Buprenorphine Induction Strategies

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Disclosures

- No conflicts of interest

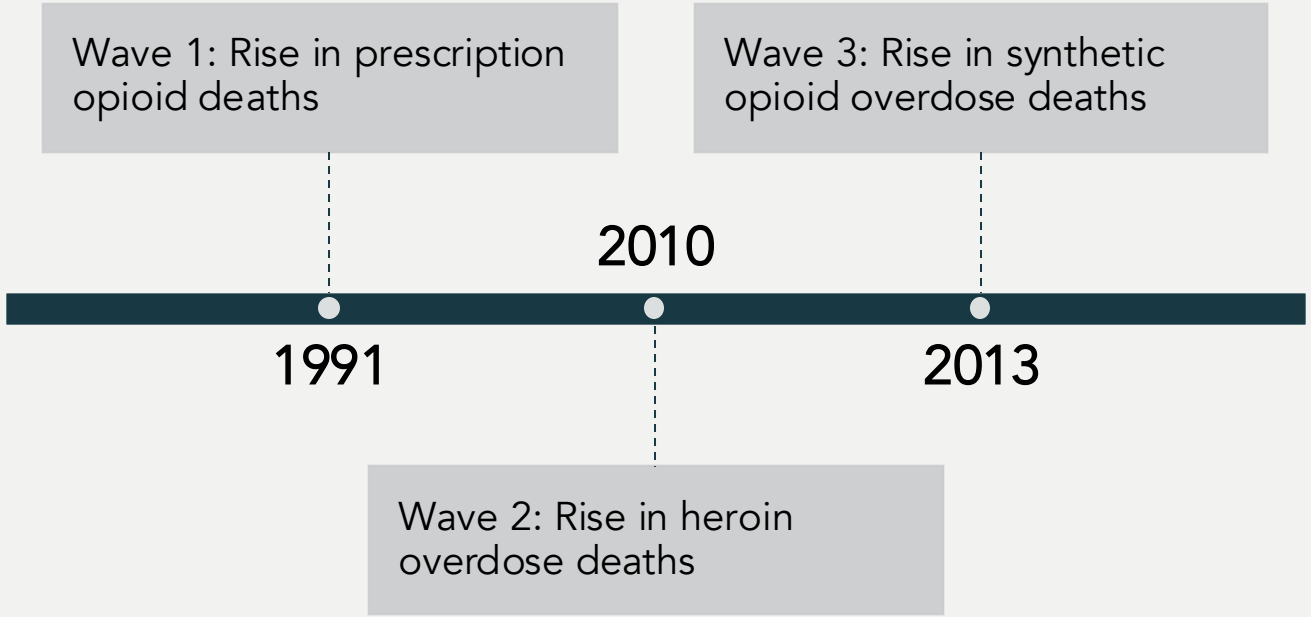
Objectives

- Discuss recent regulatory updates related to buprenorphine prescribing including implications for clinical workflows.
- Review and analyze key findings from primary literature on best practices for buprenorphine inductions.
- Compare and contrast various induction techniques with attention to patient suitability and clinical outcomes.
- Evaluate how the induction setting influences the choice of induction strategy and patient engagement.
- 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
- SOWS – Subjective Opiate Withdrawal Scale

Opioid Epidemic Evolution



Between 2019-2020:

