2025 Early Career Scholar Program

An Intensive Multi-day Opioid REMS Initiative in Pain Management

CME OUTFITTERS

This activity is supported by an independent educational grant from the Opioid Analgesic REMS Program Companies.

Please see https://www.opioidanalgesicrems.com/Resources/Docs/List_of_RPC_Companies.pdf for a listing of REMS Program Companies. This activity is intended to be fully compliant with the Opioid Analgesic REMS education requirements issued by the U.S. Food and Drug Administration (FDA).

Assessing and Mitigating Risk for Opioid Misuse

Diagnosis and Management of OUD

This activity may include discussions of products or devices that are not currently labeled for use by the U.S. Food and Drug Administration (FDA).

The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational uses (any uses not approved by the FDA) of products or devices.

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Decatur, GA

Learning Objectives

- Incorporate the DSM-5 criteria in the identification and diagnosis of OUD in patients prescribed opioids for acute and chronic pain
- Utilize best practices in discussing potential OUD diagnosis and treatment with patients

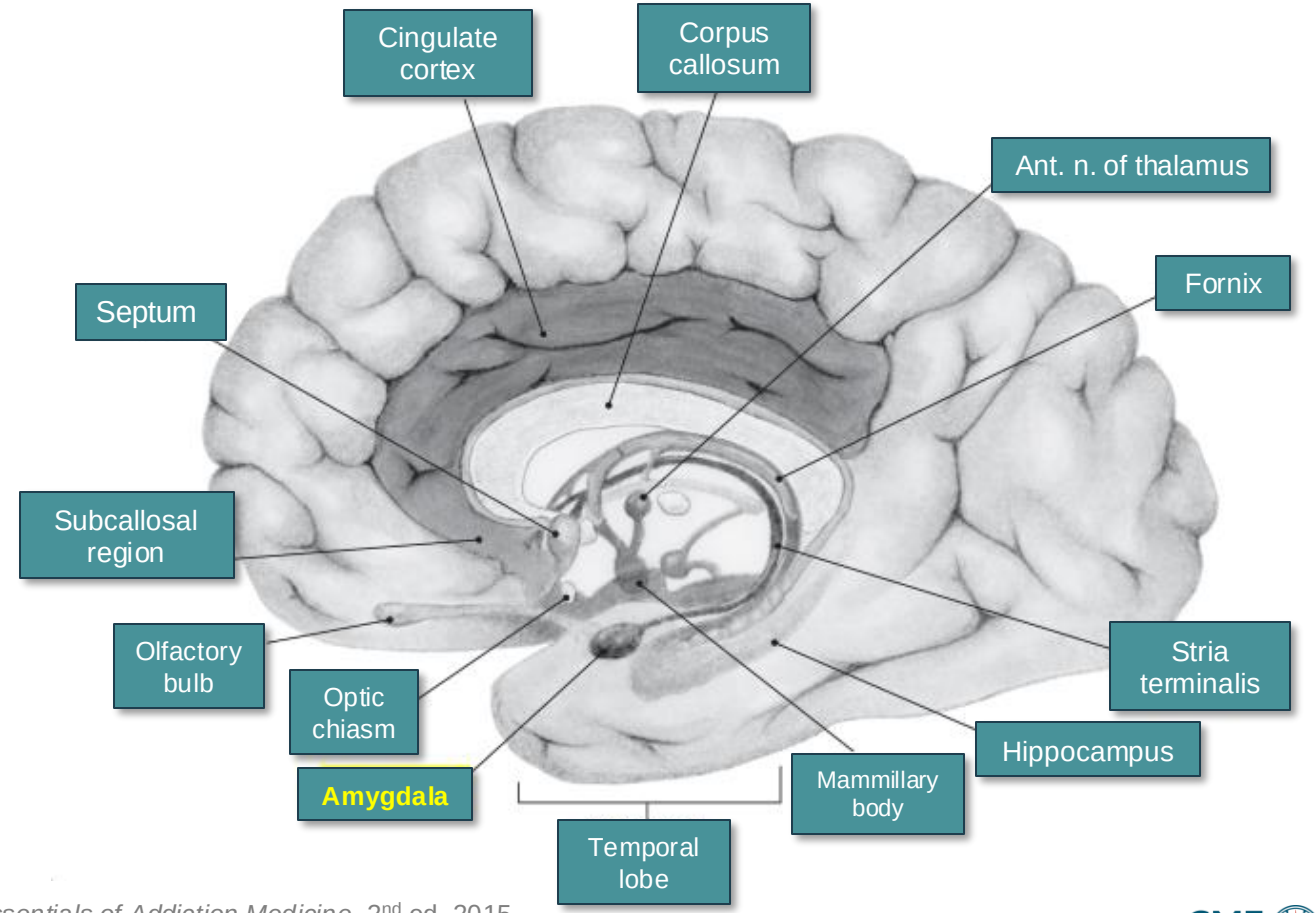
About Me

- Triple-boarded in anesthesiology, pain medicine, and addiction medicine
- I run a super-specialty multidisciplinary pain clinic for veterans on high-dose opioids or with comorbid substance use disorder (SUD) issues
- This lecture is a combination of evidence-based practice, common sense, and good old-fashioned hard knocks of clinical practice

So, How Exactly Does Addiction Happen?

Neurobiology I: Limbic System

- Emotion
- Behavior
- Memory
- Long-term motivation

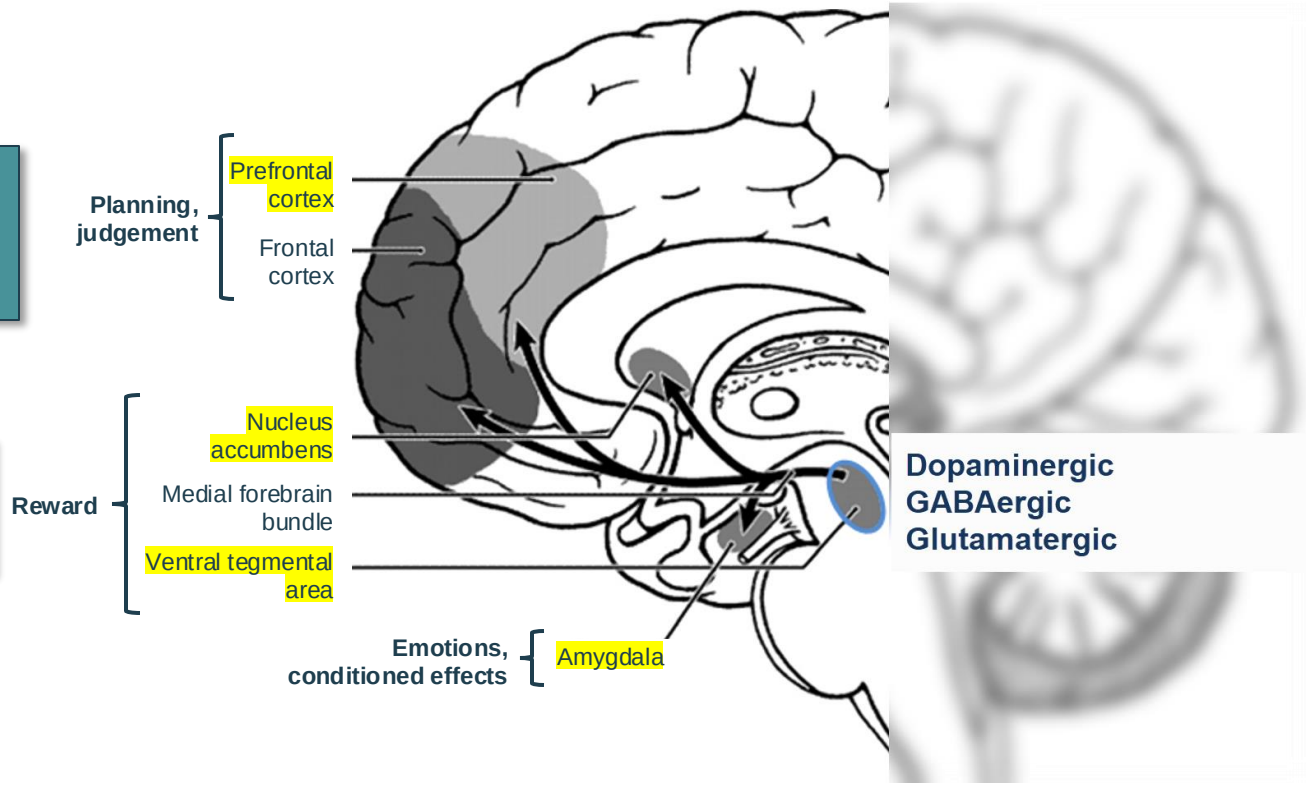


From Herron A, Brennan TK. *The ASAM Essentials of Addiction Medicine.* 2nd ed. 2015. https://clerkship.lwwhealthlibrary.com/book.aspx?bookid=1485&rotationId=0.

