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PSYCHIATRY ACADEMY

Long Acting Injectable Buprenorphine

Laura G. Kehoe, MD, MPH

Assistant Professor of Medicine

Harvard Medical School

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Disclosures

I have the following relevant financial relationship with a commercial interest to disclose:

Consultant:

MCSTAP Massachusetts Consultation Service for the Treatment of Addiction and Pain (funded by Massachusetts government)
Baycove Health and Human Services and Gavin Foundation

Advisory board, non-branded speaker:

Indivior

Medical Director:

Health Care Resources Centers OTP

Learning Objectives

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- Understand pharmacology of long-acting injectable buprenorphine
- Compare Sublocade® and Brixadi®
- Review dosing, initiation, and patient selection
- Discuss safety, monitoring, and implementation
- Discuss common clinical challenges and scenarios

BUP XR formulations

- Provide higher and more consistent serum levels than current SL dosing
- Option for patients who cannot stabilize on current sublingual (dosage, formulation, stability)
- ***Steady state not reached for 4-6 injections congruent with clinical need for SL supplementation earlier in treatment***
- Emerging use in inductions and rapid starts

Ochalek, Drug Alcohol Depend Rep. 2023
Peckham JSAT 2021
Sublocade [bup extended-release package insert] Indivior Feb 2020

For Whom?

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DSM 5 criteria moderate or severe OUD

Administration only by healthcare professional, as early as q 26 days covered

Pt goals:

- Abstinence?
- Decrease OD, less chaotic/frequent use?
- Convenience? Challenges with adherence or managing meds?
- Challenges with BUP initiation/precipitated withdrawal?
- Wish to keep OUD more private/lack of pill or film burden?
- Pending incarceration, travel?
- *Wish to taper off? (not evidence based)

Should be voluntary; Never mandated

Ling et al, 2019
Peckham AM, Kehoe LG, Gray JR, Wakeman SE. Real-world outcomes with extended-release buprenorphine (XR-BUP) in a low threshold bridge clinic: A retrospective case series. J Subst Abuse Treat. 2021 Jul;126:108316. doi: 10.1016/j.jsat.2021.108316.

Specialty Pharmacy vs. Buy and Bill

Table courtesy of Andrea Jodat, BMC OBAT

	Specialty Pharmacy	Buy and Bill
Type of Benefit	Pharmacy benefit	Medical benefit
How it Works	Healthcare clinic/office **orders** injectable buprenorphine for a **specific** patient from a REMS-certified specialty pharmacy (usually dictated by the patient's insurance). Once the medication is approved by the patient's insurance, the specialty pharmacy works with the clinic to coordinate delivery. Upon delivery, clinic staff appropriately logs and secures medication until administration to patient. Most health centers utilize this method to obtain injectable buprenorphine.	Healthcare clinic/office **purchases** injectable buprenorphine directly from a specialty distributor. The medication is delivered to the clinic, logged appropriately by clinic staff, and securely stored on-site, allowing injectable buprenorphine to be available on hand. When the medication is administered to a patient, the clinic then bills and submits a claim to the patient's insurance for reimbursement. With this method, the healthcare clinic assumes the cost of the medication upfront.
Prescription Drug Monitoring Program (PDMP) Status	Will show up on the state PDMP	Will NOT show up on the state PDMP (because it is billed as a medical, not pharmacy, benefit)
Disposal (as of current regulations) **The DEA may announce changes to the disposal process for injectable bupe in the future, making it easier and more streamlined.*	Eligible for reverse distribution through Indivior's REMS program: 1-866-258-3905.	Clinic will need to work with a DEA-certified 3rd party reverse distributor. You can find a reverse distributor by contacting your local DEA field office.

Feature	Sublocade	Brixadi
Active Ingredient	Buprenorphine (long-acting)	Buprenorphine (long-acting)
FDA Approval	2017	2023
Administration Frequency	Monthly only, (after weekly load #1 and #2)	Weekly **or** Monthly
Injection Sites	*Abdomen, thigh, buttock, upper arm	Abdomen, thigh, buttock, **upper arm**
Dose Options	100 mg & 300 mg monthly	Weekly: 8, 16, 24, 32 mg • Monthly: 64, 96, 128 mg
Storage	Refrigerate (2–8 °C)	Room temperature
Onset Requirements	*Can start after **single** dose transmucosal buprenorphine	Can start after a **single** dose of transmucosal buprenorphine
Removal if Needed	Depot can be removed within ~14 days	Not recommended / typically not removable
Flexibility for Titration	Moderate (monthly adjustments)	Higher (weekly dose adjustments)
Typical Use Case	Maintenance therapy	Induction & maintenance therapy

Parameter	**Transmucosal Buprenorphine**(SL/Buccal, daily)	**Brixadi – Weekly**	**Brixadi – Monthly**	**Sublocade 100 mg**	**Sublocade 300 mg**
Route / Formulation	Sublingual / transmucosal	SC extended-release depot	SC extended-release depot	SC polymer depot	SC polymer depot
Typical Dose Range	8–24 mg/day	8–32 mg weekly	64–128 mg monthly	100 mg monthly	300 mg monthly
Tmax (Absorption Peak)	~1–4 h	~24 h	~6–10 h	~24 h	~24 h
Apparent Half-Life*	~24–42 h (1–2 days)	~3–5 days	~19–26 days	~43–60 days	~43–60 days
Time to Steady State	~7–10 days	~4 weekly doses (~1 month)	~4 monthly doses (~4 months)	~4–6 months	~4–6 months
Steady-State Plasma Levels	Lower troughs; high daily variability	Moderate, smoother than SL	Flatter monthly profile	Sustained plateau	Highest sustained plateau
Peak–Trough Variability	**High** (daily cycling)	**Moderate**	**Low**	**Very low**	**Very low**
Estimated μ-Opioid Receptor Occupancy†	**~70–90%** (dose & timing dependent; troughs may dip)	**~80–90%**	**~85–95%**	**~90–95%**	**~95%+ sustained**
Clinical PK Characterization	Fast on/off, adherence-dependent	Flexible titration	Maintenance-oriented	Long-acting maintenance	Highest, most stable exposure

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1.SUBLOCADE. FDA Drug Label. Updated date: 2026-01-08.
2. Greenwald MK, Wiest KL, Haight BR, Laffont CM, Zhao Y. Harm Reduction Journal. 2023.
3. Shiwach R, Le Foll B, Alho H, et al. JAMA Network Open. 2025.
4.BRIXADI. FDA Drug Label.
5.Walsh SL, Comer SD, Lofwall MR, et al. JAMA Psychiatry. 2017.
6. Lofwall MR, Walsh SL, Nunes EV, et al. JAMA Internal Medicine. 2018.
7.Weimer MB, Herring AA, Kawasaki SS, et al. Journal of Addiction Medicine. 2023.

