Bridging the Gap: Updates in Substance Use Treatment in the ED

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Learning Objectives

- Discuss updates in treatment of alcohol use disorder and alcohol withdrawal in the ED
- Understand navigation between acute care and outpatient addiction treatment
- Utilize novel strategies to start buprenorphine for patients with opioid use disorder

Disclosures

No relevant financial relationship with commercial interests to disclose.

I will discuss off-label medications

Receive Funding from:

NIH and PCORI for OUD Clinical Trials

Roadmap

Part 1: How can we address alcohol use disorder in the ED?

Part 2: How can we link to outpatient addiction treatment?

Part 3: How can we start buprenorphine in the ED in the fentanyl era?

Alcohol Use Disorder: A worsening public health crisis

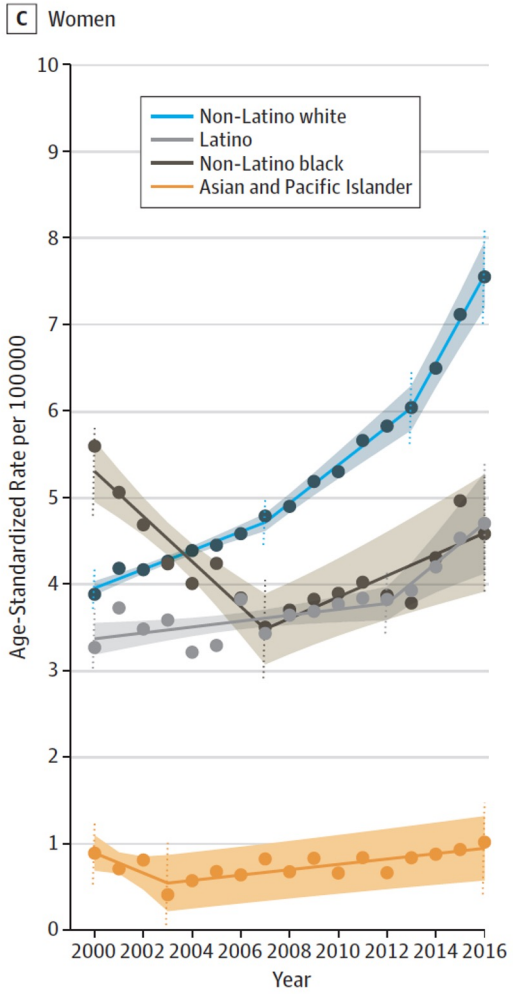
Racial & Ethnic Disparities

Mortality increasing for nearly all demographic groups

Largest increase in American Indian & Alaska Native individuals and non-Latinx White women

Specifically within AI/AN community, social determinants, historical trauma, and stigma need to be considered

Spillane 2020



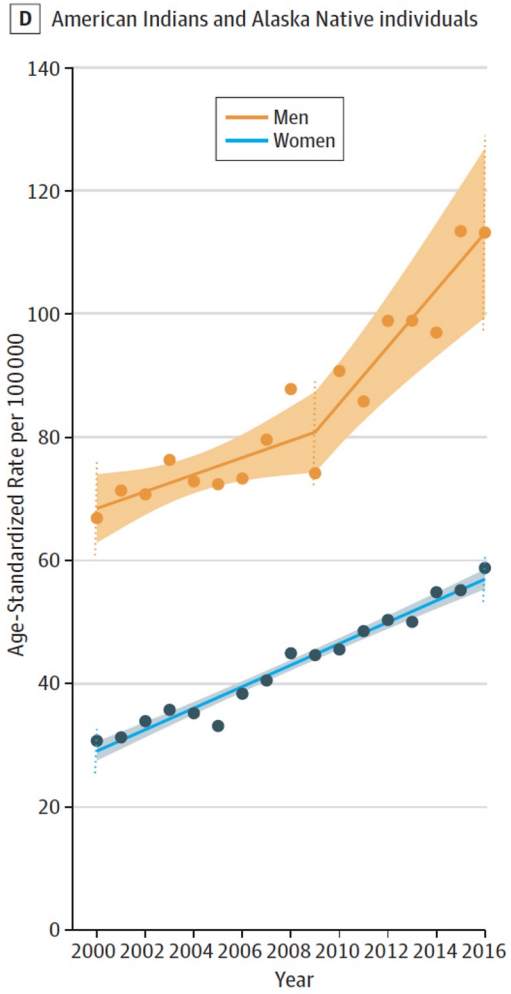
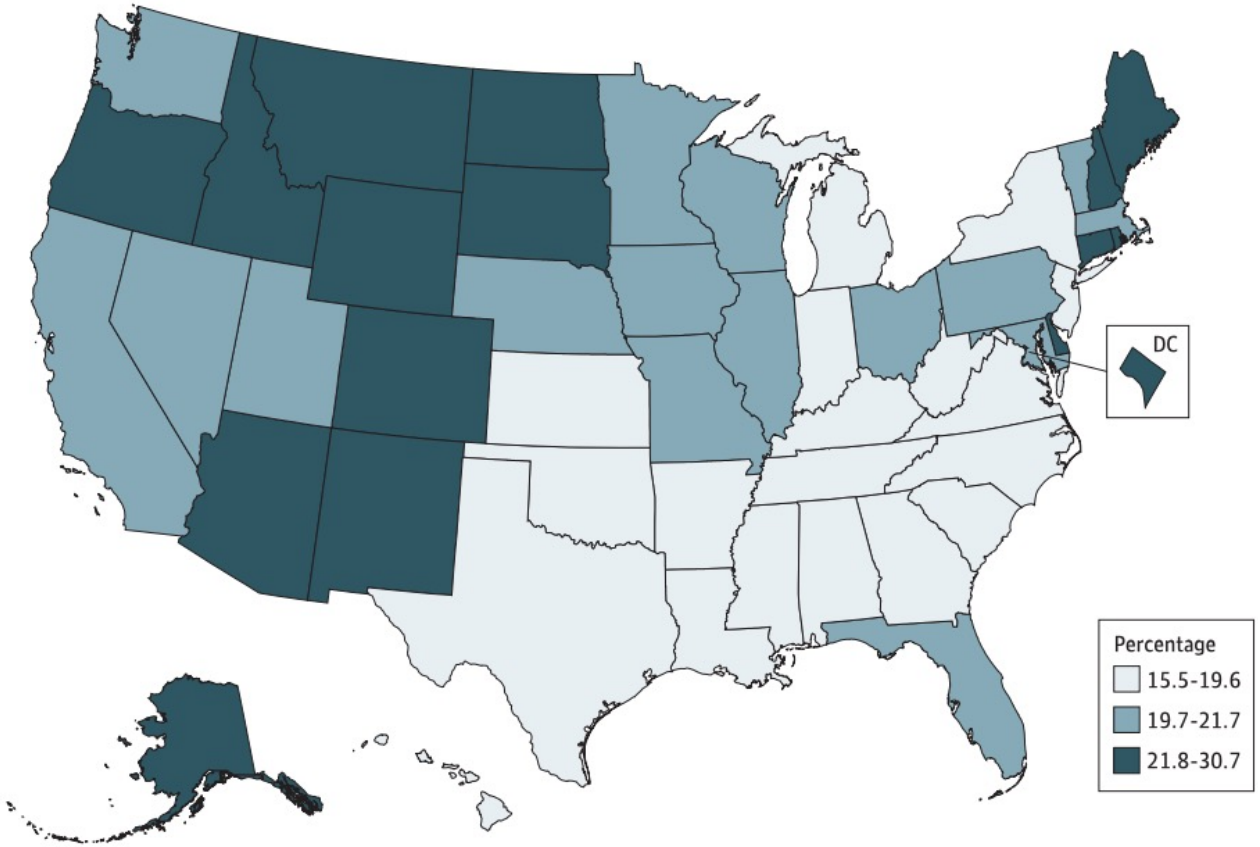