Neurobiology II: Mesolimbic System (AKA "Reward" Pathway)

Prefrontal Cortex
Higher order processing (e.g., planning/executive functioning)

Nucleus Accumbens
Reinforcement and reward for motor learning

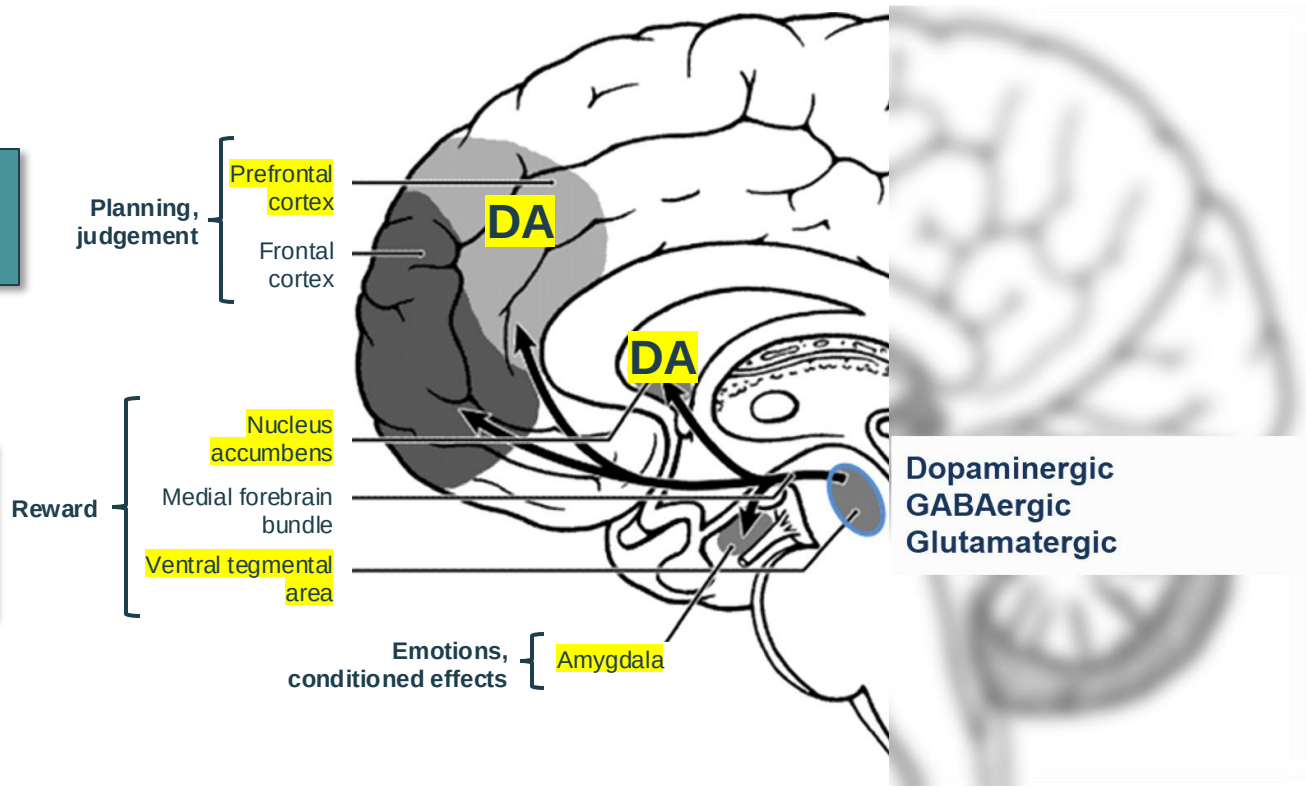


From Herron A, Brennan TK. *The ASAM Essentials of Addiction Medicine.* 2nd ed. 2015. https://clerkship.lwwhealthlibrary.com/book.aspx?bookid=1485&rotationId=0.

Neurobiology II: Mesolimbic System (AKA "Reward" Pathway)

Prefrontal Cortex
Dopamine affects executive functioning (e.g., substances)

Nucleus Accumbens
Dopamine regulates motivation, desire for stimuli, reinforces reward for motor learning

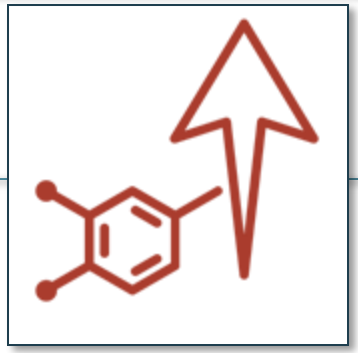


DA = dopamine

From Herron A, Brennan TK. *The ASAM Essentials of Addiction Medicine.* 2nd ed. 2015. https://clerkship.lwwhealthlibrary.com/book.aspx?bookid=1485&rotationId=0.

Dopamine: The “Pleasure” Neurotransmitter

Released when we eat, drink, sleep, have sex (i.e., life-sustaining activities)



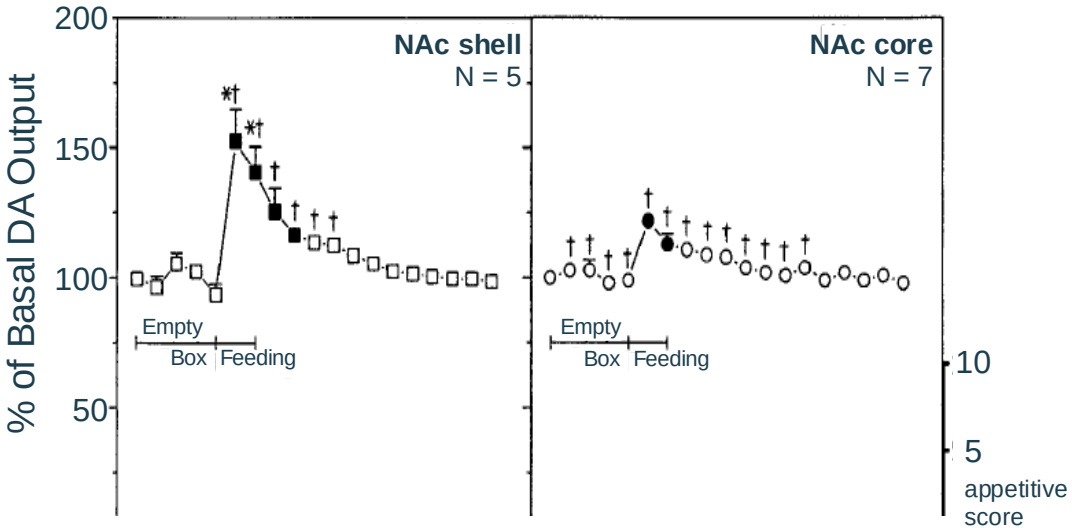
Drugs of abuse release dopamine in much higher concentrations

