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Objectives for Today

1. Discuss Opioid Use Disorder and why medications for treatment are critical
2. Review buprenorphine and its history
3. Evaluate options for buprenorphine initiation in the era of fentanyl
4. Discuss recommendations for duration of treatment

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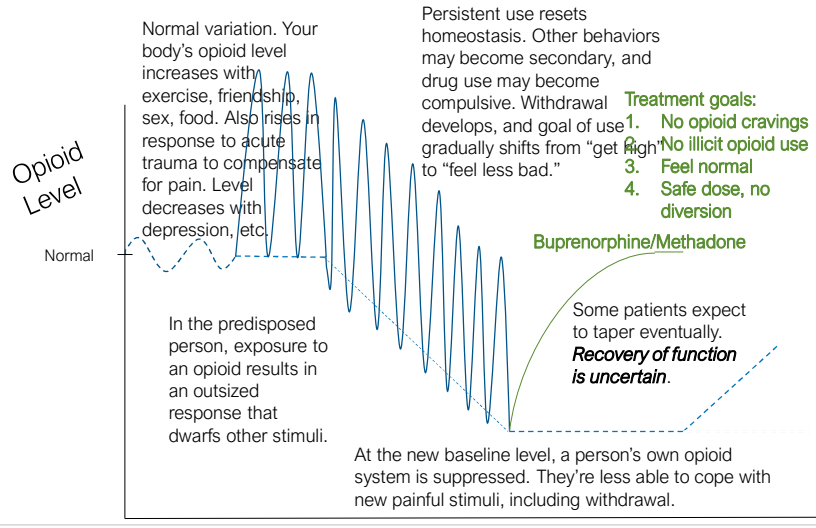
Impact of Chronic Opioid Use & MOUD



HennepinHealthcare

Created by Brian Grahan, MD, PhD on 4/1/18
Hennepin Healthcare Opioid & Addictions Care TeleECHO Group

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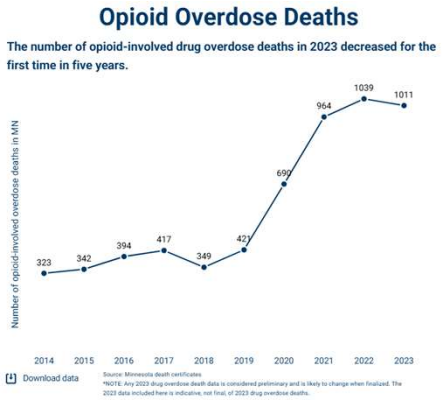
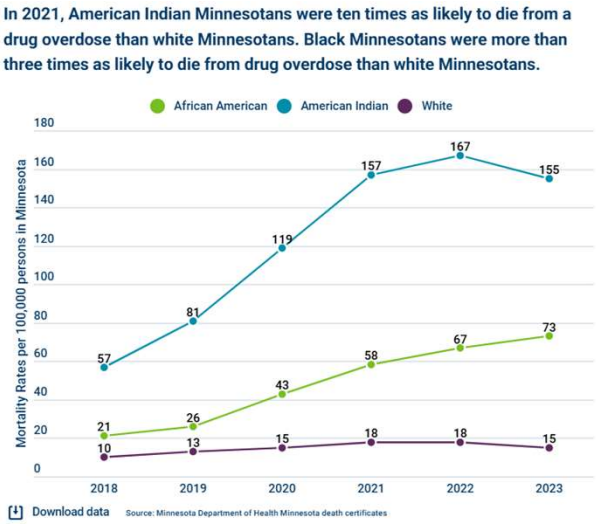
MN Opioid Overdose Statistics





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Medications for Opioid Use Disorder

- Buprenorphine
- Methadone
- Naltrexone
- Without medications, 85% of people return to illicit use