BUP XR Sublocade® Considerations

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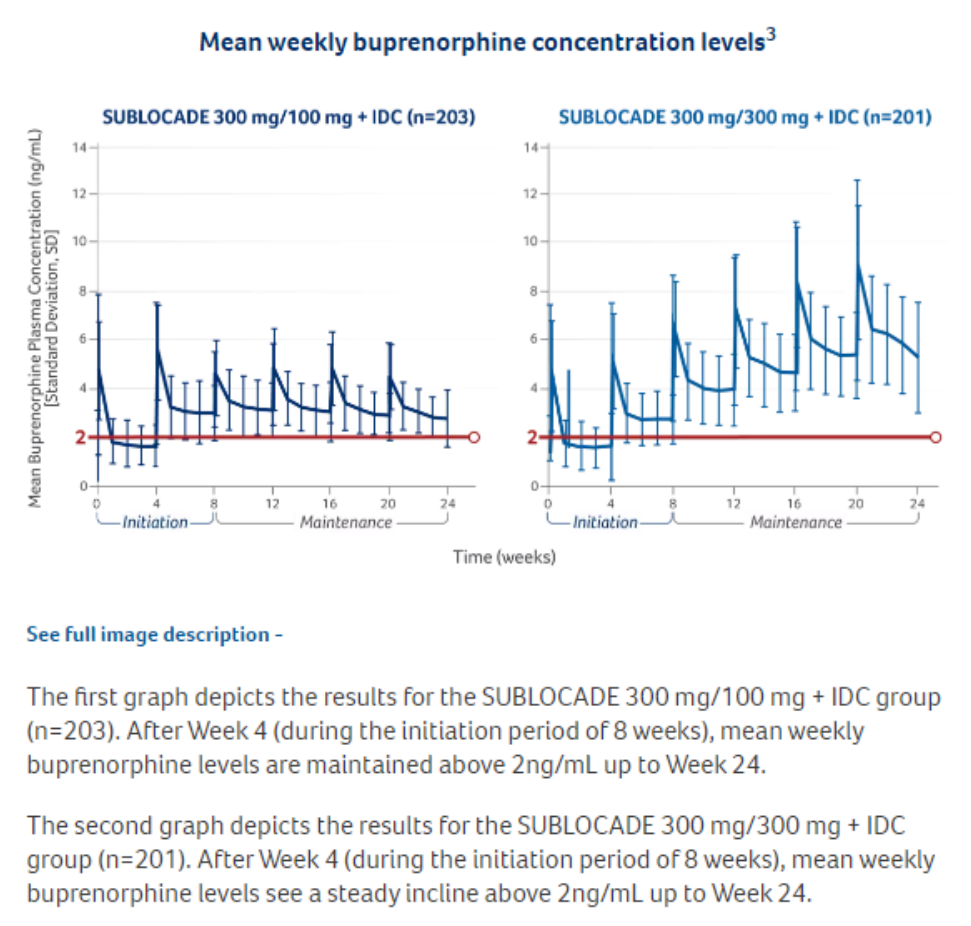

Patient Population	Initial Dose	Injection #1	Injection #2	Maintenance	Key Notes
New to buprenorphine	4 mg SL test dose (observe 1 hour)	300 mg SC	300 mg SC (1 week to 1 month later)	100 mg SC monthly	Additional SL buprenorphine up to 8 mg may be given on induction day
On 8-24 mg/day SL buprenorphine	None needed	300 mg SC	300 mg SC (1 week to 1 month later)	100 mg SC monthly	Direct transition without test dose
On 8-18 mg/day SL (well-controlled)	None needed	300 mg SC	100 mg SC (if controlled after first dose)	100 mg SC monthly	May skip second 300 mg dose if stable
Inadequate response to 100 mg	—	—	—	300 mg SC monthly	Consider if patient tolerates but doesn't respond to 100 mg

SUBLOCADE. FDA Drug Label.Updated date: 2026-01-08.

Ochalek, Drug Alcohol Depend Rep. 2023
Peckham, Kehoe, Gray JSAT 2021
Sublocade [bup extended-release package insert] Indivior Feb 2020

BRIXADI®: Dosing Regimen

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- Patients not currently receiving buprenorphine: 24 mg SQ once weekly titrated up over the first week as follows
  - Administer a test dose of transmucosal buprenorphine 4 mg if signs of mild to moderate withdrawal appear
  - Initiate 16 mg SQ, followed by an additional dose of 8 mg SQ within 3 days of the first dose to achieve the recommended 24 mg weekly dose
  - Clinical trials have also utilized single 24 mg dose without subsequent rescue doses
  - If needed, during this first week of treatment, administer an additional 8 mg dose, waiting at least 24 hours after the previous injection, for a total weekly dose of 32 mg SQ (maximum weekly dose)
  - Subsequent weekly injections based on the total weekly dose established during week 1
  - Can also use supplemental SL instead of rescue SQ doses

Patients switching from transmucosal buprenorphine-containing products to Brixadi®

Daily dose of sublingual buprenorphine	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