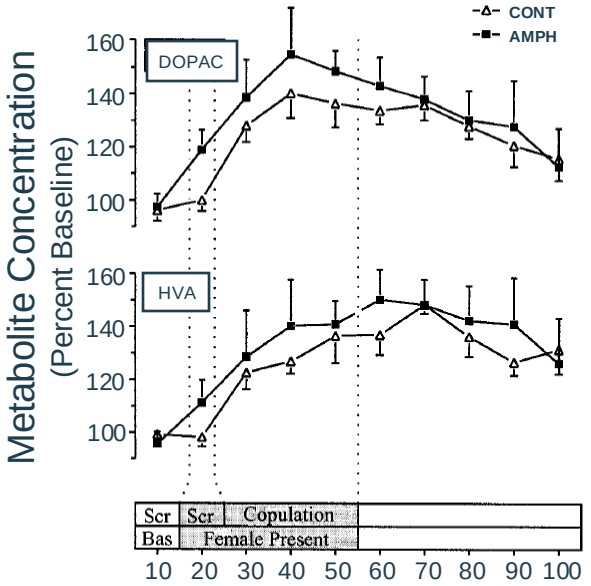
Regular life-sustaining activities provide less euphoria

This corrupts the reward pathway

Gardner EL. *Adv Psychosom Med*. 2011;30:22-60

Natural Rewards and Dopamine Release

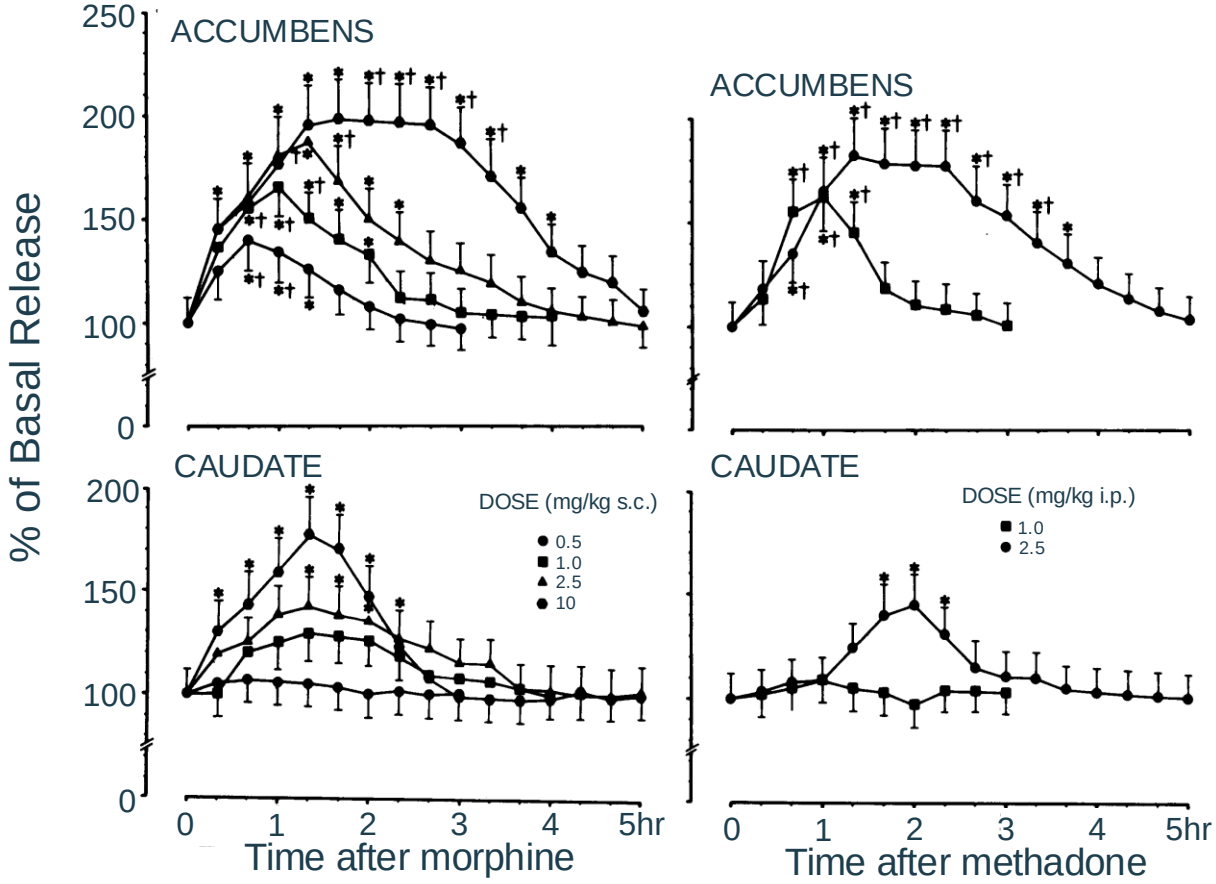




AMPH = d-amphetamine; CONT = saline control; DOPAC = dihyroxyphenylacetic acid; HVA = homovanillic acid; NAc = nucleus accumbens

Bassareo V, Di Chiara G. *Neuroscience*. 1999;89(3):637-41. Fiorino DF, Phillips AG. *J Neurosci*. 1999;19(1):456-63.

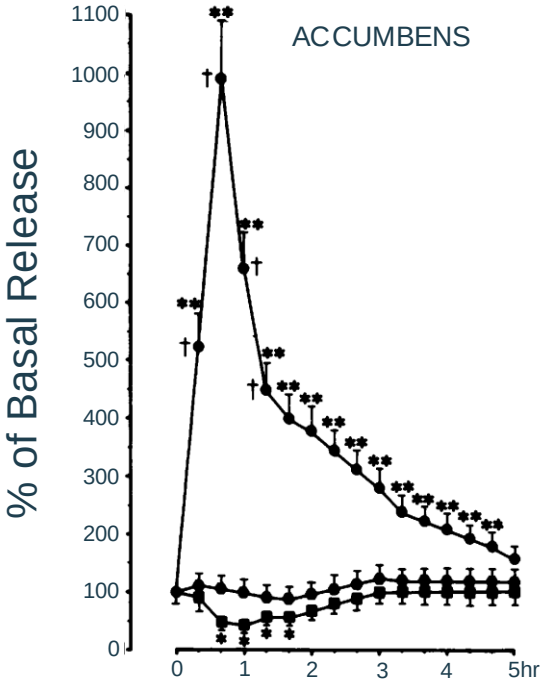
Opioids and Dopamine Release



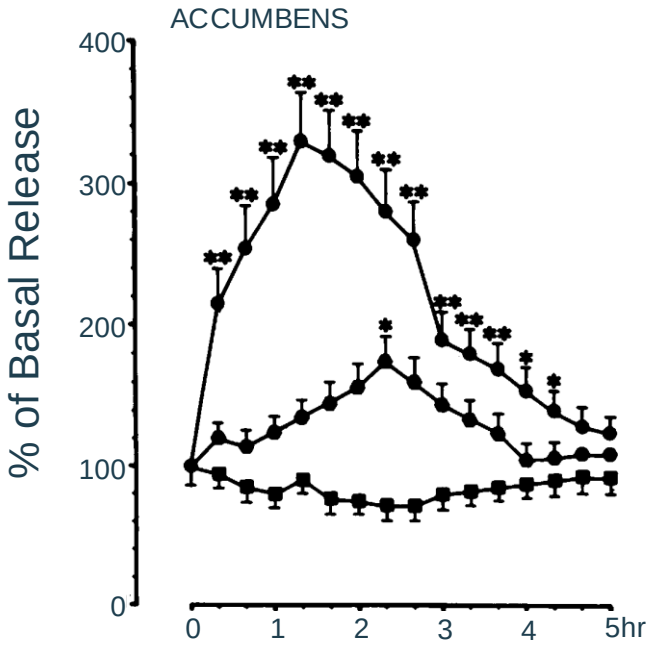
Di Chiara G, Imperato A. *Proc Natl Acad Sci USA*. 1988;85(14):5274-8.

Stimulants and Dopamine Release

Amphetamine



Cocaine



Di Chiara G, Imperato A. *Proc Natl Acad Sci USA*. 1988;85(14):5274-8.

What Causes Addiction in Some People but not Others?

