ADVANCED BUPRENORPHINE PRESCRIBING STRATEGIES

In Era of High Potency Synthetic Opioids (HPSOs)

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DISCLOSURE INFORMATION

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Commercial Interests: The presenter has no commercial interests or endorsements to declare.

Off-label Use: Discussion of off-label uses will be included where relevant.

OBJECTIVES

FORMULATION KNOWLEDGE	Gain a comprehensive understanding of various buprenorphine formulations and their specific roles in treating opioid use disorder (OUD).
CHALLENGES	Understand the clinical challenges in prescribing during the fentanyl era
NOVEL PRESCRIBING STRATEGIES	Learn innovative buprenorphine prescribing methods for induction, transitioning between formulations, and tapering off suboxone effectively.

Buprenorphine Formulations		
Short-Acting		
Formulation	**Brand Name**	**Dosage Forms**
Buprenorphine	Subutex, generic	SL tablet 2 mg, 8 mg
	Butrans*	Transdermal patch 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, 20 mcg/hr
	Belbuca*	Buccal film 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, 900 mcg
	Buprenex, generic*	IV or IM injection 0.3 mg/mL
Buprenorphine/ naloxone	Generic	SL tablet 2/0.5 mg, 8/2 mg
	Suboxone	SL film 2/0.5 mg, 4/1 mg, 8/2 mg, 12/3 mg
	Zubsolv	SL tablet 0.7/0.18 mg, 1.4/0.36 mg, 2.9/0.71 mg, 5.7/1.4 mg, 8.6/2.1 mg, 11.4/2.9 mg
	Bunavail	Buccal film 2.1/0.3 mg, 4.2/0.7 mg, 6.3/1 mg
Long-Acting		
Buprenorphine	Sublocade	SC injection 100 mg, 300 mg
	Brixadi	SC injection 8 mg, 16 mg, 24 mg, 32 mg (weekly) and 64 mg, 96 mg, 128 mg (monthly)

**Approved for pain only, not opioid use disorder*

The Changing Landscape of OUD Treatment

Impact of Fentanyl on Treatment

- The rise of fentanyl has led to a significant increase in overdose deaths, posing new challenges for treatment.
  Withdrawal symptoms may not appear for 24-48 hours after the last use
  The major research on prescribing medications for opioid use disorder (MOUD) was done before fentanyl became much more prevalent than heroin

Pharmacology

Understanding Fentanyl

Fentanyl's Key Properties

- Fentanyl is a full mu-opioid agonist that is 50-100 times more potent than morphine, leading to rapid onset of effects.
  Its high lipophilicity allows it to accumulate in adipose tissue, resulting in prolonged and unpredictable withdrawal symptoms.
  The strong receptor binding of fentanyl increases the risk of precipitated withdrawal when transitioning to other opioids such as buprenorphine.
  Traditional induction strategies for buprenorphine may not work effectively for fentanyl users due to these unique pharmacological characteristics.

Opioids

Fentanyl

Fentanyl's Dominance in the Opioid Market

- Fentanyl has surpassed heroin as the leading non-prescribed opioid in the US.
  Accounts for over 80% of opioid-related overdose deaths, according to CDC 2023.

Comparing Fentanyl and Heroin

- In 2022, fentanyl caused over 70,000 overdose deaths, mainly from synthetic opioids.
  Heroin-related deaths were about 13,000, showing a declining trend.
  Fentanyl's lower production cost and higher profitability have decreased heroin availability.

Health Risks

Adulterants in Non-Prescribed Fentanyl Supply

Why Adulterants Are Used

- To increase profits by bulking up the product.
To mimic or enhance the effects of other drugs.
To evade drug detection methods.

Common Adulterants in Fentanyl

- Xylazine ("Tranq"): A veterinary sedative not approved for human use.
Benzodiazepines: Increase sedation and respiratory depression, complicating overdose treatment.
Caffeine/Levamisole: Used to mimic stimulants or bulk up the product.

Concerns

Xylazine

Impact of Xylazine on Opioid Users

- Xylazine is a veterinary sedative increasingly found mixed with opioids like fentanyl. It enhances the risk of fatal respiratory depression when combined with opioids. Users may experience severe infections, wounds, necrosis and sometimes require

Prevalence and Public Health Concerns

- In 2021-2022, up to 80% of fentanyl-positive syringes tested positive for xylazine in Maryland. Reports indicate rising cases of xylazine-related overdoses and complications among opioid users. Public health officials are concerned about the growing prevalence and its impact on treatment strategies.
- Naloxone reversal less effective if xylazine is an adulterant

Pharmacology of Buprenorphine

Buprenorphine: Partial Mu-Opioid Agonist

- High affinity for mu-opioid receptors, providing analgesic effects.
  Slow dissociation from receptors leads to a ceiling effect on respiratory depression, enhancing safety.
  Displaces full agonists like fentanyl but can precipitate withdrawal if not managed properly.

