Opioids, Addiction, and the Treatment of Pain

Michigan Dental Society
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Disclosure

Neither I nor any members of my immediate family have a financial interest/arrangement or affiliation that could be perceived as a real or apparent conflict of interest related to the content or supporters of this activity.
Common quote:

“Opioids are the most potent medications we have for treatment of pain.”


Opioid facts

The United States has 4.6% of the world’s population.
- We use 80% of the world’s opioids!\(^1\)
- 83% of the world’s population has no access to any opioids.\(^2\)
Opioid increase

Drug distribution through the pharmaceutical supply chain was the equivalent of 96 mg of morphine per person in 1997.

and approximately 640 mg per person in 2015, an increase of >500%. That is the equivalent of 128 Vicodin tablets!

Percentage of Prescriptions Dispensed for Opioid Analgesics From Outpatient US Retail Pharmacies, 2009
Dental Opioids and Youth

Table 1. Proportion of Medicaid Patients Dispensed Opioids Following Surgical Extraction of Teeth, 2000-2010

<table>
<thead>
<tr>
<th>Year</th>
<th>National Vital Statistics System, DEA’s Automation of Reports and Consolidated Orders System, SAMHSA’s TEDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid Sales KG/10,000</td>
<td>Opioid Deaths/100,000</td>
</tr>
<tr>
<td>1999</td>
<td>0.51</td>
</tr>
<tr>
<td>2000</td>
<td>0.62</td>
</tr>
<tr>
<td>2001</td>
<td>0.73</td>
</tr>
<tr>
<td>2002</td>
<td>0.84</td>
</tr>
<tr>
<td>2003</td>
<td>0.95</td>
</tr>
<tr>
<td>2004</td>
<td>1.06</td>
</tr>
<tr>
<td>2005</td>
<td>1.17</td>
</tr>
<tr>
<td>2006</td>
<td>1.28</td>
</tr>
<tr>
<td>2007</td>
<td>1.39</td>
</tr>
<tr>
<td>2008</td>
<td>1.50</td>
</tr>
<tr>
<td>2009</td>
<td>1.61</td>
</tr>
<tr>
<td>2010</td>
<td>1.72</td>
</tr>
</tbody>
</table>

Michigan opioid deaths

Opioid pain reliever-related overdose deaths increasing at a faster rate than deaths from any major cause

<table>
<thead>
<tr>
<th>% change in number of deaths, United States, 2000-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-opioid overdose:</td>
</tr>
<tr>
<td>Alzheimer’s</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
</tr>
<tr>
<td>Nephritis</td>
</tr>
<tr>
<td>Suicide</td>
</tr>
<tr>
<td>Liver Disease</td>
</tr>
<tr>
<td>Chronic Lower Respiratory disease</td>
</tr>
<tr>
<td>Septicemia</td>
</tr>
<tr>
<td>HIV</td>
</tr>
<tr>
<td>Malignant Neoplasms</td>
</tr>
<tr>
<td>Pneumonia</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Meningitis</td>
</tr>
<tr>
<td>Pernicious Period</td>
</tr>
<tr>
<td>Heart disease</td>
</tr>
<tr>
<td>Motor vehicle traffic</td>
</tr>
<tr>
<td>Cerebrovascular</td>
</tr>
<tr>
<td>Influenza &amp; Pneumonia</td>
</tr>
<tr>
<td>Acute Aneurysm</td>
</tr>
</tbody>
</table>

WISQARS, 2000 and 2010; CDC/NCHS, National Vital Statistics System
**2014 to 2016**

U.S. life expectancy decreased for the first time in decades.

U.S. mortality rate increased.

All driven by opioid overdoses!

*Opioid overdoses counteracted all other medical advances!*

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### The State of US Health

Years lived with disability (in thousands)

<table>
<thead>
<tr>
<th>Condition</th>
<th>1990</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low back pain</td>
<td>3000</td>
<td>2500</td>
</tr>
<tr>
<td>Other MS disease</td>
<td>3500</td>
<td>3000</td>
</tr>
<tr>
<td>Neck pain</td>
<td>1500</td>
<td>1200</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>1000</td>
<td>700</td>
</tr>
</tbody>
</table>
Three key concepts:

Prescribers:
1. Don’t understand pain.
2. Don’t understand opioids.
3. Don’t understand addiction.
Pain

An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

International Association for the Study of Pain

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Acute pain: Pain < 3 months
Chronic pain: Pain > 3 months
Acute pain is a symptom
Chronic pain is a disease
4 types of pain

- Nociceptive
- Neuropathic
- Central Sensitization
- Opioid withdrawal
Which square is darker... A or B?

Better keep an eye on them...
Better keep an eye on them...

Constancy

Better keep an eye on them...

As Constancy
Better keep an eye on them...

s Constancy

Better keep an eye on them...

s Constancy
Better keep an eye on them...

