Transforming ED Care with Buprenorphine

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BRIDGE
Treatment. Equity. Connection.

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Bridging emergency care and community health to create an integrated system that improves health and equity.

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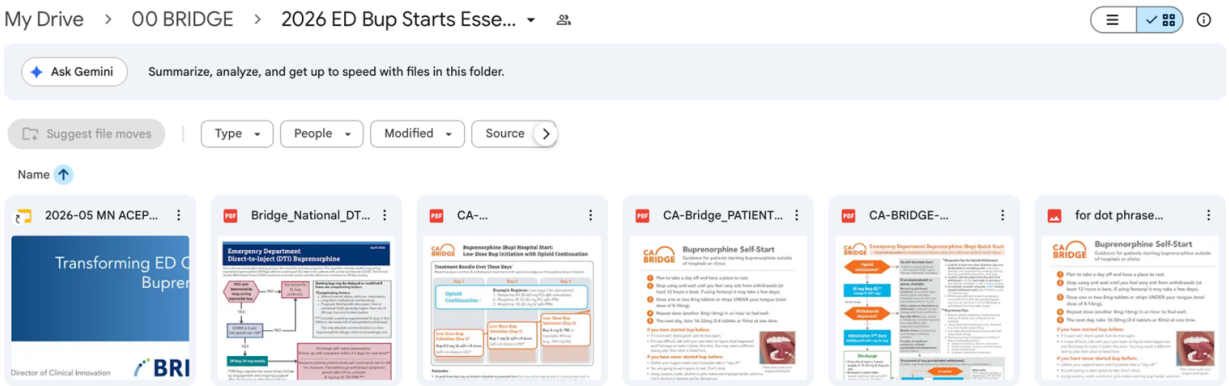
Bup Topics:

1. Why ED Bup Starts are Great
2. Ways to Start Bup in the ED

Essential Resources



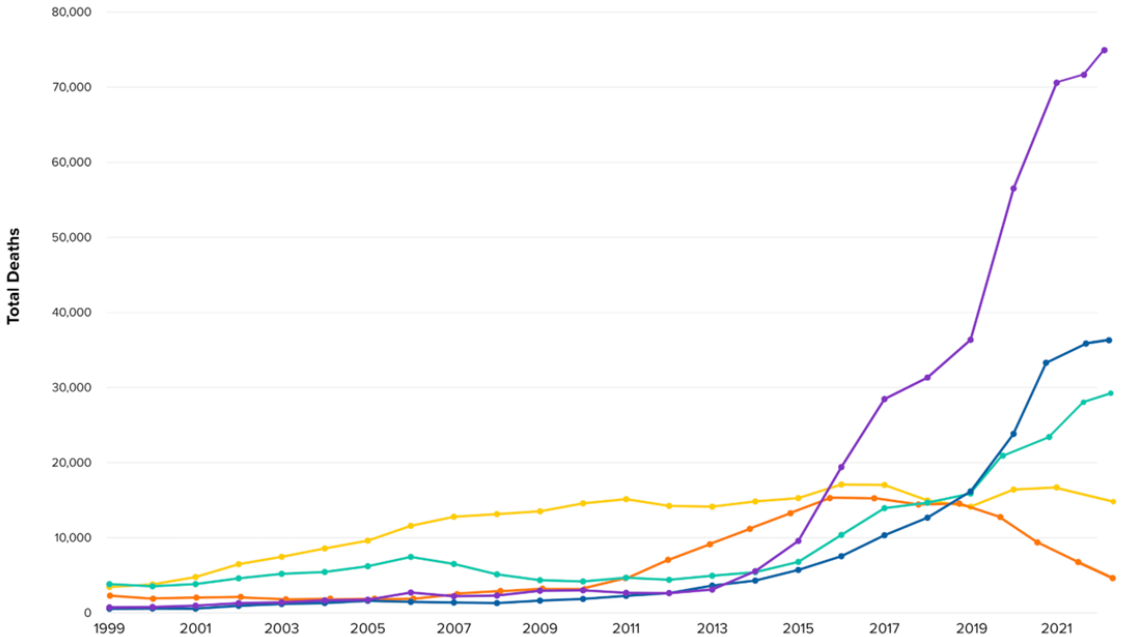
bitly

Overdose is Our #1 Public Health Problem

More Americans under age 45 die from drug overdose than from any other cause.

Fentanyl is Driving Overdose Deaths

Trends in U.S. Drug Overdose Deaths (December 1999–June 2023)



Synthetic opioids excluding methadone overdose deaths increased **103-fold**

Psychostimulants with abuse potential (primarily methamphetamine) overdose deaths increased **64-fold**

Cocaine overdose deaths increased **7.6-fold**

Rx opioid overdose deaths increased **4.1-fold**

Heroin overdose deaths increased **2.5-fold**

U.S. Department of Health & Human Services, 2023 – https://www.hhs.gov/overdose-prevention/

Vision: Low barrier, high volume SUD care

Treatment First

Patients will be offered low-threshold, evidence-based MOUD directly in the ED

Patient Navigation

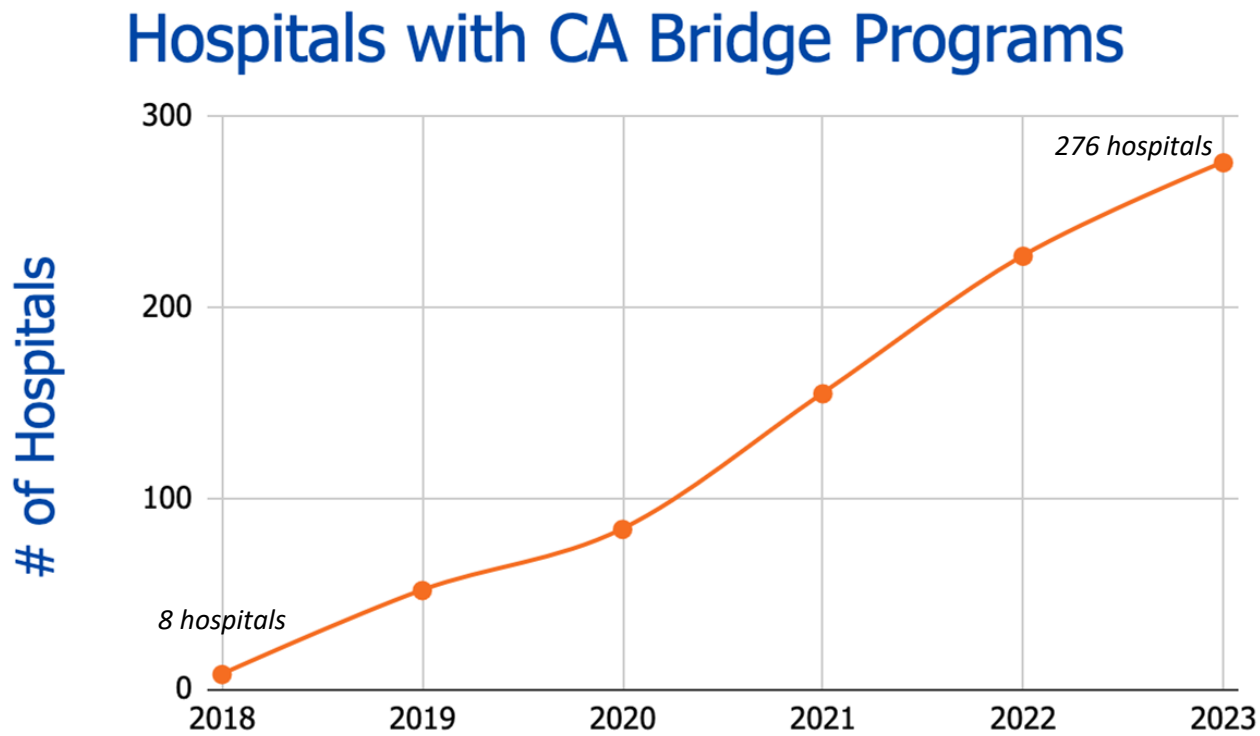
Patients will be connected with ongoing care

Culture of Care

Signs and staff in the hospital invite patient self-disclosure of drug use and desire for treatment

Successes So Far

Goal: Universal access to addiction treatment in all EDs in California



CA Bridge Impact: 2019-2024

444,875

Patients seen for substance use disorders

364,869

Patients identified with opioid use disorder

138,070

Patients prescribed or administered MAT

271,848

Naloxone kits ordered by hospitals

From 2019 through Apr 2024, 276 hospitals implemented the CA Bridge model, helping thousands of patients get treatment.

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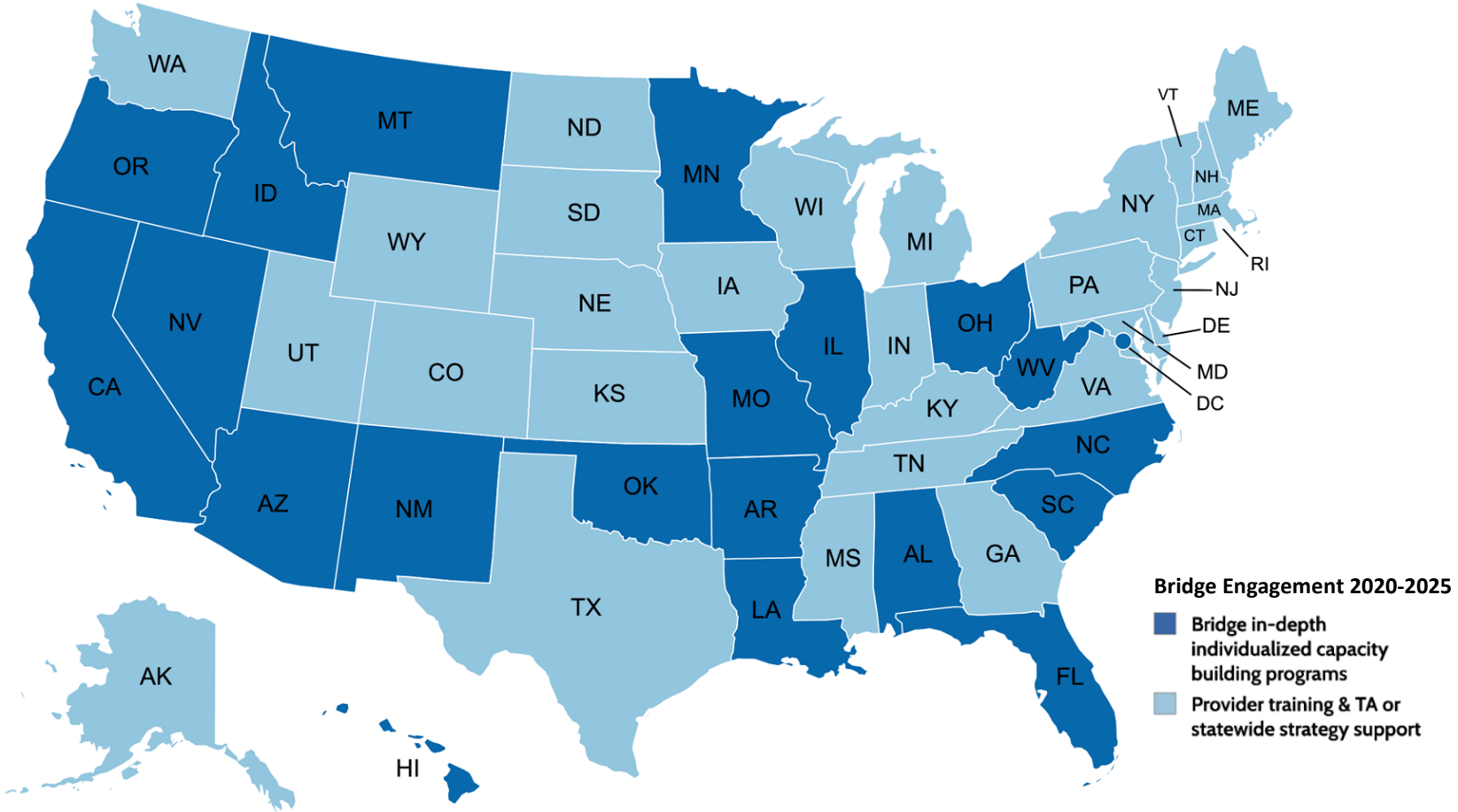
National reach as of October 2025



National Bridge Starts Program

- Cohorts: Typically 1-3 hospitals in one state
- Enhance ED based SUD treatment
- Weekly meetings with site champions x 8 weeks
- Followed by Site Visit
- Grant funded

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Why treat SUD in the Emergency Department?

28%

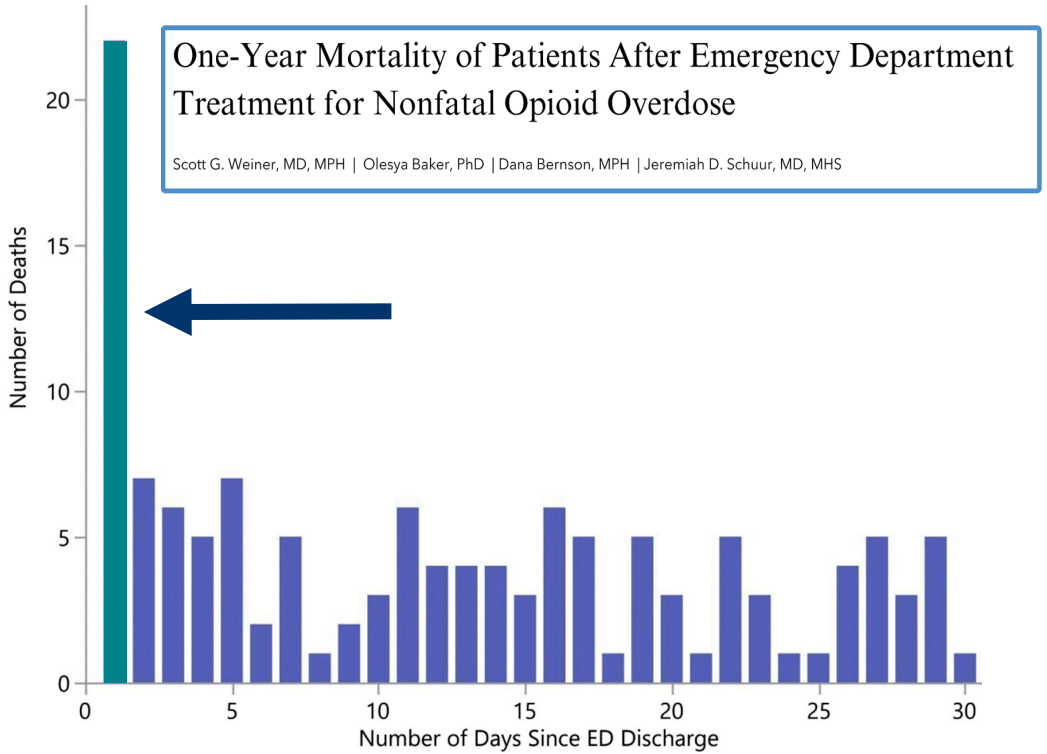
of adult ED patients screen positive for SUD.

