Non-opioid Approaches to Pain Management:
A Cochrane-based Analysis of the CDC's Recent Recommendations.
Layne Subera, DO

Lecture Contents
• Overview of the CDC Guideline for Prescribing Opioids for Chronic Pain
  • Focus on Non-opioid Treatment Provisions
  • Nonpharmacologic Recommendations
  • Opioid Pharmacologic Therapy Recommendations
• Compare CDC Recommendations to Other Evidence
  • Cochrane Database Is Used When Possible
    • Neuropathic Indications
    • Nociceptive Indications
  • RA, OA
• Consider the Efficacy and Safety of Different Modalities

Chronology of Guidelines
• Washington, 2007
• Utah, 2008
• Oklahoma, 2013
• CDC, 2016
All Opioid Guidelines Are Similar

- Focus on Clinically Meaningful Improvement in Function
- More Specific Diagnosis
- Non-pharmacological Interventions Preferred
- Non-opioid Options Before Opioid Options
- Screen for Opioid Risk Factors
- Use the Lowest Effective Dose of Opioids
- Continually Monitor
- Promote Realistic Expectations

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

- In context:
  - 20% of patients present to physician offices with noncancer pain.
  - Providers wrote 258 million prescriptions for opioids in 2012.
  - Enough for every adult in the United States to have a bottle of pills!
  - In 2010, there were 16,651 opioid related overdoses.
  - Prevalence of musculoskeletal pain conditions was estimated at 43% among adults in the United States in 2003.
  - 3%-4% of the adult U.S. population, were prescribed long-term opioid therapy in 2005.
  - At a population level, more than 165,000 persons in the United States have died from opioid pain-medication-related overdoses since 1999.

http://www.cdc.gov/drugoverdose/prescribing/guideline.html

CDC Specific Therapies

- To guide patient-specific selection of therapy, clinicians should evaluate patients and establish or confirm the diagnosis.
- An evaluation should generally include:
  - A focused history.
  - The characteristics of the pain and potentially contributing factors.
    - Function, psychological stressors, sleep, etc.
  - A physical exam.
  - Imaging or other diagnostic testing only if indicated.
CDC Principles of Chronic Pain Treatment

- Use non-opioid therapies to the extent possible.
- Identify and address co-existing mental health conditions.
- Focus on functional goals and improvement.
- Engage patients actively in their pain management.
- Use disease-specific treatments when available.
  - For example: gabapentin/pregabalin/duloxetine for neuropathic pain.
- Use first-line options preferentially.
- Use multimodal approaches for patients who have failed standard treatments, have severe functional deficits, or psychosocial risk factors.

For complex pain syndromes

- Pain specialty consultation can be considered to assist with diagnosis as well as management.
- Diagnosis can help identify disease-specific interventions to reverse or ameliorate pain. For example:
  - Improving glucose control to prevent diabetic neuropathy.
  - Immune-modulating agents for rheumatoid arthritis.
  - Physical or occupational therapy to address posture, muscle weakness, or repetitive occupational motions that contribute to musculoskeletal pain.
  - Surgical intervention to relieve mechanical/compressive pain.

Nonpharmacologic Recommendations

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

• There is high-quality evidence that exercise therapy for hip and knee osteoarthritis reduces pain and improves function immediately after treatment.
  • The improvements can sustained for at least 2–6 months.
  • Reduces pain and improves function in low back pain.
  • Improves global well-being and physical function in fibromyalgia.
Cochrane Author’s Conclusion: Muscle Energy Therapy

• The quality of research is poor. Studies are generally small and at high risk of bias due to methodological deficiencies.
• Studies conducted to date generally provide low-quality evidence that MET is not effective for patients with LBP.
• There is not sufficient evidence to reliably determine whether MET is likely to be effective in practice.

http://www.cochrane.org/CD009852/BACK_muscle-energy-technique-met-for-non-specific-low-back-pain

Cochrane Author’s Conclusion: Spinal Manipulation Therapy

• High quality evidence suggests that there is no clinically relevant difference between SMT and other interventions for reducing pain and improving function in patients with chronic low-back pain.
• Further research is likely to have an important impact on our confidence in the estimate of effect in relation to inert interventions and sham SMT, and data related to recovery.

http://www.cochrane.org/CD008112/BACK_spinal-manipulative-therapy-for-chronic-low-back-pain