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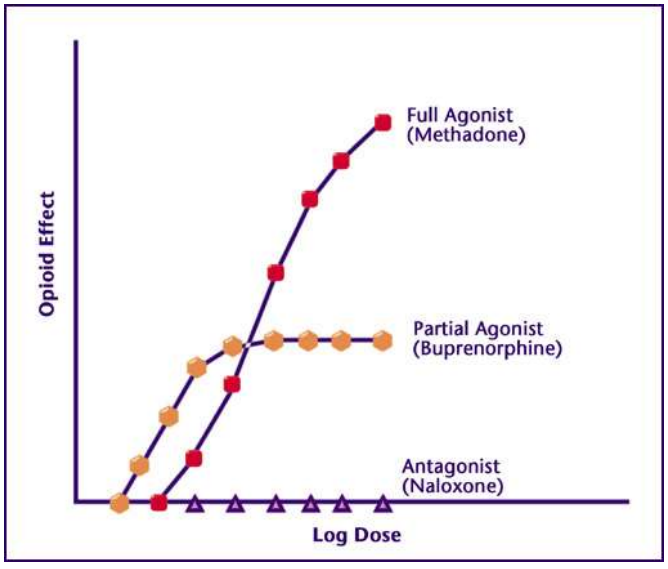

Source: naabt.org

Buprenorphine MOA

- Partial μ-receptor agonist
- High affinity and low-intrinsic activity
- Slow dissociation from receptors
- Long duration of action
  - t½ = 37 hrs

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Buprenorphine

Partial Opioid Agonist

Less respiratory depression

Decreases cravings

Decreases withdrawal symptoms

Accessible

No X waiver needed to prescribe

- Discontinued in 2023

Any provider with a DEA can prescribe

Allows for split dosing throughout the day

Risk of opioid overdose is significantly lower

62% reduction of opioid overdose risk

Maintain tolerance

Blocks fentanyl

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History of Buprenorphine

Semisynthetic opioid derived from thebaine	First synthesized in 1966	Initially used for pain management
1970s and 80s early studies demonstrated efficacy in treating OUD	Drug Addiction Treatment Act of 2000 allowed physicians to prescribe for OUD • Needed X waiver	Approved by FDA for OUD treatment in 2002

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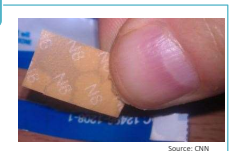
Buprenorphine Formulations

Sublingual

- Poor bioavailability
- 8-24 hours
- Suboxone = buprenorphine + naloxone
  - Naloxone added as deterrent for injection of buprenorphine
- Subutex = buprenorphine only



Source: CNN

Subcutaneous

- Long acting injectable
- 28-day formulation (Sublocade/Brixadi)
- 7-day formulation (Brixadi)

Transdermal patch

- Lower doses
- Chronic pain patients and low dose buprenorphine initiations

Source: UK-rehab.com

Buccal

- Chronic pain patients and low dose buprenorphine initiations

Source: painnewsnetwork.org

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Starting Buprenorphine

Need to decide:

Low dose or High dose initiation?

1st step:

Assess opioid withdrawal status

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Precipitated Withdrawal

Buprenorphine has a higher affinity for mu receptors than most opioids

Can replace full agonist opioid at mu receptor causing acute severe opioid withdrawal symptoms	Occurs 15-60 minutes after taking buprenorphine	It's not naloxone!

Higher risk of PW with fentanyl

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Starting Buprenorphine

COWS > 8 (more withdrawal)

- High dose buprenorphine initiation

COWS < 8 (less withdrawal)

- Low dose buprenorphine initiation or
- Wait until COWS>8, then start high dose buprenorphine initiation

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Starting Buprenorphine: High Dose Initiation

If COWS score >8: start high dose buprenorphine initiation:

- Give 8 mg buprenorphine immediately
- Can increase to 16-32 mg/day as needed
  - *Typically increase dose by 8 mg at a time*
  - *Can receive 32 mg on day 1 of treatment!*

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Starting Buprenorphine: Low Dose Initiation

Other commonly used terms:

- Microdosing
- low dose induction

Pros:

