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Psychiatry and Addictions Case Conference
UW Medicine | Psychiatry and Behavioral Sciences

BEST OPTIONS FOR BUPRENORPHINE INDUCTIONS

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project ECHO

SPEAKER DISCLOSURES

I have no actual or potential conflict of interest in relation to this program/presentation.

Planner disclosures

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

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OBJECTIVES

1. List **two** advantages of buprenorphine
2. Define precipitated withdrawal
3. Appreciate **two** emerging buprenorphine protocols and in what clinical scenarios each are indicated
4. Recognize **two** common pitfalls of buprenorphine induction and their countermeasures

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INTRODUCTION

- 3 million Americans meet criteria for opioid use disorder (OUD)
  - 47,000 deaths per year
- 35% of those with OUD get some form of treatment
  - 22% receive medication for OUD (MOUD)
- MOUD: **Buprenorphine**, Methadone, Naltrexone

-Jones CM, Han B, Baldwin GT, Einstein EB, Compton WM. Use of Medication for Opioid Use Disorder Among Adults With Past-Year Opioid Use Disorder in the US, 2021. JAMA Netw Open. 2023;6(8):e2327488. doi:10.1001/jamanetworkopen.2023.27488

INTRODUCTION

- Buprenorphine created in 1966
  - Synthetic analog of thebaine
  - Schedule III

- FDA approval
  - Acute and chronic pain
  - **Opioid dependence**

-Kumar R, Viswanath O, Saadabadi A. Buprenorphine. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. https://www.ncbi.nlm.nih.gov/books/NBK459126/
-Christian Heidbreder, Paul J. Fudala, Mark K. Greenwald. History of the discovery, development, and FDA-approval of buprenorphine medications for the treatment of opioid use disorder. Drug and Alcohol Dependence Reports, Volume 6, 2023, 100133, ISSN 2772-7246. https://doi.org/10.1016/j.dadr.2023.100133.

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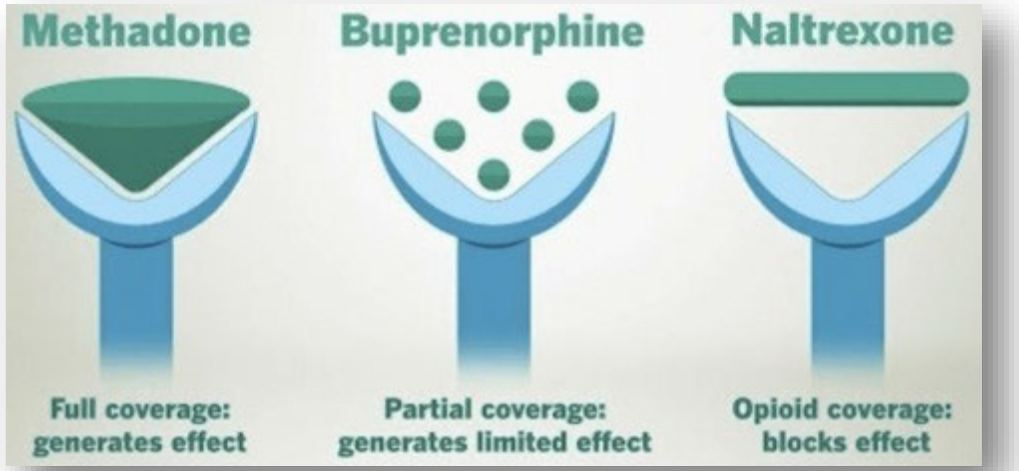
PHARMACODYNAMICS

- **Partial agonist of mu opioid receptors**
  - High affinity
  - Low efficacy
  - Slow dissociation