Patients transitioning between weekly and monthly Brixadi® formulations

BRIXADI (weekly)	BRIXADI (monthly)
16 mg	64 mg
24 mg	96 mg
32 mg	128 mg

Figure 2: Buvidal® Weekly and Buvidal® Monthly versus daily SL BPN

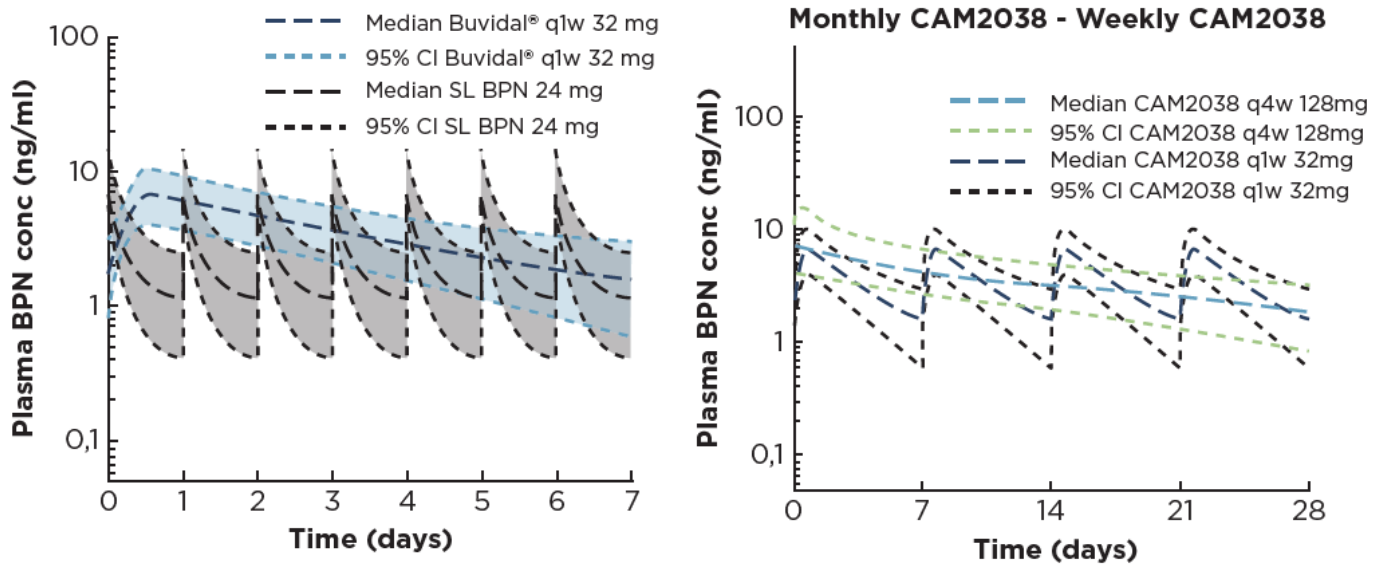
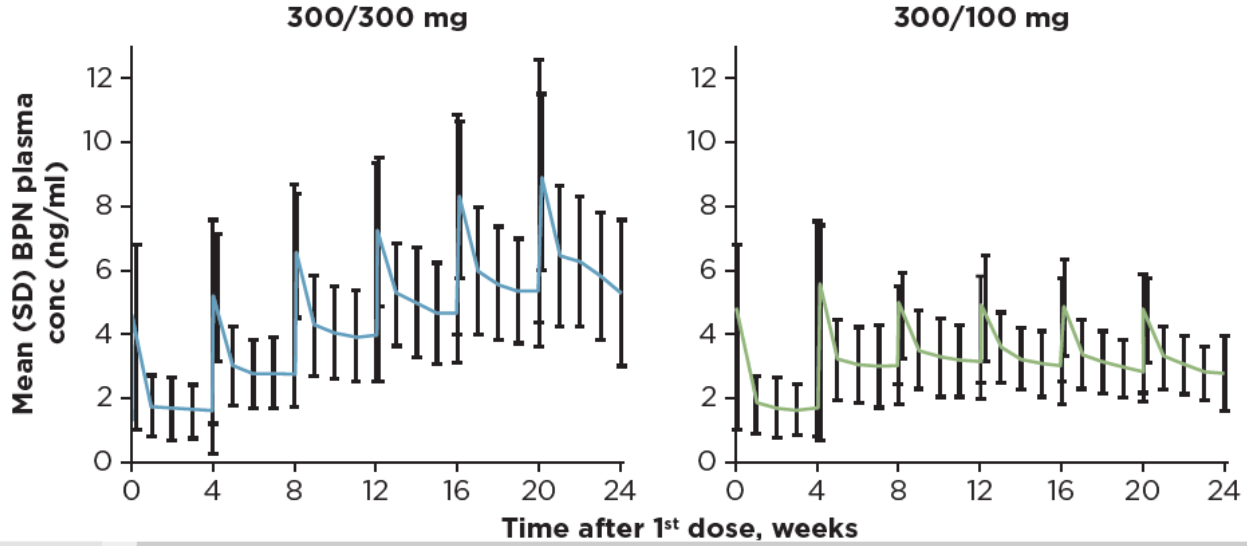
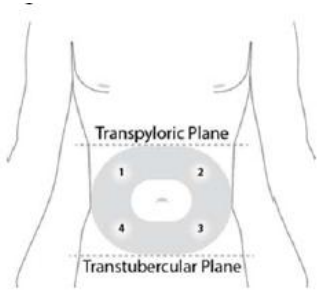


Figure 3: Sublocade® PK profile



Patient Counseling

- Long duration of action
  - If treatment is discontinued, withdrawal may not occur for weeks to months
- Risk of serious harm/death if injected intravenously
- Risk of withdrawal if depot is tampered with or removed
- Pregnancy
- *Education about nodule, mild site reactions*
- *If concern about site reaction, have ED provider contact SUD provider*
- Potential need for SL supplementation
- OD prevention, harm reduction



Anesthesia -- MGH protocol

Massachusetts General Hospital Substance Use Disorder Bridge Clinic

Optional Lidocaine injection / local anesthetic for XR buprenorphine injections

Purpose:
Some patients find topical ice is insufficient to manage the procedural pain from XR buprenorphine injections, which has led some patients to fear initiating XR buprenorphine or to discontinue injections despite preference for this formulation

Procedure:

1) Identify site for XR buprenorphine in abdominal quadrant
2) Apply ice to site while preparing lidocaine for injection into subcutaneous tissue
3) Prepare 1% Lidocaine, without epinephrine:
    - Wipe top of lidocaine bottle with alcohol pad
    - Draw up 2cc Lidocaine with large bore needle in a 3 or 5 cc syringe
    - Change needle to 1 inch, 25 or 27 gauge
4) Clean abdominal site with alcohol swab
5) Tent skin and Inject 2 cc Lidocaine at ~75 degree angle, releasing lidocaine into tissue while pulling back
6) Apply 2x2 gauze to area and massage gently in circular motion to allow lidocaine to diffuse the area
7) Keep 2x2 resting on skin and reapply ice pack

