Review of 2022 CDC Clinical Practice Guidelines for Prescribing Opioids for Pain + Neuroplastic Pain Neuroanatomy and a Comprehensive Approach to Chronic Pain

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Disclosures

- None

Outline

- CDC Guideline review
  - Briefly review the 2016 Guidelines
  - Rationale for updating the Guidelines
  - Overview the 2022 Guidelines
  - Deep dive into the evidence base and rationale for each new guideline
  - Summarize the guidelines, and THEN interject my personal opinions
- Neuroplastic pain
  - Personal professional journey from biomechanical model to biopsychosocial model
  - Neuroanatomy – ascending and descending pathways
  - Examples of pain without nociception and nociception without pain
  - Role of Cognitive therapies in assisting descending pathways
  - All patients with chronic pain should have a physical exercise regimen as well as mental health regimen
- Nonpharmacologic approaches to chronic pain

Brief background

- Opioid epidemic
- 2016 CDC released guidelines for prescribing opioids for chronic pain

2016 CDC Guidelines

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.
2. Clinicians should establish treatment goals with all patients prior to initiating opioid therapy.
3. Clinicians should discuss with patients known risks and realistic benefits of opioid therapy.
4. When starting opioid therapy for chronic pain, prescribe immediate release opioids, not ER/LA
5. Clinicians should prescribe at the lowest effective dosage. Reassess evidence of individual benefits and risk when increasing to 50 MME. Avoid increasing to 90 MME or justify decision to titrate above 90 MME.
6. Only prescribe immediate release opioids for acute pain, and for no more than the expected duration of pain.
7. Evaluate benefits and harms within 1-4 weeks of starting opioid therapy. Evaluate the benefits vs harms every 3 months.

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2016 CDC Guidelines

8. Before starting and periodically during treatment, evaluate risk factors. Consider offering naloxone when factors that increase risk for opioid overdose are present
9. Utilize PDMP data
10. Utilize UDS testing
11. Avoid prescribing opioids and benzodiazepines whenever possible
12. Offer or arrange evidence-based treatment (usually medication -assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for opioid use disorder

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2018 Arizona Law

- All prescribes are required to check PDMP before prescribing an opioid analgesic or benzodiazepine
- Prescribes who dispense in office for outpatient use may no longer dispense schedule II opioids, except for MAT
- Limit of initial prescription for a schedule II opioid to not more than a five-day supply, except postsurgical 14-day supply
  - Exceptions: surgery, cancer, trauma, hospice, MAT, infant opioid weaning
  - A pharmacist is not required to verify with the prescriber whether the prescription meets exemption
- If a provider believes a patient requires >90 MME per day, they must first consult with a licensed physician board certified in pain.
  - Exceptions: continuation of an existing prescription, cancer, trauma, hospital, hospice, MAT
- Must also prescribe naloxone if >90 MME per day
- By 1/1/2020, all prescriptions must be sent electronically
- Additional pharmacist requirements ("red cap")
- Veterinarian exemptions
- CME requirement

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2022 CDC Guidelines

1. Maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient. Discuss risks and benefits.
2. Nonopioid therapies are preferred for subacute and chronic pain. Discuss risks and benefits.
3. When starting opioid therapy, use immediate release, not ER/LA
4. When initiating opioids, use lowest effective dose. If opioids are continued for chronic therapy, use caution and evaluate risks/benefits.
5. Weigh benefits and risks when changing opioid dosages. Unless there are indications of a life -threatening issue, do NOT discontinue opioids abruptly or rapidly reduce opioid dosages
6. When rx for acute pain, prescribe no greater than needed for the expected duration of pain
7. Evaluate benefits and risks with 1-4 weeks after initiation. Regularly re-evaluate

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2022 CDC Guidelines

8. Evaluate risk and benefit periodically. Offer naloxone.
9. Review PMDP data
10. Consider toxicology testing
11. Use caution when prescribing opioid pain medication and benzodiazepines concurrently
12. Offer and arrange treatment with evidence-based medications to treat patients with opioid use disorder. Detoxification on its own, without medications for opioid use disorder, is not recommended for opioid use disorder.

