Breaking Barriers:

Pain & Addiction Updates

Mark Garofoli, PharmD, MBA, BCGP, CPE, CTTS

Disclosures

I have nothing to disclose concerning possible financial relationships with ineligible companies that may have a direct or indirect interest in the subject matter of this presentation.

Abbreviations

- MOUD (Medications for Opioid Use Disorder)
- MME (Morphine Milligram Equivalent)
- PDMP (Prescription Drug Monitoring Program)
- CS (Controlled Substance)
- UDM (Urine Drug Monitoring)
- ADF (Abuse Deterrent Formulation)

Personal Facts…

I have personal and professional opinions on pain management, but some things are better left NSAID.

Learning Objectives

1. Recall the pharmacological properties of buprenorphine.
2. Recall controlled substance “Red Flags” for prescribers and dispensers based on the National Opioid Settlement.
3. Identify the available opioid antagonist products currently available in the United States.
4. Recall the CDC Opioid Guideline Update twelve recommendations.
5. Identify pain management medications that are potentially inappropriate for utilization in older adults based on the AGS Beers Criteria
6. Recall the pharmacological properties of the most common new pain medications.

Agenda

1. Intro
2. Addiction Updates
3. Pain Management Best Practices
4. Opioid Antagonists
5. CDC Opioid Guideline Update
6. Beers List Update
7. Newer Pain Medications

US Substance-Related Deaths

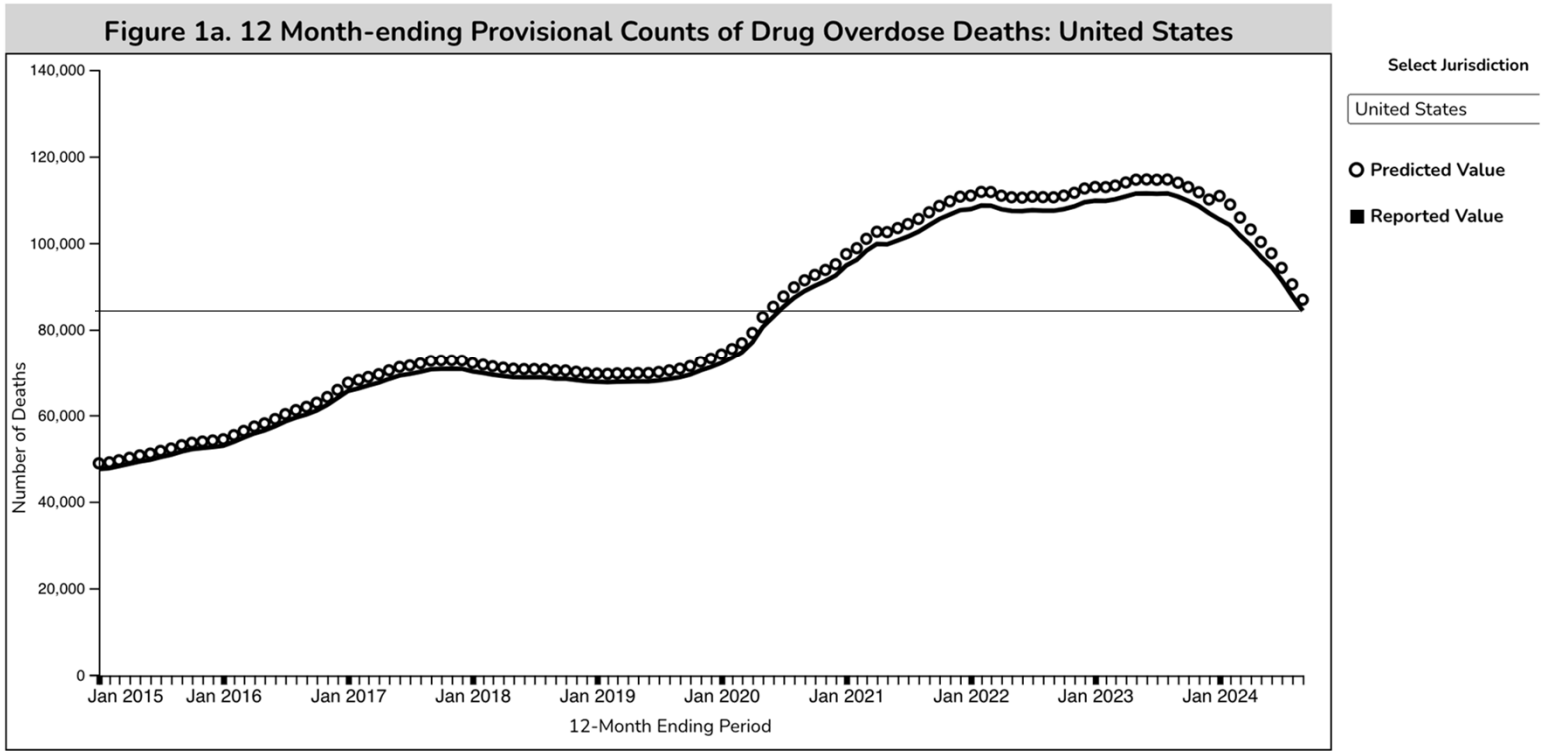
Substance	~US Annual Deaths
“Drugs”	80,000
Alcohol	150,000
Tobacco	500,000

https://www.drugwarfacts.org/node/1854
https://www.npr.org/2022/11/05/1134523220/alcohol-death-rate-cdc-report

US Drug Overdose Deaths

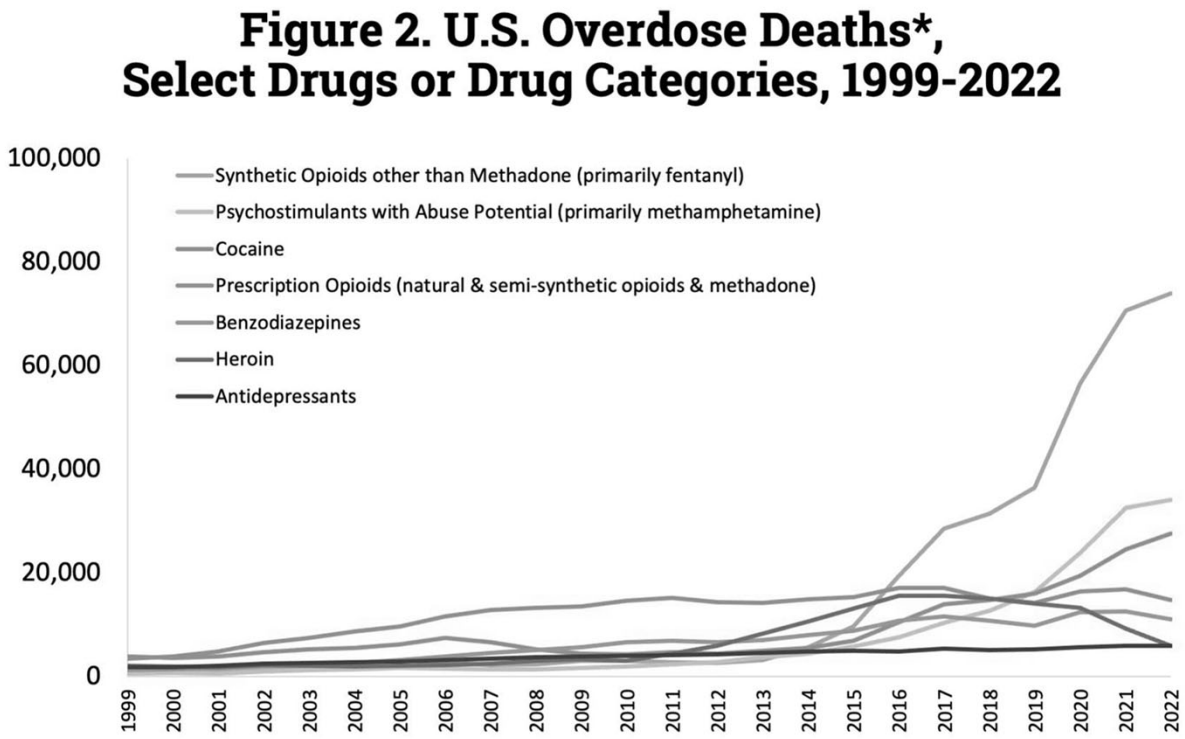
All Drugs

Based on data available for analysis on: February 2, 2025



https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
https://www.statista.com/chart/18744/the-number-of-drug-overdose-deaths-in-the-us/

US Drug Overdose Deaths



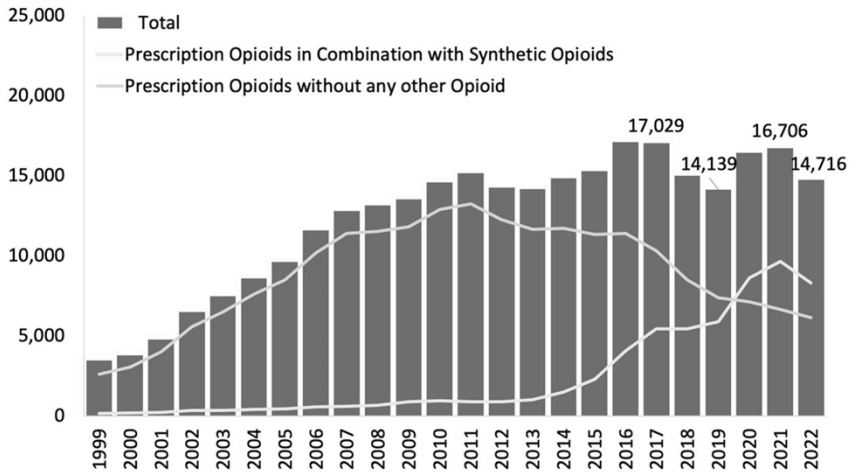
*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates

U.S. Rx Opioids

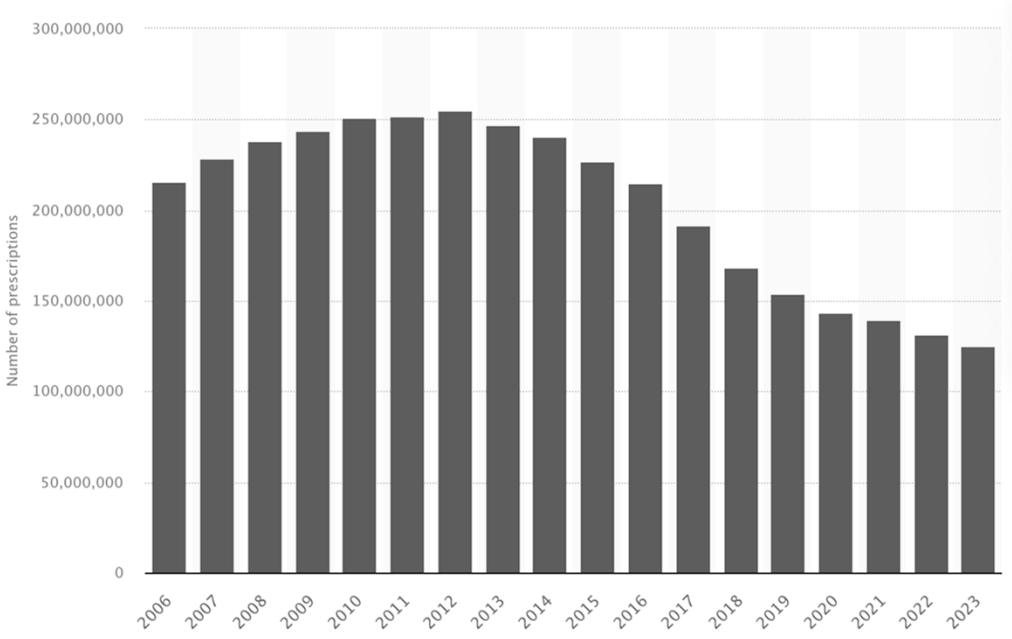
Deaths/Rx's

Figure 4. U.S. Overdose Deaths Involving Prescription Opioids*, 1999-2022



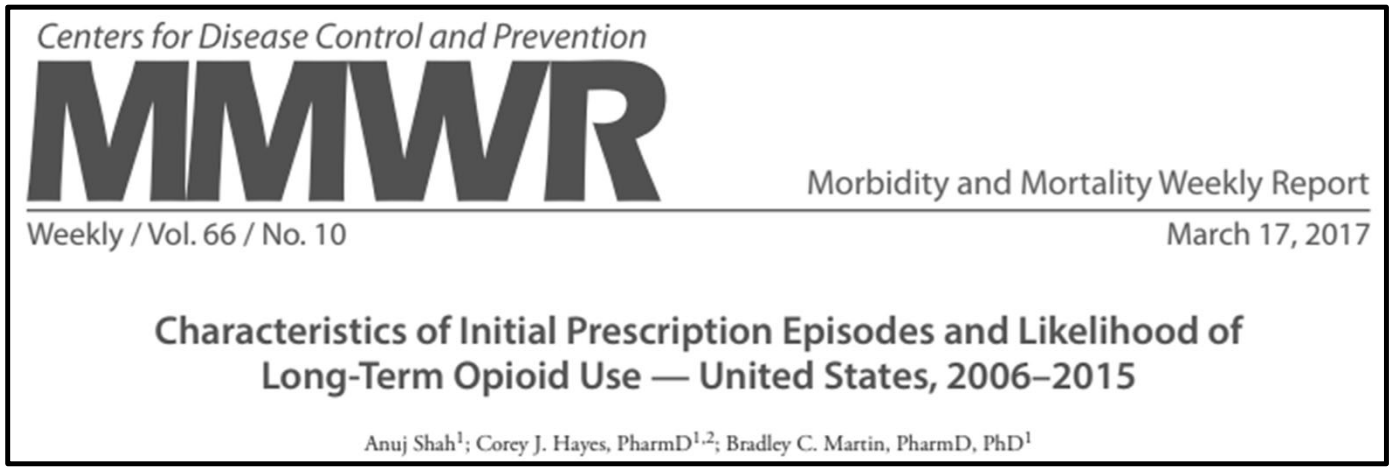
*Among deaths with drug overdose as the underlying cause, the prescription opioid subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2) or methadone (T40.3). Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2022 on CDC WONDER Online Database, released 4/2024.

Number of annual opioid prescriptions in the U.S. from 2006 to 2023



https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates
https://www.statista.com/statistics/753149/total-number-of-opioid-rx-prescriptions-in-us/

Heroin Headlines



Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Weekly / Vol. 66 / No. 10

March 17, 2017

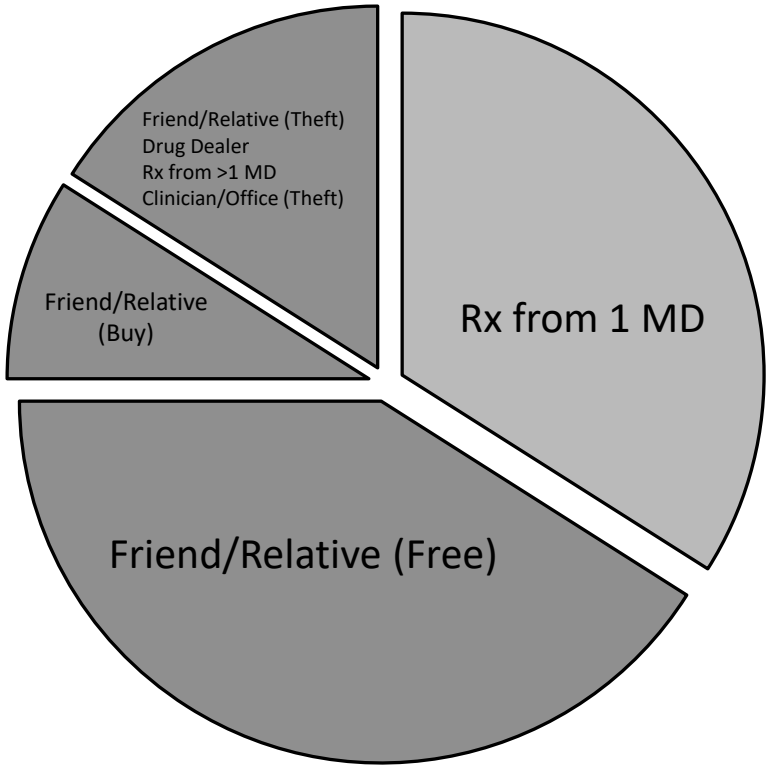
Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015

Anuj Shah[1]; Corey J. Hayes, PharmD[1,2]; Bradley C. Martin, PharmD, PhD[1]

75% of Heroin Utilizers Started with Prescription Opioids

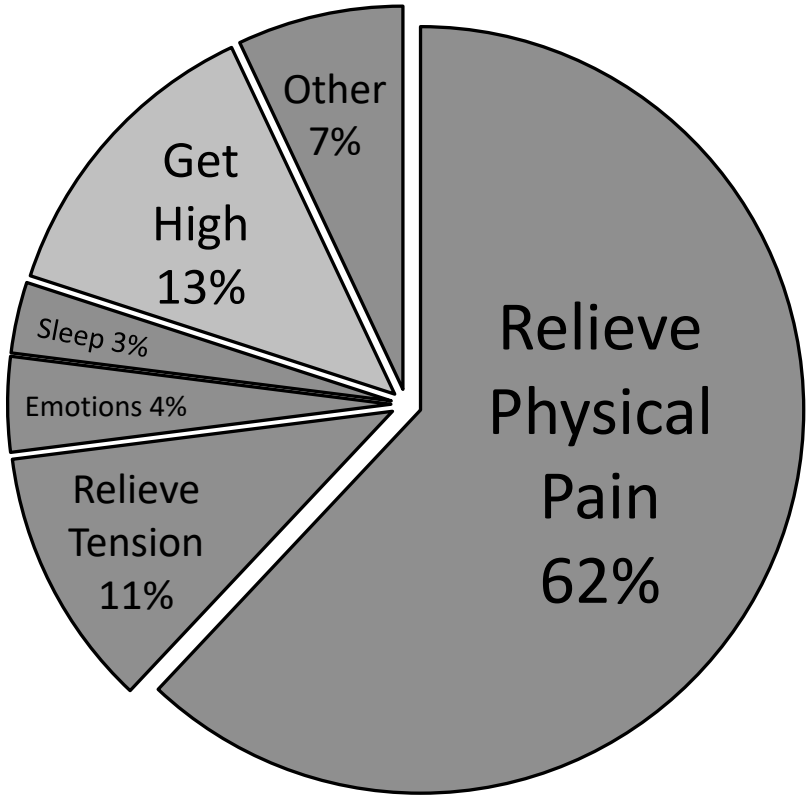
Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use – United States, 2006-2015. *Weekly* / March 17, 2017 / 66(10); 265–269.

But From Where?



2017 DEA National Drug Threat Assessment. https://www.dea.gov/docs/DIR-040-17_2017-NDTA.pdf

And WHY?