Figure. Estimated Percentage of Total Deaths Attributable to Excessive Alcohol Use Among US Adults Aged 20 to 49 Years, 2015 to 2019

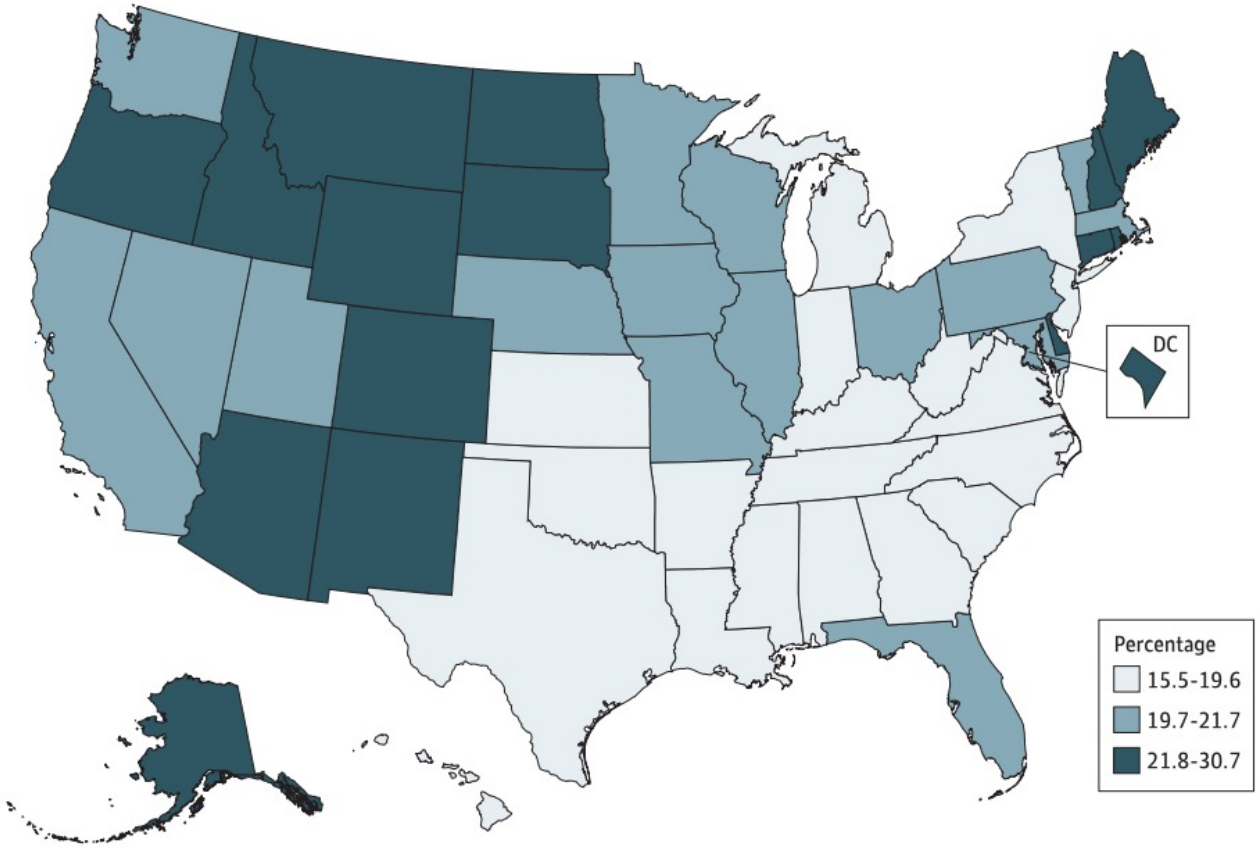


Cross sectional study 694,600 deaths age 20-64 from 2015-2019

What percentage of deaths are related to excessive alcohol use?

Esser et al. Jama Open 2022.

Figure. Estimated Percentage of Total Deaths Attributable to Excessive Alcohol Use Among US Adults Aged 20 to 49 Years, 2015 to 2019



In US:

Age 20-64: 1 in 8 deaths

Age 20-49: 1 in 5

Esser et al. Jama Open 2022.


“A condition in which the standard of care has a limited evidence base and has changed little over several decades.”
Smith et al, JAMA Open

A double-blind comparison of the efficacy and safety of lorazepam and diazepam in the treatment of the acute alcohol withdrawal syndrome.

Miller WC Jr, McCurdy L

Clinical Therapeutics, 01 Jan 1984, 6(3):364-371
PMID: 6722863

1984

Annals of Emergency Medicine
Volume 76, Issue 6, December 2020, Pages 774-781

Toxicology/original research

Lorazepam Versus Diazepam in the Management of Emergency Department Patients With Alcohol Withdrawal

Frank X. Scheuermeyer MD, MHSc [a, b], Isabelle Miles MD [a, b, c], Daniel J. Lane PhD [d], Brian Grunau MD,

2020

Framework

1

Need “loading doses” and initial treatment with benzos or phenobarbital

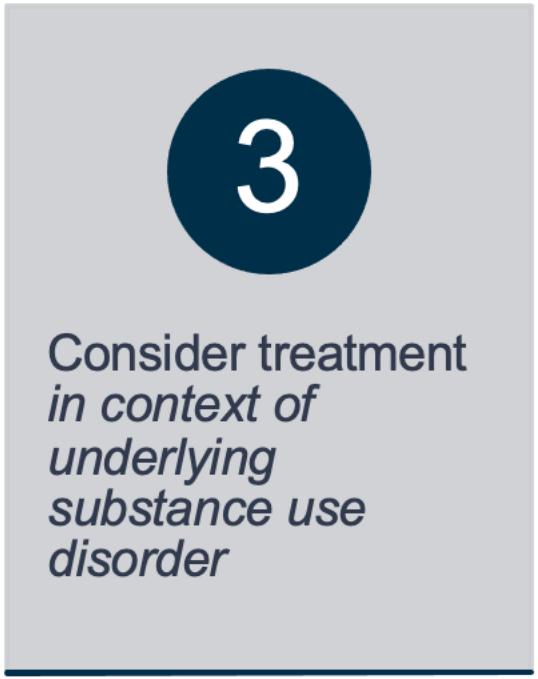
2

After stabilization, minimize harms of medications

3

Consider treatment *in context of underlying substance use disorder*

How to consider AUD treatment?



1. Bedside interventions around alcohol use

2. Start medications for AUD

Medications for AUD

FDA Approved	Off-Label
Naltrexone	**Gabapentin***
Disulfiram	Topiramate
Acamprosate	Baclofen

**Also treats AWS*

Gabapentin

AWS: Several retrospective cohort studies inpatient, only RCTs are in ambulatory settings

Can be used to promote abstinence in AUD patients with AWS history after withdrawal managment

Use supported as adjunct by ASAM and VA Clinical Practice Guideline OR as monotherapy for low-risk patients

ORIGINAL ARTICLE

MAYO CLINIC

Retrospective Analysis of Gabapentin for Alcohol Withdrawal in the Hospital Setting: The Mayo Clinic Experience

Ruth E. Bates, MD; Jonathan G. Leung, PharmD, RPh; Robert J. Morgan, III, MD; Karen M. Fischer, MPH; Kemuel L. Philbrick, MD; and Simon Kung, MD

Propensity score matched analysis (n=443):

Gabapentin monotherapy (900mg TID) vs benzos only vs both

Safe, associated with shorter LOS, faster CIWA reductions

Published in final edited form as:
Alcohol Clin Exp Res. 2009 September ; 33(9): 1582–1588. doi:10.1111/j.1530-0277.2009.00986.x.