Genetics

- 40%-60% of vulnerability to addiction

Environment

- Low socioeconomic status
- Poor parental support
- Within-group peer deviance
- Physical/psychological abuse
- Unmarried status
- Low level of education
- Unemployed
- Caucasian
- **Drug exposure**

Mental Illness

30% of people with psychiatric diagnoses abuse drugs

- 25% ETOH
- 40% nicotine
- 15% other drugs

ETOH = ethyl alcohol

DSM-V: Substance Use Disorder (2013)

Impaired control	- Craving or strong urge to use the substance - Desire or failed attempts to cut down or control substance use
Social problems	- Substance use causes failure to complete major tasks at work, school, or home - Social, work, or leisure activities given up/cut back because of substance use
Risky use	- Use in risky settings; continued use despite known problems
Pharmacologic effects	- Tolerance and withdrawal symptoms

Substances frequently associated with SUD: alcohol, cocaine, opioids, methamphetamine, benzodiazepines

SUD = substance use disorder

American Psychiatric Association. (2013). Substance use disorders. In *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. 2013. https://www.psychiatry.org/psychiatrists/practice/dsm.

Loss of Control		
1	Substance taken in larger amounts or for a longer time than intended	"I didn't mean to start using so much."
2	Persistent desire or unsuccessful effort to cut down or control use of a substance	**"I've tried to stop a few times before, but I start using this drug again every time."**
3	Great deal of time spent obtaining, using, or recovering from substance use	"Everything I do revolves around using this drug." In severe cases, most/all daily activities may revolve around substance use.
4	Craving (a strong desire or urge) to use opioids	**"I wanted to use so badly; I couldn't think of anything thing else."**
Social Problems		
5	Continued opioid use that causes failures to fulfill major obligations at work, school, or home	**"I keep having trouble at work/ have lost the trust of friends and family because of using this drug."**
6	Continued opioid use despite causing recurrent social or personal problems	**"I can't stop using, even though it's causing problems with my friends/family/boss/landlord."**
7	Important social, occupational, or recreational activities are reduced because of opioid use	"I've stopped seeing my friends and family and have given up my favorite hobby because of drugs."
Risky Use		
8	Recurrent opioid use in dangerous situations	"I keep doing things that I know are risky and dangerous to buy or use this drug."
9	Continued opioid use despite related physical or psychological problems	**"I know that using this drug causes me to feel badly/ messes with my mind, but I still use anyway."**
Pharmacological Problems		
10	**Tolerance:** Need to take higher doses of a drug to feel the same effects, or a reduced effect from the same amount	"I have to take more and more of the drug to feel the same high."
11	**Withdrawal:** Experience of pain or other uncomfortable symptoms in the absence of a drug	"When I stop using the drug for a while, I'm in a lot of pain."

SUD categorized based on number of criteria met, mild (2-3), moderate (4-5), severe (≥ 6 criteria)

American Psychiatric Association. (2013). Substance use disorders. In *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. 2013. https://www.psychiatry.org/psychiatrists/practice/dsm.

Behaviors Suggestive of Prescription Use Disorder
Deterioration in function (e.g., work, social)
Illegal activities (e.g., selling medication, forging prescriptions, buying from non-medical sources)
Altering the route of administration (e.g., snorting, injecting)
Multiple episodes of ‘lost’ or ‘stolen’ prescriptions
Resistance to change therapy despite negative outcomes
Refusal to comply with toxicology testing
Concurrent, active abuse of alcohol, illegal drugs
Use of multiple physicians or pharmacies to obtain the prescription
Behaviors Less Suggestive of Prescription Use Disorder
Medication hoarding
Requesting specific pain medications
Openly acquiring similar medications from other providers
Occasional unsanctioned dose escalation
Nonadherence to other recommendations for pain therapy

Miller SC, Frankowski D. *Current Psychiatry.* 2012;11(8):14-22.

How Do You Treat Addiction?

Nonpharmacologic Therapies for Substance Use Disorders

Herron AJ, Brennan TK. *The ASAM Essentials of Addiction Medicine.* 2nd ed. 2015. https://clerkship.lwwhealthlibrary.com/book.aspx?bookid=1485&rotationId=0.

Pharmacologic Therapies for Substance Use Disorders

Alcohol

- Disulfiram
- Acamprosate
- Naltrexone or nalmefene*
- Topiramate* or gabapentin*

Opioids

- Buprenorphine
- Naltrexone
- Buprenorphine/naltrexone
- Nalmefene
- Methadone

Benzodiazepines

- Carbamazepine* for withdrawal
- Flumazenil for oversedation or overdose

Stimulants

- No FDA-approved agents
- Tricyclic antidepressants* may help

Tobacco

- Nicotine replacement therapy
- Varenicline
- Bupropion
- Nortriptyline*

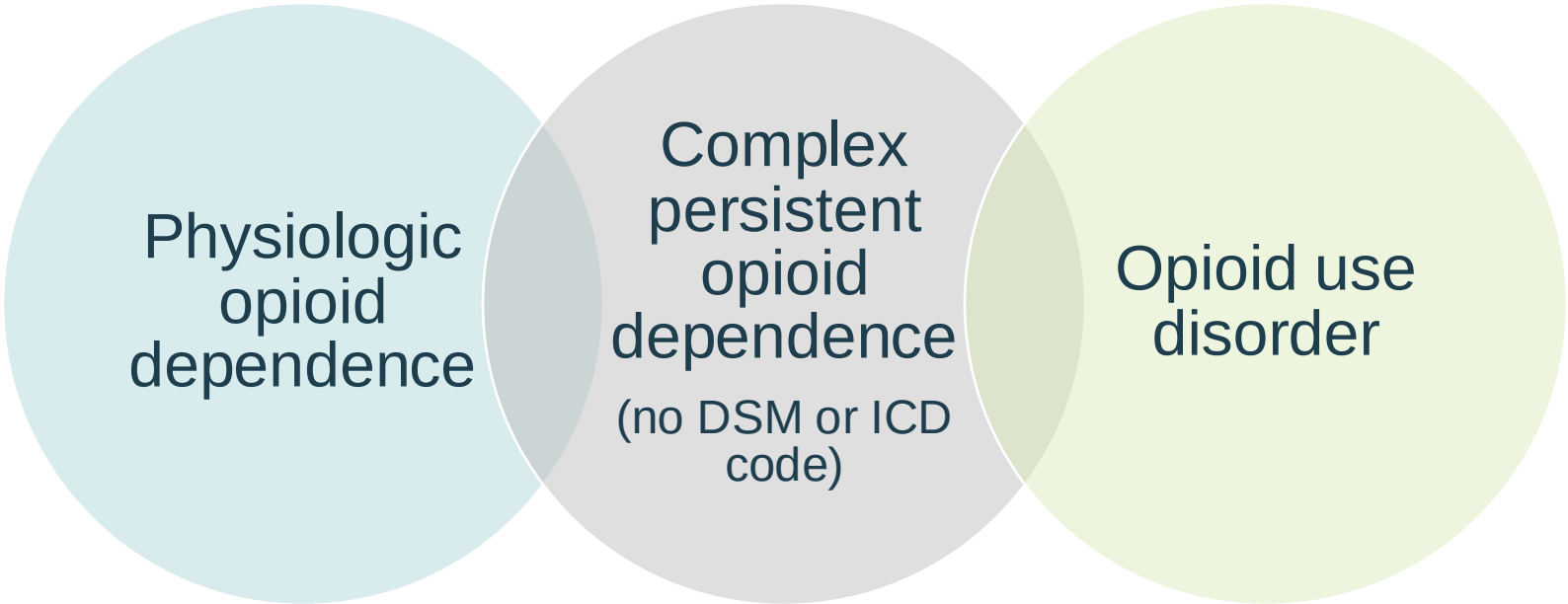
Cannabinoids

- No FDA-approved agents

*This medication is not FDA approved for the treatment of the substance it is listed under, but may be used off-label

Herron AJ, Brennan TK. *The ASAM Essentials of Addiction Medicine.* 2nd ed. 2015. https://clerkship.lwwhealthlibrary.com/book.aspx?bookid=1485&rotationId=0.

Complex Persistent Opioid Dependence



"Although OUD commonly develops through the hedonic use of opioids, illicitly and/or via prescriptive pain treatment, CPOD distinctly starts and persists within a therapeutic context of pain treatment where LTOT is initiated and continued as a therapeutic strategy through shared decisions by the patient/provider dyad."