Elder et al., 2020

OUD is an Emergency

Significant increase in mortality risk post-ED discharge (~5.5% over following year)

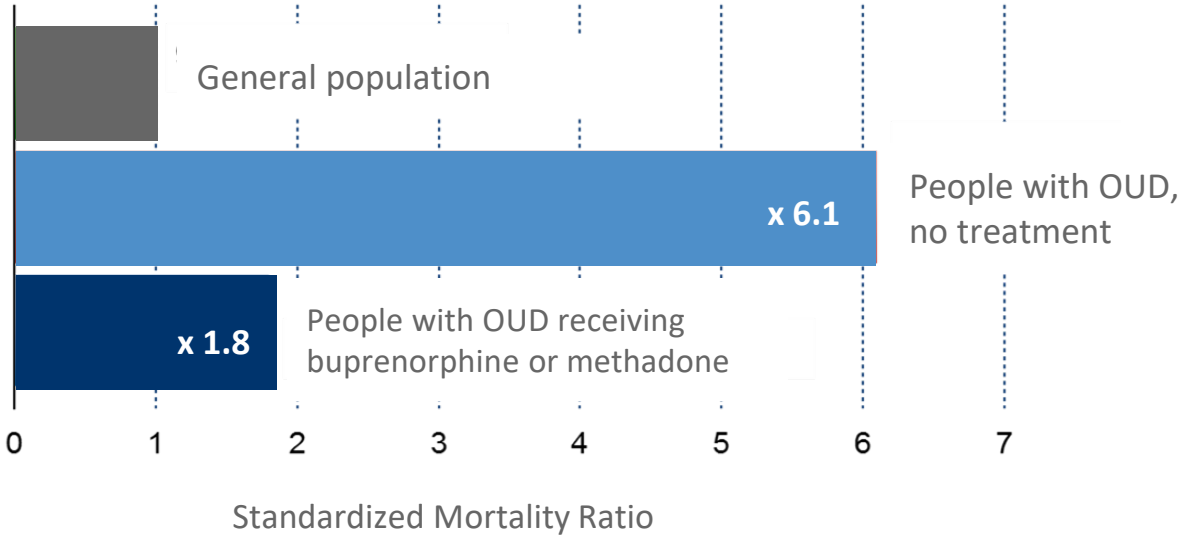
- 20% of patients that died did so in the first month
- 22% of those who died in the first month **died** within the first 2 days



Weiner et al., 2019

Medication for OUD Saves Lives

Mortality Risk Compared to the General Population



Evans et al., 2015.

Number Needed to Treat (NNT)

Aspirin in STEMI	**42** to save a life
Steroids in COPD Exacerbation	**10** to prevent treatment failure
Defibrillation in cardiac arrest	**2.5** to save a life
Bup in opioid use disorder	**2** to retain in treatment

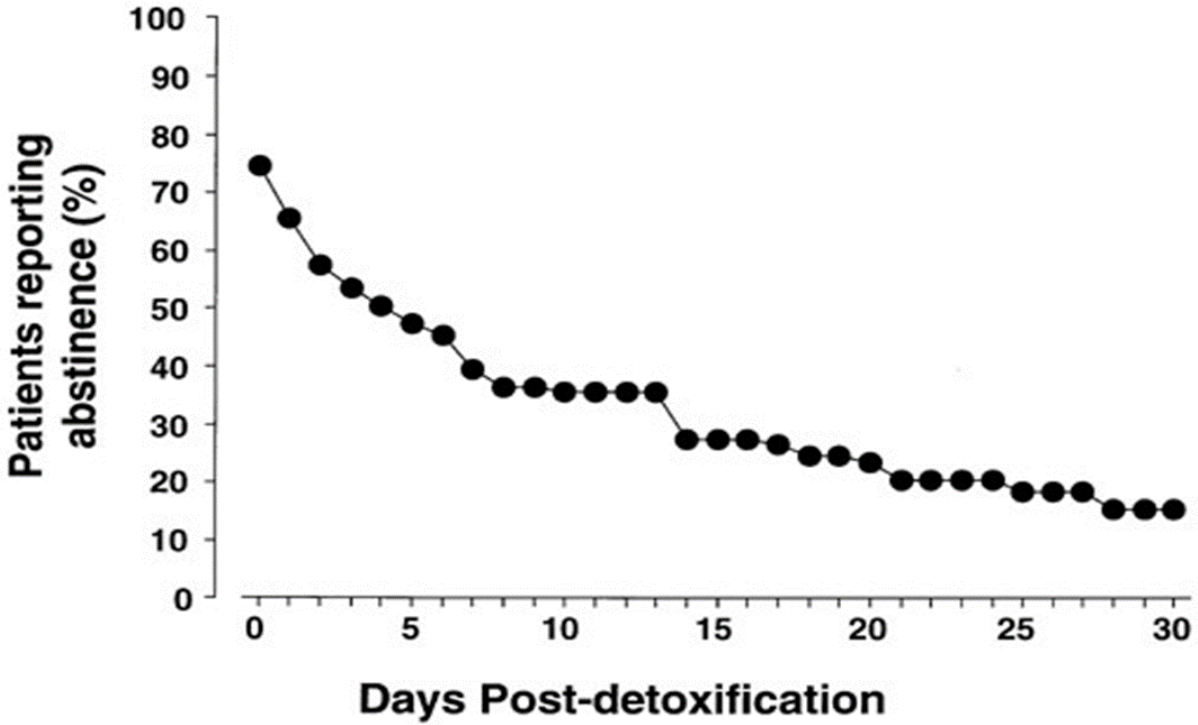
Sean P. Kane, P. D. (n.d.). Number needed to treat. Number Needed to Treat (NNT) Calculator. Retrieved August 3, 2022, from https://clincalc.com/Stats/NNT.aspx

Number Needed to Treat (NNT)

NNT	Bup Dose
1 in 4	**2-6mg**
1 in 3	**7-16mg**
1 in 2	**≥ 16mg**

Mattick RP et al. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. 2014;(2):CD002207.

“Detox” Doesn’t Last



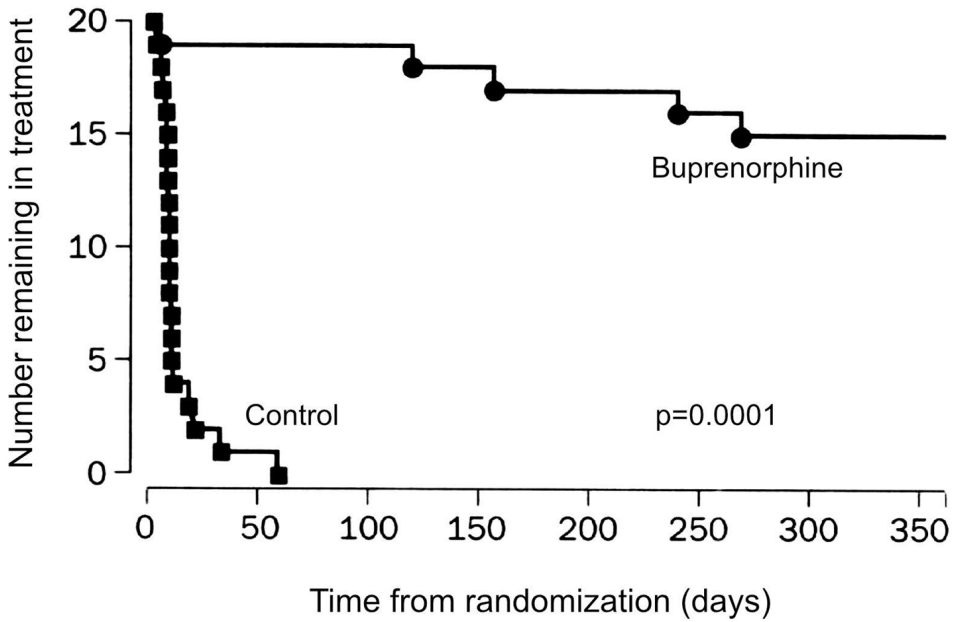
Chutuape et al., 2001

Buprenorphine Improves Retention

Compared to placebo,

75%

of patients taking daily bup **stayed in treatment 1yr**



Kakko et al., 2003

Treatment in the ED drives success

Emergency Department-Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence: A Randomized Clinical Trial

Gail D'Onofrio, MD, MS | Patrick G. O'Connor, MD, MPH | Michael V. Pantalon, PhD | Marek C. Chawarski, PhD | Susan H. Busch, PhD | Patricia H. Owens, MS | Steven L. Bernstein, MD | David A. Fiellin, MD

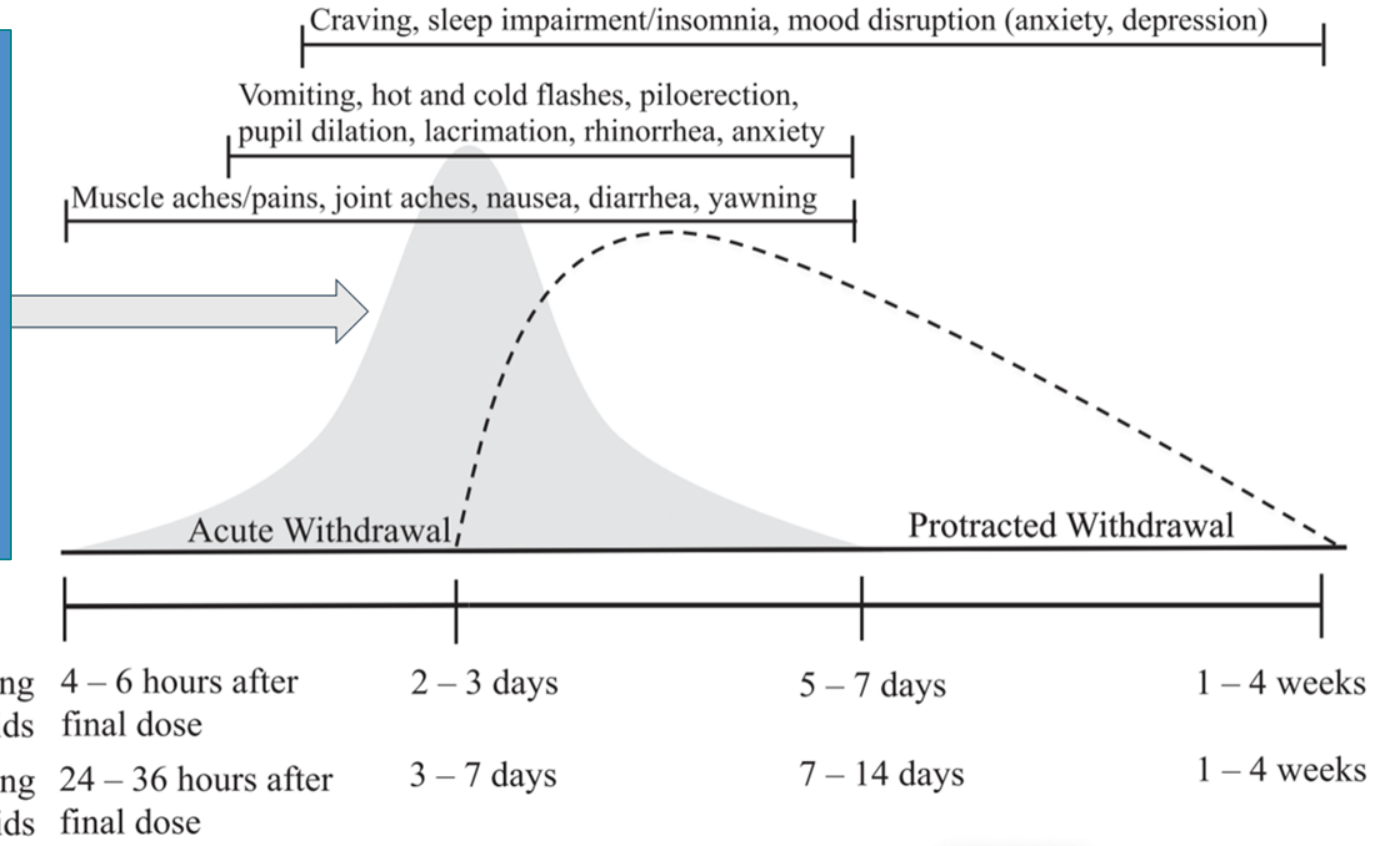
JAMA®
The Journal of the American Medical Association

78% vs. 37%

retention in treatment at 30 days

D'Onofrio et al., 2015

EDs Respond to Dynamic Situations



Bup saves lives

Buprenorphine reduces all-cause mortality by more than 50% over 5 years

Santo et al., 2021

One-year mortality after a non-fatal overdose is similar to STEMI.

Weiner et al., 2019

Starting patients on buprenorphine decreases readmissions and minimizes ED utilization.

Gryczynski et al., 2021

ED-initiated buprenorphine increases the likelihood of your patient being in treatment in 30 days.