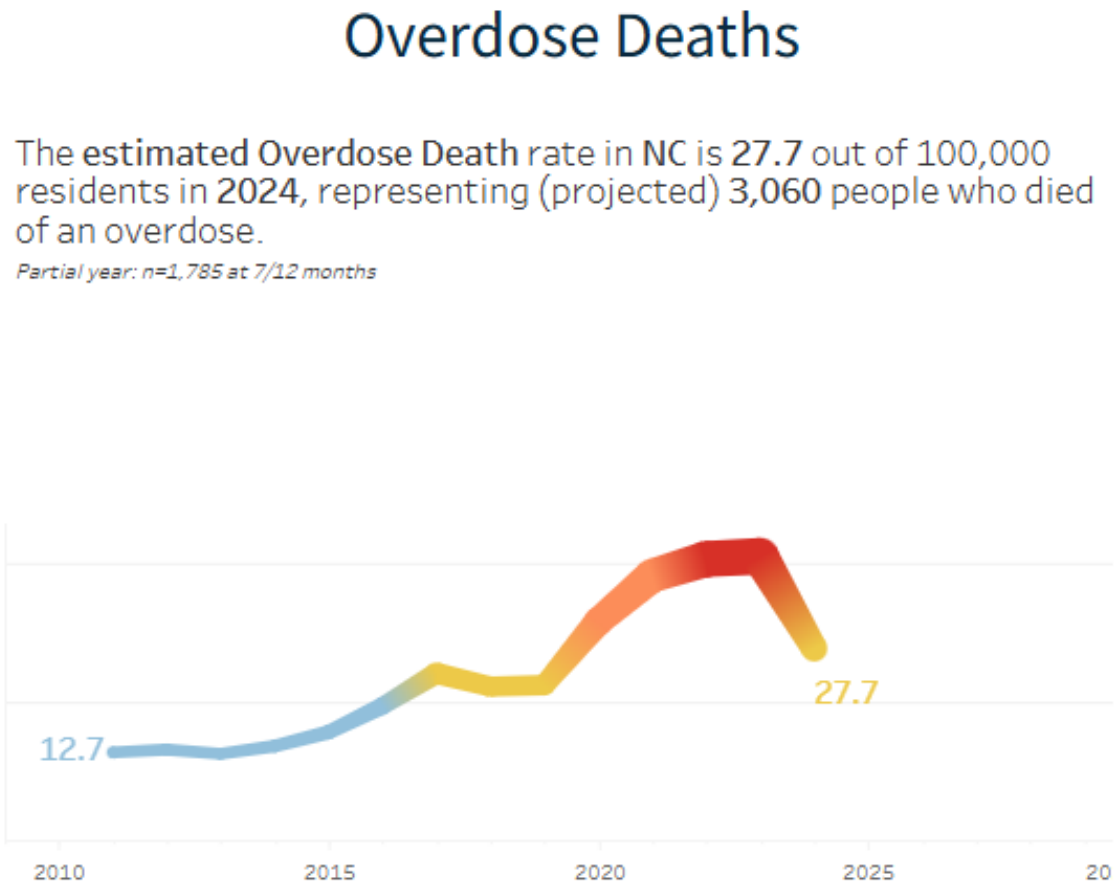
- Opioid deaths **increased 38%**
- Heroin deaths decreased by 7%
- Synthetic opioid-involved deaths (excluding methadone) **increased by 56%**