Fentanyl and Derivatives

Definition of Highly Potent Synthetic Opioids (HPSO)

- HPSOs are a class of full agonists at the μ-opioid receptor with very high potency, including fentanyl and its analogues.
  Analogues of fentanyl include sufentanil, alfentanil, remifentanil, carfentanil, and thiofentanil.

Properties and Impact

- HPSOs have a diversity among agents for selectivity at mu receptors, some with delta and kappa receptor interactions.
  Fentanyl and its analogues are now primarily sourced from illicit markets, initially from China, now increasingly from Mexico and India.
  These substances pose significant public health challenges due to their potency, potential for development of use disorders and high rates of overdose.

Novel Induction Strategies

Novel induction strategies for opioid agonist treatments (OAT) have emerged to address the challenges faced by patients physiologically dependent on fentanyl. Traditional approaches often lead to increased rates of precipitated withdrawal when standard doses of buprenorphine are used and traditional methadone dosing is too low to stabilize heavy fentanyl use

Novel Approaches

- **Low Dose Initiation / Bernese Method**
- **High Dose Buprenorphine Induction**
- **High Dose Methadone Induction**

Buprenorphine Initiation Approaches

Traditional Buprenorphine Initiation	Involves gradual dose escalation over 2-3 days. Patients are expected to abstain from full opioid agonists during this period.
Low Dose Buprenorphine with Opioid Continuation (LDB-OC)	Allows for administering small, gradually increasing doses of buprenorphine while continuing a full agonist opioid over 2-7 days. Initial doses are typically <2mg, making it suitable for patients who cannot tolerate abstinence.
High-Dose Buprenorphine Induction	Targets rapid stabilization for patients at high risk of overdose. Observed dose-response suggests that a rapid escalation to 24-32 mg SL on day 1 is well tolerated, minimizing undertreatment.

Novel Induction Strategies

LOW DOSE INITIATION (LDI) / Bernese Method

- LDI allows for small, incremental doses of buprenorphine without stopping the full agonist or waiting for withdrawal symptoms to emerge.
- This approach has been successfully employed in various situations
- Studies have shown that LDI can achieve successful induction rates comparable to traditional methods, while minimizing withdrawal and enhancing patient engagement in treatment.
- Proving to be very useful and often preferred by patients as there is no or very minimal clinically significant withdrawal symptoms.

Low Dose Induction (LDI)

Overview and Applications

- Multiple protocols in the literature.
  Typical inductions start with 0.5 to 1 mg sublingual buprenorphine and titrate up to 12-16 mg over 5-8 days.
- No RCTs yet, but hundreds of encouraging case reports over the last 5 years.
- Widely used in clinical practice based on expert consensus
- If on prescribed opioids, patients remain on their current opioids through the process until the last day of titration
- As with standard inductions, not always effective.
- Efficacy improves with higher communication during titration, RN support, messaging portal access, etc.
  Case studies have shown LDI to be effective in chronic pain patients who must come off full agonists.
- If using street fentanyl, standard induction is preferred if they are able
  - If unable, this is a preferred strategy as they are continuing to use wile titration is proceeding
  - Harm reduction education is key

Patient Instructions (Smartphrase & Printout)		Prescriber Instructions
Day	Number of film(s) per dose buprenorphine-naloxone 2 mg – 0.5 mg film strip	Dose
1	One quarter film once	0.5mg qd
2	One quarter film twice a day	0.5mg BID
3	One half film twice a day	1mg BID
4	1 film twice a day	2mg BID
5	2 films twice a day	4mg BID
6	2 films three times a day	4mg TID
7	Switch to 8mg films, take one twice a day. STOP opioids	8mg BID
	You may repeat a day if needed	Orderset: 14 2mg & 2 8mg Films. Smartphrase: documenting in plan

Low dose initiation of Buprenorphine

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Buprenorphine dose	0.5mg daily	0.5mg BID	1mg BID	2mg BID	4mg BID	4mg TID	8mg BID
Film size	2mg	2mg	2mg	2mg	2mg	2mg	8mg
Morning dose							
Afternoon Dose							
Night dose							
Full agonist	Continue	Continue	Continue	Continue	Continue	Continue	STOP

Treatment Strategy

When to Use LDI

High Opioid Tolerance

Patients with high opioid tolerance, such as those using large amounts of fentanyl, on methadone maintenance or on chronic opioids for pain, are prime candidates for LDI to mitigate withdrawal symptoms.