Pretty cool, huh?

“Lightness Constancy”
Pain pathways

- Nociceptor
- Spinothalamic nerve
- Thalamus

Amygdala (fear)
Hippocampus (memory)
Somatosensory nerve (pain)
Limbic system (emotion)
Prefrontal cortex (rational thinking)
Central sensitization

- Nociceptor
- Spinothalamic nerve
- Thalamus

Amygdala (fear)
Hippocampus (memory)
Somatosensory nerve (pain)
Limbic system (emotion)
Prefrontal cortex (rational thinking)

Central Sensitization Syndromes
- Fibromyalgia
- Chronic headaches
- Irritable bowel syndrome
- Chronic neck pain
- Chronic back pain
- TMD
- All chronic pain???
Central Sensitization

This is also an issue in acute pain....

TMD

- Central sensitization is much more common in individuals with temporomandibular disorders.60
Central sensitization Inventory

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Difficulty and exhaustion when I wake from sleeping.</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>My menses feel mild and dry.</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>I have anxiety attacks.</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>I have headaches frequently.</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>I have problems with balance and mobility.</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>I have problems getting up and down.</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>I lose sensation in my fingers.</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>I feel my heart race when I am physically active.</td>
<td>None</td>
</tr>
<tr>
<td>9</td>
<td>I feel tension in my body.</td>
<td>None</td>
</tr>
</tbody>
</table>

Subclinical = 0 - 29
Mild = 30 - 39
Moderate = 40 - 49
Severe = 50 – 59
Extreme = 60 - 100.

Opioid withdrawal pain

• Occurs with reduction in opioid dose for those who have been on opioid therapy – even for acute pain treatment.
• Usually is felt in the area where there is a history of pain.
Acute to Chronic back pain

Risk factors by significance (my interpretation of the literature):

1. Mental and emotional status prior to injury.
2. Work and home environment.
3. Reception of opioids for acute pain
4. Activity level prior to injury.
5. Severity of injury.

Radiofrequency denervation

• Over 600 patients with CLBP and no improvement with conservative measures.
• 50% received denervation. All had a standardized exercise program.
• No difference in pain at 3 months.

JAMA, 2017
Chronic pain causes

- Nociceptive
- Neuropathic
- Central Sensitization
- Opioid withdrawal
- Combination (this is most common)

Central Sensitization is a significant factor in most cases of chronic pain that cause people to see the doctor.

OPIOIDS
Poppy plant
All addictive substances stimulate dopamine

- Opioids
- Alcohol
- THC
- Cocaine
- Methamphetamine
- Nicotine
- LSD
- Ecstasy
- Others

Opioids are different...

Dopamine
+
Opioid receptors
**Dopamine**

What is the purpose of our endorphins?

Enable us to achieve a goal (short term).\textsuperscript{23,24}
- Decrease pain (minimal effect).
- Increase motivation.
- Increase confidence.
- Increase reward.
- Reduce depression and anxiety.
- Increase “warmth-liking”.\textsuperscript{25}
  - Liking warm things.
  - Interpersonal bonding.

**Opioid receptors and endorphins**
Primary purpose:

**Dopamine** – Our primary reward system. This is what we live for.

**Endorphins and opioid receptors** – These maximize our ability to achieve the reward. This is our “success system”!
The “Dorothy Reaction”

• Occurs in susceptible individuals on exposure to opioids:
  • Those with acute or chronic stress/anxiety
  • Those with depression
  • Those with high ACE scores
  • Those with a genetic predisposition
  • Those with substance use disorder (including smoking)
  • Others...

Opioids given for pain may cause the “Dorothy Reaction and:

• Mentally impairing.\textsuperscript{8,9}
• Delay recovery.\textsuperscript{10,11}
• Increase medical costs.\textsuperscript{12}
• Opioid hyperalgesia.\textsuperscript{13,14}
• Double the chance of disability (if prescribed for 7 days or more).\textsuperscript{15}
• Increase falls.\textsuperscript{16}
• Cardiac, GI?\textsuperscript{17,18}
• Treat depression.\textsuperscript{19} (They are very calming)
• Brain changes.\textsuperscript{20}
• Addiction.\textsuperscript{21,22}
Addiction

Acute rx leads to long-term use\textsuperscript{47}

Duration of acute use:
1 day - 6% chance of still using that drug a year later.
8 days - 13.5%.
31 days - 29.9%.
Acute rx leads to long-term use\textsuperscript{47}

A note about tramadol:
Of those people whose initial rx was tramadol, 13.7\% were still on opioids one year later – the highest of any type of opioid.