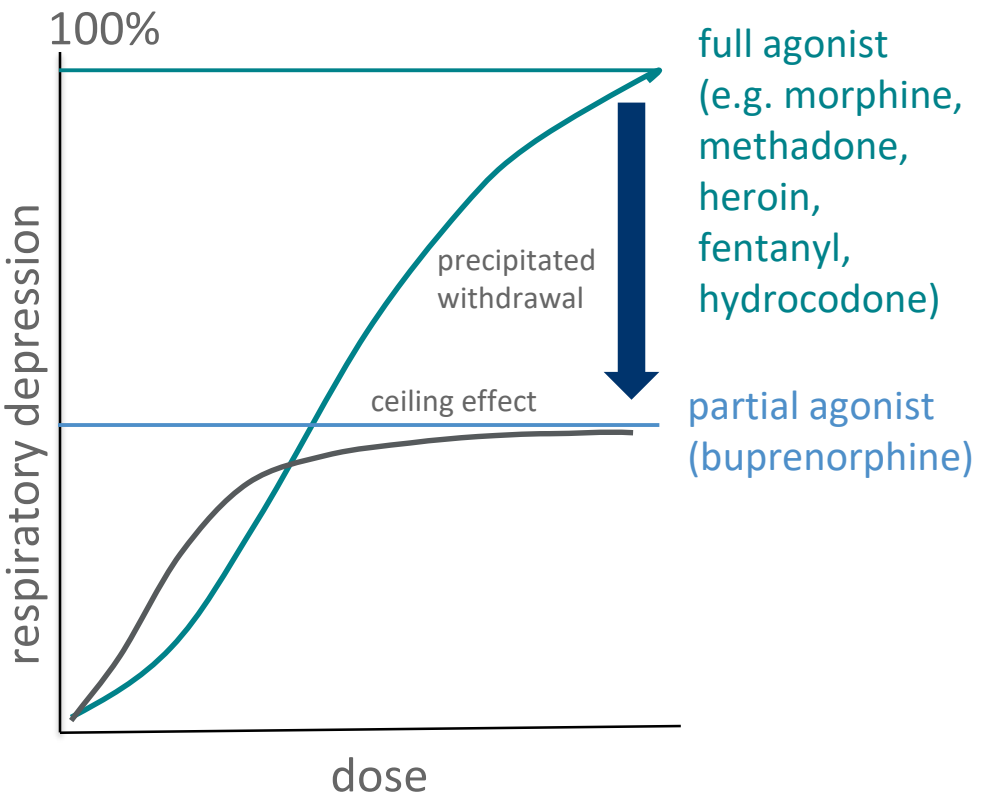
D'Onofrio et al., 2015

Buprenorphine Formulations

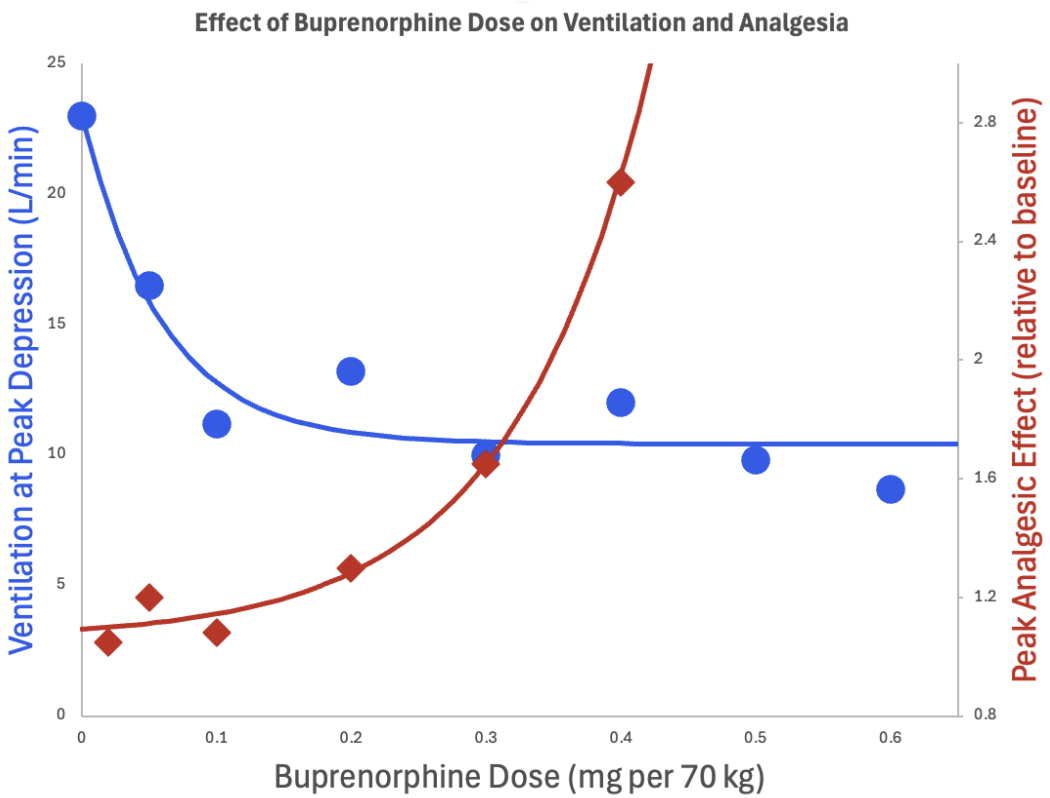
- **Buprenorphine vs. Bup-Naloxone**
  - Naloxone component *not* needed
- **Sublingual tab; buccal film**
  - ***Must dissolve in the mouth***
  - Decreased bioavailability in the stomach
- **IV, IM, transdermal patch**
- **Long-acting injectable buprenorphine (XR Bup)** available in weekly and monthly formulations

Buprenorphine:

- Safely and effectively treats withdrawal, craving, & overdose
- Partial agonist
  - Ceiling effect:
    - Respiratory depression
    - Sedation
  - No ceiling effect:
    - Analgesia
- High affinity
  - Blocks other opioids
  - Displaces other opioids
  - Can precipitate withdrawal
- Long acting
  - Half-life ~ 24-36 Hours



Bup: Ceiling on Respiratory Depression, Not Analgesia



Adapted from Dahan A et al. Br J Anaesth. 2006;96(5):627-32. Pedersen MF et al. Neuropharmacology. 2020;166:107718.

Bup: High Doses are Safe

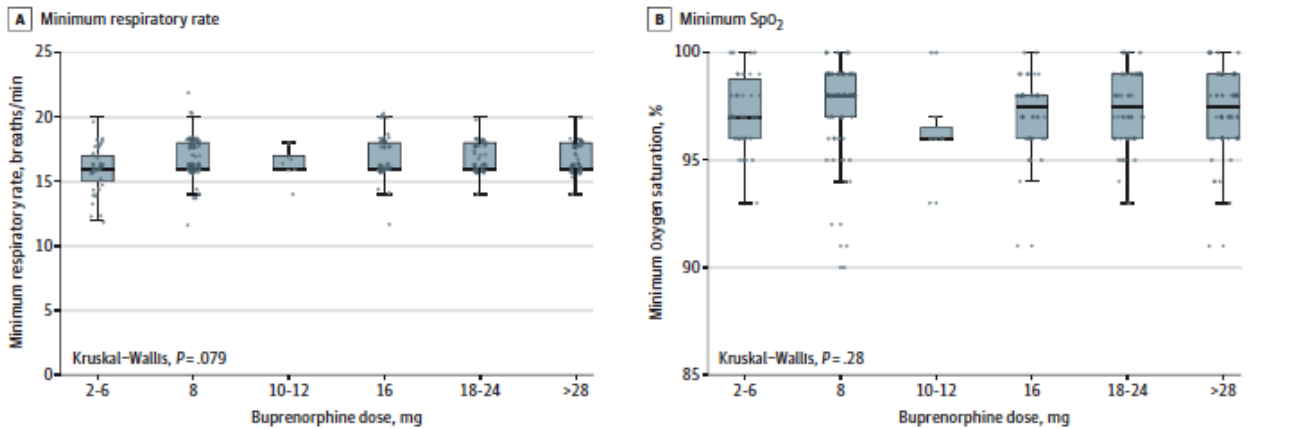
JAMA Network Open

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

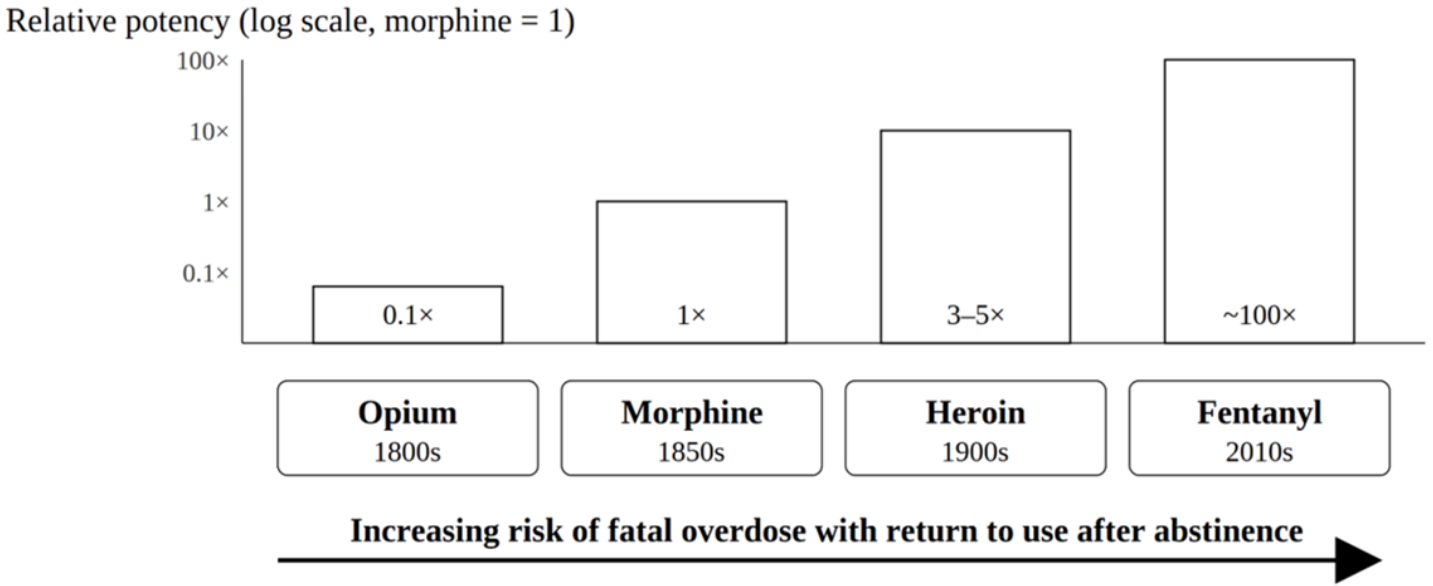
Figure 2. Minimum Respiratory Rate and Oxygen Saturation (SpO_2) Following Initial Dose by Buprenorphine Dose



Boxes correspond to 25th and 75th percentiles, with lines in boxes denoting medians. Dots denote outliers. Error bars denote 95% CIs. Kruskal-Wallis test compares distributions of respiratory rate and oxygen saturation across buprenorphine dose categories.

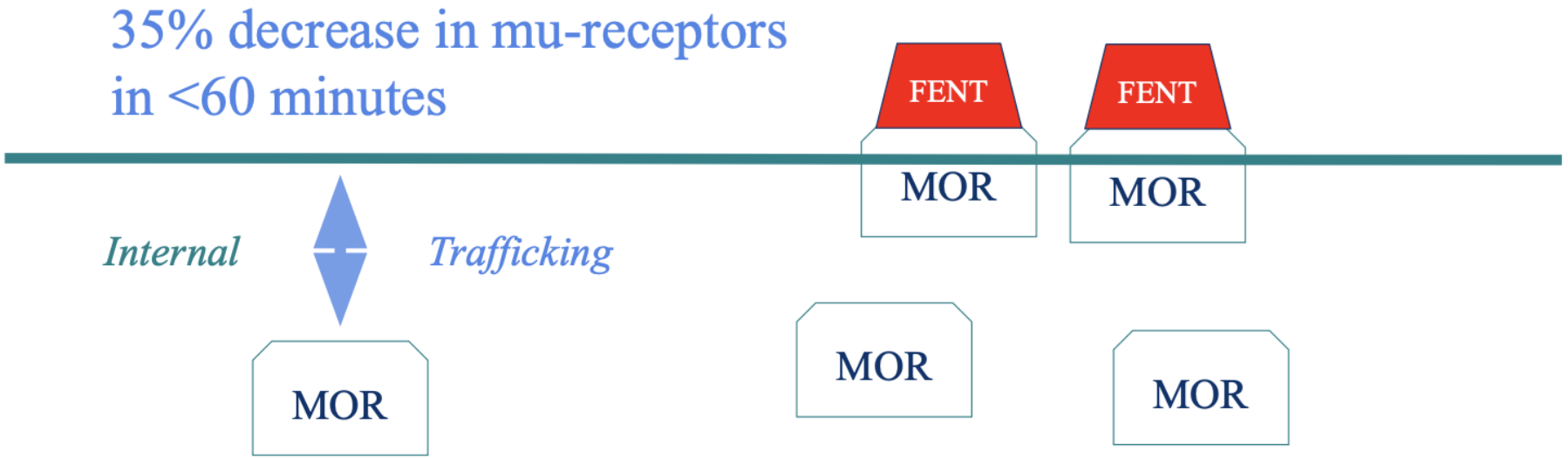
Herring, Vosooghi, and Luftig et al, 2021

USA 2026



More extensive and more persistent neuroadaptations
in reward circuitry and stress-tolerance systems

Fentanyl Rapidly Induces Profound Tolerance



MOR internalization & decreased MOR signal amplification result in tolerance & desensitization

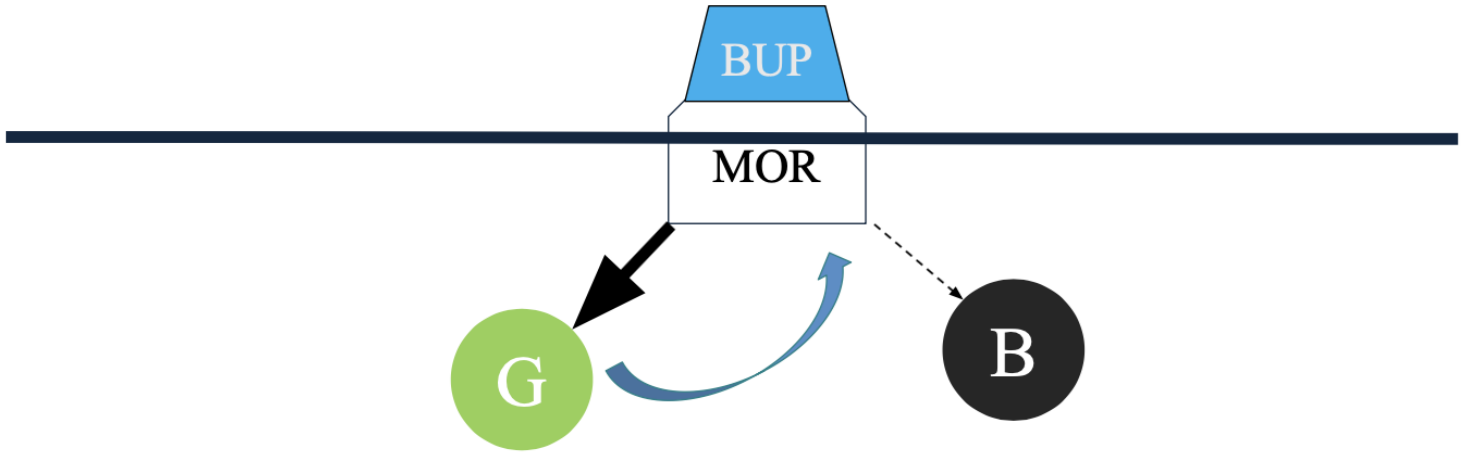
https://pubmed.ncbi.nlm.nih.gov/960064

https://pubmed.ncbi.nlm.nih.gov/9618424/

https://pubmed.ncbi.nlm.nih.gov/19108502/

https://pubmed.ncbi.nlm.nih.gov/23553842/

Bup Promotes Resensitization



- Analgesia
- Mood elevation
- Resp Depression (Ceiling effect)