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

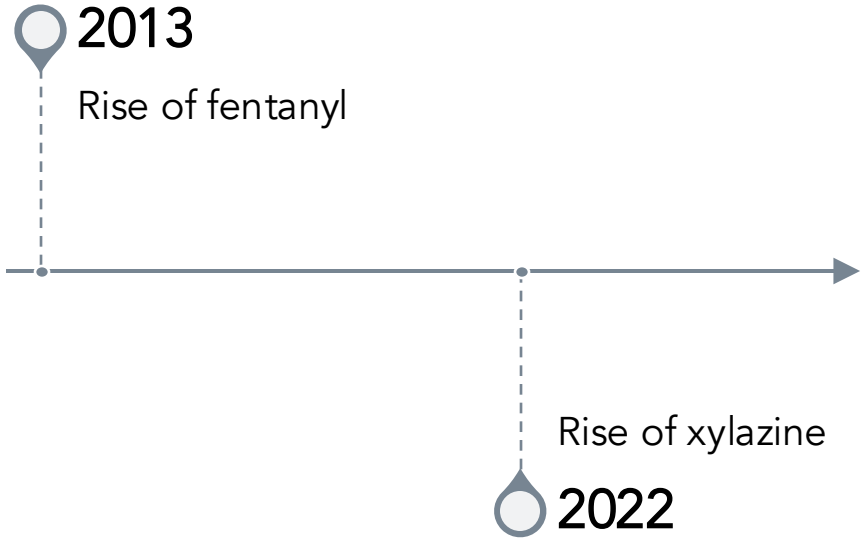


NC Department of Health and Human Services, 2025

Where Are We Now

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

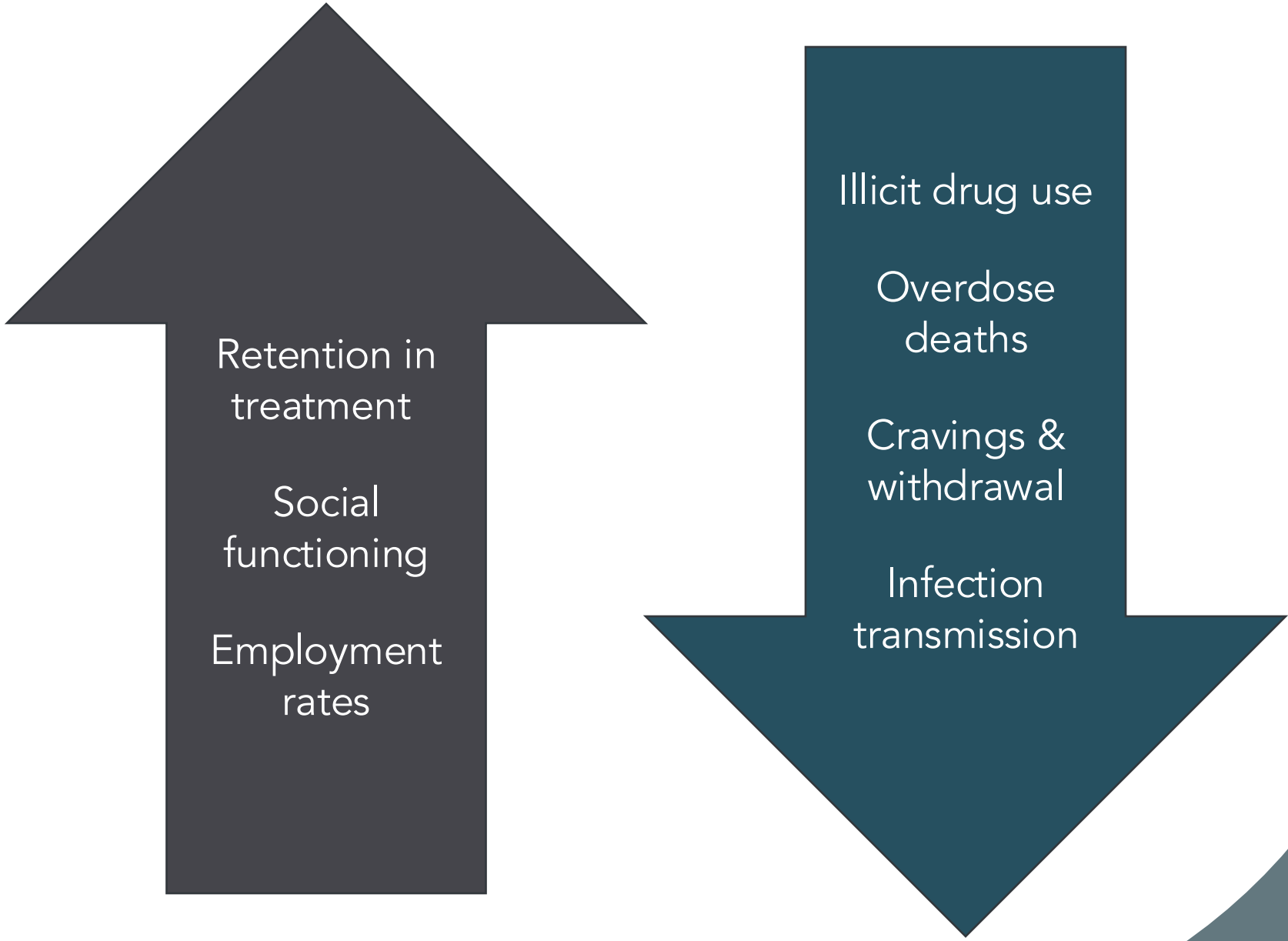
  Increased risk of overdose and death post-detox without MOUD or sustained abstinence
- Can be done inpatient or outpatient

