
- Sensitization
  - Peripheral Nociceptive Fibers
  - Sustained Activation
- Structural Remodeling
  - CNS Neuroplasticity
  - Hyperactivity
- ACUTE PAIN
- CHRONIC PAIN

References:
There are different “types” of pain, …not just different degrees of the same type.

Chronic Pain Conditions Can Be Classified Based on Type of Pain Pathophysiology

Three Main Types of Pain Pathophysiology

- **Nociceptive**: Pain related to damage of somatic or visceral tissue, due to trauma or inflammation
  - **EXAMPLES**: rheumatoid arthritis, osteoarthritis, gout

- **Neuropathic**: Pain related to damage of peripheral or central nerves
  - **EXAMPLES**: painful diabetic peripheral neuropathy (pDPN), postherpetic neuralgia

- **Sensory Hypersensitivity**: Pain without identifiable nerve or tissue damage; thought to result from persistent neuronal dysregulation, affective system disorder
  - **EXAMPLES**: Any pain

The Three Types of Pain, Separately or Together, Give Rise to Various Chronic Pain Conditions

Sensory Hypersensitivity

• Fibromyalgia
• Irritable bowel syndrome
• Functional dyspepsia
• Interstitial cystitis
• Neck and back pain without structural pathology
• Myofascial pain / Temporomandibular joint (TMJ) disorder

Nociceptive

• Gout
• Osteoarthritis
• Rheumatoid arthritis
• Tendonitis, bursitis
• Ankylosing spondylitis
• Tumor-related nociceptive pain
• Neck and back pain with structural pathology
• Sickle-cell disease
• Inflammatory bowel disease
• Postherpetic neuralgia
• Painful diabetic peripheral neuropathy
• Sclerosis/stenosis
• Spinal cord injury pain
• Tumor-related neuropathy
• Chemotherapy-induced neuropathy
• Small-fiber neuropathy
• Post-stroke pain
• Multiple sclerosis pain
• Persistent postoperative pain

Neuropathic

Chronic low back pain has been acknowledged to have multiple potential mechanisms and is often viewed as a prototypical “mixed-pain state”

Which Person Has Pain?
Acute Postoperative Pain Has Been Associated With Chronic Pain After Common Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Incidence of Chronic Postsurgical Pain</th>
<th>US Surgical Volumes (1000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td>57-62%</td>
<td>159</td>
</tr>
<tr>
<td>Breast surgery</td>
<td>27-48%</td>
<td>479</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>52-61%</td>
<td>Unknown</td>
</tr>
<tr>
<td>Inguinal hemia repair</td>
<td>19-40%</td>
<td>609</td>
</tr>
<tr>
<td>Coronary artery bypass</td>
<td>23-39%</td>
<td>598</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>12%</td>
<td>220</td>
</tr>
</tbody>
</table>

Factors correlated with the development of postsurgical chronic pain:
1. Nerve injury
2. Inflammation
3. Intense acute postoperative pain

Factors correlated with the development of chronic postsurgical pain:
1. Nerve injury
2. Inflammation
3. Intense acute postoperative pain

Severity of Acute Postoperative Pain Correlated With Development of Chronic Pain

- In the first postoperative week, thoracotomy patients who developed chronic pain (n=78)* vs those who did not (n=71) reported:
  - Greater incidence of acute pain (P=0.002)
  - More severe acute pain (P=0.0001)
  - Greater total amount of time spent having pain (P=0.02)
- The incidence of progression to chronic pain increased with the intensity of acute postoperative pain
- Genetic variation of BDNF** is associated with an increased risk of chronic postsurgical pain (Anesthesiology. 2018;128:587-597)

*Chronic pain assessed 6 months to 3.5 years postsurgery
**Brain-derived neurotrophic factor
Bio-Psycho-Social Model

Of all approaches to the treatment of pain, none has a stronger evidence basis for efficacy, cost-effectiveness than interdisciplinary care.

Establishing Pain Relief Goals

- Goals for pain management should be specific, measurable, and patient-centered.
- Goals focused solely on numeric pain ratings can be problematic.
- Clinical trials suggest that a 33% to 50% decrease in pain intensity is meaningful.
- Goal setting:
  - Collaborative, focus on functional improvement.
- Be realistic:
  - Eliminating pain is often not realistic.

Study results showed that a precipitous decrease in the number of interdisciplinary programs occurred in the U.S. between 1999 and 2012, except among the Veteran's Health Administration. During this same time period, the number of interdisciplinary programs in industrialized nations with National Health Services increased dramatically.


Assessing Patients in Pain
Pain Assessment

• Self report is the most reliable or unreliable measure of pain intensity as there are no biological markers of pain
• Simply worded questions and tools, which can be easily understood, are the most effective
• Most widely used pain intensity scales:
  – Numeric Rating Scale (NRS)
  – Verbal Descriptor Scale (VDS)
  – Faces Pain Scale-Revised (FPS-R)
• We must treat the patient, not a number!
• Focus is on functional restoration

Flaherty E. Try This: Best Practices in Nursing Care to Older Adults. 2007;7.

Elements of a Comprehensive Assessment

Use Appropriate Tools

• History/physical examination/diagnostic testing
• Be aware of risk of acute pain transitioning to chronic pain
• Psychosocial evaluation
• Risk identification
  – State prescription monitoring programs
• Special populations: pediatric, elderly, pregnancy

• State medical boards may have specific regulations, e.g., Medical Board of California:
  – History/Physical Examination
    • “A medical history and physical examination must be accomplished. This includes an assessment of the pain, physical and psychological function; a substance abuse history; history of prior pain treatment; an assessment of underlying or coexisting diseases or conditions; and documentation of the presence of a recognized medical indication for the use of a controlled substance.”
Perform Thorough Evaluation and Assessment of Pain

Seek objective confirmatory data

Components of patient evaluation for pain

Order diagnostic tests (appropriate to complaint)

General: vital signs, appearance, posture, gait, & pain behaviors

Musculoskeletal Exam
- Inspection
- Palpation
- Percussion
- Auscultation
- Provocative maneuvers

Neurologic exam

Cutaneous or trophic findings

Documentation Is Vital

- Clinical assessment
- Patient education
- Treatment agreement and informed consent
- Action plans and goals
- Periodic functional outcomes
- Monitoring for adverse events, including aberrant behaviors


Clinical Interview

Pain and Treatment History

Description of pain

<table>
<thead>
<tr>
<th>Location</th>
<th>Intensity</th>
<th>Quality</th>
<th>Onset/Duration</th>
<th>Variations / Patterns / Rhythms</th>
</tr>
</thead>
</table>

What relieves the pain?

What causes or increases pain?

Effects of pain on physical, emotional, and psychosocial function

Patient's pain & functional goals

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Pain Descriptors

<table>
<thead>
<tr>
<th>Ten Components</th>
<th>Questions to Ask</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. History of onset</td>
<td>How/when did your pain begin? What was the last time you were pain free?</td>
</tr>
<tr>
<td>2. Location</td>
<td>Where exactly is your pain?</td>
</tr>
<tr>
<td>3. Quality</td>
<td>What does it feel like (e.g., sharp, dull, burning, cramping)?</td>
</tr>
<tr>
<td>4. Intensity</td>
<td>How would you rate your pain now? When is pain the least? At the worst? On average? Use an intensity scale appropriate to patient’s language, development and cognitive level.</td>
</tr>
<tr>
<td>5. Temporal pattern</td>
<td>Is your pain constant or intermittent? If intermittent, frequency and duration of episodes; variability according to time of day, etc.</td>
</tr>
<tr>
<td>6. Aggravating factors</td>
<td>What factors make you pain worse?</td>
</tr>
<tr>
<td>7. Alleviating factors</td>
<td>What factors decrease your pain?</td>
</tr>
<tr>
<td>8. Associated symptoms</td>
<td>What other sensations are associated with your pain (e.g., nausea, vomiting, dizziness, weakness, incontinence, itching, vasomotor changes)?</td>
</tr>
<tr>
<td>9. Previous methods of treatment</td>
<td>What treatments have you tried for your pain, e.g., medications, behavioral strategies or alternative therapies such as acupuncture, massage, herbal therapies? How effective have they been?</td>
</tr>
<tr>
<td>10. Impact of pain on quality of life</td>
<td>What effect has your pain had on your quality of life? This information many not be feasible to gather on the initial evaluation, due to time or pain intensity, but should be gathered on subsequent patient contact. Areas to assess include mood, sleep, appetite, functional status/activities of daily living.</td>
</tr>
</tbody>
</table>
Pain Assessment Tools

• Brief Pain Inventory
  – Assesses severity and impact of pain on daily functions
  – Self-report or interview (5 min for short form; 10 min for long form)
  – Validated and available in many languages
  – Copyrighted but free for individual practice


• Universal Pain Assessment Tool
  – Visual / analog / linguistic pain scoring
  – Self-report or interview

Pain and Function Assessment Tools

• Graded Chronic Pain Scale
  – Pain and function assessment

Figure 2. Graded Chronic Pain Scale

http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf. Used for educational purposes only.

Primary Care Strategies

• If not already using pain assessment tools, then start with
  – Chronic Pain Scale
  – Assess pain and function at start and during therapy
• Consider having patients complete the Brief Pain Inventory at each visit while in the waiting room
Paradigm Shift from Reducing Pain to Increasing Function

- Pain relief should improve function
- Lack of functional improvement always indicates treatment failure or other problems, e.g., misuse, diversion, addiction, mood disorders, side effects, etc.