Resensitization

- ~~MOR Internalization~~
- ~~Desensitization~~
- ~~Hyperalgesia~~

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Direct-to-Inject Long Acting Injectable Bup (DTI XR Bup)

DTI XR Bup Features

1. No sublingual lead in
2. Can administer XR Bup in any state of withdrawal including low or no withdrawal
3. Multiple days of treatment with single injection

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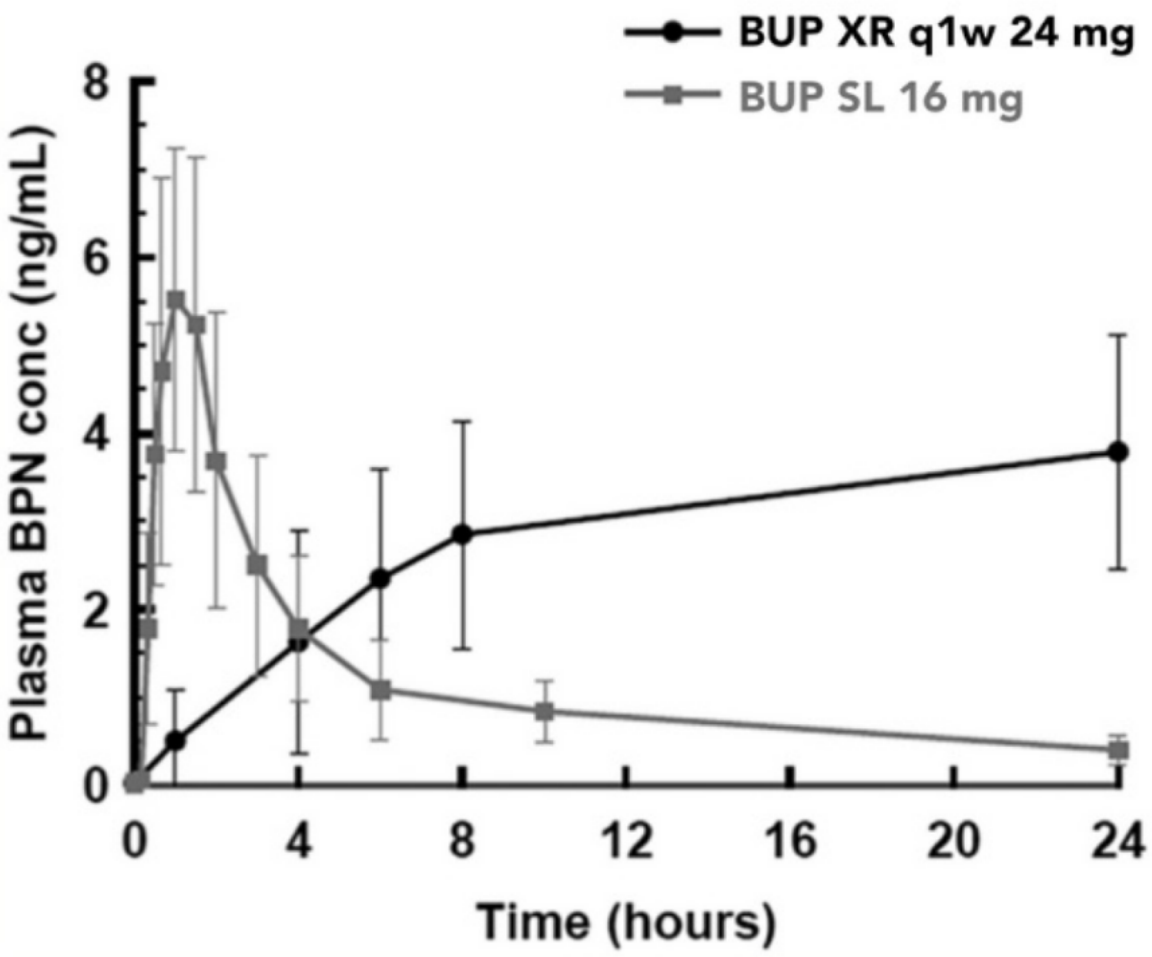
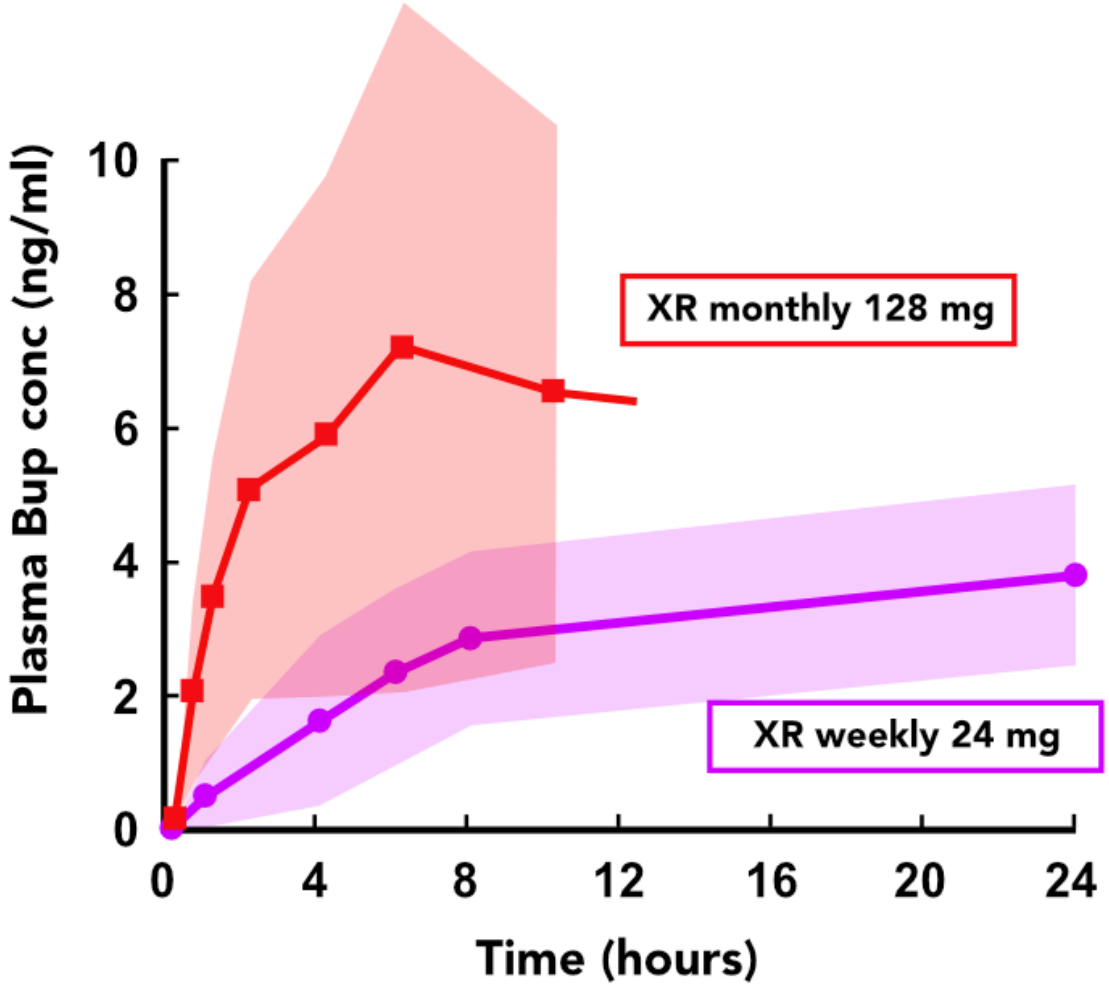
Available formulations of long acting injectable buprenorphine (XR Bup)

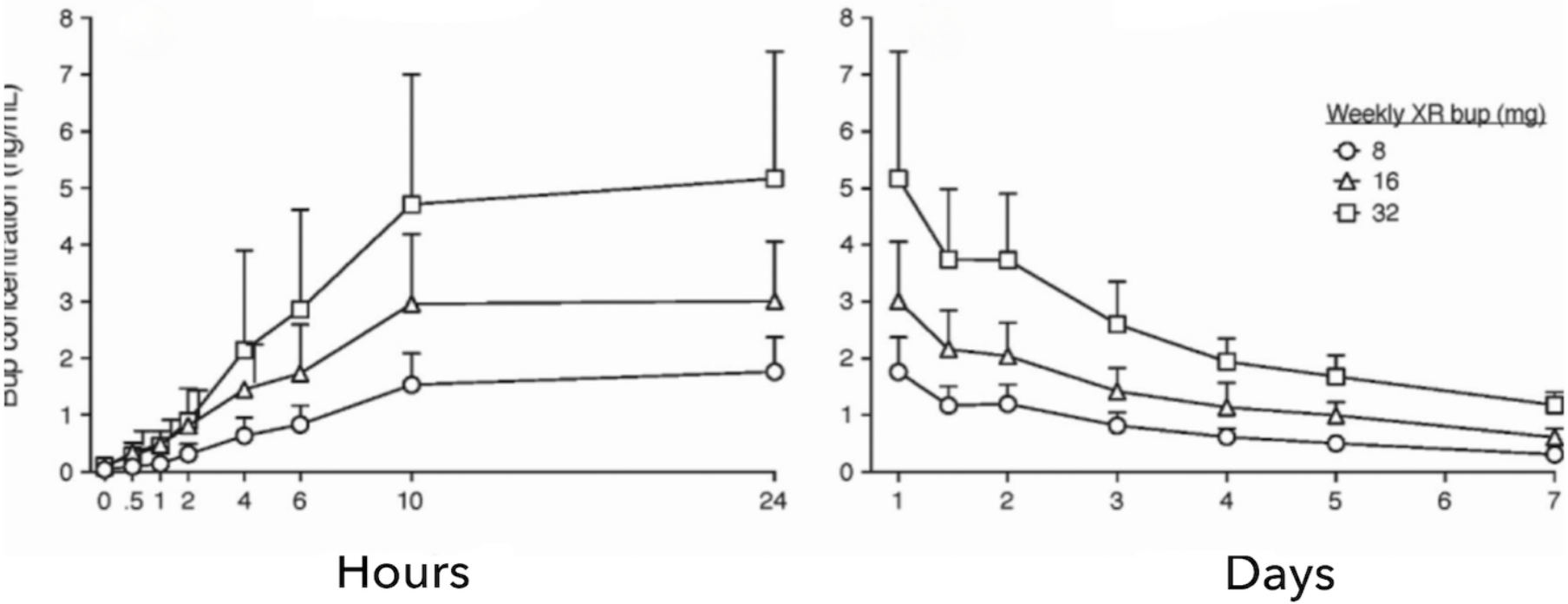
Generation	Formulation	US Brand Name	Dosage Form	Doses	Injection Volumes	Median Time to Max Concentration (Tmax)	Mean Half Life (T1/2)
2nd	XR Bup weekly (50 mg/mL)	Brixadi Weekly	Pre-filled syringe	8 mg, 16 mg, 24 mg, 32 mg	0.16 mL, 0.32 mL, 0.48 mL, 0.64 mL	24 h	5 d
2nd	XR Bup monthly (356 mg/mL)	Brixadi Monthly	Pre-filled syringe	64 mg, 96 mg, 128 mg	0.18 mL, 0.27 mL, 0.36 mL	6-10 h	19-25 d
1st	XR Bup monthly (200 mg/mL)	Sublocade	Pre-filled syringe	300 mg, 100 mg	1.5 mL, 0.5 mL	24 h	45-60 d

Pharmacokinetics of Bup XR vs Bup SL




Plasma Bup conc (ng/ml)
10
8
6
4
2
0
0
4
8
12
16
20
24
Time (hours)
XR monthly 128 mg
XR weekly 24 mg

Pharmacokinetics of Weekly XR Bup



EDINNOVATION Trial: Study Design (D'Onofrio et al. 2026)

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Overview

- Multicenter RCT across 29 US EDs (July 2020 – August 2024)
- N = 1,994 adults with untreated OUD and COWS ≥ 4
- 76% tested positive for fentanyl; 50% unstable housing

Intervention Arms

- **XR-buprenorphine:** 24 mg SC injection (≈16 mg/d equivalent) (COWS ≥ 4)
- **SL buprenorphine:** 8 mg in ED (COWS ≥ 8) or take-home instructions (COWS 4–7)
- Both groups: 7-day follow-up appointment + naloxone
- **Primary outcome:** Engagement in OUD treatment at day 7

D'Onofrio et al. JAMA. 2026.