2018 DEA National Drug Threat Assessment (NDTA). https://www.dea.gov/documents/2018/10/02/2018-national-drug-threat-assessment-ndta

Just Say NO

https://www.scientificamerican.com/article/why-just-say-no-doesnt-work/

7th Grade Speeling Bee Falure

Rolaids
Vs
Relief

https://www.npr.org/2019/05/31/728526221/8-spelling-bee-winners-named-as-co-champions-in-historic-marathon-competition

Just Say KNOW

https://www.scientificamerican.com/article/why-just-say-no-doesnt-work/

The West Virginia Way

Almost Heaven…

- Mother's Day
- Proud. Hard Working. Resilient.
- Jack Dempsey
- Jennifer Garner
- Brad Paisley
- Supersize Me (Movie)
- We are Marshall (Movie)
- Hidden Figures (Movie)
- Take Me Home, Country Roads!

Addiction Updates
MOUDs

https://yrm.org/misunderstood-book-time/

Buprenorphine

Pain MCG Narrative Reviews

Journal of Pain Research

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Benefit-Risk Analysis of Buprenorphine for Pain Management

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Robert B Raffa[3,4]

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Abstract: Health care providers in the United States are facing challenges in selecting appropriate medication for patients with acute and chronic pain in the midst of the current opioid crisis and COVID-19 pandemic. When compared with conventional opioids, the partial μ-opioid receptor agonist buprenorphine has unique pharmacologic properties that may be more desirable for pain management. The formulations of buprenorphine approved by the US Food and Drug Administration for pain management include intravenous injection, transdermal patch, and buccal film. A comparison of efficacy and safety data from studies of buprenorphine and conventional opioids suggests that buprenorphine may be a better-tolerated treatment option for many patients that provides similar or superior analgesia. Our benefit-risk assessment in this narrative review suggests that health care providers should consider that buprenorphine may be an appropriate alternative for pain management over other opioids.

Keywords: buprenorphine, buprenorphine buccal film, analgesia, pain, opioids

Journal of Multidisciplinary Healthcare

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Frontline Perspectives on Buprenorphine for the Management of Chronic Pain

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Abstract: Due to the prevalence of chronic pain and high-impact chronic pain in the US, a significant percentage of the population is prescribed opioids for pain management. However, opioid use disorder is associated with reduced quality of life, along with fatal opioid overdoses, and is a significant burden on the US economy. Considering the clinical needs of patients with intractable chronic pain and the potential harms associated with prescribed and illicit opioids in our communities, having a deep understanding of current treatment options, supporting evidence, and clinical practice guidelines is essential for optimizing treatment selections. Buprenorphine is a Schedule III opioid with a unique mechanism of action, allowing effective and long-lasting analgesia at microgram doses with fewer negative side effects and adverse events, including respiratory depression, when compared with other immediate-release, long-acting, and extended-release prescription opioids. Due to its relatively lower risk for overdose and misuse, buprenorphine was recently added to the Clinical Practice Guideline for the Use of Opioids in the Management of Chronic Pain as a first-line treatment for chronic pain managed by opioids by the US Departments of Defense and Veterans Affairs, and the Department of Health and Human Services recommends that buprenorphine be made available for the treatment of chronic pain. In this narrative review, we discuss the different buprenorphine formulations, clinical efficacy, advantages for older adults and other special populations, clinical practice guideline recommendations, and payer considerations of buprenorphine and suggest that buprenorphine products approved for chronic pain should be considered as a first-line treatment for this indication.

Hale M, Garofoli MP, Raffa R. Benefit-Risk Analysis of Buprenorphine for Pain Management. Journal of Pain Research. 24 May 2021 Volume 2021: 14 Pages 1359-1369.
Adler J, Mallick-Searle T, Garofoli M, Zimmerman A. Frontline Perspectives on Buprenorphine for the Management of Chronic Pain. *J Multidiscip Healthc*. 2024;17:1375-1383

Mu Opioid Receptor Affinity

Prescription Opioid	~K
Sufentanil	0.138
Buprenorphine	**0.216**
Hydromorphone	0.37
Naltrexone (Antagonist)	0.4 to 0.6
Oxymorphone	0.41
Levorphanol	0.42
Butorphanol	0.76
Naloxone (Antagonist)	1 to 3
Morphine	1.1
Fentanyl	1.3
Methadone	3
Diacetylmorphine	10
Hydrocodone	42
Oxycodone	25
Pentazocine	118
Codeine	734
Meperidine	450
Dextromethorphan	1,020
Tramadol	12,500

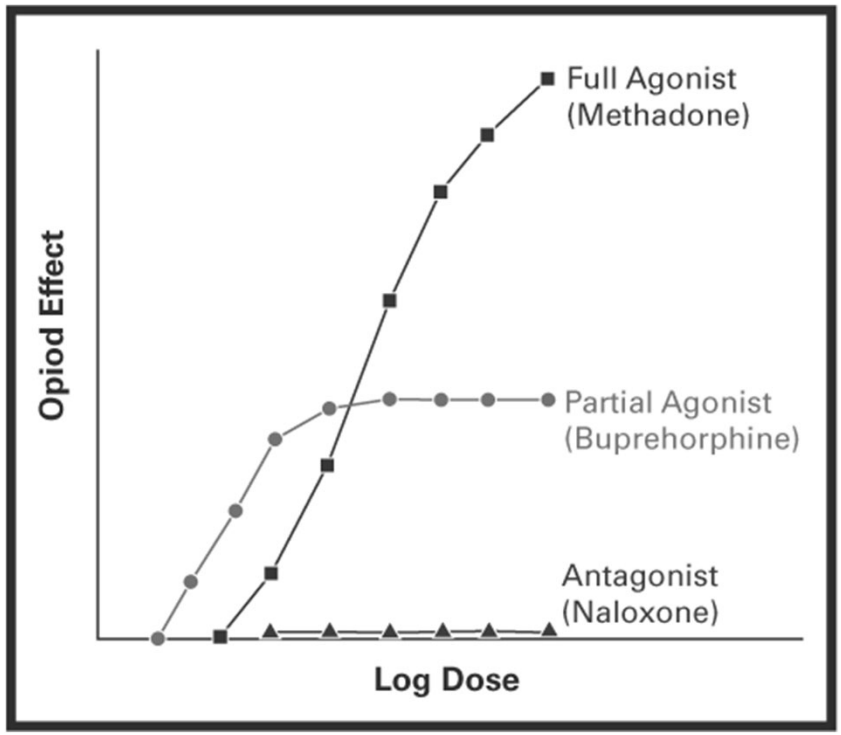
- Affinity: “Thermodynamic Chemical Attraction to Receptor”
- NOT Intrinsic Activity (NOT effect)

High to Low Affinity

Neuropsychopharmacology. 2003. 28 (11): 2000-2009.
Ellis CR, et. al.(2018) Predicting opioid receptor binding affinity of pharmacologically unclassified designer substances using molecular docking. PLoS ONE 13(5): e0197734.
Chen ZR, et. al. Life Sciences, Vol. 48, pp. Printed in the U.S.A. Mu Receptor Binding of Some Commonly Used Opioids and Their Metabolites. Life Sciences. 1991 (48), 2165-2171.
Volpe DA, et. al., Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs. Regulatory Toxicology and Pharmacology 59 (2011) 385–390..
PDSP Ki Database pdsp.unc.edu/databases/pdsp.php? recDDRadio=recDDRadio&receptorDDI 1&receptor=&speciesDDI&speciesFree Radio=speciesFreeRadio&species=hum an&sourceDDRadio=sourceDDRadio&s ourcesDDI &source=&hotDDRadio=hot DDRadio&hotLigandDDI&hotLigand=&t estDDRadio=testDDRadio&testLigandD DI&testLigand=&refDDRadio=refDDRa dio&referenceDDI&reference=&KiGreat er=&KiLess=&k

Buprenorphine

Respiratory Depression "Ceiling Effect"



Concerns

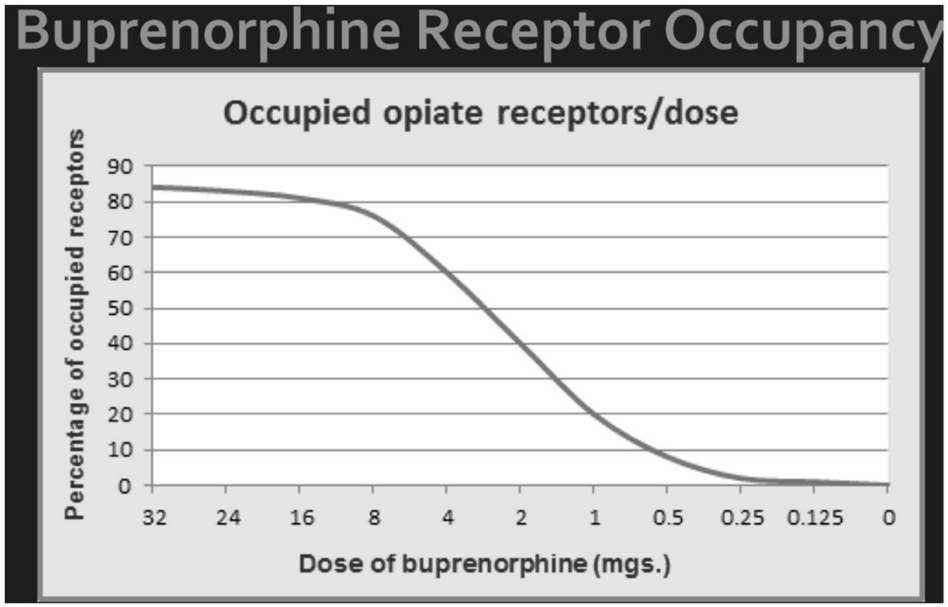
- Relapses
- Street PolyRx
- Children

Suboxone Medication Guide (Package Insert)
Roberts, James R. MD Buprenorphine: Toxicity and Overdose, Emergency Medicine News: January 2009 - Volume 31 - Issue 1 - p 7-10

Buprenorphine

Receptor Saturation

However, did these studies involve opioid-naïve or opioid-experienced (tolerant) human brains?



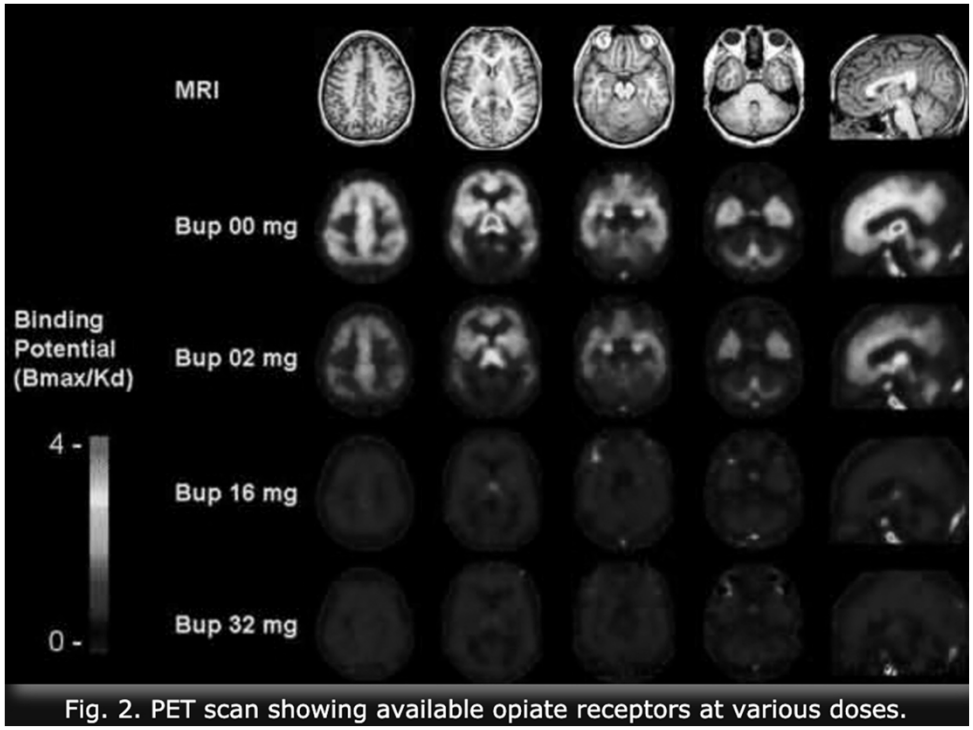


Fig. 2. PET scan showing available opiate receptors at various doses.

Clinical Pharmacology Online Database
Neuropsychopharmacology. 2003. 28 (11): 2000-2009.
https://accurateclinic.com/accurate-education-pain-medications-buprenorphine/

Buprenorphine
Morphine Milligram Equivalent Factor

- March 2016 CDC Chronic Pain Opioid Guidelines
  - Buprenorphine MME Factor: 10
- January 2017 CDC Updates
  - Buprenorphine MME Factor: 30
- 2018 CDC Updates
  - Buprenorphine MME Factor: Unlisted

Clinical Pharmacology Online Database
SAMHSA Buprenorphine Clinical Guidelines. https://www.ncbi.nlm.nih.gov/books/NBK64245/pdf/Bookshelf_NBK64245.pdf
Walsh SL, et al. Clinical Pharmacology of Buprenorphine: Ceiling Effects at High Doses. Clinical Pharmacology & Therapeutics. 1994 May; 55(5): 569-580.
http://pediatrics.aappublications.org/content/121/4/e782.long

Buprenorphine

Initiations

TRADITIONAL EXAMPLE
Observe Mild to moderate opioid withdrawal (Approximate COWS >11)
Initiation of buprenorphine should start with a dose of 2mg to 4 mg
Dosages may then be increased in increments of 2 mg to 4 mg
Once initial dose is well tolerated, can titrate fairly rapidly to 24-hour stable effects
Doses average at least 8 mg per day

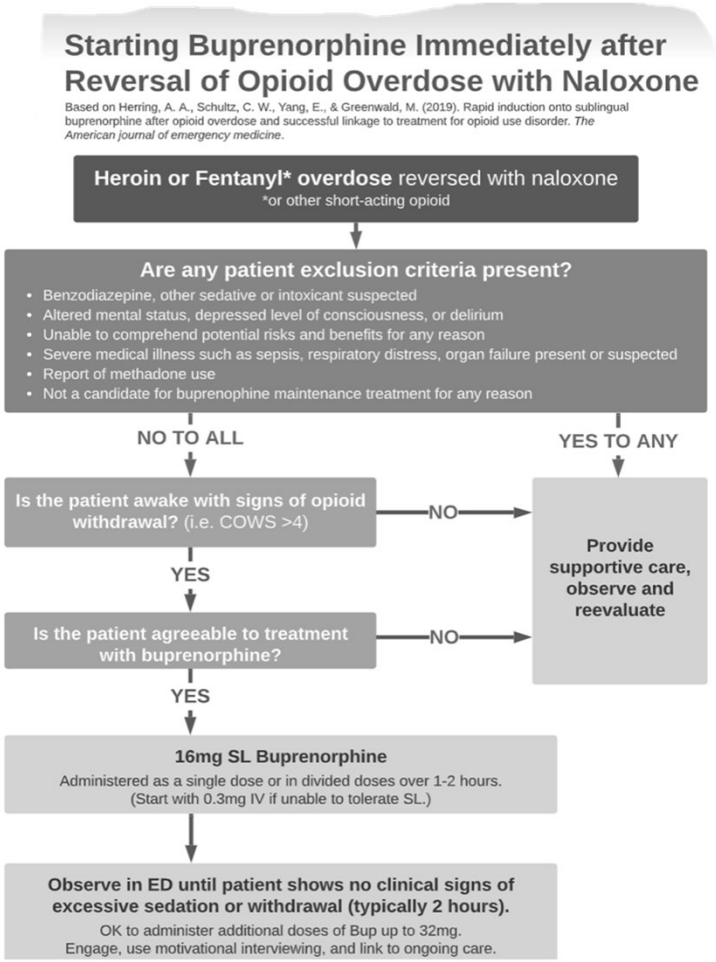
MICRODOSE EXAMPLE	
Day 1	0.5mg QD
Day 2	0.5mg BID
Day 3	1mg BID
Day 4	2mg BID
Day 5	3mg BID
Day 6	4mg BID
Day 7	12mg (stop other opioids)

Kampman K and Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med. Sep-Oct 2015;9(5):358-67.
Ahmed, S. Bhivandkar S, et. al. Microinduction of Buprenorphine/Naloxone: A Review of the Literature. The American Journal on Addictions, 30: 305–315, 2021.
Privia A. Randhawa, Rupinder Brar and Seonaid Nolan. Buprenorphine–naloxone "microdosing": an alternative induction approach for the treatment of opioid use disorder in the wake of North America's increasingly potent illicit drug market CMAJ January 20, 2020 192 (3) E73.

