



Buprenorphine for Opioid Use Disorder

Initiation Protocols in the Fentanyl Era



Lauren Graber MD, MPH
Hennepin Healthcare
Family Medicine & Addiction Medicine

Disclosures

- No financial disclosures



Katie Mackay MD
University of Minnesota Addiction Fellow
Family Medicine & Addiction Medicine

Disclosures

- No financial disclosures



Objectives for today

1. Your Words Matter
2. Fentanyl and adulterants (like xylazine)
3. Opioid Use Disorder and how buprenorphine helps
4. Protocols to start buprenorphine
5. Management of Withdrawal & precipitated withdrawal

A Note on Storytelling



Image: Google images



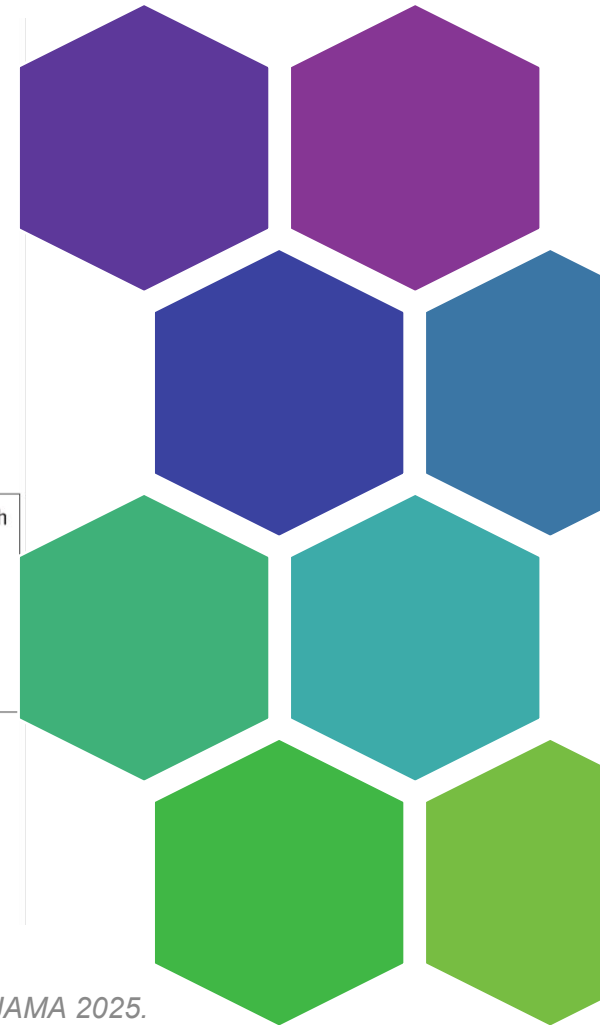
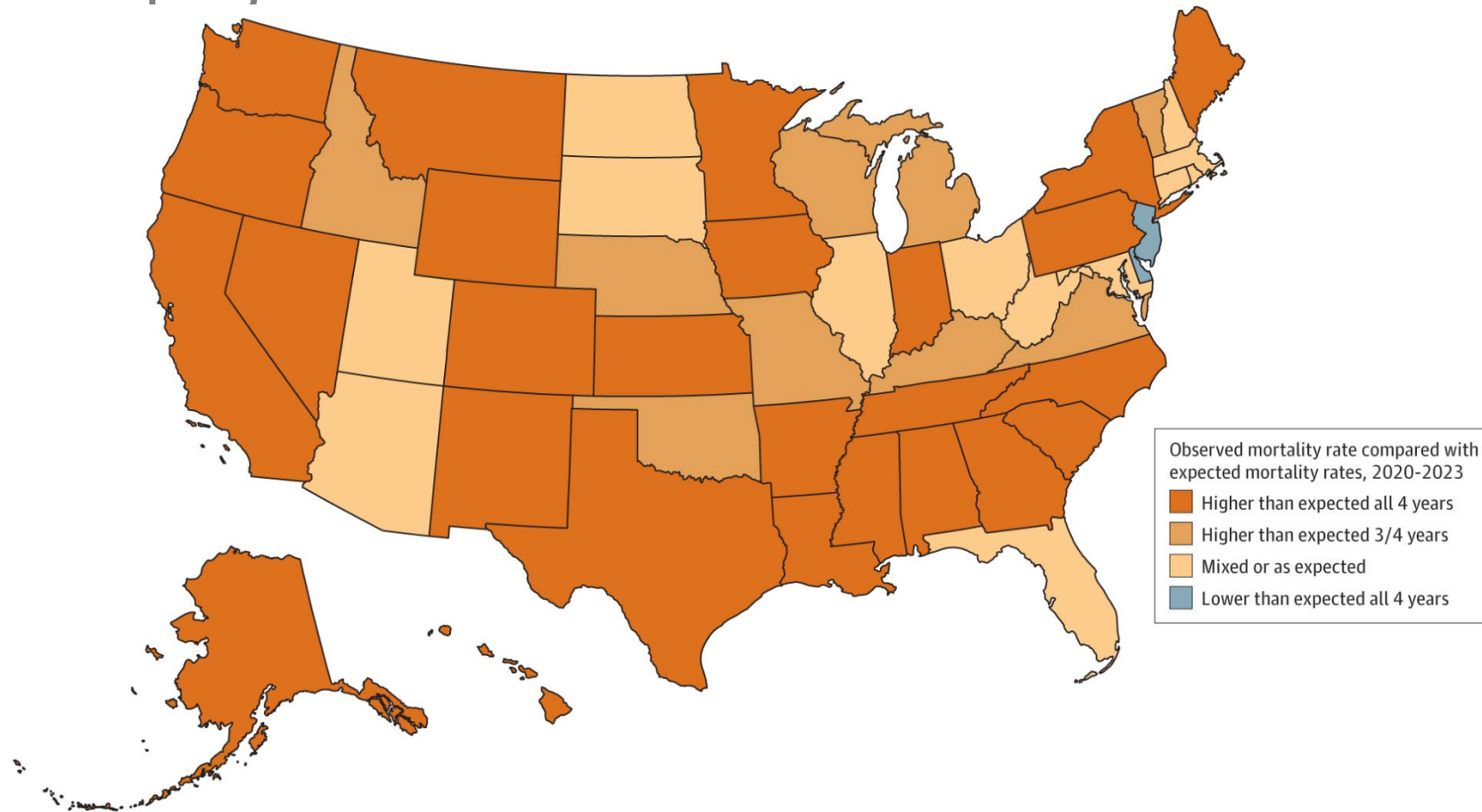
The words we ~~use~~ ^{chart} matter