- **Ceiling effect** at the receptor
  - benefits up to at least 32 mg



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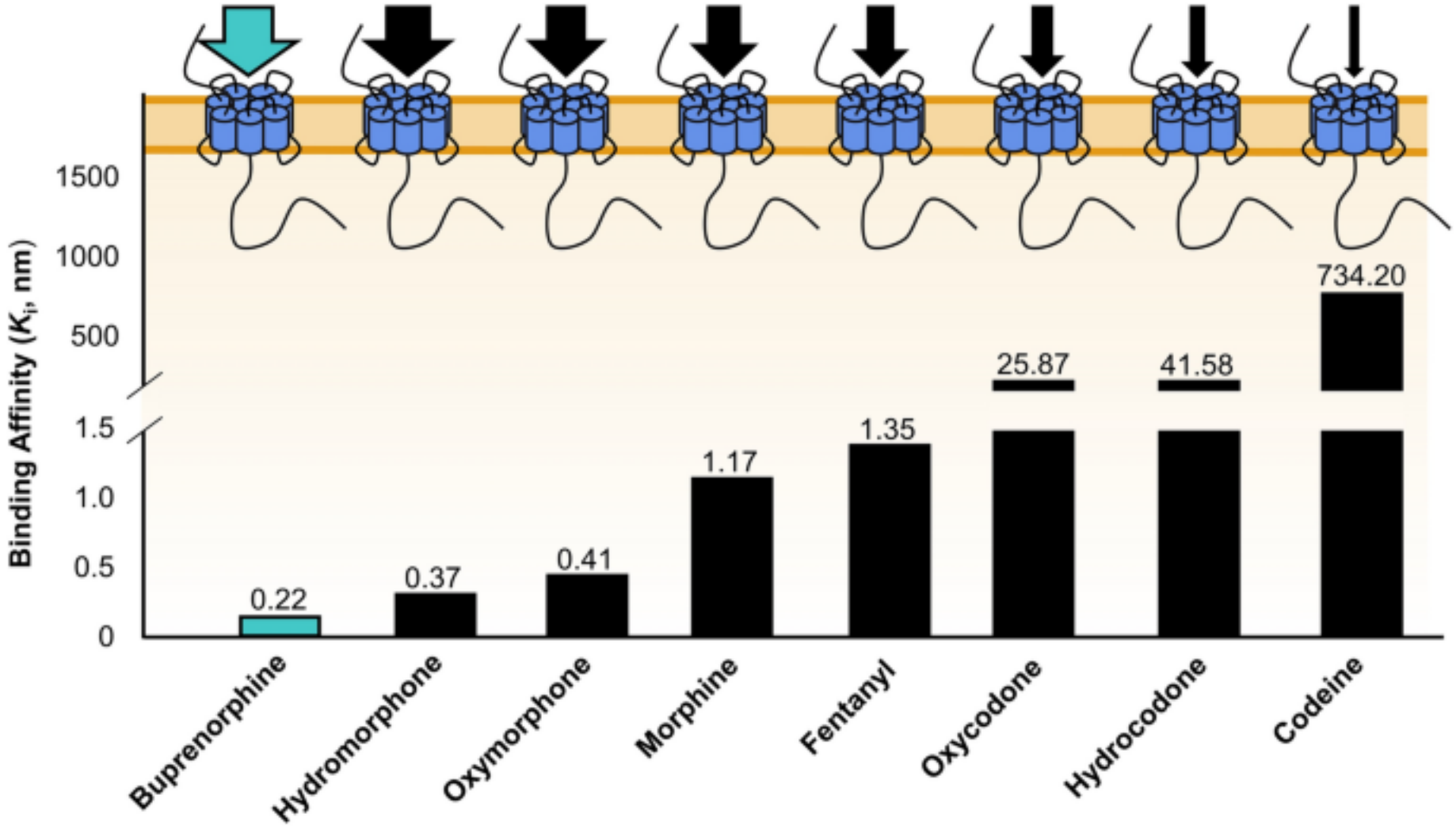

Gudin, J., Fudin, J. A Narrative Pharmacological Review of Buprenorphine: A Unique Opioid for the Treatment of Chronic Pain. Pain Ther 9, 41–54 (2020). https://doi.org/10.1007/s40122-019-00143-6

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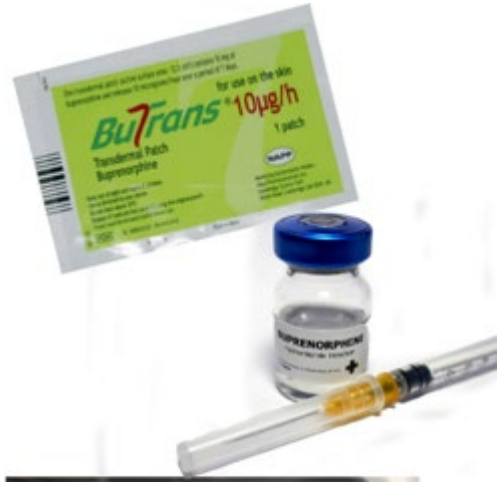
PHARMACOKINETICS

- Avoiding liver and intestine is best route for bioavailability
  - Sublingual, buccal, transdermal, subQ implants, IV, IM
- **Slow onset of action (3hrs)**
- Highly lipophilic
- Metabolized via CYP3A4
  - **34hr half life**
  - Forms norbuprenorphine



-Kumar R, Viswanath O, Saadabadi A. Buprenorphine. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. https://www.ncbi.nlm.nih.gov/books/NBK459126/

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ADVANTAGES

- **Less abuse potential**
- **Low risk of overdose**
- **Safe in pregnancy**
- **Anyone* can prescribe**
  - Mainstreaming addiction treatment (MAT) act
  - *DEA w/ schedule III permissions

Whelan PJ, Remski K. Buprenorphine vs methadone treatment: A review of evidence in both developed and developing worlds. J Neurosci Rural Pract. 2012 Jan;3(1):45-50. doi: 10.4103/0976-3147.91934.