Buprenorphine

Initiations

"Macrodosing"



https://bridgetotreatment.org/resource/starting-buprenorphine-immediately-after-reversal-of-opioid-overdose-with-naloxone/

MAT & MATE Acts

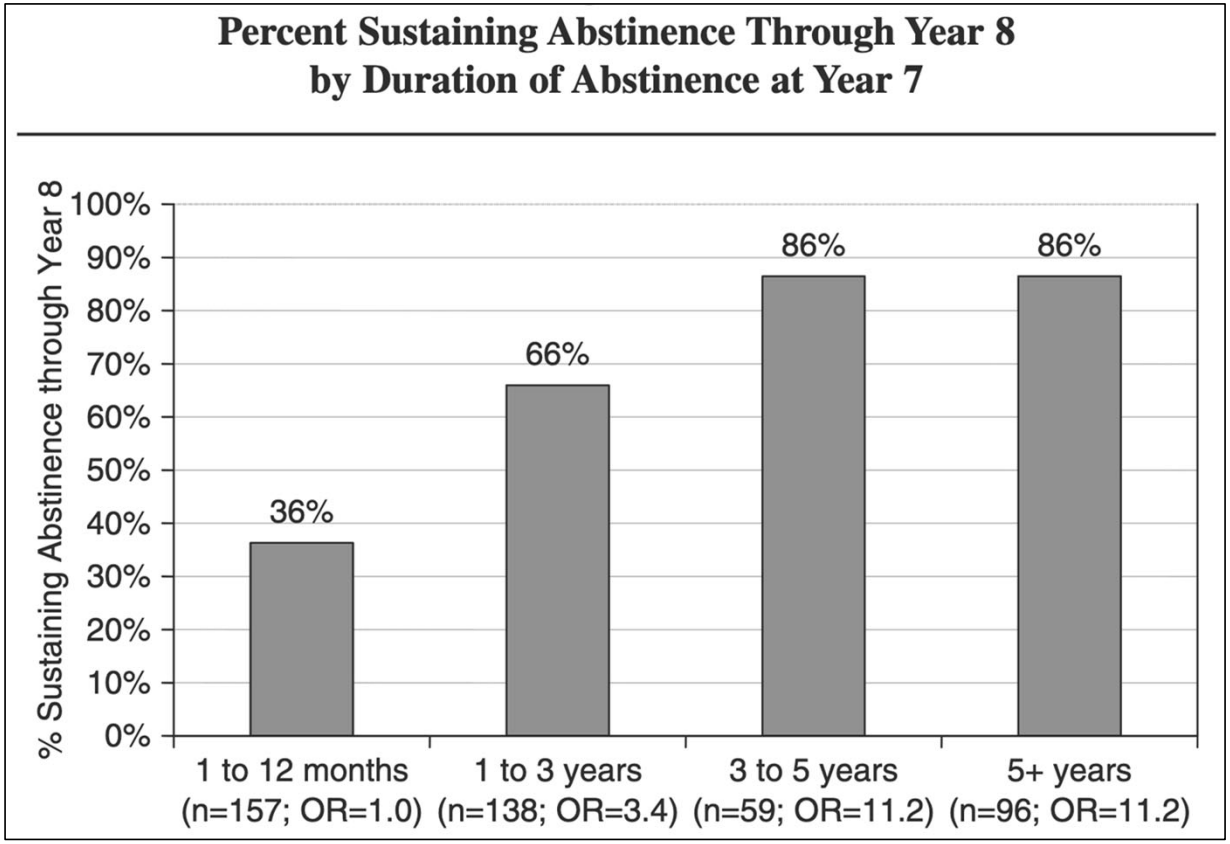
MAT Act: Buprenorphine X-Waiver eliminated

- Prescribers only need an active DEA License
- There are no limits on the number of patients for a prescriber

MATE Act: DEA renewals (q 3 years) require 8-hour Substance Use Disorder (SUD) training

https://www.medpagetoday.com/specialreports/features/102520
https://www.pewtrusts.org/en/research-andanalysis/articles/2022/12/30/president-signsbipartisan-measure-to-improve-addiction-treatment
https://www.deadiversion.usdoj.gov/pubs/docs/A-230020-Dear-Registrant-Letter-Signed.pdf

Minimum SUD Treatment???



Michael L. Dennis, Mark A. Foss, and Christy K. Scott. An Eight-Year Perspective on the Relationship Between the Duration of Abstinence and Other Aspects of Recovery. Evaluation Review 2007 31:6, 585-612.

Wouldn't Dopamine Agonists Make Sense?

Induction of Compulsions (Gambling/Sex)

Frequency of New-Onset Pathologic Compulsive Gambling or Hypersexuality After Drug Treatment of Idiopathic Parkinson Disease

J. Michael Bostwick, MD; Kathleen A. Hecksel, MD; Susanna R. Stevens, MS; James H. Bower, MD; and J. Eric Ahlskog, MD, PhD

TABLE 3. **Patients With PD and Compulsive Gambling or Hypersexuality**[a]

Patient No./sex/ age at PD onset (y)/ age at behavior onset (y)	Behaviors	Dose (mg/d)				Other psychoactive drugs at time of behavior onset (mg)
		Pramipexole	Ropinirole	Levodopa	Other PD drug	
1/M/43/49	Hypersexuality[b]		15	0		Bupropion SR, 150
2/M/40/52	Pathologic gambling, compulsive lawn care	4.5		700	Selegiline, 5; amantadine, 300	Gabapentin, 900; oxycodone, 5
3/M/65/68	Pathologic gambling, hypersexuality	4.5		600		
4/F/53/53	Pathologic gambling	4.5		600		Escitalopram, 10
5/M/64/80	Hypersexuality[b]		6	850		Trazodone, 75
6/M/55/66	Hypersexuality, pathologic gambling	4.5		1400		Amiodarone, 200
7/M/41/49	Pathologic gambling, pathologic hypersexuality, increased food and alcohol consumption, compulsive hobby work		21-24	0		

[a] PD = Parkinson disease; SR = sustained release.
[b] Not clearly pathologic.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2665974/pdf/mayoclinproc_84_4_003.pdf

Oh Oh Oh OUD

JAMA Network | Open

Research Letter | Psychiatry

Semaglutide and Opioid Overdose Risk in Patients With Type 2 Diabetes and Opioid Use Disorder

William Wang; Nora D. Volkow, MD; QuangQiu Wang, MS; Nathan A. Berger, MD; Pamela B. Davis, MD, PhD; David C. Kaelber, MD, PhD, MPH; Rong Xu, PhD

Introduction

Drug overdose fatalities in the United States remain high, with an estimated 107 543 deaths in 2023, mostly from opioids.[1] Despite the effectiveness of medications for opioid use disorder (OUD) in preventing overdoses, only an estimated 25% of individuals with OUD receive them,[2] and close to 50% discontinue treatment within 6 months. There is an urgency for alternative treatments for OUD. Glucagon-like peptide-1 receptor agonists (GLP1-RAs), used for type 2 diabetes (T2D) and obesity, modulated dopamine reward signaling and decreased drug rewards, including heroin in rodents.[3] Anecdotal reports of reduced drug craving in individuals using semaglutide, a new generation GLP-1RA, along with empirical studies showed its therapeutic benefits in alcohol and nicotine use disorders.[4,5] This led us to investigate whether semaglutide could protect against overdoses in patients with OUD.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

OUD
Opioid Use Disorder

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2824054#google_vignette

Pain Management Best Practices

Best Practices

Patient Education

- Patient & Provider Agreements/Contracts
- Treatment Goals (Pain Reduction, Improved Function, & End of Therapy)
- Proper medication storage and disposal

Treatment Selection

- Mental Health Assessments (Psychological Evaluation & Opioid Risk Screening)
- Drug Interaction Review (Drug-Drug, PD, PK, & PGx)
- Naloxone Education

Adherence & Diversion Monitoring

- Pill Counts
- Urine Drug Monitoring
- Prescription Drug Monitoring Program (PDMP) Review
- Monitoring for Controlled Substance Red Flags

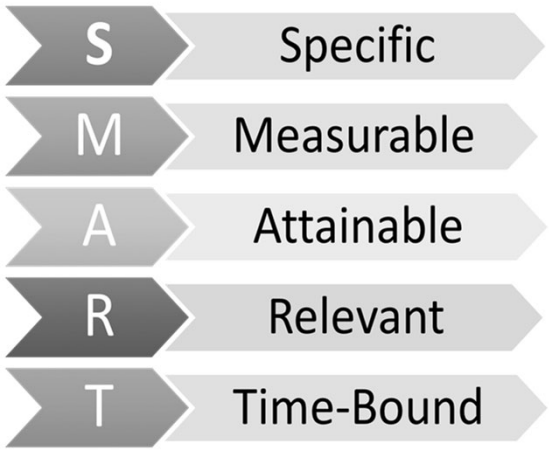
Pain Management Goals

Pain Reduction & Function Improvement

Pain = 5th Vital Sign ???

Analgesic ???

The goal is NOT necessarily to eliminate pain

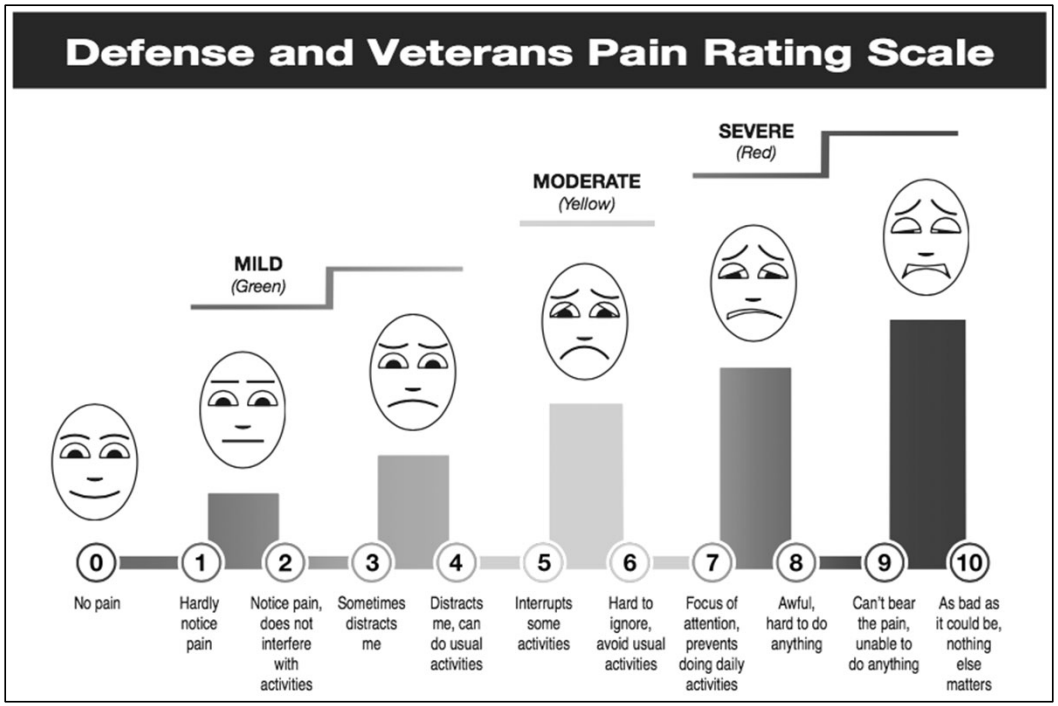


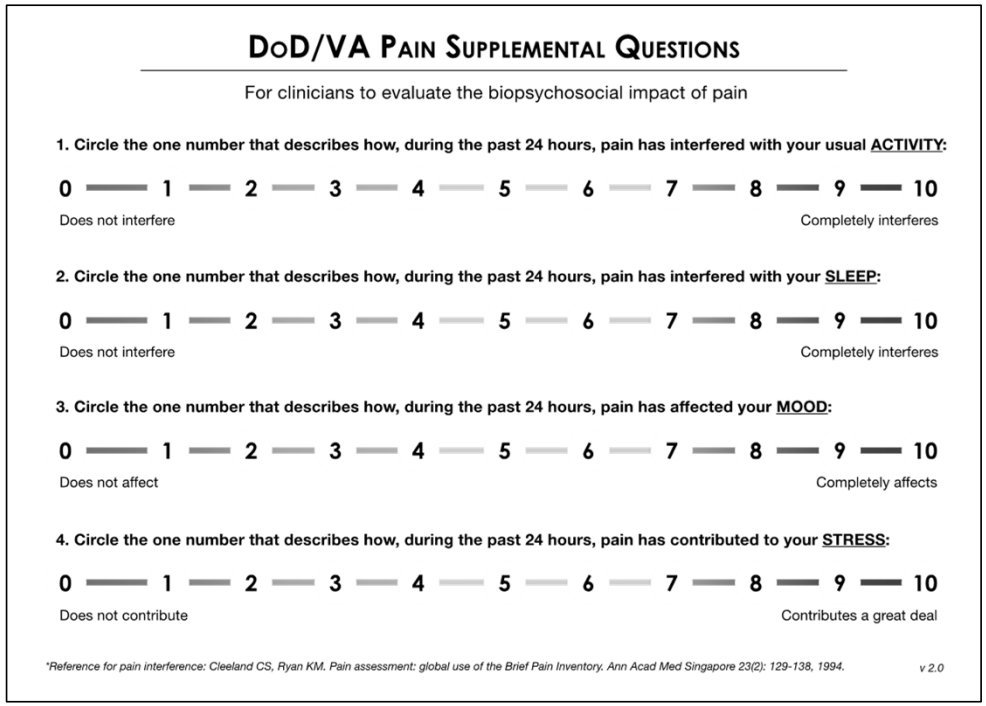
➢ **The goal is to Improve Function & Reduce Pain**

Favorite 1 to 10 Pain Scale Responses

20	Yes
13	2
8.5	3.14

DVPRS





DoD/VA Pain Supplemental Questions

For clinicians to evaluate the biopsychosocial impact of pain

1. Circle the one number that describes how, during the past 24 hours, pain has interfered with your usual ACTIVITY:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

Does not interfere — Completely interferes

2. Circle the one number that describes how, during the past 24 hours, pain has interfered with your SLEEP:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

Does not interfere — Completely interferes

3. Circle the one number that describes how, during the past 24 hours, pain has affected your MOOD:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

Does not affect — Completely affects

4. Circle the one number that describes how, during the past 24 hours, pain has contributed to your STRESS:

0 — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9 — 10

Does not contribute — Contributes a great deal

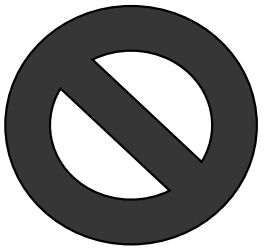
**Reference for pain interference: Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singapore 23(2): 129-138, 1994.* v 2.0

http://www.dvcipm.org/clinical-resources/defense-veterans-pain-rating-scale-dvprs/

Proper Medication Storage

Bathroom Medicine Cabinets → NO

- Humidity
- Unsecure
- Typically accessed at “groggy” times of day (AM/PM)



Lockable Safe Boxes → YES

- Away from children and pets
- Secure
- Still must incorporate into daily routine

Proper Medication Disposal

EPA

EPA United States Environmental Protection Agency

How to Dispose of Medicines Properly

DON'T: Flush expired or unwanted prescription and over-the-counter drugs down the toilet or drain unless the label or accompanying patient information specifically instructs you to do so.

DO: Return unwanted or expired prescription and over-the-counter drugs to a drug take-back program or follow the steps for household disposal below.

1ST CHOICE: DRUG TAKE-BACK EVENTS

To dispose of prescription and over-the-counter drugs, call your city or county government's household trash and recycling service and ask if a drug take-back program is available in your community. Some counties hold household hazardous waste collection days, where prescription and over-the-counter drugs are accepted at a central location for proper disposal.

Courtesy: Upper Watauga Riverkeeper and Appalachian Voices

Drug Take-Back Event

2ND CHOICE: HOUSEHOLD DISPOSAL STEPS*

1. Take your prescription drugs out of their original containers.

2. Mix drugs with an undesirable substance, such as cat litter or used coffee grounds.

3. Put the mixture into a disposable container with a lid, such as an empty margarine tub, or into a sealable bag.

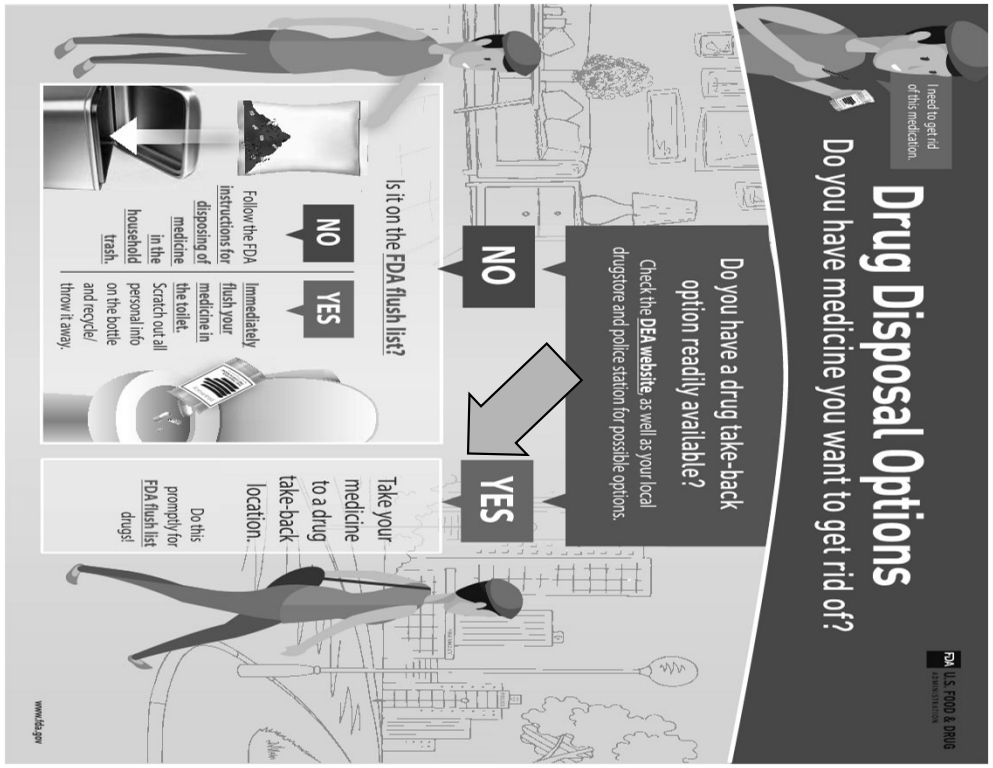
4. Conceal or remove any personal information, including Rx number, on the empty containers by covering it with permanent marker or duct tape, or by scratching it off.