  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

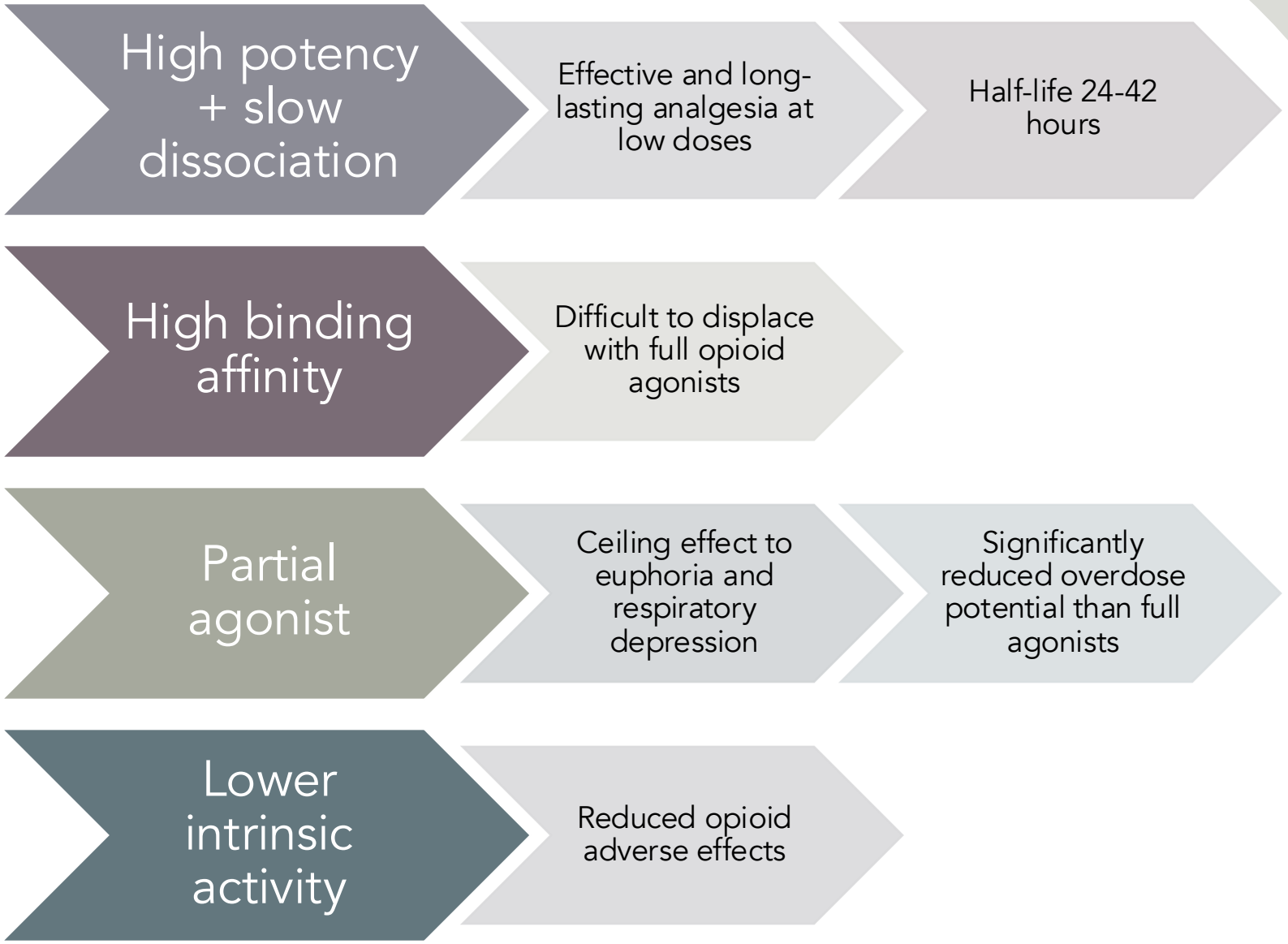
- μ-OR **antagonist**
  - *Strong receptor affinity*
  - *Competitive binding*
- Kappa opioid receptor antagonist

