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Program Evaluation and Research Unit

Pain Management for Individuals with Substance Use Disorder

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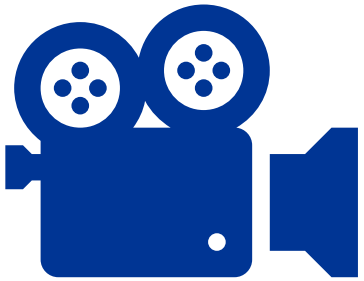

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- Everyone on every PERU webinar is **valued**. Everyone has an expectation of **mutual, positive regard** for everyone else that respects the **diversity** of everyone on the webinar.
- We operate from a **strength-based, empathetic, and supportive** framework – with the people we serve, and with each other on PERU webinars.
- We encourage the use of **affirming language** that is not discriminatory or stigmatizing.
- We treat others as **they** would like to be treated and, therefore, avoid argumentative, disruptive, and/or aggressive language.

Mutual Agreement (continued)

- We strive to: **listen** to each person, avoid interrupting others, and seek to **understand** each other through the Learning Network as we work toward the highest quality services for COE clients.
- Information presented in Learning Network sessions has been vetted. We recognize that people have different opinions, and those **diverse perspectives** are welcomed and valued. Questions and comments should be framed as **constructive feedback**.
- The Learning Network format is **not conducive to debate**. If something happens that concerns you, please send a chat during the session to the panelists and we will attempt to make room to address it either during the session or by scheduling time outside of the session to process and understand it. Alternatively, you can reach out offline to your PERU point of contact.

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Acknowledgements

- The Centers of Excellence is a partnership of the University of Pittsburgh's Program Evaluation and Research Unit and the Pennsylvania Department of Human Services; and is funded by the Pennsylvania Department of Human Services, grant number 601747.

- COE vision: The Centers of Excellence will ensure care coordination, increase access to medication-assisted treatment and integrate physical and behavioral health for individuals with opioid use disorder.

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DEPARTMENT OF HUMAN SERVICES

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Michael Palladini

April 19, 2023

Pain Management for Individuals with Substance Use Disorder

Objectives

- Recognize the effect that pain has on substance use
- Discuss stigma related to pain management for those with substance use issues
- Discuss selecting an appropriate pain management referral partner
- Understand the relationship between medications for OUD and pain

Chronic pain is very common

Table 1

How often adult respondents reported having pain over the past 3 months

Frequency	N (millions)	95% CI	% of population	95% CI
Every day	31.5	30.0-33.0	12.9	12.4-13.4
Most days	18.7	17.7-19.7	7.6	7.3-8.0
Some days	93.9	90.7-97.1	38.4	37.7-39.1
Never	100.5	97.0-104.0	41.1	40.2-41.9
Total	244.6	237.7-251.4	100	

Source: Based on data from the National Health Interview Survey, 2019

Over 50 million American adults report pain daily or on most days

- over 20% of the population

Pain was most commonly reported in the:

- Back
- Hands, arms, or shoulders
- Hips, knees, or feet

Yong RJ, et al. *Pain*. 2022 Feb 1;163(2):e328-e332

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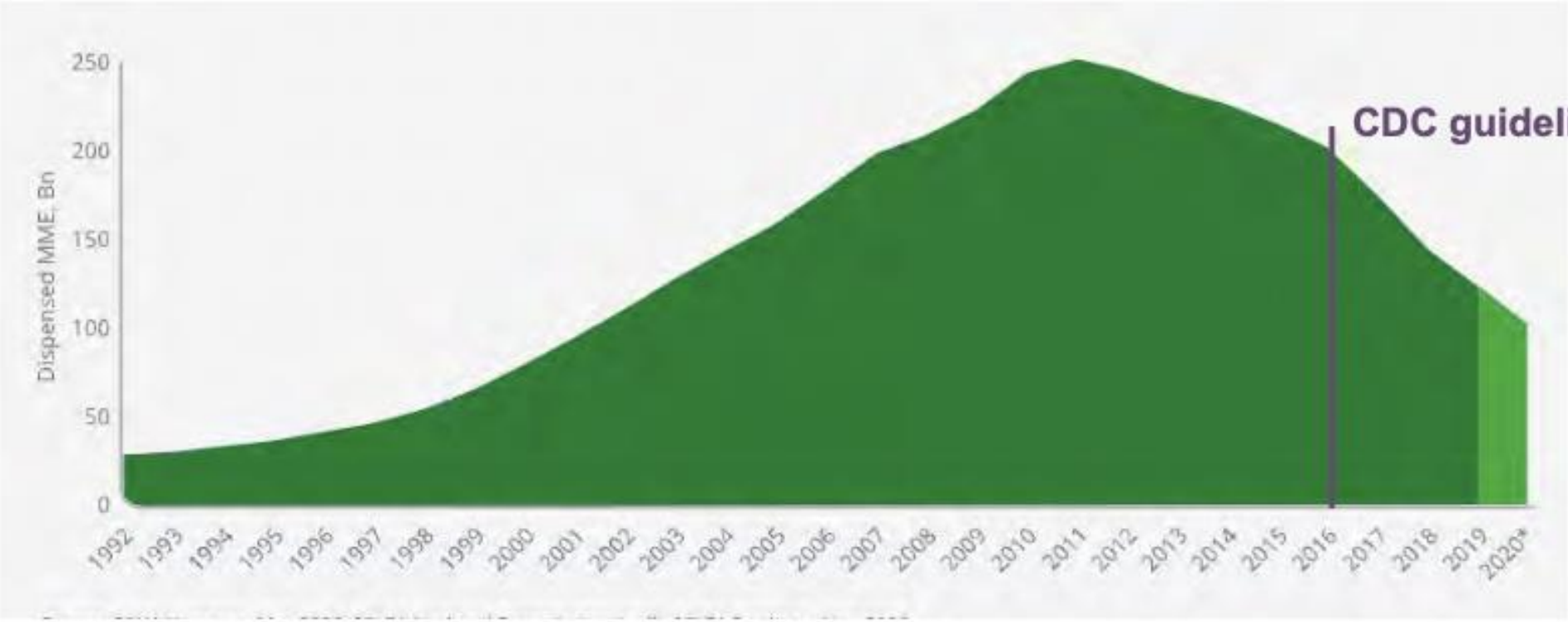
Prescription opioid prescribing trends

