Rethink Chronic Pain

A Structured Approach to the Management of Patients with Chronic Pain
1 Why Rethink Chronic Pain?
The Public Health Challenges of Chronic Pain

• Chronic pain is a serious public health issue\textsuperscript{1, 2}

• Patients with chronic pain, clinicians, payers, employers, and the government, are confronted by two dual interrelated issues\textsuperscript{1}:
  
  • Poor understanding and often inappropriate treatment of pain, including prescription therapy
  • Misuse, abuse, and diversion of medications intended to treat pain, namely opioids

• These challenges must be addressed in parallel to ensure that concerns about abuse and misuse of opioids do not preclude clinically appropriate opioid therapy for patients who need it\textsuperscript{3, 4}

• There needs to be R&D investment in new non-opioid chronic pain treatments and models of care, which could potentially help to address these challenges\textsuperscript{5}

Chronic Pain Is a Serious Public Health Burden

HIGH PREVALENCE:

~100 million American adults are affected by chronic pain1-5

- 23 million report ‘being in substantial’ pain
- Exceeds prevalence of cardiovascular disease (~27M), diabetes (~26M), and cancer (~12M) in US population
- Similar prevalence estimates globally

HIGH COST:

$560–635 billion is the estimated annual cost of chronic pain in the US1-4

- Exceeds costs of cardiovascular disease ($444B), diabetes ($174B), and cancer ($125B)
- High health care costs globally, although estimates vary

Opioid Prescriptions and Rates of Serious Health Consequences of Opioid Misuse and Abuse

Opioid Prescriptions Dispensed by Retail Pharmacies

Prescription Opioid Overdose Deaths and Emergency Department Visits
(US, 1999-2015)

50% to 80% of people who die from prescription opioid overdoses have a history of chronic pain.4

Understanding Chronic Pain
Chronic Pain Is **Different** From Acute Pain

### TIME

#### ACUTE PAIN

< 3 Months

- Usually obvious tissue damage
- Pain resolves upon healing
- Serves a protective function

#### CHRONIC PAIN

≥ 3-6 Months

- Pain for 3 months or more
- Pain beyond expected period of healing
- Usually has no protective function

CNS and Peripheral Pain Signaling Pathways

**Descending tracts** play a role in pain modulation via the midbrain periaqueductal gray matter and nucleus raphe.

**Ascending tracts** (e.g., spinothalamic) convey pain signals to the brain, where they are processed by the thalamus.
How Do Chronic Pain States Develop?

Central Sensitization
- Uncoupling of pain from peripheral stimuli
- Membrane excitability, synaptic recruitment and decreased inhibition

Peripheral Sensitization
- Nociceptor sensitization and direct pain messenger effects on nerve endings
- Reduction in pain threshold due to primary and secondary pain messenger activity

Described in the image:
- PAIN
- Spinal Cord Cross-Section
- Skin
- Trauma
- Peripheral Nociceptors
- Descenting Modulation
- Ascending Input
3 Chronic Pain Categories and Multimodal Pain Management
Chronic Pain Is a Biological, Psychological, and Social Phenomenon

• For many patients with chronic pain, effective assessment and treatment is multimodal and multidisciplinary, taking into account:
  • Biological factors (mix of symptoms, type of pain, etc.)
  • Psychological, emotional and cognitive factors (anxiety, depression, anger, fear of movement, catastrophizing)
  • Social factors (social and financial circumstances)

Multimodal Chronic Pain Management

Most patients with chronic pain will need pharmacotherapy as well

- For many patients with chronic pain, effective assessment and treatment is multimodal and multidisciplinary
  - **Nonpharmacologic intervention** that can be chosen based on the patient’s profile and treatment availability
    - Psychological therapies, such as cognitive-behavioral therapy, relaxation, biofeedback
    - Rehabilitative/physical therapies, such as stretching, exercise, massage
    - Other complementary alternative medicine, such as yoga, acupuncture
    - Patient self-management, such as pacing of activity, brief planned rests
  - **Pharmacological interventions**
  - **Interventional Techniques** (i.e., for chronic spinal pain)
    - Spinal interventional techniques (Diagnostic & therapeutic interventional techniques)
    - Cervical, thoracic, and lumbar interventional techniques (i.e., facet joint, epidurals, decompression, neurotomy)
    - Implantables (i.e., Spinal Cord Stimulators, Implantable Intrathecal Drug Administration)

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

Three Main Types of Pain Pathophysiology:

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

- **Neuropathic Pain**
  - 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
  - **EXAMPLES:** fibromyalgia


FM-PNP-0006 - 2-0
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The Three Types of Pain, Separately or Together, Give Rise to Various Chronic Pain Conditions