Prescription Opioids in Adolescence and Future Opioid Misuse

Richard Miech, PhD\textsuperscript{b}, Lloyd Johnston, PhD\textsuperscript{b}, Patrick M. O’Malley, PhD\textsuperscript{b}, Katherine M. Keyes, PhD\textsuperscript{b}, Kenneth Heard, MD\textsuperscript{b}

Teens who received a prescription for opioid pain medication by Grade 12 were at 33 percent increased risk of misusing an opioid between ages 19 and 25.

Among those with low predicted risk of future opioid use in 12th grade, having an opioid prescription increased their risk of post-high-school opioid misuse three-fold.
Treating Pain

General goals for pain treatment

• Empower patient (reduce victimhood)
  • Manage mood
  • Manage anxiety
  • CBT and mindfulness

• Distract

• Medicate
  • Nonopioid medications (oral medications and nitrous oxide)
  • Nerve blocks
  • Wound infiltration
  • Opioids if necessary – for calming effects
Efficacy of pain medications

Acute pain

<table>
<thead>
<tr>
<th>Medication</th>
<th>Percent with 50% pain relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen 200 mg</td>
<td>37</td>
</tr>
<tr>
<td>Acetaminophen 500 mg</td>
<td>28</td>
</tr>
<tr>
<td>Ibuprofen 400 mg</td>
<td>40</td>
</tr>
<tr>
<td>Oxycodone 15 mg</td>
<td>21</td>
</tr>
<tr>
<td>Oxy 10 + acet 1000</td>
<td>37</td>
</tr>
<tr>
<td>Ibu 200 + acet 500</td>
<td>62</td>
</tr>
</tbody>
</table>

Post-op pain

- Enhanced recovery after surgery (ERAS)
- 109 patients having colorectal surgery c/w 98 controls
- Protocol includes:
  - Pre-op counseling
  - Carbohydrate loading
  - Multimodal analgesia with avoidance of intravenous opioids
  - Intraoperative goal-directed fluid resuscitation
  - Immediate postoperative feeding
  - Immediate ambulation
ERAS outcomes

ERAS patients compared to controls:

• Ambulated on POD 0: 77% (0%)
• Total morphine equivalents: 63 (280)
• Any complication: 15% (30%)
• Length of stay in days: 4.6 (6.8)
• Hospital costs: $13,306 ($20,435)
• Press-Ganey patient satisfaction: 98% (43%)

Renal colic

Delivering safe and effective analgesia for management of renal colic in the emergency department: a double-blind, multigroup, randomised controlled trial

Samer Al Pathan, Bisswadee Mitra, Lohn D Strange, Muhammad Shoaib Afzal, Shahzad Aajur, Elharameh Shukri, Konstantinos Morley, Shatsho A Al Hill, Khalid Al Rumaithi, Stephen H Thomas, Peter A Cameron


Figure 2: Proportion of patients with ureteric calculi who did not achieve a significant pain reduction (45% reduction from initial pain score) with a numerical pain rating scale score.
Acute pain conclusion:

We must prescribe fewer opioids for acute pain!
The CDC guidelines recommend 3 days or less – but most outpatient pain can be treated without any opioids!
The combination of ibuprofen + acetaminophen is the best treatment with the least side effects.
**Excerpt from:**
*University of Minnesota School of Dentistry Guideline*  
(This is a *mandatory* guideline)

If NSAIDS can be tolerated:

<table>
<thead>
<tr>
<th>Pain Severity</th>
<th>Analgesic Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Ibuprofen (200-400 mg) q4-6 hours prn for pain</td>
</tr>
</tbody>
</table>
| Mild to Moderate    | **Step 1:** Ibuprofen (400-600 mg) q6 hours: fixed intervals for 24 hours  
**Step 2:** Ibuprofen (400 mg) q4-6 hours prn for pain |
| Moderate to Severe  | **Step 1:** Ibuprofen (400-600 mg) with APAP (500 mg) q6 hours: fixed interval for 24 hours  
**Step 2:** Ibuprofen (400 mg) with APAP (500 mg) q6 hours prn for pain |
| Severe              | **Step 1:** Ibuprofen (400-600 mg) with APAP (650 mg) with (5mg) hydrocodone q6 hours: 3-day supply.  
**Step 2:** Ibuprofen (400-600 mg) with APAP Ibuprofen (400-600 mg) with APAP (500 mg) q6 hours: prn for pain |

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**Total Opioid Prescriptions per Quarter**

- *Protocol introduced to Clinical Affairs Committee*
- **Protocol Official Policy of Department of OMFS**