2022 Guidelines

- Preamble
  - Pain is a complex phenomenon influenced by multiple factors, including biologic, psychological and social factors
  - Patients with chronic pain are also at increased risk for suicidal ideation and behaviors
  - Subconscious and overt gender and racial discrimination occurs with respect to pain management
    - Black patients are less likely to be referred to a pain specialist
    - Black patients receive prescription opioids at lower doses than white patients
    - Adults in rural areas are more likely to be prescribed opioids for nonmalignant pain
    - White populations have experienced much higher rates of prescription related opioid overdose deaths than black populations

2022 Guidelines

- Preamble
  - "An important aim of pain management is the provision of person-centered care built on trust between patients and clinicians. Such care includes appropriate evaluation to identify potentially reversible causes of pain and establish a diagnosis and measurable treatment outcomes that focus on optimizing function and quality of life."
  - Insufficient evidence to demonstrate long-term benefits of prescription opioid treatment for chronic pain

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2022 Guidelines

- Preamble
  - "Although some laws, regulations, and policies that appear to support recommendations in the 2016 CD Opioid Prescribing Guideline might have had positive results for some patients, they are inconsistent with a central tenet of the guideline:
    - **The recommendations are voluntary and intended to be flexible to support, not supplant, individualized, patient-centered care."**
  - Some policies purportedly drawn from the 2016 Guideline have been notably inconsistent with it and have gone well beyond its clinical recommendations
    - Extension to non-covered populations such as cancer and palliative care
    - Rapid opioid tapers
    - Abrupt discontinuation without collaboration with patients
    - Rigid application of opioid dosage thresholds

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2022 Guidelines

- Preamble
  - "These actions are not consistent with the 2016 Guideline and have contributed to patient harm, including untreated and undertreated pain, serious withdrawal symptoms, worsening pain outcomes, psychological distress, overdose, and suicidal ideation and behavior."
  - Guidelines do NOT replace clinical judgement and individualized patient-centered decision-making.
  - Flexibility is paramount
  - Should not be used as inflexible standards of care
  - **Not intended to be implemented as absolute limits for policy or practice across populations**

2022 Guidelines

- "The recommendations do not apply to care provided to patients who are hospitalized or in an emergency department… do apply to prescribing for pain management for patients when they are discharged from hospitals, emergency departments or other facilities."

2022 Guidelines

- "Pain management specialists often have extensive training and expertise in pain management modalities that other clinicians do not, and they might treat patients with clinical situations that are more complex, less prevalent, and not well addressed by the available evidence; therefore, the balance of benefits and risks to patients might differ when the treating clinician is a pain management specialist."

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2022 Guidelines

- For sickle cell disease, cancer, palliative care, and opioid use disorder, other clinical guidelines exist

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Category Recommendations and Evidence Types

- Category A = Applies to all patients
- Category B = Individual decision-making needed

- Type 1: RCTs; overwhelming evidence from observational studies
- Type 2: RCTs with limitations; strong evidence from obs studies
- Type 3: Observational studies or RCTs with notable limitations
- Type 4: Clinical experience/observations; studies with major limitations

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2022 Guidelines – Recommendation 1

- Nonopioid therapies are at least as effective as opioids for many common types of acute pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider opioid therapy for acute pain if the benefits are anticipated to outweigh risks to the patient. Before prescribing opioid therapy for acute pain, clinicians should discuss with patients the realistic benefits and known risks of opioid therapy (recommendation category B; evidence type 3)

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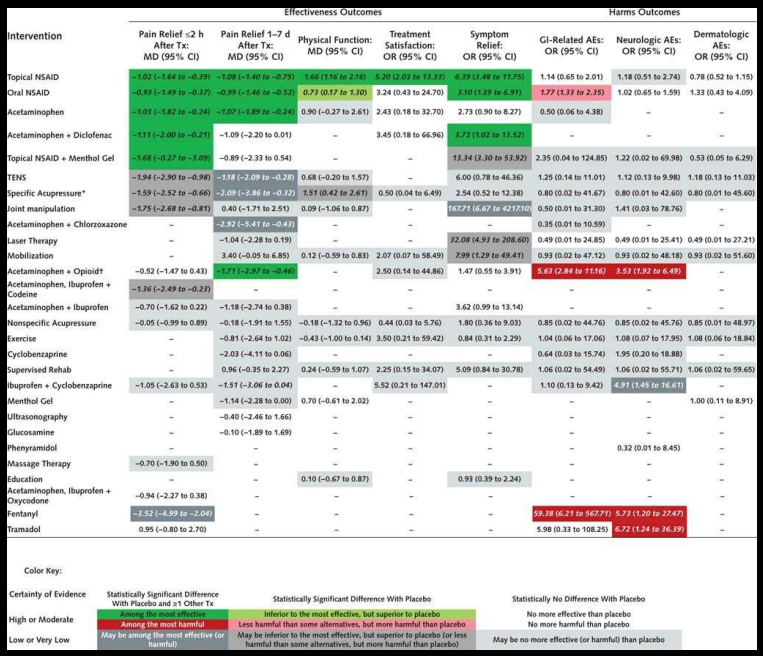
2022 Guidelines – Recommendation 1 commentary

- ACP recommends nonpharmacologic treatment with superficial heat, massage, acupuncture or spinal manipulation
- Health insurers and health systems can contribute to improved pain management and reduced medication use by increasing access to noninvasive nonpharmacologic therapies with evidence of effectiveness
- A systematic review found that for MSK injuries such as sprains, whiplash and muscle strains, topical NSAIDs provided the greatest benefit-harm ration, followed by oral NSAIDS or acetaminophen. (122)
- NSAIDS have been found to be more effective than opioids for surgical dental pain and kidney stone pain and similarly effective to opioids for low back pain (10)