CPOD = complex persistent opioid dependence; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Diseases; LTOT = long-term opioid therapy

Manhapra AJ, et al. *J Gen Intern Med.* 2020;35(Suppl 3):964-971.

Complex Persistent Opioid Dependence vs. Opioid Use Disorder: Characteristics

Characteristics	CPOD	OUD
Clinical presentation	Poor pain control Declining physical function Medical instability Aberrant behaviors	Opioid use related to social, work, and behavioral problems
Motivation to take opioids	Pain Suffering Inability to function	Dysphoria Anhedonia Need for euphoria Pain (occasionally)
Opioid tolerance	Not applicable Increased dose needed for pain relief and functional improvement	Applicable Increased dose needed to relieve dysphoria and anhedonia
Opioid craving and compulsivity	Not present	Prominent
Acute withdrawal symptoms with cessation	Yes	Yes
Protracted withdrawal syndrome after dose reduction or cessation	Yes, difficulty tolerating tapers, symptoms dominated by worsening pain and severe functional decline	Yes, symptoms may include anxiety, dysphoria, irritability, sleep disturbances

Manhapra AJ, et al. *J Gen Intern Med.* 2020;35(Suppl 3):964-971.

Complex Persistent Opioid Dependence vs Opioid Use Disorder: Treatment

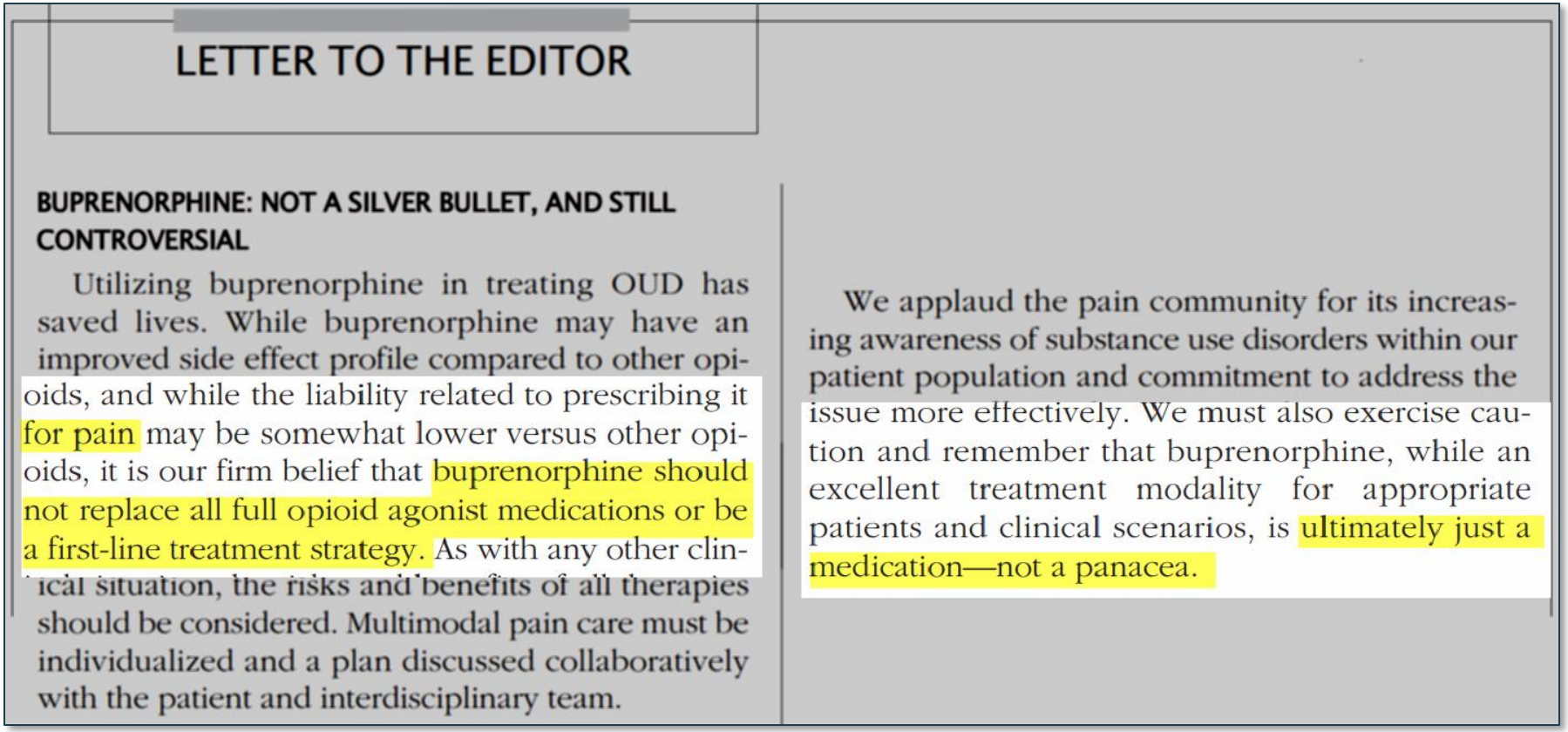
Treatment	CPOD	OUD
Buprenorphine* transdermal patch, buccal film, or tablet Some planned withdrawal initiation protocols can be a barrier	Preliminarily effective Some patients benefit	Effective
Methadone	May be effective Minimal experience	Effective
Naltrexone IM depot injection **Naltrexone oral** Requires 7–10-day opioid free interval	Unknown	Effective Initiation and adherence are concerns Oral has a higher dropout rate
Combination medications (e.g., buprenorphine/naltrexone, buprenorphine/naloxone)	Unknown	Effective, but higher dropout rates
Effective behavioral treatment foci	Pain Functional recovery	Behaviors related to opioid use Relapse prevention Recovery resilience

Pharmacologic management of CPOD is under-researched, most studies focus on OUD

*The DATA waiver (X-waiver) restrictions for prescribing buprenorphine were removed in 2023, any physician with a DEA license that includes schedule 3 authority can prescribe buprenorphine for OUD. IM = intramuscular

Manhapra A, et al. *J Gen Intern Med*. 2020;35(Suppl 3):964-971. Manhapra A, et al. *Br J Clin Pharmacol*. 2024;90(12):2962-2976. Koehl JL, et al. *Am J Health Syst Pharm*. 2019 18;76(15):1097-1103. Miller JC. *Drugs R D*. 2023;23(4):339-362. Substance Abuse and Mental Health Services Administration [SAMHSA]. 2024. https://www.samhsa.gov/substance-use/treatment/statutes-regulations-guidelines/matact#:~:text=Section%201262%20of%20the%20Consolidated,opioid%20use%20disorder%20(OUD).

Buprenorphine Still Controversial



LETTER TO THE EDITOR

BUPRENORPHINE: NOT A SILVER BULLET, AND STILL CONTROVERSIAL

Utilizing buprenorphine in treating OUD has saved lives. While buprenorphine may have an improved side effect profile compared to other opioids, and while the liability related to prescribing it for pain may be somewhat lower versus other opioids, it is our firm belief that buprenorphine should not replace all full opioid agonist medications or be a first-line treatment strategy. As with any other clinical situation, the risks and benefits of all therapies should be considered. Multimodal pain care must be individualized and a plan discussed collaboratively with the patient and interdisciplinary team.

We applaud the pain community for its increasing awareness of substance use disorders within our patient population and commitment to address the issue more effectively. We must also exercise caution and remember that buprenorphine, while an excellent treatment modality for appropriate patients and clinical scenarios, is ultimately just a medication—not a panacea.

Potru S, et al. *J Opioid Manag.* 2021;17(7):9-10.

Audience Poll

Have you used an opioid risk assessment tool successfully in your practice?

