ADDICTION MEDICINE

GOVERNOR'S INSTITUTE

The Art of the Start: Strategies for Successful Buprenorphine Induction

Olivia Caron, PharmD, CPP, BCACP

PGY2 Pharmacy Residency Program Director, MAHEC Department of Pharmacy

Assistant Professor of Clinical Education, UNC-Chapel Hill Eshelman School of Pharmacy

Clinical Assistant Professor, UNC School of Medicine

4/11/2026 Asheville, NC

Disclosures

- No conflicts of interest

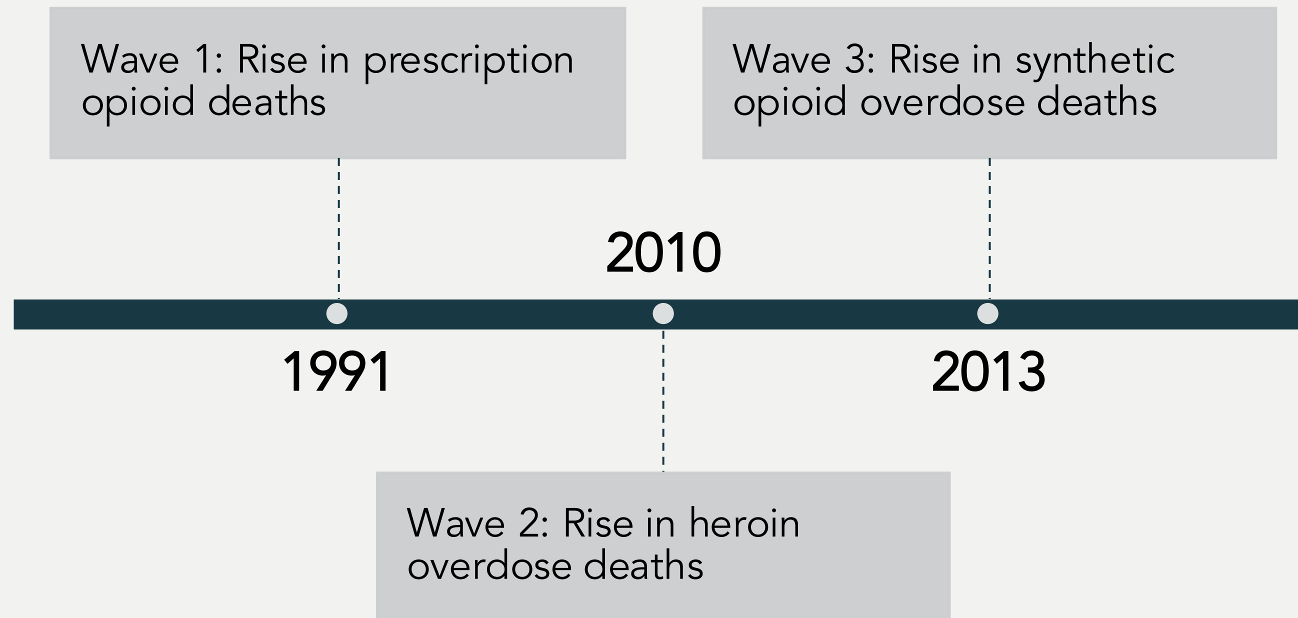
Objectives

1. Discuss recent regulatory updates related to buprenorphine prescribing including implications for clinical workflows.
2. Review and analyze key findings from primary literature on best practices for buprenorphine inductions.
3. Compare and contrast various induction techniques with attention to patient suitability and clinical outcomes.
4. Evaluate how the induction setting influences the choice of induction strategy and patient engagement.
5. Apply updated knowledge to clinical scenarios to choose appropriate induction approaches based on patient presentation.

Abbreviations

- ASAM – American Society of Addiction Medicine
- COWS – Clinical Opiate Withdrawal Scale
- CPP – Clinical Pharmacist Practitioner
- DEA – Drug Enforcement Administration
- DSM-V – Diagnostic and Statistical Manual of Mental Disorders, 5th edition
- HDB – High-Dose Buprenorphine
- LDB – Low-Dose Buprenorphine
- MAT – Medication Assisted Treatment
- MME – Morphine Milligram Equivalents
- MOUD – Medications for Opioid Use Disorder
- NMDA - N-methyl-D-aspartate
- OR – Opioid Receptor
- OTP – Opioid Treatment Program
- OUD – Opioid Use Disorder
- SAMHSA – Substance Abuse and Mental Health Services Administration
- SL – Sublingual
- SOWS – Subjective Opiate Withdrawal Scale
- XR – Extended Release

Opioid Epidemic Evolution



Between 2019-2020:

- Opioid deaths **increased 38%**
- Heroin deaths decreased by 7%
- Synthetic opioid-involved deaths (excluding methadone) **increased by 56%**

Centers for Disease Control and Prevention, 2022

North Carolina

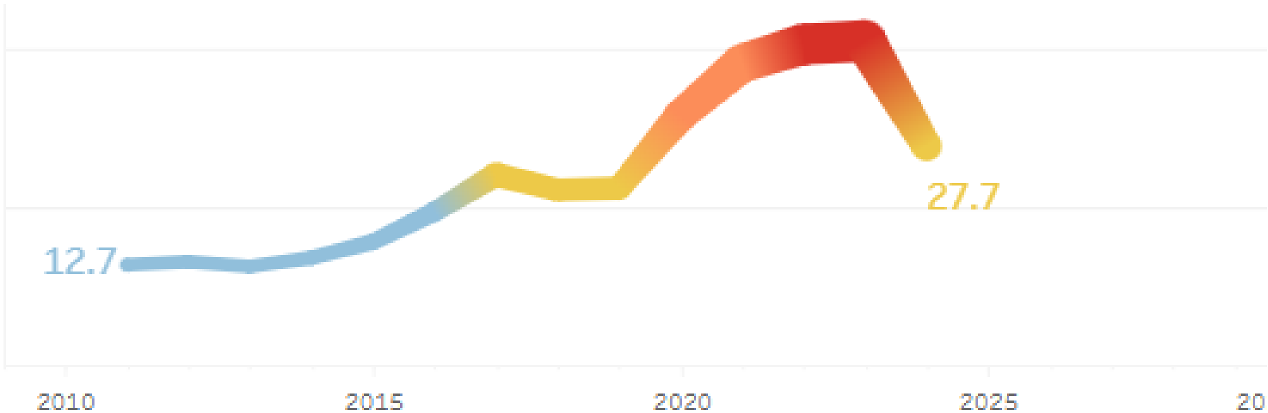
- Significant decrease first noted in 2024
- Continues to decline!