- Prescription opioid dispensing rates have decreased from a peak of 81.2 prescriptions/100 persons in 2012 to 43.3 prescriptions/100 persons in 2020
- Centers for Disease Control (CDC) Guidelines for Prescribing Opioids for Chronic Pain led to steeper reductions in opioid prescribing



Goldstick et al. *JAMA Netw Open*. 2021 Jul 1;4(7):e2116860. https://www.iqvia.com/insights/the-iqvia-institute/reports/prescription-opioid-trends-in-the-united-states

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Acute vs. Chronic pain

- Acute: caused by obvious tissue injury and typically fades with healing
  - Self-limited
  - Expectation of decreasing pain over time

- Transition from acute and sub-acute pain to chronic pain is not clear, though generally this is considered to be 90 days.

- Chronic: pain lasts longer than 90 days or beyond the time of normal tissue healing

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Nociceptive pain

- Caused by the normal activation of nociceptors
  - Normal response to tissue damage, irritation, or inflammation
  - Protective
  - Generally constant, well-localized
  - Described as aching or throbbing

- Examples
  - Arthritis (OA)
  - Trauma (ankle sprain, hip fracture)
  - Post-operative pain

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Neuropathic pain

- Results from an injury to the nervous system
  - maladaptive
  - abnormal neuronal firing in the absence of active tissue damage
  - may be continuous or episodic
  - varies widely in its presentation, but characterized by:
    - Stimulus independent pain that is shooting, lancinating, or burning
    - Paresthesias: Pins and needles
    - Loss of sensation
- Examples
  - Diabetic neuropathy
  - Post-herpetic neuralgia
  - Trigeminal Neuralgia

Woolf CJ. *Lancet*. 1999;353:1959-1964

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Other pain syndromes

- Complex and without clear etiology
  - Fibromyalgia
  - Non-anatomic lower back pain
  - Phantom limb pain
  - Migraine

Assessment: Take a history

- Main source: self-report and caregiver's report
- Pain assessment should be comprehensive
  - pain location, quality, and duration
  - aggravating or alleviating factors
  - previous treatments and their efficacy
- Assess impact of pain on functional status and sleep
- Screen for any mental health conditions (e.g., depression, anxiety, memory screening)
  - may be useful for pain assessment and management.

Gordon DB, et al. *Arch Intern Med*. 2005; 165: 1574-1580.

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Assessment Tools: PEG scale

- **P**ain average, interference with **E**njoyment of life, and interference with **G**eneral activity (PEG)
- Three item scale, ranking each statement from 0 to 10
- May be used to assess response to opioids in chronic pain (~30% reduction is meaningful)

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

Krebs EE, et al. *J Gen Intern Med.* 2009;24:733-8.

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Managing patient expectations regarding acute pain

- Acute pain is a normal response to tissue injury
- Most forms of acute nociceptive pain will subside within weeks and do not require substantial intervention (e.g. nonspecific low back pain)
- The goal of pain treatment is **not** to eliminate pain
- Instead, the goals of optimal pain management are to:
  - 1) relieve suffering

  AND
  - 2) improve function (e.g. hasten return to work)

  WHILE
  - 3) minimize the harms and risks associated with treatment

Carey TS, et al. *N Engl J Med.* 1995; 333: 913-7.

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Management strategies for pain

- Non-pharmacologic options
  - Physical therapy
  - Yoga, tai chi
  - Massage
  - Mindfulness meditation

- Non-opioid pharmacotherapy
  - Acetaminophen
  - NSAIDs
  - Topical options (e.g., lidocaine, NSAIDs)
  - Antidepressants (SNRI's e.g. Duloxetine; TCA's)
  - Gabapentinoids

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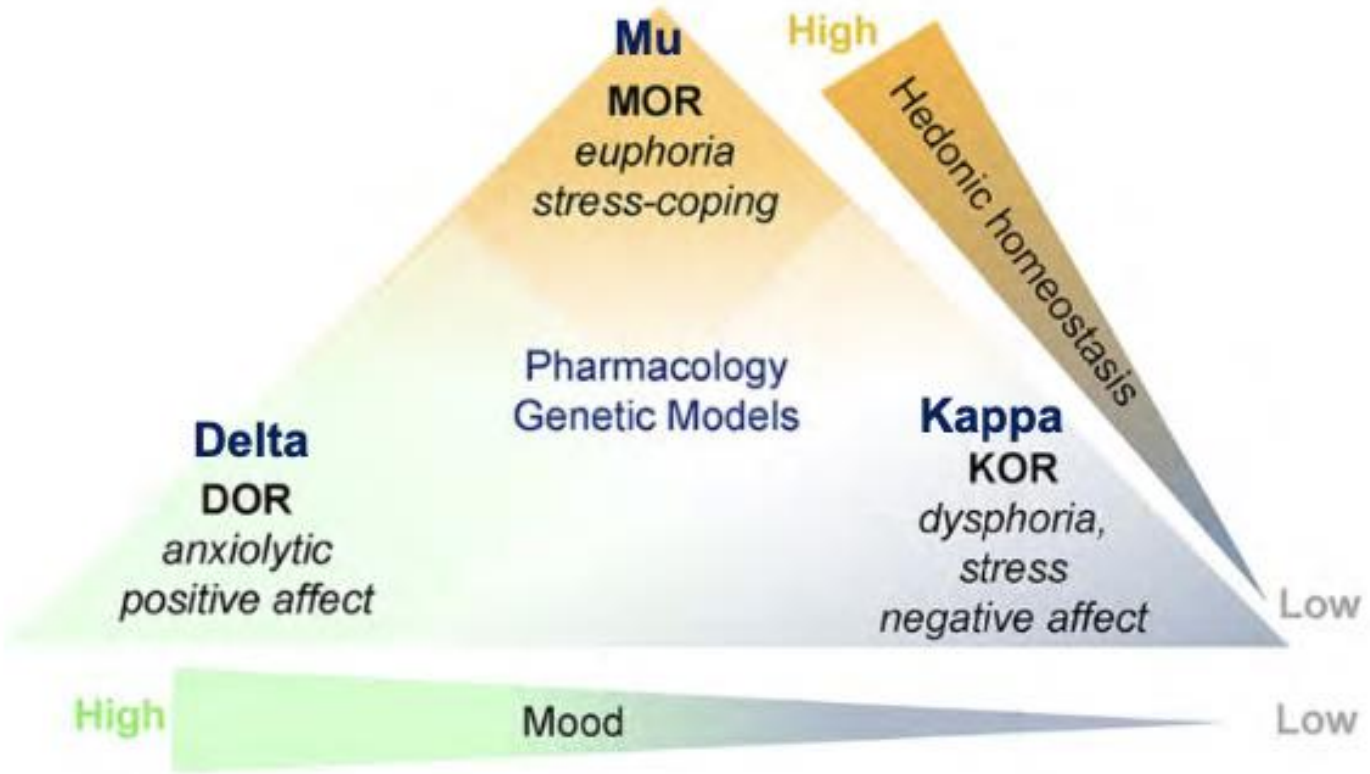
Opioid mechanism of action