Outcomes to Assess

- Progress towards therapeutic goals
- Changes in functional status
- Presence of opioid-related adverse effects
- Changes in underlying pain condition
- Changes in medical or psychological comorbidities
- Opioid tolerance
- Aberrant behaviors, addiction, diversion
The Goal of **treatment** in chronic pain is to **Improve Function** and **Control the Pain** with minimal side effects.

**Multiple Pathways of Pain Transmission Provide Multiple Targets for Pain Relief**

**A Depiction of How Therapeutic Choices May Affect Pain Pathways**

**Inhibiting ascending pathways**\(^1\)-\(^4\),\(^6\)
- Opioids†
- Local anesthetics
- Antiepileptics\(^7\)
- NSAIDs/acetaminophen

**Enhancing descending pathways**\(^1\),\(^3\)-\(^5\)
- Norepinephrine reuptake inhibitors
- Serotonin reuptake inhibitors
- Tricyclic antidepressants
- Opioids†

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*Theoretical mechanisms of action
†It is well established that opioids inhibit the ascending transmission of nociceptive signals. Additional mechanisms have been reported in the literature, including the activation of descending inhibitory pathways and modulation of thymic system activity.*\(^1\),\(^3\),\(^4\),\(^6\)
Undertreatment of Pain May Involve Multiple Factors

Communication between physician and patient

Fear of disciplinary action or prosecution

Fear of addiction, tolerance & side effects

Potential for abuse

Socioeconomic and psychological factors

Lack of training in opioid titration

Poor patient knowledge

Governmental and public policy on payment for opioid analgesics

Physician factors

Patient factors

Combination of factors


Special Considerations: Pregnant Women

Managing Chronic Pain in Pregnant Women is Challenging, and Affects Both Mother and Fetus

• Potential risks of opioid therapy to the newborn include:
  – Low birth weight
  – Premature birth
  – Hypoxic-ischemic brain injury
  – Neonatal death
  – Prolonged QT syndrome
  – Neonatal opioid withdrawal syndrome

• Given these potential risks, clinicians should:
  – Counsel women of childbearing potential about risks & benefits of opioid therapy during pregnancy & after delivery
  – Encourage minimal/no opioid use during pregnancy unless potential benefits outweigh risks

• If chronic opioid therapy is used during pregnancy, anticipate and manage risks to the patient and newborns

Special Considerations: Children (<18 years)

- Safety and effectiveness of most ER/LA opioids unestablished
  - Pediatric analgesic trials pose challenges
  - Transdermal fentanyl approved in children aged ≥2 yrs
- Most opioid studies focus on inpatient safety
  - Opioids are common sources of drug error
- Opioid indications are primarily life-limiting conditions
  - Few children with chronic pain due to non-life-limiting conditions should receive opioids
- When prescribing opioids to children:
  - Consult pediatric palliative care team or pediatric pain specialist or refer to a specialized multidisciplinary pain clinic


Special Considerations: Elderly Patients

Does Patient Have Medical Problems That Increase Risk of Opioid-related AEs?

- Respiratory depression more likely in elderly, cachectic, or debilitated patients
  - Altered pharmacokinetics due to poor fat stores, muscle wasting, or altered clearance
  - Monitor closely, particularly when
    - Initiating & titrating ER/LA opioids
    - Given concomitantly w/ other drugs that depress respiration
  - Reduce starting dose to 1/3 to 1/2 the usual dosage in debilitated, non-opioid-tolerant patients
  - Titrate dose cautiously
- Older adults more likely to develop constipation
  - Routinely initiate a bowel regimen before it develops
- Is patient/caregiver likely to manage opioid therapy responsibly?

“Nothing is intrinsically good or evil but its manner of usage may make it so”

Thomas Aquinas

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk Factor</th>
<th>Score if Female</th>
<th>Score if Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History of Substance Abuse</td>
<td>Alcohol</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Illegal Drugs</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Prescription Drugs</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Personal History of Substance Abuse</td>
<td>Alcohol</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Illegal Drugs</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Prescription Drugs</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Age</td>
<td>Age 16-45 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>History of Preadolescent Sexual Abuse</td>
<td>ADD, OCD, Bipolar Disorder, Schizophrenia Depression</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Psychological Disease</td>
<td>Depression</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Total Risk Score

OCD, obsessive compulsive disorder.
SOAPP — Sample Questions

Please answer the questions below, using the following scale:
0 = Never, 1 = Seldom, 2 = Sometimes, 3 = Often, 4 = Very Often

1. How often do you have mood swings? 0 1 2 3 4
2. How often do you smoke a cigarette within an hour after you wake up? 0 1 2 3 4
3. How often have you taken medication other than the way that it was prescribed? 0 1 2 3 4
4. How often have you used illegal drugs (for example, marijuana, cocaine, etc) in the past five years? 0 1 2 3 4
5. How often, in your lifetime, have you had legal problems or been arrested? 0 1 2 3 4

Risk Factors for Aberrant Behaviors/Harm

BIOLOGICAL
- Age ≤45 years
- Gender
- Family history of prescription drug or alcohol abuse
- Cigarette smoking
- Sleep disorder

PSYCHIATRIC
- Substance use disorder
- Preadolescent sexual abuse (in women)
- Major psychiatric disorder (e.g., personality disorder, anxiety or depressive disorder, bipolar disorder)

SOCIAL
- Prior legal problems
- History of motor vehicle accidents
- Poor family support
- Involvement in a problematic subculture

Stratify Risk

Low Risk
- No past/current history of substance abuse
- Noncontributory family history of substance abuse
- No major or untreated psychological disorder

Moderate Risk
- History of treated substance abuse
- Significant family history of substance abuse
- Past/Comorbid psychological disorder

High Risk
- Active substance abuse
- Active addiction
- Major untreated psychological disorder
- Significant risk to self and practitioner

Consider referring high-risk patients or any patient you have concerns about to a pain specialist


Primary Care Strategies

- If not using any risk assessment tools, then start with
  - ORT to screen for potential for ADRBs
  - PHQ-9 to screen for depression
  - CAGE-AID to screen for alcohol and/or drug problems
  - PEG for pain, function, and quality of life
- For monitoring at follow-up visits, start with
  - 2-4 weeks determined by risk
- Check state prescription monitoring program at first visit and continuously monitor during treatment (interval often stipulated by medical board)
- Comply with local regulations and laws
Know the Risk Factors for Respiratory Depression

• Generally preceded by sedation and decreased respiratory rate
• Risk factors for respiratory depression include:

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Conditions/Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep apnea or a sleep disorder diagnosis</td>
<td>Morbid obesity with a high risk of sleep apnea</td>
</tr>
<tr>
<td>Risk increases with age (&gt;60)</td>
<td>No recent opioid use</td>
</tr>
<tr>
<td>Use of other sedating agents (CNS depressants),</td>
<td>Preexisting pulmonary or cardiac disease or dysfunction or major organ failure</td>
</tr>
<tr>
<td>such as benzodiazepines and alcohol</td>
<td>Smoking</td>
</tr>
<tr>
<td>Post-surgery (particularly upper abdominal or thoracic)</td>
<td></td>
</tr>
</tbody>
</table>


Components to an Effective Treatment Plan and General Principals of Nonpharmacologic Approaches
Principles of Pain Therapy Selection

- Standard of care for particular pain conditions and pain patients
- Consider therapies that may provide a better risk-benefit profile
- Patient comorbidities
- Ability of patient to adhere to the rules of therapy

Treatment Goals

**ACUTE PAIN**
- Facilitate recovery from the underlying injury, surgery, or disease
  - Reduce neuroendocrine stress
  - Minimize impact of pain on recovery
- Control and reduction of pain to acceptable level
- Minimize pharmacologic side effects
- Prevent chronic pain

**CHRONIC PAIN**
- Restore function
  - Physical, emotional, social
- Improve quality of life
- Decrease pain
  - Treat underlying cause where possible
  - Minimize medication use
- Correct secondary consequences of pain
  - Postural deficits, weakness, overuse
  - Maladaptive behavior, poor coping


Multimodal Therapeutic Pain Strategies

Therapeutic Considerations
Setting Priorities

- Efficacy
  - Clinical trial data
  - Clinical experience
- Safety/tolerability
- Ease of use
  - Frequency
  - Patient acceptability
- Cost

Principles of Responsible Opioid Prescribing

Treatment Plan

- I have resolved key points before initiating opioid therapy
  - Diagnosis established and opioid treatment plan developed
  - Established level of risk
  - I can treat this patient alone/I need to enlist other consultants to co-manage this patient (pain or addiction specialists)
- I have considered nonopioid modalities
  - Pain rehabilitation program
  - Behavioral strategies
  - Non-invasive and interventional techniques

Principles of Responsible Opioid Prescribing

Treatment Plan (continued)

- Drug selection, route of administration, dosing/dose titration
- Managing adverse effects of opioid therapy
- Assessing outcomes
- Written agreements in place outlining patient expectations/responsibilities
- Consultation as needed
- Periodic review of treatment efficacy, side effects, aberrant drug-taking behaviors
- Comply with the FDA label
**Informed Consent and Treatment Agreement**