  Considered to be multifactorial
- Fentanyl-positive deaths declining when compared to 2024

Overdose Deaths

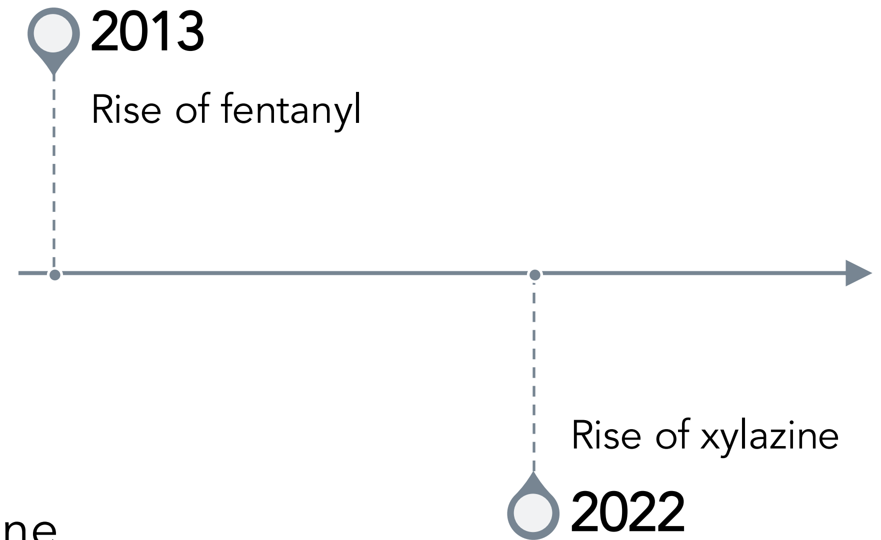
The **estimated Overdose Death** rate in **NC** is **27.7** out of 100,000 residents in **2024**, representing (projected) **3,060** people who died of an overdose.

Partial year: n=1,785 at 7/12 months



NC Department of Health and Human Services, 2025

Emerging Substances



Fentanyl

- Synthetic opioid
- Pharmaceutical fentanyl vs. Illicit fentanyl
- 50x stronger than heroin, 100x stronger than morphine

Xylazine

- Non-opiate sedative, analgesic, and muscle relaxant only approved for veterinary use
- Used as an adulterant for multi-drug mixtures, often containing fentanyl
- Increases the potential for a fatal outcome of an overdose

Drug Enforcement Administration, 2022

Fentanyl Pearls

- More potent at μ-OR compared to other full agonist opioids
  - *Higher concentration of naloxone required to reverse respiratory depression*
- High lipid solubility
  - *Rapidly enter the CNS compared to other full agonist opioids*
  - *Large volume of distribution*
- Low cross tolerance to heroin

Luba et al., 2023
Kelly et al., 2023

Withdrawal

Spontaneous opioid withdrawal

- A decrease or discontinuation in agonist opioid use
- Time of withdrawal depends on short versus long acting

Precipitated opioid withdrawal

- Happens rapidly
- Usually caused by administering a partial opioid agonist or antagonist
- Displaces opioid from receptor

SAMHSA, 2021
Kampman et al., 2015

Opioid Withdrawal

Signs and Symptoms		
Restlessness	Anxiety	Insomnia
Insomnia	Yawning	Abdominal cramps
Diarrhea	Vomiting	Irritability
Dilated pupils	Sweating	Piloerection

SAMHSA, 2021

Medically Supervised Withdrawal

- Commonly referred to as "detoxification"
- Over 90% of patients who complete detox return to use
- Consider maintenance plan or long-term goals prior to detoxing

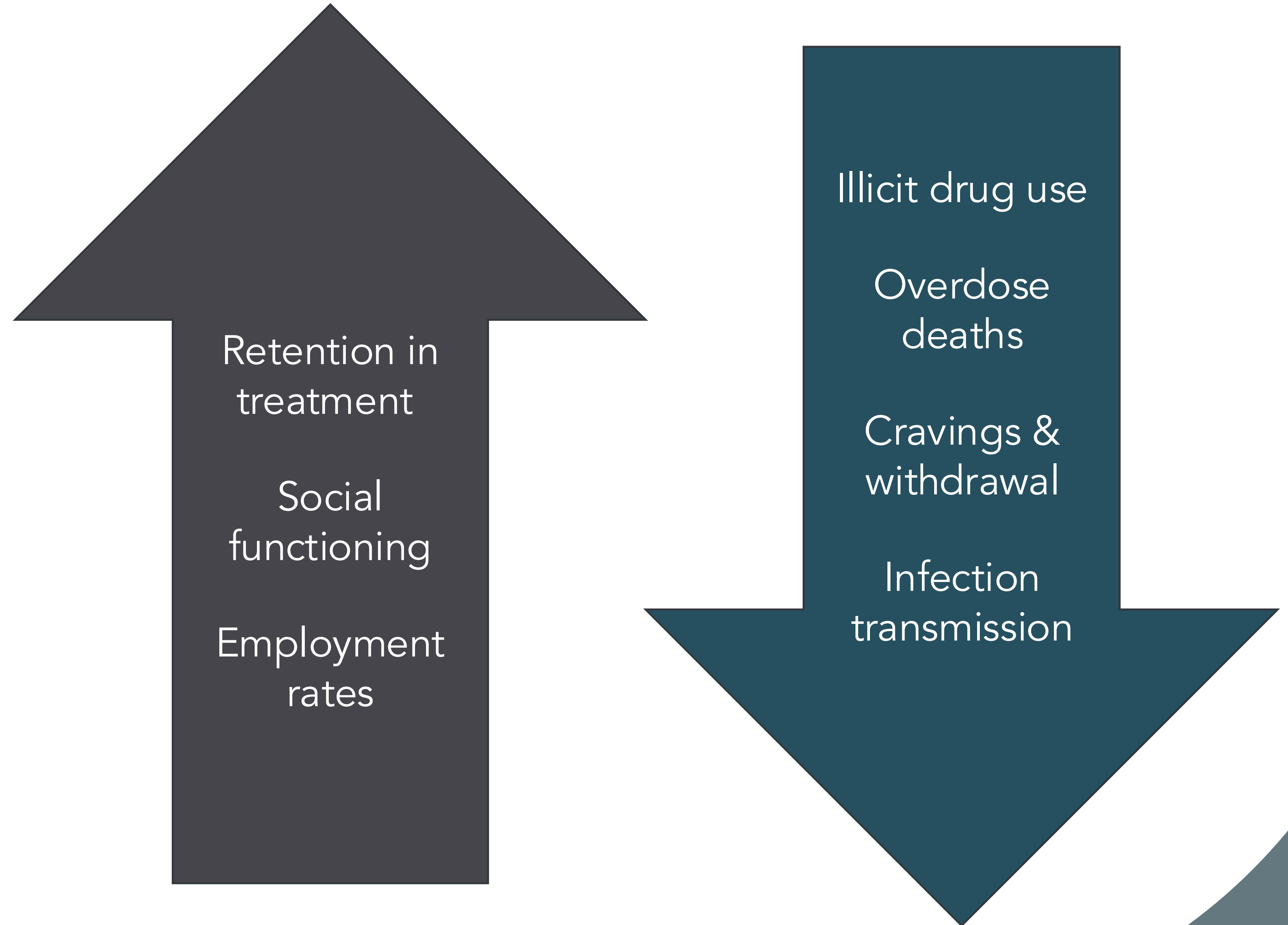
  Increased risk of overdose and death post-detox without MOUD or sustained abstinence
- Can be done inpatient or outpatient