A DOUBLE BLIND TRIAL OF GABAPENTIN VS. LORAZEPAM IN THE TREATMENT OF ALCOHOL WITHDRAWAL

Hugh Myrick, MD[1,2], **Robert Malcolm, MD**[2], **Patrick K. Randall, PhD**[2], **Elizabeth Boyle, MSW**[2], **Raymond F. Anton, MD**[2], **Howard C. Becker, PhD**[1,2], and **Carrie L. Randall, PhD**[2]

[1]Ralph H. Johnson Department of Veterans Affairs Medical Center, Research and Development Service, Charleston, SC

[2]Medical University of South Carolina, Department of Psychiatry and Behavioral Sciences, Alcohol Research Center, Charleston, SC

RCT n=100 Ambulatory patients CIWA ~12-14:

RCT 400mg TID gabapentin vs 2mg TID loraz

Safe and effective, lower rates return to drinking

JAMA Intern Med. 2014 January 1; 174(1): 70–77. doi:10.1001/jamainternmed.2013.11950.

Gabapentin Treatment for Alcohol Dependence: A Randomized Controlled Trial

Barbara J. Mason, PhD[a], **Susan Quello, BA, BS**[a], **Vivian Goodell, MPH**[a], **Farhad Shadan, MD**[b], **Mark Kyle, MD**[b], and **Adnan Begovic, MD**[b]

[a]The Scripps Research Institute, Pearson Center for Alcoholism and Addiction Research, 10550 North Torrey Pines Road, TPC-5, La Jolla, CA 92037

RCT n=150 for AUD

600mg TID Gabapentin vs 300mg TID vs placebo

High dose NNT 5 heavy drinking; NNT 8 abstinence

Gabapentin for AWS (and AUD)

Alcohol Withdrawal

600-900 mg PO TID

Alcohol Use Disorder

600-900 mg PO TID

Naltrexone

Number needed to treat (NNT) 12 prevents return to heavy drinking

Effective in an office-based setting

Once daily dosing vs. monthly injection

Extended-release is promising for acute care patients

Naltrexone in Acute Care setting

Two cohort studies for hospitalized patients implemented XR-Naltrexone	• Found to have lower ED visits, readmissions
Two ED studies with PO and/or XR-Naltrexone	• High rates of treatment engagement, reduced drinking and improved QOL at follow up

Wei et al.; Kirchoff et al.; Anderson et al; Murphy et al

When you should *not* use Naltrexone

- Opioid use (clear history or naloxone challenge)
- Liver function tests >5-10x upper limit of normal (ULN) or decompensated cirrhosis*

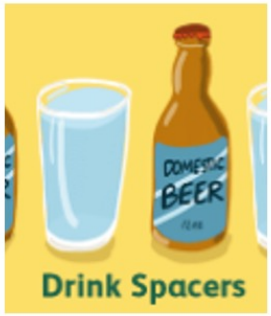
Harm Reduction for Alcohol Use Disorder

AUD is 10x more prevalent, 6x mortality in PEH

Harm reduction counseling + XR-NTX is efficacious

Improved mental, physical quality of life; fewer drinks per day; lower harms from drinking

Collins et al Lancet Psych



Harm Reduction for Alcohol

Harm Reduction – On Demand Naltrexone

- Many patients have risky drinking patterns, may not have AUD or withdrawal history
- ”Targeted Naltrexone” is an effective approach to reducing excessive alcohol use
- RCT: NNT 2 to reduce number of binge drinking days
- Sustained effect on number of drinks per month at 6 months

Santos et al Am J Psych

Alcohol Summary

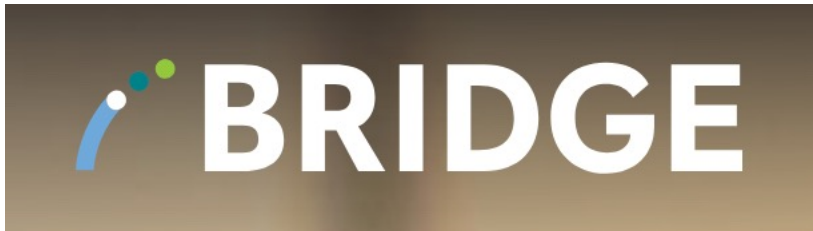
- Thoughtful approach to AWS may have acute and long term benefits
- Gabapentin and NTX most useful in ED
- AUD treatment can and should be started in the ED
- Social context of alcohol can tailor harm reduction interventions

Linkage to care from Emergency Department to Addiction Treatment

- Initiating treatment should be paired with active efforts to link to ongoing treatment
- Connection to clinics can be challenging in many settings

ED Substance Use Navigation

- Large body of evidence that bedside brief interventions for SUD in the ED has an impact long term outcomes
- Bup + navigation has high rate of follow up in clinical trials
- Substance use navigators (SUNs) are now widespread across CA and other parts of the country



What is a Substance Use Navigation?

Bedside Counseling	Substance Use History	Motivational Interviewing
Harm Reduction	Supplies	Strategies
Whole Person Care	Personalized Treatment Plans	SDOH
Medications	Refer providers to guidelines	Troubleshoot barriers

ED Substance Use Navigation

- 1,328 patients discharged from HGH ED; propensity score matched study

- Control: Experienced ED Clinicians trained in SUD meds
- Intervention: On-site SUNs with whole person care approach
    - Some with lived experience, all from East Bay communities impacted by substance use

- All Patients: high volume, 5 day a week low-threshold clinic, in-person or telemedicine