Intervention	Effectiveness Outcomes					Harms Outcomes		
	Pain Relief ≤2 h After Tx: MD (95% CI)	Pain Relief 1–7 d After Tx: MD (95% CI)	Physical Function: MD (95% CI)	Treatment Satisfaction: OR (95% CI)	Symptom Relief: OR (95% CI)	GI-Related AEs: OR (95% CI)	Neurologic AEs: OR (95% CI)	Dermatologic AEs: OR (95% CI)
Topical NSAID	*−1.02 (−1.64 to −0.39)*	*−1.08 (−1.40 to −0.75)*	*1.66 (1.16 to 2.16)*	*5.20 (2.03 to 13.33)*	*6.39 (3.48 to 11.75)*	1.14 (0.65 to 2.01)	1.18 (0.51 to 2.74)	0.78 (0.52 to 1.15)
Oral NSAID	*−0.93 (−1.49 to −0.37)*	*−0.99 (−1.46 to −0.52)*	*0.73 (0.17 to 1.30)*	3.24 (0.43 to 24.70)	*3.10 (1.39 to 6.91)*	*1.77 (1.33 to 2.35)*	1.02 (0.65 to 1.59)	1.33 (0.43 to 4.09)
Acetaminophen	*−1.03 (−1.82 to −0.24)*	*−1.07 (−1.89 to −0.24)*	0.90 (−0.27 to 2.61)	2.43 (0.18 to 32.70)	2.73 (0.90 to 8.27)	0.50 (0.06 to 4.38)	–	–
Acetaminophen + Diclofenac	*−1.11 (−2.00 to −0.21)*	−1.09 (−2.20 to 0.01)	–	3.45 (0.18 to 66.96)	*3.72 (1.02 to 13.52)*	–	–	–
Topical NSAID + Menthol Gel	*−1.68 (−0.27 to −3.09)*	−0.89 (−2.33 to 0.54)	–	–	*13.34 (3.30 to 53.92)*	2.35 (0.04 to 124.85)	1.22 (0.02 to 69.98)	0.53 (0.05 to 6.29)
TENS	*−1.94 (−2.90 to −0.98)*	*−1.18 (−2.09 to −0.28)*	0.68 (−0.20 to 1.57)	–	6.00 (0.78 to 46.36)	1.25 (0.14 to 11.01)	1.12 (0.13 to 9.98)	1.18 (0.13 to 11.03)
Specific Acupressure*	*−1.59 (−2.52 to −0.66)*	*−2.09 (−2.86 to −0.32)*	*1.51 (0.42 to 2.61)*	0.50 (0.04 to 6.49)	2.54 (0.52 to 12.38)	0.80 (0.02 to 41.67)	0.80 (0.01 to 42.60)	0.80 (0.01 to 45.60)
Joint manipulation	*−1.75 (−2.68 to −0.81)*	0.40 (−1.71 to 2.51)	0.09 (−1.06 to 0.87)	–	*167.71 (6.67 to 4217.10)*	0.50 (0.01 to 31.30)	1.41 (0.03 to 78.76)	–
Acetaminophen + Chlorzoxazone	–	*−2.92 (−5.41 to −0.43)*	–	–	–	0.35 (0.01 to 10.59)	–	–
Laser Therapy	–	−1.04 (−2.28 to 0.19)	–	–	*32.08 (4.93 to 208.60)*	0.49 (0.01 to 24.85)	0.49 (0.01 to 25.41)	0.49 (0.01 to 27.21)
Mobilization	–	3.40 (−0.05 to 6.85)	0.12 (−0.59 to 0.83)	2.07 (0.07 to 58.49)	*7.99 (1.29 to 49.41)*	0.93 (0.02 to 47.12)	0.93 (0.02 to 48.18)	0.93 (0.02 to 51.60)
Acetaminophen + Opioid†	−0.52 (−1.47 to 0.43)	*−1.71 (−2.97 to −0.46)*	–	2.50 (0.14 to 44.86)	1.47 (0.55 to 3.91)	*5.63 (2.84 to 11.16)*	*3.53 (1.92 to 6.49)*	–
Acetaminophen, Ibuprofen + Codeine	*−1.36 (−2.49 to −0.23)*	–	–	–	–	–	–	–
Acetaminophen + Ibuprofen	−0.70 (−1.62 to 0.22)	−1.18 (−2.74 to 0.38)	–	–	3.62 (0.99 to 13.14)	–	–	–
Nonspecific Acupressure	−0.05 (−0.99 to 0.89)	−0.18 (−1.91 to 1.55)	−0.18 (−1.32 to 0.96)	0.44 (0.03 to 5.76)	1.80 (0.36 to 9.03)	0.85 (0.02 to 44.76)	0.85 (0.02 to 45.76)	0.85 (0.01 to 48.97)
Exercise	–	−0.81 (−2.64 to 1.02)	−0.43 (−1.00 to 0.14)	3.50 (0.21 to 59.42)	0.84 (0.31 to 2.29)	1.04 (0.06 to 17.06)	1.08 (0.07 to 17.95)	1.08 (0.06 to 18.84)
Cyclobenzaprine	–	−2.03 (−4.11 to 0.06)	–	–	–	0.64 (0.03 to 15.74)	1.95 (0.20 to 18.88)	–
Supervised Rehab	–	0.96 (−0.35 to 2.27)	0.24 (−0.59 to 1.07)	2.25 (0.15 to 34.07)	5.09 (0.84 to 30.78)	1.06 (0.02 to 54.49)	1.06 (0.02 to 55.71)	1.06 (0.02 to 59.65)
Ibuprofen + Cyclobenzaprine	−1.05 (−2.63 to 0.53)	*−1.51 (−3.06 to 0.04)*	–	5.52 (0.21 to 147.01)	–	1.10 (0.13 to 9.42)	*4.91 (1.45 to 16.61)*	–
Menthol Gel	–	−1.14 (−2.28 to 0.00)	0.70 (−0.61 to 2.02)	–	–	–	–	1.00 (0.11 to 8.91)
Ultrasonography	–	−0.40 (−2.46 to 1.66)	–	–	–	–	–	–
Glucosamine	–	−0.10 (−1.89 to 1.69)	–	–	–	–	–	–
Phenyramidol	–	–	–	–	–	–	0.32 (0.01 to 8.45)	–
Massage Therapy	−0.70 (−1.90 to 0.50)	–	–	–	–	–	–	–
Education	–	–	0.10 (−0.67 to 0.87)	–	0.93 (0.39 to 2.24)	–	–	–
Acetaminophen, Ibuprofen + Oxycodone	−0.94 (−2.27 to 0.38)	–	–	–	–	–	–	–
Fentanyl	*−3.52 (−4.99 to −2.04)*	–	–	–	–	*59.38 (6.21 to 567.71)*	*5.73 (1.20 to 27.47)*	–
Tramadol	0.95 (−0.80 to 2.70)	–	–	–	–	5.98 (0.33 to 108.25)	*6.72 (1.24 to 36.39)*	–