5. The sealed container with the drug mixture, and the empty drug containers, can now be placed in the trash.

https://www.epa.gov/hwgenerators/collecting-and-disposing-unwanted-medicines

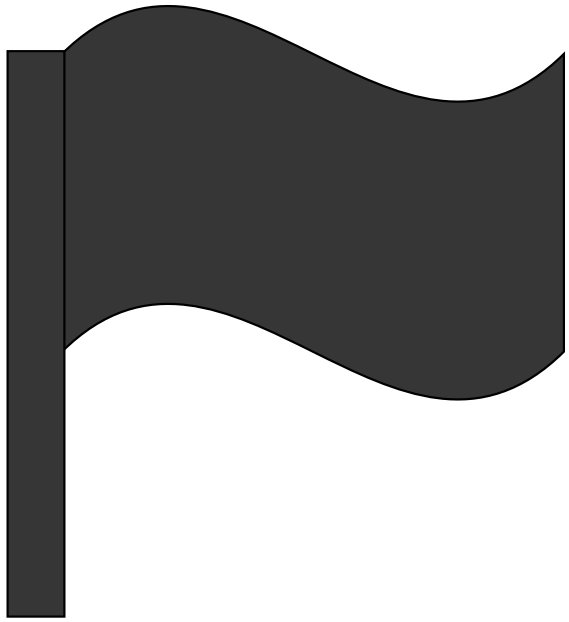
Proper Medication Disposal

FDA



https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm#steps
https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm576167.htm

Controlled Substances Red Flags



Publication of Red Flags

Prior to 2022

DEA Red Flags

(Court Cases)

2022

Practical Pain Management

(Now: Med Central)

2023

National Opioid Settlement

Garofoli MP, "Prescribing and Dispensing Controlled Substances: When to Pump the Brakes". Practical Pain Management. 2022; 22(6).
https://nationalopioidsettlement.com/

Red Flags

National Opioid Settlement

Teva & Allergen Settlements

Walmart, Walgreens, & CVS Settlements

Distributor & Janssen Settlements

FAQs, Explanatory Charts, & Frequently Referenced Documents

State Participation Chart & Documents

https://www.drugtopics.com/view/national-pharmacy-chain-opioid-settlements-poised-to-affect-independent-pharmacies
https://nationalopioidsettlement.com/

Red Flags

National Opioid Settlement

- A Red Flag shall not automatically mean prescription is illegitimate, yet must be resolved
- Resolution → RPh believes legitimate diagnosis & scope
- Resolutions & Rejections → Documentation

https://nationalopioidsettlement.com/

Red Flags

National Opioid Settlement

Red Flags (Patient)

1. CS-2 Refill Too Soon by > 3 Days
2. Doctor Shopping (CS > 4 Previous Prescribers of Separate Practices over 6 months)
3. Prescriber has > 10 documented CS refusals within 6 months
4. Previous 3 other CS from multiple prescribers with overlapping days within 30 days
5. Distance between patient's residence and pharmacy > 50 miles
6. Distance between patient's residence and prescriber > 100 miles
7. Previous 2 CS refusals within 30 days
8. Cash pay despite having prescription insurance coverage
9. >/= 3 Patients appear together for the same CS
10. Slang Term Medication Request (e.g., "Mallinckrodt blues," "M's", or "the blue pill")
11. Patient appears visibly altered, intoxicated, or incoherent

https://nationalopioidsettlement.com/

Red Flags

National Opioid Settlement

RED FLAGS (PRESCRIPTION)

1. Fails to meet law requirements
2. Misspellings
3. Atypical Abbreviations
4. Multiple Colors of Ink or Multiple Handwritings

RED FLAGS (PRESCRIBER)

1. CS-2 + Benzodiazepine + Carisoprodol
2. Prescriber has no office within 50 miles of pharmacy
3. Prescriber utilizes preprinted or stamped prescription pads

https://nationalopioidsettlement.com/

Corresponding Legal Responsibility

Title 21 Code of Federal Regulations

§1306.04 (a) Purpose of issue of prescription

- A prescription for a controlled substance to be effective must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice

➢The responsibility for the proper prescribing and dispensing of controlled substances is upon the prescribing practitioner, but a corresponding responsibility rests with the pharmacist who fills the prescription

https://www.deadiversion.usdoj.gov/21cfr/cfr/1306/1306_04.htm

OBRA '90

It is an expected best practice, to not only offer patient counseling as required by OBRA 1990 law, but to proactively counsel (discuss) any and all dispensed prescriptions with respective patients.

https://www.cms.gov/files/document/patientcounselingbooklet111414pdf

Patient Counseling At Its Best

- ~~I need you to sign here.~~

- ~~Do you have any questions?~~

➢ This medication might turn your urine purple.
Pause Do you have any questions?

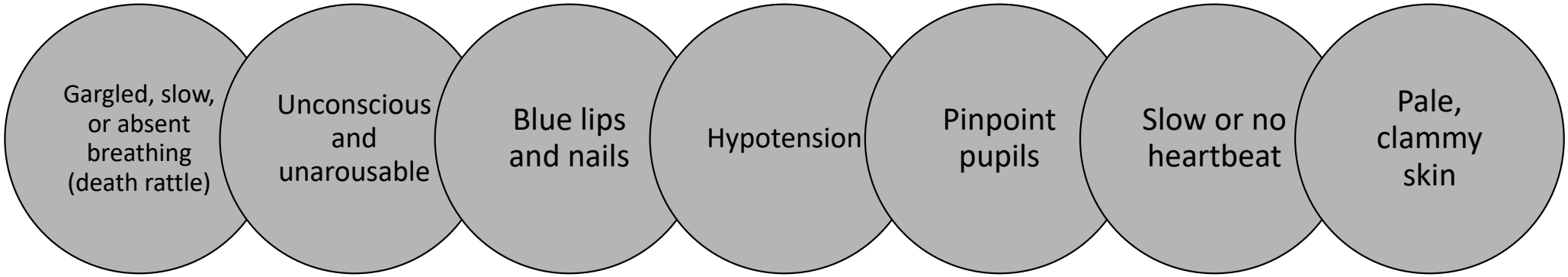
Avoiding Stigmatic Communications

Stigmatic Terminology	Recommended Terminology
Aberrant Behaviors	Using Medication Not as Prescribed or Intended
Abuse	Non-Medical Use
Addict	Person with Substance-Use Disorder
Clean/Dirty Urine	Negative versus Positive, or Unexpected

https://www.samhsa.gov/capt/sites/default/files/resources/sud-stigma-tool.pdf
https://www.whitehouse.gov/sites/whitehouse.gov/files/images/Memo%20-%20Changing%20Federal%20Terminology%20Regrading%20Substance%20Use%20and%20Substance%20Use%20Disorders.pdf

Opioid Antagonists

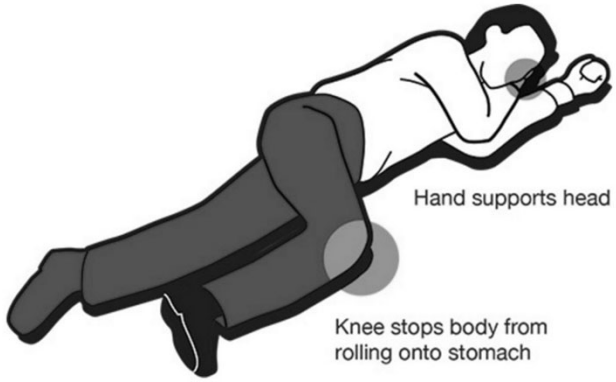
Opioid Overdose Symptoms



https://www.samhsa.gov/medication-assisted-treatment/treatment/naloxone

Opioid Antagonist Administration

SAMHSA Guidelines



1. Check for signs of opioid overdose
2. Call EMS to access immediate medical attention*
3. Administer antagonist (rescue position)*
4. Rescue breathe if patient not breathing
5. Stay with the person and monitor their response until emergency medical assistance arrives. After 2 to 5 minutes, repeat the dose if person is not awakening or breathing well enough (10 or more breaths per minute)

*Order depending on the source of guidance.

https://www.samhsa.gov/medication-assisted-treatment/treatment/naloxone

Naloxone
FDA "Perfect Dose" Panel

MEDPAGETODAY®

Specialties COVID-19 Opinion Health Policy Meetings Special Reports Break Room Conditions Society Part

Neurology > General Neurology

FDA Splits on Naloxone Dose

— Most agreed there was insufficient evidence to decide if 0.4-mg standard is too low

by Kristina Fiore, Associate Editor, MedPage Today October 6, 2016

A joint FDA advisory panel was split on whether the injectable 0.4-mg dose of naloxone should remain the current standard by which products containing the opioid overdose reversal drug should be measured -- though they agreed that a lack of data made their decision more challenging.

Slightly more panelists voted to increase the minimum acceptable dose rather than maintain it (15-to-13) during the joint meeting of the Anasthetic and Analgesic Drug Products Advisory Committee (AADPAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM).

ADVERTISEMENT
AND WE ARE NOT STOPPING NOW
gastroenteritis (0.9%),
• In children 6 weeks thro commonly reported soli injection site tenderness decreased appetite, de

No conclusion on "best" or "perfect" naloxone dose for all situations

Fiore, Kristina. "FDA Splits on Naloxone Dose." *Medical News*, MedpageToday, 6 Oct. 2016, www.medpagetoday.com/neurology/generalneurology/60632.

Naloxone 8mg vs 4mg NS

- No benefits to administration of 8-mg intranasal naloxone compared with 4-mg product
- 8-mg product had a significantly higher prevalence of opioid withdrawal

Payne ER, Stancliff S, Rowe K, Christie JA, Dailey MW. Comparison of Administration of 8-Milligram and 4-Milligram Intranasal Naloxone by Law Enforcement During Response to Suspected Opioid Overdose — New York, March 2022–August 2023. MMWR Morb Mortal Wkly Rep 2024;73:110–113.

Naloxone

Shelf Life

FDA announces shelf-life extension for naloxone nasal spray

Today, FDA is announcing that Emergent BioSolutions is extending the shelf-life of newly manufactured NARCAN (naloxone hydrochloride) 4 milligram (mg) Nasal Spray products from 3-years to 4-years. This action was taken at the request of the FDA and is the latest of multiple steps the Agency has recently taken to prevent overdoses and reduce overdose-related deaths by expanding access to naloxone and other overdose reversal agents.

Center for Drug Evaluation and Research. "FDA Announces Shelf-Life Extension for Naloxone Nasal Spray." *U.S. Food and Drug Administration*, FDA, www.fda.gov/drugs/drug-safety-and-availability/fda-announces-shelf-life-extension-naloxone-nasal-spray.

Location & Individuals

- Anyone can be trained to save a life with an opioid antagonist, yet what happens if there is none available on scene?

- Consider storing antagonist alongside AEDs, which are commonly located in public areas (malls, libraries, restaurants, and even airplanes)

- Location, Location, LOCATION!!!

Harm Reduction

WEBER*RENEW

Rhode Island's Center for Harm Reduction and Recovery Services

As encountered by Pain Guy™ in Burnside Park in Providence, Rhode Island

Naloxone Products

Product	Dose	Directions	Rx/OTC
Generic Injectable	0.4mg	Inject 1mL in shoulder/thigh, may repeat in 2 to 3 min Use 3mL 23G syringe and 1” needle	Rx
Zimhi®	5mg	Inject in thigh, may repeat in 2 to 3 minutes	Rx
Auto Injector	10mg	Military Utilization	
Generic Intranasal (Kits)	1mg	Spray 1mL (half of syringe) in each nostril with atomizer, may repeat in 2 to 3 minutes	Rx
Narcan® Nasal Spray + Generic	4mg	Spray into one nostril; may repeat in 2 to 3 minute with 2nd device in alternate nostril	Rx & OTC
Kloxxado® Nasal Spray	8mg		Rx
Rivive®	3mg		OTC
Pocket Naloxone®	1 swab	Swab one nostril, may repeat in 2 to 3 minutes	OTC

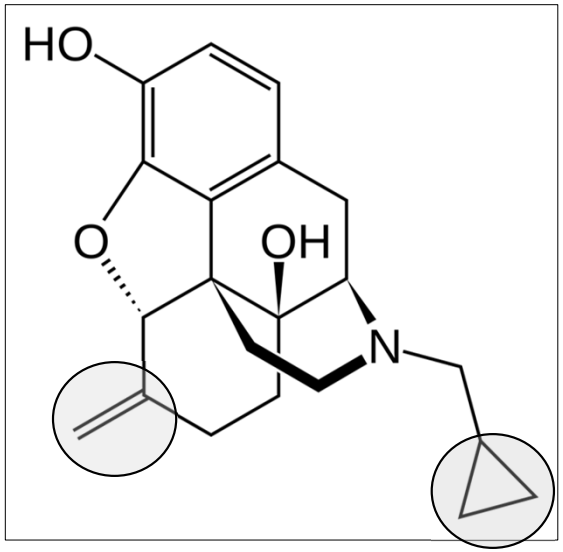
Clinical Pharmacology Online Database.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212045s000lbl.pdf
https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212854s000lbl.pdf

Nalmefene

Pharmacology

Stronger ?
Longer ?

- Compared to Naltrexone
  - Longer t ½ (~8 Hours)
  - Greater PO bioavailability
  - Similar Mu binding affinity
- Compared to Naloxone
  - 5x Mu binding affinity



Nalmefene

History

- 1975: Discovered
- 1995: FDA approved (Revex™) parenteral opioid overdose reversal
- 2008: Manufacturer discontinued
- 2013: European countries began approving for alcohol dependence
- 2020s: Studies for opioid overdose reversal product (US)

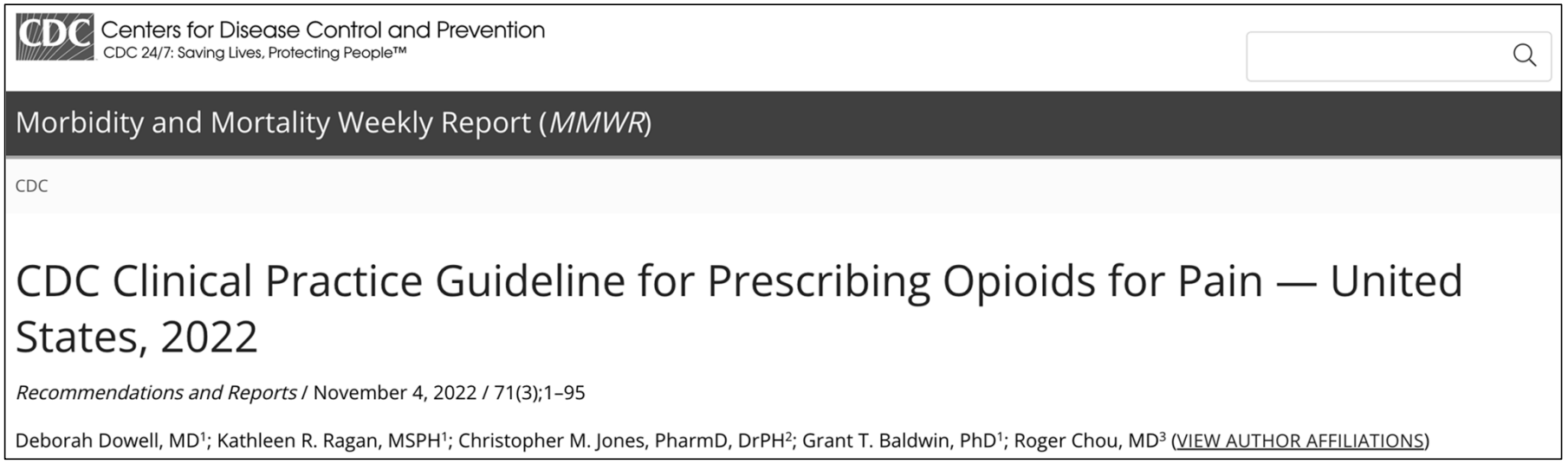
Nalmefene Products

Product	Dose	Directions	Rx/OTC
Generic Injectable	2 mL vials (1 mg/1 mL)	Weight-Based IV Bolus or IM/SC	Rx
Zurnai® Auto-Injector	1.5mg in 0.5mL	Single-Dose Auto-Injector	Rx
Opvee® Nasal Spray	2.7mg	Spray into one nostril; may repeat in 2 to 3 minute with 2nd device in alternate nostril	Rx

Pain Guidelines

2022 CDC Opioid Guideline Update

Published Online Thursday November 3rd, 2022



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022

Recommendations and Reports / November 4, 2022 / 71(3);1–95

Deborah Dowell, MD[1]; Kathleen R. Ragan, MSPH[1]; Christopher M. Jones, PharmD, DrPH[2]; Grant T. Baldwin, PhD[1]; Roger Chou, MD[3] (VIEW AUTHOR AFFILIATIONS)

https://www.regulations.gov/docket/CDC-2022-0024/document

CDC Opioid Workgroup

2022 CDC Opioid Guideline Update

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- Ross, Melanie R., MPH, MCHES (Designated Federal Officer)

https://www.cdc.gov/injury/bsc/opioid-workgroup-2019.html#:~:text=The%20Opioid%20Workgroup%20(OWG)%20of,prepared%20by%20CDC)%20and%20to

2022 CDC Opioid Guideline Updates

What's Updated???

1. Settings (All Outpatient)
2. Expanded Time Frames (Acute, Subacute, and Chronic)
3. Specific Pain Conditions
   - OA, Neuropathic, Fibromyalgia, DPN, & PHN
   - Not including palliative, cancer, nor sickle cell
4. Taper only when appropriate & only gradually (Avoid rapid tapers)
5. Massaged MME limits and thresholds wording
   - Updated Hydromorphone, Methadone, & Tramadol MME Factors

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Update

12 Recommendations

Opioid Yes/No

1. Nonopioid therapies are effective for many common types of acute pain
2. Nonopioid therapies are preferred for subacute and chronic pain

Opioid Selection

3. Utilize Immediate-Release (IR) before Extended-Release (ER) opioids
4. Start low, go slow, and avoid increasing to high-risk dosage levels
5. Current high-risk opioid dosages: continually reassess risk/benefits, only taper gradually if risks > benefits

Duration & Follow-Up

6. When opioids are utilized in acute pain, only provide for expected duration
7. Reevaluate chronic/subacute opioid utilization at least every 3 months (within 1 to 4 weeks initially)

Risk Reduction

8. Opioid risk screening and naloxone education
9. PDMP review initially and periodically
10. Toxicology testing (UDM)
11. Caution with opioid/benzo combinations (or opioids with any CNS depressant)
12. Arrange MOUD for patients with OUD

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Updates

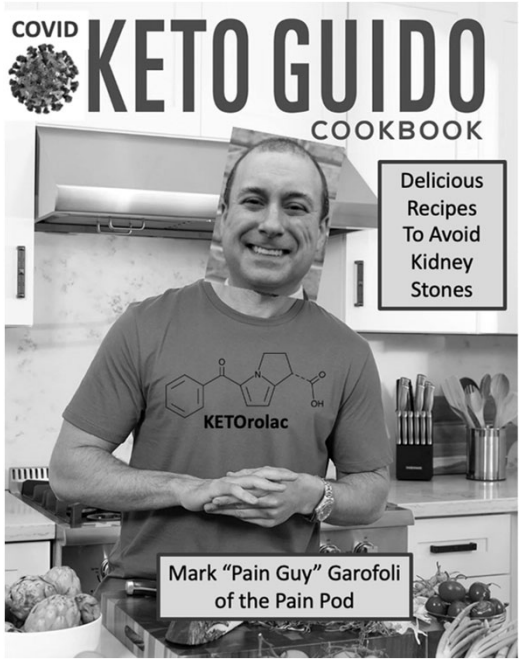
Section 1: Recommendation 1

- Nonopioid therapies are at least as effective as opioids for many common types of acute pain
  - Maximize Non-Rx and Non-Opioid Treatments
  - Only utilize Rx Opioid when Benefits > Risks
  - Discuss benefits & risks of opioid therapy with patient
  - Reference: AHRQ Review Article of 183 RCTs

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

Opioids in Acute Pain

Kidney Stones



- 8 trials w/ ~2K Patients with kidney stone pain
  - Opioids
    - 1 Trial: Morphine
    - 7 Trials: Meperidine (Not commonly utilized in U.S.)
  - NSAIDs
    - 1 Trial: Indomethacin
    - 4 Trials: Ketorolac
    - 3 Trials: Diclofenac
  - Summary
    - Opioid therapy *probably* less effective than NSAIDs for kidney stone pain
    - Less effective than APAP for kidney stone pain

❖All single dose Inpatient IV Therapy, yet guideline scope: OUTPATIENT ???

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.