ADVANTAGES

- Provides relief from withdrawal and craving
  - Allows focus on treatment
- Improves quality of life
  - Breaks the circle of seeking/using
  - Improves finances
- Reduces morbidity and mortality rates

Whelan PJ, Remski K. Buprenorphine vs methadone treatment: A review of evidence in both developed and developing worlds. J Neurosci Rural Pract. 2012 Jan;3(1):45-50. doi: 10.4103/0976-3147.91934.

OPIOID WITHDRAWAL

- **Physical manifestation of opioid dependence**
- **Usually not deadly**, but very uncomfortable
- May be sole reason for continued use of opioids
- Primary reason patients avoid buprenorphine

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DSM 5 Opioid Withdrawal

- A. Presence of either of the following:
  - **1. Cessation of or reduction in opioid use that has been heavy and prolonged**
  - **2. Administration of an opioid antagonist after a period of opioid use**
- B. **Three or more** of the following developing within **minutes to several days** after Criterion A
  - **1. Dysphoric mood**
  - **2. Nausea or Vomiting**
  - **3. Muscle Aches**
  - **4. Lacrimation or rhinorrhea**
  - **5. Pupillary dilation, piloerection, or sweating**
  - **6. Diarrhea**
  - **7. Yawning**
  - **8. Fever**
  - **9. Insomnia**
- C. Signs and Symptoms in B cause clinically significant distress or impairment….
- D. Signs or Symptoms..medical, mental, including **intoxication or withdrawal**…

American Psychiatric Association. (2022). Substance use disorders. In Diagnostic and statistical manual of mental disorders (5th ed., text rev.).

CLINICAL OPIATE WITHDRAWL SCALE

Patient's Name:_____ Date and Time ____/____/____:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.

***Goal for MOUD: COWS=11-12**

Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). J Psychoactive Drugs, 35(2), 253–9.

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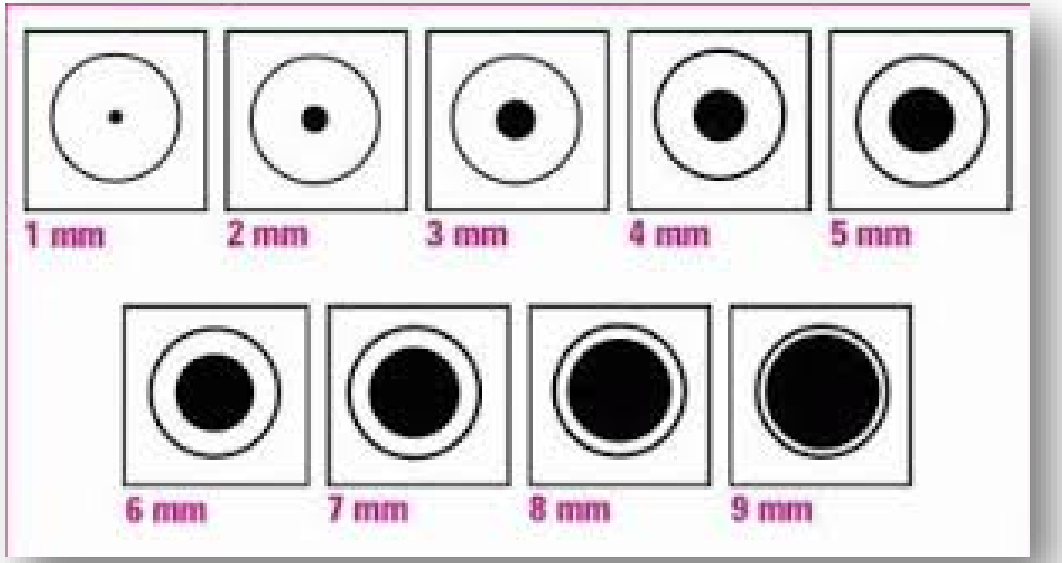
VALIDITY & RELIABILITY

- Highly subjective
- Shown to be both valid and reliable



Christian A. Tomaszewski, Faith Quenzer, Bryan Corbett, Andrew Lafree, Daniel Lasoff, Jorge Romo, Leslie Mukau, Interobserver agreement between emergency clinicians and nurses for Clinical Opiate Withdrawal Scale, JACEP Open, Volume 2, Issue 3, 2021, e12462, ISSN 2688-1152, https://doi.org/10.1002/emp2.12462.