- Agonists
  - Morphine, codeine, hydromorphone, hydrocodone (etc.)
    - stimulate at least one of the opioid receptors
    - continued analgesia with increasing dose
- Partial Agonists
  - Buprenorphine
    - high affinity/low dissociation from mu-receptor
    - have a ceiling effect on respiration and CNS depression. Ceiling effect on analgesia is unclear
- Antagonists
  - Naloxone, naltrexone
    - competitive binding with agonists, but do not have analgesic effect

Opioids work at three main receptors: mu, kappa, delta



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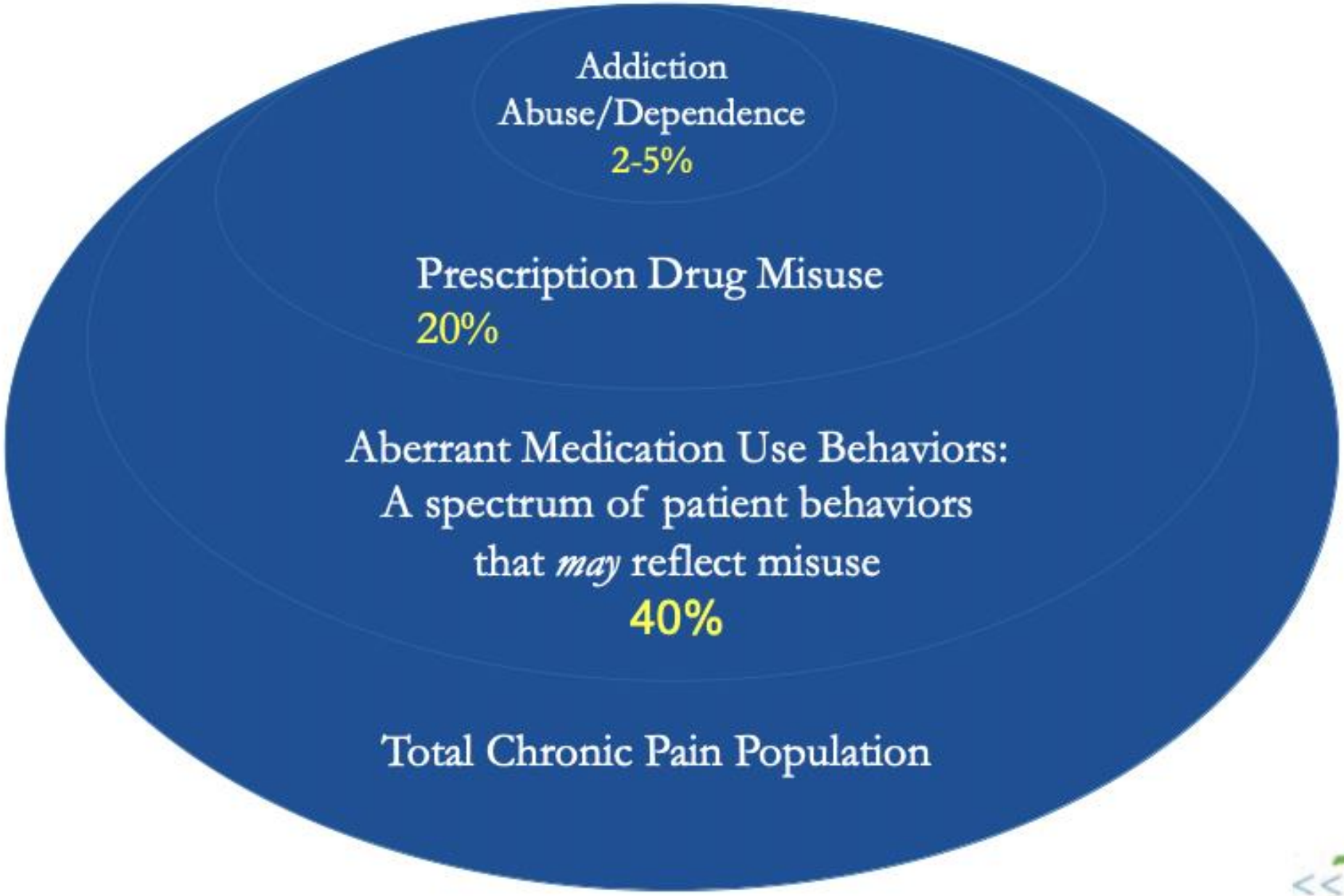

Adapted from Passik. APS Resident Course, 2007

Behaviors of misuse in primary care

- Assess behaviors indicative of opioid misuse

Behavior	Percent
Requested early refills	47
Increased dose on own	39
Felt intoxicated from pain medication	35
Lost or had medication stolen	30
Purposely over sedated oneself	26
Used opioids for purpose other than pain	18

Fleming MF, et al. *Pain*. Jul 2007;8(7):573-582.