2022 CDC Opioid Guideline Updates

Section 1: Recommendation 2

- Non-Opioids Preferred For Subacute & Chronic Pain
  - Maximize Non-Rx and Non-Opioid Treatments
  - Only utilize Rx Opioid when Benefits > Risks
  - Discuss Benefits & Risks Of Opioid Therapy with Patient
  - Discuss Opioid Discontinuation if Risks Eventually > Benefits
- Non-Opioid Options Should Have Insurance Coverage

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Updates

Section 1: Recommendation 2

Osteoarthritis

Non-Rx →

Topical NSAIDs →

Duloxetine or NSAIDs

Neuropathic Pain

TCAs, SNRIs, Gabapentin, Pregabalin, Oxcarbazepine, Capsaicin Patches, & Lidocaine Patches

Fibromyalgia

TCAs, SNRIs, NSAIDs, Gabapentin, & Pregabalin

(Duloxetine, Milnacipran, & Pregabalin are FDA-approved)

DPN

Duloxetine & pregabalin

(FDA-Approved)

PHN

Pregabalin & gabapentin

(FDA-Approved)

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Updates

Section 2: Recommendation 3

➢Opioid Initiation: IR Before ER/LA

- ER/LA opioids should be reserved for severe, continuous pain
  - FDA: Some ER/LA opioids only after IR opioids daily for at least 1 week
- Be careful with opioid rotation & renal/hepatic dysfunction
- Methadone should not be 1st Line option for ER/LA Rx pain opioid
- TD Fentanyl only with clinicians aware of dosing/absorption

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Updates

Section 2: Recommendation 4

➢Opioid Initiation: Start Low, Go Slow

- Many patients do not experience benefit in pain and function from ≥50 MME/day but are exposed to progressive risk

➢Opioid-Naïve Starting Dose:

- 5 to 10 MME single dose, or 20 to 30 MME/Day

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

MME Factors

2022 CDC Guidelines

Rx Opioid	MME Factor
Codeine	0.15
Fentanyl (Transdermal)	2.4
Hydrocodone	1.0
Hydromorphone	5.0
Methadone	4.7
Morphine	1.0
Oxycodone	1.5
Oxymorphone	3.0
Tapentadol	0.4
Tramadol	0.2

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

MME Practice Case #1

Oxycodone

Ms. Faye Kinet is prescribed oxycodone 40mg BID for the management of chronic lower back pain. How many Morphine Milligram Equivalents (MMEs) per day are being utilized?

40mg tablet x 2/Day = 80mg/Day
80mg/Day x 1.5 (MME Factor) = 120 MME/Day

120 MMEs/Day

https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

MME Practice Case #2

Tramadol

Thomas Payne is utilizing tramadol 50mg QID PRN. How many Morphine Milligram Equivalents (MMEs) per day are being utilized?

Tramadol 50mg tablet x 4/Day= 200mg/Day
200mg/Day x 0.2 (MME Factor) = 40 MMEs/Day

40 MMEs/Day

https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

MME Potential Limitations

Patient Variability

- Age, Height, Weight
- Genetics
- Hepatic/Renal Function
- Medications, etc.

Conversion Estimates

Dose-Response Curves

- Respiratory Depression
- Analgesia

Formulation Bioavailability Variability

Mixed-Action Opioids

Tolerance

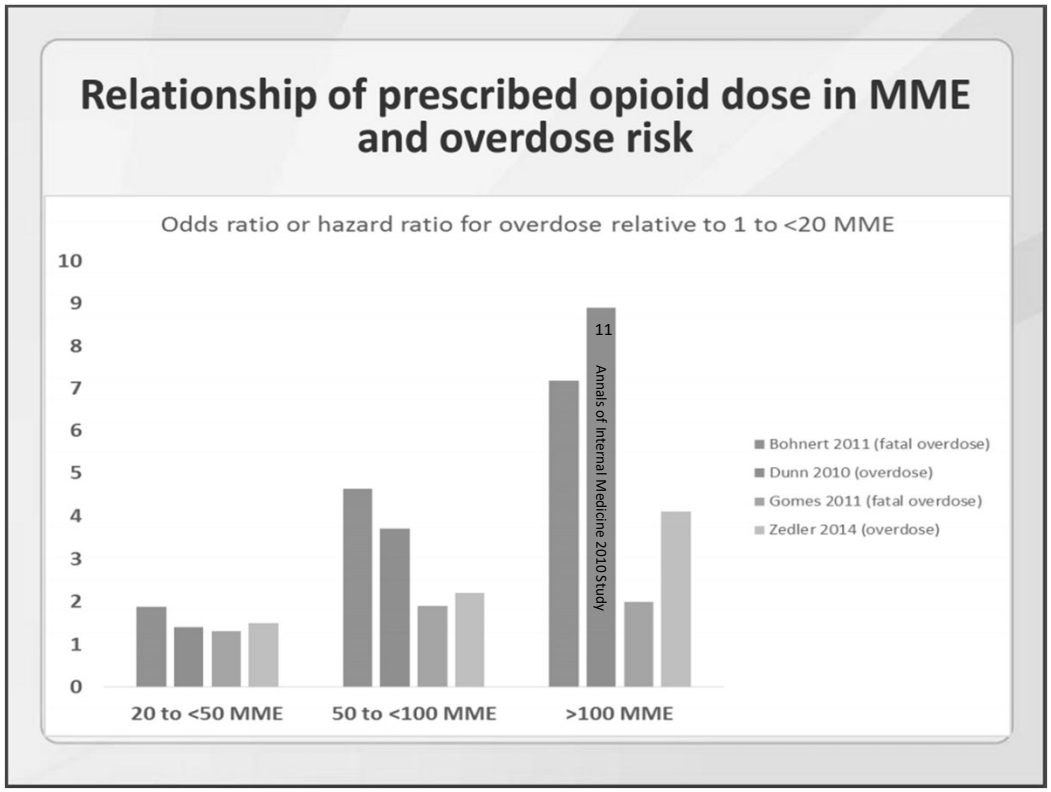
Methadone

- 2016: 4/8/10/12
- 2022: 4.7 (Source 2008)

Transdermal Fentanyl

- Before 2016: Variable

MMEs & Overdose Risk



https://i1.wp.com/face-facts.org/wp-content/uploads/2017/04/Opioid-dose-vs-overdose-risk.jpg


Inferring
causation
from
correlation

2022 CDC Opioid Guideline Updates

Section 2: Recommendation 5

- If Opioid Risks > Benefits: Optimize Other Tx's (& *Gradually* Taper Opioid)
  - 10% Monthly, and may need to pause/restart (rapid tapers only if life threatening)
  - Counsel on decreased tolerance (Overdose risk with previous doses)

- Payers, health systems, & state medical boards should *not* use this clinical practice guideline to set rigid standards

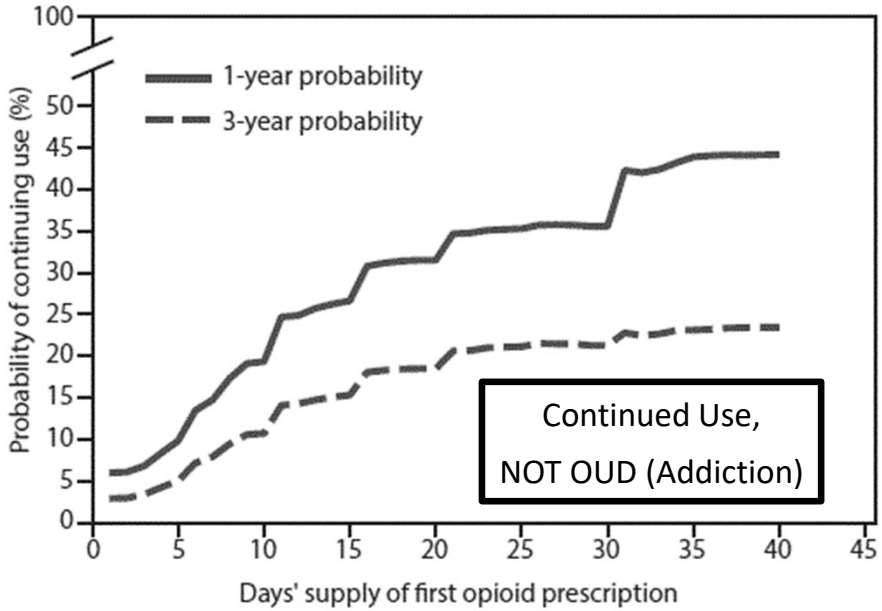
Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Updates

Section 3: Recommendation 6

- **Acute Pain**

Utilize no greater quantity than needed for the pain's expected duration



Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.
Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015. MMWR Morb Mortal Wkly Rep 2017;66:265–269.

2022 CDC Opioid Guideline Updates

Section 3: Recommendation 7

➢Regular Follow-Up

- Evaluate Risks/Benefits within 1 to 4 weeks of opioid initiation or dosage escalation
- Regularly reevaluate Risks/Benefits of continued utilization

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Updates

Section 4: Recommendation 8

- Opioid Risk Assessment (Initially & Continually)
- Naloxone Education (*ALREADY DISCUSSED*)

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

Opioid Risk Screenings

	Opioid-Naïve	Opioid-Experienced
Self	• Drug Abuse Screening Test (DAST) • Screener and Opioid Assessment for Patients with Pain (SOAPP)	• Current Opioid Misuse Measure (COMM) • Pain Medication Questionnaire (PMQ) • Prescription Drug Use Questionnaire, Patient (PDUQp)
Provider	• Opioid Risk Tool (ORT) • Opioid Risk Tool for Substance-Use Disorder (ORT-SUD) • Diagnosis, Intractability, Risk, and Efficacy Score (DIRE)	• Prescription Drug Use Questionnaire (PDUQ)

2022 CDC Opioid Guideline Updates

Section 4: Recommendation 9

➢PDMP Review: Initially & minimum q 3 months

- Part of the overall risk reduction strategy (not sole)
- Assess Complete Opioid Daily Dosage & Risks
- PDMP Risk Scores are not validated (to clinical outcomes such as overdose) and should not supplant clinical judgement
- Clinicians should not dismiss patients based on PDMP alone

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Updates

Section 4: Recommendation 10

- Consider Urine Drug Monitoring (Subacute/Chronic Pain)
- Screening vs. Testing
- Not Punitive (Should not dismiss based on UDM alone)

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

2022 CDC Opioid Guideline Updates

Section 4: Recommendation 11

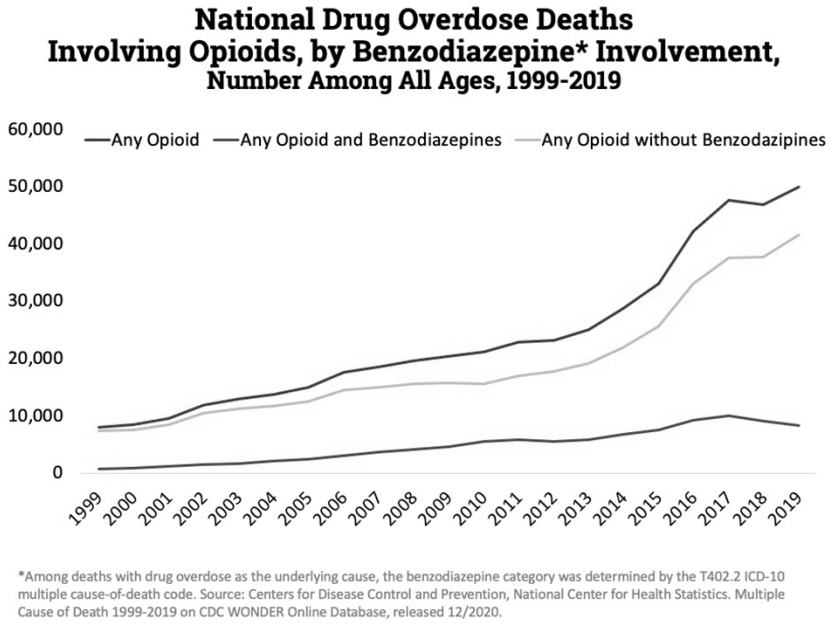
- Caution with Opioids & Benzos (Risks vs Benefits)

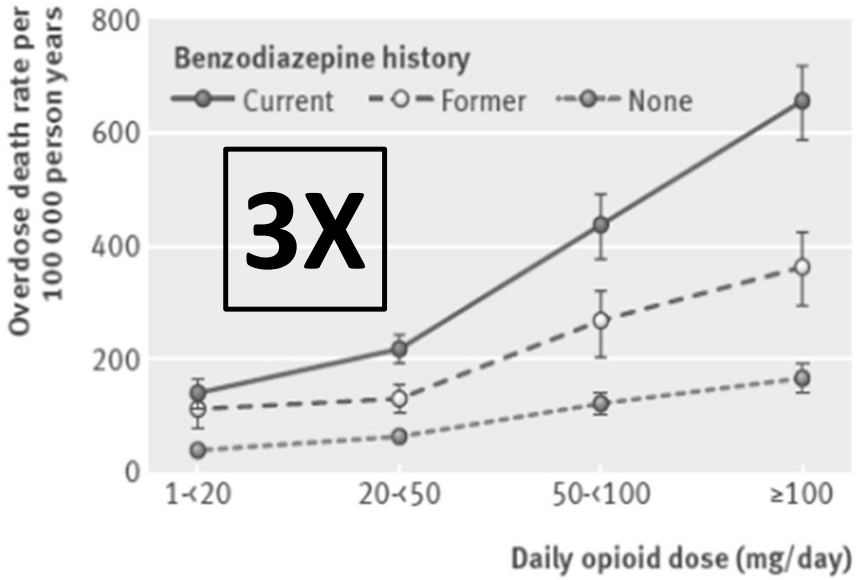
- Incidents of the combo do occur
  - Patient utilizing chronic Benzo experiencing Acute Pain, etc.

- Benzo's require a personalized gradual taper to avoid withdrawal symptoms (seizures, etc.)

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

Opioids & Benzos





https://www.drugabuse.gov/drug-topics/opioids/benzodiazepines-opioids

Tae Woo Park, et al. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ* 2015;350:h2698

2022 CDC Opioid Guideline Updates

Section 4: Recommendation 12

- OUD → MOUD

- This is a Pain Guideline Right?

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.

Beers Criteria Update

Aging Anatomy & Physiology

Cardiovascular

- Heart wall thickens, HR decreases, & Systolic BP increases

Pulmonary

- Chest wall thickens & Central airways widen = Decreased pulmonary Flow

Central Nervous System (CNS)

- Brain Size & BBB decreases

Endocrine

- Kidney size decreases GFR decreases

Hepatic System

- Liver Mass & CYP450 decreases

Immune System

- Entire immune system function decreases

Gastrointestinal

- Gastric emptying frequency decreases
- Gastric emptying time duration increases

Overall Body

- Body water/muscle ratio decreases
- Body fat increases

http://www.merckmanuals.com/professional/geriatrics.html

Painful Paperwork

- Living Wills
  - Advanced Directives for healthcare, life sustainment, treatment, etc.
- Power of Attorney
  - Invalid if patient becomes incompetent
- Durable Power of Attorney
  - Valid if patient becomes incompetent
- Durable Power of Attorney for Healthcare Decisions
  - Valid if patient becomes incapacitated
- DNR Orders
  - Do Not Resuscitate Orders, made by patient while competent
  - Made by Family/Practitioner if not competent

http://www.merckmanuals.com/professional/geriatrics.html

Geriatric Medication Toolbelt

Medication Selection & Utilization Tools for Patients >/= 65yo	
AGS Beers	American Geriatrics Society Beers List
STOPP	Screening Tool of Older Peoples Prescriptions
START	Screening Tool to Alert to Right Treatment
FORTA	Fit fOR The Aged
MAI	Medication Appropriateness Index
ADS	Anticholinergic Drug Scale
ACB	Anticholinergic Cognitive Burden Scale
ARS	Anticholinergic Risk Scale

2023 AGS Beers List Update

SPECIAL ARTICLE

Journal of the
American Geriatrics Society

American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults

By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel

AGS BEERS CRITERIA® 2023
Potentially Inappropriate Medications for Older Adults

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023; 1- 30.

2019 AGS Beers List (10 Tables)

Table	Descriptions
1	Designations Of Quality Of Evidence And Strength Of Recommendations
2	Potentially Inappropriate Medication Use In Older Adults (PIMs)
3	PIMs Due To Drug-disease Or Drug-syndrome Interactions That May Exacerbate The Disease/Syndrome
4	PIMs: Drugs To Be Used With Caution In Older Adults
5	Potentially Inappropriate Drug-Drug Interactions That Should Be Avoided In Older Adults
6	Medications to Avoid or Have Dosage Reduced With Varying Levels of Kidney Function in Older Adults
7	Drugs With Strong Anticholinergic Properties
8	Medications/Criteria Removed Since Previous AGS Beers List
9	Medications/Criteria Added Since Previous AGS Beers List
10	Medications/Criteria Modified Since Previous AGS Beers List

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023; 1- 30.

Table 1: PIMs (Pain Related)

Drug Class	Alternative(s)
TCA's: ALL except Doxepin </= 6 mg/day Paroxetine Barbiturates (Butalbital/Phenobarbital) Benzodiazepines (ALL) Z-Hypnotics Eszopiclone, Zaleplon, & Zolpidem	SSRI's (Not Paroxetine) SNRI's Bupropion Trazodone Topicals (Neuro Pain)

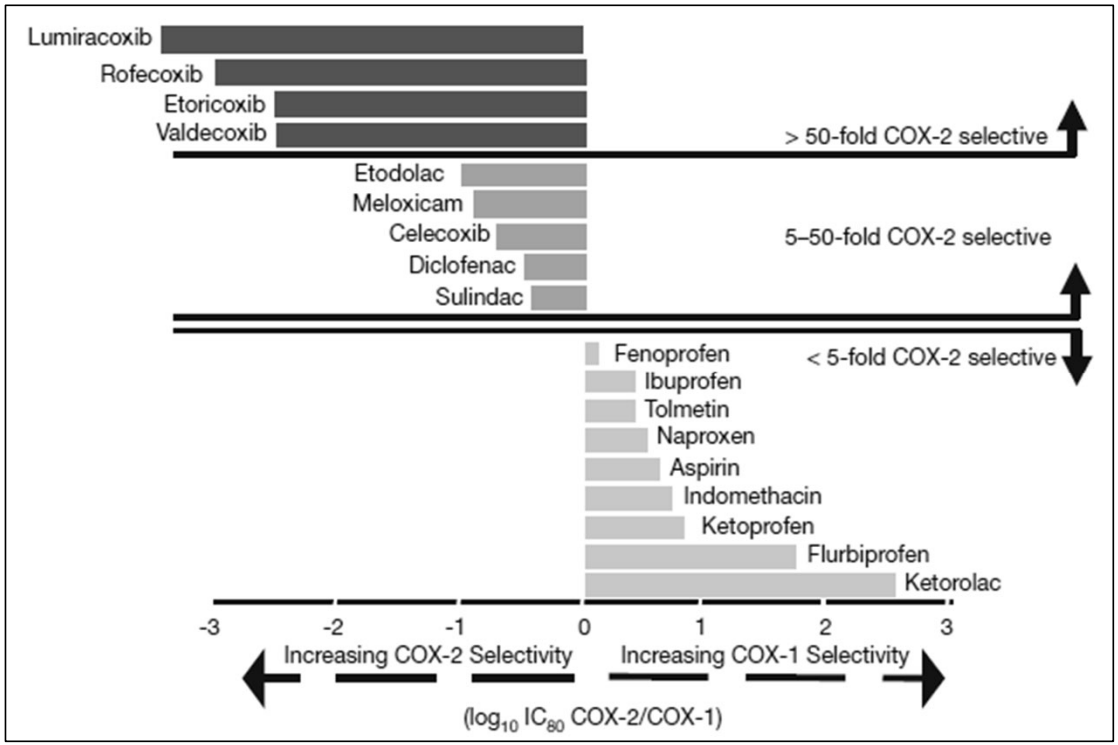
2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023; 1- 30.