History of Precipitated Withdrawal

Individuals with a history of precipitated withdrawal may benefit from LDI, as it allows for a more controlled transition to buprenorphine.

Anxiety About Withdrawal Symptoms

Patients with significant fear or anxiety about withdrawal symptoms often prefer this approach.

Tips for Successful Initiation

Tips for Successful Initiation

- Only use strips if possible; pills do not split well.
  Take it slow unless there is a time constraint; if symptoms of withdrawal occur, repeat that day's dose for an additional day before gradually increasing again.
  Use symptomatic treatment to assist the process
- involving peer navigators or nurse specialists can enhance support.

Considerations

- Some providers believe it is more effective to use monoproducts due to potentially less gastrointestinal symptoms.
  No significant overdose protection until upper end of titration
  - Harm reduction:
    - Overdose and naloxone education, use with someone with naloxone that knows how to use it
    - Reduce use during the process as tolerated
    - No sourcing from unknown / new dealers
    - No mixing with alcohol or other substances

Novel Induction Strategies

HIGH-DOSE BUPRENORPHINE INDUCTION

Core Principles:

- Traditional buprenorphine induction often insufficient for HPSO-dependent individuals
- Failure to use adequate dosing results in:
  - Untreated withdrawal symptoms
  - Early treatment discontinuation
  - Patient loss of confidence in treatment effectiveness
- Key study (D'Onofrio et al., JAMA Network Open 2023):
  - 1200 enrolled patients
  - 70% fentanyl-positive
  - Only 0.76% precipitated opioid withdrawal (POW)
- Contrasts with previous study showing up to 22% (POW)
- Until clarified, **primarily for patients in ED or inpatient**

High Dose Buprenorphine – “Macro-induction” Strategy

01

Dosing Targets and Protocols

- Traditional buprenorphine involves gradual dose escalation over 2-3 days.
  Observed dose-response suggests rapid escalation to a 24-32 mg SL on day 1 is well tolerated per the D’Onofrio study, though data is mixed
  Wait 36-48 hours from last use to give >16mg at one time.
  Wait 6-12 hours from last use to give >24mg at one time.

02

Patient Outcomes and Considerations

- Minimizes period of undertreatment and rapidly maximizes agonism.
  Accelerates dosing once withdrawal has begun with initial target of ≥24 mg SL in 1 or 2 doses.
  High-dose strategy is especially beneficial for individuals at very high risk of overdose.
- If POW occurs, can require more aggressive treatment than LDI

High vs. Low-Dose Buprenorphine

High-Dose Buprenorphine

- High-dose induction typically involves administration of 8-16 mg in under 2 hours.
  A study of 391 ED patients found that after 4-8 mg starting dose, 63% had inadequate symptom control, leading to recommendations for >12 mg dosing.
  Precipitated withdrawal was more common in the non-high dose cohort.
  Patients who received higher doses reported better control of withdrawal symptoms and reduced dropout rates during treatment.
- Recommended for ED and inpatients
- For outpatients, a less aggressive approach is recommended but more aggressive than standard induction for HPSO users
- Agonism > antagonism at higher buprenorphine doses

Low-Dose Buprenorphine

- Low-dose induction often starts with 0.5 to 1 mg SL buprenorphine, titrating up to 12-16 mg over 5-8 days. **Success rates identical to traditional induction but much more versatile and comfortable for the patient**
- Versatility:
  - Can use for people who cannot stop use / fearful of withdrawal
  - People who need to transition from methadone even if they can’t reduce to 30mg
  - People on chronic opioids for pain who are transitioning for safety profile or aberrant use

Patient Discomfort During Buprenorphine Initiation

Causes of Discomfort:

• Ongoing Opioid Withdrawal Symptoms (OWS) - Most common cause, occurs when combined agonism of buprenorphine and FAO is below baseline tolerance

• Withdrawal from other substances - May complicate the clinical picture

• Adverse effects - Including nausea and other medication side effects

• Precipitated Opioid Withdrawal (POW) - Rare (<1% in ED initiations)

Key Mechanisms:

• Patient comfort depends on balance between buprenorphine agonist effects and FAO effects