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STANDARD INDUCTION

- Advantages:
  - Most well studied and described technique
  - Works for most mild to moderate potency opioids

- Considerations:
  - Requires withdrawal
  - May need adjuvant medications
  - Takes 1-3 days to stabilize
  - **Must know what opioid your patient is taking**

STANDARD INDUCTION

- Protocol:
  1. Patient in mild/moderate withdrawal
  2. Start buprenorphine 2-4mg
  3. Wait 1-2 hours and reassess withdrawal
  4. Additional buprenorphine 2-4mg if continued withdrawal symptoms
  5. Repeat steps 3 & 4 until withdrawal controlled or 16-24mg total dose for day 1
  6. Take day 1 dose at start of day 2, repeat steps 3 & 4 as needed until withdrawal controlled or 32mg total dose
  7. Repeat day 2 dose for subsequent days

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THE FENTANYL PROBLEM

- High Potency Synthetic Opioid
  - **50-100x potency of morphine**
  - Rapid onset, rapid fat sequestration
  - Delayed clearance
  - **Unpredictable withdrawal course**
  - Implicated in buprenorphine precipitated withdrawal

- **Illicit opioids are Fentanyl until proven otherwise**

Kehoe L. *Buprenorphine: Novel Induction Strategies.* [Powerpoint Slides]. Psychiatry Academy. Massachusetts General Hospital. www.mghcme.org.

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PREBUPRENORPHINE OPIOID BALANCE

- **Higher the balance, likelihood of precipitated withdrawal**

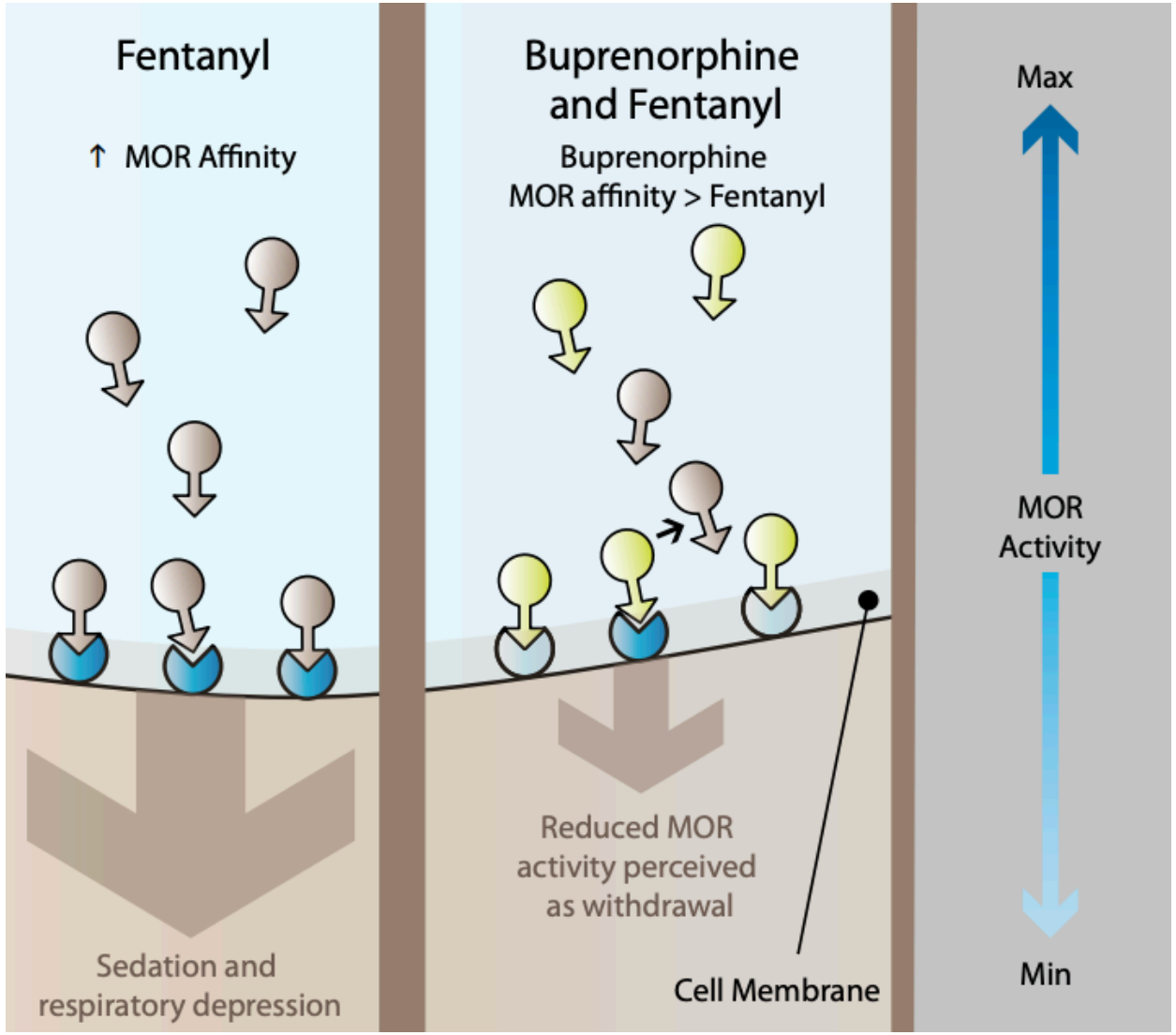
- Characteristics of importance
  - Affinity for receptor
  - Effect size
  - Lipophilicity