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Tramadol: Another opioid?

- Schedule IV per DEA due to abuse potential and adverse events are similar to those of other opioids.
- Abrupt cessation from tramadol has been associated with two types of withdrawal syndromes:
  - One is typical of opioid drugs with flu-like symptoms, restlessness and drug craving (90% of cases)
  - Another withdrawal syndrome (about 10%of cases of tramadol withdrawal) is atypical of opioids and is associated with hallucinations, paranoia, extreme anxiety, panic attacks, confusion, and numbness
- 2020 NSDUH survey:
  - 16.7 million people in the US aged 12 or older used tramadol in the past year
  - 1.5 million people in the US aged 12 or older misused tramadol in the past year

DEA's Diversion Control Division website; 2020 National Survey on Drug Use and Health
https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases Accessed Jan 2022.

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Tramadol

- Is a partial agonist of the mu-opioid receptor and a serotonin/norepinephrine reuptake inhibitor

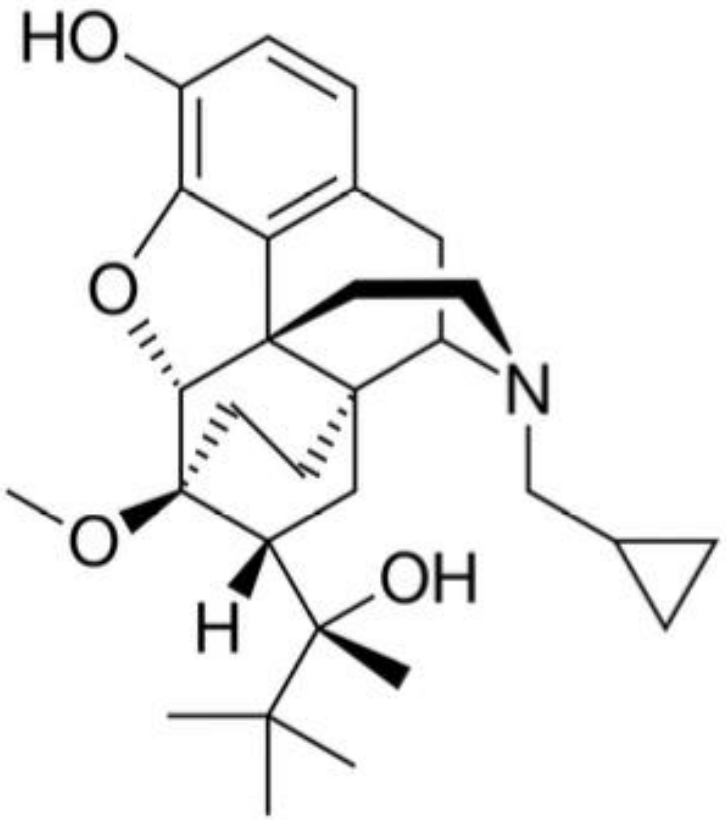
- Monitor for side effects, which are similar to opioids:
  - Nausea, vomiting
  - Constipation
  - Drowsiness

- Potential risk of serotonin syndrome when combined with:
  - Serotonergic antidepressants as SSRIs, SNRIs, TCAs, MAOI's
  - Triptans

1. Malonne H, et al. Clin Ther. 2004;26(11):1774-1782.
2. J Am Geriatr Soc. 2009;57(8):1331-1346.

Buprenorphine pharmacology

- Atypical opioid with a mixed mechanism of action
  - Mu opioid receptor (MOR) partial agonist
  - Kappa antagonist
  - Opioid-receptor like 1 (ORL1) activation (reduces tolerance to opioids)
  - β-arrestin activity antagonism (additive effects with other opioids)
  - Anti-hyperalgesic effects
- Due to high affinity will displace other MOR agonists
- No ceiling effect on analgesia but does have ceiling effect on respiratory depression
- Poor oral bioavailability (approximately 10%) and is available primarily in non-oral formulations



Fishman et al. *Curr Pain Headache Rep*. 2018 Oct 5;22(12):83.

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Original FDA registration study that showed therapeutic efficacy of buprenorphine for pain

Analgesic Efficacy and Tolerability of Transdermal Buprenorphine in Patients with Inadequately Controlled Chronic Pain Related to Cancer and Other Disorders: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

Reinhard Sittl, MD,[1] Norbert Griessinger, MD,[1] and Rudolf Likar, MD[2]

[1]University of Erlangen, Pain Clinic, Erlangen, Germany, and [2]Pain Clinic, General Hospital, Klagenfurt, Austria