*Wait at least 3 minutes before injecting XR buprenorphine

XR Buprenorphine injection:

1) Clean abdominal site with alcohol wipe where lidocaine was injected, identifying the lidocaine puncture site
2) Tent skin and inject XR Buprenorphine into the same puncture site and track of lidocaine
3) Apply band-aid
4) Have patient lay for recommended time per manufacturer

Kehoe, LG, Gray, J, MGH SUD Bridge Clinic

Summary of Buprenorphine Initiation Approaches

TABLE 2. Clinical Decision Support for Buprenorphine Initiation Techniques Based on the Clinical Setting

	Fastest		Slowest
Initiation Strategy*	**HDB†**	**Standard‡**	**LDB-OC§**
Possible advantages	-Quick stabilization -Bridge access barriers to ongoing buprenorphine	-Most common and well-described technique	-Opioid abstinence not initially required
Need for opioid withdrawal?	Yes	Yes	No
Premedicate with adjuvant medications?‖	Consider	Yes	Yes
Initial starting dose¶ (buprenorphine SL formulation)	8–16+ mg	2–8 mg	0.25 mg–1 mg
Duration of initiation until stabilization	≤2 h	1–3 days	3–10 d (may be longer in certain situations)
Need for opioid continuation	No	No	Yes
Full agonist opioid continuation dose	None	None	Examples: Methadone 30 mg PO daily or Hydromorphone 4 mg PO every 4 hr or Self-directed illicit/nonprescribed opioid use
Care coordination required	Moderate	Moderate	High

Weimer, Herring J Addict Med 2023

- Fentanyl analogs
  - Rapid onset crossing blood brain barrier
  - 50-100x potency vs. morphine
  - Highly lipophilic, rapid fat sequestration
  - Regular use leads to delayed renal clearance (Mean ~2 weeks, may take 4+ weeks[1)]
  - Unpredictable withdrawal course
  - Implicated in buprenorphine-precipitated withdrawal
  - Might extend opioid withdrawal and post withdrawal sequalae
- Polysubstance use / exposure
  - Contributing to morbidity + overdose mortality
  - Complicating withdrawal experience for patients
- Adulterants like Xylazine /Medetomidine
  - Complicating withdrawal management

Bottom Line: Unclear how to guide our patients when we don't know what they are taking or how it impacts them

Huhn AS, Hobelmann JG, Oyler GA, Strain EC. Protracted renal clearance of fentanyl in persons with opioid use disorder. Drug Alcohol Depend. 2020 Sep 1;214:108147. doi: 10.1016/j.drugalcdep.2020.108147.

Silverstein SM, Daniulaityte R, Martins SS, Miller SC, Carlson RG, 2019 "Everything is not right anymore": Buprenorphine experiences in an era of illicit fentanyl. International Journal of Drug Policy. 74, 76–83.

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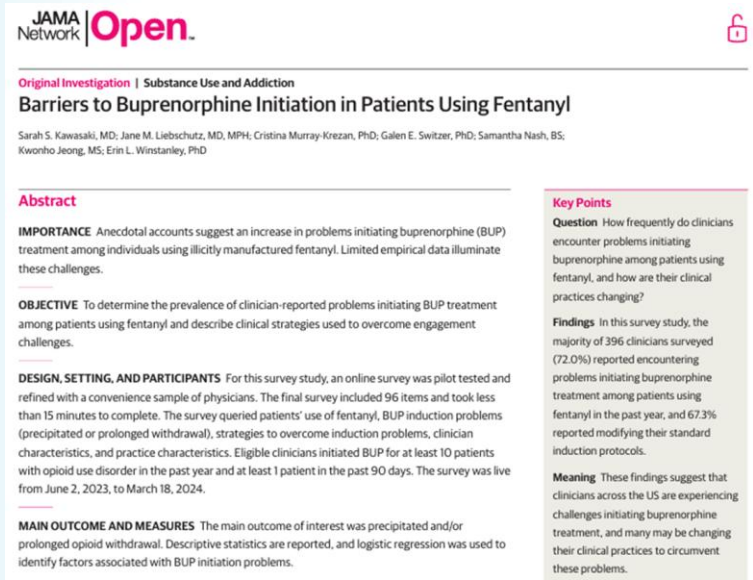
COMMENTARY

A Plea From People Who Use Drugs to Clinicians: New Ways to Initiate Buprenorphine are Urgently Needed in the Fentanyl Era

Kimberly L. Sue, MD, PhD, Shawn Cohen, MD, Jess Tilley, and Avi Yocheved

J Addict Med. 2022 Jul-Aug 01;16(4):389-391.



JAMA Network Open.

Original Investigation | Substance Use and Addiction

Barriers to Buprenorphine Initiation in Patients Using Fentanyl

Sarah S. Kawasaki, MD; Jane M. Liebschutz, MD, MPH; Cristina Murray-Krezan, PhD; Galen E. Switzer, PhD; Samantha Nash, BS; Kwonho Jeong, MS; Erin L. Winstanley, PhD

Abstract

IMPORTANCE Anecdotal accounts suggest an increase in problems initiating buprenorphine (BUP) treatment among individuals using illicitly manufactured fentanyl. Limited empirical data illuminate these challenges.

OBJECTIVE To determine the prevalence of clinician-reported problems initiating BUP treatment among patients using fentanyl and describe clinical strategies used to overcome engagement challenges.

DESIGN, SETTING, AND PARTICIPANTS For this survey study, an online survey was pilot tested and refined with a convenience sample of physicians. The final survey included 96 items and took less than 15 minutes to complete. The survey queried patients' use of fentanyl, BUP induction problems (precipitated or prolonged withdrawal), strategies to overcome induction problems, clinician characteristics, and practice characteristics. Eligible clinicians initiated BUP for at least 10 patients with opioid use disorder in the past year and at least 1 patient in the past 90 days. The survey was live from June 2, 2023, to March 18, 2024.