Instead of...	Use...
<ul style="list-style-type: none">• Drug abuse	<ul style="list-style-type: none">• Use• Misuse
<ul style="list-style-type: none">• Clean / Sober	<ul style="list-style-type: none">• Being in remission or recovery• Abstinent from substances• Testing negative
<ul style="list-style-type: none">• Habit	<ul style="list-style-type: none">• Substance use disorder
<ul style="list-style-type: none">• Addict or user	<ul style="list-style-type: none">• Person with substance use disorder
<ul style="list-style-type: none">• Addicted baby	<ul style="list-style-type: none">• Baby born to parent who used drugs while pregnant• Baby with signs of withdrawal from prenatal substance exposure• Baby with Neonatal Opioid Withdrawal Syndrome

[Words Matter - Terms to Use and Avoid When Talking About Addiction | National Institute on Drug Abuse \(NIDA\)](#)



Despite national coverage that overdoses are slowing, ongoing trend continues to exceed projections



Kiang and Humphreys. *JAMA* 2025.

Fentanyl & Other Opioids



Source: Harm Reduction Ohio



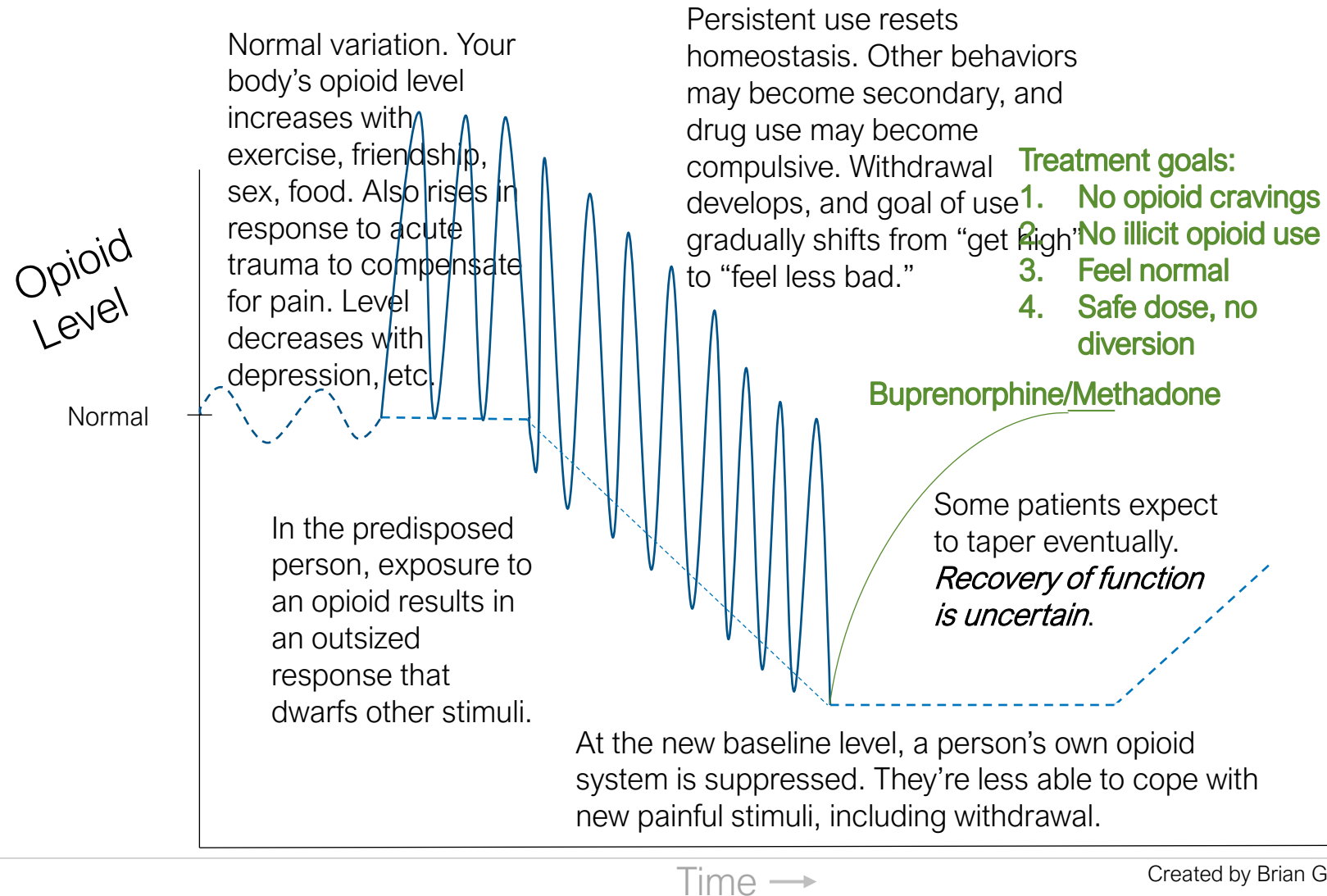