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

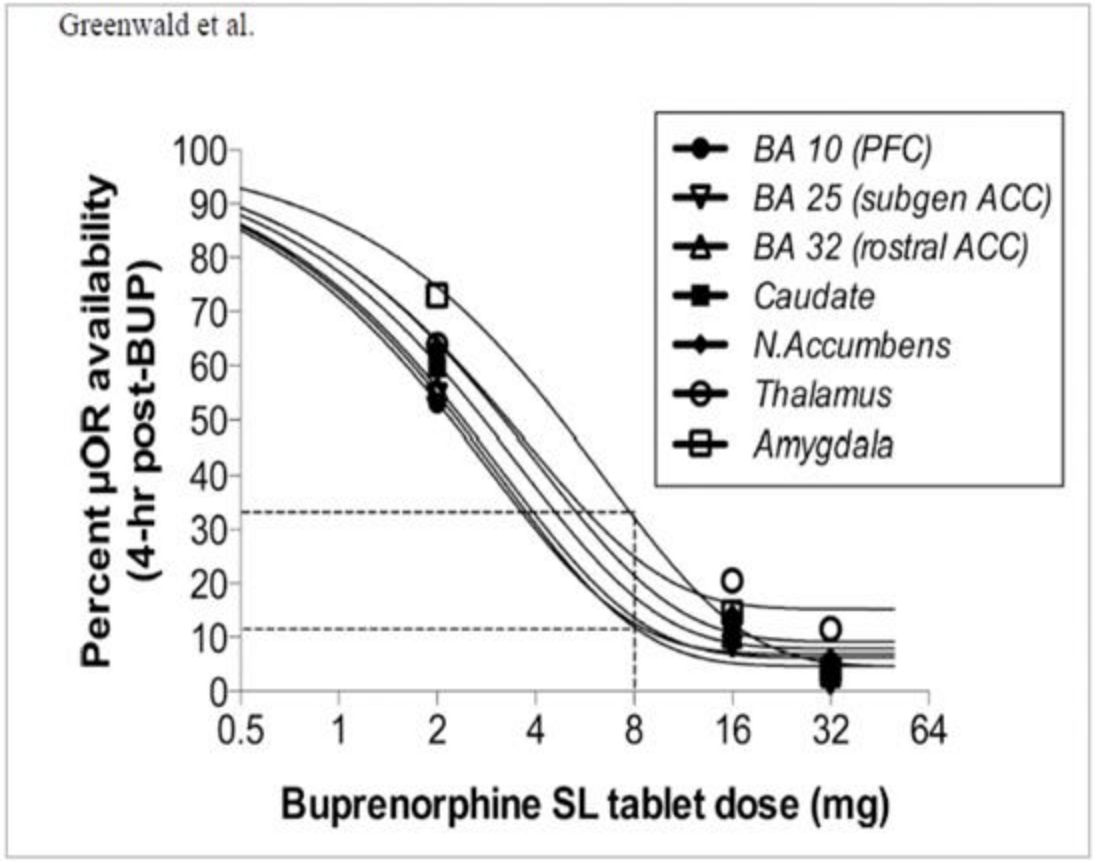
Buprenorphine Pearls

- 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

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

- 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

Buprenorphine Inductions Summary

	Standard	LDB	HDB
Withdrawal	Yes	No	Yes
Opioid Continuation	No	Yes	No
Duration of Induction	2 to 3 days	3 to 7 days	1-2 days
Initial Day Dose of Buprenorphine	4-12 mg	~0.5 mg	16-32+ 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?