• Most effective treatment is additional buprenorphine once MORs are bound

• Ceiling effect well-demonstrated for respiratory depression but unknown for other effects

Managing Mild to Moderate OWS

Primary Treatment Strategy:

- Rapid dose escalation of buprenorphine up to 24-32mg SL per day
- Considered safe and most effective first-line approach
- Particularly indicated for patients with high opioid tolerance

Supporting Interventions:

- Alpha-2 agonists - Premedication recommended to reduce OWS severity
- Symptom-directed adjunctive medications

Severe OWS and Intracrable POW Management

Emergency Department Care:

- Required for severe cases unresponsive to initial treatment
- Rapid maximization of buprenorphine MOR activation
- Dose escalation up to 64mg SL reported in literature

Advanced Interventions:

- Ketamine: 0.3 mg/kg boluses over 10-15 minutes or continuous infusion
- Dexmedetomidine (IV alpha-2 agonist)
- High-affinity FAOs while maintaining buprenorphine

Adjunct Medications:

- Benzodiazepines - Targeted for persistent agitation/anxiety
- Antipsychotics - Used sparingly for severe cases
- Multimodal approach often necessary for intractable cases

High-Dose Induction - Methadone

- Methadone does not precipitate withdrawal as it is a full agonist, but it is difficult to switch someone from methadone to a partial agonist.
- Buprenorphine is typically preferred choice of MOUD given less risk of respiratory depression, overdose, and availability through office-based prescribing
- Methadone requires going to a specialized methadone clinic or Opioid Treatment Program (OTP) regularly and at strict times, which limits access

High-Dose Induction - Methadone

- Typical methadone induction was 30 mg to start, then 5-10 mg increase every 3 - 5 days. It would take over 1 month to reach 120 mg a day typically needed for those HPSO-dependent, so dropout would be excessive and higher risk of overdose.
- New inductions as rapid as 40-60-80 mg over 3 days, followed by 10-20 mg every 4 days are described but MUST monitor closely for over-accumulation!
- A less aggressive acceleration is starting at 30 mg, then 50 mg day 3, followed by 20 mg increase per week.

Opioid Treatment Programs (OTPs)

Role of Medical Director

The medical director must be a physician and oversees all clinical operations of the treatment program.

Methadone Prescribing Restrictions

Office-based methadone prescribing is restricted to pain management, not for OUD, requiring federal/state approved OTPs.

Methadone Dispensing

Methadone is dispensed in a metered fashion to prevent diversion and misuse

Role of Program Sponsor

The program sponsor oversees regulatory compliance, staffing, and finances of the OTP.

Drug Testing for Compliance

OTPs must perform urine drug testing upon admission and at least eight additional times yearly to monitor compliance.

Clinical Considerations

Methadone Contraindications & Precautions

01

Hypersensitivity

Patients with known hypersensitivity to methadone or any of its components should not receive methadone treatment.

02

Respiratory Depression

Methadone should not be administered to individuals experiencing respiratory depression, including those with severe COPD or severe obstructive sleep apnea.

03

Concurrent CNS Depressants

Caution is advised when prescribing methadone alongside other CNS depressants, including alcohol, other opioids, and benzodiazepines.

04

Liver Disease Risks

Patients with liver disease require careful monitoring and may have an increased risk of adverse effects due to altered drug metabolism.

05

QTc Prolongation

An electrocardiogram (ECG) should be performed if QTc exceeds 450ms, and treatment should be closely monitored for those with QTc over 500ms.

Extended -Release Buprenorphine (BXR)

Introduction

- Sublingual formulation of buprenorphine approved in US in 2002 for opioid use disorder
  - Very effective and adopted widely
  - Main disadvantages are noncompliance and diversion
- 1st BXR approved in the US in 2017 (Sublocade) for the treatment of moderate-severe OUD after stabilization on SL buprenorphine for 1 week (available since 2019)
  - Two available strengths, 300 mg and 100 mg
  - SC abdominal injection every 4 weeks
  - Cost is approximately $1700 per injection
  - Rapid induction to Sublocade may be safe and feasible (Mariani 2020, Mariani 2021)

Extended - Release Buprenorphine (BXR)

2nd BXR approved in 2018 (Brixadi US; Buvidal EU).
Commercially available in the US in 2023

- Weekly (8, 16, 24 or 32 mg)
- Monthly (64, 96, 128)
- Can be injected into buttock, thigh, abdomen, or upper arm
- Initiate treatment with 4 mg test dose SL buprenorphine, then weekly Brixadi injection
- Monthly formulation not studied for new buprenorphine treatment starts, but fine if already on some form of buprenorphine

Extended -Release Buprenorphine (BXR)

- High effectiveness, better results than traditional methods.
  Improved retention, patient satisfaction.
  Beneficial for patients at very high risk, with compliance issues or who have had insufficient response to SL treatment.
- Known overdose protection for > 1 month

- High cost per injection, approximately $1700, which may be prohibitive for some patients or healthcare systems.
  Risk of noticeable injection site nodules and reactions
  Limited availability in some regions.