- Ethically obliged to discuss risk/benefit with patient
  - Plan to manage AEs, safeguard meds, alternative Tx
- Treatment agreement
  - Set clear boundaries
  - Outline physician and patient responsibilities
    - Facilitate mutually agreed-upon Tx course, improve communication and adherence, prevent misunderstandings
    - Not proven to do so
- Provisions, e.g., UDT, frequency of office visits, pill counts, not sharing/obtaining meds from others, no illicit drug use, Rx from single prescriber


**Non-pharmacologic Options**

- Interventional
  - Injections
  - Neuro-augmentation*

- Non-interventional
  - Physical Rehab
  - CBT
  - Comp/Alternative

*Exception is Intrathecal Medications
Interventional Therapies for Pain

- Epidural Steroid Injection
- Sacroiliac Joint Injection and RFA
- Facet Joint Injection and RFA
- Sympathetic Block
- Celiac and Hypogastric Plexus Block
- Spinal Cord Stimulation
- Spinal Drug Delivery

Complementary/Alternative

- Mind Body
  - Mindfulness
  - CBT
- Manipulative
  - Acupuncture
  - Massage/Yoga
  - Herbals
Definition of Integrative Pain Treatment

“Integrative pain treatment is the practice of caring for individuals with pain that focuses on the whole person, reaffirms the importance of the relationship between practitioner and patient, uses the least invasive treatments whenever possible, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals and disciplines to achieve optimal health and healing.”

– Martha Menard, PhD
PAINS, 2013

Cochrane Reviews (CAM)

• **Touch Therapy**: Areas of the body where energy field is weak or congested are assessed, and practitioner uses his/her hands to direct energy into the field to balance it, thereby relieving pain

• **Music Therapy**: Music may have beneficial effects on anxiety, fatigue, depression, pain, and quality of life for patients with cancer; reduces the need for pain medication after surgery

• **P6 Therapy for Post-op Nausea**: P6 acupoint stimulation is comparable to antiemetics in preventing postoperative nausea and vomiting after anesthesia and surgery

• **Aromatherapy**: Essential oils are massaged into the skin, inhaled, or placed in baths to relieve stress, anxiety, and other ailments, such as pain

• **Caffeine**: Use of an analgesic plus caffeine resulted in a higher number of patients with good pain relief compared with use of an analgesic alone

Pain Treatment Options

Non-pharmacologic Approach

- Mind-body therapy
- Heat/cold therapy
- Massage
- Acupuncture
- Tai-chi
- PT/OT
- Transcutaneous electrical nerve stimulator (TENS)

Osteoarthritis Treatment Options

Considered Before Opioids

- Exercise
  - Aquatic/aerobic strengthening
- Self-management
- Education
- Braces
- Patellar tape
- TENS/acupuncture
- Orthopedic consult
- NSAIDs + PPI
- NSAIDs + misoprostol
- COX-2 inhibitors
- Glucosamine
- Chondroitin
- Topical NSAIDs
- Topical capsaicin
- IA corticosteroids

COX-2, cyclooxygenase-2; IA, intra-articular; PPI, proton-pump inhibitor; NSAID, nonsteroidal anti-inflammatory drugs; TENS, transcutaneous electrical nerve stimulation.

Spinal Pain Treatment Options Considered Before Opioids

- Exercise
- TENS/acupuncture
- Osteopathy
- Facet joint injections
- Root sleeve injections
- Acetaminophen
- NSAIDs
- Antidepressants
- Pregabalin/gabapentin
- Other anticonvulsants

Neuropathic Pain Treatment Options Considered Before Opioids

- Non-drug therapy
  - Education
  - TENS
  - Spinal cord simulation
  - Entrapment release
- Pharmacotherapy
  - TCAs
  - SNRIs
  - Pregabalin/gabapentin
  - Topical lidocaine
  - Topical capsaicin
  - NMDA antagonists

NMDA, N-methyl-D-aspartate; SNRI, serotonin norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.
Common Neuropathic Pain Diagnoses

- Diabetic Peripheral Neuropathy*
- Post Herpetic Neuralgia*
- Radicular Pain (neuropathic low back pain)
- Traumatic Peripheral Nerve Injury
- Complex Regional Pain Syndrome
- Chronic Postop Pain
- Phantom Limb Pain
- HIV related neuropathy
- Spinal Cord Injury*
- Post-stroke pain
- Trigeminal Neuralgia*
- Small Fiber Polyneuropathy*

* FDA-approved medications available

Polyneuropathies May Involve Small and Large Nerve Fibers

<table>
<thead>
<tr>
<th>Large-fiber Neuropathy</th>
<th>Small-fiber Neuropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Pain: burning, electric shocks, stabbing pain, numbness</td>
</tr>
<tr>
<td>Numbness, pins and needles, tingling,</td>
<td></td>
</tr>
<tr>
<td>poor balance</td>
<td></td>
</tr>
<tr>
<td>Exam Findings</td>
<td>Thermal, pin-prick sensation, allodynia</td>
</tr>
<tr>
<td>Reflexes, proprioception</td>
<td></td>
</tr>
<tr>
<td>Vibration, +/- motor</td>
<td></td>
</tr>
<tr>
<td>Functional changes</td>
<td>Nociception; protective sensation</td>
</tr>
<tr>
<td>Pressure, balance, fall risk</td>
<td></td>
</tr>
<tr>
<td>Diagnostic test</td>
<td>QST, nerve biopsy, intraepidermal nerve fiber density</td>
</tr>
<tr>
<td>EMG/NCV, sural nerve biopsy</td>
<td>(skin biopsy)</td>
</tr>
</tbody>
</table>
Common Diagnostic Studies and Limitations

**Studies**
- Blood studies
- X-ray, CT, MRI
- Electromyography (EMG)
- Nerve conduction velocity (NCV)
- Quantitative sensory testing (QST)
- Skin biopsy

**Limitations of EMG/NCV**
- Insensitive in acute injury
- Normal result does not rule out neuropathic pain
- Cannot assess function of small-fiber nerves involved in most neuropathic pain


Neuropathic Pain

**Recommendations of Various Societies**

<table>
<thead>
<tr>
<th></th>
<th>EFNS, Europe Neurology</th>
<th>Canadian Pain Society</th>
<th>IASP NeuPSIG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First line</strong></td>
<td>TCA</td>
<td>TCA</td>
<td>TCA, SNRI</td>
</tr>
<tr>
<td></td>
<td>GBP/PGB</td>
<td>GBP/PGB</td>
<td>GBP/PGB</td>
</tr>
<tr>
<td></td>
<td>Lidocaine 5% plaster</td>
<td>Lidocaine 5% plaster</td>
<td>Lidocaine 5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Opioid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Opioid</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(specific circumstances)</td>
</tr>
<tr>
<td><strong>Second line</strong></td>
<td>SNRI</td>
<td>SNRI</td>
<td>SNRI</td>
</tr>
<tr>
<td></td>
<td>(Opioid)</td>
<td></td>
<td><strong>Opioid</strong></td>
</tr>
<tr>
<td></td>
<td>Lidocaine 5%</td>
<td></td>
<td>Tramadol</td>
</tr>
<tr>
<td><strong>Third line</strong></td>
<td><strong>Opioid</strong></td>
<td><strong>Opioid</strong></td>
<td>Paroxetine</td>
</tr>
<tr>
<td></td>
<td>Lamotrigine</td>
<td>(except methadone)</td>
<td>Bupropion</td>
</tr>
<tr>
<td></td>
<td>Capsaicin</td>
<td></td>
<td>NMDA</td>
</tr>
<tr>
<td><strong>Fourth line</strong></td>
<td></td>
<td>Methadone</td>
<td>antagonist</td>
</tr>
</tbody>
</table>

EFNS, European Federation of Neurological Societies; IASP, International Association for the Study of Pain; NeuPSIG, Neuropathic Pain Special Interest Group
**Pharmacotherapeutics I**

*General Principles of Pharmacologic Analgesic Therapy*

---

**Selecting Correct Drug for Corresponding Pain Type**

**A. Nociceptive Pain**
- Noxious peripheral stimulus
- Brain
- **EXAMPLES**
  - APAP, NSAIDS, antidepressants, opioids

**B. Neuropathic Pain**
- Peripheral nerve damage
- Brain
- **EXAMPLES**
  - Antidepressants, anticonvulsants, antiarrhythmic opioids (?)

**C. Sensory Hypersensitivity**
- No known tissue or nerve damage
- Abnormal central processing
- Brain
- **EXAMPLES**
  - Antidepressants (SNRIs), NSAIDs, APAP, opioids

*Patients may experience multiple pain states simultaneously.*

---


*Chong MS, Bajwa ZH. J Pain Symptom Manage. 2003;25:S4-S11.

Used for educational purposes only.
Multimodal Therapy

Although formal pain management treatment protocols are lacking, most experts propose conservative nonpharmacological modalities as primary and adjunctive treatment, with opioids reserved for those patients who fail to respond to other therapies.