  Can use MOUD to help with de-escalation plan or abstinence

  Supportive meds used in both settings

Nunes et al., 2020
Polydorou et al., 2008
Weiss et al., 2008

Benefits of MOUD



National Institute on Drug Abuse, 2016
Fairley M et al., 2021
SAMHSA, 2021

Medications for Opioid Use Disorder

Methadone

- μ-OR **full agonist**
- Kappa and delta opioid receptor binding
- Inhibits reuptake of serotonin and norepinephrine
- NMDA receptor antagonist

Naltrexone

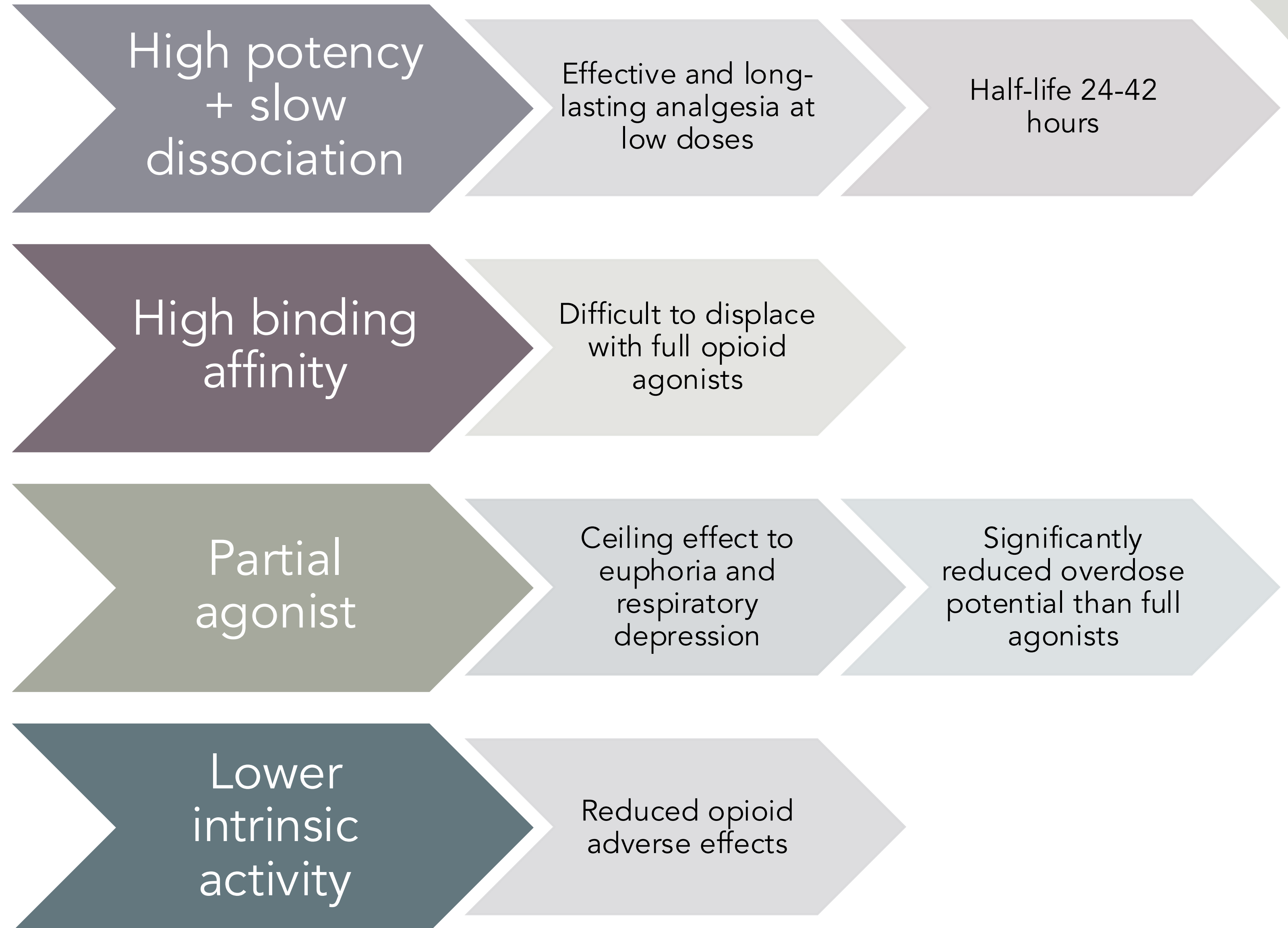
- μ-OR **antagonist**
  - *Strong receptor affinity*
  - *Competitive binding*
- Kappa opioid receptor antagonist