Color Key:

Certainty of Evidence	Statistically Significant Difference With Placebo and ≥1 Other Tx	Statistically Significant Difference With Placebo	Statistically No Difference With Placebo
High or Moderate	Among the most effective Among the most harmful	Inferior to the most effective, but superior to placebo Less harmful than some alternatives, but more harmful than placebo	No more effective than placebo No more harmful than placebo
Low or Very Low	May be among the most effective (or harmful)	May be inferior to the most effective, but superior to placebo (or less harmful than some alternatives, but more harmful than placebo)	May be no more effective (or harmful) than placebo

Figure 1. NMA results, sorted based on GRADE certainty of evidence and effect estimate for the comparisons of active treatments versus placebo for effectiveness and harm outcomes.

Busse JW, Sadeghirad B, Oparin Y, Chen E, Goshua A, May C, Hong PJ, Agarwal A, Chang Y, Ross SA, Enary P, Florea ID, Noor ST, Yao W, Lok A, Ali SH, Craigie S, Couban R, Morgan RL, Culig K, Brar S, Akbari-Kelachayeh K, Pozdnyakov A, Shergill Y, Sivanamthan L, Zihayat B, Das A, Guyatt GH. Management of Acute Pain From Non-Low Back, Musculoskeletal Injuries : A Systematic Review and Network Meta-analysis of Randomized Trials. Ann Intern Med. 2020 Nov 3;173(9):730-738. doi: 10.7326/M19-3601. Epub 2020 Aug 18. PMID: 32805127.

Chou R, Wagner J, Ahmed AY, et al. Treatments for Acute Pain: A Systematic Review [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2020 Dec. (Comparative Effectiveness Review, No. 240.) Evidence Summary. Available from: https://www.ncbi.nlm.nih.gov/books/NBK566511/

- "Opioid therapy was associated with decreased or similar effectiveness for pain versus an NSAID for surgical dental pain, kidney stone pain, and low back pain. Opioids and NSAIDs were more effective than acetaminophen for pain for surgical dental pain, but opioids were less effective than acetaminophen for kidney stone pain."
- No graphs/charts/data to illustrate. Just statements of findings.