Cochrane Author’s Conclusion: Massage Therapy

• Very little confidence that massage is an effective treatment for LBP.
• Acute, sub-acute and chronic LBP had improvements in pain outcomes with massage only in the short-term follow-up.
• Functional improvement was observed in participants with sub-acute and chronic LBP when compared with inactive controls, but only for the short-term follow-up.

http://www.cochrane.org/CD001929/BACK_massage-low-back-pain
**Primary Care & Cognitive Behavioral Technique**

- CBT addresses psychosocial contributors to pain and improves function.
- Primary care clinicians can integrate cognitive behavioral approaches.
  - Encouraging patients to take an active role in the care plan.
  - Supporting patients in engaging in beneficial but potentially anxiety-provoking activities, such as exercise.
  - Providing education in relaxation techniques and coping strategies.
- Patients with more entrenched anxiety or fear related to pain can be referred for formal therapy with a mental health specialists.

**Cochrane Author’s Conclusion: Psychological Therapy for Adults**

- CBT but not behaviour therapy has weak effects in improving pain, but only immediately post-treatment and when compared with treatment as usual/waiting list.
- Small to moderate benefits, more for disability, mood and catastrophic thinking than for pain, were found in trials which compared CBT with no treatment.
- CBT is a useful approach to the management of chronic pain.


**The Efficacy of CBT for Chronic Pain**

- Compared with treatment-as-usual or wait-list control conditions, CBT had statistically significant but small effects on pain and disability, and moderate effects on mood and catastrophizing.
  - At 6- to 12- months, the only significant effect was for mood.
  - Compared with active control conditions, CBT was not superior.

Interventional Approaches

- Interventional approaches such as arthrocentesis and intraarticular glucocorticoid injection can provide short-term improvement in pain and function.
  - Rheumatoid arthritis.
  - Osteoarthritis.
  - Rotator cuff disease.
- Evidence is insufficient to determine the extent to which repeated glucocorticoid injection increases potential risks such as articular cartilage changes and sepsis.

Cochrane Author’s Conclusion: Injection Therapy for Low Back Pain

- There is insufficient evidence to support the use of injection therapy in subacute and chronic low-back pain.
- However, it cannot be ruled out that specific subgroups of patients may respond to a specific type of injection therapy.

http://www.cochrane.org/CD001824/BACK_injection-therapy-for-subacute-and-chronic-low-back-pain

Nonopioid Pharmacologic Therapy Recommendations

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Categorizing the Character of Pain

- The underlying mechanism for most pain syndromes can be categorized.
  - Neuropathic (e.g., diabetic neuropathy, postherpetic neuralgia, fibromyalgia).
  - Nociceptive (e.g., osteoarthritis, muscular back pain).
- NSAIDs (and opioids) can be used for exacerbations of nociceptive pain.
- Tricyclics, gabapentinoids, anticonvulsants, or transdermal lidocaine generally are recommended for neuropathic pain.

Nonopioid Medications

- Acetaminophen.
- NSAIDs.
- Gabapentin/pregabalin.
- Tricyclic antidepressants and serotonin/norepinephrine reuptake inhibitors.
- Topical agents (lidocaine, capsaicin, NSAIDs).

CDC NSAIDS and Acetaminophen

- Several nonopioid pharmacologic therapies are effective for chronic pain.
  - “In particular, acetaminophen and NSAIDs can be useful for arthritis and low back pain.”
- Nonopioid pharmacologic therapies are not generally associated with a substance use disorder.
- The numbers of fatal overdoses associated with nonopioid medications are a fraction of those associated with opioid medications.
**Acetaminophen**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnitude of Benefit</td>
<td>Small</td>
</tr>
<tr>
<td>Potential Harms</td>
<td>Hepatotoxic, particularly at higher doses</td>
</tr>
<tr>
<td>CDC Comments</td>
<td>First-line analgesic, probably less effective than NSAIDs</td>
</tr>
<tr>
<td>NNT</td>
<td>4 to 5</td>
</tr>
<tr>
<td>NNH</td>
<td>12</td>
</tr>
</tbody>
</table>

**BMJ: Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomised placebo controlled trials**

- 12 reports (13 randomised trials) were included.
- For hip or knee osteoarthritis there was "high quality" evidence that paracetamol provides a significant, although not clinically important, effect on pain and disability in the short term.
- "High quality" evidence showed that patients taking paracetamol are nearly four times more likely to have abnormal results on liver function tests.
- CONCLUSION: Paracetamol is ineffective in the treatment of low back pain and provides minimal short term benefit for people with osteoarthritis.