Table 1: PIMs (Pain Related)

Drug Class	Alternative(s)
• Meperidine • Muscle Relaxants (Spasmodics) • Carisoprodol, Chlorzoxazone, Cyclobenzaprine, Metaxalone, Methocarbamol, & Orphenadrine • Non-Selective NSAIDs (all except celecoxib)	Non-Pharm APAP Celecoxib Topicals Antispasticity Agents (baclofen/tizanidine)

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023; 1- 30.

COX Selectivity



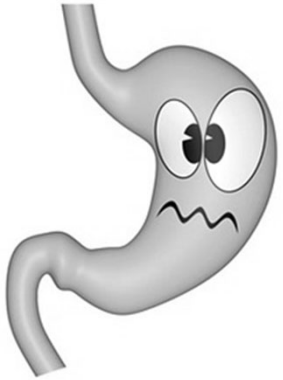
COX-1 to COX-2 Ratio	
Flurbiprofen	10.27
Ketoprofen	8.16
Fenoprofen	5.14
Tolmetin	3.93
Aspirin	3.12
Oxaprozin	2.52
Naproxen	1.79
Indomethacin	1.78
Ibuprofen	1.69
Ketorolac	1.64
Piroxicam	0.79
Nabumetone	0.64
Etodolac	0.11
Celecoxib	0.11
Meloxicam	0.09
Mefenamic acid	0.08
Diclofenac	0.05
Rofecoxib	0.05

Herndon, C. et al. Management of Chronic Nonmalignant Pain with Nonsteroidal Anti-inflammatory Drugs. Pharmacotherapy. 2008; 28 (6): 788-805.

Feldman, M, et al. Do Cyclooxygenase-2 Inhibitors Provide Benefits Similar to Those of Traditional Nonsteroidal Anti-Inflammatory Drugs, with Less Gastrointestinal Toxicity. Ann Intern Med. 2000; 132: 134-143.

COX-1 & COX-2

COX-1 Selective



COX-2 Selective

Feldman M & McMahon A. Do Cyclooxygenase-2 Inhibitors Provide Benefits Similar to Those of Traditional Nonsteroidal Anti-Inflammatory Drugs, with Less Gastrointestinal Toxicity? Ann Intern Med. 2000;132:134-143.

Table 3: PIMs Due to Disease/Syndrome

Pain Related

- Heart Failure (Avoid NSAIDs)
- Syncope (Avoid Tertiary TCAs: Amitriptyline, Imipramine, Clomipramine, Doxepin)
- Delirium (Avoid Opioids, Benzo's, Corticosteroids, etc.)
- Dementia (Avoid Anticholinergics, Antipsychotics, Benzo's, & Z-Hypnotics)
- History of Falls/Fractures (Avoid Benzo's, Opioids, Z-Hypnotics, TCAs, SSRIs, & SNRIs)
- Gastric/Duodenal Ulcer (Avoid NSAIDs except celecoxib)
- CKD Stages 4 & 5 (Avoid all NSAIDs)

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023; 1- 30.

Table 4: Medications to Use with Caution in Elderly

Pain Related

- Antipsychotics
- Mirtazapine
- SNRIs
- SSRIs
- TCAs
- Tramadol

2023 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023; 1- 30.

Table 5: Drug/Drug Interactions

Pain Related

- Multiple Anticholinergic Medications (Cognitive Decline, delirium, & falls/fractures)
- Opioids & Benzos/Gabapentinoids (Sedation/Overdose)
- >/= 3 CNS Active Medications (Falls/Fractures)
  - Antidepressants, Antipsychotics, Antiepileptics, Benzos, Z-Hypnotics, Muscle Relaxants, & Opioids

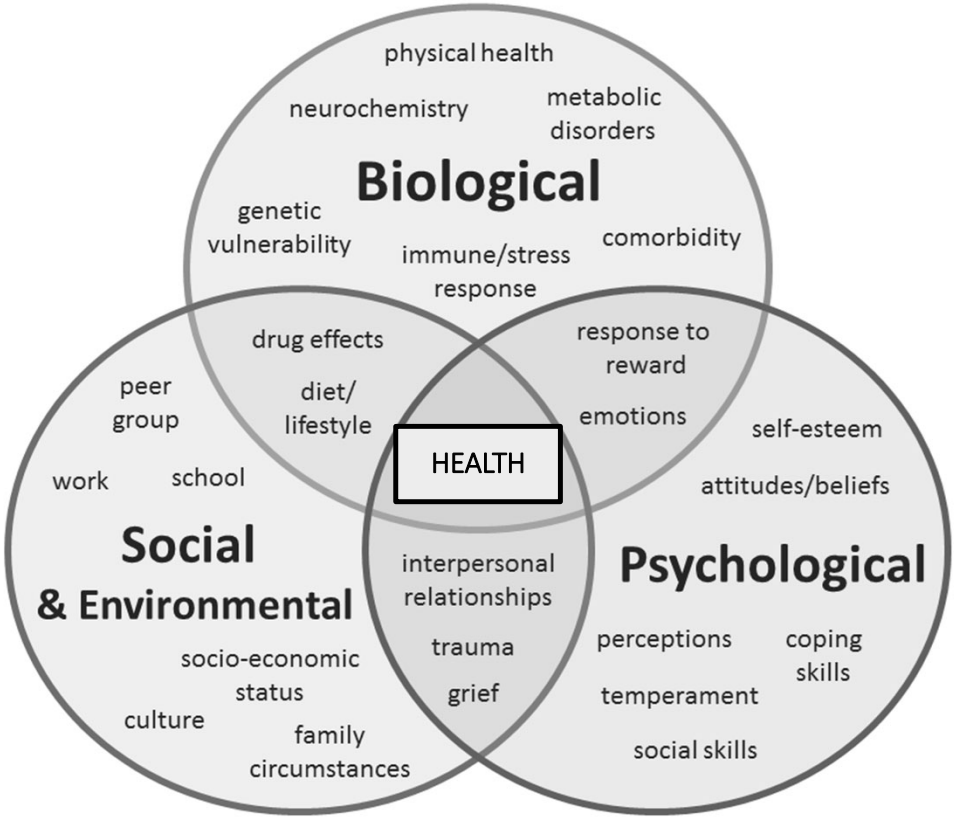

LEFT LANE
CLOSED
1500 FT
R
RIGHT LANE
CLOSED
1500 FT

If Not Anything, Then Something?

Patient by patient scenarios

- Clinical judgment
- Monitoring
- Documentation

BioPsychoSocial Model of Pain



https://www.physio-pedia.com/Biopsychosocial_Model

New Pain Medications

The Opioids

Tamayta, Toemaatoe, Opiate, Opioid

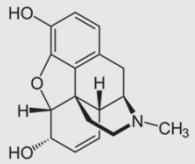
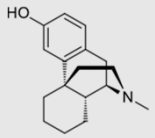
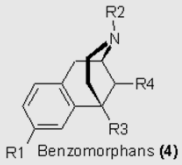
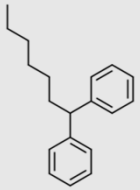
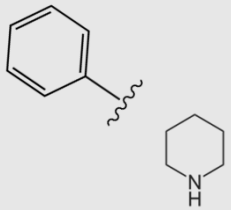
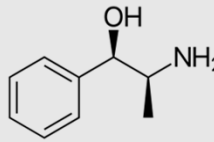
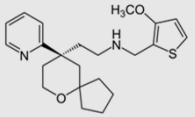
Opiate

"Natural"
Thebaine
Morphine
Codeine

Opioid

"Semi/Synthetic"
Heroin
Hydrocodone
Oxycodone
Fentanyl

Opioid Structural Classes

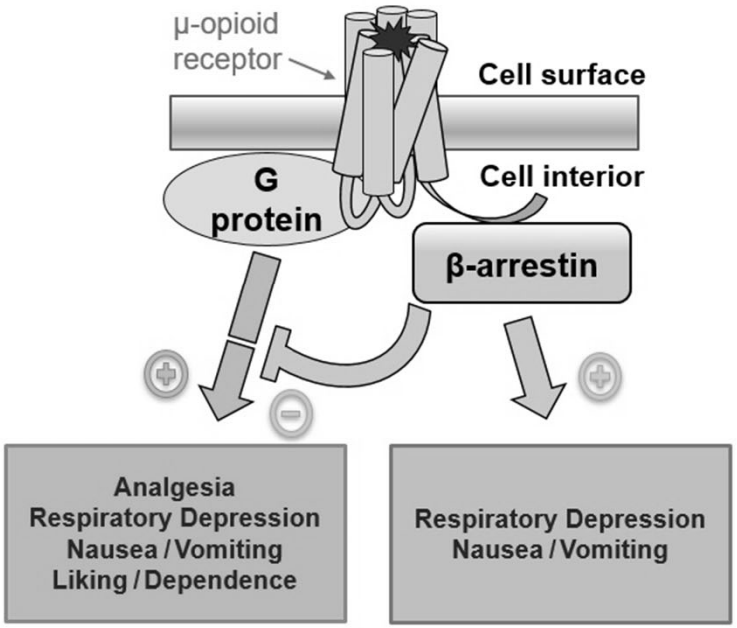
Structural Class	Phenanthrenes		Benzomorphan	Dipheylheptanes	Phenylpiperidines	Phenylpropylamines	New Entity
Rings	5 Rings	4 Rings	3 Rings	2 Rings	2 Rings	1 Ring	4 Rings
Structure							
Medication(s)	Opium Codeine Diacetylmorphine Hydrocodone Hydromorphone Benz-Hydrocodone Morphine Oxycodone Oxymorphone Naloxone Naltrexone Nalmefene Buprenorphine	Butorphanol Levorphanol	Pentazocine	Methadone Propoxyphene	Fentanyl/Analogs Sufentanil Meperidine Diphenoxylate Loperamide	Tapentadol Tramadol	Oliceridine

Adapted from Trescot AM, Datta S, Lee M, Hansen H. Opioid pharmacology. Pain Physician. 2008 Mar;11(2 Suppl):S133-53.

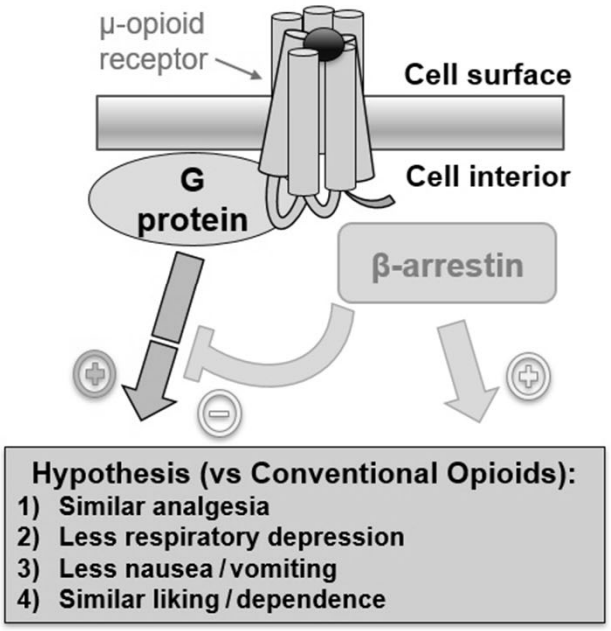
Oliceridine

Specificity Matters

Conventional Opioids



Oliceridine



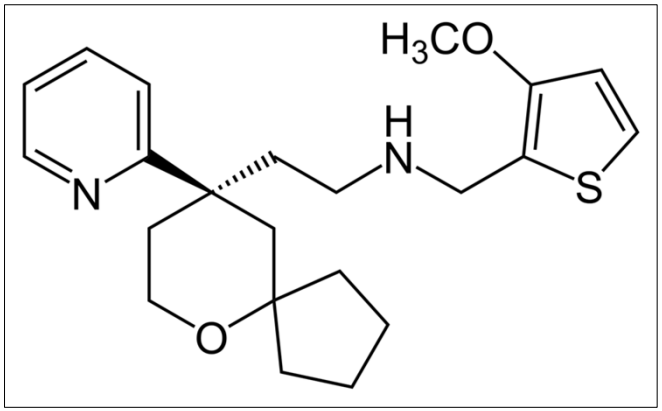
Oliceridine

OLINVYK™

- IV administration only (No Dilution)
- Dosing
  - Initial dose of 1.5 mg
  - Max single subsequent doses of 3 mg
  - Max cumulative daily dose of 27 mg

➢Oliceridine 1 mg IV ≈ morphine 5 mg IV

- CYP 2D6 & 3A4 Primary Metabolism
- Bolus & PCA Dosing
- No Renal & Hepatic Dosage Adjustment



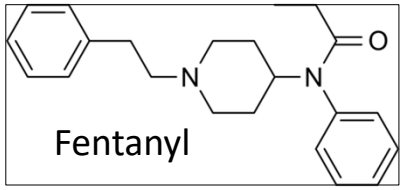
Trevena. Oliceridine Briefing Document: October 11, 2018 FDA Advisory Committee Meeting
https://olinvyk.com/dosing.html

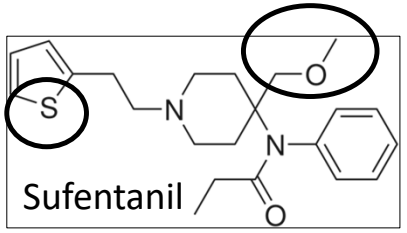
Sufentanil

Dsuvia®

CII

- Each 30mcg tablet is 3mm, blue, & flat-faced
- Dosage is 1 SL tablet, minimum of 1-hour between doses
- Do not exceed 12 tablets in 24 hours (360mcg)
- Use beyond 72 hours has not been studied
- 30mcg Sufentanil SL Tablet = 5 MMEs (MME Factor ~500)
- CYP-3A4 Substrate
- Minimize talking & avoid food/drink for 10 minutes post dosage
- Provide ice chips if excessive dry mouth prior to administration

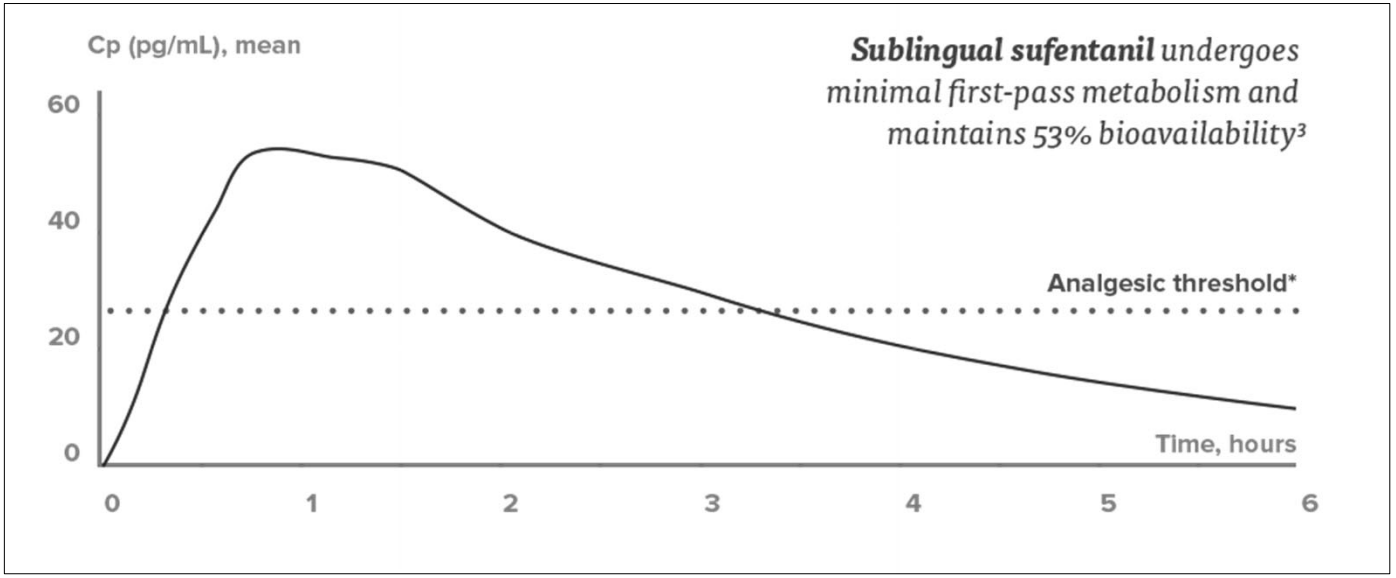


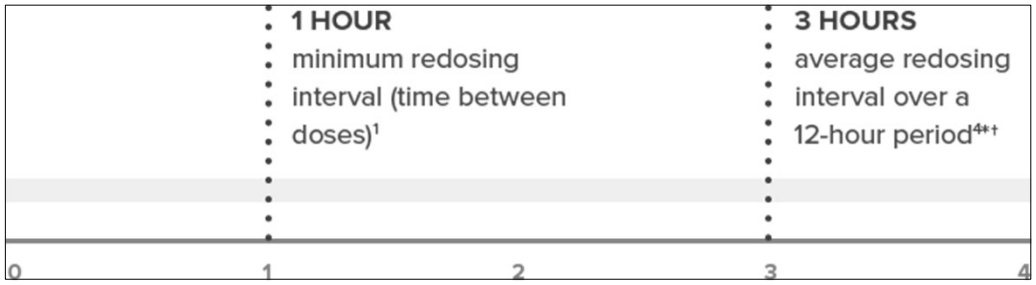


Clinical Pharmacology Online Database
Tvetenstrand CD, Wolff ME (2020) Reduced Opioid Use and Reduced Time in the Postanesthesia Care Unit Following Preoperative Administration of Sublingual Sufentanil in an Ambulatory Surgery Setting. J Clin Anesth Pain Manag 4(2):123-128..