Fentanyl & Other Opioids



Source: NYTimes



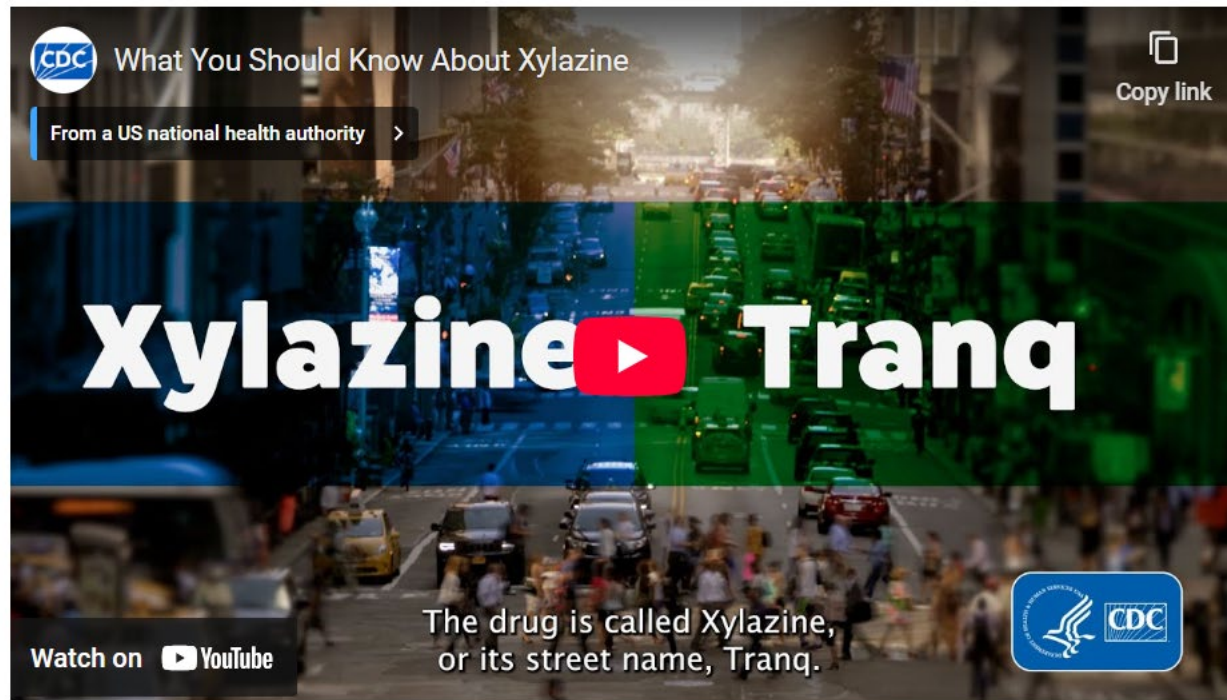
Impact of Chronic Opioid Use & MOUD



Adulterants

Xylazine

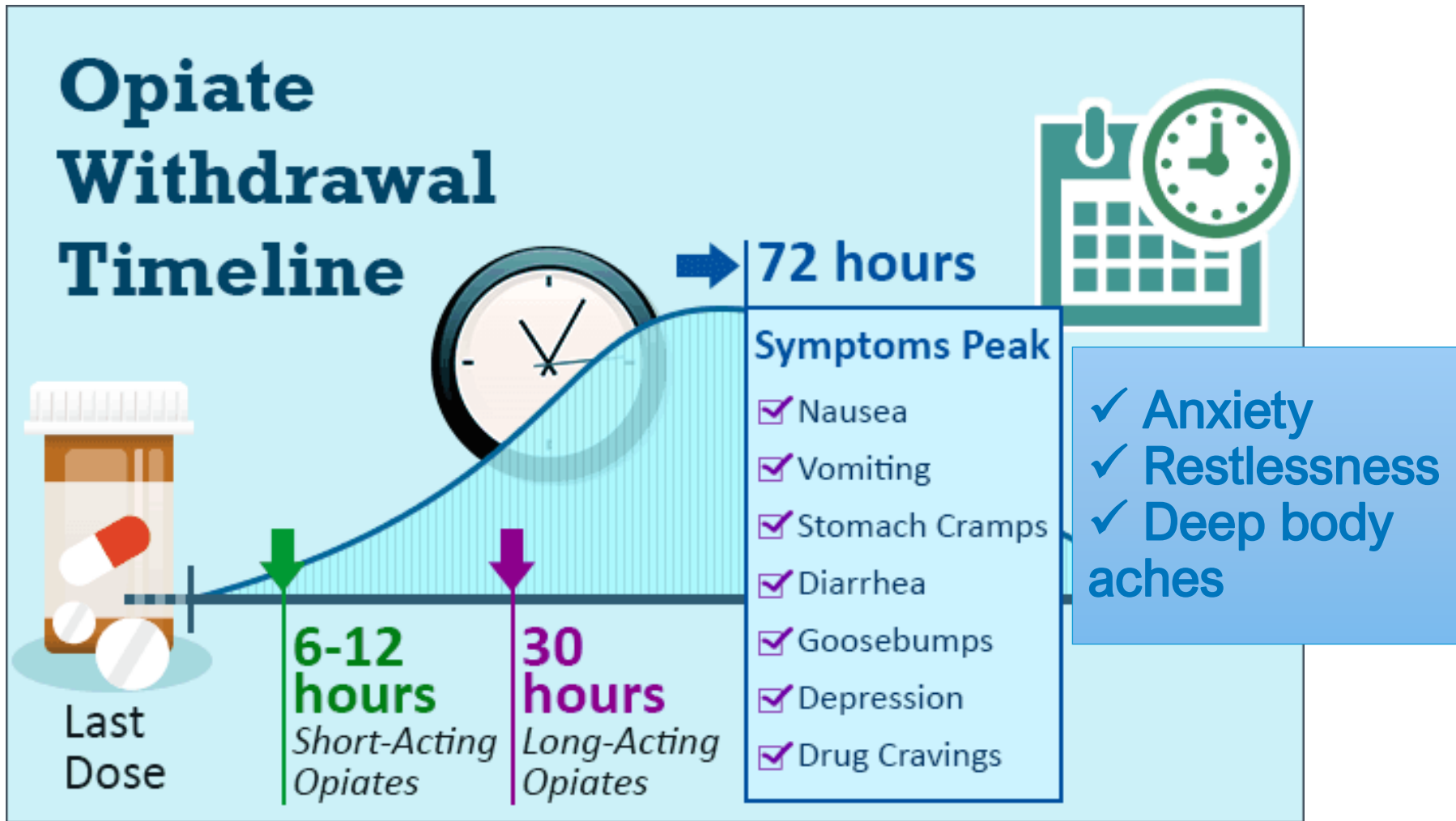
A tranquilizer called xylazine, a non-opioid sedative, is increasingly being found in the US illegal drug supply and linked to overdose deaths. [1] Xylazine—which is not approved for use in people and can slow down the brain and breathing, make the heart beat slower, and lower blood pressure in people, is especially dangerous when combined with opioids like fentanyl. [2]