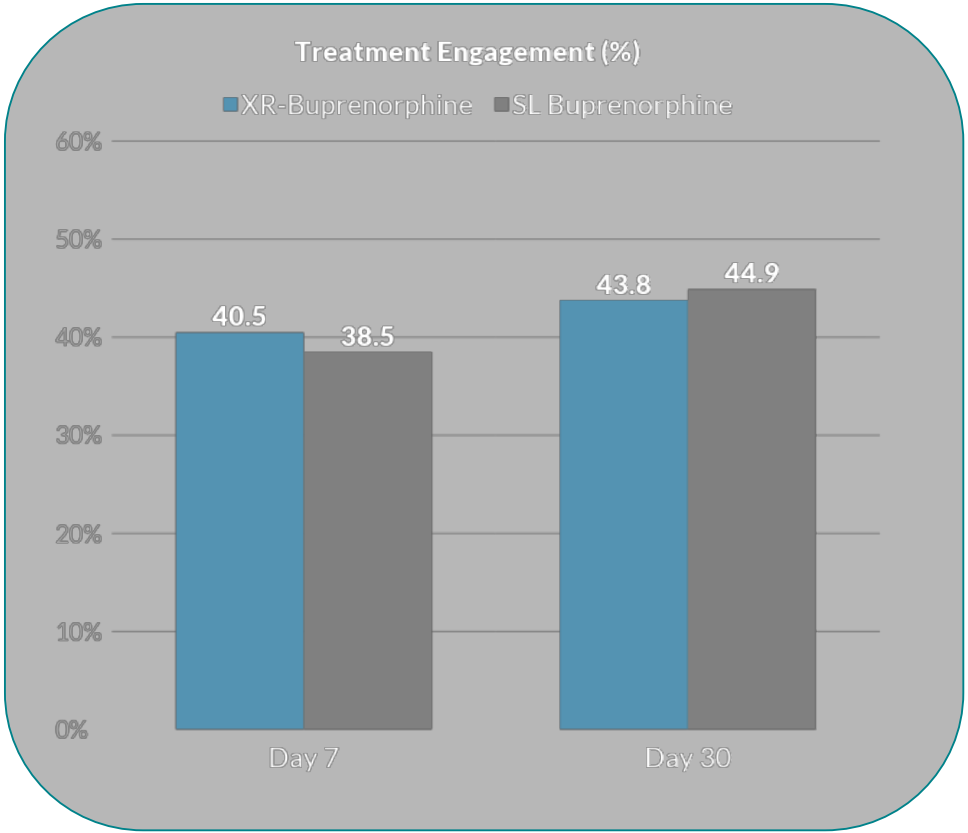
EDINNOVATION: Key Results

Primary Outcome

- Day 7 engagement: **40.5% vs 38.5%**
- Diff +1.6% (95% CI −2.8 to 6.0)
- Day 30: 43.8% vs 44.9%

XR-Bup Advantages

- Lower craving at day 7
- Fewer return ED visits
- Higher patient satisfaction
- PW <1% in both groups



D'Onofrio et al. JAMA. 2026.

EDINNOVATION: Implications for DTI Practice

Safety in the Fentanyl Era

- ~2,000 initiations with <1% precipitated withdrawal — even at COWS ≥4
- Gradual XR bup plasma rise may reduce PW risk vs rapid SL onset

Expanding Access

- Initiation at low withdrawal thresholds — no waiting for COWS ≥ 8
- Eliminates daily adherence barrier — critical for unstable housing, transportation issues, limited pharmacy access
- Fewer ED return visits with XR-bup could reduce system burden

A Key Insight

Day-7 engagement is a downstream, system-dependent measure. DTI Bup-XR's decisive advantage is upstream: ***one injection = 7 full days of steady buprenorphine levels*** *— no Rx to fill, no self-start adherence required.*

D'Onofrio et al. JAMA. 2026.

Waters et al. 2025: Injectable-Only Protocol

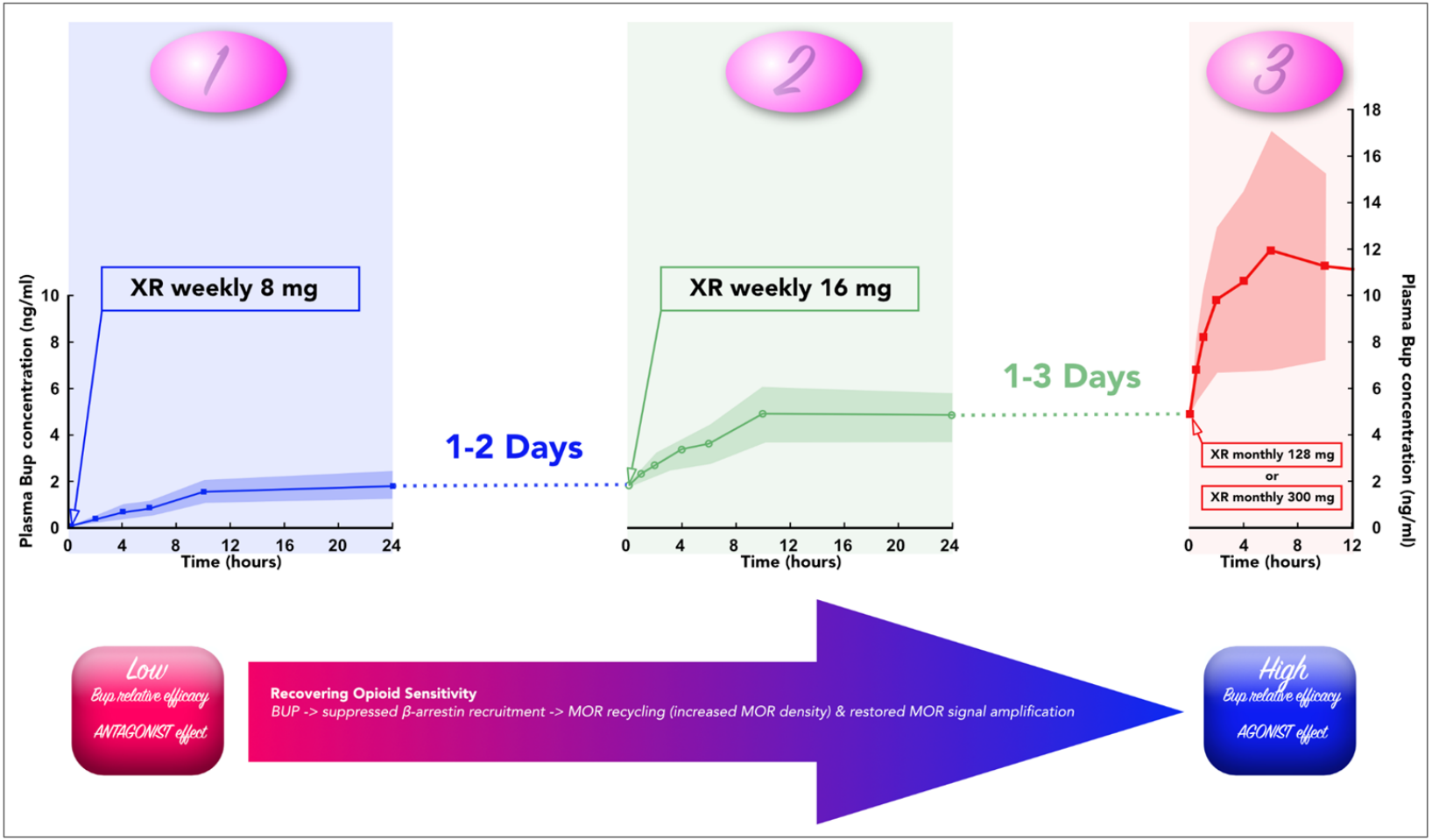
Study Design

- **Retrospective observational cohort study** (EHR data; low-threshold outpatient program + outreach in Seattle)
- **n = 95 patients** with moderate-to-severe OUD actively using fentanyl (79% experiencing homelessness or in permanent supportive housing) who elected the protocol
- Injectable-only 3-dose overlapping buprenorphine start (Day 1: weekly **8 mg**; Day 2: weekly **16 mg**; Day 3: monthly **128 mg or 300 mg**) with *continued fentanyl use allowed*
- Low-threshold clinic + field-based setting (Downtown Emergency Service Center / DESC Opioid Treatment Network)
- No sublingual buprenorphine required at any point
- Multiple doses may be a barrier to broad adoption (noted in study)

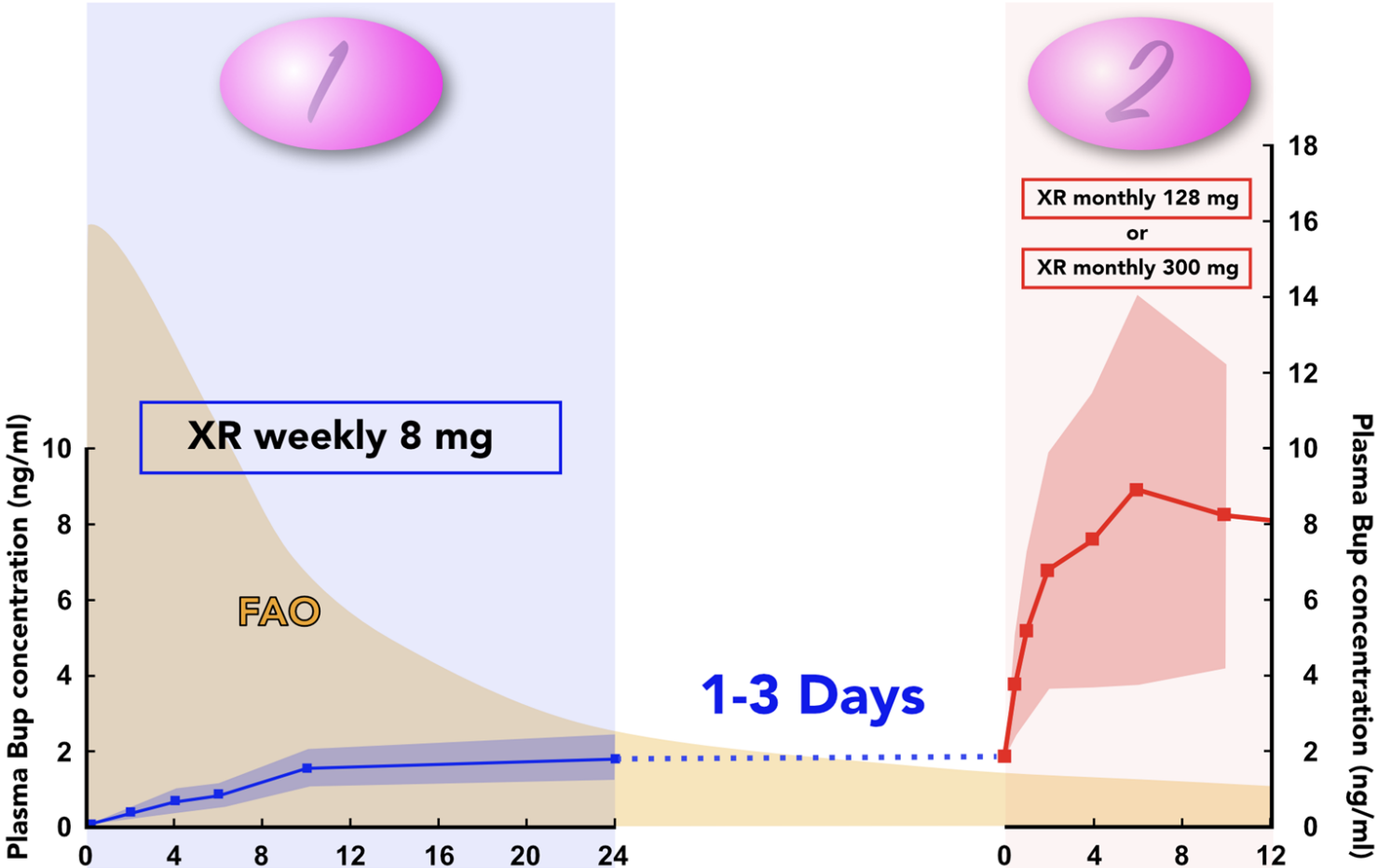
Key Outcomes

- **90% (85/95) successful protocol initiation** without prior sublingual buprenorphine (received first 8-mg weekly injection)
- **75% (71/95) completed the full 3-dose protocol**
- **64% (61/95) 2-month treatment retention** (received second monthly long-acting injectable buprenorphine dose within 45 days of the first; 72% of those who initiated)
- **Favorable safety profile** with overlapping dosing: no serious adverse events reported; withdrawal symptoms possible (counseled and managed supportively with adjuncts); continued fentanyl use permitted
- **Effective treatment engagement** in a real-world low-threshold setting serving highly marginalized patients

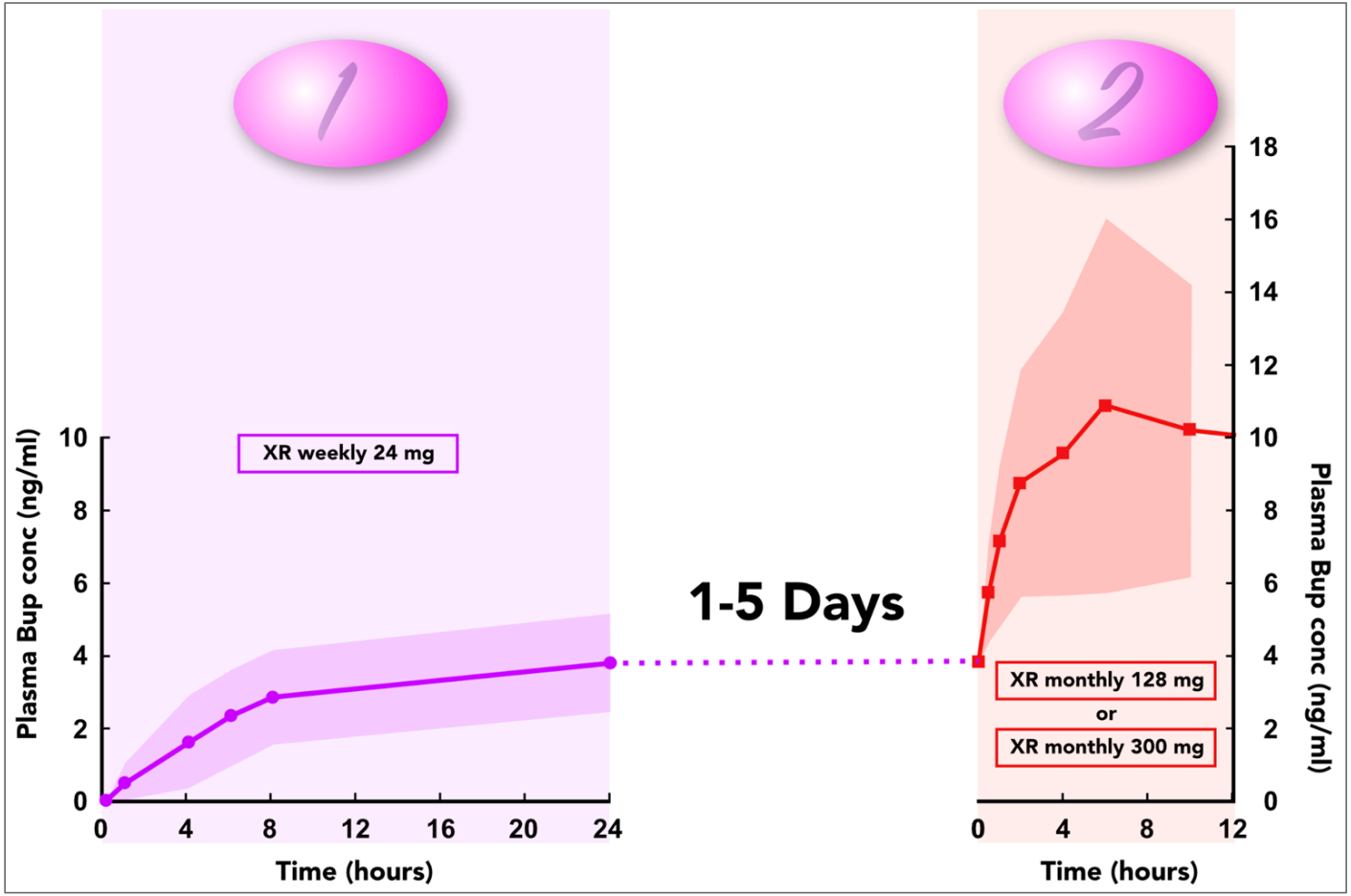
3-Step DTI Protocol: No Withdrawal + Opioid Continuation