- High: **fentanyl**, fentanyl analogs, hydromorphone

- Intermediate: methadone

- Low: oxycodone, hydrocodone, heroin, morphine, kratom, codeine

Greenwald MK, Herring AA, Perrone J, Nelson LS, Azar P. A Neuropharmacological Model to Explain Buprenorphine Induction Challenges. Ann Emerg Med. 2022 Dec;80(6):509-524. doi: 10.1016/j.annemergmed.2022.05.032.



De Aquino JP, Parida S, Sofuoglu M. The Pharmacology of Buprenorphine Microinduction for Opioid Use Disorder. Clinical Drug Investigation. 2021 May;41(5):425-436.

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PRECIPITATED WITHDRAWAL

- Rapid worsening of withdrawal symptoms post opioid partial agonist/antagonist
  - **COWS increase >5**
- Leads to poor outcomes and buprenorphine avoidance
- Different than undertreated withdrawal
  - Some or no improvement in symptoms

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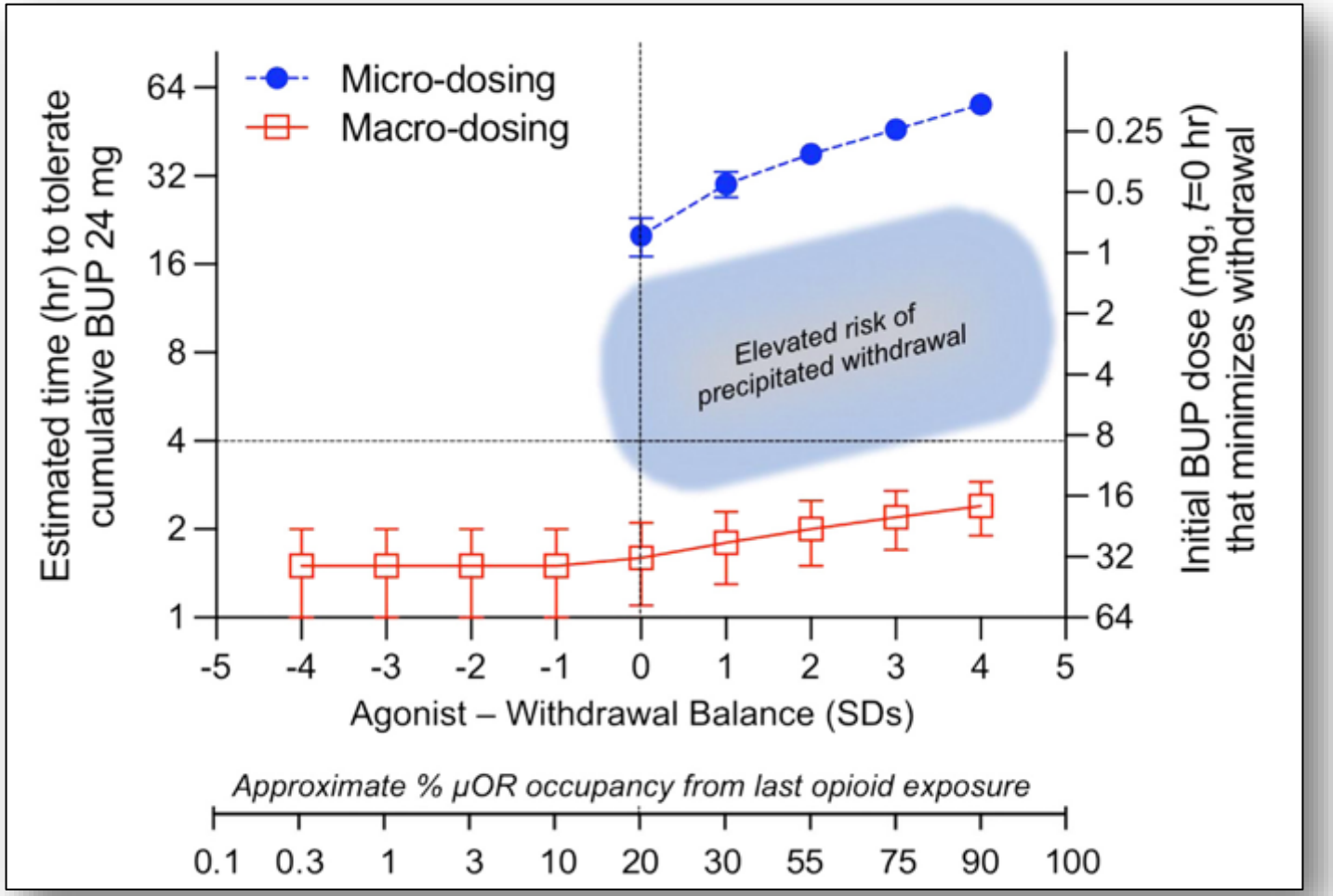
PRECIPITATED WITHDRAWAL