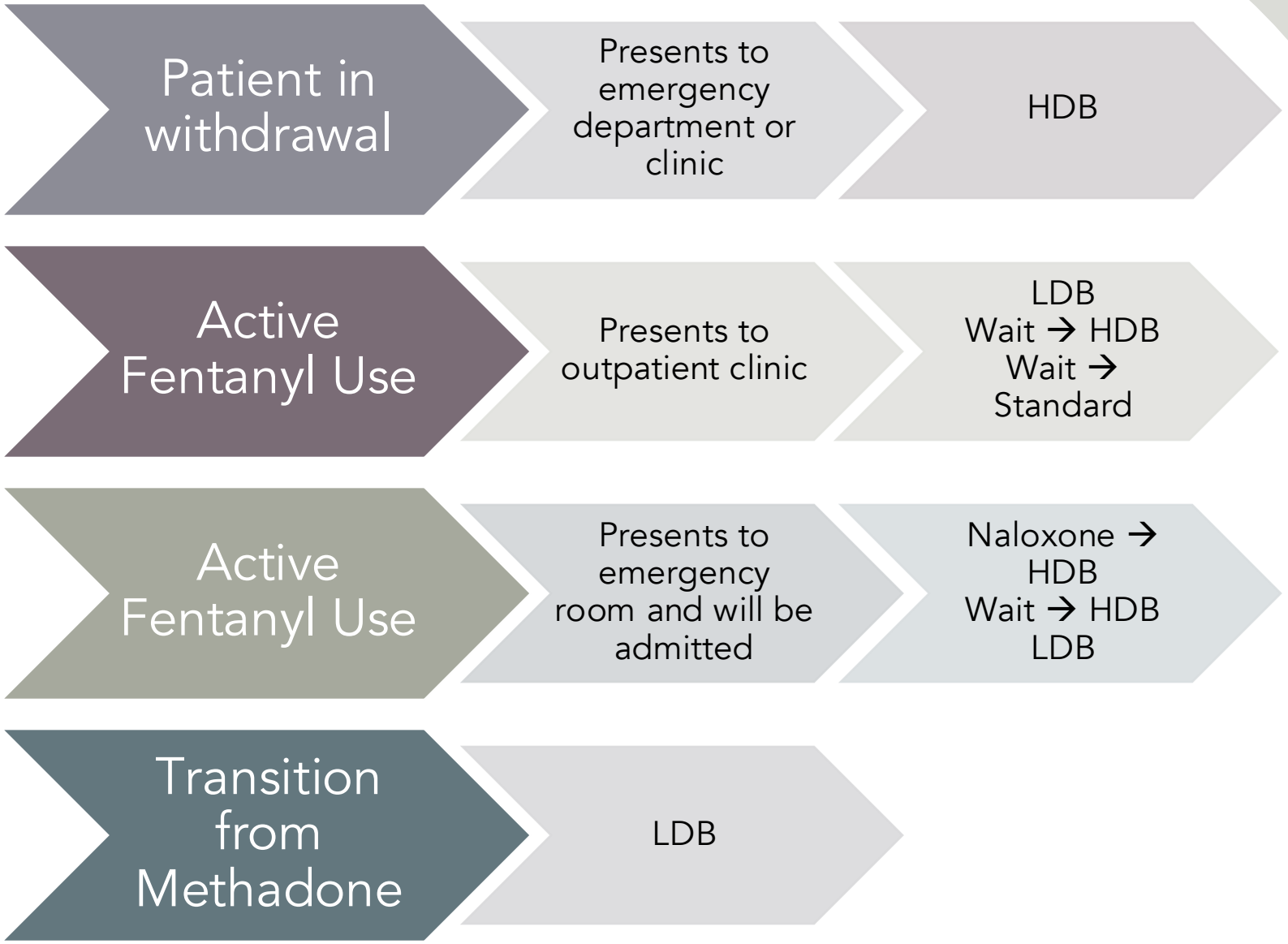
Case 4

- 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.