A. Yes, I have one that I like, and it works well
B. Yes, but I would like to find one that is easier/more reliable
C. No, I've tried but haven't had much success
D. No, I have never used an opioid risk assessment tool

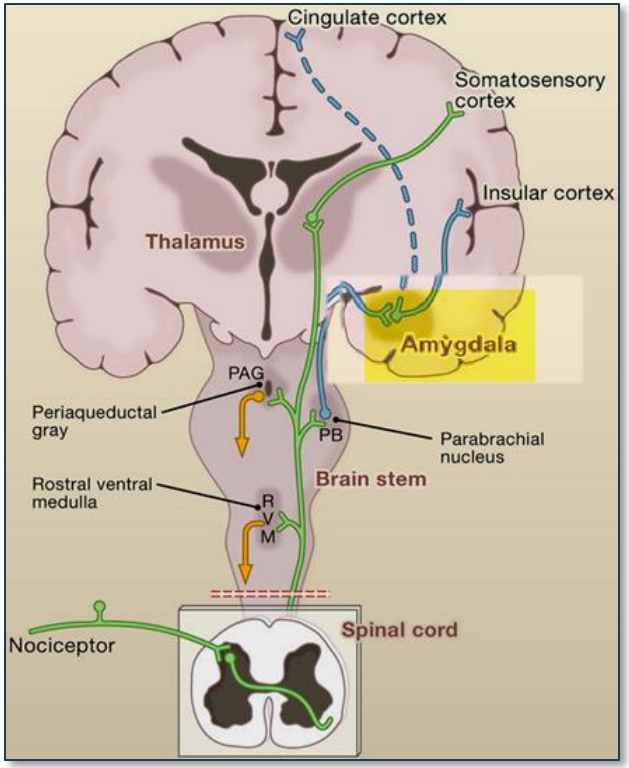
Opioid Risk Tool

Mark each box that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Prescription drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Prescription drugs	5	5
Age between 16-45 years	1	1
History of preadolescent sexual abuse	3	0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	2	2
Depression	1	1
Scoring totals		

ADD = attention deficit disorder; OCD = obsessive compulsive disorder

Webster LR, et al. *Pain Med*. 2005;6(6):432-42.

Simplified Pain Pathway



Chen J, et al. Pain. In: *Neuroscience in the 21st Century.* 3rd ed. 2022: pp.1375–1433. https://link.springer.com/referenceworkentry/10.1007/978-3-030-88832-9_32.

Mental Health, Pain, and Addiction

"My clinical experience is that, often, the highest opioid doses end up going to those with history of physical or emotional trauma (stated or unstated)."

Use the Opioid Risk Tool!!!

Mark each box that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Prescription drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Prescription drugs	5	5
Age between 16-45 years	1	1
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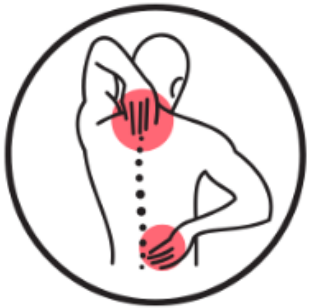
Psychological disease		
ADD, OCD, bipolar, schizophrenia	2	2
Depression	1	1
Scoring totals		

Webster LR, et al. *Pain Med*. 2005;6(6):432-42.

Mental Health, Pain, and Addiction

16% of Americans have mental health disorders

- These Americans receive ≥ 50% of opioids prescribed



Are we treating physical pain, emotional suffering, or both?

- Manifestation of trauma as centralized pain syndromes
- Examples: fibromyalgia, IBS, migraine

Possible mechanisms

- Amygdala?
- Glial cell activation?

IBS = irritable bowel syndrome

Davis MA, et al. *J Am Board Fam Med*. 2017;30(4):407-417. Spiegel DR, et al. *Health* Serv Res *Manag Epidemiol*. 2015;2:2333392814567920.

How Do I Approach the Patient with SUD and Chronic Pain Clinically?

Ask Yourself the Big Question

Do you want this patient in your clinic or not?

Everything starts from that!

Clinical Evaluation

If long-term sobriety:

- Will admit to issues in the past: “I don’t want medications”
- Will repeatedly ask if certain treatments are habit-forming
- Will ask if treatments are likely to affect their mood

If undiagnosed:

- None of the above
- Will perseverate on getting psychoactive medications

If short-term sobriety: Who knows?

- Remember that there are permanent brain changes that take years to change in some instances

Clinical Evaluation

Disguise your SUD evaluation as a pain evaluation

Start by asking how long ago they started using pain medications

Ask in detail how they use their medications

Do they run out early often?
Do they have withdrawal?

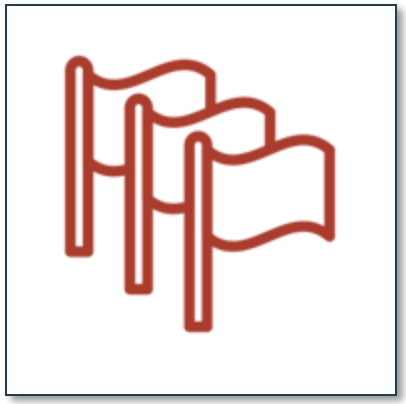
Some OUD patients will complain of compulsions to be “out of pain”

Clinical Evaluation

Generate genuine empathy	Imagine a close family member sitting in the exam room with you, dealing with both pain and addiction
Frame everything in the context of safety	"I don't want anything bad to happen to you"
Chronic pain patients with substance use disorders will have pain flares/exacerbations	• Treat them appropriately • Uncontrolled pain is a factor for relapse!! • SUD patients resemble opioid-TOLERANT → they need MORE, not less

Clinical Evaluation

- With an unexpected test result, it's time to (gently) ask more questions
- If you're unsatisfied with the answer or if it's inconsistent with objective findings (PDMP, UDS, random pill count, etc.), it's time to ask more questions
- When someone says, "the medication relaxes me" or "I take it and then I can finally go to sleep", it's time to ask more questions
- You may discover SUD, CPOD, or some underlying mental health issue
- If so, it's time to refer to a specialist or start buprenorphine if OUD/CPOD



PDMP = prescription drug monitoring program; UDS = urine drug screen

Prescribing Chronic Opioids to Patients With SUD in Recovery

- Try to wait until at least one year of sobriety if possible
  - Early remission: 90-364 days
  - Sustained remission: ≥ 365 days
- Discuss the opioid agreement at length
- Consider short-term prescriptions to start (e.g., every 1 to 2 weeks)
- Document function carefully
  - "Mr. Jones can walk XX feet without pain without his medications and can walk YY feet while using his pain medications."
- Urine drug screens, PDMP checks, random pill counts as usual

American Psychiatric Association [APA]. Substance use disorders. In Diagnostic and Statistical Manual of Mental Disorders. 5th ed. 2013. https://www.psychiatry.org/psychiatrists/practice/dsm FDA. Opioid Patient Prescriber Agreement https://www.fda.gov/files/drugs/published/Opioid-Patient-Prescriber-Agreement-(PPA).pdf. Dowell D, et al. MMWR Recomm Rep. 2016;65(1):1-49. Califf RM, et al. *N Engl J Med*. 2016;374(15):1480-1485. FDA. *FDA's Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain*. 2023. https://www.fda.gov/media/173774/download?attachment.

Prescribing Chronic Opioids to Patients With SUD in Recovery

- Abuse-deterrent formulations (ADFs) may be considered
- Effective at decreasing abuse, misuse, and diversion
- Cannot decrease risk of taking more oral doses than prescribed
- Access/cost may be a barrier to use

Generic ADF*	Abuse-Deterrent Route of Administration	
Oxycodone hydrochloride ER	IV injection: viscous in liquid and hard to inject	Intranasal: tablet hard to crush and inhale
Oxycodone hydrochloride IR		Intranasal: chemical compound slows and decreases absorption
Oxycodone ER		Intranasal/oral: ER properties are maintained when crushed, chewed, or inhaled
Hydrocodone bitartrate ER		Intranasal: tablet hard to crush and inhale

*There are 4 total approved ADFs available, none of these products are currently available as a generic.
The FDA list of products is available at: https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/abuse-deterrent-opioid-analgesics.
ER = extended release; IR = instant release
Webster L, Gudin J. *J Pain Res*. 2024;17:1989-2000. U.S. Food & Drug Administration [FDA]. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/abuse-deterrent-opioid-analgesics.

CDC Guideline Recommendations for OUD in Pregnancy OUD

- Medications for OUD are preferred over withdrawal management (i.e., discontinuation of opioids through either short- or medium-term tapering)
- Clinicians should access appropriate expertise if considering tapering opioids during pregnancy because of possible risks to the pregnant patient and the fetus if the patient goes into withdrawal.
- Medications for OUD (buprenorphine or methadone) are the recommended therapy and should be offered as early as possible in pregnancy to prevent harms to both the patient and the fetus.