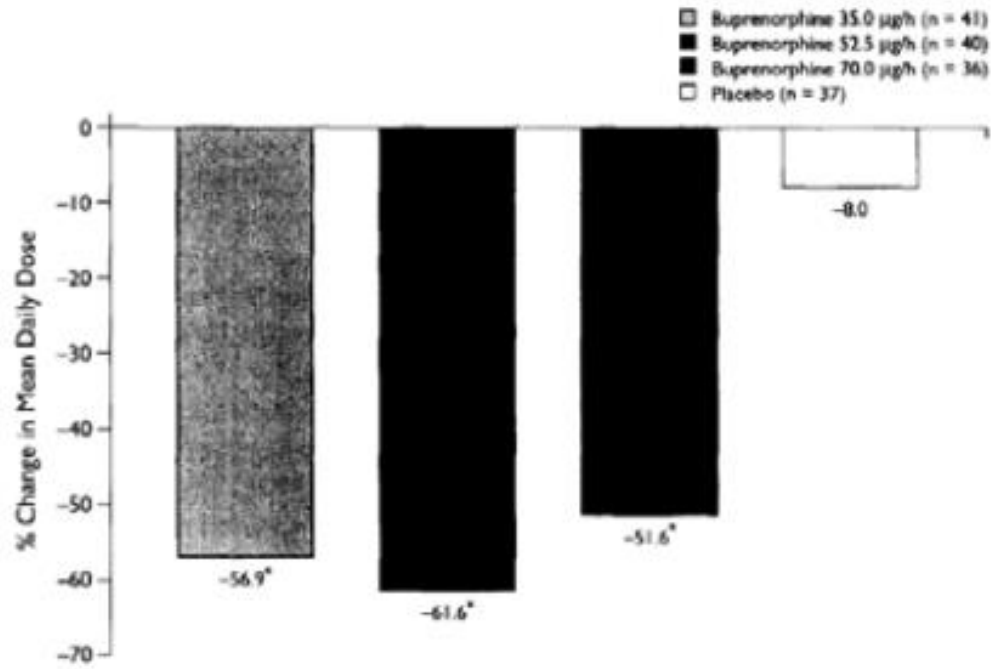
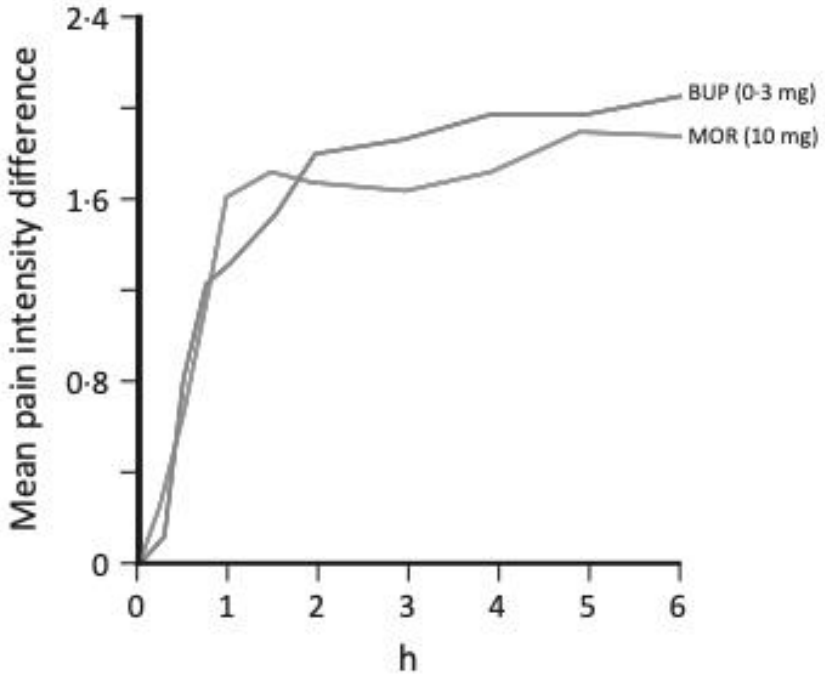


Figure 2. Percentage reduction in consumption of additional oral opioid analgesic medication for breakthrough pain during the study period. *$P < 0.05$ versus placebo group (least significant difference test).

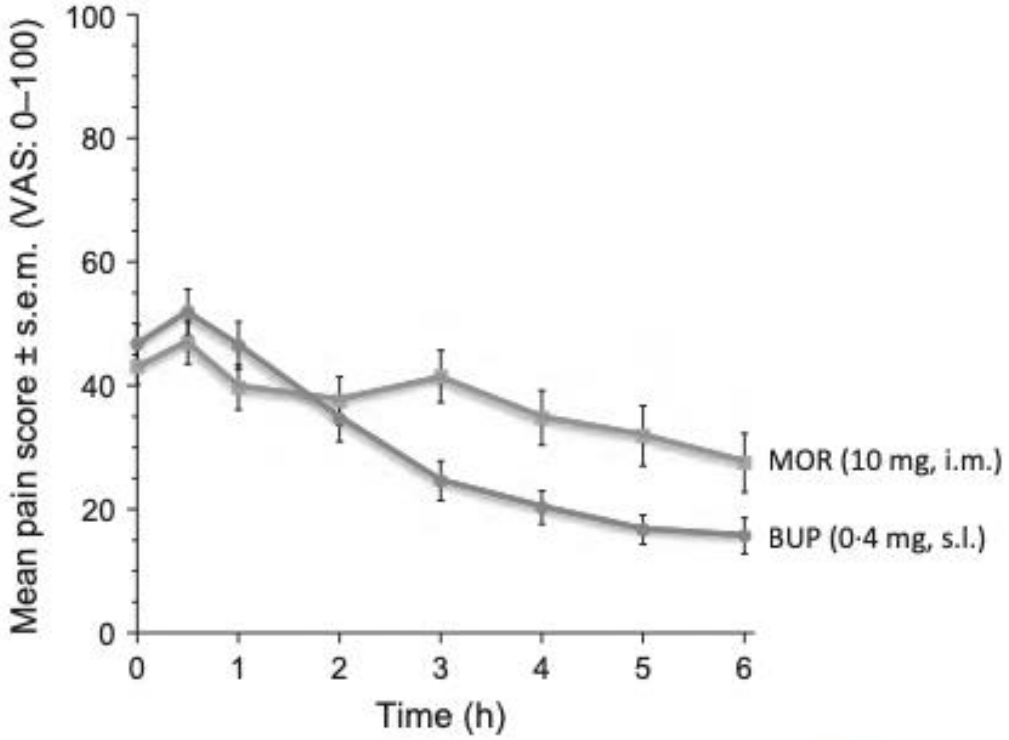
AIOSA Health

Is it as good as other opioids?