2022 Guidelines – Recommendation 1 commentary

- Triptans, NSAIDs, combined triptans with NSAIDs, antiemetics, dihydroergotamine, and acetaminophen are established acute treatment for migraine.
- When not contraindicated, NSAIDs should be used for low back pain, painful musculoskeletal injuries, dental pain, postoperative pain and kidney stone pain

2022 Guidelines – Recommendation 2

- Nonopioid therapies are preferred for subacute and chronic pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider initiating opioid therapy if expected benefits for pain and function are anticipated to outweigh the risks to the patient. Before starting opioid therapy… discuss with patients the realistic benefits and known risks of opioid therapy

Recommendation 2 – What noninvasive options?

- Fibromyalgia – CBT, myofascial release massage, mindfulness practices, tai chi, quigong, acupuncture
- Low back pain – exercise therapy, psychological therapy, spinal manipulation, laser therapy, massage, mindfulness, yoga, acupuncture
- Joint osteoarthritis – weight loss, manual therapies
- Tension headache – spinal manipulation

Recommendations 2, cont'd

- Health insurers and health systems can improve pain management and reduce medication use and associated risks by increasing reimbursement for and access to noninvasive nonpharmacologic therapies

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Recommendations 2 – nonopioid Rx

- Osteoarthritis – topical NSAIDs, duloxetine, systemic NSAIDs
- Chronic low back pain – NSAIDs, duloxetine
- Neuropathic pain – tricyclic, tetracyclic, SNRI; pregabalin, gabapentin; capsaicin and lidocaine patches
- Diabetic peripheral neuropathy – pregabalin, duloxetine
- Fibromyalgia – pregabalin, duloxetine, milnacipran (savella)

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Recommendations 2, cont'd

- Opioids should not be considered first-line or routine therapy for subacute or chronic pain. This does not mean that patients should be required to sequentially fail nonpharmacologic and nonopioid pharmacologic therapy or be required to use any specific treatment before proceeding to opioid therapy.
- Opioid therapy should not be initiated without consideration by the clinician and patient of an exit strategy to be used if opioid therapy is unsuccessful.
- Clinicians should avoid rapid tapering or abrupt discontinuation of opioids.
- Clinical evidence reviews found no instrument with high accuracy for predicting opioid-related harms, such as overdose or opioid use disorder.

Recommendation 2 – Interventional approaches

- Osteoarthritis, rheumatoid arthritis, RTC disorders – intra-articular glucocorticoid injection
- Spinal pain – epidural steroid injections, nerve ablation procedures, neurostimulation procedures

Recommendation 3

- When starting opioid therapy for acute, subacute, or chronic pain, clinicians should prescribe immediate-release opioids instead of ER/LA opioids

Recommendation 3 – Considerations

- Do not use ER/LA opioids as PRN
- ER/LA should be reserved for severe, continuous pain.
- When switching between opioids, reduce total daily dosage to account for incomplete opioid cross-tolerance.
- No studies were found in the clinical evidence reviews assessing the effectiveness of “abuse-deterrent” technologies as a risk mitigation strategy for deterring or preventing opioid misuse, opioid use disorder or overdose. (195,7)

Recommendations 3 – ER/LA more dangerous?

- Miller M, Barber CW, Leatherman S, et al. Prescription Opioid Duration of Action and the Risk of Unintentional Overdose Among Patients Receiving Opioid Therapy. *JAMA Intern Med.* 2015;175(4):608–615. doi:10.1001/jamainternmed.2014.8071

- "After adjustment for age, sex, opioid dose, and other clinical characteristics, patients receiving long-acting opioids had a significantly higher rate of overdose injury than did those receiving short-acting opioids (hazard ratio [HR], 2.33; 95% CI, 1.26-4.32)"

Recommendation 3 – Methadone

- "methadone is associated with cardiac arrhythmias along with QT prolongation on the electrocardiogram, and it has complicated pharmacokinetics and pharmacodynamics, including a long and variable half-life and peak respiratory depressant effect occurring later and lasting longer than peak analgesic effect."

- "only clinicians who are familiar with methadone's unique risk profile and who are prepared to educate and closely monitor their patients, including risk assessment for QT prolongation and consideration of electrocardiographic monitoring, should consider prescribing methadone for pain."

Recommendation 4

- When opioids are initiated for opioid-naïve patients, clinicians should prescribe the lowest effective dosage… carefully evaluate individual benefits and risks when considering increasing dosage and should avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients.

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Recommendation 4 – Implementation

- Lowest starting dose 5-10 MME per dose; 20-30 MME/day
- Before increasing total opioid dosage >50 MME, pause and carefully reassess evidence of individual benefits and risks
- Additional dosage increases beyond 50 MME/day are progressively more likely to yield diminishing returns in benefits for pain and function

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Recommendation 4 – Rationale

- Opioid dosages for chronic pain of 50-100 MME in observational studies have been associated with increased risks for opioid overdose by factors of 1.9-4.6 compared with dosages of 1-20 MME.

- When opioids are prescribed for acute pain, similar associations have been found, with dosages of 50-100 MME/day 4.73x risk of overdose and >100 MME/day 6.64x risk of overdose compared to <20 MME.