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HIGH DOSE INDUCTION

- Advantages:
  - **Rapid dose stabilization (hours) minimizes period of undertreatment**
  - Simple instructions
  - Bridges access barriers to medication
  - Protective against overdose

- Considerations:
  - **Requires opioid withdrawal (COWS 11-12+)**
  - Patient will be on high dose of buprenorphine
  - Emergency department, hospitalize, or outpatient

Greenwald MK, Herring AA, Perrone J, Nelson LS, Azar P. A Neuropharmacological Model to Explain Buprenorphine Induction Challenges. Ann Emerg Med. 2022 Dec;80(6):509-524. doi: 10.1016/j.annemergmed.2022.05.032.

HIGH DOSE INDUCTION

1. Patient is in withdrawal (16+ hours)
2. **Start buprenorphine 16-24mg*****
3. Wait 1-2 hours and reassess withdrawal
4. If withdrawal partially improved, give 4-8mg and reassess
5. If precipitated withdrawal, repeat initial dose
6. Repeat steps 3-5 until withdrawal controlled **(up to 64mg TDD)**
7. Take day 1 dose for subsequent days

***earlier in withdrawal the larger the first dose**

Kehoe L. *Buprenorphine: Novel Induction Strategies.* [Powerpoint Slides]. Psychiatry Academy. Massachusetts General Hospital. www.mghcme.org.

LOW DOSE INDUCTION

- Advantages:
  - **Patient does not need to be in withdrawal**
  - **Does not require patient to be abstinent first**

- Considerations:
  - **High care coordination**
  - Longest period before stabilization (3-10+ days)
  - Can be done with or without opioid continuation
  - **Hospitalized** or outpatient with close follow up

Greenwald MK, Herring AA, Perrone J, Nelson LS, Azar P. A Neuropharmacological Model to Explain Buprenorphine Induction Challenges. Ann Emerg Med. 2022 Dec;80(6):509-524. doi: 10.1016/j.annemergmed.2022.05.032.