MAIN OUTCOME AND MEASURES The main outcome of interest was precipitated and/or prolonged opioid withdrawal. Descriptive statistics are reported, and logistic regression was used to identify factors associated with BUP initiation problems.

Key Points

Question How frequently do clinicians encounter problems initiating buprenorphine among patients using fentanyl, and how are their clinical practices changing?

Findings In this survey study, the majority of 396 clinicians surveyed (72.0%) reported encountering problems initiating buprenorphine treatment among patients using fentanyl in the past year, and 67.3% reported modifying their standard induction protocols.

Meaning These findings suggest that clinicians across the US are experiencing challenges initiating buprenorphine treatment, and many may be changing their clinical practices to circumvent these problems.

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High dose buprenorphine initiation in ED: what can we learn?

- 1 Prospective cohort study of ED patients across country, 75% w/confirmed HPSO exposure, received bup >8mg
  - POW <1%

- 2 retrospective cohort studies of HDB across 16 ED's in California reported no increased AE compared with standard initiation
  - Precipitated withdrawal was rare (<2%)

  - *Applicability to practice?*
    - *1 study occurred before widespread HPSO*
    - *1 study reported low incidence of HPSO use*
    - *Does not match what many providers are seeing clinically*


Research Letter | Substance Use and Addiction

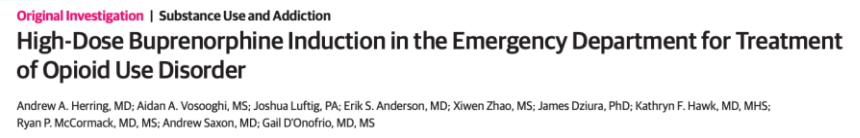
Incidence of Precipitated Withdrawal During a Multisite Emergency Department–Initiated Buprenorphine Clinical Trial in the Era of Fentanyl

Gail D'Onofrio, MD, MS; Kathryn F. Hawk, MD, MHS; Jeanmarie Perrone, MD; Sharon L. Walsh, PhD; Michelle R. Lofwall, MD; David A. Fiellin, MD; Andrew Herring, MD


Research Letter | Substance Use and Addiction

High-Dose Buprenorphine Initiation in the Emergency Department Among Patients Using Fentanyl and Other Opioids

Hannah Snyder, MD; Brendon Chau, MPH; Mariah M. Kalmin, PhD; Melissa Speener, MPH; Arianna Campbell, PA; Aimee Moulin, MD, MAS; Andrew A. Herring, MD


Original Investigation | Substance Use and Addiction

High-Dose Buprenorphine Induction in the Emergency Department for Treatment of Opioid Use Disorder

Andrew A. Herring, MD; Aidan A. Vosooghi, MS; Joshua Luftig, PA; Erik S. Anderson, MD; Xiwen Zhao, MS; James Dziura, PhD; Kathryn F. Hawk, MD, MHS; Ryan P. McCormack, MD, MS; Andrew Saxon, MD; Gail D'Onofrio, MD, MS

Case

- 32 yom with severe OUD with numerous complications, PTSD, challenges with med adherence, internalized and externalized stigma MOUD, repeat experience stopping and returning to fentanyl use
- Last fentanyl use > 3 days ago
- Detained, in severe WD with COWS 17 by the time you see him
- Goal: stop OD, eventual opioid abstinence, no daily meds

Considerations?

High dose buprenorphine learning points

- Ensure in opioid withdrawal
- The earlier in withdrawal the higher the initial dose needed (at least 24mg, case reports up to 64mg in 16mg increments)
  - Day 2+ return to 16-24mg
- Go BIG or get stuck in withdrawal; avoid 2-4mg dose
- Harm reduction education and support key
- Consider comfort meds to aid fear of POW
- Need more data re: outpatient experience not aligning with ED case series

Case continued

- After discussion of options, he chooses Sublocade
- Receives 300 mg, injection #1 and #2 booked in 4 weeks
- Ongoing cravings and mild withdrawal symptoms
- Does not have access to SL BUP
- Used fentanyl this AM

Considerations?

Low Dose Initiation: ED-INNOVATION Trial

- Multisite study aiming to rapidly expand access to ED-initiated BUP across 28 diverse EDs in the US (mix of geography, urban/suburban, and academic/community)
- Patients with COWS 4+ given 24 mg SC injection, observed for 2 H, and discharged (no rescue doses or supplemental SL) w/ follow-up in 7 days
- Vast majority of individuals in this trial tolerated 7-day XR-BUP injectable, even at low levels of withdrawal (COWS scores of 4), allowing for initiation of BUP early in the ED visit
- Very low rates (>0.5%) of precipitated withdrawal

D'Onofrio G, Perrone J, Hawk KF, Cowan E, McCormack R, Coupet E Jr, Owens PH, Martel SH, Huntley K, Walsh SL, Lofwall MR, Herring A; ED-INNOVATION Investigators. Early emergency department experience with 7-day extended-release injectable buprenorphine for opioid use disorder. Acad Emerg Med. 2023 Dec;30(12):1264-1271. doi: 10.1111/acem.14782. Epub 2023 Aug 22. PMID: 37501652; PMCID: PMC10822018.

Case

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- 27 yo unhoused with 10yr hx severe OUD, uses fentanyl IV, cocaine, benzodiazepines
- hx of necrotizing fasciitis, numerous OD, GAD.
- Goals: abstinence and transition to XR Buprenorphine
- “I’m desperate. Please help me.”
- She is terrified of POW, having experienced it numerous times
- Adamantly opposed to methadone
- Asks to try Low dose Brixadi initiation today after a friend successfully transitioned onto bupe

Low Dose Initiation: Direct to Inject (DTI) XR Buprenorphine

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Drug and Alcohol Dependence 278 (2026) 113011

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journal homepage: www.elsevier.com/locate/drugalcdep

ELSEVIER

Outpatient initiation of direct-to-inject buprenorphine

Sarah Rosenwohl-Mack [a,*], Megan Heeney [b], Lysa Samuel [b], Erik Anderson [b], Andrew A. Herring [b], Lauren Roller Sirey [b], Damian Peterson [c], Alexander R. Bazazi [d], Hannah Snyder [a], Leslie W. Suen [e]

[a] Department of Family and Community Medicine, University of California San Francisco, San Francisco, CA, United States
[b] Division of Addiction Medicine, Highland Hospital - Alameda Health System, Oakland, CA, United States
[c] San Francisco Department of Public Health, San Francisco, CA, United States
[d] Division of Substance Use and Addiction Medicine at San Francisco General Hospital, Department of Psychiatry and Behavioral Sciences, University of California, San Francisco, San Francisco CA, United States
[e] Division of General Internal Medicine at San Francisco General Hospital, Department of Medicine, University of California San Francisco, San Francisco, CA, United States

Objective: To evaluate 90-day treatment retention and withdrawal tolerability following DTI buprenorphine initiation across multiple outpatient safety-net settings.