Transition of Patients Established on Long-term Treatment with Transmucosal Buprenorphine Whose Disease Symptoms are Controlled

Transmucosal Buprenorphine Doses	SUBLOCADE		
	Injection #1	Injection #2	Maintenance Dose
8 – 18 mg/day	300 mg	100 mg*	100 mg
20 – 24 mg/day	300 mg	300 mg	100 mg

*For patients still experiencing craving or withdrawal symptoms after the initial 300-mg dose, consider giving 300 mg as the second dose

Pharmacokinetic parameters	Transmucosal Buprenorphine				SUBLOCADE	
	8 mg	12 mg	16 mg	24 mg	100 mg	300 mg
$C_{avg,ss}$ (ng/mL)	1.37 (40)	1.79 (40)	2.16 (40)	2.84 (40)	2.87 (32)	6.32 (32)
$C_{max,ss}$ (ng/mL)	4.27 (45)	5.60 (45)	6.77 (45)	8.86 (45)	5.10 (33)	11.81 (35)
$C_{trough,ss}$ (ng/mL)	0.66 (63)	0.87 (63)	1.04 (61)	1.37 (62)	2.46 (40)	5.47 (39)

Drug product dose			C_{av} (ng/mL)			C_{max} (ng/mL)			C_{trough}[a] (ng/mL)		
SL BPN	Brixadi (weekly)	Brixadi (monthly)	SL BPN *	Brixadi (weekly)	Brixadi (monthly)	SL BPN *	Brixadi (weekly)	Brixadi (monthly)	SL BPN *	Brixadi (weekly)	Brixadi (monthly)
8 mg	16 mg	64 mg	1.2	2.1	2.0 $	4.7	4.3	4.0 $	0.7	0.8	1.3 $
16 mg	24 mg	96 mg	1.8	2.9 $	2.9 $	6.5	5.5 $	6.0 $	1.0	1.4 $	2.0 $
24 mg	32 mg	128 mg	2.5	4.2	3.9	8.2	6.9	11.1	1.4	2.6	2.1

Novel Prescribing Strategies for HPSO era

Switch to BXR

- Risky patients w/ multiple ODs and/or heavy fentanyl users i.e multiple “bundles (grams)” per day - despite SL bup 20+ mg/day, or who are inconsistent w/ adherence
- Two 300mg loading doses, may require ongoing 300mg doses qmo if destabilize at 100mg dose reduction. Often 300mg qmo can stabilize. OD protection higher even if they continue to use.
- If 300mg ineffective, refer to methadone clinic/OTP. Methadone has no ceiling dose.