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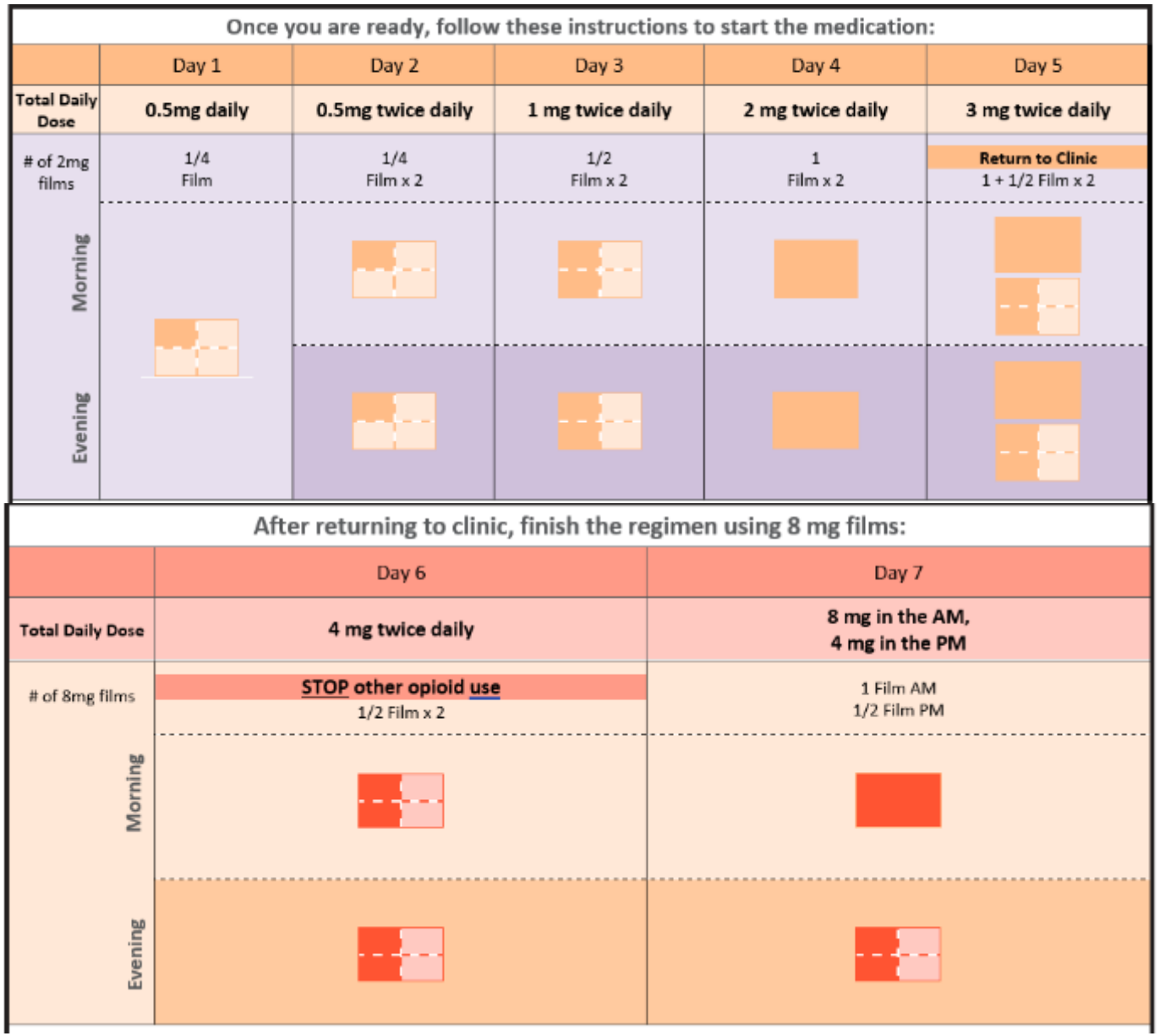
LOW DOSE INDUCTION



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LOW DOSE INDUCTION

Day of transition	Becker, et al. Bup/nlx dose	Terasaki, et al. Bup/nlx dose	Weimer, et al. Buccal Bup + Bup/nlx Hospital Based
1	Bup/nlx 0.5mg BID (+ OA)	Bup/nlx 0.5mg daily (+ OA)	Bucccal Bup 225mcg (+OA)
2	Bup/nlx 1mg BID (+ OA)	Bup/nlx 0.5mg BID (+ OA)	Buccal Bup 225mcg BID (+ OA)
3	Bup/nlx 1mg TID (+ OA)	Bup/nlx 1mg BID (+ OA)	Buccal Bup 450mcg BID (+ OA)
4	Bup/nlx 2mg TID (+ OA)	Bup/nlx 2mg BID (+ OA)	Bup/nlx 2mg BID (+ OA)
5	Bup/nlx 4mg TID (+ OA)	Bup/nlx 4mg BID (+ OA)	Bup/nlx 4mg BID (+ OA)
6	Full transition complete	Bup/nlx 4mg TID (+ OA)	Bup/nlx 4mg TID (+ OA)
7		Full transition complete	Full transition complete

Kehoe L. *Buprenorphine: Novel Induction Strategies.* [Powerpoint Slides]. Psychiatry Academy. Massachusetts General Hospital. www.mghcme.org.