60 patients, post op pain relief following upper abdominal surgery. Double blind randomized



101 patients, post op pain relief, double blind randomized



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If opioids are necessary, use one with a better safety profile

Buprenorphine

- Partial agonist with the favorable property of a ceiling effect for respiratory depression, but no ceiling effect for pain
  - pain relief similar to other opioids[19,20]
  - can be used to treat pain in patients with and without opioid use disorder (OUD)
- Products FDA-approved for pain:
  - available as buccal (Belbuca) and transdermal product (Butrans)
  - dosed in micrograms
  - sublingual formulations can be used, but are not FDA-approved for chronic pain
- Cost may be a barrier to receiving buprenorphine medications

Tramadol

- Fewer opioid side effects (like respiratory depression) at maximum daily dose, but still has overdose and misuse potential[21,22]
- May be combined with SSRI and SNRI medications at recommended doses, but be aware of drug interactions that increase the risk of serotonin syndrome[23-25]

Avoid combining ***any*** opioid with a respiratory depressant, such as a benzodiazepine.

Gabapentinoid schedule and FDA-approved indications

Gabapentin

(Neurontin, Gralise, Horizant, generics)

- **No DEA schedule**
  - State scheduled Schedule V in Virginia
  - State mandated reporting on PDMP in Kansas
- FDA approved indications:
  - Postherpetic neuralgia
  - Adjunctive treatment for partial-onset seizures (Neurontin, Horizant)
  - Moderate to severe primary Restless leg syndrome (Horizant only)

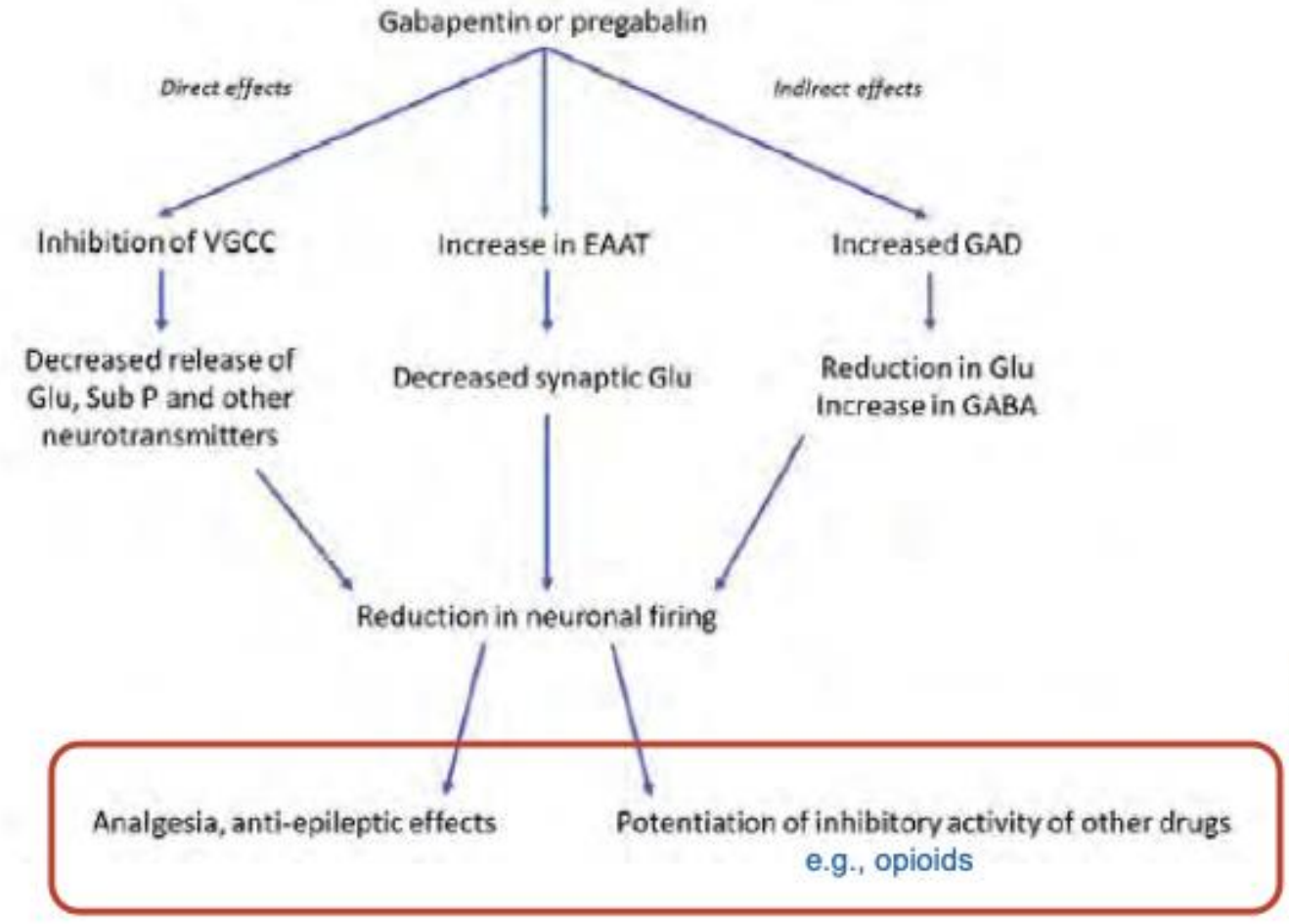
Pregabalin

(Lyrica, Lyrica CR, generics)

- **DEA Schedule V**
  - *"In clinical trials, pregabalin produces some pharmacological effects characteristic of diazepam and alprazolam and is likely to be abused for its positive psychic effects. The percentage of individuals that experienced acute euphoric effects was unusually high for pregabalin in clinical trials."*
- FDA approved indications:
  - Neuropathic pain (i.e., diabetic peripheral neuropathy, postherpetic neuralgia, associate with spinal cord injury)
  - Fibromyalgia
  - Adjunctive treatment for partial-onset seizures

Collins S. *Pharmacy Today.* 2021 Oct 01;27(10);33.
deadiversion.usdoj.gov/fed_regs/rules/2005/fr0728.htm

Mechanism of action



EAAT: excitatory amino acid transporters
GABA: gamma aminobutyric acid
GAD: glutamic acid decarboxylase
Glu: glutamate
Sub P: substance P
VGCC: voltage-gated Ca2+ channels

Evoy KE, et al. *J Clin Pharmacol.* 2021 Aug;61 Suppl 2:S89-S99.