Buprenorphine

- μ-OR **partial agonist**
- Kappa opioid receptor antagonist

SAMHSA, 2021
Coe et al., 2019

Buprenorphine at the μ-OR



Coe, et al., 2019
Webster et al., 2020

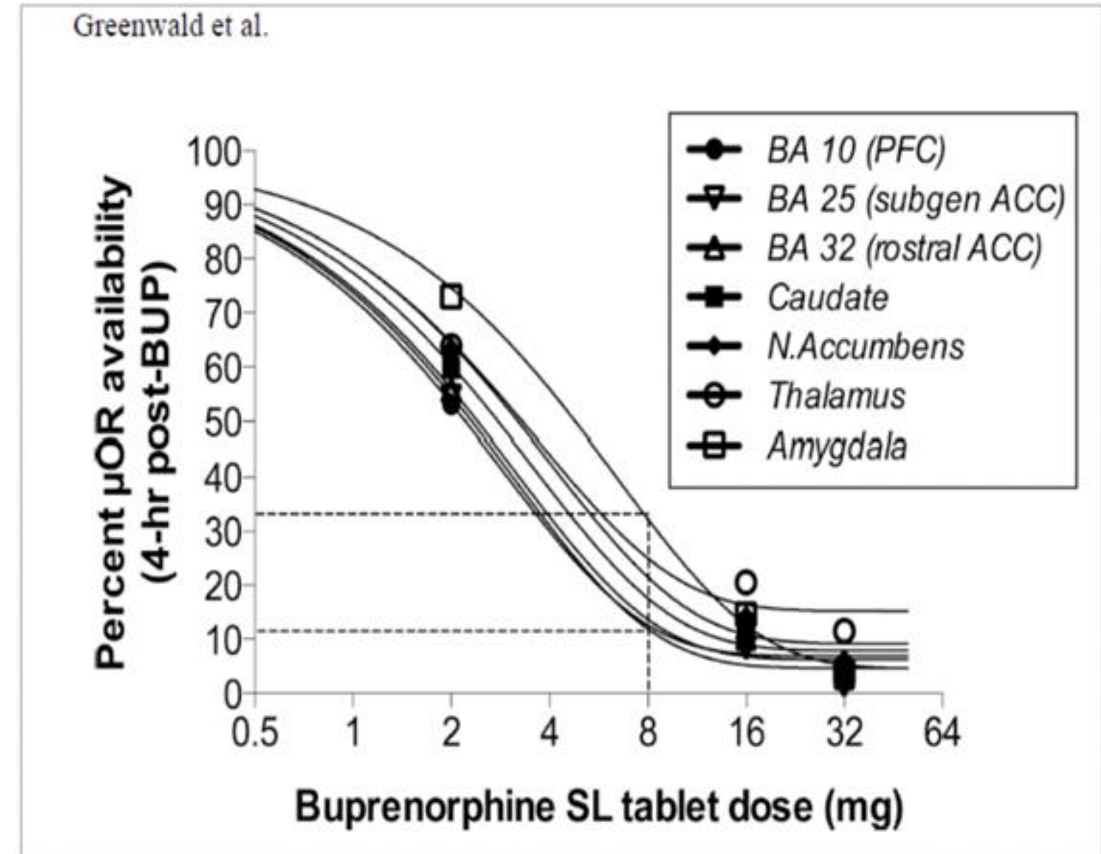
Buprenorphine Pearls

- 4mg/d is enough to prevent withdrawal symptoms

  50% opioid receptors occupancy

- 16mg/d is enough to block cravings

  >80% of opioid receptors occupancy



Greenwald et al., 2014

Buprenorphine Formulations

Type	Buprenorphine	Buprenorphine/ Naloxone	Buprenorphine Long-Acting
FDA Indication	Pain	Opioid Use Disorder	Opioid Use Disorder
Brands	Belbuca® Butrans®	Suboxone® Zubsolv®	Sublocade® Brixadi®

Arbuck, 2019

December 2022

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

Federal Legislation Changes

- X-Waiver requirement removed

  Only a DEA number needed to prescribe buprenorphine

- Removal of limits or patient caps

- 8-hour of substance use training for all DEA-licensed prescribers

  Decreased from 24 hours for non-physician prescribers

SAMHSA, 2023

Stages of Treatment with Buprenorphine

Standard Buprenorphine

- Patient needs to be in mild to moderate withdrawal
- Initiation lasts 2 to 3 days
- Starts with 2 to 4 mg dose, max of 16 mg on day 1
- Follows manufacturer's guidelines
- Common practice to have patient do at home

SAMHSA, 2021
ASAM, 2015
Lee et al., 2009

Example Standard Outpatient Protocol

Conduct Clinical Opiate Withdrawal Scale (COWS)

If COWS ≥ 12

- Buprenorphine-naloxone 4-1 mg
- Wait 2-4 hours

Withdrawal symptoms relieved?

- No → Buprenorphine-naloxone 4-1 mg
- Wait 2-4 hours

Withdrawal symptoms relieved?

- No → Buprenorphine-naloxone 4-1 mg
- End of Day 1

Day 2

- Give Day 1 total dose + additional buprenorphine-naloxone 4-1 mg

Withdrawal symptoms relieved?

- No → Buprenorphine-naloxone 4-1 mg
- Wait 2-4 hours

Withdrawal symptoms relieved?

- No → Buprenorphine-naloxone 4-1 mg
- End Day 2

SAMHSA, 2021

Why isn't *standard* induction enough?