Source: CDC [▶ Low Resolution Video](#)



Withdrawal Symptoms



Source: DrStacyGreen.com

How to respond to a patient's disclosure of opioid use

- Honor that the patient felt safe to share
- Affirm commitment to supporting them to be healthy and that this is a safe place
- Share:
 - Harm reduction
 - Substance use treatment programs
 - Medications



Medications for Opioid Use Disorder



Without medications, >85% of people
return to illicit use



Medications for Opioid Use Disorder

Buprenorphine

Methadone

Naltrexone



Buprenorphine



Partial Opioid Agonist

Less respiratory depression
Decreases cravings
Decreases withdrawal symptoms



Accessible

No X waiver needed to prescribe
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

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



Starting Buprenorphine



Need to decide:

Low dose or High dose
initiation?



1st step:

Assess opioid withdrawal
status



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!



Starting Buprenorphine: Assess Withdrawal Status

- Ask your patient:
 - Are you in withdrawal?
 - Goosebumps?
 - Dilated pupils?

MD CALC Search "QT interval" or "QT"

COWS Score for Opiate Withdrawal
Quantifies severity of opiate withdrawal.

When to Use ▾ Pearls/Pitfalls ▾ Why Use ▾

Resting Pulse Rate (BPM)	≤80	0
Measure pulse rate after patient is sitting or lying down for 1 minute	81-100	+1
	101-120	+2
	>120	+4

Goosebumps skin	Skin is smooth	0
	Piloerection of skin can be felt or hairs standing up on arms	+3

COWS Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9. **Clinical Opiate Withdrawal Scale**

Resting Pulse Rate: beats/minute Measured after patient is sitting or lying for one minute	GI Upset: over last 1/2 hour
0 Pulse rate 80 or below	0 No GI symptoms
1 Pulse rate 81-100	1 Stomach cramps
2 Pulse rate 101-120	2 Nausea or loose stool
3 Pulse rate greater than 120	3 Vomiting or diarrhea
	4 Multiple episodes of diarrhea or vomiting
Sweating: over past 1/2 hour not accounted for by room temperature or patient activity	Tremor: observation of outstretched hands
0 No report of chills or flushing	0 No tremor
1 Subjective report of chills or flushing	1 Tremor can be felt, but not observed
2 Flushed or observable moistness on face	2 Slight tremor observable
3 Beads of sweat on brow or face	4 Gross tremor or muscle twitching
4 Sweat streaming off face	
Restlessness: Observation during assessment	Yawning: Observation during assessment
0 Able to sit still	0 No yawning
1 Reports difficulty sitting still, but is able to do so	1 Yawning once or twice during assessment
3 Frequent shifting or extraneous movements of legs/arms	2 Yawning three or more times during assessment
4 Unable to sit still for more than a few seconds	4 Yawning several times/minute
Pupil size	Anxiety or irritability
0 Pupils pinned or normal size for room light	0 None
1 Pupils possibly larger than normal for room light	1 Patient reports increasing irritability or anxiousness
2 Pupils moderately dilated	2 Patient obviously irritable or anxious
3 Pupils so dilated that only the rim of the iris is visible	4 Patient so irritable or anxious that participation in the assessment is difficult
Bone or joint aches: If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored	Goosebumps skin
0 Not present	0 Skin is smooth
1 Mild diffuse discomfort	3 Piloerection of skin can be felt or hairs standing up on arms
2 Patient reports severe diffuse aching of joints/ muscles	5 Prominent piloerection
4 Patient is rubbing joints or muscles and is unable to sit still because of discomfort	
Runny nose or tearing: Not accounted for by cold symptoms or allergies	
0	



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

**Regardless of
severity of
withdrawal
symptoms:**

- Offer supportive care immediately



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!