Advantages
- Multimechanistic effect
- Improved efficacy
- Reduction in end organ toxicity
- Reduction in side effects
- Functional improvement

Disadvantages
- Requires knowledge of drugs, PK data, and pharmacodynamics
- Every analgesic has its own unique adverse event profile
- May increase drug-drug interactions

Table 1. Categories of Pain Treatments

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonopioid drugs</td>
<td>Acetaminophen, nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>Adjunct analgesics</td>
<td>Antidepressants, anticonvulsants</td>
</tr>
<tr>
<td>Opioids</td>
<td>Morphine, oxycodone, fentanyl, methadone, oxymorphone, hydromorphone</td>
</tr>
<tr>
<td>Rehabilitative approaches</td>
<td>Modalities (heat, cold, transcutaneous electrical nerve stimulation), physical therapy, occupational therapy</td>
</tr>
<tr>
<td>Psychological approaches</td>
<td>Cognitive behavioral therapy, specific techniques (biofeedback, hypnosis, relaxation), other psychotherapies</td>
</tr>
<tr>
<td>Injection therapies</td>
<td>Trigger point injections, joint injections, spinal injections</td>
</tr>
<tr>
<td>Neural blockade</td>
<td>Sympathetic nerve blocks, medial branch block, celiac plexus block</td>
</tr>
<tr>
<td>Implant therapies</td>
<td>Spinal cord stimulator, intrathecal pump</td>
</tr>
<tr>
<td>Surgical approaches</td>
<td>Cordotomy, neurectomy</td>
</tr>
<tr>
<td>Complementary and alternative medicine approaches</td>
<td>Acupuncture, chiropractic therapy, massage, nutritional approaches and nutraceuticals, energy therapies</td>
</tr>
<tr>
<td>Lifestyle changes</td>
<td>Weight loss, exercise</td>
</tr>
</tbody>
</table>

Non-opioids Limited by Efficacy and AEs

Considerations for Antidepressants

- TCAs vs Beer's Criteria*
- Pharmacology
  - TCAs
  - SNRIs
  - SARIs
  - Atypicals
- See http://www.paindr.com/antidepressant%20chart.pdf
- Drug Interactions to consider
  - 2D6, 3A4, others

*Beer's Criteria: guidelines for healthcare professionals to help improve the safety of prescribing medications for older adults.
Anticonvulsants
Available in US, Excluding Benzodiazepines

<table>
<thead>
<tr>
<th>1st Generation Anticonvulsants</th>
<th>2nd / 3rd Generation Anticonvulsants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine (Tegretol, others)</td>
<td>Eslicarbazepine (Aptiom)</td>
</tr>
<tr>
<td>Ethosuximide (Zarontin)</td>
<td>Ezogabine (Potiga)</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Felbamate (Felbatol)</td>
</tr>
<tr>
<td>Phenytoin / Fosphenytoin (Dilantin)</td>
<td>Gabapentin (Neurontin)</td>
</tr>
<tr>
<td>Primidone (Mysoline)</td>
<td>Lacosamide (Vimpat)</td>
</tr>
<tr>
<td>Valproic Acid (Depakote, others)</td>
<td>Lamotrigine (Lamictal)</td>
</tr>
<tr>
<td></td>
<td>Levetiracetam (Keppra)</td>
</tr>
<tr>
<td></td>
<td>Oxcarbazepine (Trileptal, others)</td>
</tr>
<tr>
<td></td>
<td>Perampanel (Fycompa)</td>
</tr>
<tr>
<td></td>
<td>Pregabalin (Lyrica)</td>
</tr>
<tr>
<td></td>
<td>Rufinamide (Banzel)</td>
</tr>
<tr>
<td></td>
<td>Tiagabine (Gabitril)</td>
</tr>
<tr>
<td></td>
<td>Topiramate (Topamax, others)</td>
</tr>
<tr>
<td></td>
<td>Vigabatrin (Sabril)</td>
</tr>
<tr>
<td></td>
<td>Zonisamide (Zonegran)</td>
</tr>
</tbody>
</table>

Inflammation
Ongoing Chemical Activation of Pain Sensors

- Capsaicin
- Heat
- ATP
- H+
- PGs
- Na⁺, K⁺, Ca²⁺ channels
- 5HT
- NGF
- C-fiber
- Cytokines

Sensitize, activate
Nerve Growth Factor

Direct Peripheral, Direct and Indirect Gene Effects
Conditions of Tissue Damage, Deep Inputs, Neuromas

Potential functions and mechanisms of action of NGF in development of post-injury pain


NGF In Lower Back Pain

Opioid Consumption: Just the US?
2014 Prescribed Opioid Consumption of Australia, Canada, Germany and US

• Australia 2014: 358 mg ME* (minus methadone) per person and 481 mg ME including methadone
  – Methadone is frequently used for chronic pain management in Australia
• Canada 2014: 732 mg ME (minus methadone) per person
• Germany 2014: 480 mg ME (minus methadone) per person
• United States 2014: 500 mg ME (minus methadone) per person

*ME = Morphine Equivalence

Alternative Facts
Percentage of US Counties with Changes in Opioid Prescribing, 2010–2015

<table>
<thead>
<tr>
<th>Opioid Prescribing Measures</th>
<th>Decrease (%)</th>
<th>Stable (%)</th>
<th>Increase (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDD per capita</td>
<td>49.6</td>
<td>27.8</td>
<td>22.6</td>
</tr>
<tr>
<td>Overall prescribing rate</td>
<td>46.5</td>
<td>33.8</td>
<td>19.6</td>
</tr>
<tr>
<td>High-dose prescribing rate</td>
<td>86.5</td>
<td>6.7</td>
<td>6.9</td>
</tr>
<tr>
<td>Average daily MEDD per prescription</td>
<td>72.1</td>
<td>25.7</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Individual Response to Treatment

Pharmacogenetics
The science of how genetic variability impacts individual responses to medications

4A’s As a Template

Adverse Effects  Aberrant Behavior

HARM

Analgesia  Activities of Daily Living

BENEFIT

Patient Response Variability

Pharmacogenetic Variability and Response

- General population has 40-60% phenotype variability
- CYP450 enzymes most frequently involved
  - CYP2D6, CYP2C19, CYP2C9, CYP3A4, CYP1A2, CYP2E1
- Genetic differences impact 25% of all drugs
Benzodiazepines and Chronic Pain Patients

- Enhance the respiratory depressant effects of opioids
  - Frequently co-prescribed with opioids (up to 50% of patients)
    - In 1 population, 80% of patients prescribed high-dose opioids were co-prescribed benzodiazepines
    - More common in chronic pain patients with substance use disorders
  - Consider an alternative
    - For anxiety disorders
    - When a sleep aid is indicated, e.g., an anticonvulsant or low-dose trazodone
      - For patients with neuropathic pain, low-dose trazodone at bedtime may be dually beneficial

Opioid Analgesics

Risk Evaluation and Mitigation Strategy (REMS)

For Immediate Release

August 31, 2016

FDA News Release

FDA requires strong warnings for opioid analgesics, prescription opioid cough products, and benzodiazepine labeling related to serious risks and death from combined use

Action to better inform prescribers and protect patients as part of Agency’s Opioids Action Plan


Opioid Involvement in Benzodiazepine Overdose

National Center for Health Statistics, CDC Wonder. Used for educational purposes only.
**Benzodiazepine History**

![Benzodiazepine History Chart](chart.png)

**Opioids for Chronic Pain**

- **Short-acting (immediate release)**
  - Higher peaks, higher toxicity profiles
  - Intermittent effect on hypoadrenal axis
  - Possible lower overall 24 hour dose
  - Consider toxicity if combo w/ ASA, IBU, or APAP
- **Long-acting (ER-LA)**
  - Generally have lower Cmax
  - Sleep through night, but greater effect on REM sleep
  - Continuous effect at hypoadrenal axis
Managing Opioid Side Effects

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>Increase fluid intake; use of cathartics, stool softeners, PAMORAs, and nonopioid analgesics</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Switch opioid v. use antiemetic / Lower dose</td>
</tr>
<tr>
<td>Itching</td>
<td>Switch opioid; antihistamines</td>
</tr>
<tr>
<td>Edema and sweating</td>
<td>Switch opioid</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Anti vertiginous agents</td>
</tr>
<tr>
<td>Confusion</td>
<td>Titrate dose; switch opioid; add neuroleptic</td>
</tr>
<tr>
<td>Endocrine dysfunction</td>
<td>Endocrine monitoring; testosterone replacement</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>Switch opioid</td>
</tr>
<tr>
<td>Risk of falling for the elderly</td>
<td>Lower dose; use nonopioid analgesics</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>Reduce dose or discontinue</td>
</tr>
</tbody>
</table>

Select Opioid Formulations

- Available with co-analgesic
  - Oxycodone, tramadol, codeine, hydrocodone
- Pure m-opioid receptor agonists
  - Morphine, hydromorphone, fentanyl, oxycodone, hydrocodone
- Two or more mechanisms
  - Methadone, levorphanol
- Rapid onset (transmucosal)
  - Fentanyl
- Immediate release without co-analgesic
  - Tramadol, oxycodone, tapentadol, hydrocodone, hydromorphone, oxymorphone, others
- Modified release (long acting)
  - Morphine, methadone, oxycodone, hydromorphone, hydrocodone, others
- Partial agonists
  - Tramadol, pentazocine, butorphanol
- Partial agonists/antagonists
  - Buprenorphine
Opioid Formulations: Points to Consider