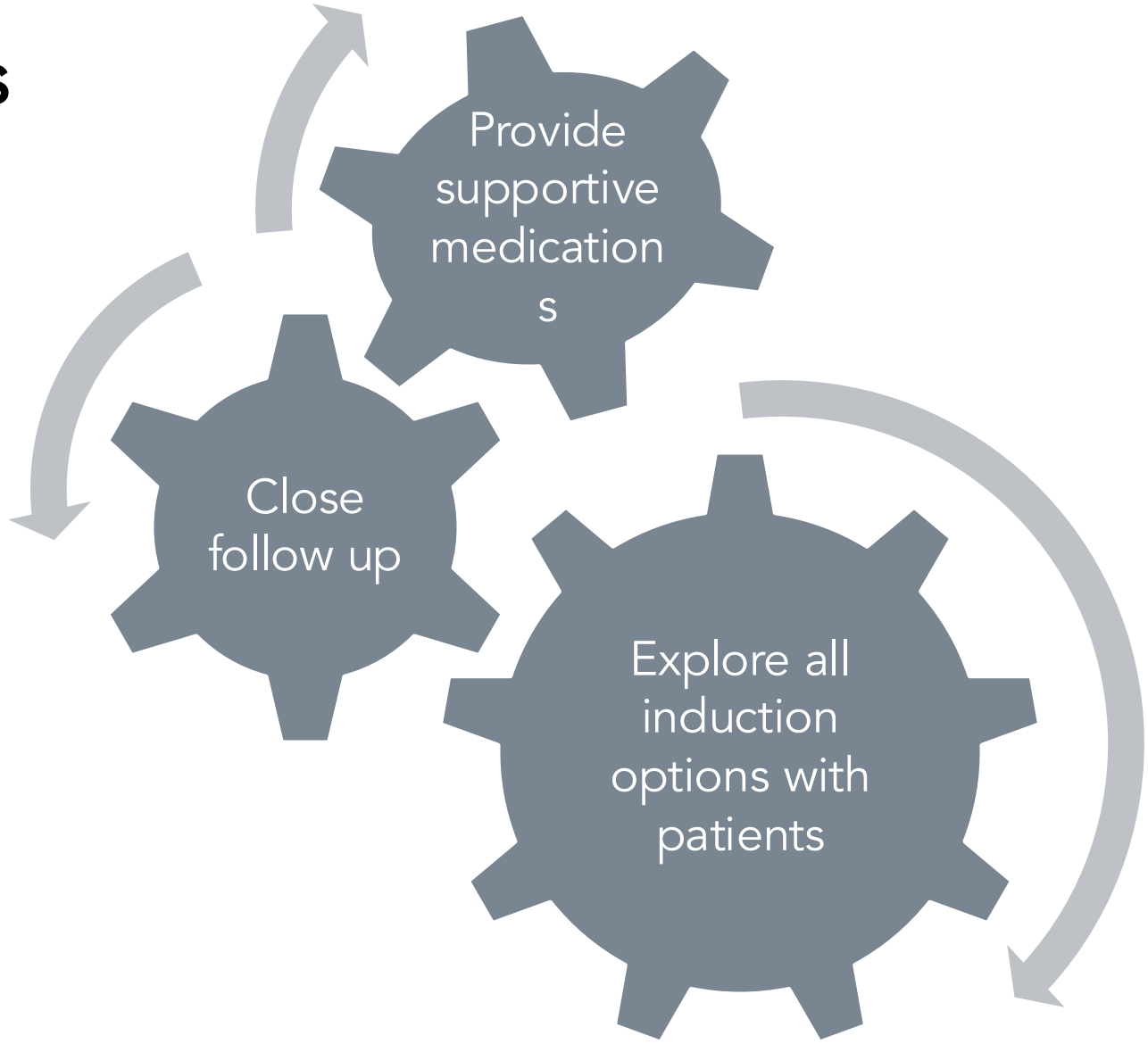
Would you offer this patient buprenorphine?

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

Considerations for Inductions



Key Takeaways



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Questions or Comments?

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