Sufentanil

Dsuvia®



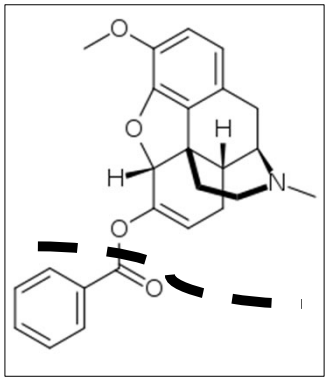


https://www.dsuvia.com/dosing-administration.

Benz-hydrocodone/APAP

Apadaz®

- Prodrug covalently bonded with benzoic acid
  - Benzoic Acid: Typical food preservative
  - Ligand-Activated Technology (LAT®)
  - Also being studied with a methylphenidate prodrug



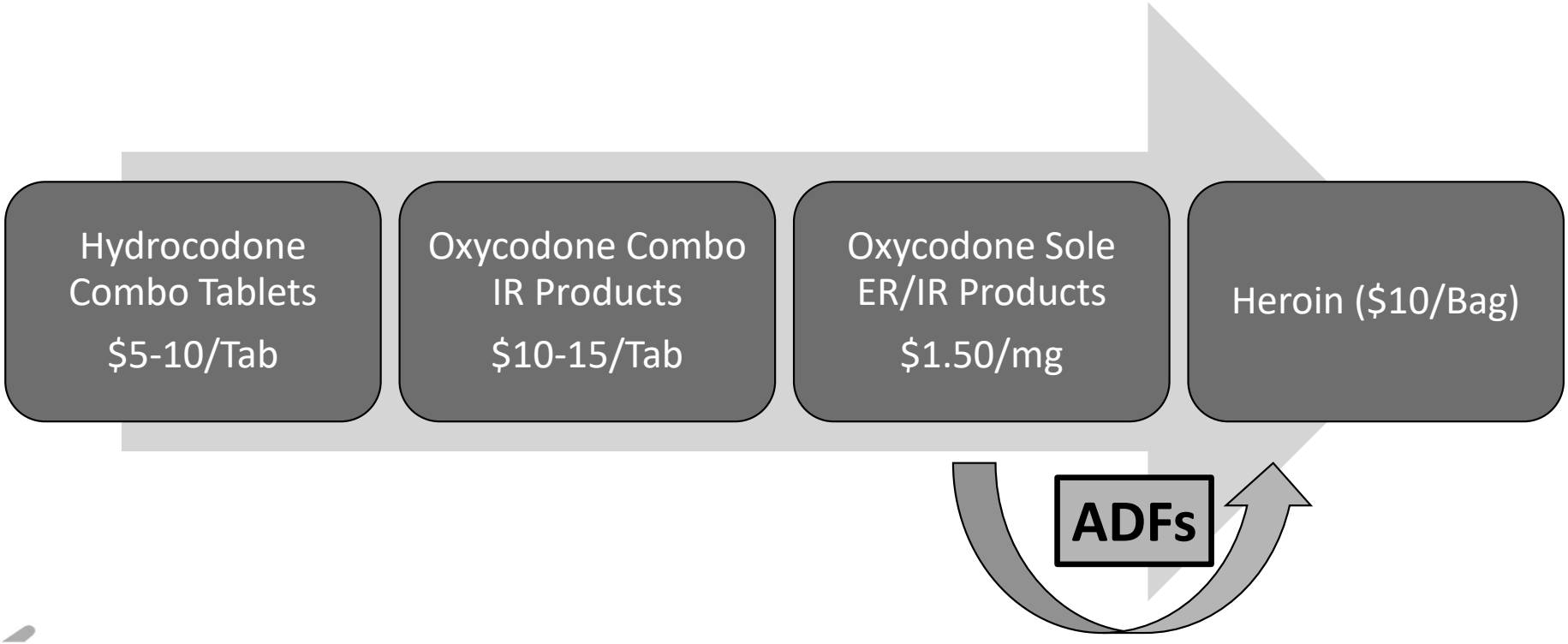
- NOT FDA approved as an abuse-deterrent formulation (ADF) opioid

- Indicated for the short-term (*no more than 14 days*) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate

Benzhydrocodone/APAP 6.12/325mg = hydrocodone/APAP 7.5/325mg

Clinical Pharmacology Online Database.
Apadaz Package Insert. 2018

Opioid Abuse Transition



- www.bluelight.org
- Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use – United States, 2006-2015. Weekly / March 17, 2017 / 66(10); 265–269.

Abuse-Deterrent Formulations

ADF Type	Description
1. Physical Barrier	Prevent chewing, crushing, cutting, grating, or grinding
2. Chemical Barrier	Resist extraction of the opioid through use of common solvents including water, alcohol or other organic solvents
3. Agonist/Antagonist Combinations	Antagonist is added to the formulation to interfere with release if taken in any other way than it was intended
4. Aversion	Substances are added to the dosage form to produce an unpleasant effect if the dosage form is manipulated prior to ingestion or if a higher dosage than directed is used
5. Delivery System	Alternative delivery systems that are more difficult to manipulate (such as a depot injectable, an implant, or transdermal application)
6. Prodrug	Medication contains a prodrug that lacks opioid activity until it has been transformed in the gastrointestinal tract
7. Combination of the above	

Webster L, Gudin J. Review of Opioid Abuse-Deterrent Formulations: Impact and Barriers to Access. J Pain Res. 2024 Jun 5;17:1989-2000.

FDA ADF Studies

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

Category 3

Abuse Potential Studies

Physically Manipulation	Routes of Administration
Cutting Grafting Milling Chewing +/- Heat	Ingestion (Oral Route) Injection (Parenteral Route) Insufflation (Nasal Route) Smoking (Inhalation Route)

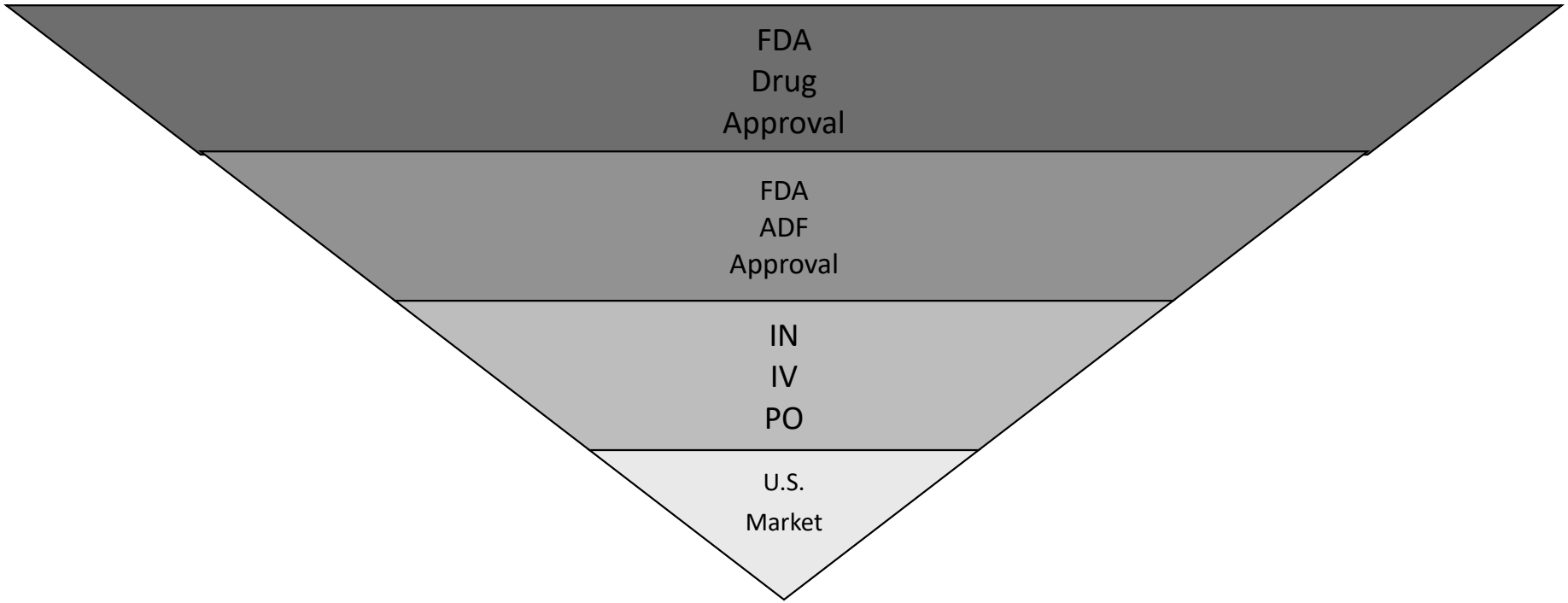
https://www.fda.gov/downloads/Drugs/.../Guidances/UCM492172.pdf

Category 3
Abuse Potential Studies

In Vitro Studies (Lab)	In Vivo Studies (Body)
Extractability studies	Nasal and oral PK
Performed at both room temp and elevated temp	Multiple strengths tested
Solvents • Level 1: deionized water • Level 2: vinegar, 0.2% baking soda solution, 40% ethanol, & carbonated drink • Level 3: 100% ethanol, 100% isopropyl alcohol, acetone, 0.1 N HCl, & 0.1N NaOH	Agonist/Antagonist Levels

https://www.fda.gov/downloads/Drugs/.../Guidances/UCM492172.pdf

ADF Opioid Availability Cascade



https://www.fda.gov/downloads/Drugs/.../Guidances/UCM492172.pdf

Abuse Deterrent Formulation (ADF) Opioids "Attempts"

Active Ingredient	Product	FDA ADF Approval	Formulation
oxycodone	Xtampza ER®	IN, IV, & PO Chew	Capsule
	Xartemis ER® (+APAP)	-	IR/ER Tablet
	OxyContin®	IN & IV	Tablet
	Troxyca®	IN, IV, PO Crush	Capsule
	Targiniq®	-	Tablet
	Oxaydo®	-	IR Tablet
	RoxyBond®	IN & IV	IR Tablet
tapentadol	Nucynta ER®	-	Tablet
hydromorphone	Exalgo®	-	Tablet
morphine	Embeda®	IN & PO Crush	Tablet
	Arymo®	IV	Tablet
	MorphaBond®	IN & IV	Tablet
hydrocodone	Hysingla®	IN, IV, & PO Chew	Tablet
	Zohydro ER®	-	Capsule
	Vantrela ER®	IV	Tablet
	Hydromet®	-	Liquid
	Tussigon®	-	Tablet
benzhydrocodone	Apadaz®	-	Tablet
pentazocine	Talwin NX®	-	Tablet
Oxymorphone	Opana ER®	-	Tablet

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411218/
https://www.sciencedirect.com/science/article/pii/S0378517316304884
https://www.futuremedicine.com/doi/pdf/10.2217/pmt-2015-0005
https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm

So, Who Made the Cut?…Pun Intended

FDA Approved ADF Opioids on US Market (2025)

Medicine	Product	FDA ADF Approval			Formulation	Generic Available
hydrocodone	Hysingla®	IN	IV	PO Chew	ER Tablet	Yes
oxycodone	OxyContin®	IN	IV	n/a	ER Tablet	Yes
	Xtampza ER®	IN	IV	PO Chew	ER Capsule	No
	RoxyBond®	IN	IV	PO Chew	***IR Tablet***	No

Adapted from Clinical Pharmacology Online Database.

Oxycodone IR ADF

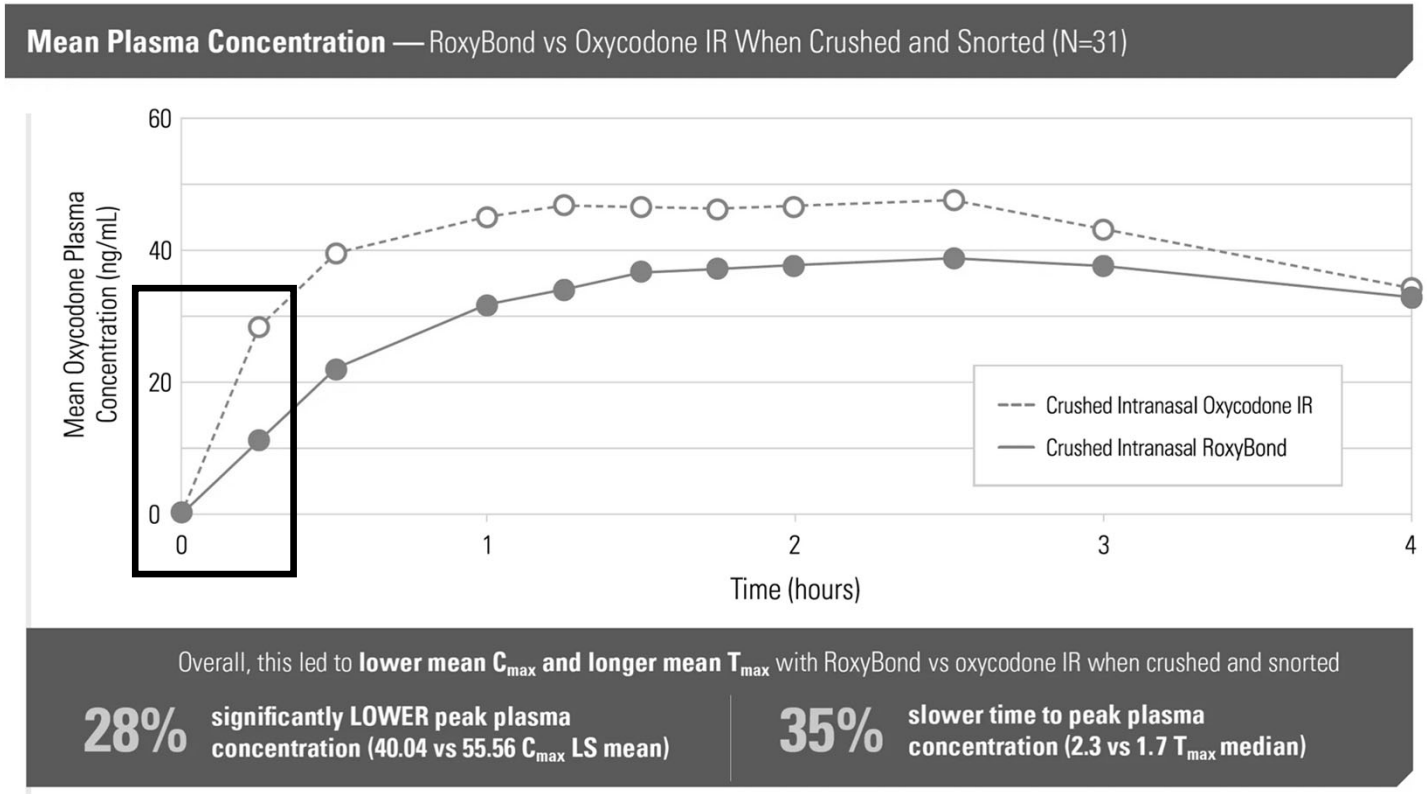
RoxyBond™

- Oxycodone IR 5mg, 15mg, & 30mg
- 1-to-1 Dosing Conversion with Oxycodone IR
- SentryBond™ Technology
  - Resists Physical Manipulation
  - Resists Chemical Extraction
  - Resists manipulation or transformation for injection

