### No One Dies a Preventable Death

The Role of EMS in Addiction Care & the Science of Opioid Addiction

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

#### We have no disclosures.



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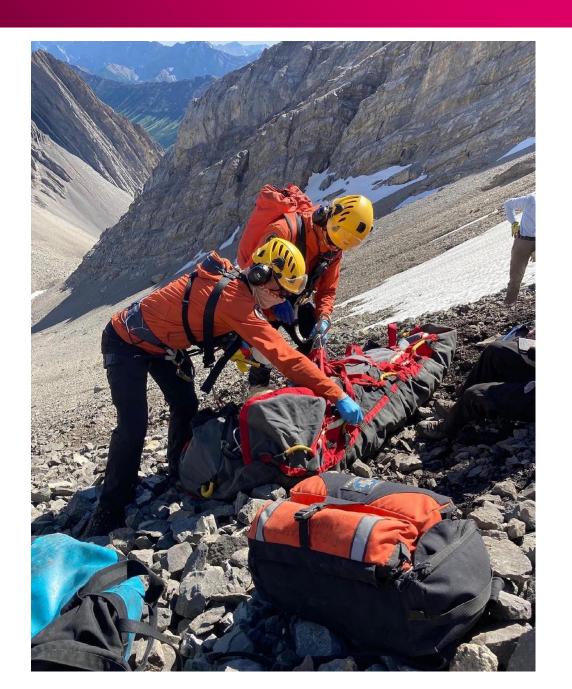
Special thanks to:











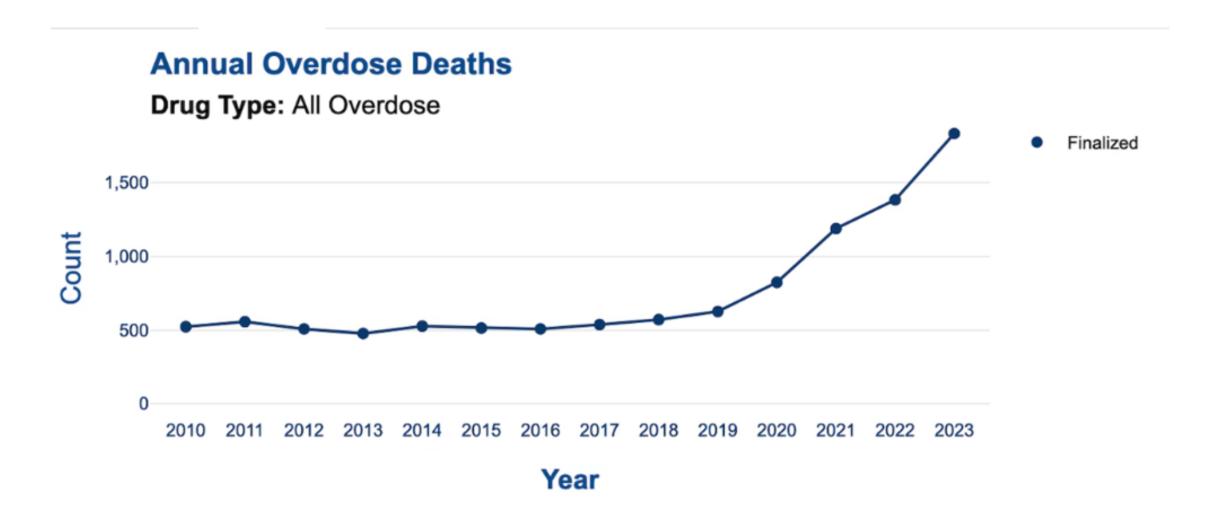




## NO ONE DIES A PREVENTABLE DEATH

## Oregon overdose deaths grew 33% in 2023, health data shows

Published: Dec. 12, 2024, 4:28 p.m.







## Home from boot camp, Army recruit from Oregon dies of fentanyl OD

Updated: Jan. 23, 2025, 10:17 p.m. | Published: Jan. 23, 2025, 7:00 a.m.