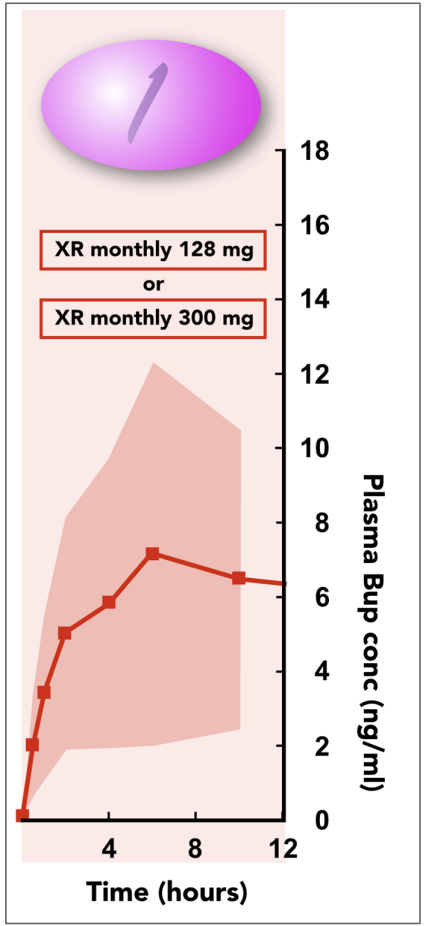
2-Step DTI Protocol: No Withdrawal + Opioid Cessation



2-Step DTI protocol: Withdrawal (COWS≥4), +/- Opioid Continuation



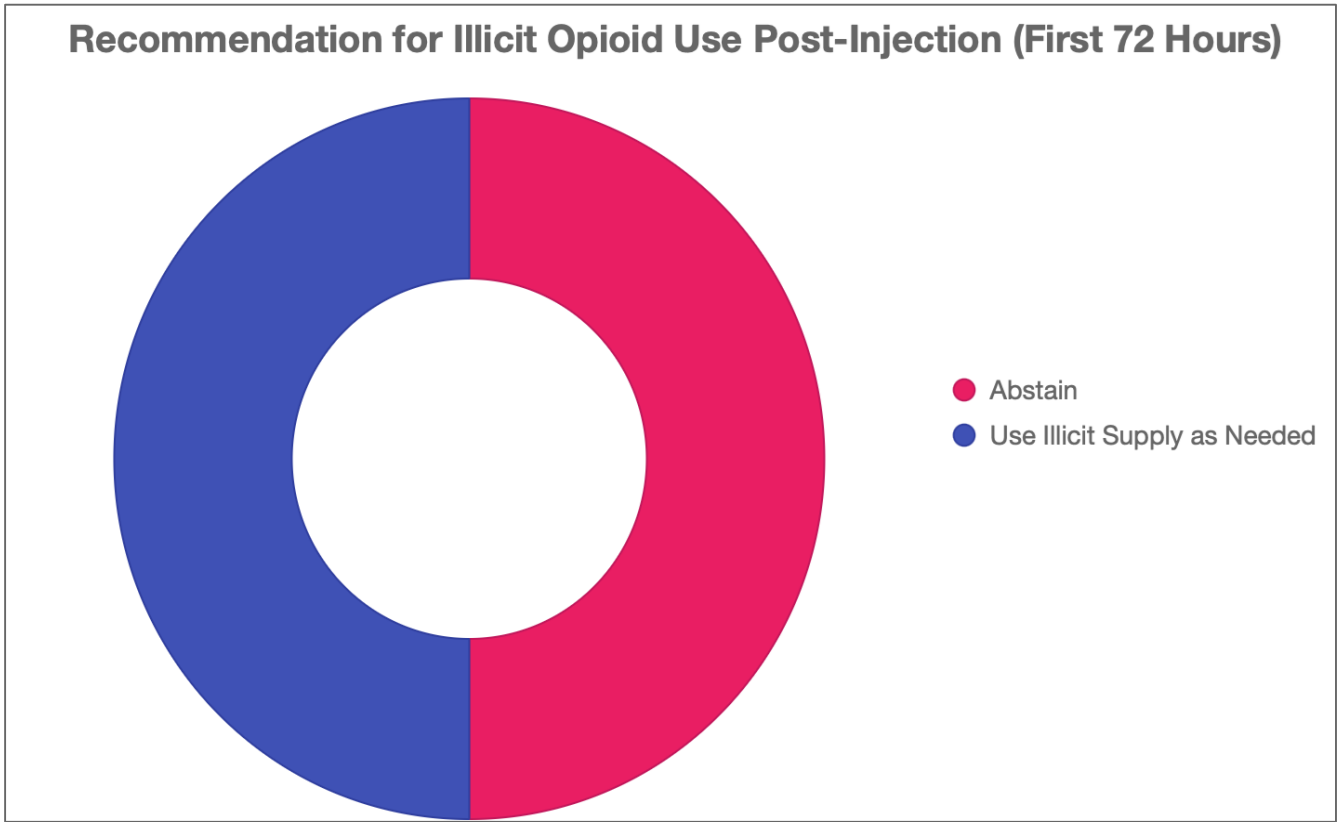
1-Step DTI protocol: In more severe withdrawal at start, +/- Opioid Continuation

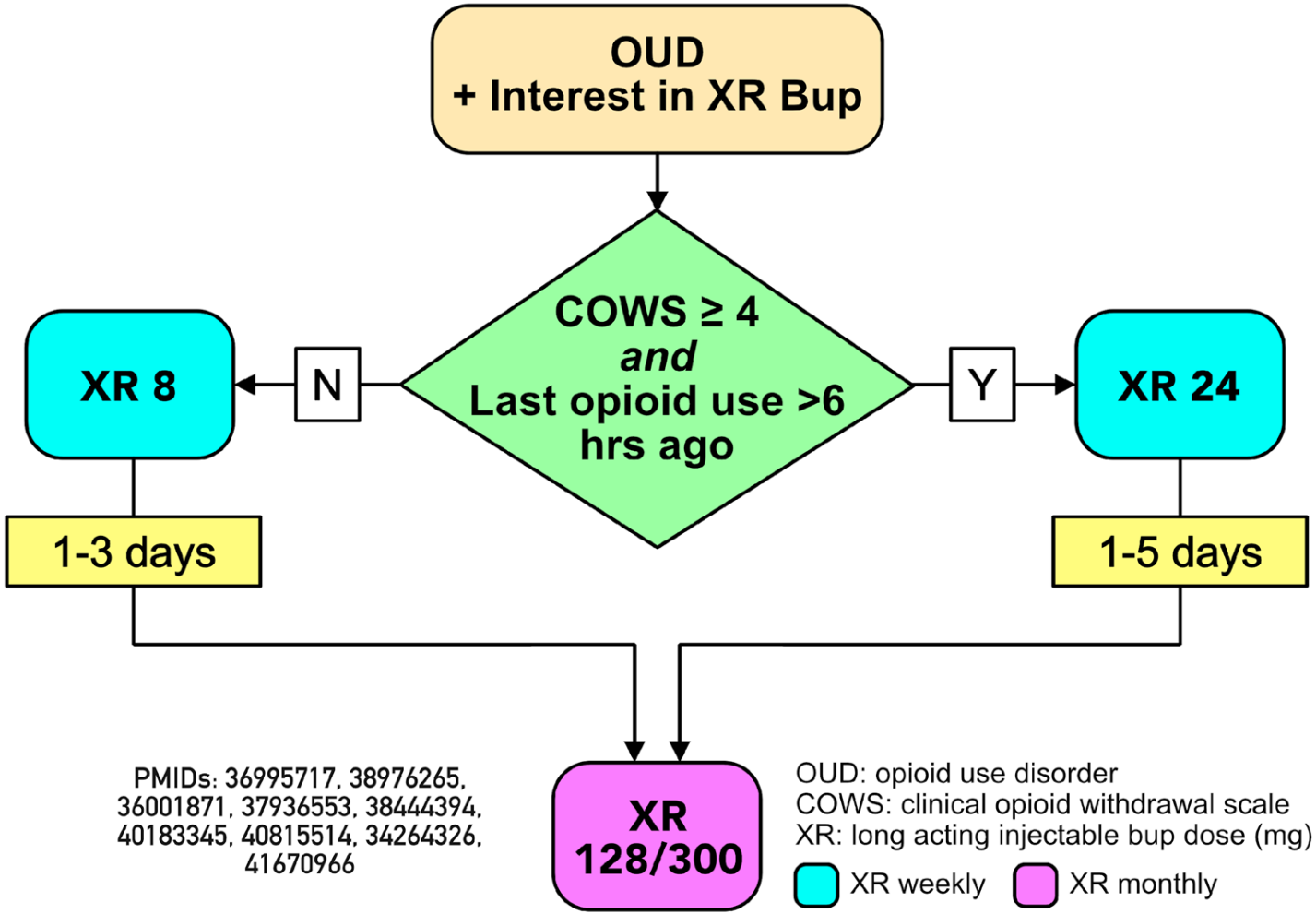


Creating A Useable DTI Guideline

1. Existing XR Bup Research
2. National DTI Clinician Survey
3. National DTI Hackathons
4. DTI Expert Review Panels

DTI Survey Responses




OUD
+ Interest in XR Bup
COWS ≥ 4
and
Last opioid use >6 hrs ago
N
Y
XR 8
XR 24
1-3 days
1-5 days
XR 128/300
PMIDs: 36995717, 38976265, 36001871, 37936553, 38444394, 40183345, 40815514, 34264326, 41670966
OUD: opioid use disorder
COWS: clinical opioid withdrawal scale
XR: long acting injectable bup dose (mg)
XR weekly
XR monthly

Emergency Department Direct-to-Inject (DTI) Buprenorphine

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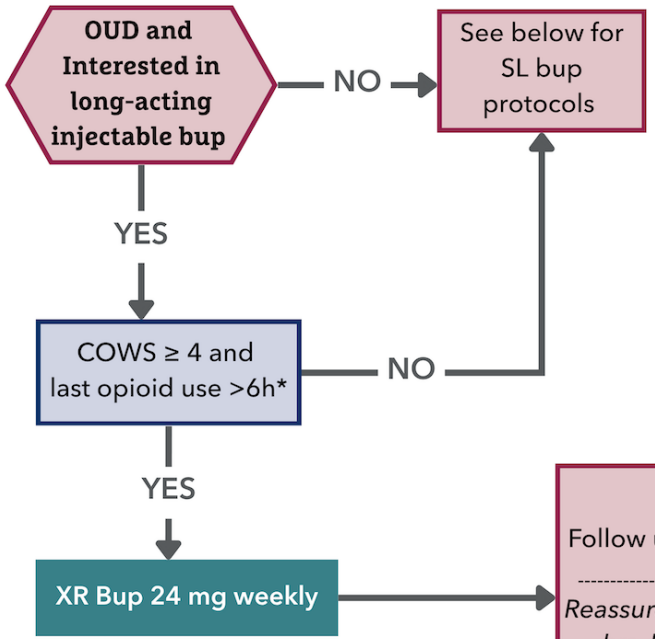
This is the recommended starting protocol for most EDs and new programs. This algorithm initiates weekly long-acting injectable buprenorphine (XR Bup) without a sublingual (SL) lead-in for patients with opioid use disorder (OUD). The Clinical Opiate Withdrawal Scale (COWS) and time since last opioid use help determine readiness for XR Bup dosing.



**XR Bup requires the same timely follow-up engagement and ongoing support after discharge as other formulations.

Starting bup may be delayed or modified if there are complicating factors.

***Complicating factors:**

- Altered mental status, delirium, intoxication,
- Long-term methadone maintenance.
- ~~Pregnant: Risk/benefit discussion. Risk of untreated OUD generally higher than risk of XR bup, but only limited studies.~~

*** Consider avoiding supplemental SL bup in first 24hrs to decrease risk of precipitated withdrawal.

The only absolute contraindication is a true buprenorphine allergy, which is exceedingly rare.

OK in Pregnancy and Breastfeeding

Discharge with return precautions.
Follow up with outpatient within 3-5 days for next dose**

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*Reassure patients plasma levels will continue to rise for 24 hrs, however, if breakthrough withdrawal symptoms persist after 24 hrs consider 8 mg bup SL TID PRN ****

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COWS ≥ 8 + 2 objective signs of withdrawal

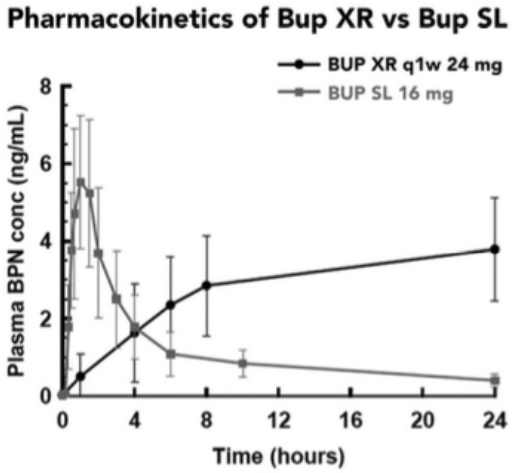
OK for high dose start.