Novel Prescribing Strategies for HPSO era

OD risk mitigation

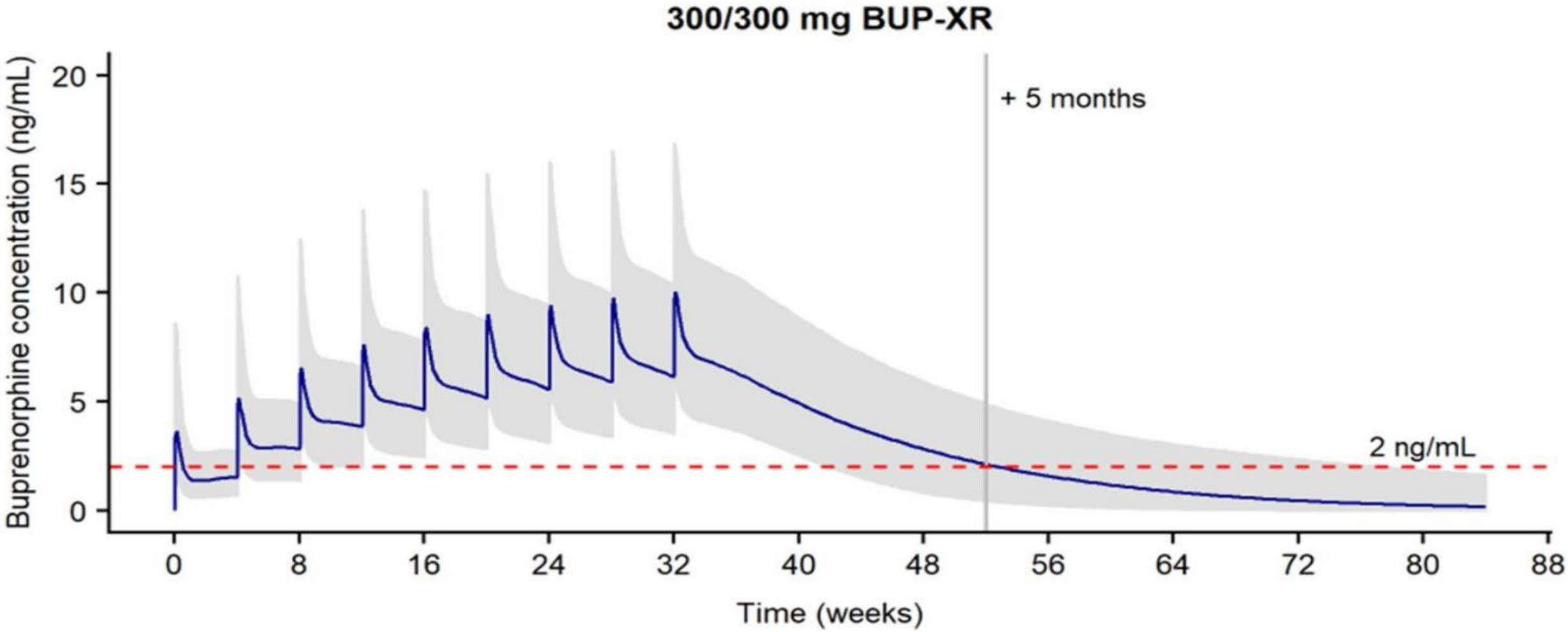
- BXR x1 from ED, residential or hospital at discharge for high-risk patients, such as those who came in w/ OD – very likely provides mortality benefit for several weeks as compared to 3–7-day suboxone rx. Discharge is very high OD risk period
- Consider in pt's who have overdosed or otherwise very high risk and discharging from hospital / residential treatment. Must prove toleration with at least one SL dose challenge
- Cons: Rapid induction is off label use. Supported by some rapid XR induction case series only.

Novel Prescribing Strategies

- Addiction docs increasingly using BXR to taper people off SL bup if stuck
  - BXR self tapers more gradually than possible w/ cutting strips/pills
- Only two published case series showing effectiveness of this approach
  - many colleagues having success however, with happy patients!
- My approach, stop SL w/in one week of injection:
  - If SL bup dose >12 mg qd, start w/ 300mg x1
    - If SL < 12 mg qd, 100mg x1 ,
  - If pt later reports w/d, repeat x1 or try clonidine + PRNs
- Case studies vary- show success w/ single dosing and longer term dosing up to 11x.
  - 7 patients total, one relapse. All did meet goal of d/c
- Half life up to 60 days for 300mg dose, can take nearly a year to eliminate fully, self tapering. Had patient get dose in July ’24, January’25 requested repeat.

Novel Prescribing Strategies

- Case studies vary- show success w/ single dosing and longer term dosing up to 11 injections.
  - First series 3 patients all tapered w/ 100mg x1. No relapses. All successful.
  - Second 4 patients – pts continued until ready to stop 3-11x. All ultimately met goal of d/c but there was one brief relapse.
- Half life up to 60 days for 300mg dose, can take nearly a year to eliminate fully, self tapering.
  - One pt of mine was dosed 300mg x1 in July ’24, started to feel withdrawal in January. S/p 100mg x1 booster now
- Consider for those in long term recovery who want to come of buprenorphine and feel ready.
  - Stable patients who wanted to stop bup for 5, 10+ years now are ideal candidates



Pharmacokinetics: C_{avg} mean plasma concentration

Key Takeaways & Implementation Tips:

Easing into to novel strategies

Highest Impact, most versatile, and best strategies to start with:

- **Low dose induction – LDI**
  - Familiarize with one protocol. (I have used the same for 6 yrs)
  - Identify a patient who did not have a successful induction and is still using fentanyl or non prescribed opioids
    - If on methadone, probably not the best to start with – trickiest. OTP can usually do it for patient.
- **Buprenorphine XR - BXR**
  - Familiarize with one product and where pt may obtain it
  - Sublocade more straightforward, highest mean dose option
    - Limited utility of weekly XR dosing, though can consider for pregnancy – less ingredients
  - Identify a patient whose outcome may be helped
- **Teach them** about the options. If they are very interested, start, bring in a colleague, or refer to addiction med/psych.
- The chances lives will be saved are **VERY HIGH**