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

4 Assessing and Managing Chronic Pain
Comprehensive Pain Assessment Involves the Evaluation of Three Elements

Record **pain severity, impact on function, mood, and sleep**

- Assess and record pain severity, e.g., using VAS
- Evaluate impact on function, sleep, mood
  - At present, rarely done in primary care setting, and rarely (if ever) included in available EMR modules

Identify and document potential **underlying cause of pain**

- Evaluate health status, medical history, comorbid illnesses, prior and current medications, family history, etc
- Assess duration, location, and the likely source of pain
- Use advanced diagnostic techniques for certain patients

Identify and document **type(s) of pain pathophysiology**

- Evaluate pain descriptors, presence of allodynia, hyperalgesia
- Use tools to help determine the type of pain pathophysiology:
  - ID Pain® screening tool (6-item scale to identify non-nociceptive pain)
  - PainDETECT (detects neuropathic pain in low back pain patients)
  - Wolfe FM Questionnaire or FM Survey Questionnaire

**References**


**Abbreviations**

BPI: Brief Pain Inventory; EMR: electronic medical record; VAS: visual analog scale; FM: fibromyalgia
ID Pain® screening tool
(6-item scale to identify non-nociceptive pain)

- Score of ≥ 3 was shown to indicate the presence of a neuropathic component of pain
- ID-Pain consists of 5 sensory descriptor items and 1 item relating to whether pain is located in the joints (used to identify nociceptive pain)
- Developed in 586 patients with chronic pain of nociceptive, mixed or neuropathic etiology, and validated in 308 patients with similar classifications as determined by pain specialist diagnoses
- In the validation study, 22% of the nociceptive group, 39% of the mixed group, and 58% of the neuropathic group scored above the cutpoint score of 3

### ID PAIN® Screener

<table>
<thead>
<tr>
<th>Question</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Did the pain feel like pins and needles?</td>
<td>1</td>
</tr>
<tr>
<td>2. Did the pain feel hot/burning?</td>
<td>1</td>
</tr>
<tr>
<td>3. Did the pain feel numb?</td>
<td>1</td>
</tr>
<tr>
<td>4. Did the pain feel like electrical shocks?</td>
<td>1</td>
</tr>
<tr>
<td>5. Is the pain made worse with the touch of clothing or bed sheets?</td>
<td>1</td>
</tr>
<tr>
<td>6. Is the pain limited to your joints?</td>
<td>-1</td>
</tr>
</tbody>
</table>

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Treatment of Chronic Pain Includes Opioid Pain Medications Only When Appropriate

### Step 1
**Identify Pain Type**
- **Nociceptive Pain**
- **Neuropathic Pain**
- **Sensory Hypersensitivity**

### Step 2
**Use Guideline Driven First Line Treatment**
- **NSAIDs**, acetaminophen
  Treatment of underlying inflammatory condition may include corticosteroids, biologics and disease-modifying agents
- **Selected AEDs, SNRIs, and TCAs**

### Step 3
**Optimize First Line Treatment**
- Titrate, when appropriate, to FDA approved therapeutic doses based on tolerability prior to treatment being deemed inadequate and necessitating change

### Step 4
**Switch to Alternative Non-Opioid Treatment**
- When first line therapy is deemed inadequate, consider switching to another drug in the class or alternative non-opioid drug class

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15. Franklin G. Neurology 2014;83;1277-1284.
# Treatment of Chronic Pain Includes Opioid Pain Medications Only When Appropriate

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
<th>Nociceptive Pain</th>
<th>Neuropathic Pain</th>
<th>Sensory Hypersensitivity</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<td></td>
<td></td>
<td></td>
</tr>
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<td>Selected AEDs, SNRIs, and TCAs</td>
</tr>
<tr>
<td>3</td>
<td>Optimize First Line Treatment</td>
<td>Titrate, when appropriate, to FDA approved therapeutic doses based on tolerability prior to treatment being deemed inadequate and necessitating change</td>
<td></td>
<td></td>
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<tr>
<td>4</td>
<td>Switch to Alternative Non-Opioid Treatment</td>
<td>When first line therapy is deemed inadequate, consider switching to another drug in the class or alternative non-opioid drug class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Consider Opioids for When Non-Opioid Treatments are Inadequate</td>
<td>Reserve ER/LA Opioids for the management of pain severe enough to require daily, around-the-clock, long-term treatment in patients with nociceptive or neuropathic pain.</td>
<td>Opioids should be avoided in patients with sensory hypersensitivity</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Mitigate Risk</td>
<td>When prescribing an opioid, employ risk mitigation strategies, such as: assess patient risk, use abuse-deterrent opioids, prescribe lowest effective dose, and monitor for abuse, misuse and diversion (e.g., PDMP, UDT)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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## Risks Associated with Opioid Use in Special Populations