**Cochrane Author’s Conclusion: Acetaminophen**

- Acetaminophen compared to placebo
- The studies show that people who took acetaminophen has less pain (when resting, moving, sleeping and overall) and felt better overall than people who took a placebo.
- Pain, physical function and stiffness were about the same.
- Pain decreased by 4 more points on a scale of 0-100 for people who took acetaminophen instead of a placebo.

http://www.Cochrane.org/CD004257/MUSKEL_acetaminophen-for-osteoarthritis
**NSAIDs**

<table>
<thead>
<tr>
<th>NSAID</th>
<th>Magnitude of Benefit</th>
<th>Potential Harms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Small-moderate</td>
<td>Cardiac, GI, renal</td>
</tr>
<tr>
<td>CDC Comments</td>
<td>First-line analgesic; COX-2 selective NSAIDs less GI toxicity</td>
<td></td>
</tr>
</tbody>
</table>

- **NNT**: 1.8 to 3.9
- **NNH**: 11 to 53

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**Cochrane Author’s Conclusion:**

NSAIDS (Low back Pain)

- Six of the 13 included RCTs showed that NSAIDs are more effective than placebo regarding pain intensity.
- NSAIDs are slightly more effective than placebo regarding disability.
- We identified no difference in efficacy between different NSAID types including selective versus non-selective NSAIDs.
- We cannot make firm statements about the occurrence of adverse events or whether NSAIDs are safe for long-term use.


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**Subtypes of NSAIDS**

<table>
<thead>
<tr>
<th>NSAID Class</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propionic Acids</td>
<td>Ibuprofen, Ketoprofen, Naproxen</td>
</tr>
<tr>
<td>Acetic Acids</td>
<td>Diclofenac, Etodolac, Ketorolac</td>
</tr>
<tr>
<td>Fenamates (1-naphthaleneacetic acids)</td>
<td>Nabumetone</td>
</tr>
<tr>
<td>Oxoxams</td>
<td>Meloxicam, Profescom</td>
</tr>
<tr>
<td>Salicylates</td>
<td>Aspirin, Diflunisal, Choline Magnesium Trisalicylate</td>
</tr>
<tr>
<td>COX-2 Inhibitors</td>
<td>Celecoxib</td>
</tr>
</tbody>
</table>
### Are some NSAIDs safer?

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Case-control studies</th>
<th>Cohort study</th>
<th>Oral route vs control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen</td>
<td>1.6 (1.3 to 2.0)</td>
<td>1.0</td>
<td>2.1 (1.6 to 2.7)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1.6 (1.3 to 2.0)</td>
<td>1.0</td>
<td>1.8 (1.0 to 2.8)</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>2.3 (1.8 to 2.7)</td>
<td>1.6 (1.0 to 2.1)</td>
<td>2.7 (1.6 to 4.8)</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>2.8 (2.3 to 4.6)</td>
<td>2.6 (1.9 to 3.1)</td>
<td>2.5 (1.6 to 10.4)</td>
</tr>
<tr>
<td>Tolmetin</td>
<td>3.8 (2.7 to 6.2)</td>
<td>2.6 (1.9 to 2.6)</td>
<td>3.2 (2.6 to 11.9)</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>2.6 (1.7 to 3.6)</td>
<td>2.3 (1.7 to 2.6)</td>
<td>2.8 (1.9 to 11.9)</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>1.8 (1.4 to 2.3)</td>
<td>1.4 (0.7 to 2.8)</td>
<td>2.7 (1.5 to 4.8)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>2.2 (1.7 to 2.9)</td>
<td>1.6 (1.0 to 2.0)</td>
<td>2.3 (1.6 to 11.2)</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>2.2 (1.6 to 2.7)</td>
<td>1.6 (1.0 to 2.1)</td>
<td>2.7 (1.6 to 4.8)</td>
</tr>
<tr>
<td>Sulindac</td>
<td>2.2 (1.7 to 2.9)</td>
<td>1.6 (1.0 to 2.0)</td>
<td>2.3 (1.6 to 11.2)</td>
</tr>
<tr>
<td>Diflusinal</td>
<td>2.2 (1.6 to 2.7)</td>
<td>1.6 (1.0 to 2.1)</td>
<td>2.7 (1.6 to 4.8)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>2.2 (1.7 to 2.9)</td>
<td>1.6 (1.0 to 2.0)</td>
<td>2.7 (1.6 to 4.8)</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>2.2 (1.6 to 2.7)</td>
<td>1.6 (1.0 to 2.1)</td>
<td>2.7 (1.6 to 4.8)</td>
</tr>
</tbody>
</table>