Methods: *R*etrospective cohort study of 131 DTI initiations among 114 high risk patients with OUD across San Francisco and Oakland safety-net clinics from March 2024 to May 2025.

Patients were initiated on weekly long-acting buprenorphine and evaluated for withdrawal severity in the first 24 h and calculated continuous treatment retention at 7, 30, and 90 days using pharmacy and chart data.

Results*:* Mean age was 42 years; 79 % reported fentanyl use, and 67 % were unstably housed or unhoused. **In the 24 h after injection, 37 % experienced no withdrawal, 31 % experienced mild-moderate withdrawal, and 11 % experienced severe withdrawal, with 21 % missing data. Overall, 72 % continued buprenorphine beyond initial injection, with most transitioning to monthly formulations. Retention rates were 69 % at 7 days, 68 % at 30 days, and 43 % at 90 days.** No demographic or clinical factors predicted 90-day retention.

Pharmacokinetics of Brixadi®

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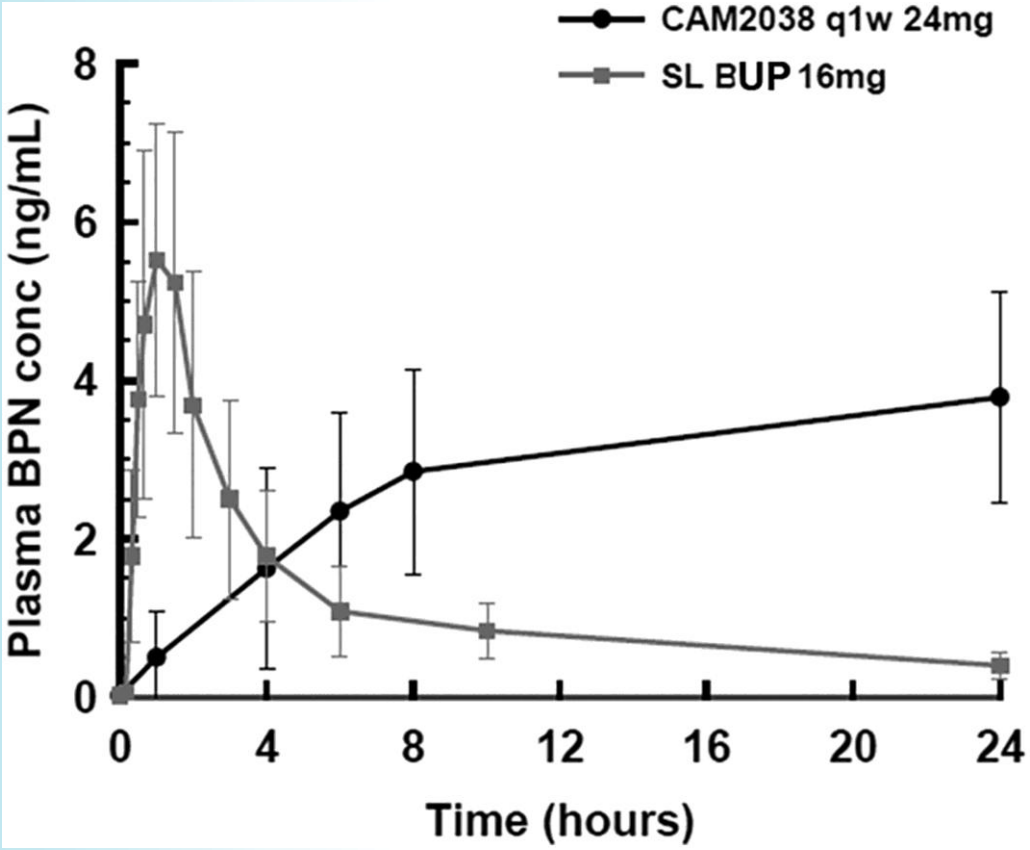
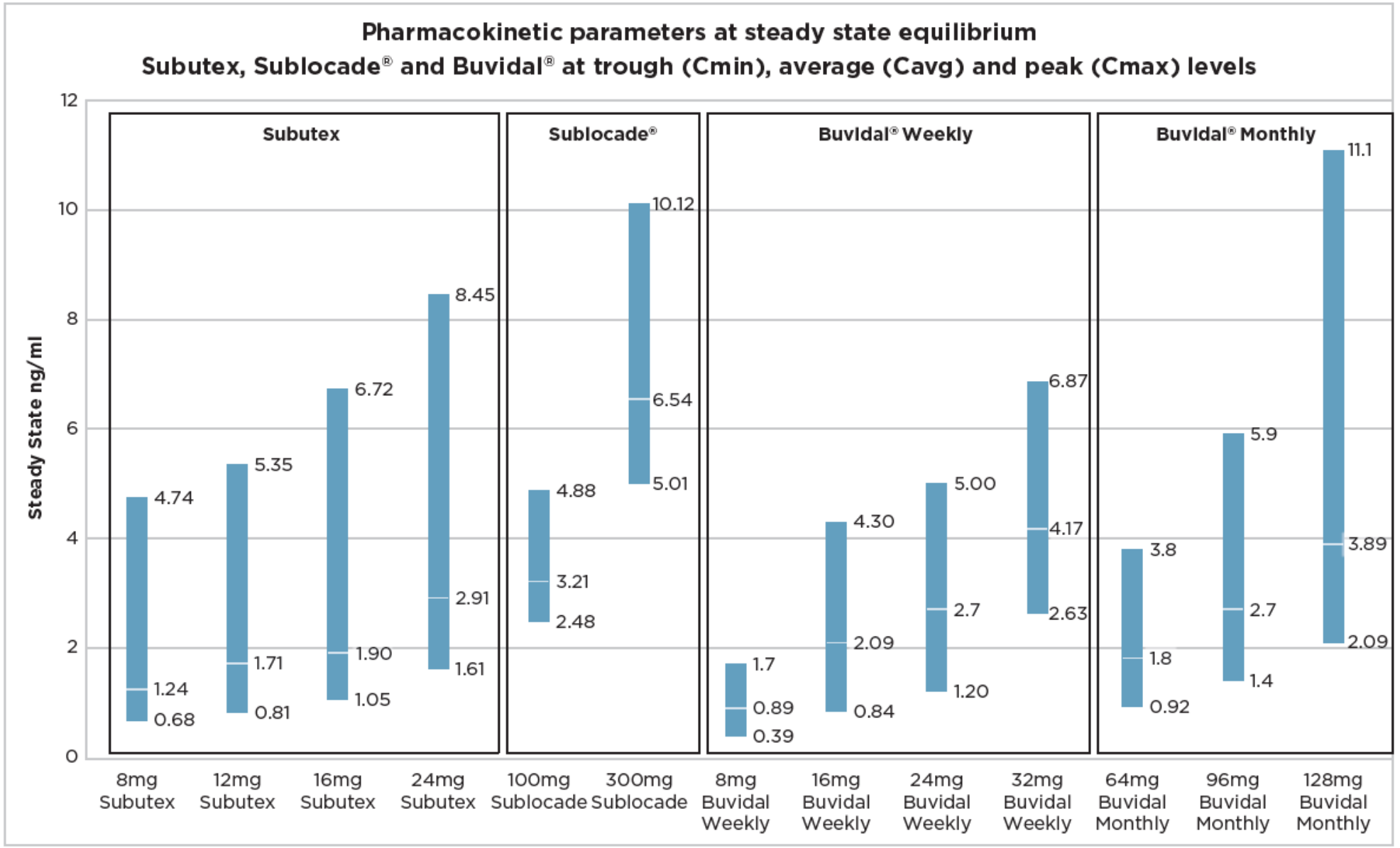
- SL buprenorphine has rapid absorption, but low oral bioavailability; reaches peak in 60 min
- After 24 mg SC injection Brixadi®, plasma concentrations are therapeutic for craving and withdrawal between 6-8 hours, peak level usually within 20 hours achieved within 20 h. Terminal half-life is between 70 and 107 hours
- Slower rise in blood plasma level makes it a possible agent for low-dose initiation (as opposed to rapid rise from Sublocade®)