Low-Dose Buprenorphine (LDB)

- Patient does not need to go into withdrawal
- Induction can take up to 1 week
- Starts with max dose of 0.5 mg on day 1
- Continue full agonist while titrating buprenorphine
- Case and Case series
- Different protocols

Cohen et al., 2021
Teraski et al., 2019
Becker et al., 2020
Weimer et al., 2021
Robbins et al., 2021

Example LDB Hospital Protocol

Buprenorphine 225 mcg
- Continue full agonist

Buprenorphine 225 mcg twice daily
- Continue full agonist

Buprenorphine 450 mcg twice daily
- Continue full agonist

Buprenorphine-naloxone 2-0.5 mg twice daily
- Continue full agonist

Buprenorphine-naloxone 4-1 mg twice daily
- Continue full agonist

Buprenorphine-naloxone 4 mg three times daily
- Continue full agonist

Establish maintenance dose
- Discontinue full agonist

Weimer, et al. JAM 2021

Outpatient LDB Keys to Success

- Shared decision making
- Ongoing access to full agonist opioid
- Frequent monitoring and follow up
  - *Review signs and symptoms of withdrawal*
  - *Provide supportive medications*
- Pack medications together
  - *Help cut films or put into bottles/bubble packs/etc.*
  - *Access to naloxone*

High-Dose Buprenorphine (HDB)

- Patient in mild to severe withdrawal
- Induction takes 1 to 2 days
- Max doses up to 32 mg (or higher) on day 1
- Higher doses to mitigate long induction and symptoms of withdrawal
- Case series and reports
- Mainly implemented in emergency department (ED)

Herring et al., 2021
Ahmadi et al., 2018
Danilewitz et al., 2020
Mariani et al., 2021

Example HDB Emergency Room Protocol

Conduct Clinical Opiate Withdrawal Scale (COWS)

Buprenorphine 4-8 mg SL

- If COWS ≥ 8

Buprenorphine 8-24 mg

- Every 30-60 minutes if COWS ≥ 8 persists

Buprenorphine 16+ mg daily

- Discharge prescription with quantity sufficient until follow up appointment

Herring et al., 2021

Rapid Induction to Injectable Buprenorphine (RITI)

- Induction takes 1 day

    Test dose with buprenorphine SL and then administer XR

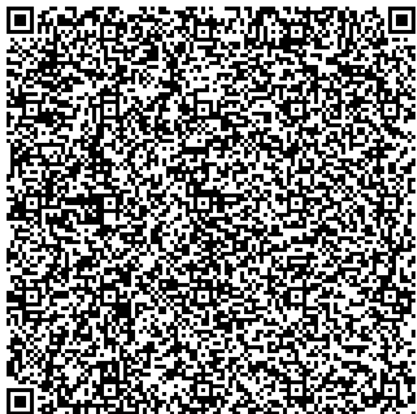
- Multicenter, open-label randomized clinical trial O

    Over 700 patients randomized

- Majority of patient had used fentanyl at screening urine drug screen
- Rapid induction was noninferior with higher retention than standard induction

Shiwach et al., 2025

Example RITI Outpatient Protocol



Conduct Clinical Opiate Withdrawal Scale (COWS)

Administer buprenorphine 4 mg SL

- If COWS ≥ 8

Administer 300 mg buprenorphine XR

- Clinically sedated → reschedule or wait in clinic
- Precipitated withdrawal → reschedule or wait in clinic

Prescribe adjunctive withdrawal medications

- Consider supplemental buprenorphine SL

Administer 300 mg buprenorphine XR

- 1 week after initial injection

Shiwach et al., 2025

Direct-to-Inject Buprenorphine (DTI)

- Direct initiation of injectable buprenorphine without test dose

  Excluded patients who had > 4 mg of SL in last 24 hours

- Retrospective cohort study in 21 patients
- Two different techniques based on if patient in active use
- First 24 hours resulted mixed withdrawal experience
- High retention at 7 and 30 days (greater than 70%)

Rosenwohl-Mack et al., 2025

Example 2-Injection DTI Outpatient Protocol

Conduct Clinical Opiate Withdrawal Scale (COWS)

Administer weekly injectable buprenorphine (8, 16, 24, or 32 mg)

- Ideally, COWS ≥ 4, at least 6-12 hours since last use
- No recent methadone

Consider supplemental buprenorphine SL

- Patient to start buprenorphine SL 24 hours after first injection
- Prescribe adjunct withdrawal medications

Administer monthly injectable buprenorphine (100, 300, 64, 96, or 128 mg)

- If patient received 16 mg, give second dose within 4 days
- If patient receive 24 or 32 mg, give second dose with in 7 days

Rosenwohl-Mack et al., 2025

Example 3-Injection DTI Outpatient Protocol

Conduct Clinical Opiate Withdrawal Scale (COWS)

Administer weekly injectable buprenorphine (8 mg)

- No minimum COWS, can continue to use full-agonist opioid
- Prescribe adjunct withdrawal medications

Administer weekly injectable buprenorphine (16 mg)

- No sooner than 24 hours after first injection
- Continue adjunct meds and/or full-agonist

Consider additional buprenorphine SL

- Recommended to start 24 hours after 16 mg dose

Administer monthly injectable buprenorphine (100, 300, 64, 96, or 128 mg)

- Dose administered ~3-4 days post initial injection

Rosenwohl-Mack et al., 2025

Buprenorphine Inductions Summary

	Standard	LDB	HDB	RITI	2-DTI	3-DTI
Withdrawal at Induction	Yes	No	Yes	Yes	Yes	No
Opioid Continuation	No	Yes	No	No	No	Yes
Duration of Induction	2 to 3 days	3 to 7 days	1-2 days	1 day	4 to 9 days	3 to 7 days
Initial Day Dose of Buprenorphine	4-12 mg	~0.5 mg	16-32+ mg	4 mg SL 300 mg XR	16-24 mg XR	8 mg

Which induction strategy should I pick?

Shared decision making with your patient!

Case 1

- 26-year-old female presents to the clinic after taking a home pregnancy test that resulted positive. She is here today for confirmatory testing. She endorses using 3 points of fentanyl daily. She last used this morning. She is asking about buprenorphine and is wondering if she could start today. She currently lives with one roommate and works 4 days a week at a local bank.

Is this patient a candidate for buprenorphine? If so, how would you induce her?

What harm reduction modalities can you offer her?