- *Bohnert ASB, Valenstein M, Bair MJ, et al. Association Between Opioid Prescribing Patterns and Opioid Overdose-Related Deaths. JAMA. 2011;305(13):1315–1321. doi:10.1001/jama.2011.370*
  - Data from the VA from 2004-2008

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Recommendation 5

- For patients already receiving opioid therapy, clinicians should carefully weigh benefits and risks and exercise care when changing opioid dosage. If benefits outweigh the risks, clinicians should work closely with patients to optimize nonopioid therapies while continuing opioid therapy. If benefits do not outweigh risks… appropriately taper and discontinue opioids. Unless there are indications of a life-threatening issue such as warning signs of impending overdose, opioid therapy should not be discontinued abruptly, and clinicians should not rapidly reduce opioid dosages from higher dosages.

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Recommendation 5 – Implementation

- Longer duration of previous opioid therapy might require a longer taper. For patients who have taken opioids >1 year, tapers can be completed over several months to years depending on the opioid dosage and should be individualized based on the patients goals and concerns.
  - Tapers of 10% per month or slower are likely to be better tolerated
- Clinicians should access appropriate expertise if considering tapering opioids during pregnancy

Recommendation 5 – Implementation

- Payers, health systems, and state medical boards should not use this clinical practice guideline to set rigid standards or performance incentives related to dose or duration of opioid therapy; should ensure that policies based on cautionary dosage thresholds do not result in rapid tapers or abrupt discontinuation of opioids; and should ensure that policies do not penalize clinicians for accepting new patients who are using prescribed opioids for chronic pain, including those receiving high dosages of opioids or for refraining from rapidly tapering patients prescribed long-term opioid medications

Recommendation 5 – Implementation

- Integrating behavioral and nonopioid pain therapies and treatment for comorbid mental health conditions before and during a taper can help manage pain.
- Nonpharmacologic and nonopioid treatments should be integrated into the patients' pain management plans after an individualized assessment of benefits and risks that considers the patient's diagnosis, circumstances and unique needs.
- "pain management" does NOT mean "opioids"

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Recommendation 5 – Managing withdrawal symptoms

- Alpha 2 agonists clonidine and lofexidine are more effective than placebo in reducing severity of withdrawal from heroin or methadone in the context of abrupt discontinuation
- Similar research could not be found on clonidine and lofexidine in patients tapering from long-term opioid treatment for pain.
- However, alpha-2 agonist tizanidine has been used to help taper patients from long-term, high dosage opioids for pain.
- Clinicians should closely monitor patients who are unable to taper and who continue on high-dosage or otherwise high-risk opioid regimens
- Clinicians can use periodic and strategic motivational questions and statements to encourage movement toward appropriate therapeutic changes.

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Sidebar conversation – Opioid risks

- Tolerance, dependence, abuse
- Opioid overdose, accidental
- Intentional overdose
- Diversion
- Opioid-induced hyperalgesia
- Drowsiness; confusion
- Lowered respiratory rate
- Immunosuppression
- Liver toxicity
- Constipation
- Hormonal dysfunction
- Osteoporosis

Recommendation 6

- When opioids are needed for acute pain, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids
- If patients already receiving long-term opioid therapy require additional opioids for superimposed severe acute pain, opioids should be continued only for the duration of pain severe enough to require additional opioids, returning to the patient's baseline opioid dosage as soon as possible.

Recommendation 6 – Implementation

- If patients already receiving long-term opioid therapy require additional opioids for superimposed severe acute pain, opioids should be continued only for the duration of pain severe enough to require additional opioids, returning to the patient's baseline opioid dosage as soon as possible.
- Clinicians, practices and health systems should have mechanisms in place for the subset of patients who experience severe acute pain that continues longer than the expected duration.
- Patients should be evaluated at least every 2 weeks if prescribed opioids for acute pain

Recommendation 7

- Clinicians should evaluate benefits and risks with patients within 1-4 weeks of starting opioid therapy for subacute or chronic pain or of dosage escalation.

Recommendation 7 – implementation

- ER/LA opioids have increased risk of OD within the first 2 weeks of treatment
- Shorter follow-up intervals when starting or increasing methadone
- Establish treatment goals, including functional goals, for continued opioid therapy
- Reevaluate patients who are at higher risk for opioid use disorder or overdose more frequently than 3 months
- If virtual visits are part of standard care, follow-up assessments that allow the clinician to communicate with and observe the patient through telehealth modalities might be conducted.
- Ensure treatment for depression, anxiety or other psychological comorbitities is optimized.

Recommendation 7 – implementation

- Clinicians should ensure that opioid prescribing for acute pain does not unintentionally become long-term opioid therapy simply because medications are continued without reassessment but only as an intentional decision that benefits are likely to outweigh risks after discussion between the clinician and patient.