<table>
<thead>
<tr>
<th>Special Populations</th>
<th>Risks</th>
</tr>
</thead>
</table>
| Older Adults                         | • Smaller therapeutic window  
• Greater risk of respiratory depression and overdose  
• Increased risk of falls and fractures                                                                                                   |
| Renal/Hepatic insufficiency          | • Smaller therapeutic window  
• Greater risk of respiratory depression and overdose                                                                                   |
| Pregnant Women                       | • Risk to mother and fetus  
  • Some evidence of birth defects: neural tube defects, congenital heart defects, preterm delivery, stillbirth  
  • Neonatal opioid withdrawal                                                                                                              |
| Depression                           | • Higher risk for opioid use disorder                                                                                                                                                                 |
| Alcohol or other substance abuse     | • Higher risk for opioid use disorder                                                                                                                                                                 |
| Sleep Apnea                          | • Opioid therapy can worsen central sleep apnea; further desaturation                                                                                                                                    |
Guidelines Vary, But They Do Align on Certain Aspects of Assessment and Treatment

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Year</th>
<th>Topic</th>
<th>Multimodal Management</th>
<th>Multidisciplinary Approach</th>
<th>Assess Pain Mechanism</th>
<th>Use of Opioids</th>
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<tbody>
<tr>
<td>CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016</td>
<td>2016</td>
<td>Opioid use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2nd line</td>
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<tr>
<td>ASIPP: Responsible, Safe and Effective Prescription of Opioids for Chronic Non-cancer pain</td>
<td>2017</td>
<td>Opioid use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2nd line</td>
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<tr>
<td>VA-DOD: Guideline for Opioid Therapy for Chronic Pain</td>
<td>2017</td>
<td>Opioid use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2nd line</td>
</tr>
<tr>
<td>Washington State Interagency Guideline on Opioid Dosing for Chronic Non-cancer pain</td>
<td>2010</td>
<td>Opioid use</td>
<td>✓</td>
<td>✓</td>
<td>No mention</td>
<td>2nd line</td>
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<tr>
<td>Washington State Interagency Guideline on Prescribing Opioids for Pain</td>
<td>2015</td>
<td>Opioid Use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2nd or 3rd line</td>
</tr>
<tr>
<td>APS-AAPM: Use of Chronic Opioid Therapy in Chronic Noncancer Pain</td>
<td>2009</td>
<td>Opioid use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2nd line</td>
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<tr>
<td>Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain</td>
<td>2009</td>
<td>Opioid use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2nd line</td>
</tr>
<tr>
<td>ICSI Pain: Assessment, non-opioid treatment Approaches and Opioid Management</td>
<td>2016</td>
<td>Opioid Use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2nd or 3rd line</td>
</tr>
<tr>
<td>ICSI Health Care Guideline: Assessment and Management of Chronic Pain (2013 update)</td>
<td>2013</td>
<td>Chronic noncancer pain</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>2nd line</td>
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<tr>
<td>ACR: Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, &amp; Knee</td>
<td>2012</td>
<td>OA</td>
<td>✓</td>
<td>✓</td>
<td>No mention</td>
<td>2nd line</td>
</tr>
<tr>
<td>ACR: Guidelines for the Management of Rheumatoid Arthritis (2015 update)</td>
<td>2015</td>
<td>RA</td>
<td>✓</td>
<td>✓</td>
<td>No mention</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>AAN/AANEM/AAMP&amp;R: Evidence-based Guideline: Treatment of Painful Diabetic Neuropathy</td>
<td>2011</td>
<td>pDPN</td>
<td>✓</td>
<td>No mention</td>
<td>No mention</td>
<td>Level B evidence</td>
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<tr>
<td>Diabetic Neuropathy: a position statement by the American Diabetes Association</td>
<td>2016</td>
<td>pDPN</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Discouraged</td>
</tr>
<tr>
<td>IASP/NeuPSIG: Pharmacologic Management of Neuropathic Pain: Evidence-based Recommendations (updated review)</td>
<td>2015</td>
<td>Neuropathic</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>3rd line</td>
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<tr>
<td>EFNS Guidelines on the Pharmacological Treatment of Neuropathic Pain (2010 Revision)</td>
<td>2010</td>
<td>Neuropathic</td>
<td>No mention</td>
<td>No mention</td>
<td>✓</td>
<td>2nd or 3rd line</td>
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<td>Canadian Guidelines for the Diagnosis and Management of Fibromyalgia Syndrome</td>
<td>2012</td>
<td>FM</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Discouraged</td>
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<tr>
<td>EULAR: Evidence Based Recommendations for the Management of Fibromyalgia Syndrome (2016 update)</td>
<td>2016</td>
<td>FM</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
5 Addressing the Opioid Problem
While Clinical Guidelines Do Not Recommend Opioids as 1st Line, Up to 50% of Patients Receive Them 1st Line ( Alone or in Combination)

In the US, opioid medication utilization as first treatment post-diagnosis for chronic pain conditions* (prescribed alone or in combination with other pain therapy) does not appear to follow opioid treatment guidelines

Opioids Prescribed as First-line Pharmacologic Treatment by Condition

*Based on national claims data analysis between March 2008 and February 2012.