### GI Risk

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>No history of ulcer or antiulcer drug</td>
<td>1.0</td>
</tr>
<tr>
<td>Dyspepsia or antiulcer drug user</td>
<td>0.7 (0.3 to 1.5)</td>
</tr>
<tr>
<td>Ulcer without complication</td>
<td>5.3 (4.2 to 6.7)</td>
</tr>
<tr>
<td>Ulcer with complication</td>
<td>25 (14 to 41)</td>
</tr>
</tbody>
</table>


### “Safer” Not “Safe”

**From the CDC:**
- Acetaminophen: 228
- NSAIDS: 2,200
- Opioids: 16,831

**From the UK:**
- Acetaminophen: 25 million
- NSAIDS: 70 million
- Opioids: 10 million

Cardiovascular Risk


Gabapentin/pregabalin

<table>
<thead>
<tr>
<th>Gabapentin/pregabalin</th>
<th>Magnitude of Benefit</th>
<th>Potential Harms</th>
<th>CDC Comments</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Small-moderate</td>
<td>Sedation, dizziness, ataxia</td>
<td>First-line for neuropathic pain; TCAs and SNRIs for fibromyalgia, TCAs for headaches</td>
<td>7.2</td>
<td>3.7</td>
</tr>
</tbody>
</table>

CDC Non-opioid Risks: Gabapoids & Anticonvulsants

- Selected anticonvulsants such as pregabalin and gabapentin can improve pain in diabetic neuropathy and post-herpetic neuralgia.
- Pregabalin, gabapentin, and carbamazepine are FDA-approved for treatment of certain neuropathic pain conditions.
- Pregabalin is FDA approved for fibromyalgia management.
Cochrane Author's Conclusion: Gabapentin (Neuropathic Pain)

• There was no top tier evidence that was unequivocally unbiased.
• Second tier evidence, showed that gabapentin at doses of 1200 mg or more was effective for some people with some painful neuropathic pain conditions.
• About 35% achieved at least 50% pain intensity reduction with gabapentin, compared with 21% for placebo.
• Over half of those treated with gabapentin will not have worthwhile pain relief.
• The levels of efficacy found for gabapentin are consistent with those found for other drug therapies in postherpetic neuralgia and painful diabetic neuropathy.


Cochrane Author's Conclusion: Pregabalin (Neuropathic Pain)

• Pregabalin has proven efficacy in neuropathic pain conditions and fibromyalgia.
• A minority of patients will have substantial benefit with pregabalin, and more will have moderate benefit.
• Many will have no or trivial benefit, or will discontinue because of adverse events.
• There is no evidence to support the use of pregabalin in acute pain scenarios.


Cochrane Author's Conclusion: Antiepileptic drugs (Neuropathic Pain)

• Clinical trial evidence supported the use of only gabapentin and pregabalin in some neuropathic pain conditions and fibromyalgia.
• For other antiepileptic drugs there was no evidence, insufficient evidence, or evidence of a lack of effect; this included carbamazepine.
• Evidence from clinical practice and experience is that some patients can achieve good results with antiepileptics other than gabapentin or pregabalin.

http://www.Cochrane.org/CD010567/SYMPT_antiepileptic-drugs-to-treat-neuropathic-pain-or-fibromyalgia-an-overview-of-Cochrane-Author’s-Conclusion-reviews
Tricyclics and Serotonin/Norepinephrine Reuptake Inhibitors

<table>
<thead>
<tr>
<th>Tricyclic antidepressants and serotonin/norepinephrine reuptake inhibitors</th>
<th>Magnitude of Benefit</th>
<th>Potential Harms</th>
<th>CDC Comments</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small-moderate</td>
<td>TCA/venlafaxine: anticholinergic and cardiac toxicities; SNRI: safer and better tolerated</td>
<td>First-line for neuropathic pain; TCA/venlafaxine: for fibromyalgia, TCA for headaches</td>
<td>2 to 3.6</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

Cochrane Author’s Conclusion: TCAs/SNRI (Neuropathic Pain)

- There is still limited evidence for the role of SSRIs.
- TCAs and venlafaxine have NNTs of approximately three.
  - This means that for approximately every three patients with neuropathic pain who are treated with either of these antidepressants, one will get at least moderate pain relief.
- There is evidence to suggest that other antidepressants may be effective but numbers of participants are insufficient to calculate robust NNTs.