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Prevalence of gabapentinoid misuse and abuse

- Nearly 1 in 5 respondents reported ever use of gabapentin or pregabalin in a survey of 1,843 adults ages 18-59.
  - 6.6% (n=121) of all respondents met criteria for misuse/abuse/non-medical use
    - Misuse/abuse was more common in patients with a self-reported substance use disorder and prior addiction treatment
  - Reasons for abuse of both gabapentin and pregabalin:
    - Calms/relaxes
    - Improved sociability/reduces inhibitions
    - Euphoria
    - Improves mood
  - Reasons for misuse:
    - Other medications not relieving symptoms
    - No longer able to obtain other medications

Evoy KE, et al. *Int J Clin Pharm*. 2021 Aug;43(4):1055-1064.
Evoy KE, et al. *Drugs*. 2021 Jan;81(1):125-156.

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Gabapentin and OUD

- 9.3% (n=766) of OUD patients (N=12,792) reported using gabapentin non-medically in the past month
  - 64% of these used an opioid agonist medication as well
    - Buprenorphine co-use reported by nearly half of gabapentin+opioid users

- Patients living in the south, on the streets or have a history of chronic pain were most likely to report misuse.

- Results suggest some use of gabapentin with buprenorphine to self-medicate for OUD or manage withdrawal symptoms

Ellis MS, et al. *Drug Alcohol Depend*. 2022 May 1;234:109400
Evoy KE, et al. *Drugs*. 2021 Jan;81(1):125-156.

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Gabapentinoid take homes

- The actual prevalence in the general population is not well understood.
- Post-mortem samples suggest about 10% of drug related deaths involved a gabapentinoid, usually in combination with other substances.
  - Small baseline overdose risk with gabapentin alone
  - Increasing risk when combined with prescription opioids
  - Combining gabapentinoids with fentanyl has highest risk
- Patients admitted to OUD treatment report using gabapentinoids illicitly

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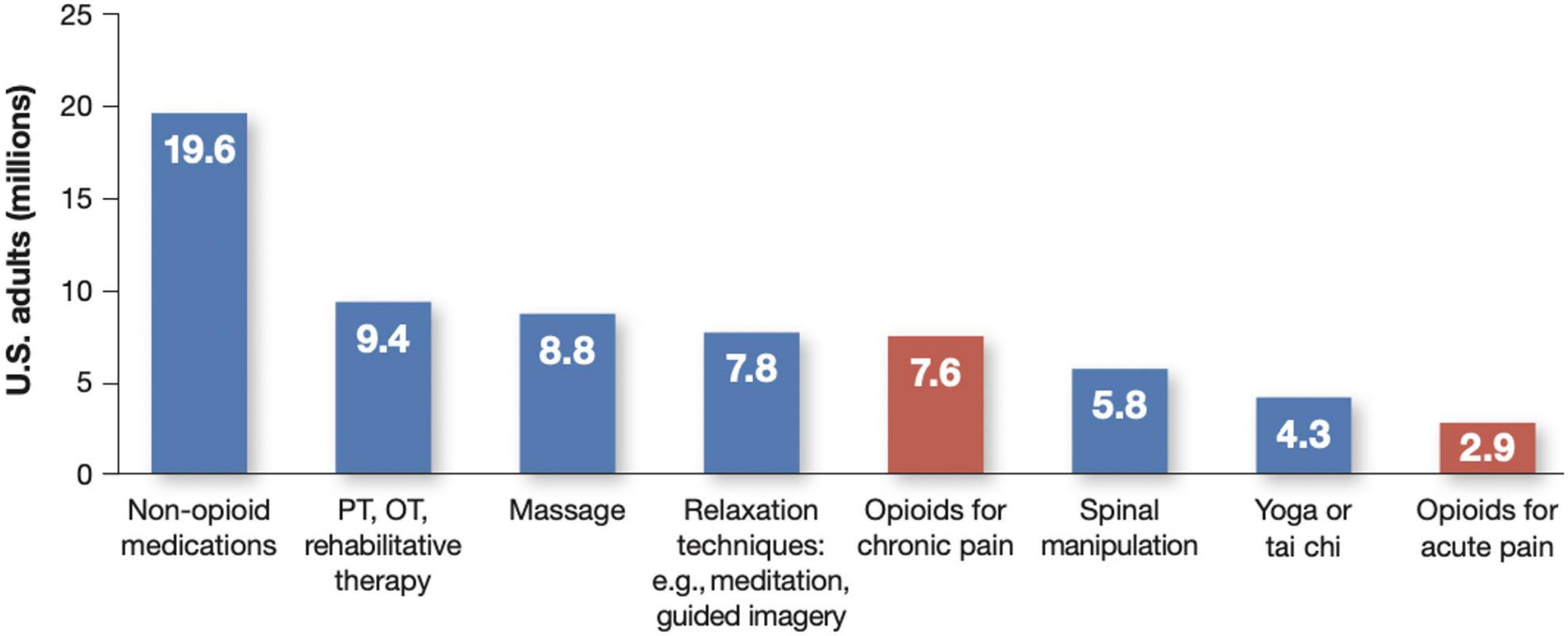
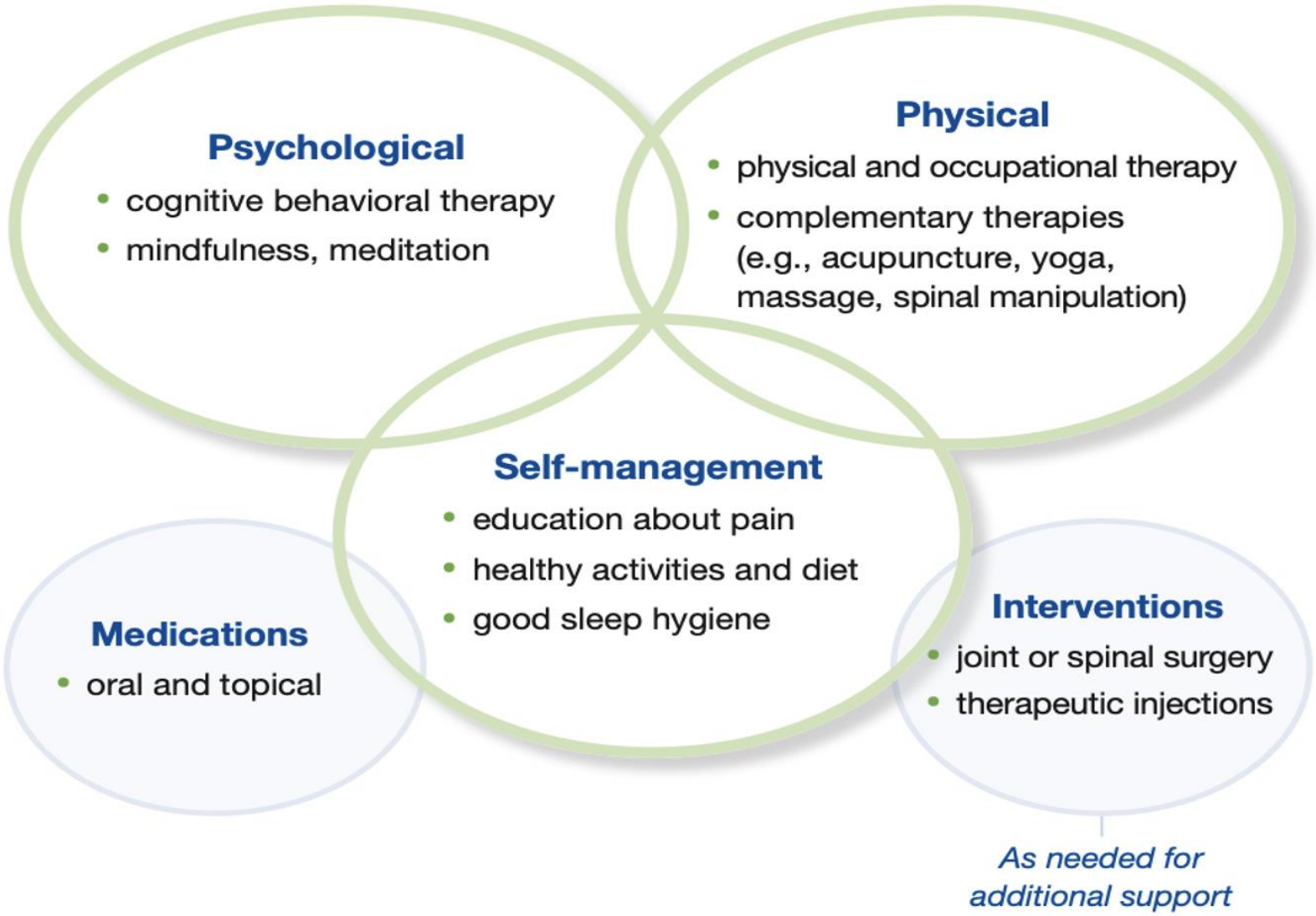
Putting it all together