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Total Opioid Prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 QTR 2015</td>
<td>915</td>
</tr>
<tr>
<td>2 QTR 2015</td>
<td>1138</td>
</tr>
<tr>
<td>3 QTR 2015</td>
<td>1007</td>
</tr>
<tr>
<td>4 QTR 2015</td>
<td>1076</td>
</tr>
<tr>
<td>1 QTR 2016</td>
<td>1126</td>
</tr>
<tr>
<td>2 QTR 2016</td>
<td>330</td>
</tr>
<tr>
<td>3 QTR 2016</td>
<td>169</td>
</tr>
<tr>
<td>4 QTR 2016</td>
<td>454</td>
</tr>
<tr>
<td>1 QTR 2017</td>
<td>336</td>
</tr>
<tr>
<td>2 QTR 2017</td>
<td>209</td>
</tr>
</tbody>
</table>
Combining ibuprofen and acetaminophen for acute pain management after third-molar extractions

Translating clinical research to dental practice

Paul A. Moore, DMD, PhD, MPH; Elliot V. Hersh, DMD, MS, PhD


Other dental articles.
If you use opioids for acute pain:

• They are most helpful for their calming effects.
• Use for 3 days or less.
• Check MAPS first!

Chronic pain

• Completely different from acute pain!
• If the pain is severe or disabling, **MOST** is from central sensitization and/or opioid withdrawal!
  • Pain medications will not work well on this type of pain.
Chronic pain

No evidence that opioids are effective for long-term treatment of chronic pain.\textsuperscript{30}

Epidemiologic studies have shown that those on chronic opioid therapy have worse quality of life than those with chronic pain who are not.\textsuperscript{31}

The AAN recommends against using opioids for back pain, headaches, or fibromyalgia.\textsuperscript{37}

A Cochrane review recommends against using opioids for OA of the hip or knee.\textsuperscript{36}

Opioid efficacy for chronic back pain\textsuperscript{45}

- Short term studies (<3 mo) pain decrease 10.1 (100 pt scale)
- Medium term studies (3 mo - <6 mo) pain decrease 8.1
- Long term (6 mo or more) – NO STUDIES

Experts believe that there must be a decrease of 15 points to be clinically significant.
Treatment of chronic pain

• Behavioral therapy

• PT

• Treatment of mood disorders

• Exercise

• Acupuncture

• Yoga and other alternative therapies

• Amitriptyline, duloxetine, gabapentin and similar drugs may help a little.

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Treatment of chronic pain

• Behavioral therapy:
  • Cognitive Behavioral Therapy
    • (redirect your thoughts)
  • Mindfulness training
    • (acknowledge your thoughts)
  • Decatastrophizing

There is very limited availability of this type of therapy.
Additional thoughts:

• If your patient on opioids is not doing functionally better, you should wean them off.

• If you believe your patient has developed opioid use disorder, you must treat them or refer them for treatment. MAT is the most effective treatment of OUD.

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**Centers for Disease Control and Prevention**

**MMWR**

Morbidity and Mortality Weekly Report

Early Release / Vol. 65

March 15, 2016

**CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016**

https://www.cdc.gov/drugoverdose/prescribing/guideline.html
Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

9. Clinicians should review the patient’s history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

CDC Guidelines

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient.

2. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

6. For acute pain. Use opioids for 3 days or less.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies).
PEG
Pain Screening Tool

1. What number best describes your pain on average in the past week:
   0 1 2 3 4 5 6 7 8 9 10
   No pain
   Pain as bad as you can imagine

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere
   Completely interferes

3. What number best describes how, during the past week, pain has interfered with your general activity?
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere
   Completely interferes

For patients already on opioids for COT

• Do not prescribe additional opioids.
• Utilize acetaminophen and/or NSAIDs.
• Call the prescribing doctor. Have them manage pain.
When are opioids definitely indicated?

• Following severe trauma (for a short period)
• End of life

A survey of patients in the waiting room found that 37% had misused opioids in the past month.
(2) Before prescribing or dispensing a controlled substance to a patient, a licensed prescriber shall ask the patient about other controlled substances the patient may be using. The prescriber shall record the patient’s response in the patient’s medical or clinical record.

(3) Beginning June 1, 2018, before prescribing or dispensing to a patient a controlled substance in a quantity that exceeds a 3-day supply, a licensed prescriber shall obtain and review a report concerning that patient from the electronic system for monitoring schedule 2, 3, 4, and 5 controlled substances established under section 7333a. This subsection does not apply under any of the following circumstances:

The difficult dental patient

• The individual “allergic” to NSAIDs and acetaminophen.

• The individual who calls back after 3 days with severe pain and wanting a refill.

• The individual on chronic opioid therapy for chronic pain.

• The individual on buprenorphine or methadone for treatment of opioid use disorder.
If you think abuse or addiction is a possibility:

Refer for treatment!

Goals for pain treatment

- Consider every dose of opioid
- Keep opioid naïve patients, opioid naïve
- Remember that:
  - No one dies from acute pain
  - Over 100 people die every day from opioids
“To write prescriptions is easy, but to come to an understanding with people is hard.”

-- Franz Kafka, “A Country Doctor”

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References:


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