Anderson et al Ann Emerg Med

ED Substance Use Navigation

30 day engagement in addiction treatment

- **50% with SUN vs 16% without SUN**

Medication for SUD administered

- **40% with SUN vs 17% without SUN**

Medication for SUD prescribed at discharge

- **47% with SUN vs 21% without SUN**

Anderson et al Ann Emerg Med

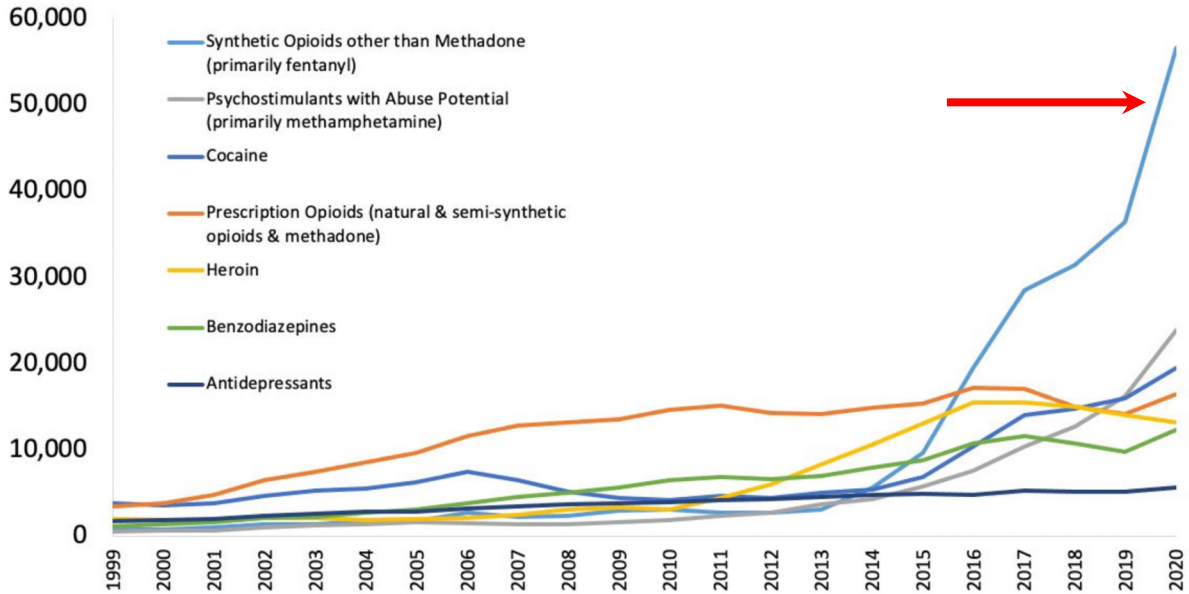
ED Substance Use Navigation

- Substance use navigation is independent predictor of engaging in addiction treatment after acute care
- A whole person care approach may be a useful framework to use
- Care from SUNs that is culturally competent from the community will improve efforts

Opioids

The Problem: Overdose deaths are *skyrocketing*

Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2020



- **91,799** overdose deaths in 2020
- **107,622** overdose deaths in 2021
- **110,000** overdose deaths in 2022
- **112,000** overdose deaths 2023
- Annual drug overdose deaths exceed those from motor vehicle crashes, gun violence, and HIV at its peak
- **Fentanyl** use and overdose is **on the rise** in our region

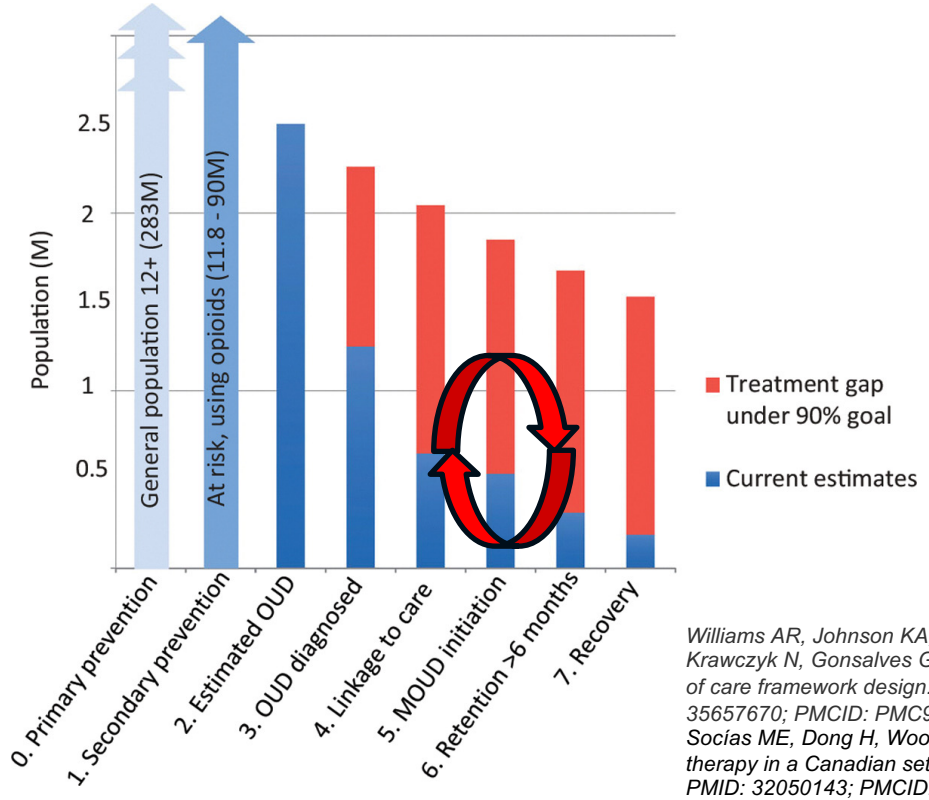
Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021
Ahmad FB, Cisewski JA, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2022.