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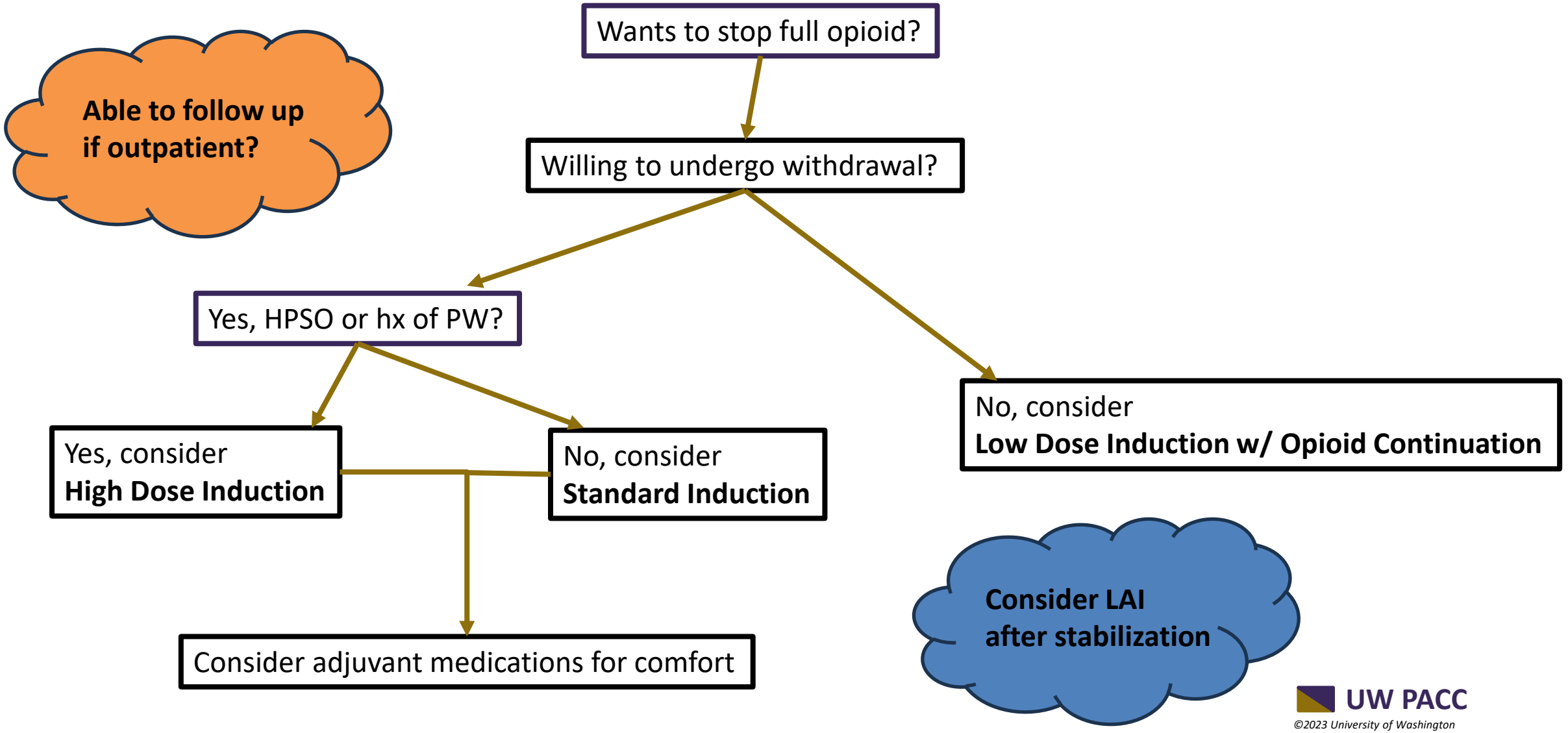
PATHWAY



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PITFALLS

- “I can’t wait long enough”
- “It doesn’t work for me”
- “It makes me sick”
- “It doesn’t help my pain”

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ADJUVANT MEDICATIONS

- **Clonidine**, loratadine: autonomic symptoms
- **Hydroxyzine**, BZNs, SGAs: agitation/anxiety
- **Metoclopramide, ondansetron**: nausea
- **Dicyclomine**: GI cramping
- **Ibuprofen, Acetaminophen**, gabapentin: aches/pains/headaches

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OTHER CONSIDERATIONS

- Emerging induction strategies
  - Ketamine
  - Hydromorphone or Methadone in IP
- Transition to injectable buprenorphine
  - Sublocade (monthly)
  - Brixadi (weekly & monthly)

Daily Sublingual Buprenorphine Dose*	BRIXADI Weekly	BRIXADI Monthly
≤6 mg	8 mg	-
8-10 mg	16 mg	64 mg
12-16 mg	24 mg	96 mg
18-24 mg	32 mg	128 mg

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SUMMARY AND KEY TAKE AWAYS

- Buprenorphine has high affinity for opioid receptor and low efficacy which makes it safe and effective for treating OUD
- Can treat opioid withdrawal if full opioid agonist balance is low
- Can cause precipitated withdrawal if balance is high (common in fentanyl era)
- High dose and low dose w/ OC buprenorphine initiations help to mitigate the risk of PW and improve likelihood of success

SUMMARY AND KEY TAKE AWAYS

- High dose useful in ED and outpatient settings when patient in withdrawal
- Low dose w/ OC useful in hospital and outpatient settings when patient is still using opioids or is fearful of withdrawal
- Use comfort medications!
- Consider transition to LAI

RESOURCES

- Psychiatry Consult Line
  - https://pcl.psychiatry.uw.edu/
  - 877-WA-PSYCH (877-927-7924)
  - Prescribing providers call any time, 24/7, Non-prescribing providers call Mon-Fri, 8-5 (excluding holidays)
  - **They take all OUD questions**

- https://scalanw.org/
  - Provides tools for clinicians and patients for opioid inductions
  - Information on syringe service programs, infectious disease screening, naloxone distribution, and low barrier drop in MAT programs

THANK YOU!

QUESTIONS?

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