- Opioid use remains common
- Side effects of opioids include constipation, nausea/vomiting, and sedation
- Opioid-related harms include misuse, addiction, and overdose.
- Additional associated risks include falls, fracture, immunosuppression, MI, and sexual dysfunction
- Tramadol is an opioid (can cause withdrawal) that is less potent and may have a role in managing pain in some patients.
- Buprenorphine, also an opioid, has a ceiling effect with respiratory depression that may make it safer to initiate than full mu agonists in patients requiring an opioid for pain
- Gabapentinoids can be misused/abused. Universal screening is necessary.

FIGURE 2. Non-opioid management options are safe and effective, and are now used more than opioids. Opioid prescribing has declined with better recognition of its risks and effective alternatives.[1]



PT: physical therapy; OT: occupational therapy


Psychological
cognitive behavioral therapy
mindfulness, meditation
Physical
physical and occupational therapy
complementary therapies (e.g., acupuncture, yoga, massage, spinal manipulation)
Self-management
education about pain
healthy activities and diet
good sleep hygiene
Medications
oral and topical
Interventions
joint or spinal surgery
therapeutic injections
As needed for additional support

Patients Face Stigma

- Patients with chronic pain, mainly those treated with opioids can experience stigma
- Hidden and obvious from family, friends, co-workers, healthcare providers and society at large
- Guilt, shame, judgment, embarrassment results in increased risk of behavioral health issues such as anxiety and depression
- Chronic pain is common among individuals with SUD, yet stigma remains a major barrier to treatment, especially associated with MOUD (methadone and buprenorphine)

ONLY 12.2%

of people who require treatment
for a SUD actually seek treatment.

Stigma is found to be a significant barrier, with **20.5%** not seeking treatment because of negative consequences associated with their work

and around **17%** being concerned about negative judgements by friends or community.

Clinicians and Stigma

- Clinicians who treat acute and chronic pain, particularly with opioids, may experience **stigma from colleagues and society** in general that — in addition to fear of scrutiny from state medical boards and the Drug Enforcement Administration (DEA) — may dissuade them from using opioids appropriately.

- Stigma leads to **over-referral and patient abandonment.**

Recommendations

- Increase patient, physician, clinician, nonclinical staff, and societal education on the underlying disease processes of acute and chronic pain, and the disease of addiction, to reduce stigma.
- The national crisis of illicit drug use, with overdose deaths, is confused with appropriate therapy for patients who are being treated for pain. This confusion has created a stigma that contributes to barriers to proper access to care.
- Identify strategies to reduce stigma in opioid use

Thank you

Michael Palladini, RPh MBA

Clinical Educator Pharmacist

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michaelp@alosahealth.org

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