Inspired by an uncle, Tyson Richardson joined the Army and had dreams of serving as a cavalry scout to specialize in reconnaissance and gathering information about enemy positions, weapons and activity. "He wanted to serve his country, to be part of something greater than himself," said Clifford Richardson, his father. Courtesy of Family

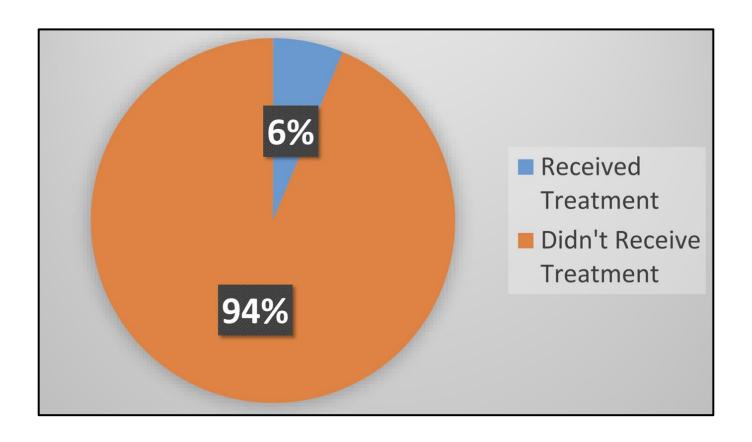


# About 46 million Americans, or 15% of the population, have a substance use disorder (SUD).

Source: Substance Abuse and Mental Health Services Administration. (2020). Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/



## Receipt of *Any* Substance Use Treatment Among People with a Past Year SUD



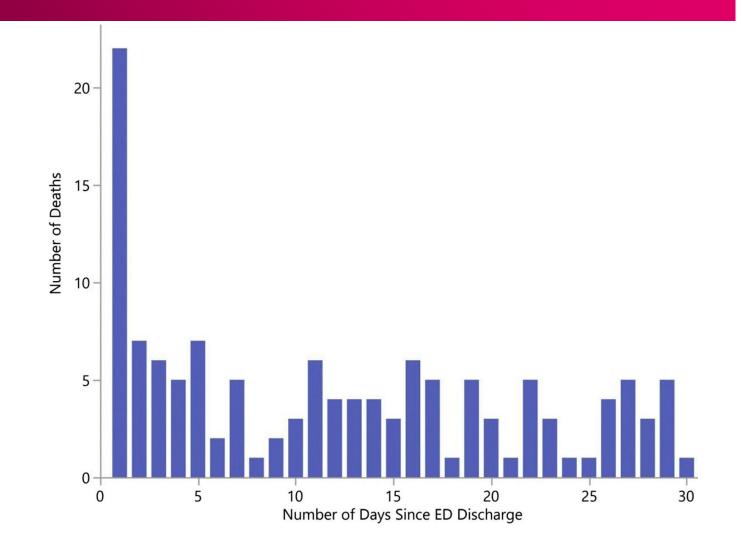


## Why is this an EMS problem?

#### OUD is an Emergency

Significant increased mortality risk post-ED discharge

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

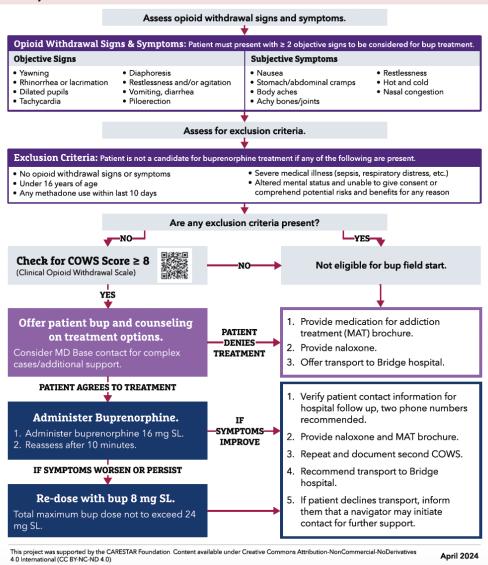




#### Emergency Medical Services: Buprenorphine (Bup) Field Start Protocol



This treatment protocol can be used for patients experiencing opioid withdrawal symptoms and for patients recently administered naloxone.