- Able to start buprenorphine when patient is not in withdrawal
- Able to start buprenorphine when patient is on full-agonist opioid

Cons:

- Longer duration to stabilization
- Initiation protocol more complicated

Patient Selection:

- Patient endorses difficulty starting buprenorphine previously
- Patient is currently requiring full-agonist opioids for pain control
- Patient is NOT currently in withdrawal

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7-day Low Dose Buprenorphine Initiation Protocol

Day	Buprenorphine Dose	Full Agonist Opioid
1	0.5 mg (1/4 of 2 mg film) buprenorphine SL daily	Continue
2	0.5 mg (1/4 of 2 mg film) buprenorphine SL BID	Continue
3	1 mg (1/2 of 2 mg film) buprenorphine SL BID	Continue
4	2 mg(1 film of 2 mg film) buprenorphine SL BID	Continue
5	3 mg (1.5 film of 2 mg film) buprenorphine SL BID	Continue
6	4 mg (2 of 2 mg film) buprenorphine SL BID	Continue
7	8 mg (1 film of 8 mg film) buprenorphine SL TID	Wean or stop

Prescribe: 2 mg buprenorphine SL strips #15, 8 mg buprenorphine strips #4 for 7 day supply

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XR-BUP (Brixadi)

2018

Approved by European Medicines Agency in 2018 for those 16 years and older

Approved by US Food and Drug Administration for those 18 years and older in 2023 for patients with moderate to severe opioid use disorder

2023

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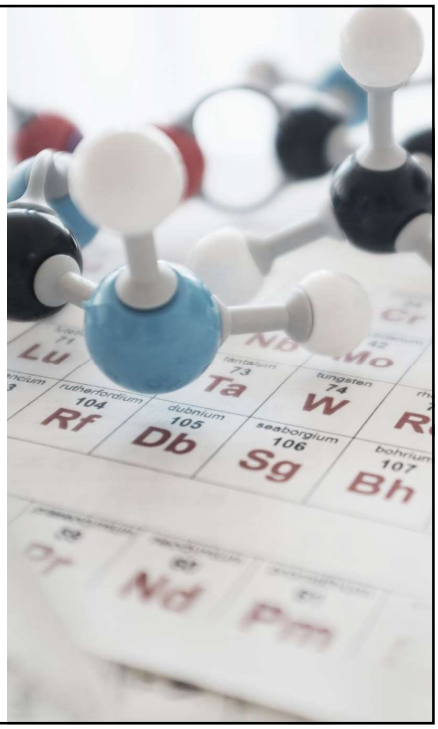
Brixadi vs SL-BUP

7-day XR-BUP:

- Bioavailability 6-8 x higher than SL-BUP, lower total dose needed to achieve equivalent plasma concentration
- Terminal half-life is between 70-107 hours, appropriate for weekly dosing
  - *Terminal half-life of SL-bup is 32 h*
- Safety profile similar
  - *Exception: mild-moderate injection site pain reported by small number of patients*
- Viscous liquid crystalline gel that encapsulated the BUP solution
  - *Over time, gel biodegrades releasing BUP at **steady rate over 1 week period***
  - *Avoids daily peaks and troughs associated with daily SL-BUP dosing*
- Comes in prefilled syringes with different doses, all <1 ml
- Injection needle small, 23-gauge



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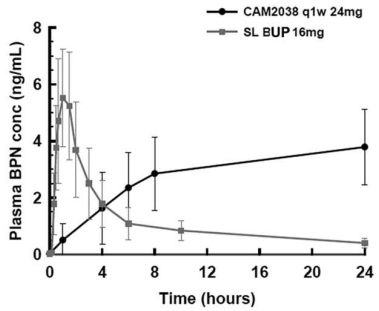
Early emergency department experience with 7-day extended-release injectable buprenorphine for opioid use disorder



Academic Emergency Medicine, Volume: 30, Issue: 12, Pages: 1264-1271, First published: 28 July 2023, DOI: (10.1111/acem.14782)

Plasma concentration-time curves of BUP

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