Case 1 Part 2

- Patient tried to start buprenorphine at home but has had friends go through withdrawal and is nervous to start alone. She presents to the ED 3 days after her last use and is yawning, shaking, and feels nauseous. Her heart rate is elevated, appears agitated, and has goosebumps on her skin. She lets the clinicians in the ED know she is interested in starting MOUD.

How can you assess this patient?

If starting buprenorphine, what induction technique would be appropriate?

Case 2

- 47-year-old female presents to the hospital and is admitted for infective endocarditis. The patient reports taking oxycodone 30mg 4 times daily (180 MME) for chronic pain and has a remote history of cocaine misuse. Her hospitalist discuss buprenorphine with her. She is hesitant to start treatment and worried about the induction period as well as adequate pain control.

How would you counsel this patient?

If starting buprenorphine, what induction technique might be most appropriate?

Case 3

- 33-year-old patient is brought to the hospital by EMS after a non-fatal overdose that was reversed with naloxone. Patient reports history of severe opioid use disorder, primarily fentanyl and occasionally oxycodone. He is admitted for aspirational pneumonia. By the time the attending sees the patient, his COWS score is 8. No major complaints. He is interested in starting buprenorphine.

What induction technique might be most appropriate?

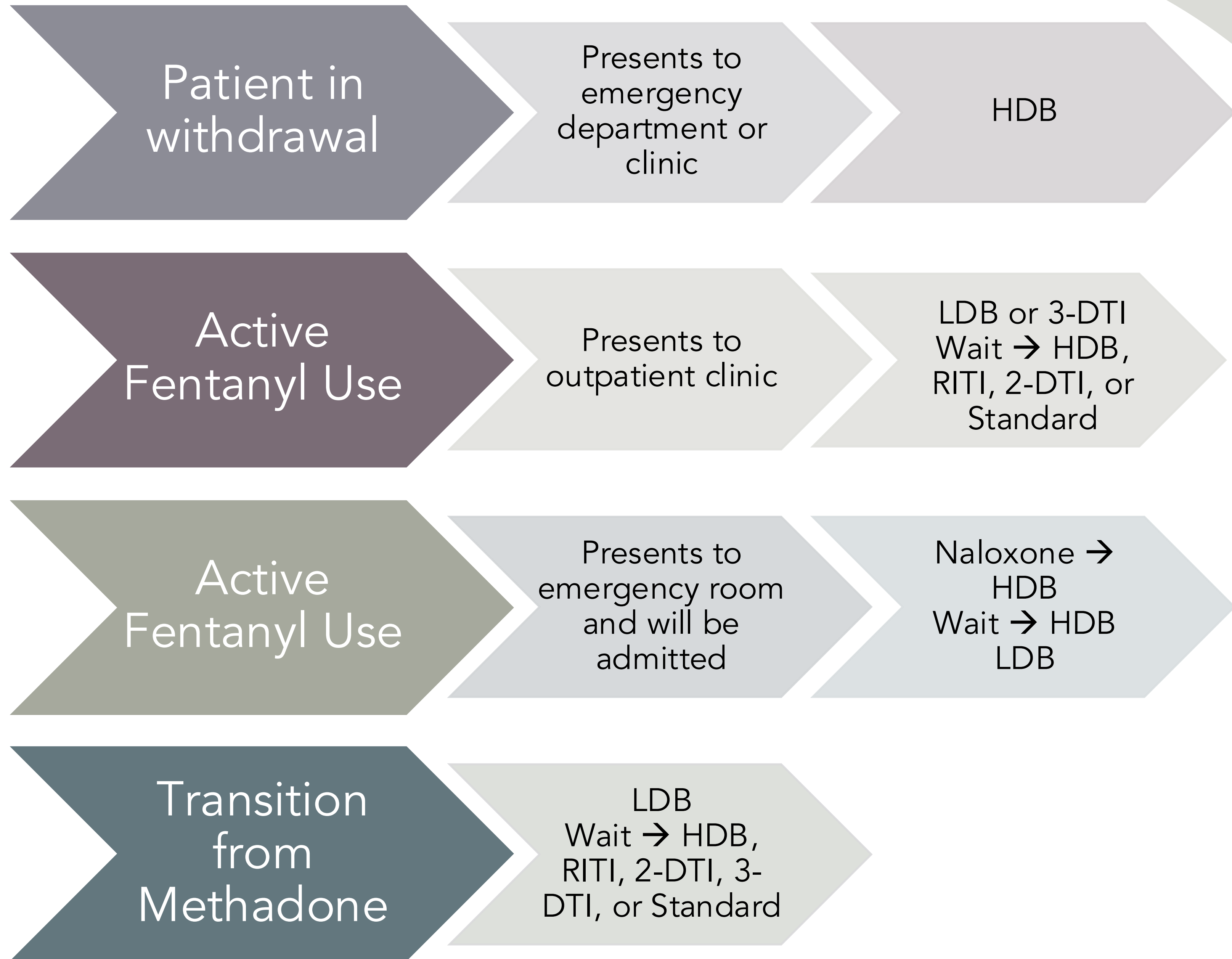
Case 4

- 21-year-old female presents to a primary care clinic for a contraception consult. She discloses occasional substance use, namely cocaine and fentanyl. She is unable to establish her last day of use. Her COWS is 2. She states she is just here to discuss birth control options. She's tried buprenorphine in the past and it has not worked for her and mentions she was taking 4 mg daily.