- Dose-limiting issues and toxicity with co-analgesics
  - 4 g/day acetaminophen limit
- Importance of titration
  - Risk of overdose, challenges of dose conversion during rotation
- Pharmacokinetics vs temporal patterns of pain
- Issues that influence the opioid selection
  - Pain pattern
  - Genetic factors that can influence metabolism
  - Comorbid medical conditions that may alter drug metabolism or clearance
  - Past history with opioid therapy and route of administration issues
- Adherence and care-giving issues
- Cost and convenience

Abuse-deterrent formulations (ADFs)

One Component to Address Prescription Opioid Epidemic

- Full impact cannot be realized until all opioids are abuse-deterrent
- FDA's goal: ADFs for all major opioids
Common Routes of Administration or Abuse

- Crushing and swallowing
- Crushing and snorting
- Crushing and smoking
- Crushing and/or extracting for injection
- Oral intact
- Co-ingestion with alcohol/benzodiazepines

Development of Prescription Opioid Abuse

Possible Adverse Outcomes:
- Addiction
- Overdose
- Death

References:
### Theoretical Roles of Opioids with Abuse-deterrent Properties

- **Pain Patient**
- **Guidelines**
- **Susceptible Person**
- **Recreational User**

#### Behaviors
- **Intact**
- **Crushed**

- **ADF**

- **Addiction**
- **Overdose**
- **Death**

---

**Webster LR. Drug Discovery and Development. July, 30. 2009.**

---

### Speed of CNS Entry and Concentration Determines Liking

- The “abuse potential” of a drug increases as the value of the AQ increases

- **Cmax / Tmax**

  In this ratio, as Cmax INCREASES and as Tmax DECREASES, the ratio becomes relatively larger, signaling potentially increased attractiveness as a drug of abuse

---

**Webster LR. Drug Discovery and Development. July, 30. 2009.**
Key Assessments

• Subjective Abuse Liability Assessments
  – Bipolar VAS
    • Drug Liking
    • TDA
  – Unipolar VAS
    • Drug High
  – Likert, T/F
    • ARCI, POMS

Difference in $C_{\text{max}}$

Do you LIKE the drug?

TIME (hours post-dose)

$C_{\text{max}}$

75 – Comparator

10% or less

68.5 – Generic ADF
Comparison of FDA Approved ADFs vs Claimed AD Properties

<table>
<thead>
<tr>
<th>With FDA-approved Abuse-deterrence Claims¹</th>
<th>Without FDA-approved Abuse-deterrence Claims²⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug product</td>
<td>Drug substance(s)</td>
</tr>
<tr>
<td>MORPHABOND™ ER</td>
<td>morphine</td>
</tr>
<tr>
<td>ARYMO™ ER</td>
<td>morphine</td>
</tr>
<tr>
<td>EMBEDA®</td>
<td>morphine + naltrexone (sequestered)</td>
</tr>
<tr>
<td>HYSINGLA® ER</td>
<td>hydrocodone</td>
</tr>
<tr>
<td>VANTRELA™ ER</td>
<td>hydrocodone</td>
</tr>
<tr>
<td>OXYCONTIN®</td>
<td>oxycodone</td>
</tr>
<tr>
<td>XTAMPZA®ER</td>
<td>oxycodone</td>
</tr>
<tr>
<td>TARGINQ®ER</td>
<td>oxycodone + naloxone</td>
</tr>
<tr>
<td>TROXYCA®ER</td>
<td>oxycodone + naloxone (sequestered)</td>
</tr>
</tbody>
</table>


These tables are derived from the Prescribing Information for the respective products. They are not intended to compare efficacy, safety, mechanism of action, or uses between any of the products listed. The products listed in the table on the left are expected to reduce abuse and misuse; however, abuse and misuse of all of these products are still possible.

Please see presenter for full Prescribing Information for MORPHABOND ER, including BOXED WARNINGS and Medication Guide.
ICER Summary

“…ADFs have the potential to substantially reduce the incidence of opioid abuse relative to non-ADF formulations among patients initially prescribed these drugs...

…but will also increase overall costs to the health system…”

CDC Opioid Guidelines

ADFs not included in the guidelines “because they do not prevent misuse through oral intake or unintentional overdose”
Eight Opioid Prescribing Principles for Providers®
Help Minimize Harm Prescribing Opioids and Other Psychotherapeutics

1. Assess patients for risk of abuse before starting opioid therapy and manage accordingly
2. Watch for and treat comorbid mental disease if present
3. Conventional conversion tables can cause harm and should be used cautiously when rotating (switching) from one opioid to another
4. Avoid combining benzodiazepines with opioids, especially during sleep hours
5. Start methadone at a very low dose and titrate slowly regardless of whether your patient is opioid tolerant or not
6. Assess for sleep apnea in patients on high daily doses of methadone or other opioids and in patients with a predisposition
7. Tell patients on long-term opioid therapy to reduce opioid dose during upper respiratory infections or asthmatic episodes
8. Avoid using long-acting opioid formulations for acute, post-operative, or trauma-related pain


Issues with Morphine Equivalent Daily Dose and Opioid Conversion

- Body weight
- Pharmacogenetic variability
- Drug interactions
- Lack of universal morphine equivalence

- Specific opioids that should never have an MEDD
  - Methadone
  - Buprenorphine
  - Tapentadol
  - Tramadol

Challenge of Equal Analgesic Conversion

- Tables use for risk stratification and should not be used to establish equianalgesic conversion
- Subjects with limited opioid exposure
- Do not reflect clinical realities of chronic opioid administration


Available Online Opioid Conversion Calculators

- Med Calc
- WA State Agency
- Pain Research
- Pain Physicians
- Hopkins
- Palliative Care
- Global RPh
- Practical Pain Management

CDC Calculator Lacks Accuracy with Methadone Conversion!

1. DETERMINE the total daily amount of each opioid the patient takes.
2. CONVERT each to MMEs—multiply the dose for each opioid by the conversion factor. (see table)
3. ADD them together.

Calculating morphine milligram equivalents (MME)

<table>
<thead>
<tr>
<th>OPIOID (doses in mg/day except where noted)</th>
<th>CONVERSION FACTOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>0.15</td>
</tr>
<tr>
<td>Fentanyl transdermal (in mcg/hr)</td>
<td>2.4</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>1</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4</td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
</tr>
<tr>
<td>1-20 mg/day</td>
<td>4</td>
</tr>
<tr>
<td>21-40 mg/day</td>
<td>8</td>
</tr>
<tr>
<td>41-60 mg/day</td>
<td>10</td>
</tr>
<tr>
<td>&gt; 61-80 mg/day</td>
<td>12</td>
</tr>
<tr>
<td>Morphine</td>
<td>1</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1.5</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>3</td>
</tr>
</tbody>
</table>

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.


An Actual Example from the CDC Smart Phone App

<table>
<thead>
<tr>
<th>Guideline Resources: CDC Opioid Guideline Mobile App</th>
<th>“Morphine Equivalent” (mg)</th>
<th>Methadone Daily Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>168</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>320</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>410</td>
<td>41</td>
</tr>
</tbody>
</table>

Serum Fentanyl Concentrations Following Multiple Applications of Fentanyl TD 100mcg/h (n=10)

This presents a huge risk even with 50% dose reduction!

Risks for Opioid Overdose

- Substance abuse
- High daily morphine equivalent dose (MED)
- Age
- Gender
- Accidental exposure to young children in the home
- Chronic lung disease
- Chronic kidney and/or liver impairment
- Sleep apnea
- Concomitant use of benzodiazepines and/or alcohol with or without other sedative-hypnotics


Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression

- Two major studies
  - Linear regression multivariate analysis
  - VA population
    - 17 questions, 115 highest possible score
  - General population
    - 16 questions, 146 highest possible score


Non-VA Population
16 Questions, 146 Highest Possible Score

- Retrospective case-control study of 18,365,497 patients
- IMS PharMetrics Plus integrated commercial health plan opioid claims in the US
- 7,234 patients experience OSORD
- OSORD found to be associated with:
  - ER/LA opioid formulations
  - Daily morphine equivalence dose
  - Interacting medications
  - ED visits and hospital admissions
  - Coexisting health conditions

OSORD = Overdose or Serious Opioid-Induced Respiratory Depression
Discussing Continued Lack of Benefit

- Stress how much you believe/empathize with patient’s pain severity and impact
- Express frustration re: lack of good pill to fix it
- Focus on patient’s strengths
- Encourage therapies for “coping with” pain
- Show commitment to continue caring about patient and pain, even without opioids i.e., you are abandoning the treatment, not the patient
- Schedule close follow-ups during and after taper

Opioid Exit Strategy: Possible Paths

- **Patient’s behavior consistent with drug addiction**
  - Refer for addiction management or comanagement

- **Patient unable or unwilling to cooperate with outpatient taper**
  - Provide sufficient opioid for 1-month taper or maint until admission
  - Refer to inpatient or outpatient program or similar service, as available

- **No apparent addiction problem**
  - Patient able to cooperate with office-based taper
  - Taper gradually over 1 month (Longer tx duration → longer taper)
  - Implement nonopioid pain management (psychosocial support, CBT, PT, nonopioid analgesics)

CBT, cognitive behavioral therapy; PT, physical therapy.

Recent CDC Guidelines
Who I Should Target for Take-home Naloxone?