https://www.roxybond.com/

Oxycodone IR ADF

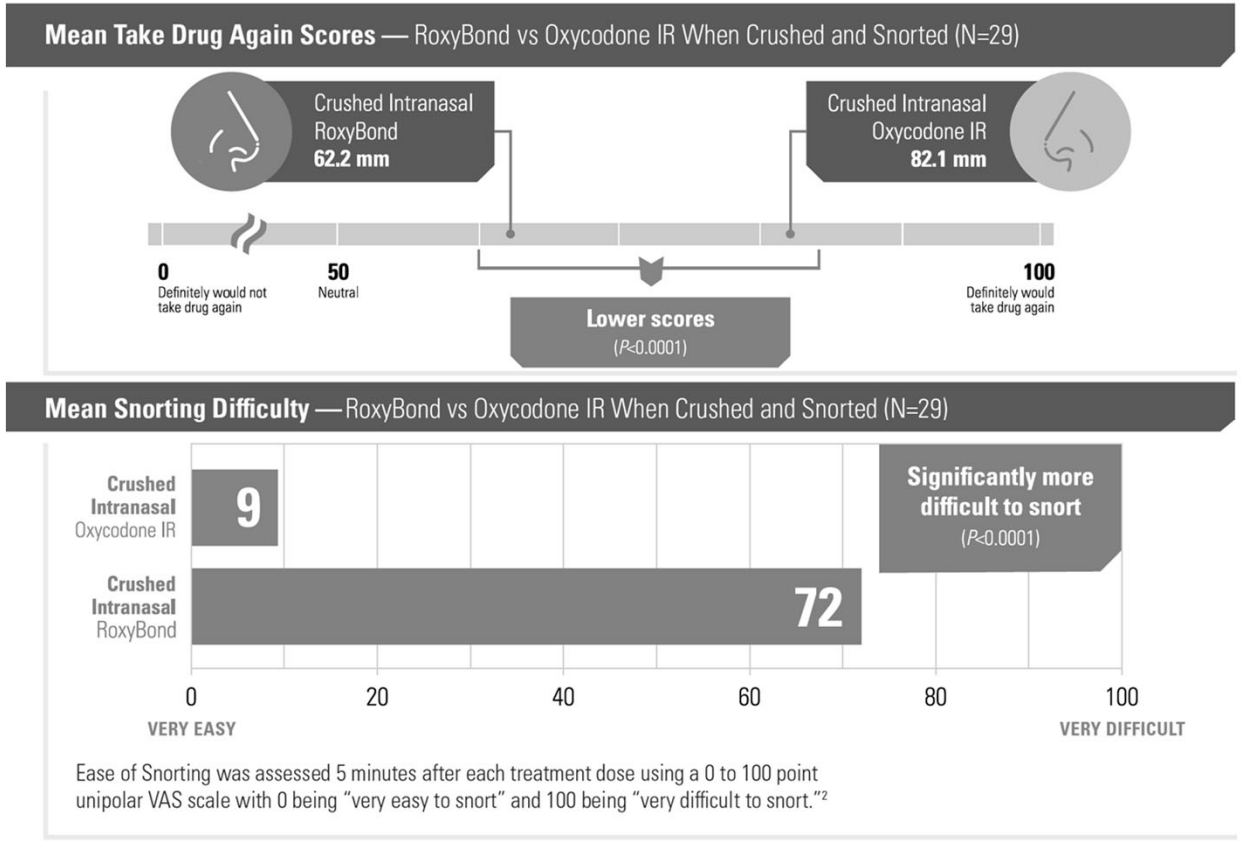
RoxyBond™



https://www.roxybond.com/

Oxycodone IR ADF

RoxyBond™



https://www.roxybond.com/

New Pain Medications

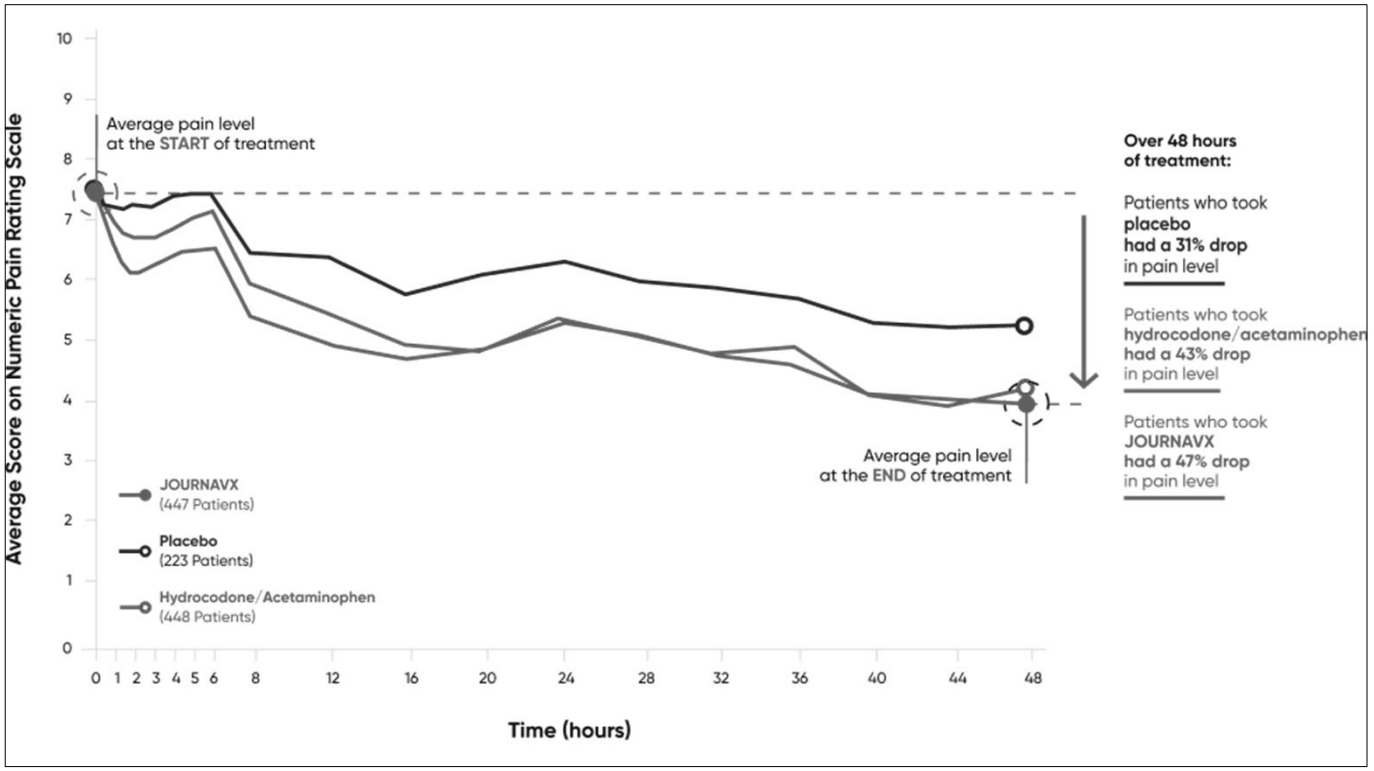
The Non-Opioid

Journavx™
suzetrigine

- Non-Opioid
- NaV1.8 Antagonist (Blocks action potential that typically shifts Na into cell)
- FDA Approval: Moderate-to-Severe (NPS 4 to 10) Acute Pain in Adults
- Dosage:
  - 100mg, 50mg q12 x 3, then 50mg QD (<14d)
  - 1st Dose: 1 hour before 2 hours after food; Subsequent doses +/- food
- 3A Substrate
- $15/pill

Journavx™

Tummy Tuck Trial



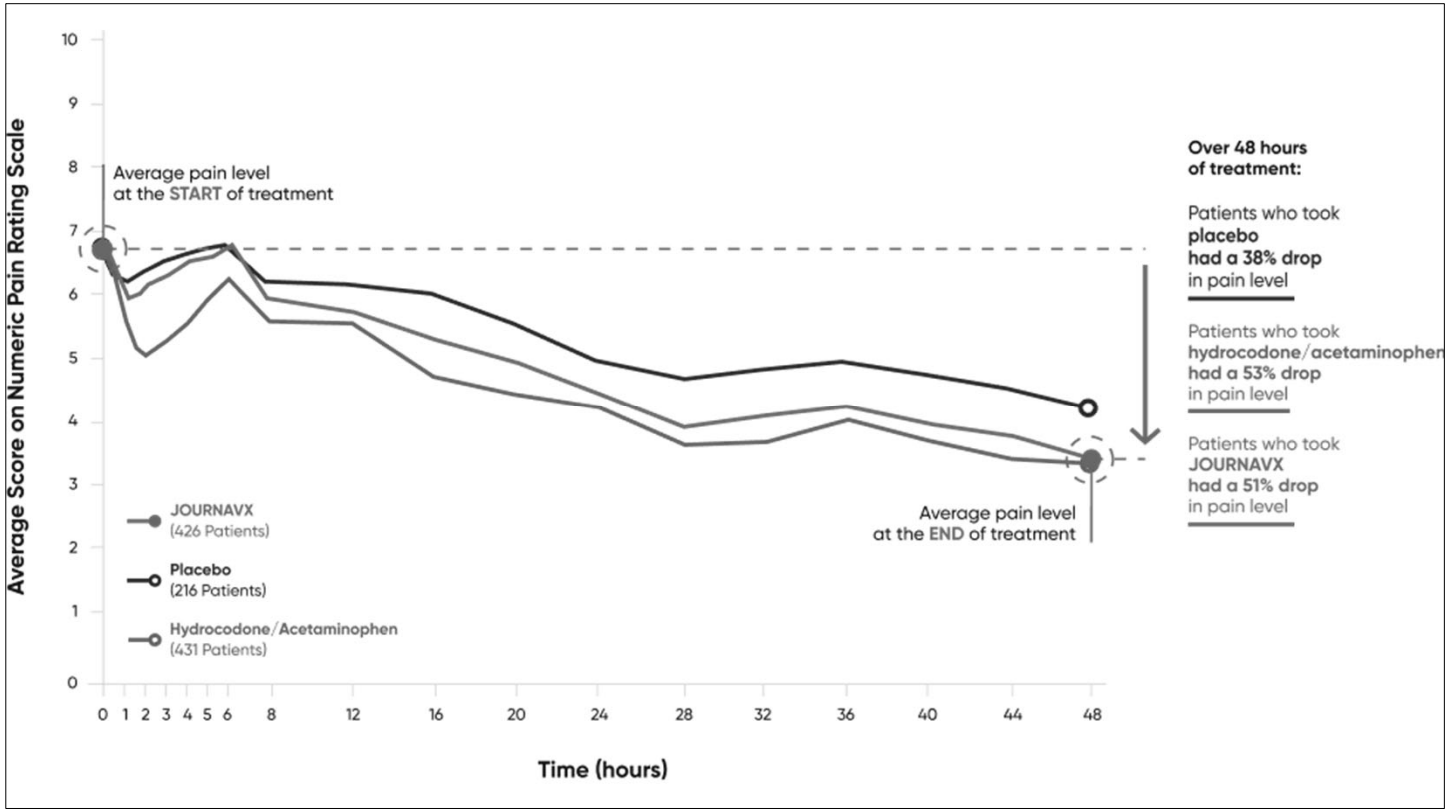
ADEs (<~2%)

- Itching
- Rash
- Muscle Spasms
- CPK Increase

https://www.journavx.com/#how-it-works

Journavx™

Bunion Removal Trial



https://www.journavx.com/#how-it-works

Summary

Patient CARE

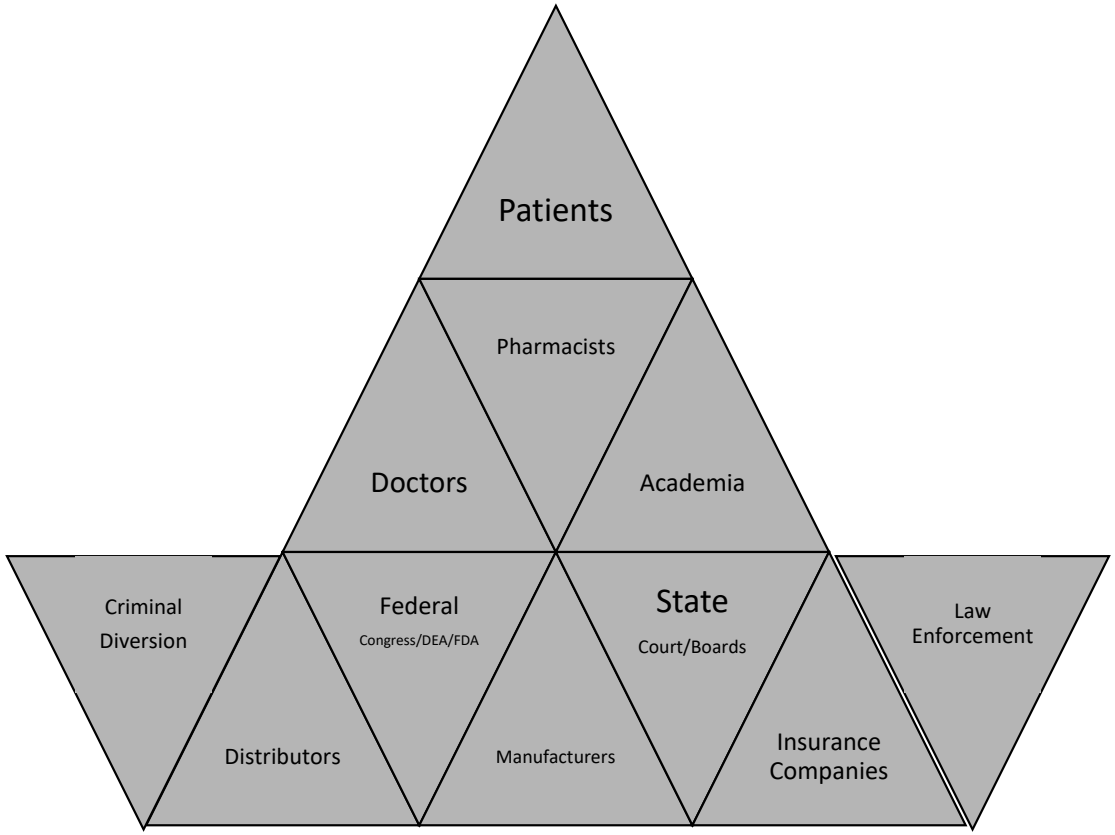
People Respect What You Inspect, Not What You Expect

An Ounce of Prevention, is Worth a Pound of Treatment

Never Stop Learning

Hippocratic Oath: Do No Harm

Everyone Keeps the Boat Afloat



Resources

- 2023 Beers Criteria Update
- 2022 CDC Opioid Guideline Update
- 2016 West Virginia Safe & Effective Management of Pain (SEMP) Guidelines (Updating in 2025)
- https://www.nationalopioidsettlement.com/

Key Takeaways

- MAT Act eliminated buprenorphine “X Waiver”
- Buprenorphine is a partial Mu agonist with a respiratory depression ceiling effect
- Controlled Substance Red Flags in the National Opioid Settlement include, but are not limited to:
  - CS-2 Refill Too Soon by > 3 Days
  - Doctor Shopping (CS > 4 Previous Prescribers of Separate Practices over 6 months)
  - Distance between patient’s residence and pharmacy > 50 miles
  - Distance between patient’s residence and prescriber > 100 miles
  - Prescriber has no office within 50 miles of pharmacy
  - Cash pay despite having prescription insurance coverage
  - CS-2 + Benzodiazepine + Carisoprodol
- Opioid overdose symptoms include gargled, slow, or absent breathing (death rattle); being unconscious & unarousable; blue lips & nails (hypoxia); hypotension; pinpoint pupils; slow/no heartbeat; & pale clammy skin
- Naloxone is a highly lipophilic, low oral bioavailability, short duration of action mu-opioid antagonist which is FDA approved for opioid agonist overdose (respiratory depression)
- Nalmefene is a mu-opioid antagonist that has great oral bioavailability, a longer half-life compared to naltrexone, 5-times the mu-opioid receptor affinity of naloxone, and is available as injectable, auto-injector, and intranasal products, with nasal administration mirroring that of naloxone prepackage nasal products (1st Dose being 1 spray in one nostril)

Key Takeaways

- The CDC recommends prescription opioid utilization considerations including utilization of immediate-release (IR) before extended-release (ER) opioids; a start low, go slow dosage strategy, and avoid increasing to high-risk dosage levels; reevaluating risks versus benefits for legacy or inherited patient utilizing high-risk prescription opioid dosages; when prescription opioid tapering is appropriate, only utilize a gradual tapering; when opioids are utilized in acute pain, only provide for expected duration; & to reevaluate chronic/subacute opioid utilization at least every 3 months (within 1 to 4 weeks initially)
- The CDC recommends universal pain management best practices including opioid risk screening, naloxone education, PDMP review, urine drug monitoring, avoidance of opioid and other sedatives combinations, and offering MOUD for patient with OUD
- Meperidine is the only opioid on the Beers Criteria List of Potentially Inappropriate Medications (PIMs) for all geriatric patients, yet for patients with a history of falls, all opioids are on the PIMs list
- The FDA-approved ADF opioid medications available on the U.S. market include the hydrocodone product of Hysingla® and the three oxycodone products of OxyContin®, Xtampza ER®, & RoxyBond®
- Suzetrigine is a Non-Opioid NaV1.8 Antagonist FDA Approval: Moderate-to-Severe (NPS 4 to 10) Acute Pain in Adults

Question 1

1. Which of the following described current buprenorphine regulations?

   a) There is no “X-Waiver” nor provider patient limits

   b) There is no “X-Waiver” but a provider patient limit of 100

   c) There is an “X-Waiver” with a provider patient limit of 100

   d) There is an “X-Waiver” with a provider patient limit of 250

Question 2

1. According to the National Opioid Settlement, which of the following are controlled substance red flags?
   a) 60 miles between patient's residence and pharmacy
   b) 60 miles between patient's residence and prescriber
   c) 75 miles between patient's residence and prescriber
   d) 30 miles between pharmacy and prescriber

Question 3

1. According to the National Opioid Settlement, which of the following are controlled substance red flags?
   a) Oxycodone, Diazepam, & Zolpidem
   b) Oxycodone, Diazepam, & Carisoprodol
   c) Hydrocodone, Morphine, & Alprazolam
   d) Hydrocodone, Tramadol, & Zolpidem

Question 4

1. Which of the following naloxone products is available as both prescription and over-the-counter?
   a) 5mg Injectable
   b) 10mg Auto Injector
   c) 4mg Nasal Spray
   d) 8mg Nasal Spray

Question 5

1. What is the dose of the nalmefene nasal spray products available with a prescription?
   a) 2.7mg
   b) 3.6mg
   c) 5.4mg
   d) 7.6mg

Question 6

1. According to the CDC Opioid Guideline update, what is a recommended gradual opioid taper (when appropriate)?
   a) 10% Monthly
   b) 10% Weekly
   c) 15% Monthly
   d) 15% Weekly

Question 7

1. According to the most recent AGS Beers Criteria, which of the following NSAIDs is recommended for an older adult without any comorbidities?
   a) Celecoxib
   b) Diclofenac
   c) Ibuprofen
   d) Naproxen

Question 8

1. Which of the following medications has a novel mechanism of action aiming to avoid the B-Arrestin portion of the Opioid Mu Receptor?
   a) Buprenorphine
   b) Levorphanol
   c) Oliceridine
   d) Pentazocine

Question 9

1. Which prescription opioid is is an FDA-Approved immediate-release ADF product?
   a) Hysingla®
   b) OxyContin®
   c) RoxyBond®
   d) Xtampza®

Question 10

1. What are appropriate patient counseling points for the non-opioid Journavx®?
   a) Take with a full glass of water to avoid hypernatremia
   b) Take 1 hour before or 2 hours after food
   c) Take 2 hours before or 1 hour after food
   d) Review for Significant interaction with 2C9 NSAIDs

CE Evaluation Access Code

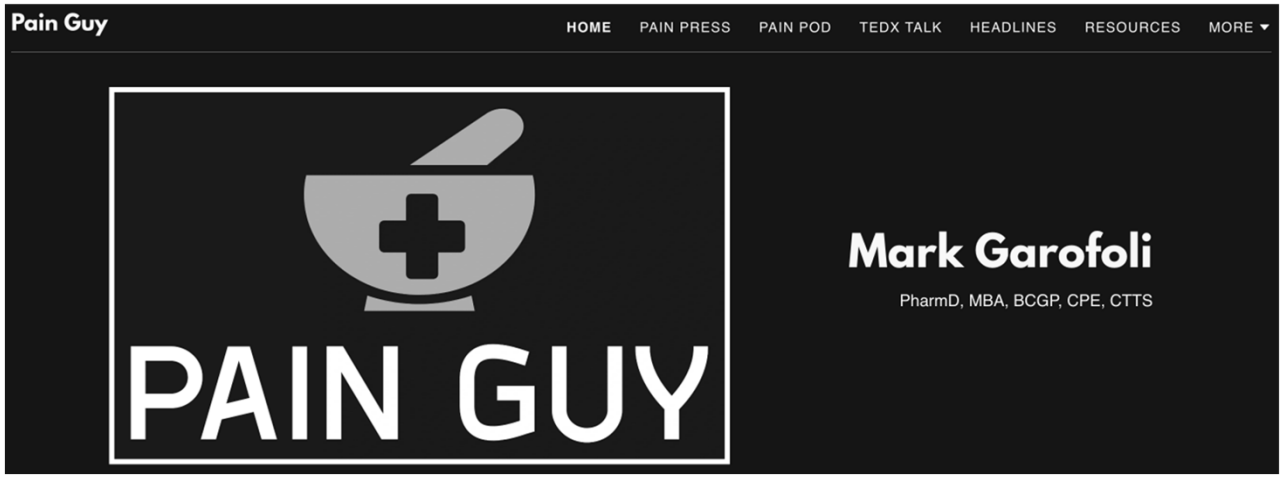
XXXXXX

Capital Letters, No Spaces

Please complete the online evaluation by **03/16/2025**

Note: CE credit will be reported to NABP CPE Monitor within 4-6 weeks

www.painguy.us



SCAN ME

Pain & Addiction Updates

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