Medication treatment for opioid use disorder *reduces the risk of death from any cause by more than 50%* and represents the standard of care.

***Yet*, only about 1 in 5 people with OUD receive any medication treatment.**

Santo T, Clark B, Hickman M, et al. Association of Opioid Agonist Treatment With All-Cause Mortality and Specific Causes of Death Among People With Opioid Dependence: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2021;78(9):979–993. doi:10.1001/jamapsychiatry.2021.0976
Jones CM, Han B, Baldwin GT, Einstein EB, Compton WM. Use of Medication for Opioid Use Disorder Among Adults With Past-Year Opioid Use Disorder in the US, 2021. JAMA Netw Open. 2023;6(8):e2327488. doi:10.1001/jamanetworkopen.2023.27488

OUD Cascade of Care

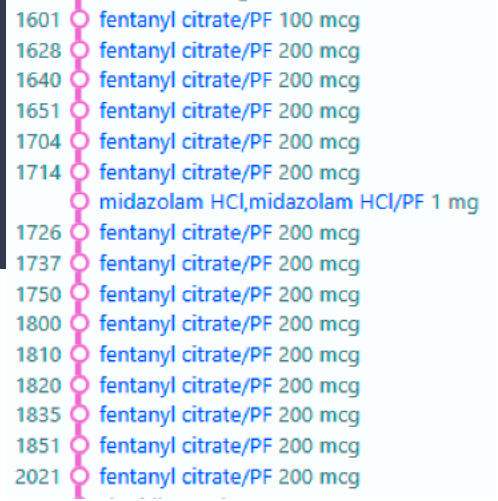


- SUD as a relapsing-remitting chronic condition
- Care trajectories are often non-linear
- ED 24/7 Open Door

Williams AR, Johnson KA, Thomas CP, Reif S, Socías ME, Henry BF, Neighbors C, Gordon AJ, Horgan C, Nosyk B, Drexler K, Krawczyk N, Gonsalves GS, Hadland SE, Stein BD, Fishman M, Kelley AT, Pincus HA, Olfson M. Opioid use disorder Cascade of care framework design: A roadmap. Subst Abus. 2022;43(1):1207-1214. doi: 10.1080/08897077.2022.2074604. PMID: 35657670; PMCID: PMC9577537.

Socías ME, Dong H, Wood E, Brar R, Richardson L, Hayashi K, Kerr T, Milloy MJ. Trajectories of retention in opioid agonist therapy in a Canadian setting. Int J Drug Policy. 2020 Mar;77:102696. doi: 10.1016/j.drugpo.2020.102696. Epub 2020 Feb 9. PMID: 32050143; PMCID: PMC7577708.

Landscape has changed



- Typical patient who says “I smoke 2g of fentanyl a day”
  - Smoking fentanyl has >90% bioavailability
  - Purity is approximately 20% in SF drug testing programs
- 2g of fentanyl = 2,000,000 mcg x 20% = **400,000 mcg of fentanyl daily**
- Patients managed with iOAT in Canada receive 2000-4000mcg iv fentanyl q1h prn

Starting Buprenorphine

- Typical approach
- Challenging cases

Case 1: Typical Buprenorphine Initiation from Fentanyl

- 22 yo F smoking 1g of fentanyl for 3 years, last use 48 hours ago
- Presents to ED with a COWS of 14, large pupils, yawning, piloerection

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- Receives 16mg SL bup → COWS 10
- Repeats 16mg SL bup 2 hours later → COWS 2

- Discharged with naloxone and appointment next day

Home-Based Simplified Bup Start Guide

- Great for uncomplicated starts
- ***Need 2 objective withdrawal signs***
- Advise >24 hours
- *Utilize other supportive meds*

CA BRIDGE
TREATMENT STARTS HERE

Wait, Withdraw, Dose

Starting Buprenorphine (Bup), "Subs," Suboxone

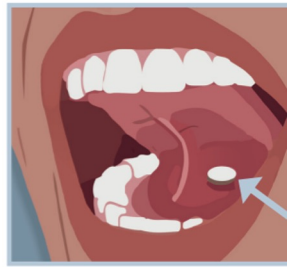
1. **Plan to take a day off and have a place to rest.**
2. **Stop using and wait until you feel sick from withdrawals (at least 12 hours is best).**
3. **Dose an 8mg tablet or strip UNDER your tongue.**
4. **Repeat dose (another 8mg) in an hour to feel well.**
5. **Start 16mg per day the next day.**

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 what happened and find ways to make it better this time.

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 actually makes starting Bup harder, but that is up to you. Be safe.



Place dose under your tongue (sublingual).

Novel Strategies for Buprenorphine Initiation:

Who needs them?