Starting Buprenorphine: High Dose Initiation

- Titrate dose as needed:
 - Typical therapeutic dose 16-24 mg
 - In fentanyl era, 24 mg TDD = more engaged in care
- Goal:
 - Minimal to no cravings for opioids
 - No opioid withdrawal symptoms
 - Avoid side effects



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



Low Dose Buprenorphine Initiation Protocols

- **The basics:**

- Start with low dose buprenorphine (less than 1 mg)
- CONTINUE full agonist opioids:
 - Self-directed illicit/nonprescribed opioids outpatient
 - Methadone or hydromorphone recommended inpatient

- **Typical timeline:**




- 3-7 days

- **Goals = same as high dose initiation**

- By day 7:
- Therapeutic dose of buprenorphine (typically 16-24 mg TDD)
- Discontinue full-agonist opioids







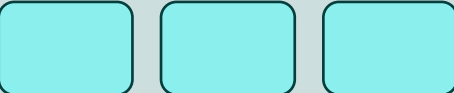


Example 3-day Low Dose Initiation Buprenorphine Protocol

Day	Buprenorphine Dose		Full-Agonist Opioids
1	0.5 mg (1/4 of 2 mg film) SL buprenorphine Q3 hours		Continue
2	1 mg (1/2 of 2 mg film) SL buprenorphine Q3 hours		Continue
3	8 mg (1 film) TID SL buprenorphine		Wean or stop

- **Prescribe: 2 mg buprenorphine films #6, 8 mg buprenorphine films #3 for 3 day supply**

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

Treatment for Opioid Withdrawal

Opioid Withdrawal Symptoms	Supportive Care Medications
Anxiety, irritability, restlessness	Clonidine Hydroxyzine Gabapentin Tizanidine Lorazepam Olanzapine
Nausea, vomiting	Ondansetron
Diarrhea	Loperamide
Body aches/Pain	Tizanidine



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!



Treatment for Precipitated Withdrawal

Give more buprenorphine!
16-32 mg more helps flood the opioid receptors

Treat opioid withdrawal symptoms with other supportive medications



Resources

California
Bridgetotreatment.org:



Boston Medical Center
MAT Quick Start



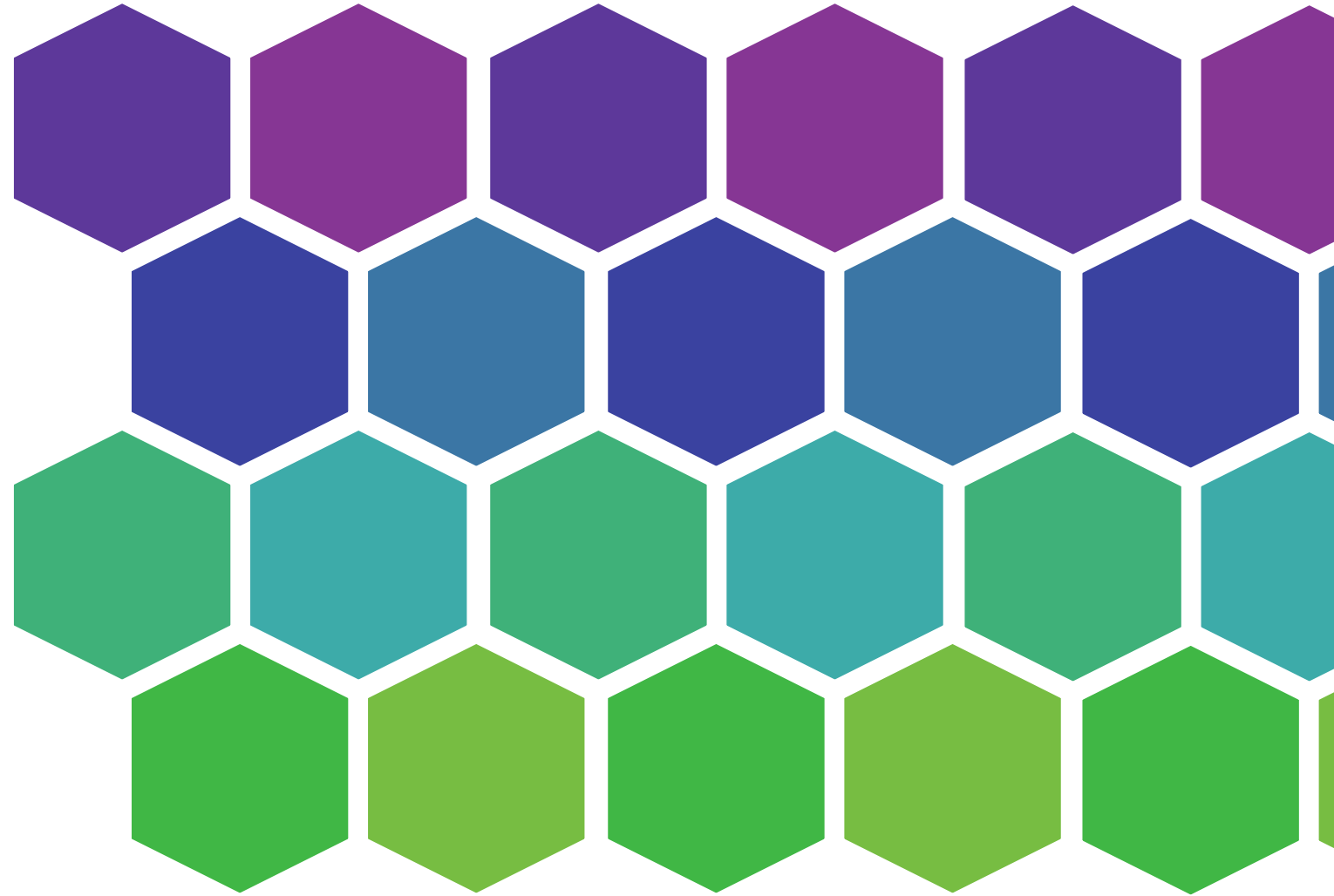
In summary

1. The words we use & chart matter
2. Fentanyl is different, but treatable
3. Protocols can help start buprenorphine
4. Treat and prevent withdrawal

Questions?
Thank you!

Lauren Graber MD, MPH
lauren.graber@hcmed.org

Katie Mackay MD
macka100@umn.edu



Perinatal Substance Use ECHO

Supporting Breastfeeding in Substance Use Disorder: A Patient-Centered Approach

With Katherine Standish, MD, MS

Wednesday, April 23rd
12:15 pm - 1:15 pm Central Time
via Zoom

Register on the iECHO program page [HERE](#)
or scan the QR code:



Email Rachel Langer at
rachel.langer@hcmcd.org with any questions.



ADOLESCENT SUBSTANCE USE CLINIC

Thursday mornings

Clinic & Specialty Center, Level 3
715 South 8th Street, Minneapolis 55404

- Meet medical providers who specialize in addiction care
- Medication for opioid and alcohol use
- Drug and alcohol testing
- Support and education for adolescents and their families
- Referral to primary care and psychiatric services

Contact **612-873-9360** or **612-873-5500**

*Other appointment times available at our main Addiction Medicine Clinic at 914 S 8th St.