Patient Instructions (Smartphrase & Printout)		Prescriber Instructions
Day	Number of film(s) per dose buprenorphine-naloxone 2 mg – 0.5 mg film strip	Dose
1	One quarter film once	0.5mg qd
2	One quarter film twice a day	0.5mg BID
3	One half film twice a day	1mg BID
4	1 film twice a day	2mg BID
5	2 films twice a day	4mg BID
6	2 films three times a day	4mg TID
7	Switch to 8mg films, take one twice a day. STOP opioids	8mg BID
	You may repeat a day if needed	**Orderset**: 14 2mg & 2 8mg Films. **Smartphrase**: documenting in plan

Tailor to the patient

Supportive medication (non-benzo, non-barbiturate)

Drug	Class/action	Target
Ibuprofen 400mg PO Q6hrs	NSAID	Pain
Loperamide 4g PO Q4hrs	Gut opioid stimulant	diarrhea
Clonidine 0.3 mg QID	Alpha-2 agonist	Anxiety, restlessness
Gabapentin 900mg TID	Gaba+ reduces CNS excitation	Anxiety
Ondansetron 4mg PO Q 4hs	5-HT3	nausea
Baclofen 20mg TID	GabaB agonist	anxiety , tremor
Pramipexole 0.25 mg TID	Dopamine D3 agonist	Restlessness and depression
Trazodone 100mg PO	5-HT2 and alpha-1 antagonist	Sleep

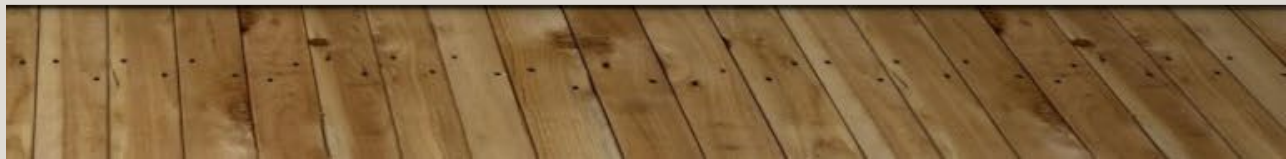
Case Studies

CASE 1

- Clinical Situation: A 35-year-old woman injecting 2 bundles of heroin daily per records. There are 10 bags per bundle, a bundle approximately a gram. She presents seeking treatment. You ask her if she's still using 2 bundles of heroin and she says yes. She has made several attempts to quit, during which she has tried to stop long enough to enter withdrawal but has been unable to maintain abstinence long enough to avoid withdrawal when trying to get on buprenorphine.

What is the best approach for this patient?

- A) Traditional buprenorphine induction
  B) Low-Dose Induction (LDI)
  C) Rapid High-Dose Buprenorphine (HDB) Initiation



Case Studies

- # CASE 1: OUTCOME AND EXPLANATION

First, always assume it’s fentanyl, it’s rarely, rarely heroin. The term is now used interchangeably unfortunately.

B) Low-Dose Induction (LDI).
LDI is chosen due to her high fentanyl tolerance and history o
severe withdrawal. High and standard dose inductions are
better for patients already in withdrawal. High dose ideally in
more supervised setting such as ED.

Her dose is gradually increased over 7 days, reaching 16 m.
day 7, she stops using fentanyl and experiences mild withdra
well managed with clonidine and loperamide.
She is stabilized on 20 mg daily and has no desire to use, sh
feeling excellent.

Patients with this level of use nearly always require at least 16mg qd for stabilization, often 24 or 32 if comorbid chronic pain.

Case 4

- A 45-year-old woman on 120 mg of methadone daily presents to an outpatient clinic seeking to switch to buprenorphine. She has been on methadone for 10 years and is concerned about withdrawal symptoms during the transition. She has been able to get down to 50mg before but never the 30mg her OTP requires to do a standard switch.