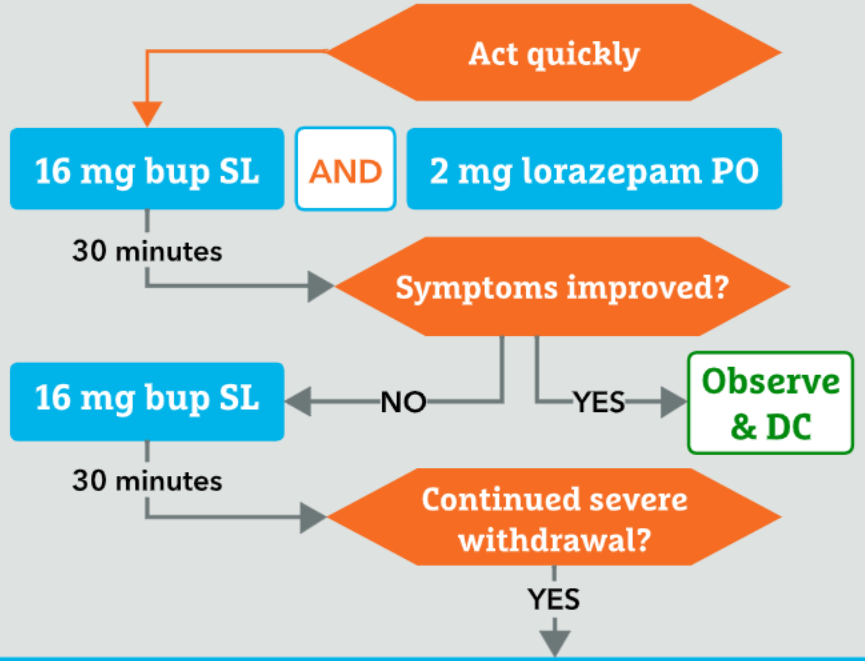
- Prior precipitated withdrawal
- Difficulty with withdrawal > 1 day
- >2-3g/day of fentanyl and co-occurring meth use

Case 2: Precipitated withdrawal to XR

- 44 yo F with fentanyl use disorder, 2g/day smoking and uses meth by injection
- Presented to ED with COWS of ~7, 1 objective sign of withdrawal (mid-range pupils), last use 20 hours prior
- COWS post 8mg SL bup x 2 → COWS of ~25

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 CO2 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

Buprenorphine SL
Initial treatment: 8mg + 8mg
POW treatment: 16mg SL
Total 32mg SL
(Plus Lorazepam 2mg PO x1)

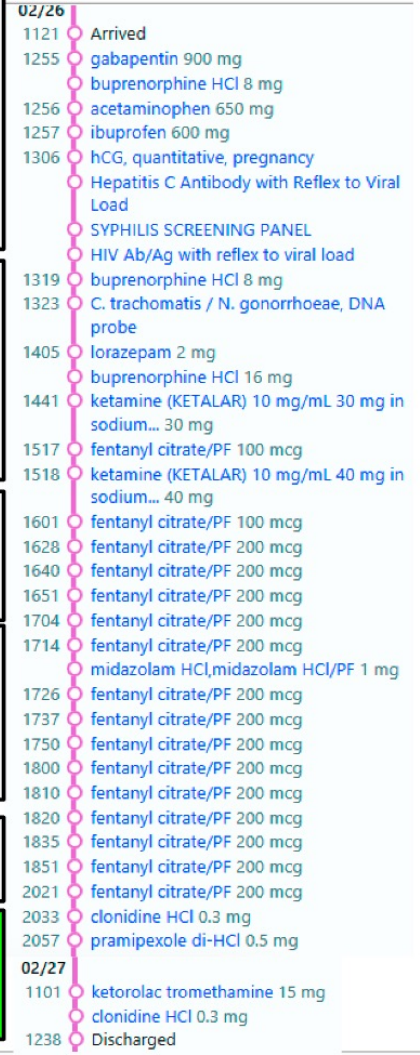
Ketamine brief infusions
30mg then 40mg
Total 70mg IV
(Plus versed 1mg IVx 1)

Fentanyl 200mcg IV boluses
Total 3,000 mcg over 5 hrs

After Fentanyl (restless)
Clonidine 0.3mg PO x1
Pramipexole 0.5mg PO x 1

Sleep under ED observation

Next morning
Sublocade 300mg SC



Case 2: Precipitated withdrawal to XR

- Precipitated withdrawal protocols available and can help
- Most improve with oral/IM benzo and additional SL bup
- Once recognized and treated, goal is XR-Bup