Recommendation 8

- Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk for opioid related harms and discuss risk with patients. Clinicians should work with patients to incorporate into the management plan strategies to mitigate risk, including offering naloxone.

Recommendation 8 – Implementation

- Screen for drug and alcohol use
- Work to optimize treatment for depression and other mental health conditions
- Offer naloxone when prescribing opioids, particularly patients at increased risk for overdose
  - History of overdose, substance use disorder, sleep-disordered breathing, >50MME, taking BZDs
- Naloxone should be offered to patients, not required in order to fill an opioid prescription
- Avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing, when possible, to minimize risk for respiratory depression

Recommendation 9

- When prescribing initial opioid therapy for acute, subacute or chronic pain, clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data

Recommendation 9 – Implementation

- PDMP data should be reviewed before an initial opioid prescription and then every 3 months or more frequently.
- PDMP generated risk scores have not been validated against clinical outcomes such as overdose and should not take the place of clinical judgement

PDMP Inconsistencies

- Clinicians should not dismiss patients from their practice on the basis of PDMP information
  - Can adversely affect patient safety
- Discuss information from the PDMP (occasionally, can be incorrect)
- Discuss safety concerns; including discussion with other physicians on the PDMP

Recommendation 10

- When prescribing opioids for subacute or chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances.

Recommendation 10 – Implementation

- Clinicians should not dismiss patients from care on the basis of a toxicology test result.
  - Dismissal could have adverse consequences for patient safety, including obtaining opioids or other drugs from alternative sources and the clinician missing opportunities to facilitate treatment for substance use disorder
- Clinicians, practices and health systems should aim to minimize bias in testing and should not apply this recommendation differentially on the basis of assumptions about patients.
- Restricting confirmatory testing to situations and substances for which results can reasonably be expected to affect patient management can reduce costs of toxicology testing.

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Recommendation 10 – Implementation

- Avoid use of potentially stigmatizing language (“dirty” or “clean”)
- Offer treatment or refer the patient for treatment with medications for opioid use disorder

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Recommendation 11

- Clinicians should use particular caution when prescribing opioid pain medication and benzodiazepines concurrently and consider whether benefits outweigh risks of concurrent prescribing of opioids and other central nervous system depressants.

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Recommendation 12

- Clinicians should offer or arrange treatment with evidence-based medications to treat patients with opioid use disorder. Detoxification on its own, without medications for opioid use disorder, is not recommended for opioid use disorder because of increased risks for resuming drug use, overdose, and overdose death. (A; 1)

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Opioid Use Disorder (DSM5)

At least 2 of the following; 10 & 11 exempt if medically prescribed

1. Taking larger amounts or taking drugs over a longer period than intended.
2. Persistent desire or unsuccessful efforts to cut down or control opioid use.
3. Spending a great deal of time obtaining or using the opioid or recovering from its effects.
4. Craving, or a strong desire or urge to use opioids
5. Problems fulfilling obligations at work, school or home.
6. Continued opioid use despite having recurring social or interpersonal problems.
7. Giving up or reducing activities because of opioid use.
8. Using opioids in physically hazardous situations such as driving while under the influence of opiates.

1. Continued opioid use despite ongoing physical or psychological problem likely to have been caused or worsened by opioids.
2. Tolerance (i.e., need for increased amounts or diminished effect with continued use of the same amount)
3. Experiencing withdrawal (opioid withdrawal syndrome) or taking opioids (or a closely related substance) to relieve or avoid withdrawal symptoms.

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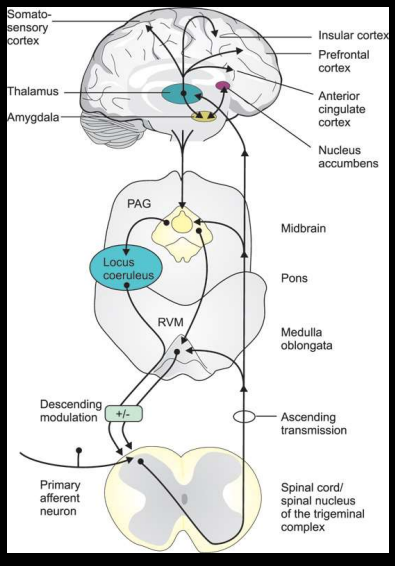
Neurobiology of Pain



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Brain Pathways

- Thalamus
  - Grand Central Station for information for sensory, motor, consciousness, alertness, cognition and memory
- Ventral Posterior Nucleus
  - Transmits information for pain, temperature and crude touch
- Amygdala
  - Plays a key role in emotional responses and affective states and disorders such as learned fear, anxiety and depression. **The amygdala has also emerged as an important brain center for the emotional-affective dimension of pain and for pain modulation**

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Amygdala and Chronic Pain

In chronic pain states, the Amygdala activates emotional-affective states. **Chronic pain is emotional pain**.