Consider Take-home Naloxone

- Candidates for a naloxone prescription to use in the event of a suspected opioid overdose include those:
  - Taking high doses of opioids
  - Taking opioid preparations that may increase risk for overdose; e.g., ER/LA opioids, including methadone
  - Undergoing opioid rotation
  - Discharged from emergency medical care following opioid intoxication/poisoning
  - With a legitimate medical need for analgesia, coupled with suspected/confirmed substance abuse

ER/LA=extended-release/long-acting
Recommendations That Naloxone Be Readily Accessible

SAMHSA: “With proper education, patients on long-term opioid therapy and others at risk for overdose may benefit from having a naloxone kit containing naloxone, syringes, and needles or prescribing naloxone auto-injector which delivers a single dose of naloxone via a hand-held auto-injector that can be carried in a pocket or stored in a medicine cabinet to use in the event of known or suspected overdose.”

“The AMA has been a longtime supporter of increasing the availability of naloxone for patients, first responders and bystanders who can help save lives.”


Naloxone Access

States with naloxone access and drug overdose good samaritan laws
States with drug overdose good samaritan laws only
States with naloxone access laws only

Utilizing Pharmacists to Increase Naloxone Access

Based on Data Collected by NASPA, as of January 2018

Naloxone Access in Community Pharmacies


Critical Naloxone Comparisons

<table>
<thead>
<tr>
<th>NXN Auto-injector</th>
<th>NXN Intranasal (FDA Approved)</th>
<th>NXN Intranasal (Makeshift)</th>
<th>NXN IM Traditional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complexity</td>
<td>Usability studies show 90% and 100% correct adm c/t NXN makeshift¹</td>
<td>Usability studies show &gt;90% correct adm²</td>
<td>60-100% failure rates¹,³</td>
</tr>
<tr>
<td>Instructions</td>
<td>Audio stepwise direction and written directions</td>
<td>Written directions</td>
<td>No FDA approved written directions</td>
</tr>
<tr>
<td>Considerations</td>
<td>May inject through seam of jeans</td>
<td>Reduced Cmax due to altered nasal mucosa (DS, cong)</td>
<td>Requires sig dexterity and familiarity</td>
</tr>
<tr>
<td>FDA Approved</td>
<td>YES, Known or suspected Op OD, EVEN IF NOT TRAINED</td>
<td>YES, Known or suspected Op OD, EVEN IF NOT TRAINED</td>
<td>NO</td>
</tr>
<tr>
<td>for in-home use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>0.4 mg/0.4 mL injection</td>
<td>4 mg/0.1 mL spray</td>
<td>0.5 mg/0.5 mL</td>
</tr>
<tr>
<td>Tmax (median)</td>
<td>0.25 hour (0.4 mg dose)</td>
<td>0.33 hour (8 mg) (2 x 4 mg doses)</td>
<td>*N/A, but consider Kelly et al.²</td>
</tr>
<tr>
<td>Cost</td>
<td>170x</td>
<td>10.75x</td>
<td>2x</td>
</tr>
<tr>
<td>Private 3rd party pay</td>
<td>Discussion...</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: 2 mg IM vs 2 mg IN
Neurobiology of Addiction

Definition of Terms

Misuse
- Use of a medication (for a medical purpose) other than as directed or as indicated, whether willful or unintentional, and whether harm results or not

Abuse
- Any use of an illegal drug
- The intentional self-administration of a medication for a nonmedical purpose such as altering one’s state of consciousness, e.g., getting high

Diversion
- The intentional removal of a medication from legitimate and dispensing channels

Dependency
- Physical neuroadaptation to an exogenous substance or
- Associated Abstinence Syndrome

Pseudoaddiction
- Syndrome of abnormal behavior resulting from undertreatment of pain that is misidentified by the clinician as inappropriate drug-seeking behavior
- Behavior ceases when adequate pain relief is provided
- Not a diagnosis; rather, a description of the clinical intention

Opioid Use Disorder (OUD)

- DSM-I (1952-1968) – “Addiction” is usually symptomatic of a personality disorder.
- DSM-II (1968-1980) – “Addiction” requires evidence of habitual use ... withdrawal symptoms are not the only evidence of dependence.
- DSM-III (1980-1994) – Essential feature of “Opioid Abuse” ... pattern of pathological use for at least one month ... impairment in social or occupational functioning ... “Opioid Dependence” essential feature is tolerance or withdrawal.
- DSM-IV (1994-2000) – “Opioid Dependence” includes ... compulsive, prolonged self-administration of opioid substances ... for no legitimate medical purpose ... doses that are greatly in excess of the amount needed for pain relief.
- DSM-V (2013-Present) – Categories of substance abuse and substance dependence have been eliminated and replaced with an overarching new category of “substance use disorders” with the specific substance defining the disorder.
  - Tolerance and withdrawal that previously defined dependence are normal responses.

Risk of Addiction by Type of Substance*

<table>
<thead>
<tr>
<th>Substance</th>
<th>Ever Used (%)</th>
<th>Dependence (%)</th>
<th>Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td>75.6</td>
<td>24.1</td>
<td>31.9</td>
</tr>
<tr>
<td>Cocaine</td>
<td>16.2</td>
<td>2.7</td>
<td>16.7</td>
</tr>
<tr>
<td>Heroin</td>
<td>1.5</td>
<td>0.4</td>
<td>23.1</td>
</tr>
<tr>
<td>Stimulant</td>
<td>15.3</td>
<td>1.7</td>
<td>11.2</td>
</tr>
<tr>
<td>Alcohol</td>
<td>91.5</td>
<td>14.1</td>
<td>15.4</td>
</tr>
<tr>
<td>Cannabis</td>
<td>46.3</td>
<td>4.2</td>
<td>9.1</td>
</tr>
</tbody>
</table>

*Weighted estimates from the National Comorbidity Survey data gathered 1990-1992 for persons 15-54 years old (n=8,098).

**Triangle of the Disease of Abuse/Addiction**

- Genetics
- Social / Environment
- Drug Properties

**Vulnerability Factor: Drug Properties**

- Drug-induced effect
- On/Off; frequency
- Rate and quantity of dopamine release

Adapted with permission. Webster publication pending.


Vulnerability Factor: Environment

- Set, setting
- Cuing
- Peer pressure
- Stress, stressors
- Home

Level of Abuse in Stressful Environments

Vulnerability Factor: Genetics

- Approximately 50%
- Many polymorphisms
- Comorbidity with mental disorders

Adapted with permission
Webster publication pending

Vulnerability to Opioid Addiction
*Individuals Respond Differently To Opioid Exposure*

- No addictive disease with exposure
- Addictive disease after opioid exposure
- No addictive disease due to lack of exposure
Three Vulnerability Factors

Adapted from Webster in preparation.

US Unique Approach to MAT
Two Treatment Settings Available

1. Outpatient Treatment Program (OTP)
   - Example: Methadone clinic

2. Office-Based Opioid Treatment (OBOT)
   - Example: Suboxone clinic

Outpatient Treatment Program (OTP)
Example: Methadone Clinic

- Most common approach used worldwide
- Intensive treatment program
- Recommended for high-risk patients
- Required evaluations with psychiatrist/counseling
- Patients present daily for observed medication administration
- OTP’s can offer both methadone and buprenorphine
- Cash ONLY ($12/day)
- May earn right to “carry” or take home medication for a few days

MAT Pharmacology/Pharmacokinetics

<table>
<thead>
<tr>
<th>Pharmacology</th>
<th>Buprenorphine</th>
<th>Methadone</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid agonist activity</td>
<td>μ, Partial agonist</td>
<td>μ</td>
<td>N/A</td>
</tr>
<tr>
<td>Opioid antagonist activity</td>
<td>κ, δ</td>
<td>N/A</td>
<td>μ, κ, δ</td>
</tr>
<tr>
<td>NE reuptake blockade</td>
<td>N/A</td>
<td>✓</td>
<td>N/A</td>
</tr>
<tr>
<td>NMDA inhibition</td>
<td>N/A</td>
<td>✓</td>
<td>N/A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pharmacokinetics</th>
<th>Buprenorphine</th>
<th>Methadone</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half-life</td>
<td>32-36 hours</td>
<td>15-60 hours</td>
<td>5-10 days</td>
</tr>
<tr>
<td>Metabolic pathway</td>
<td>3A4 mediated N-dealkylation to norbuprenorphine and glucuronidation</td>
<td>3A4, 2B6, 2C19 mediated N-demethylation to 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidene (EDDP)</td>
<td>6β-naltrexol mediated by dihydrodiol dehydrogenase to glucuronidation</td>
</tr>
<tr>
<td>Excretion</td>
<td>Urine (30%); Feces (69%)</td>
<td>Urine (30-50%); Feces (20-70%)</td>
<td>Urine (50-80%); Feces (20%)</td>
</tr>
<tr>
<td>Opioid chemistry</td>
<td>Dehydroxylated phenanthrene</td>
<td>Diphenylheptane</td>
<td>Dehydroxylated phenanthrene</td>
</tr>
<tr>
<td>Dosing</td>
<td>SL, Buccal</td>
<td>PO</td>
<td>IM</td>
</tr>
<tr>
<td>PO equivalent dose to 30 mg/day of PO morphine</td>
<td>1 mg SL</td>
<td>7.5 mg PO</td>
<td>N/A</td>
</tr>
<tr>
<td>Starting Dose</td>
<td>Up to 8 mg</td>
<td>40 mg</td>
<td>380 mg</td>
</tr>
<tr>
<td>Usual Maintenance Dose</td>
<td>8-16 mg</td>
<td>80-120 mg</td>
<td>380 mg</td>
</tr>
</tbody>
</table>