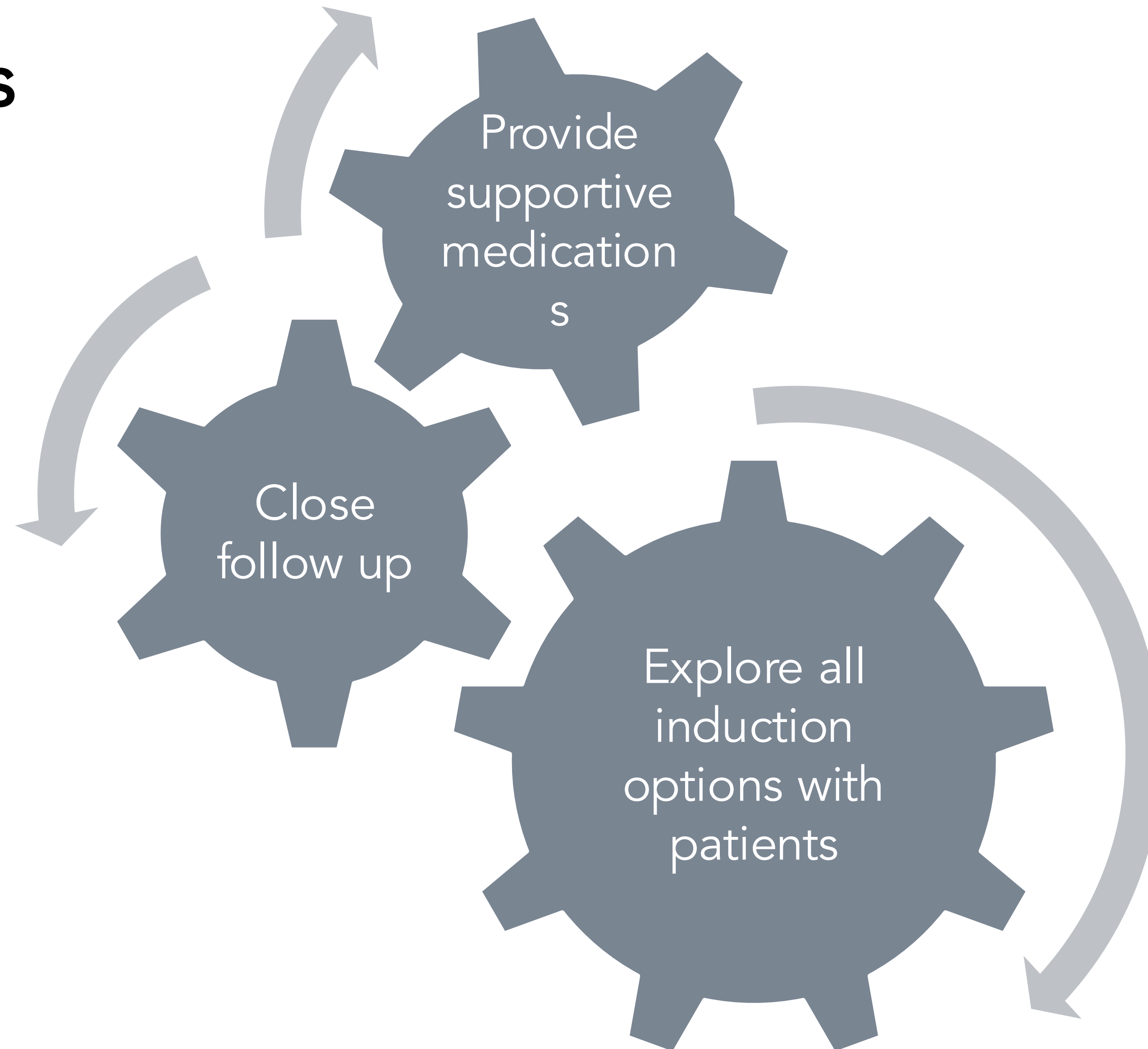
Would you offer this patient buprenorphine?

If so, what induction strategy would you use? If not, why not?

Considerations for Inductions



Key Takeaways



References

- Becker WC, Frank JW, Edens EL. Switching From High-Dose, Long-Term Opioids to Buprenorphine: A Case Series. *Ann Intern Med*. 2020;173(1):70-71. doi:10.7326/L19-0725
- Coe MA, Lofwall MR, Walsh SL. Buprenorphine Pharmacology Review: Update on Transmucosal and Long-acting Formulations. *J Addict Med*. 2019;13(2):93-103. doi:10.1097/ADM.0000000000000457
- Cohen SM, Weimer MB, Levander XA, Peckham AM, Tetrault JM, Morford KL. Low Dose Initiation of Buprenorphine: A Narrative Review and Practical Approach. *J Addict Med*. 2022;16(4):399-406. doi:10.1097/ADM.0000000000000
- Fairley M, Humphreys K, Joyce VR, et al. Cost-effectiveness of Treatments for Opioid Use Disorder. *JAMA Psychiatry*. 2021;78(7):767-777. doi:10.1001/jamapsychiatry.2021.0247
- Greenwald MK, Comer SD, Fiellin DA. Buprenorphine maintenance and mu-opioid receptor availability in the treatment of opioid use disorder: implications for clinical use and policy. *Drug Alcohol Depend*. 2014;144:1-11. doi:10.1016/j.drugalcdep.2014.07.035
- Kampman K, 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*. 2015;9(5):358-367. doi:10.1097/ADM.0000000000000166
- Lee JD, Grossman E, DiRocco D, Gourevitch MN. Home buprenorphine/naloxone induction in primary care. *J Gen Intern Med*. 2009;24(2):226-232. doi:10.1007/s11606-008-0866-8
- Nunes EV, Shulman M. Commentary on Stein et al. (2020): Whither detoxification in the face of the opioid epidemic? *Addict Abingdon Engl*. 2020;115(1):95-96. doi:10.1111/add.14834
- Robbins JL, Englander H, Gregg J. Buprenorphine Microdose Induction for the Management of Prescription Opioid Dependence. *J Am Board* Fam Med JABFM. 2021;34(Suppl):S141-S146. doi:10.3122/jabfm.2021.S1.200236
- Says T. The COVID-19 Pandemic and the Opioid Overdose Epidemic: A Perfect Storm for Workers? | Blogs | CDC. Published September 14, 2020. Accessed May 7, 2023. https://blogs.cdc.gov/niosh-science-blog/2020/09/14/covid-19-and-oud/
- NC Department of Health and Human Services Division of Public Health Injury & Violence Prevention Branch. "North Carolina Overdose Epidemic Data | Division of Public Health." North Carolina Overdose Epidemic Data. Accessed <10/12/2025>. https://www.dph.ncdhhs.gov/ivpb-overdose-data.
- Rosenwohl-Mack S, Suen LW, Logan AA, Peterson D, Snyder HR. Outpatient initiation of 7-day injectable buprenorphine: a direct-to-inject case series. Drug Alcohol Depend. 2025;260:111337. doi:10.1016/j.drugalcdep.2025.111337