Dowell D, et al. *MMWR Recomm Rep*. 2016;65(1):1-49. Dowell D, et al. *MMWR Recomm Rep.* 2022;71(3):1-95.

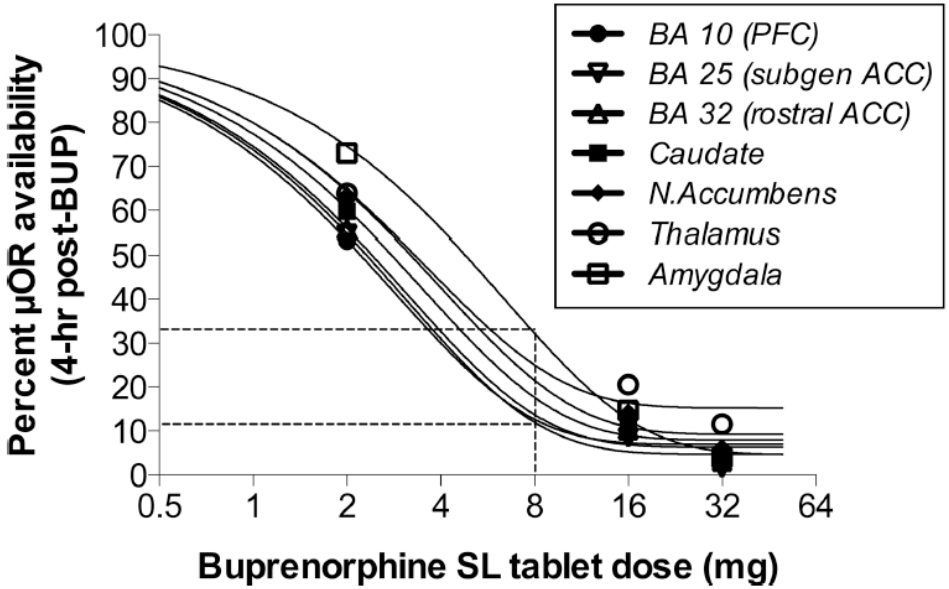
If You Don’t Want to Prescribe Opioids in SUD

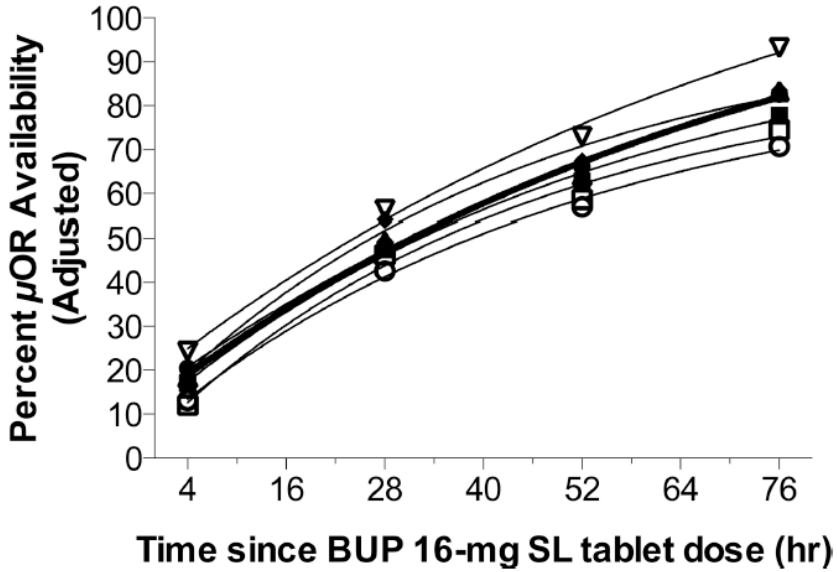
- Think about a buprenorphine patch to bridge these patients if you don’t want to give Schedule II medications
  - Virtually impossible to overdose, except with significant amounts of concomitant CNS depressants
  - May be somewhat protective, although receptor occupancy likely too low
- Assume fentanyl products are in all pills from non-medical sources
- This is a big problem with stimulants as patients may be opioid naïve

CNS = central nervous system

National Institute on Drug Abuse [NIH]. 2023. https://nida.nih.gov/news-events/news-releases/2023/01/overdose-deaths-involving-buprenorphine-did-not-proportionally-increase-with-new-flexibilities-in-prescribing#:~:text=During%20this%20study%20period%2C%20there,recorded%20in%20the%20SUDORS%20dataset.

Buprenorphine Receptor Availability





ACC = anterior cingulate cortex; BUP = buprenorphine; PFC = prefrontal cortex

Greenwald MK, et al. *Drug Alcohol Depend*. 2014;144:1–11.

Buprenorphine Receptor Availability

Estimated Percentages of Mu-Opioid Receptor Availability at Different Times Following Daily Sublingual Tablet Buprenorphine (BUP) Maintenance Doses in Heroin Dependent Volunteers

Study Details	1mg	2mg	4mg	8mg	12mg	16mg	24mg	32mg
Comer et al. (2005) ¶; n =7 heroin vs. n = 8 controls; maintenance for 14 days at each dose, with tests at 15-hr post-BUP/NAL		21 – 31%		11 – 22%				6 – 12%
Greenwald et al. (2003) §; n = 5; maintenance for 12 days at each dose, with tests at 4-hr post-BUP	(71 – 85%)	53 – 72%	(36 – 55%)	(20 – 35%)	(13 – 24%)	9 – 20%	(4 – 15%)	2 – 12%
Greenwald et al. (2007) £; n = 10; maintenance for 14 days minimum, with tests at: 4-hr post-BUP 28-hr post-BUP 52-hr post-BUP 76-hr post-BUP						27 – 31% 54 – 61% 65 – 75% 77 – 94%		

¶Comer et al. reported the mean proportion of receptors (assumed to be μORs) remaining for each of four pharmacodynamic measures (intranasal heroin self-administration, and ratings of "good drug effect", "high", and "potent" following heroin). Ranges of values reflect estimated variation in mean percent receptor availability during buprenorphine/naloxone sublingual tablet dosing, relative to a different heroin-detoxified comparison group.

§Ranges of values reflect variation in mean percent μOR availability across 7 brain regions of interest with high concentrations of μORs listed in Figure 1) during buprenorphine-mono sublingual tablet dosing, relative to the within-subject placebo control condition. Italicized μOR availability data from doses that were not directly studied reflect estimates from the non-linear curves in Figure 1.

£Ranges of values reflect variation in mean percent μOR availability across 7 brain regions of interest in Greenwald et al. (2007), relative to the placebo condition in Greenwald et al. (2003), as a function of buprenorphine-mono sublingual tablet discontinuation time. Although the 4-hr discontinuation time in this study is identical to the Greenwald et al. study (2003) study, the percentage μOR availability differs because this study used a between-subject placebo control group whereas the earlier study used a within-subject placebo control condition. This discrepancy thus reflects differences between the two subject samples and should lead to cautious interpretation of the absolute levels of μOR availability (but not its rate of decline).

NAL = naloxone

Greenwald MK, et al. *Drug Alcohol Depend*. 2014;144:1–11.

How to Have the Conversation With Patients With SUD

How to Talk to Patients With SUD

Avoid judgment and frame everything in the context of safety

If you want to keep the patient

- "I really want to help treat your pain, but I also need some help ensuring that what I'm going to do is safe for you."

If you'd prefer not to keep the patient

- "Honestly, it's a little dangerous for me to care for you with the tools I have at my disposal. It's time for us to find you some real help."
- "When we've resolved/improved the other things going on in your life, we'll have you come back."
- **Do not discharge, always have them "follow-up prn"**
- Remember that choosing not to prescribe opioids is not the same as discharge!!