See "Emergency Department Buprenorphine Quick Start."

COWS < 4

Low dose initiation.

See "Buprenorphine Hospital Start: Low-Dose Bup Initiation with Opioid Continuation."



Return Precautions:

1. Overshoot: Sedation, nausea, headache
2. Undershoot: Progressing or under-treated withdrawal
3. Buprenorphine induced withdrawal (precipitated withdrawal)
4. Injection site: Bump ok; red, warm, tender not ok

Emerging Practice: Direct-to-Inject (DTI) Buprenorphine

1st Dose in No or Low Withdrawal

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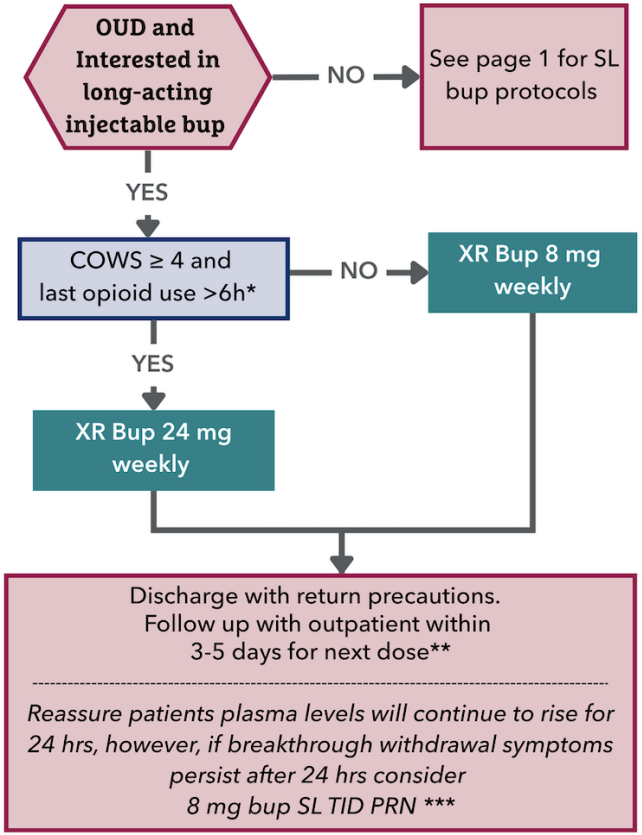
This emerging practice accommodates patients who are in no or low withdrawal in ED or clinic settings.



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***Complicating factors:**

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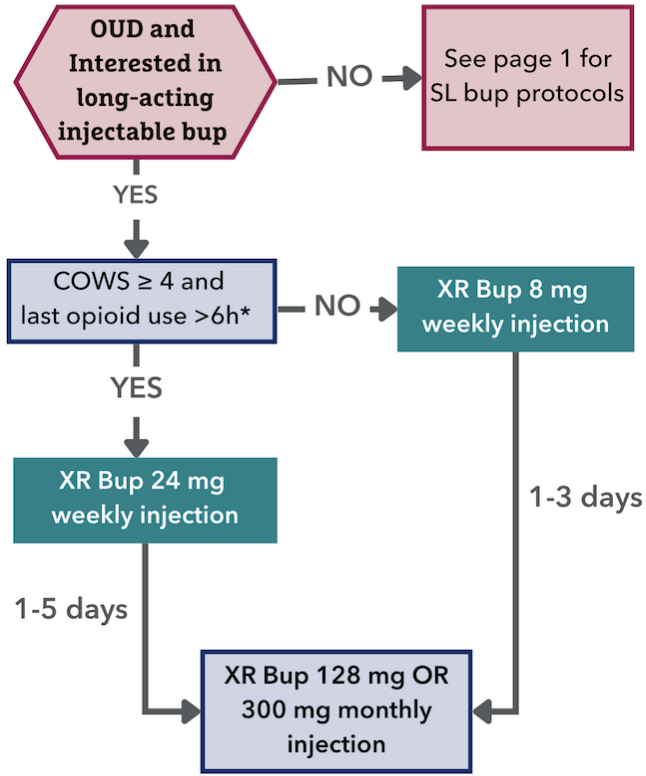
Emerging Practice: Direct-to-Inject (DTI) Buprenorphine
Routes to XR Bup Monthly

This emerging practice supports patients who receive their 1st dose in the ED or clinic and 2nd dose in a clinic setting.



Starting bup may be delayed or modified if there are complicating factors.

***Complicating factors:**

- Altered mental status, delirium, intoxication,
- Long-term methadone maintenance.
- Pregnant: Risk/benefit discussion. Risk of untreated OUD generally higher than risk of XR bup, but only limited studies.

*** Consider avoiding supplemental SL bup in first 24hrs to decrease risk of precipitated withdrawal.

The only absolute contraindication is a true buprenorphine allergy, which is exceedingly rare.

Return Precautions:

1. Overshoot: Sedation, nausea, headache
2. Undershoot: Progressing or under-treated withdrawal
3. Buprenorphine induced withdrawal (precipitated withdrawal)
4. Injection site: Bump ok; red, warm, tender not ok

May consider symptom targeted treatments for breakthrough withdrawal during XR initiation, including:

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Restlessness, sweating, tachycardia

- **Clonidine** 0.1-0.3 mg q6-8h prn sweating/racing heart/chills/hot flashes/anxiety, #28 *onset in 30-60 min* or **Lofexidine** 0.18 mg 3-4 tabs q6h sweating/chills/anxiety, #112 *onset in 30-60 min* or **Tizanidine** 4 mg q6h prn muscle aches/restlessness/anxiety, #28 *onset in 30-60 min* or **Guanfacine** ER 4mg daily prn anxiety/restlessness/sweating, #7 *onset in 2-4 hrs*
- **Ketamine** 16 mg troche [or 16 mg/ml syrup] 8–16 mg sublingual q8-12h prn withdrawal symptoms, max 48 mg/day, #8 troches [or 8 ml].

Emergency Department Buprenorphine (Bup) Quick Start

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Connect with your patient: Accurate diagnosis and treatment requires trust, collaboration, and shared decision making.

Opioid withdrawal*?

NO → **Rx self-directed start:**
- Wait for severe withdrawal then start with 8–24+ mg SL.
- Rx per "Discharge" box below.

YES ↓

16 mg bup SL**
(range 8–24+ mg)

30-60 minutes ↓

Withdrawal improved?

NO → **If no improvement or worse, consider:**

Worsening withdrawal (common): Occurs with lower starting doses and heavy tolerance; improves with more bup (additional 8–16 mg SL).

Other substance intoxication or withdrawal: Continue bup and manage additional syndromes.

Bup side-effects: e.g., nausea or headache. Continue bup and treat side-effects with supportive medications.

Medical illness: Continue bup and manage underlying condition.

If sudden & significant worsening, consider precipitated withdrawal (rare): See box below.

30-60 minutes YES ↓

Administer 2nd dose
Additional 8–24+ mg SL bup

↓

*Diagnosis Tips for Opioid Withdrawal:

1. **Look for at least two clear objective signs not attributable to something else:** large pupils, yawning, runny nose & tearing, sweating, vomiting, diarrhea, gooseflesh/piloerection, tachycardia.
2. **Confirm with the patient that they feel 'bad' withdrawal** and they **feel ready to start bup.** If they feel their withdrawal is mild, it is likely too soon.
3. **As needed, consider using the COWS (clinical opioid withdrawal scale).** Start if COWS ≥ 8 with ≥ 2 objective signs.
4. Withdrawal sufficient to start bup typically occurs 24–36 hrs after decreased/stopped use, but can vary from 6–72 hrs. Methadone withdrawal commonly takes longer.

**Bup Dosing Tips:

1. Respect patient preference. Shared decision making, flexibility, and collaboration are essential.
2. Heavy dependence/tolerance (e.g., fentanyl) may need higher doses of bup.
3. Low dependence/tolerance may do well with lower doses of bup.
4. Starting bup may be delayed or modified if there complicating factors:
   - Altered mental status, delirium, intoxication
   - Severe acute pain, trauma, or planned surgery
   - Severe medical illness
   - Long-term methadone maintenance

Step 1: Look for 2 Objective Signs

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Common Mimics:

1. Anxiety
2. Meth
3. Viral syndrome

Bup Buddy!

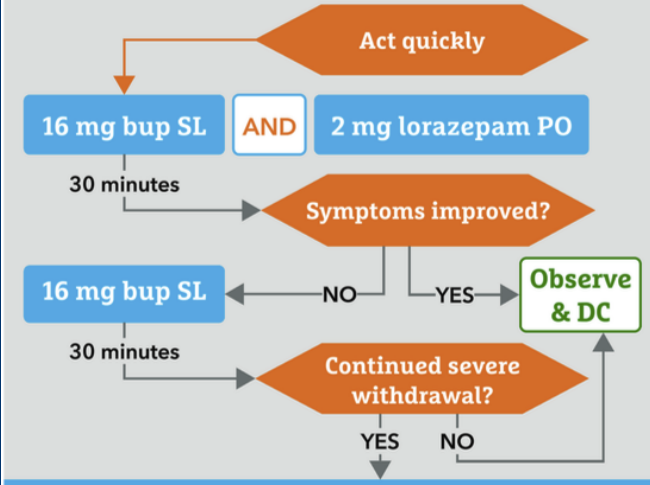
Include 2+ *objective* signs!

- Dilated pupils
- “Goose bumps”
- Vomiting
- Tachycardia
- Yawning
- Runny nose & eyes

In the event of buprenorphine precipitated withdrawal (sudden severe worsening of withdrawal symptoms, e.g., abrupt COWS score increase of >5):

Treatment of bup precipitated withdrawal

(Sudden, significant worsening of withdrawal soon after bup administration.)



Adjuvants:
OK but should not delay or replace bup. Use sparingly with appropriate caution.

Benzodiazepines:
- Lorazepam 2 mg PO/IV

Antipsychotics:
- Olanzapine 5 mg PO/IM

Alpha-agonists:
- Clonidine 0.1-0.3 mg PO

D2/D3 agonists:
- Pramipexole 0.25 mg PO

Gabapentinoids:
- Pregabalin 150 mg PO

Escalate level of care to manage potential moderate to deep sedation including cardiac, pulse oximetry, and end tidal CO_2 monitoring:

1. Ketamine (0.3 mg/kg IV slow push q 15 minutes and/or infusion).
2. Fentanyl 200 mcg IV q10 minutes. Total dose of > 2000 mcg has been reported.

After clinical resolution, observe and discharge with bup Rx and/or XR-bup

Source: CA Bridge's "Emergency Department Buprenorphine Quick Start"

For refractory precipitated withdrawl not responding to bup / fentanyl / ketamine, consider dexmedetomidine. Typically need higher dosing, e.g., starting at 1-1.5 mcg/kg/hr and titrating up as needed.

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Buprenorphine Self-Start

Guidance for patients starting buprenorphine outside of hospitals or clinics

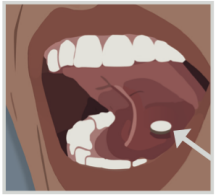
1. **Plan to take a day off and have a place to rest.**
2. **Stop using and wait until you feel very sick from withdrawals (at least 12 hours is best, if using fentanyl it may take a few days).**
3. **Dose one or two 8mg tablets or strips UNDER your tongue (total dose of 8-16mg).**
4. **Repeat dose (another 8mg-16mg) in an hour to feel well.**
5. **The next day, take 16-32mg (2-4 tablets or films) at one time.**

If you have started bup before:

- If it went well, that's great! Just do that again.
- If it was difficult, talk with your care team to figure out what happened and find ways to make it better this time. You may need a different dosing plan than what is listed here.

If you have never started bup before:

- Gather your support team and if possible take a "day off."
- You are going to want space to rest. Don't drive.
- Using cocaine, meth, alcohol or pills makes starting bup harder, and mixing in alcohol or benzos can be dangerous.



Place dose under your tongue (sublingual).

If you have a light habit: *(For example, 5 "Norco 10's" a day)*

- Consider a low dose: start with 4mg and stop at 8mg total.
- **WARNING:** Withdrawal will continue if you don't take enough bup.

If you have a heavy habit: *(For example, injecting 2g heroin a day or smoking 1g fentanyl a day)*

- Consider a high dose: start with a first dose of 16mg.
- For most people, the effects of bup max out at around 24-32mg.
- **WARNING:** Too much bup can make you feel sick and sleepy.