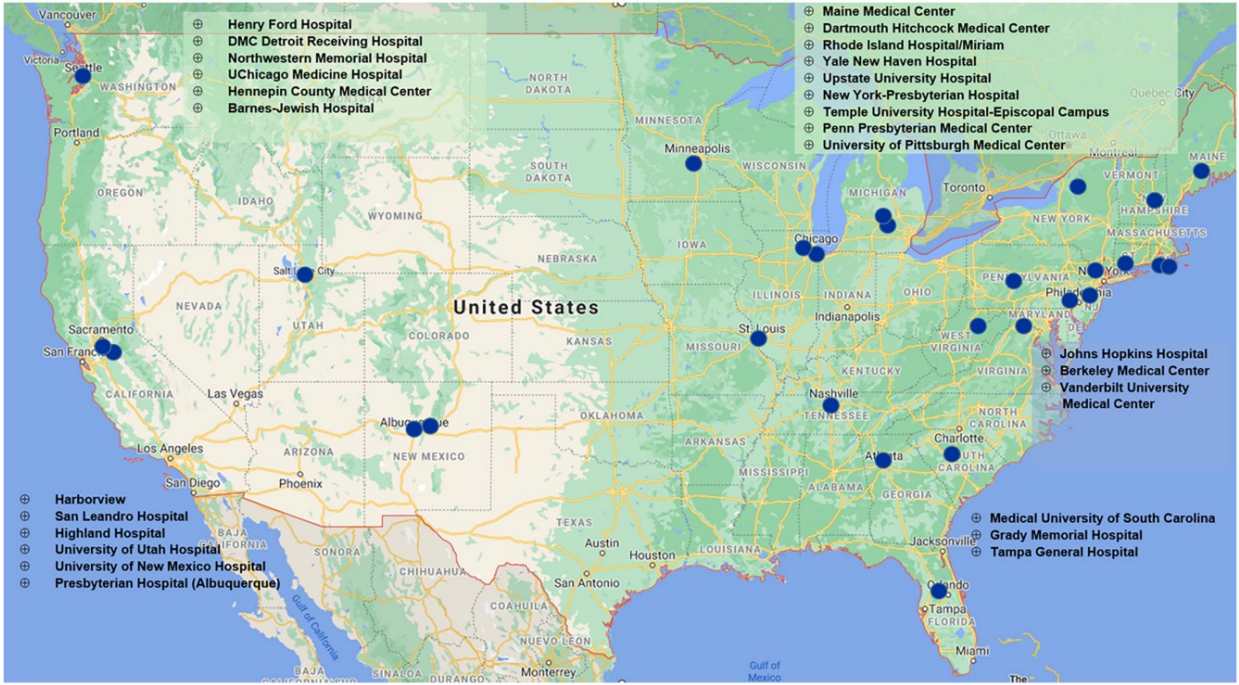
- Rescue for severe or refractory cases is frequent pushes of fentanyl titrated to comfort ***with buprenorphine continuation***
    - Of severe cases requiring fent: 12/14 leave on therapeutic MOUD; 7/14 remain engaged at 30 days. (AHS Bridge)

Case 3: Direct to Injection

- 38 year old female with OUD, smokes 1g/fentanyl daily
- Presents with COWS of 7, last use 30 hours prior
- Randomized as part of clinical trial to 24mg XR-Buprenorphine (Brixadi)

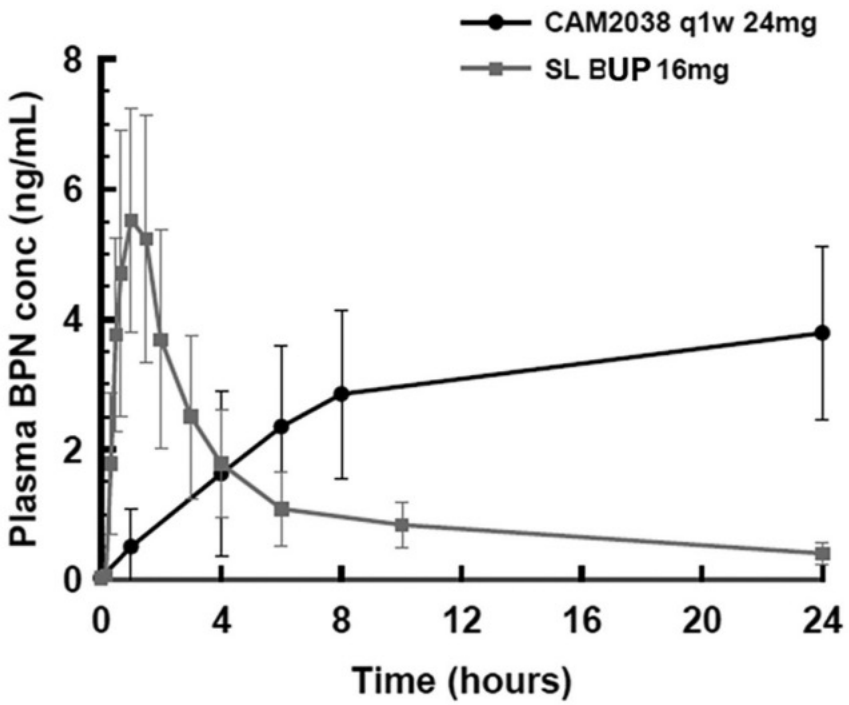
Case 3: Direct to Injection

- Multicenter RCT, nearing 2000 enrollments
- Bup SL vs XR
- Primary outcome 7 day follow up
- COWS 4+ eligible for XR vs home start
- COWS 8+ eligible for XR vs SL induction



Case 3: Direct to Injection

- Brixadi XR-Bup is now approved by FDA, covered by MCAL
- Weekly or monthly formulations
- On-label use after 4mg SL bup



Case 3: Direct to Injection

- Tolerates injection well, COWS decreases to 2 within 2 hours
- Presents to clinic 5 days later, has not used fentanyl
- Receives month long injection of buprenorphine
- Remains engaged in addiction treatment 4 months later

Summary: Opioids

- Fentanyl has made OUD a more fatal disease
- Precipitated withdrawal protocols can help improve treatment (CA Bridge has multispecialty endorsed protocol)
- Injectables a promising opportunity for ED patients

Summary

- Alcohol use disorder treatment should be integrated into withdrawal management for ED and hospitalized patients
- ED Substance Use Navigators can improve linkage to care and treatment outcomes
- Buprenorphine is a life saving medication with novel treatment approaches in the era of high-potency illicit opioids

Thanks!