- Neugebauer V, Li W, Bird GC, Han JS. The Amygdala and Persistent Pain. The Neuroscientist. 2004;10(3):221-234. doi:10.1177/1073858403261077
- Narita, M., Kaneko, C., Miyoshi, K. *et al.* Chronic Pain Induces Anxiety with Concomitant Changes in Opioidergic Function in the Amygdala. *Neuropsychopharmacol* **31**, 739–750 (2006). https://doi.org/10.1038/sj.npp.1300858

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Descending Pain Pathways

- Periaqueductal Gray (PAG) – enkephalin producing cells which modulate pain via opioid pathways
  - Enkephalins are hormones; endogenous opioids
  - Like any other hormone, if you administer exogenous opioids, your body will downregulate the endogenous variety

- The cortex probably influences pain by two different mechanisms. There is good evidence that the cortex can reduce pain by interrupting the transmission of noxious information from the spinal cord level by activating descending pain modulatory systems located in the brainstem. Ohara PT, Vit JP, Jasmin L. Cortical modulation of pain. Cell Mol Life Sci. 2005 Jan;62(1):44-52. doi: 10.1007/s00018-004-4283-9. PMID: 15619006.

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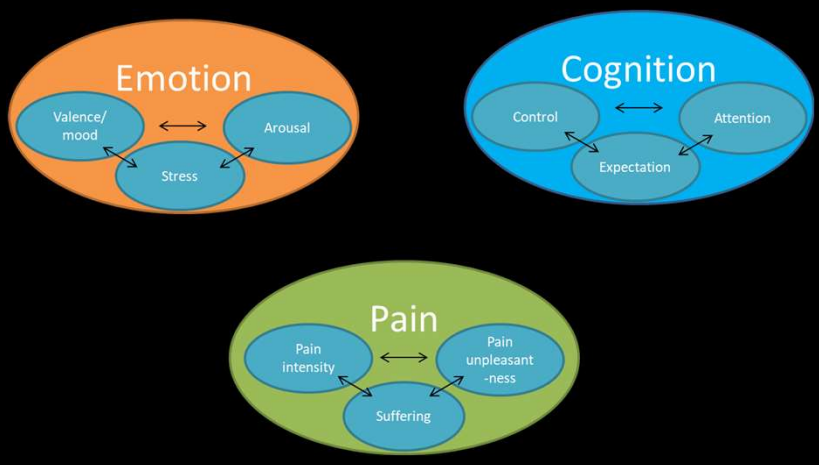

Figure 1: *A common theoretical framework illustrating the effects of cognitive and emotional factors on pain, reversed effects of pain on cognition and emotional state, as well as reciprocal within each domain. Based on (Bushnell et al., 2013).* Bushnell, M. C., Čeko, M., & Low (2013). Cognitive and emotional control of pain and its disruption in chronic pain. *Nature Reviews Neuroscience, 14*(7), 502.

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Is Chronic Pain in your head?

- Chronic pain is not conscious nor subconsciously "created" or "made up" by the mind
- Chronic pain is, however, perceived in the brain
- It is modulated by ALL emotional experiences prior to its onset
- It can be further modulated by the descending (cortical) pathway; i.e., Cognitive Behavioral Therapy

Categorizing chronic pain as "physical" or "emotional" is not helpful. **Chronic pain is *always* both physical and emotional**.

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Nociception vs Pain

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Chronic Pain and Trauma

What about low-dose opioid patients?

- They are likely not at a “therapeutic level”
- Their escalation was probably curtailed by self-imposed descending pathway homeostasis
  - Better coping mechanisms
  - “less trauma”?
  - Support systems
  - External factors – employment, child custody, etc
- They could probably still taper down to zero, but not without disrupting the homeostasis

Role of Psychotherapy in Chronic Pain

- Can help people cope with their pain using techniques such as breathing, mindfulness, de-catastrophizing, etc.
- Can also unlock previous traumatic events as triggers for the creation of chronic pain states
- Chronic pain brains “light up” differently on PET scans than brains not in chronic pain

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Treating the “physical” side of pain

- Spine
  - Epidural steroid injections (lumbar radiculopathy, spinal stenosis)
  - Facet joint interventions (facet pain, spondylolysis)
  - Kyphoplasty (osteoporotic fractures)
  - Intradiscal procedures (discogenic pain)
  - Spinal cord stimulation (post-laminectomy; “failed back”)
  - Intrathecal drug delivery
- Knee
  - Corticosteroid injections
  - Hyaluronic acid injections
  - Genicular nerve blocks / RFA / peripheral nerve stimulation

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Physical Activity

- Core strengthening
- Stretching vs strengthening
- Bracing
- Aerobic activity

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DESERT SKY
SPINE & PAIN
FOCUSED ON FUNCTION

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