- What is the best approach for this patient?
  A) Traditional buprenorphine induction
  B) Low-Dose Induction (LDI)
  C) Rapid High-Dose Buprenorphine (HDB) Initiation

Case Study

CASE 4: OUTCOME AND EXPLANATION

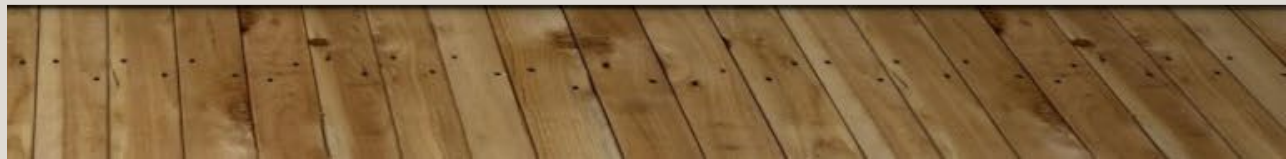
- B) Low-Dose Induction (LDI).
  LDI is chosen due to her high methadone dose and long-term use. Y
- You have her get down to 50mg again over time before starting. Once started, she ended up prolonging the LDI taper a few days by repeating doses due to symptoms, as you told her she could
- Aggressive PRNs helped her get through it without too much discomfort. She is pleased to no longer have to go to the clinic all the time.

CASE 5:

A 30-year-old man presents to an outpatient clinic in moderate opioid withdrawal. He uses a few bags of fentanyl a day, he's been able cut down over time as he previously used a bundle/day, but he tells you he can't seem to stop fully on his own and needs help. His last use was 2-3 days ago. "I don't want to go back to it doc!"

What is the best approach for this patient?

- A) Low-Dose Induction (LDI)
- B) Rapid High-Dose Buprenorphine (HDB) Initiation
- C) Standard buprenorphine induction
- D) Methadone maintenance.



Case Studies

CASE 5: OUTCOME AND EXPLANATION

C) Standard buprenorphine induction

The patient starts with 4 mg of buprenorphine sublingually and is monitored for withdrawal symptoms. He feels better so the dose is gradually increased to 8-16 mg over the next 24-48 hours, he’s given supportive PRNs and stabilizes on 16 mg of buprenorphine daily.

CASE 6:

A 40-year-old woman with bipolar d/o and OUD is on 24 mg of suboxone daily presents to an outpatient clinic. She has been struggling with adherence, stopping suboxone for a couple of days to get high and then restarting. She has overdosed twice recently, and her supply often has contaminants. She underwent debridement for a large wound on her forearm a months ago

A) Increase suboxone dose
B) Switch to methadone
C) Transition to XR buprenorphine

D) B or C

Case Study

CASE 6:

C) BXR

Chosen due to her difficulty with adherence and high-risk profile.

- Her bipolar is driving some of her impulsivity and she's relieved with the steady concentration BXR gives her. She started using again when decreased to 100mg but stabilized when increased to 300mg qmo thereafter.
- Methadone would be appropriate if she had better adherence, but requires even more discipline.
- She's now in sustained remission, her bipolar meds work better without the substances and she's back in her career and has regained custody of her children.

Case Study

CASE 7:

19yo 240 lb young adult from the local university is on medical leave due to severe polysubstance use disorders, he's been repeatedly hospitalized for combined opioid and benzo withdrawal and has had multiple overdoses.

His family is traumatized from having to resuscitate him at home may times and already had a tragic loss recently. He's using large amounts of fentanyl, cocaine and has a TBI from a recent car accident. He's avoided benzos for two months but still using cocaine. He's in severe fentanyl withdrawal and threatens to leave AMA because the two 4mg doses he's received in the ED over the past 6 hours have not provided any relief. Initially he was offered a methadone taper but refused as that didn't provide relieve the last time he was in the ED either. His last use was 30 hours ago.

What is the best approach for this patient?
A) Low-Dose Induction (LDI)
B) Rapid High-Dose Buprenorphine (HDB) Initiation
C) Methadone taper

Case Study

CASE 7:

B) Rapid High-Dose Buprenorphine (HDB) Initiation. "Macro-dosing"

- Patient is in a highly supervised ED, very high risk and in need of rapid stabilization. He's given 24 mg of buprenorphine at once and stabilizes quickly, discharged on same the following day, doing much better and has an intake for IOP.
- Traditional doses not effective due to delayed release of fentanyl from adipose, standard doses have more antagonism than agonism at the mu receptor, higher doses have higher agonism.
- High dose methadone induction with follow up at an OTP might be fine, though this would require brief hospitalization. However, the choice provided was methadone taper, not induction.
  - Methadone tapers are detox, not treatment. They increase OD risk at discharge and make it more difficult to get on buprenorphine
    - methadone is very long acting and the partial agonism of bup can more easily precipitate withdrawal.

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