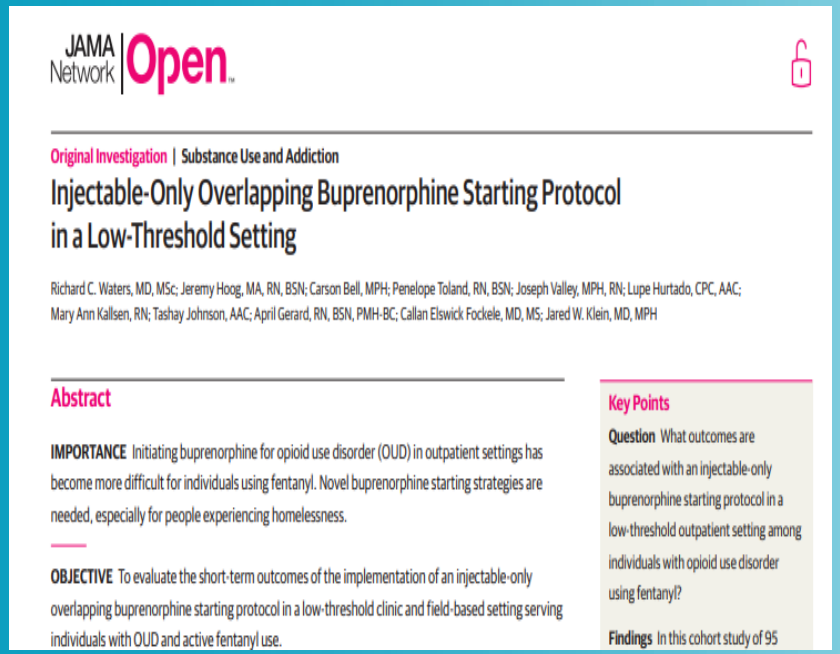


- D'Onofrio G, Perrone J, Hawk KF, Cowan E, McCormack R, Coupet E Jr, Owens PH, Martel SH, Huntley K, Walsh SL, Lofwall MR, Herring A; ED-INNOVATION Investigators. Early emergency department experience with 7-day extended-release injectable buprenorphine for opioid use disorder. Acad Emerg Med. 2023 Dec;30(12):1264-1271. doi: 10.1111/acem.14782. Epub 2023 Aug 22. PMID: 37501652; PMCID: PMC10822018.

Figure 1: Pharmacokinetic parameters – steady state



DTI in Low Threshold Setting



JAMA Network Open

Original Investigation | Substance Use and Addiction

Injectable-Only Overlapping Buprenorphine Starting Protocol in a Low-Threshold Setting

Richard C. Waters, MD, MSc; Jeremy Hoog, MA, RN, BSN; Carson Bell, MPH; Penelope Toland, RN, BSN; Joseph Valley, MPH, RN; Lupe Hurtado, CPC, AAC; Mary Ann Kallsen, RN; Tashay Johnson, AAC; April Gerard, RN, BSN, PMH-BC; Callan Elswick Fockele, MD, MS; Jared W. Klein, MD, MPH

Abstract

IMPORTANCE Initiating buprenorphine for opioid use disorder (OUD) in outpatient settings has become more difficult for individuals using fentanyl. Novel buprenorphine starting strategies are needed, especially for people experiencing homelessness.

OBJECTIVE To evaluate the short-term outcomes of the implementation of an injectable-only overlapping buprenorphine starting protocol in a low-threshold clinic and field-based setting serving individuals with OUD and active fentanyl use.

Key Points

Question What outcomes are associated with an injectable-only buprenorphine starting protocol in a low-threshold outpatient setting among individuals with opioid use disorder using fentanyl?