US Unique Approach to MAT
Two Treatment Settings Available

1. Outpatient Treatment Program (OTP)
   – Example: Methadone clinic

2. Office-Based Opioid Treatment (OBOT)
   – Example: Suboxone clinic


Office-Based Opioid Treatment (OBOT)
Example: Suboxone Clinic

- DATA 2000 allows physicians to prescribe buprenorphine for OUD in office practice
  - 24 hours of training, submit waiver notification form, DEA assigns X license #
  - 1st year 30 patients
  - NOI-Request increase to 100 patients
- Comprehensive Addiction Recovery Act (CARA) Effective 7/22/2016
  - Section 303 – authorizes NPs and PAs to obtain waiver for DEA X license
  - Increase to 275 patients

Opioid Analgesics
Risk Evaluation and Mitigation Strategy (REMS)

Buprenorphine Prescribing Is Increasing

• Traditional opioid prescribing is declining
• DEA announced mandatory 25% reduction in production of opioids from pharmaceutical companies
• Result of decreased prescribing

Buprenorphine prescribing is increasing
– Opioid Use Disorder (OUD)
  • Probuphine® (5/26/16)
  • Bunavail® (6/6/2014)
  • Zubsov® (7/3/2013)
  • Suboxone®
    • Sublingual tablet (10/8/2002)
    • Buccal Film (8/30/2010)
– Chronic Pain
  • Belbuca® (10/13/2015)
  • Butrans® (6/30/2010)

Buprenorphine Pharmacology

Receptor Activation
- µ-opioid agonist – partial
- κ-opioid antagonist
- δ-opioid antagonist

Receptor Kinetics
- Highest affinity of all opioids
- Slow receptor association (30 min)
- Very slow receptor dissociation (166 min)

Receptor Saturation
- 2 mg SL tablet – 36%-50% saturation
- 16 mg SL tablet – 79%-95% saturation

Pharmacology
- Semi-synthetic derivative of thebaine
- 20-40 times more potent than morphine

Reversal
- 2-3 times more potent at displacing fentanyl
- 40 times dose of naloxone required to reverse buprenorphine compared to fentanyl

Elimination Half-life
- Single administration (25 hrs)
- Multiple administrations (32-36 hrs)

Establishing Care in Opioid Use Disorder

US Office-Based Opioid Treatment (OBOT)

<table>
<thead>
<tr>
<th>Provider Action</th>
<th>ASAM</th>
<th>SAMHSA</th>
<th>VA/DoD</th>
<th>FSMB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Past Medical History and Physical Assessment</td>
<td>Comprehensive medical history; physical exam; evaluate for infectious diseases; pregnancy; lab tests</td>
<td>Comprehensive assessment; Physical exam; complications related to drug abuse; lab tests</td>
<td>History and physical exam, lab tests</td>
<td>Physical exam; thorough medical history; communicable diseases; UDT; POMP</td>
</tr>
<tr>
<td>Mental Health Assessment</td>
<td>Psychiatric stability; Psychiatric disorders</td>
<td>Mental status examination; Psychiatric stability</td>
<td>Mental Status examination; Psychiatric disorders</td>
<td>Psychiatric history; Psychiatric disorders; Readiness to participate in Tx</td>
</tr>
<tr>
<td>Substance Use History</td>
<td>Confirm OUD Diagnosis; Substance abuse history</td>
<td>Confirm OUD diagnosis; screen for drug or alcohol-related disorders</td>
<td>Confirm OUD Diagnosis; Treatment should be offered for each SUD</td>
<td>Confirm OUD Diagnosis; Use of other substances; Past treatment experience</td>
</tr>
<tr>
<td>Social History</td>
<td>Identify barriers to recovery; living situation, financial concerns, social support</td>
<td>Social support; family history, readiness to change</td>
<td>Assess psychosocial functioning and environment</td>
<td>Access to social supports, family, friends, housing, employment, finances and legal problems</td>
</tr>
<tr>
<td>Psychosocial Assessment</td>
<td>Assessment of psychosocial needs; Medications but one aspect of treatment</td>
<td>Needs assessment; incorporate plan for engaging in psychosocial interventions into treatment plan</td>
<td>Needs Assessment; Supportive counseling; Referral to community services</td>
<td>Baseline Assessment; Level of psychological and social functioning or impairment</td>
</tr>
<tr>
<td>Patient Selection</td>
<td>OBOT vs OTP consider: • Psychosocial situation • Co-occurring disorders • Treatment retention vs risk of diversion • Active use of other drugs, associated with poorer prognosis • Not a reason to deny Tx</td>
<td>OBOT: • Reasonable compliance • Motivation &amp; desire to Tx • History of stable treatment • Psychosocial supports • Psychiatric stability • Adequate treatment resources • Comorbid substance abuse</td>
<td>OBOT vs OTP: • Patient preference • Stable patients • Provide needed resources • None/new failed attempts at Tx • Difficulty accessing OTP</td>
<td>OBOT: • Ability to offer/refer for psychosocial services • Readiness to change • May be candidates even with previous failures</td>
</tr>
<tr>
<td>Agreement</td>
<td>Informed consent</td>
<td>Informed consent; treatment plan; provider and patient sign</td>
<td>Not specified</td>
<td>Treatment agreement and informed consent should be signed by patient</td>
</tr>
</tbody>
</table>

© 2019 Rockpointe
Provider Risk Assessment Tools for OUD

- NIDA Modified Assist
  - Assess past-year drug use and risk level on a substance
- CRAFFT
  - Designed to screen for Adolescent Drug Abuse
- AUDIT
  - Alcohol Use Disorder Identification Test
- 4Ps
  - Screen for substance abuse during pregnancy


Patient Follow-up and Monitoring in OUD
US Office-Based Opioid Treatment (OBOT)

<table>
<thead>
<tr>
<th>Provider Action</th>
<th>ASAM</th>
<th>SAMHSA</th>
<th>VA/DoD</th>
<th>FSMB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit Frequency</td>
<td>Frequently during initiation (at least weekly); stable patients (at least monthly)</td>
<td>Frequently during induction, stabilization. Weekly, biweekly, or monthly depending on stability.</td>
<td>Twice weekly, then weekly, then biweekly or up to 12 weeks</td>
<td>Frequently until stable; follow-up frequency based on compliance and high risk behaviors</td>
</tr>
<tr>
<td>Duration</td>
<td>No time limit.</td>
<td>Maintenance can be short-term (1 year) up to lifetime. Duration depends on patient: • Stability • Preference</td>
<td>No time limit</td>
<td>Recommend at least a year; Longer duration associated with better outcomes. Relapse risk is highest in first 6-12 months of abstinence</td>
</tr>
<tr>
<td>Prescription Frequency</td>
<td>Weekly or monthly</td>
<td>Weekly or monthly</td>
<td>Not specified</td>
<td>As needed until next visit, Coincides with follow-up based on compliance and high risk behaviors</td>
</tr>
<tr>
<td>Usual Dosing</td>
<td>8-16 mg daily</td>
<td>Nearly all patients will stabilize on daily doses of 16-24 mg; some; however, may require up to 32 mg daily.</td>
<td>Not specified</td>
<td>8-24 mg; some may require up to 32 mg daily.</td>
</tr>
<tr>
<td>UDT</td>
<td>Baseline; Frequently; Random preferred</td>
<td>Baseline; At least monthly</td>
<td>Baseline; Frequent, at provider discretion</td>
<td>Baseline; Routinely; Recommended and included in treatment agreement</td>
</tr>
<tr>
<td>Pill Counts</td>
<td>Unscheduled recall visits</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Recommended and included in treatment agreement</td>
</tr>
<tr>
<td>PDMP</td>
<td>Verify abstinence</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Baseline; Routinely; Recommended to verify abstinence and included in treatment agreement</td>
</tr>
</tbody>
</table>

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### Psychosocial Interventions and Care Coordination in OUD