Partial Agonists + Full Agonists

Co-administration example:

Buprenorphine → Promotes sensitivity recovery

+

Hydromorphone → Prevents withdrawal

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Buprenorphine (Bup) Hospital Start: Low-Dose Bup Initiation with Opioid Continuation

Treatment Bundle Over Three Days[1]

Maximize pain control & withdrawal treatment with opioid analgesics throughout bup initiation

Day 1

Opioid Continuation [2]

Example Regimen: (*see page 2 for alternatives*)

1. Morphine ER 30–60 mg PO q8h scheduled
2. Morphine IR 15–30 mg PO q4h PRN
3. Morphine 10–20 mg IV q4h PRN

Low-Dose Bup Initiation (Day 1)[3]

Bup 0.5 mg SL q3h x 8 doses

(q4h x 6 doses is OK)[4]

Day 2

Low-Dose Bup Initiation (Day 2)

Bup 1 mg SL q3h x 8 doses

(q4h x 6 doses is OK)[4]

Day 3

Low-Dose Bup Initiation (Day 3)

Bup 8 mg SL TID or

Injectable XR bup

(e.g., 300 mg SQ)

Low Dose Initiation with Opioid Continuation

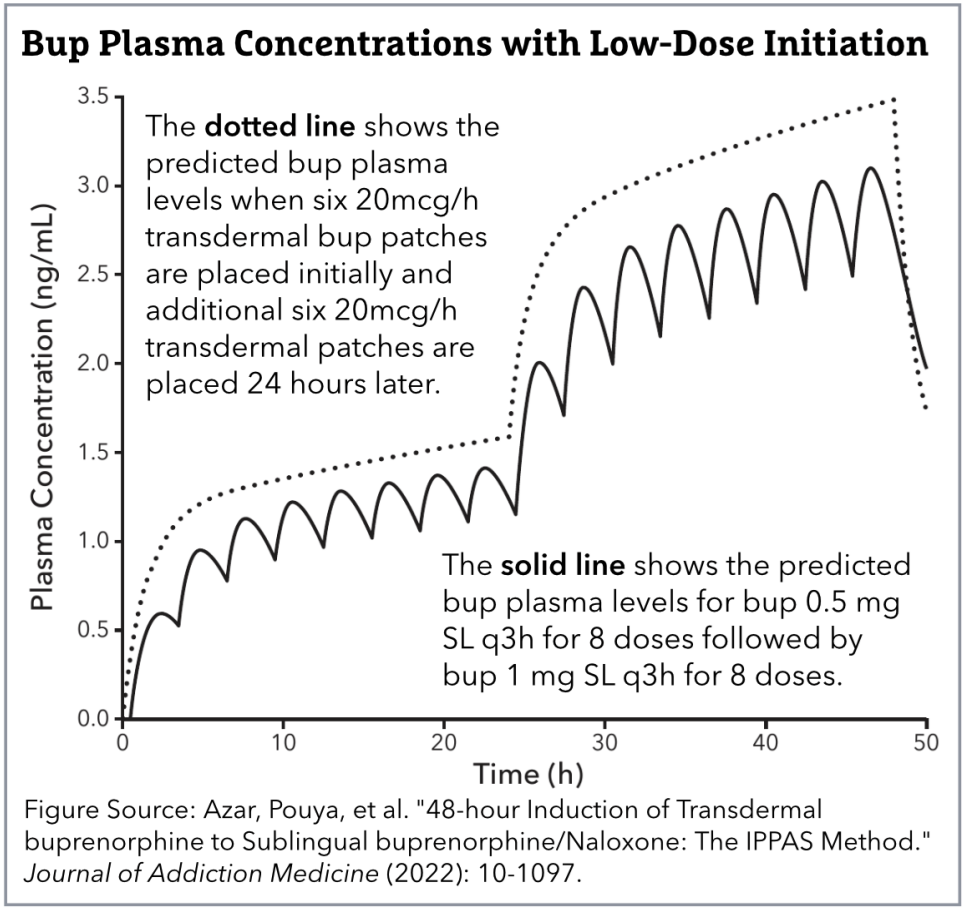
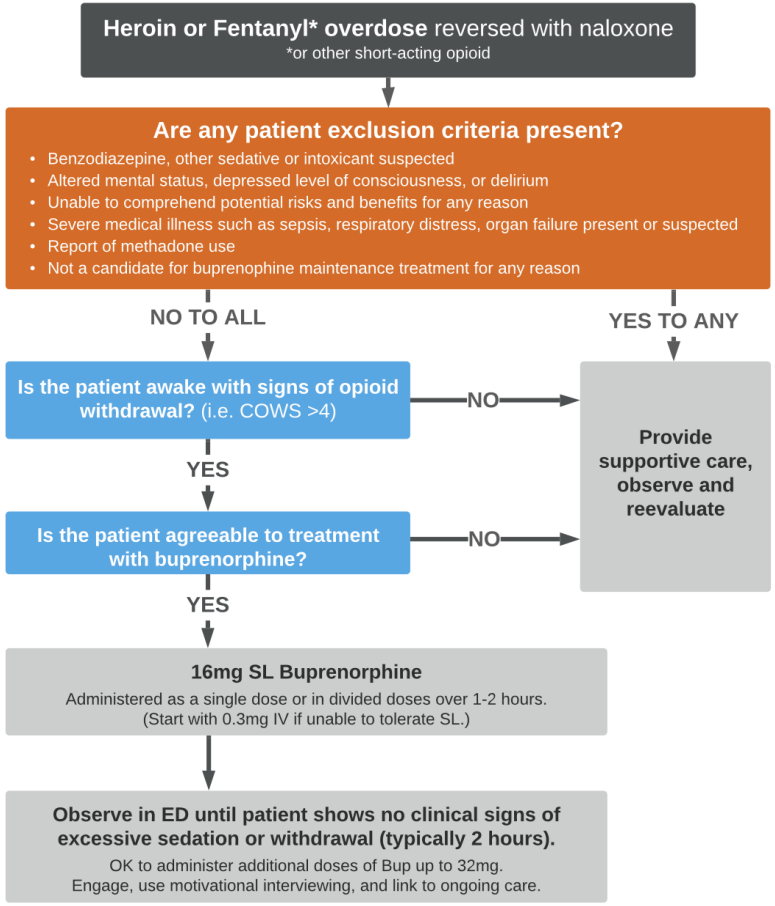


Figure Source: Azar, Pouya, et al. "48-hour Induction of Transdermal buprenorphine to Sublingual buprenorphine/Naloxone: The IPPAS Method." *Journal of Addiction Medicine* (2022): 10-1097.

Starting Buprenorphine Immediately after Reversal of Opioid Overdose with Naloxone

Based on Herring, A. A., Schultz, C. W., Yang, E., & Greenwald, M. (2019). Rapid induction onto sublingual buprenorphine after opioid overdose and successful linkage to treatment for opioid use disorder. *The American journal of emergency medicine*.



DTI Potential to Expand Treatment Access

- Can be used in patients with low or no withdrawal
  - Highest-risk patients can struggle to present in withdrawal
- Bup serum levels gradually increase over 24 hours after injection of weekly formulation, decreasing risk of precipitated withdrawal
- Meets patients “where they are at,” at the moment they engage in care
- Can consider giving monthly formulation for quicker onset if patient presents in severe withdrawal and/or unable to return within a week (potential increased risk of precipitated withdrawal)

Dahan et al., 2006.

DTI Potential to Expand Treatment Access

- Potential for improved adherence, “set it and forget it”
- Access for patients who struggle with sublingual meds
  - Taste
  - Mucosal irritation

Dahan et al., 2006.

DTI in Pregnancy

MOM study (2026)

- n=140, XR Bup vs SL Bup
- superior opioid abstinence vs. sublingual bup (82.5% vs. 72.6%)
- comparable rates of neonatal opioid withdrawal syndrome requiring treatment (~28–30% in both arms)
- fewer serious maternal adverse events

Winhusen, et al., *JAMA Intern Med* 2026

DTI Advantages

Increased convenience:

- ED/clinic/street initiation: immediate injection, no SL-BUP lead-in or test dose
- Can start in any withdrawal state, including NOT in withdrawal
- Low-complexity start: steadily escalating plasma bupe levels without complicated SL-BUP ramp-up dosing
- ED setting: Rx is optional

DTI Challenges

- Injection
  - Pain, itching, redness, lumps (less of an issue with 2nd gen XR-BUP)
  - Needle phobia
- REMS: limited specialty pharmacy distribution network, REMS certification
- Cost: buy/bill vs bill/buy model. Prior-authorizations, grant funding often required

Survey & Hackathon Shared Resources

Name	Owner
Guides and Algorithms	me
Literature and prescribing info	me
DTI Hackathon	me
May 28 DTI Chat.txt	aosoria
NEAT Webinar DTI	me
XR BUP Direct to Inject! How do you do it? (...	

https://bit.ly/DTIHackResources

Strategies for XR-Bup Medication Access

Procurement Models

- **340B Drug Pricing** — deep discounts for safety-net facilities
- **Buy-and-bill** — stock in clinic/inpatient pharmacy; eliminates external delays
- **Specialty pharmacy** (e.g., Genoa) — order → ship to clinic; REMS certification required
- **Retail pharmacy** (e.g., Safeway/Albertsons) — pharmacist-administered injections on-site
- **Infusion Clinics** — quick visits (much faster than chemo infusions), profitable, highly sustainable

Patient Assistance Programs

- **INSUPPORT** (Sublocade) — copay assistance + uninsured options
- **ByYourSide** (Brixadi) — copay as low as $0 + uninsured options
- **State Medicaid formulary** — coverage high but PA requirements vary by state

Targeting High-Risk Patients: The ROI Case for XR-Bup

Prioritize Patients Who Drive System Costs

- Frequent ED visits and repeat overdose presentations
- Prior hospital/ICU admissions for opioid-related complications
- Repeat EMS transports for opioid-related events

Evidence for Cost Offset

- 57% lower odds of all-cause ED visits vs no MOUD
- Nonfatal overdoses ↓22%, ED visits ↓78%, hospitalizations ↓77% at 1 year
- Inpatient costs nearly 5x lower vs daily oral buprenorphine
- ***Upfront XR-Bup cost is offset by reduced acute care utilization***

Gaiazov et al. 2025; Yarborough et al. 2024; Marion-Bellemare et al. 2025; Indivior RWE 2025

Prior Authorization & Workflow Quick Wins

Reducing Prior Authorization Barriers

- Pre-approved standing protocols for ED/inpatient settings
- Leverage inpatient pharmacy inventory for same-day initiation
- Same-day authorization via manufacturer support programs
- Template letters, benefit investigation forms via Bridge toolkit

Practical Quick Wins by Setting

- **ED/Inpatient** — internal buy-and-bill eliminates external delays
- **Outpatient/Clinic** — Genoa + advance Rx for reliable scheduled delivery
- **Community access** — retail pharmacy (Safeway) for pharmacist-administered injections
- **Infusion centers** — partner for sustainable insurance billing

Health Equity and DTI: Closing the Gap

- Black, Latino, and Native American communities experience disproportionate rates of opioid overdose deaths yet face the greatest barriers to treatment
- Traditional induction requirements create additional obstacles for persons experiencing homelessness or unstable housing
- DTI eliminates withdrawal requirement, daily dosing, and safe storage needs
- Implementation data drawn from safety-net hospitals, street medicine programs, and community clinics serving predominantly underserved populations
- DTI expands equitable access to life-saving medication for communities most affected by the overdose crisis

Every encounter is an opportunity to offer treatment

Herring et al. Ann Emerg Med. 2019;73(5):e13-e68. Matheson et al. J Subst Abuse Treat. 2022;139:108781.

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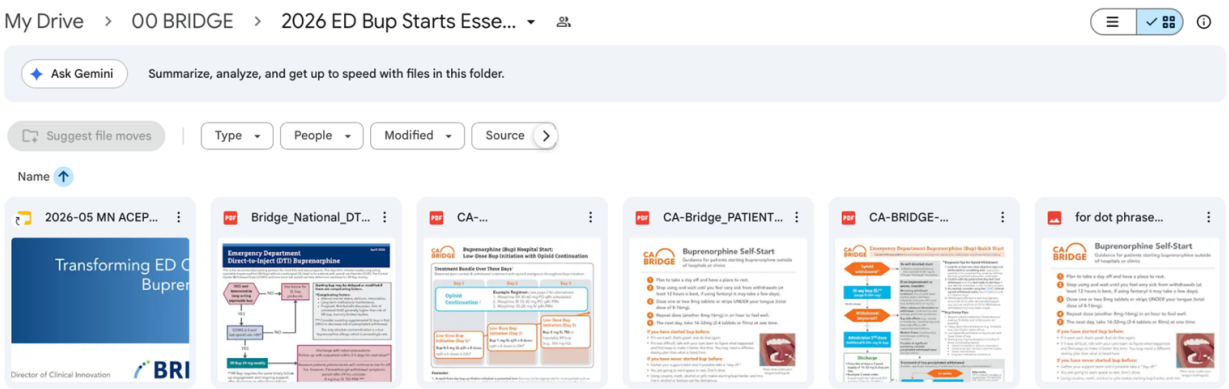
All people deserve rapid access to evidence-based treatment *with dignity.*

Direct-To-Inject Buprenorphine is an evidence-based option to initiate buprenorphine at a lower COWS

Precipitated Withdrawal remains <1% in large national RCT

There are multiple pathways to support patients initiate buprenorphine treatment and recovery opioid sensitivity

Essential Resources



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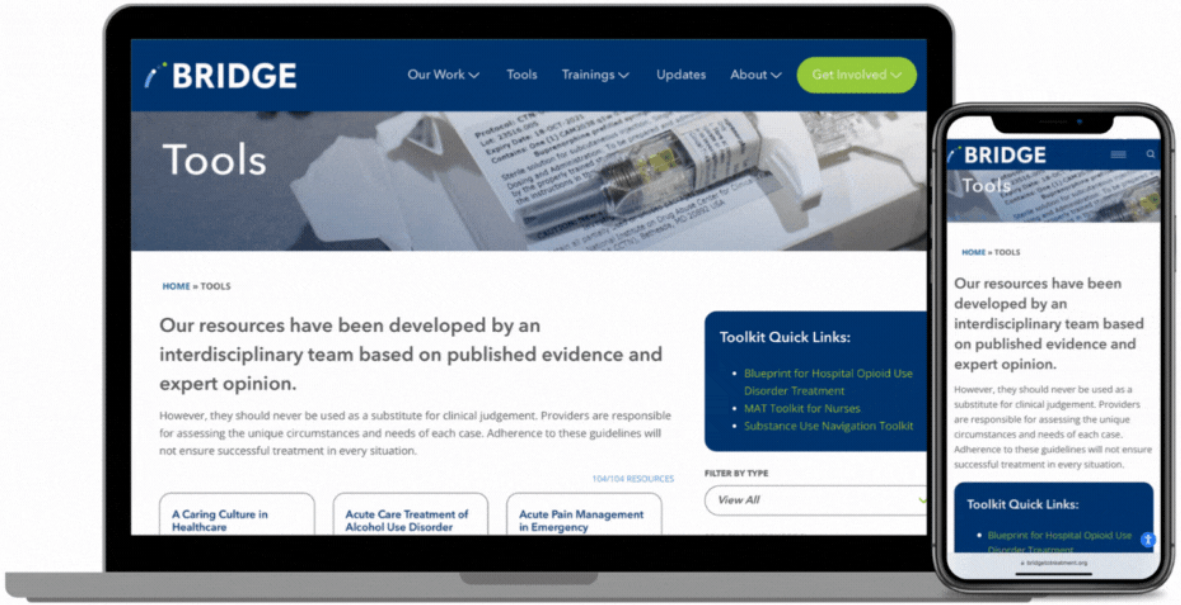
Resources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Our resources have been developed by an interdisciplinary team based on published evidence and expert opinion.
However, they should never be used as a substitute for clinical judgement. Providers are responsible for assessing the unique circumstances and needs of each case. Adherence to these guidelines will not ensure successful treatment in every situation.
Toolkit Quick Links:
Blueprint for Hospital Opioid Use Disorder Treatment
MAT Toolkit for Nurses
Substance Use Navigation Toolkit
104/104 RESOURCES
FILTER BY TYPE
View All
A Caring Culture in Healthcare
Acute Care Treatment of Alcohol Use Disorder
Acute Pain Management in Emergency

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