Cochrane Author’s Conclusion: Amitriptyline (Neuropathic Pain)

- There is no supportive unbiased evidence for a beneficial effect.
  - But... that has to be balanced against decades of successful treatment.
- There is no good evidence of a lack of effect; rather our concern should be of overestimation of treatment effect.
- Amitriptyline should continue to be used as part of the treatment of neuropathic pain.
- Only a minority of people will achieve satisfactory pain relief.

Cochrane Author's Conclusion: TCAs/SNRI (Rheumatoid Arthritis)

- There is currently insufficient evidence to support the routine prescription of antidepressants as analgesics in patients with RA.
- No reliable conclusions about their efficacy can be drawn from eight placebo RCTs.
- The use of these agents may be associated with adverse events which are generally mild and do not lead to cessation of treatment.


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Topical agents (lidocaine, capsaicin, NSAIDs)

<table>
<thead>
<tr>
<th>Topical agents (lidocaine, capsaicin, NSAIDs)</th>
<th>Magnitude of Benefit</th>
<th>Potential Harms</th>
<th>CDC Comments</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Small-moderate</td>
<td>Capsaicin initial flare/ burning, irritation of mucus membranes</td>
<td>Consider as alternative first-line, thought to be safer than systemic medications. Lidocaine for neuropathic pain, topical NSAIDs for localized osteoarthritis, topical capsaicin for musculoskeletal and neuropathic pain</td>
<td>6.4</td>
<td>Minimal</td>
</tr>
</tbody>
</table>

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Cochrane Author's Conclusion: Topical NSAIDs (Nociceptive Pain)

- Topical NSAIDs provided good levels of pain relief in acute conditions such as sprains, strains and overuse injuries.
- Probably similar benefit to that provided by oral NSAIDs.
- The gel formulations of diclofenac (as Emugel®), ibuprofen, and ketoprofen provided the best effects.
- Topical NSAIDs are effective in providing pain relief and certain formulations provide the best results.
  - NNT Diclofenac was 1.8
  - NNT Ketoprofen was 2.5
  - NNT Ibuprofen was 3.9

Cochrane Author's Conclusion: Topical capsaicin (Neuropathic Pain)

- High-concentration topical capsaicin generates more participants with high levels of pain relief than does control treatment with lower concentrations.
- Benefit over control is not large, but for those who do obtain high levels of pain relief there are additional improvements in sleep, fatigue, depression and an improved quality of life.
- Even when efficacy is established, there are unknown risks, especially on epidermal innervation due to repeated application.


Cochrane Author's Conclusion: Topical Lidocaine (Neuropathic Pain)

- No evidence from good quality randomized controlled studies to support the use of topical lidocaine to treat neuropathic pain
- Clinical experience supports efficacy in some patients.


Opioid Pharmacologic Therapy Recommendations

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
CDC Deciding to Add Opioids to the Treatment Plan

- Non-pharmacologic therapy and non-opioid 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.
- If opioids are used, they should be combined with non-pharmacologic therapy and non-opioid pharmacologic therapy.
- Recommendation Category: A, Evidence Type: 3

CDC Opioids & Reason

- CDC experts agreed that opioids should not be considered first-line or routine therapy for chronic pain outside of active cancer, palliative, and end-of-life care.
- Although evidence on long-term benefits of non-opioid therapies is also limited, these therapies are also associated with short-term benefits, and risks are much lower.
- Patients should not be required to sequentially “fail” non-pharmacologic and non-opioid pharmacologic therapy before proceeding to opioid therapy.