Why Are Opioids Overprescribed?

• Opioids may be perceived as an easy choice since they can provide relief for various types of pain
  • The prescriber may not consider etiologies/pathophysiology of pain or differential diagnosis

• Payers may provide greater access to generic opioids vs branded non-opioid medicines for pain or branded abuse-deterrent opioids

• Clinicians often underestimate patient risk for prescription opioid abuse

• Even when a patient is identified as being high risk, there is limited use of opioid risk reduction strategies

Assessing risk for misuse and abuse, and detecting such behaviors in patients already receiving opioids is difficult. Therefore, risk reduction strategies should be applied universally with every patient.

Abuse of Prescription Opioids May Progress from Oral Ingestion to Snorting and Injection

Routes of Administration of Extended-Release (ER) Oxycodone at Initiation of Use and at Addiction-treatment Admission (October 2000 to March 2002; N=187)

Patients admitted to substance abuse treatment centers reported progression from primarily oral ingestion to snorting/injection of ER oxycodone in <2 years (average time)

Initial Route of Administration (n=112/187)
- Oral: 83%
- Snorting: 16%
- Injection: 1%

Route of Administration at Admission (n=133/187)
- Oral: 62%
- Snorting: 26%
- Injection: 14%

Mean 19.2 Months*

*Average time between first use/misuse and addiction-treatment admission.

Note: Percentages at admission do not add up to 100% because respondents could report multiple routes of administration.

Extended-Release (ER) Opioids Are Tampered With for Purposes of Misuse and Abuse

Abuse of ER Formulations of Prescription Opioid Medications by Route of Administration

June 1, 2009 to August 8, 2010*

140,496 individuals assessed for substance use problems from 357 US centers participating in the National Addictions Vigilance Intervention and Prevention Program (NAVIPPRO) surveillance system

* Prior to introduction of reformulated ER oxycodone and ER oxymorphone.

Note: Percentages for each drug do not add up to 100% because respondents could report multiple routes of administration.

Knowing **When** to Use Opioid Medications Is as Important as Knowing **How** to Use Them

**Clinically Appropriate Treatment Selection for Chronic Pain**

**Universal Precautions for Opioid Prescribing**

1. **Assess Risk**
2. **Select Opioid**
3. **Dialogue With Patient**
4. **Monitor Treatment**

**WHEN to use opioids?**

Prescribe ER/LA opioids only for patients with pain severe enough to require daily, around-the-clock, long-term treatment and for whom alternative treatment options are inadequate.

**HOW to use opioids appropriately?**

A set of uniform prescribing practices should be applied to all patients to help address misuse, abuse, and diversion.*

Know When to Refer the Patient With Pain

• Certain findings (or the need for the more extensive assessments) are likely to trigger a referral to a pain specialist, neurologist, rheumatologist, or oncologist\(^1,2\)
  - Unexplained weight loss and/or history of cancer with new onset of pain
  - Fever and/or inflammation
  - Neurological deficits or progressive motor weakness
  - Urinary retention, fecal incontinence, etc.

• The need for treatment modalities such as regional anesthetic interventions and surgery may require referral to a pain specialist\(^3\)

• Referral should also be considered in the following situations\(^4,5\):
  - The patient has not responded to conservative/conventional treatments for pain
  - The pain continues to have a negative impact on patient’s quality of life, family/work life
  - The health care provider feels uncomfortable with dosage, number, or type of medications needed
  - Complicated and/or rare pain conditions such as chronic regional pain syndromes (reflex sympathetic dystrophy and causalgia) are suspected

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Taking Action on Chronic Pain
Adopting These Principles May Help Clinicians Achieve Better Outcomes in Chronic Pain

• There are significant public health problems that must be addressed in parallel
  • Poor understanding and often inappropriate treatment of pain
  • Misuse, abuse, and diversion of opioid medications
  • Development of new non-opioid chronic pain treatments and new models of care

• Clinical considerations
  • Consider psychological and social risk factors
  • Establish the pathophysiologic pain type(s) using available screening tools
  • Document pain assessments to enable effective management and monitoring
  • Use the pathophysiologic pain type(s) to help guide 1st line treatment selection
  • Consider opioid medications second line, unless contraindicated
  • Employ universal precautions to opioid prescribing
  • Set treatment goals with follow-up reevaluation of pain type and severity, impact, medication management and referrals to specialists, when appropriate