References

- Adams, K.K., Waters, K. & Sobieraj, D.M. Initiating buprenorphine to treat opioid use disorder without prerequisite withdrawal: an updated systematic review. *Addict Sci Clin Pract* 20, 19 (2025). <https://doi.org/10.1186/s13722-025-00548-z>
- Ahmed, S., Bhivandkar, S., Lonergan, B.B. and Suzuki, J. (2021), Microinduction of Buprenorphine/Naloxone: A Review of the Literature. *Am J Addict*, 30: 305-315. <https://doi.org/10.1111/ajad.13135>
- Boland H, DiSalvo M, Fried R, Woodworth KY, Wilens T, Faraone SV, Biederman J. A literature review and meta-analysis on the effects of ADHD medications on functional outcomes. *J Psychiatr Res*. 2020 Apr;123:21-30. doi: 10.1016/j.jpsychires.2020.01.006. Epub 2020 Jan 27. PMID: 32014701.
- Brar, R., Fairbairn, N., Sutherland, C. and Nolan, S. (2020), Use of a novel prescribing approach for the treatment of opioid use disorder: Buprenorphine/naloxone micro-dosing – a case series. *Drug Alcohol Rev.*, 39: 588-594. <https://doi.org/10.1111/dar.13113>
- Casey BJ, Getz S, Galvan A. The adolescent brain. *Dev Rev*. 2008;28(1):62-77. doi: 10.1016/j.dr.2007.08.003. PMID: 18688292; PMCID: PMC2500212.
- Compton WM, Thomas YF, Stinson FS, Grant BF. Prevalence, Correlates, Disability, and Comorbidity of DSM-IV Drug Abuse and Dependence in the United States: Results From the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2007;64(5):566–576. doi:10.1001/archpsyc.64.5.566Frank CJ, Morrison L. Cannabis use during pregnancy. Letters to the editor. *Am Fam Physician*. 2022;160(4):364-365.
- D'Onofrio G, Hawk KF, Perrone J, et al. Incidence of Precipitated Withdrawal During a Multisite Emergency Department–Initiated Buprenorphine Clinical Trial in the Era of Fentanyl. *JAMA Netw Open*. 2023;6(3):e236108
- Frank CJ, Morrison L. Cannabis use during pregnancy. Letters to the editor. *Am Fam Physician*. 2022;160(4):364-365.
- Friedman J, Godvin M, Shover CL, Gone JP, Hansen H, Schriger DL. Trends in Drug Overdose Deaths Among US Adolescents, January 2010 to June 2021. *JAMA*. 2022;327(14):1398–1400. doi:10.1001/jama.2022.2847
- Grande, L. A., Cundiff, D., Greenwald, M. K., Murray, M., Wright, T. E., & Martin, S. A. (2023). Evidence on Buprenorphine Dose Limits: A Review. *Journal of Addiction Medicine*, 17(5), 509–516. <https://doi.org/10.1097/ADM.0000000000001189>
- Humphreys KL, Eng T, Lee SS. Stimulant medication and substance use outcomes: a meta-analysis. *JAMA Psychiatry*. 2013 Jul;70(7):740-9. doi: 10.1001/jamapsychiatry.2013.1273. PMID: 23754458; PMCID: PMC6688478. Humphreys KL, Eng T, Lee SS. Stimulant medication and substance use outcomes: a meta-analysis. *JAMA Psychiatry*. 2013 Jul;70(7):740-9. doi: 10.1001/jamapsychiatry.2013.1273. PMID: 23754458; PMCID: PMC6688478.
- Kaltenbach K, O'Grady KE, Heil SH, Salisbury AL, Coyle MG, Fischer G, Martin PR, Stine S, Jones HE. Prenatal exposure to methadone or buprenorphine: Early childhood developmental outcomes. *Drug Alcohol Depend*. 2018 Apr 1;185:40-49.
- Kiang MV, Humphreys K. Recent Drug Overdose Mortality Decline Compared With Pre–COVID-19 Trend. *JAMA Netw Open*. 2025;8(2):e2458090. doi:10.1001/jamanetworkopen.2024.58090
- Kimmel SD, Gaeta JM, Hadland SE, Hallett E, Marshall BDL. Principles of Harm Reduction for Young People Who Use Drugs. *Pediatrics*. 2021 Jan;147(Suppl 2):S240-S248. doi: 10.1542/peds.2020-023523G. PMID: 33386326; PMCID: PMC7907587.
- Knight JR, Sherritt L, Shrier LA, Harris SK, Chang G. Validity of the CRAFFT Substance Abuse Screening Test Among Adolescent Clinic Patients. *Arch Pediatr Adolesc Med*. 2002;156(6):607–614. doi:10.1001/archpedi.156.6.607
- Molina, B.S.G., Howard, A.L., Swanson, J.M., Stehli, A., Mitchell, J.T., Kennedy, T.M., Epstein, J.N., Arnold, L.E., Hechtman, L., Vitiello, B. and Hoza, B. (2018), Substance use through adolescence into early adulthood after childhood-diagnosed ADHD: findings from the MTA longitudinal study. *J Child Psychol Psychiatr*, 59: 692-702. <https://doi.org/10.1111/jcpp.12855>
- Monitoring the Future, 2023. NIDA. <https://monitoringthefuture.org/wp-content/uploads/2023/12/mtf2023.pdf>
- NIDA. 2023, December 13. Reported drug use among adolescents continued to hold below pre-pandemic levels in 2023. Retrieved from <https://nida.nih.gov/news-events/news-releases/2023/12/reported-drug-use-among-adolescents-continued-to-hold-below-pre-pandemic-levels-in-2023> on 2024, November 16
- Suen LW, Chiang AY, Jones BLH, et al. Outpatient Low-Dose Initiation of Buprenorphine for People Using Fentanyl. *JAMA Netw Open*. 2025;8(1):e2456253. doi:10.1001/jamanetworkopen.2024.56253
- Weimer MB, Herring AA, Kawasaki SS, Meyer M, Kleykamp BA, Ramsey KS. ASAM Clinical Considerations: Buprenorphine Treatment of Opioid Use Disorder for Individuals Using High-potency Synthetic Opioids. *J Addict Med*. 2023 Nov-Dec 01;17(6):632-639. doi: 10.1097/ADM.0000000000001202. Epub 2023 Jul 28. PMID: 37934520.
- Yuan, M., Cross, S.J., Loughlin, S.E. and Leslie, F.M. (2015), Nicotine and the adolescent brain. *J Physiol*, 593: 3397-3412. <https://doi.org/10.1113/JP270492>