CDC Opioids In Treatment Plans

- In some clinical contexts (e.g., headache or fibromyalgia), expected benefits of initiating opioids are unlikely to outweigh risks regardless of previous non-pharmacologic and non-opioid pharmacologic therapies used.
- In other situations (e.g., serious illness in a patient with poor prognosis for return to previous level of function, contraindications to other therapies, and clinician and patient agreement that the overriding goal is patient comfort), opioids might be appropriate regardless of previous therapies used.
- In addition, when opioid pain medication is used, it is more likely to be effective if integrated with non-pharmacologic therapy.
CDC Long-term Opioids

- The clinical evidence review found insufficient evidence to determine whether pain relief is sustained and whether function or quality of life improves with long-term opioid therapy.
- While benefits for pain relief, function, and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant.
- Based on the clinical evidence review, long-term opioid use for chronic pain is associated with serious risks including increased risk for opioid use disorder, overdose, myocardial infarction, and motor vehicle injury.

Cochrane Author’s Conclusion: Opioids (Neuropathic pain)

- Cochrane studied four opioids for neuropathic pain: morphine, oxycodone (Roxicodone), methadone, and levorphanol (Levo-Dromoran).
- Pooled results from seven of the nine studies in this review (405 total patients) showed that patients treated with low to moderate doses of opioids had a 13-point mean decrease in pain intensity on a 100-point scale compared with placebo.
- A 13-point reduction on a visual analog scale is on the threshold of clinical significance. It was not possible to determine clinically significant pain reduction.
- This clinical benefit is comparable to that achieved by the maximal daily dose of gabapentin (Neurontin; 3,600 mg per day).


Safety & Efficacy

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

• Patients with pain should receive treatment that provides the greatest benefits relative to risks.

Moving Beyond Relative Risk

• Relative Risk vs. Absolute Risk
• Chronic Opioid Therapy
  • 1.8% risk of overdose/year vs 100% chance of pain/day.
  • A concurrent co-sedating drug may increase risk by 42%
    • 2.5% risk of overdose/year

About Numbers Needed to Treat and Harm

• Studies require dichotomous data sets.
• Start with the Absolute Risk Difference (ARD) between the control and experimental group event rates.
  • ARD = Control Event Rate (CER) minus Experimental Event Rate (EER).
  • CER and EER are probability values and from 0.0 to 1.0.
• The NNT is the inverse reciprocal of the Absolute Risk Difference
  • NNT = 1/ARD

*Pain-Topics News/Research UPDATES:* Calculating Benefits & Harms in Pain Research
### NNT and NNH for Various Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Condition</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neupathic pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>Neupathic pain</td>
<td>3.5 to 4.3</td>
<td>6.3 to 8.3</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Neupathic pain</td>
<td>3.4 to 4.7</td>
<td>8.1</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Postsurgical pain</td>
<td>2.4 to 4.8</td>
<td>8.3</td>
</tr>
<tr>
<td>TCAs</td>
<td>Neupathic pain</td>
<td>2 to 3.6</td>
<td>6 (minor), 28 (major)</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Neupathic pain</td>
<td>7.2 to 7.7</td>
<td>3.7</td>
</tr>
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<td>Venlafaxine</td>
<td>Neupathic pain</td>
<td>3.3</td>
<td>16.2</td>
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<td>Duloxetine</td>
<td>Neupathic pain</td>
<td>9 to 8</td>
<td>0.9</td>
</tr>
<tr>
<td>Acacetaminophen</td>
<td>Nociceptive pain</td>
<td>4 to 5</td>
<td>12</td>
</tr>
<tr>
<td>Lidocaine patch</td>
<td>Peripheral neuropathic pain</td>
<td>6.4</td>
<td>Minimal</td>
</tr>
<tr>
<td>Capsaicin patch</td>
<td>Peripheral neuropathic pain</td>
<td>10.6</td>
<td>Minimal</td>
</tr>
<tr>
<td>MAID</td>
<td>Nociceptive pain</td>
<td>2.8 to 3.8</td>
<td>11 to 53</td>
</tr>
</tbody>
</table>


### In Conclusion

- Exercise and fitness are the best long-term treatments.
- All medications should be used with caution.

### Cochrane Author’s Conclusion: Balneotherapy (Spa-therapy) for Osteoarthritis

- We found silver level evidence ([www.cochranemsk.org](http://www.cochranemsk.org)) concerning the beneficial effects of mineral baths compared to no treatment.
- Of all other balneological treatments no clear effects were found.
- Given the absence of an adequate statistical analysis and data presentation, the noted “positive findings” should be viewed with caution.

[http://www.Cochrane.org/CD006864/MUSKEL_balneotherapy-or-spa-therapy-for-osteoarthritis](http://www.Cochrane.org/CD006864/MUSKEL_balneotherapy-or-spa-therapy-for-osteoarthritis)