Let’s Talk a Little Bit More About Buprenorphine

Buprenorphine

Formulation (not all-inclusive)	Indication	Strengths	Frequency
Sublingual tablet*	Opioid dependence	2 mg; 8 mg	Once daily
Sublingual tablet plus naloxone (some doses available in generic)	Opioid dependence	2 mg/0.5 mg*; 8 mg/2 mg* 0.7 mg/0.18 mg; 1.4 mg/0.36mg 2.9 mg/0.71 mg; 5.7 mg/1.4 mg; 8.6 mg/2.1 mg; 11.4 mg/2.9 mg	Once daily
Sublingual film plus naloxone*	Opioid dependence	2 mg/0.5 mg; 4 mg/1 mg; 8 mg/2 mg; 12 mg/3 mg	Once daily
Buccal film	Chronic pain	75 mcg; 150 mcg; 300 mcg; 450 mcg; 600 mcg; 750 mcg; 900 mcg	Every 12 hours
Intravenous*	Acute pain	0.3 mg/mL	Every 6 hours as needed
Subcutaneous extended -release subcutaneous injection	Moderate-to-severe opioid use disorder	8 mg/0.16 mL; 16 mg/0.32 mL; 24 mg/0.48 mL; 32 mg/0.64 mL	Weekly
Subcutaneous extended -release subcutaneous injection	Moderate-to-severe opioid use disorder	64 mg/0.18 mL; 96 mg/0.27 mL; 100 mg/0.5 mL;128 mg/0.36 mL; 300 mg/1.5 mL	Monthly
Transdermal patch*	Chronic pain	5 mcg/hr; 7.5 mcg/hr; 10 mcg/hr; 15 mcg/hr; 20 mcg/hr	Weekly

*Available in generic form

Warner NS, et al. *Mayo Clin Proc*. 2020;95(6):1253-1267.
Buprenorphine [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022410s033,020732s019,020733s023lbl.pdf.

Conversion to Buprenorphine

For patients taking doses below the following amounts (~≤ 90 MME):

- Fentanyl transdermal: ≤ 25 µg/h
- Oxycodone: ≤ 60 mg/d
- Hydrocodone or morphine: ≤ 90 mg/d
- Hydromorphone: ≤ 16 mg/d
- Oxymorphone: ≤ 45 mg/d
- Tapentadol: Any dose

1. Discontinue after the last nighttime dose.

2. Consider initiating an adrenergic α_2 agonist (e.g., clonidine, lofexidine) or an immediate-release opioid (e.g., current opioid) to reduce the risk of withdrawal.

3. Initiate buprenorphine the following morning per the prescribing information, as either 10-µg/h transdermal buprenorphine or 150-µg buccal buprenorphine twice daily. Titrate buprenorphine as needed for pain per recommendations in the prescribing information.

In patients transitioning to buprenorphine from higher doses of opioids (~> 90 MME):

- Fentanyl transdermal: > 25 µg/h
- Oxycodone: > 60 mg/d
- Hydrocodone or morphine: > 90 mg/d
- Hydromorphone: > 16 mg/d
- Oxymorphone: > 45 mg/d

1. Discontinue after the last nighttime dose.

2. Consider initiating an adrenergic α2 agonist (e.g., clonidine, lofexidine) or an immediate-release opioid (e.g., current opioid) to reduce the risk of withdrawal.

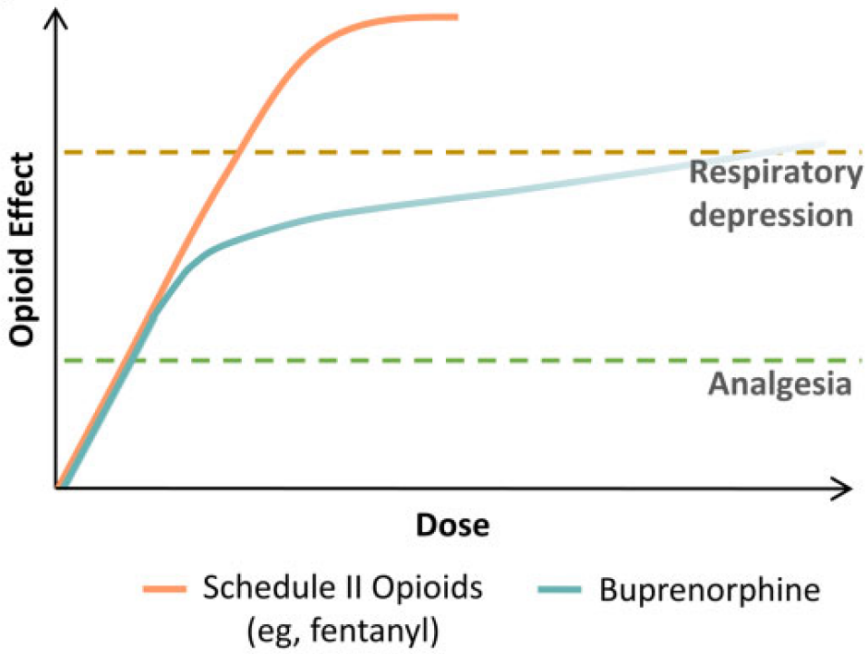
3. Initiate buprenorphine the following morning as either 20-µg/h transdermal buprenorphine once daily or 300-µg buccal buprenorphine twice daily and follow the recommendations in the prescribing information for upward titration as needed. Note that 20 µg/h is the highest dose of transdermal buprenorphine currently available in the United States. If these doses are ineffective, consider higher doses of the buccal formulation on the basis of risk/benefit analysis.

Webster L, et al. *Pain Med*. 2020;21(4):714-723.

Is Buprenorphine Effective for Chronic Pain?

Analgesic Effects of Buprenorphine

- Buprenorphine μ-receptor binding
  - Reaches analgesic threshold equal to Schedule II opioids
  - Exhibits a ceiling effect for respiratory depression



Webster L, et al. *Pain Med*. 2020;21(4):714-723.

Analgesic Effects of Buprenorphine

- The classification as a μ-receptor partial agonist may be misleading when predicting analgesic effect
  - IV buprenorphine has equally effective/more effective analgesia than IV morphine in surgical models
  - Buccal buprenorphine is effective in opioid-naïve and opioid-experienced patients
  - Buprenorphine is effective for chronic low back pain (including neuropathic pain) and chronic pain
  - Chronic pain (compared with morphine sulfate, oxycodone, and placebo)

Webster L, et al. *Pain Med.* 2020;21(4):714-723. Rauck RL, et al. *Postgrad Med.* 2016 Jan;128(1):1-11. Gimbel J, et al. *Pain.* 2016;157(11):2517-2526. Aiyer R, et al. *Anesth Analg.* 2018;127(2):529-538.

Data for the Efficacy of Buprenorphine in Chronic Noncancer Pain

- Meta-analysis of 4 clinical trials comparing buprenorphine and placebo
- Transdermal and buccal buprenorphine had a statistically significant, but small decrease in chronic noncancer pain
- Patients had better sleep quality and higher ratings for effectiveness
- Overall, still a paucity of data

Wong SSC, et al. Anesth Analg. 2023;137(1):59-71.

Conversion of Chronic Pain Patients to Sublingual Buprenorphine

- Patients were taking morphine, oxycodone, or fentanyl and then switched to sublingual buprenorphine
- Mean pain scores decreased 2.3 points
- Patients taking 100 to 199 MME/day had the largest reduction in pain at 2.7 points
- Patients taking > 400 MME/day had the least reduction in pain at 1.1 points
- No significant change in QoL

Daitch J,et al. *Pain Physician.* 2012;15(3 Suppl):ES59-66.

Take Home Points

Addiction is a terrible neurobiological disease and not a “moral failing” – be compassionate

Always frame every discussion in the context of safety

Remember that uncontrolled pain is a risk for relapse

Think about prescribing buprenorphine for pain or OUD yourself. Very safe and often very effective for analgesia.

Should we be using buprenorphine over full opioid agonists?

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Implement a multimodal pain management strategy for patients with SUD and chronic pain, including non-opioid medications, physical therapy, and cognitive behavioral therapy
- Incorporate the Opioid Risk Tool (ORT) into the standard assessment for all patients considered for opioid therapy
- Successfully initiate buprenorphine treatment for appropriate patients

If You are Interested in Difficult Conversations…

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