Findings In this cohort study of 95

Objective: Evaluate short-term outcomes of an injectable-only overlapping buprenorphine initiation protocol

Design & Setting:

- Retrospective cohort study (Sept 2024–Jan 2025)
- Urban low-threshold clinic with field-based outreach

Participants:

- 95 adults with moderate–severe OUD and active fentanyl use
- 79% experiencing homelessness or in supportive housing

Protocol (No fentanyl cessation required):

- Day 1: Weekly 8 mg injectable buprenorphine
- Day 2: Weekly 16 mg injectable buprenorphine
- Day 3: Monthly 128 mg or 300 mg injectable buprenorphine

Outcomes: Initiation, protocol completion, and 2-month retention

Results:

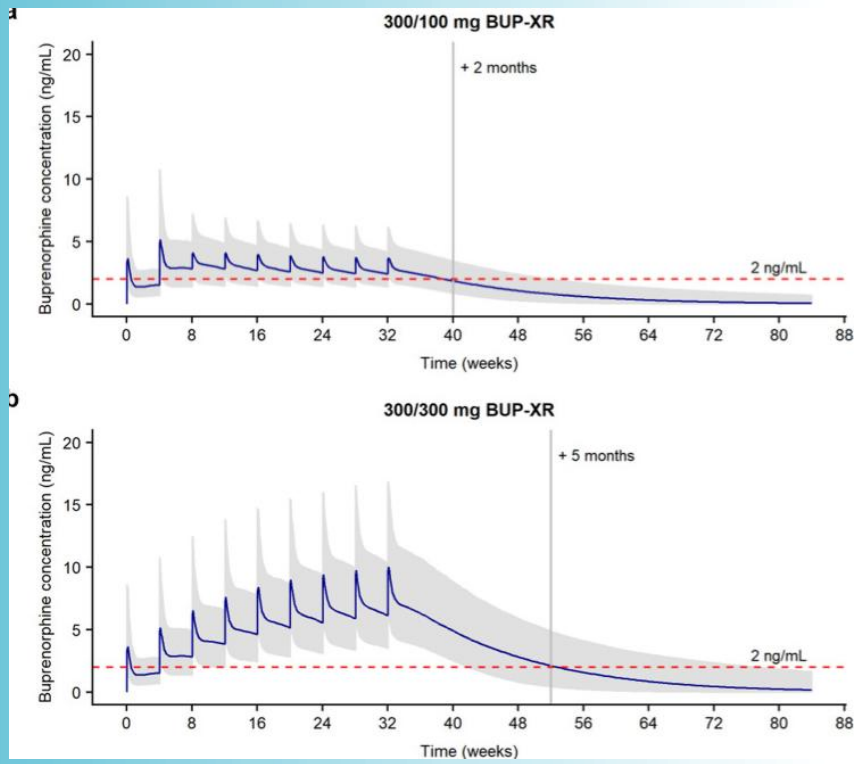
- 90% initiated protocol
- 75% completed all injections
- 64% retained at 2 months

Case 5

- 40 yom with MDD, PTSD, severe OUD in sustained remission on BUP XR x 12 months, requests discontinuation.
- Received 6+ months 300 mg, followed by 100 mg monthly injections
- Currently no breakthrough sx, working, feeling well supported and just tired of receiving monthly injections and feels he no longer needs MOUD.

Considerations?

Taper



-Model simulations indicate that steady-state buprenorphine plasma concentrations decreased slowly over time following the last injection. Concentration levels remained at therapeutic levels for 2 to 5 months on average, depending on the dosage administered

-After achieving steady state, patients discontinuing SUBLOCADE may have detectable plasma levels of buprenorphine for 12 months or longer

-NIDA study underway

-OUD is a chronic recurring condition and patients should be informed of risk of recurrence of symptoms and return to use

Indivior prescribing information

BRIXADI®

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PSYCHIATRY ACADEMY

At what intervals will insurance cover injections?

If previously stabilized on buprenorphine

- From Sublocade or SL buprenorphine: at any point; insurance does not factor recent Brixadi in covering Sublocade
- From Monthly Brixadi: as early as 26 days will be covered for monthly
- From Weekly Brixadi: at any point without insurance objections

If new to buprenorphine

- From weekly Brixadi:
  - May Dose monthly Brixadi as early as 24h after
- From fentanyl: see ED INNOVATION for COWS>4 and Seattle DTI overlapping protocol with weekly Brixadi
  - May Dose monthly Brixadi as early as 24h after
- Insurance: time of weekly Brixadi does not impact monthly timing
- Pharmacologically: recommend wait at least 24h from having the equivalent of weekly Brixadi 24mg (including SL buprenorphine) prior to monthly dose, unless COWS>4 and counseled appropriately

Missed injections:

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- If Received Brixadi® and had a return to fentanyl use
  - Very limited data
  - half-life of **monthly** Brixadi (19-26d) is far shorter than that of Sublocade (40-60d);
    - recommend oral lead-in or weekly doses (DTI) if exceeding ~6 weeks
- half-life of **weekly** Brixadi (4-5d) is very short
    - proceed with caution if >8 days from last Brixadi

- If received Sublocade® :
  - Half-life is 40-60 days
  - One injection of 300 mg and then missed -- may administer injection up to 2 months later
  - Previously stabilized on 300 mg and then missed -- may administer injection up to 4-5 months
  - Previously stabilized on 100 mg and then missed - May administer injection up to 2 months

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

Take home thoughts

- Individualize your approach, listen to your patient and goals of care
- Each approach has risks and benefits that should be discussed with patients
- Sublocade
  - Long half-life (40–60 days) → forgiving if doses delayed
  - Insurance allows early dosing (~26 days)
  - No oral lead-in needed if within accepted late windows
  - Rapid initiation possible after SL or Brixadi
- Brixadi
  - Weekly and monthly formulations
  - Shorter half-life than Sublocade → less forgiving if late
  - Useful for fentanyl DTI protocols
  - Monthly dose can be given 24–72h after weekly in DTI
- Expect maintenance doses to be higher in fentanyl era
- Time to steady state: may need SL supplementation
- More data needed
- Don’t forget methadone!

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