**US Office-Based Opioid Treatment (OBOT)**

<table>
<thead>
<tr>
<th>Provider Action</th>
<th>ASAM</th>
<th>SAMHSA</th>
<th>VA/DoD</th>
<th>FSMB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Risk (OBOT Questionable)</strong></td>
<td>Alcohol use disorder, Benzodiazepine use, Sedative/hypnotic use disorder. May not be suitable for OBOT:</td>
<td>Alcohol abuse/dependence, Benzodiazepine or sedative/hypnotic abuse/dependence, Sedative/hypnotic use disorder. Significant unmetled psychiatric comorbidity. Frecuent relapses or multiple failed treatments. Poor motivation or psychosocial support.</td>
<td>Pain requiring IR opioids. Many failed attempts at treatment.</td>
<td>Use of sedatives or alcohol. Continue to misuse and experience withdrawal at 32 mg daily. Persistent aberrant behaviors despite adjustments to treatment.</td>
</tr>
<tr>
<td><strong>Psychosocial Treatment</strong></td>
<td>Recommended for every patient on MAT. Individual or group counseling. Cognitive Behavioral Therapy (CBT). Contingency Management (CM). Release prevention. Multidisciplinary Interventions. Mutual help – not equivalent to professional psychosocial Tx.</td>
<td>Necessary for most patients on MAT.</td>
<td>No treatment can be recommended over another: Behavioral Couples Therapy, Cognitive Behavioral Therapy (CBT), Contingency Management (CM), Community Reinforcement Approach (CRA).</td>
<td>Recommended for patients on MAT. Evidence that MAT + psychosocial superior to either alone. Regular assessment of patient’s level of engagement in treatment. Counseling. 12-Step Facilitation.</td>
</tr>
<tr>
<td><strong>Care Coordination</strong></td>
<td>Linkages to existing family support systems.</td>
<td>Social and environmental factors can impact recovery if not addressed.</td>
<td>Develop recovery support system.</td>
<td>Assess changes in social functioning and relationships: Family, Friends, Employment, Housing, Legal.</td>
</tr>
<tr>
<td><strong>Relapse</strong></td>
<td>Increase treatment intensity. Increase change psychosocial supports.</td>
<td>Plan should be in place for relapse in treatment agreement. Physicians should be familiar with brief intervention:</td>
<td>Adapt treatment to meet patient’s needs. Add or substitute another psychosocial or medication intervention. Change intensity with med or therapy adjustments.</td>
<td>Relapse treatment plan: intensify structure and/or intensity of services. Assess and develop coping skills: Identify and plan for relapse triggers.</td>
</tr>
</tbody>
</table>

#### Provider/Patient Counseling Strategies

- **Contingency Management (CM)**
  - Employs stimulus control and positive reinforcement to change behavior.

- **Cognitive Behavioral Therapy (CBT)**
  - Problem-solving approach to modify dysfunctional emotions, behaviors, and thoughts.

- **Community Reinforcement Approach (CRA)**
  - Aims to eliminate positive reinforcement (PR) for substance use, and promote PR for abstinence.

- **Motivational Interviewing (MI)**
  - Helps solve ambivalent feelings and insecurities to find internal motivation needed.

- **Individual Counseling**

- **12-Step Facilitation (AA, NA)**
  - Guidelines inconsistent in value assessment of 12-step facilitation.

[www.drugabuse.gov/publications/effective-treatments-opioid-addiction/effective-treatments-opioid-addiction]
Care Coordination/Case Management

- Assess changes in social functioning and relationships across:
  - Family
  - Housing
  - Employment
  - Legal
  - Medicaid
  - Food assistance programs
- Instability in any of these areas can serve as triggers for relapse

Care Coordination/Case Management

- Social and environmental factors may impact recovery
- Providers should be aware of community resources
  - Develop relationships
    - Case management
    - Social worker
- Develop linkages to existing family support systems
  - Family encouragement
  - Spiritual support
- Develop recovery support system
- Rapid growth of care coordination services:
  - Managed Care chronic disease management teams
  - Private case management consulting agreements with treatment facilities
  - New case management codes for Medicare/Medicaid reimbursement
    - Promotes practice adoption
The National Council for Behavioral Health

• Serving 10 million + adults, children and families with mental illnesses and/or addictions.
• Drive mental health and addictions policy, practice, and education initiatives that improve access to effective care

Big Tent - Mental health; addictions; children to older adults; not for profits, government, and peer run; housing, and school and employment services; hospital and community based; prevention, treatment, and recovery supports.

The National Council for Behavioral Health

Who Are We

• Over 3,000 Members providing or supporting treatment for Mental Illnesses and Addiction

• Services
  – Mental Health First Aid – over 1 million trained
  – Center for Integrated Health Solutions (HHS)
  – CDC National Networks
  – Improving Business & Clinical Practices
  – Advocacy and Policy
  – Medical Director Institute
National Council Resources

- Dedicated Webpages
- Infographics
- Assessment Tools
- Training and consultation services
- Online Training
- Medical Directors Institute

https://www.thenationalcouncil.org/opioid-use-disorders/

Dedicated Website

- Interactive map of drug use trends
- State sponsored programs
- Infographics

https://www.thenationalcouncil.org/opioid-use-disorders/
Strategic Partnerships

- American Academy of Addiction Psychiatry (AAAP)
- Opioid Response Network
- Physician’s Clinical Support System (PCSS)
- National Association of Recovery Residences (NARR)
- Addiction Technology Transfer Centers (ATTC)

Physician’s Clinical Support System (PCSS)

Discover the rewards of treating patients with Opioid Use Disorders

https://pcssnow.org/
Opioid Response Network

Education and Training Start Here.

General Resources

• CDC guidelines for prescribing opioids for chronic pain

• CDC Recommendations for Nonopioid Treatments in the Management of Chronic Pain
  https://emergency.cdc.gov/coca/calls/2016/callinfo_072716.asp

• SAMHSA’s Center for Integrated Health Solutions
  https://www.integration.samhsa.gov/clinical-practice/pain-management
Summary

- Chronic pain is a high prevalence/low priority disease state that requires comprehensive HCP education to improve
- Chronic pain assessment and treatment is function and goal-oriented
- Effective treatment employs multimodal therapy potentially including interventional, nonpharmacologic, and nonopioid options
- Pain pharmacotherapy emphasizes nonopioid adjunct medications through evidence-based targeting of pain mechanism
- Opioid therapy is reserved for severe refractory pain, emphasizing risk mitigation and individualized therapy as part of multimodal treatment
Evaluation Reminders

• The onsite evaluation form must be completed to receive credit
• If seeking MOC credit, in addition to completing the onsite evaluation form, please visit www.rockpointe.com/remsmoc (this link is also provided on page 4 of your syllabus)
• You must include your 3-digit keypad number on the evaluation form

MACRA Credit – What to Do

1. Follow instructions, How to Apply, provided on the handout in your syllabus
2. Incorporate at least one of the following required measures into your practice:
   - Document the patient’s level of pain at each office visit
   - Reassess the patient’s treatment plan at each office visit
   - Re-evaluate the patient’s pain relief goals at each office visit
An informational handout has been provided in your syllabus. In order to receive MACRA Credit you must:

1. Attend the CME program for the full duration and apply for CME credit
2. Check the box at the bottom of the evaluation to indicate you are interested in the MACRA credit
3. Provide a valid email address to receive follow-up surveys
4. Incorporate at least one of the required measures into your practice
5. Complete 2 brief follow-up surveys sent at 30 and 90 days after the program

Certificate of completion will be sent following the completion of the 90-day survey
6. Attest to completing the Improvement Activity in the CMS system

Thank you for joining us today!

Please remember to turn in your completed EVALUATION FORM.

Your participation will help shape future CME/CE activities.
Information on MACRA Credit – How to Apply

What is MACRA:

MACRA is the Medicare Access and CHIP Reauthorization Act and is the latest legislation from CMS regarding physician reimbursements. MACRA replaces the current Medicare reimbursement schedule with a new pay-for-performance program that’s focused on quality, value, and accountability. The Centers for Medicare and Medicaid Services (CMS) stated that MACRA enacts a new payment framework that rewards healthcare providers for giving better care instead of more service. It defines the “QPP” (quality payment program) under which you’ll be paid “for quality.” The program has 2 subsets; MIPS (Merit Based Incentive Payment System) and APM (alternative payment model).

What type of MACRA Credit does this program pertain to:

This program qualifies as a medium weight improvement activity under MACRA’s MIPS (Merit Based Incentive Payment System) and participants who have completed all the steps to receive credit listed below can claim this activity as completion of an IA_PSPA_28 Accredited Safety or Quality Improvement Program.

How to receive Credit:

1. Attend the CME program for the full duration and apply for CME credit
2. Check the box at the bottom of the evaluation sheet that indicates you are interested in the MACRA credit
3. Provide a valid email address to receive follow-up surveys
4. Incorporate at least one of the following required measures into your practice:
   a. Document the patient’s level of pain at each office visit (sample provided on the back of this sheet)
   b. Reassess the patient’s treatment plan at each office visit
   c. Re-evaluate the patient’s pain relief goals at each office visit
5. Complete 2 brief follow-up surveys sent at 30 and 90 days after the program – a certificate of completion will be provided upon completion of the 90-day survey
6. Attest to completing the Improvement Activity in the CMS system. Contact your practice administrator with any questions.

Does the CMS have any resources available on Improvement Activities?

Visit the CMS website for more information on Improvement Activities: https://qpp.cms.gov/mips/improvement-activities

Where can I go to check my MIPS Status?

You can check your participation status using the National Provider Identifier (NPI) Look-up Tool on https://qpp.cms.gov.

Enter your 10-digit NPI to view your QPP participation status by performance.

QPP Participation Status includes APM Participation, as well as MIPS Participation.
## Two Item Graded Chronic Pain Scale

**Graded chronic pain scale: a two-item tool to assess pain intensity and pain interference**

In the last month, on average, how would you rate your pain? Use a scale from 0 to 10, where 0 is "no pain" and 10 is "pain as bad as could be"? *That is, your usual pain at times you were in pain.*

<table>
<thead>
<tr>
<th>No pain</th>
<th>Pain as bad as could be</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>

In the last month, how much has pain interfered with your daily activities? Use a scale from 0 to 10, where 0 is "no interference" and 10 is "unable to carry on any activities."

<table>
<thead>
<tr>
<th>No interference</th>
<th>Unable to carry on any activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>