- Terasaki D, Smith C, Calcaterra SL. Transitioning Hospitalized Patients with Opioid Use Disorder from Methadone to Buprenorphine without a Period of Opioid Abstinence Using a Microdosing Protocol. Pharmacotherapy. 2019;39(10):1023-1029. doi:10.1002/phar.2313
- Webster L, Gudin J, Raffa RB, et al. Understanding Buprenorphine for Use in Chronic Pain: Expert Opinion. Pain Med Malden Mass. 2020;21(4):714-723. doi:10.1093/pm/pnz356
- Weimer MB, Guerra M, Morrow G, Adams K. Hospital-based Buprenorphine Micro-dose Initiation. J Addict Med. 2021;15(3):255. doi:10.1097/ADM.0000000000000745
- Weiss RD, Potter JS, Fiellin DA, et al. Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid dependence: a 2-phase randomized controlled trial. *Arch Gen Psychiatry*. 2011;68(12):1238-1246. doi:10.1001/archgenpsychiatry.2011.121
- American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,. Washington, DC, American Psychiatric Association page 541.
- DEA Reports Widespread Threat of Fentanyl Mixed with Xylazine l DEA.gov. Accessed May 7, 2023. https://www.dea.gov/alert/dea-reports-widespread-threat-fentanyl-mixed-xylazine
- Harm Reduction Principles. National Harm Reduction Coalition. Accessed May 14, 2023. https://harmreduction.org/about-us/principles-of-harm-reduction/
- Polydorou, S., & Kleber, H. D. (2008). Detoxification of Opioids. In M Galanter & H Kleber (Eds.), Textbook of Substance Abuse and Treatment (4th ed.) Arlington, VA: American Psychiatric Publishing.
- *Weiss, R. D., Potter, J. S., & Iannucci, R. A. (2008). Inpatient Treatment. In M. Galanter & H. Kleber (Eds.), Textbook of Substance Abuse and Treatment (4th Ed.) Arlington, VA: American Psychiatric Publishing.*
- Effective Treatments for Opioid Addiction. National Institute on Drug Abuse. Published November 1, 2016. Accessed May 15, 2023. https://nida.nih.gov/publications/effective-treatments-opioid-addiction
- Kelly E, Sutcliffe K, Cavallo D, Ramos-Gonzalez N, Alhosan N, Henderson G. The anomalous pharmacology of fentanyl. Br J Pharmacol. 2023;180(7):797-812. doi:10.1111/bph.15573
- Shiwach R, Le Foll B, Alho H, et al. Rapid vs standard induction to injectable extended-release buprenorphine: a randomized clinical trial. JAMA Netw Open. 2025;8(10):e2537319. doi:10.1001/jamanetworkopen.2025.37319

- Arbuck D. Buprenorphine: A Promising Yet Overlooked Tool. Published June 11, 2019. Accessed May 15, 2023. https://www.practicalpainmanagement.com/treatments/addiction-medicine/opioid-use-disorder/buprenorphine-promising-yet-overlooked-tool
- COVID-19 Pandemic Impact on Patients, Families & Individuals in Recovery from a SUD. APF. Published June 8, 2020. Accessed May 7, 2023. https://www.addictionpolicy.org/post/covid-19-pandemic-impact-on-patients-families-individuals-in-recovery-fromsubstance-use-disorder
- Substance Abuse and Mental Health Administration. TIP 63: Medications for Opioid Use Disorder. Published February 5, 2021. Accessed May 15, 2023. https://www.samhsa.gov/resource/ebp/tip-63-medications-opioid-use-disorder
- Herring AA, Vosooghi AA, Luftig J, et al. High-Dose Buprenorphine Induction in the Emergency Department for Treatment of O pioid Use Disorder. JAMA Netw Open. 2021;4(7):e2117128.
- Ahmadi J, Jahromi MS, Ghahremani D, London ED. Single high-dose buprenorphine for opioid craving during withdrawal. Trials. 2018;19(1):675. Published 2018 Dec 10. doi:10.1186/s13063-018-3055-z
- Danilewitz M, McLean M. High-dose buprenorphine for treatment of high potency opioid use disorder. Drug Alcohol Rev. 2020;39(2):135-137. doi:10.1111/dar.13017
- Mariani JJ, Mahony AL, Podell SC, et al. Open-label trial of a single-day induction onto buprenorphine extended-release injection for users of heroin and fentanyl. Am J Addict. 2021;30(5):470-476. doi:10.1111/ajad.13193
- The Spike in Drug Overdose Deaths During the COVID-19 Pandemic and Policy Options to Move Forward. doi:10.26099/gyf5-3z4
- ICYMI: Dr. Gupta Op-Ed on Transforming Management of Opioid Use Disorder with Universal Treatment l ONDCP. The White House. Published September 22, 2022. Accessed May 15, 2023. https://www.whitehouse.gov/ondcp/briefing-room/2022/09/22/icymi-dr-gupta-op-ed-on-transforming-management-of-opioid-use-disorder-with-universal-treatment/
- Removal of DATA Waiver (X-Waiver) Requirement. Published January 10, 2023. Accessed May 10, 2023. https://www.samhsa.gov/medications-substance-use-disorders/removal-data-waiver-requirement
- Drug Overdose Death Rates. National Institute on Drug Abuse. Published February 9, 2023. Accessed May 7, 2023. https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates
- Luba R, Jones J, Choi CJ, Comer S. Fentanyl withdrawal: Understanding symptom severity and exploring the role of body mass index on withdrawal symptoms and clearance. Addiction. 2023;118(4):719-726. doi:10.1111/add.16100

Questions or Comments?

Olivia Caron, PharmD, CPP, BCACP

PGY2 Pharmacy Program Director, MAHEC Department of Pharmacy
Assistant Professor of Clinical Education, UNC-Chapel Hill ESOP
Clinical Assistant Professor, UNC School of Medicine
Asheville, NC

Olivia.Caron@mahec.net