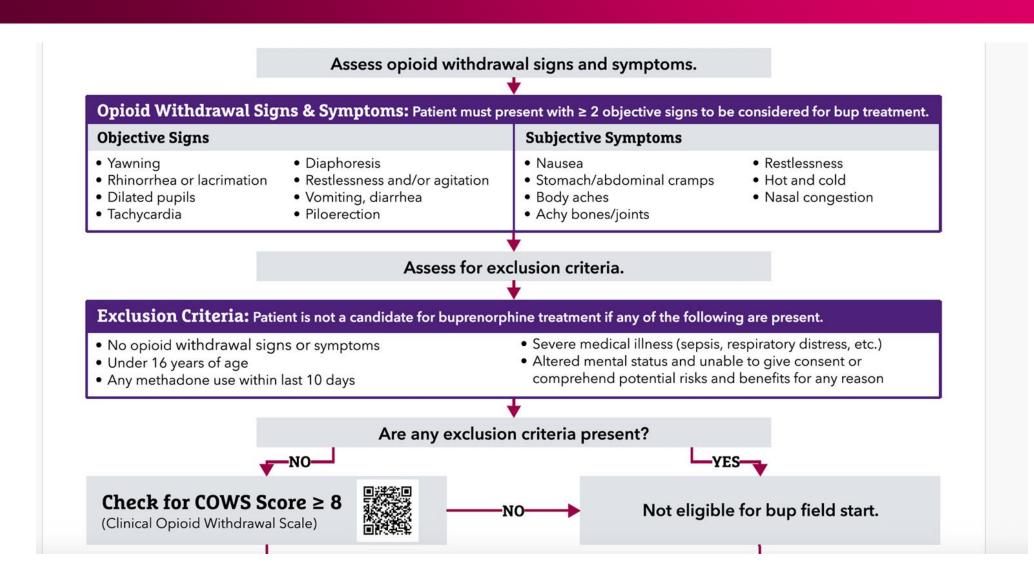


#### EMS Bridge Field Protocol:

- Follow the arrows, like ACLS
- 1300 paramedics across California use this protocol
- Currently 1/3 of all Californians live in an area where EMS has been trained to provide field bup



### Steps 1 & 2



### Steps 3 & 4

Offer patient bup and counseling 1. Provide medication for addiction PATIENT treatment (MAT) brochure. on treatment options. DENIES Provide naloxone. Consider MD Base contact for complex TREATMENT 3. Offer transport to Bridge hospital. cases/additional support. PATIENT AGREES TO TREATMENT 1. Verify patient contact information for hospital follow up, two phone numbers Administer Buprenorphine. recommended. IF SYMPTOMS— 1. Administer buprenorphine 16 mg SL. 2. Provide naloxone and MAT brochure. **IMPROVE** 2. Reassess after 10 minutes. 3. Repeat and document second COWS. IF SYMPTOMS WORSEN OR PERSIST 4. Recommend transport to Bridge hospital. Re-dose with bup 8 mg SL. 5. If patient declines transport, inform them that a navigator may initiate Total maximum bup dose not to exceed 24 contact for further support. mg SL.



# Successful Implementation in the EMS Setting





## Annals of Emergency Medicine

Emergency medical services/original research

Impact of Administering Buprenorphine to Overdose Survivors Using Emergency Medical Services

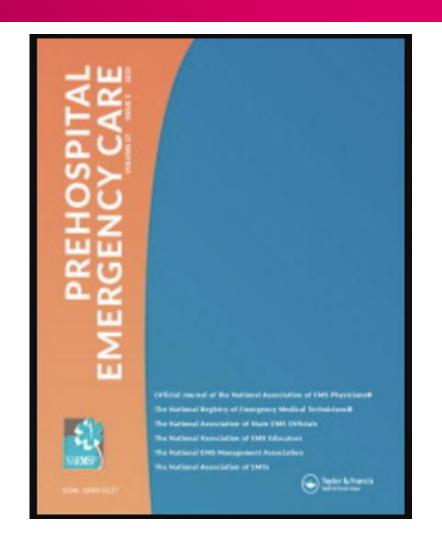
#### **Key Findings:**

- "Patients who received buprenorphine had a 12-fold increase in being engaged in treatment at 30 days"
- No precipitated withdrawal
- Decrease in Clinical Opioid
   Withdrawal Scale (COWS) from
   9.3 to 2.2
- Increased scene time of 6 minutes

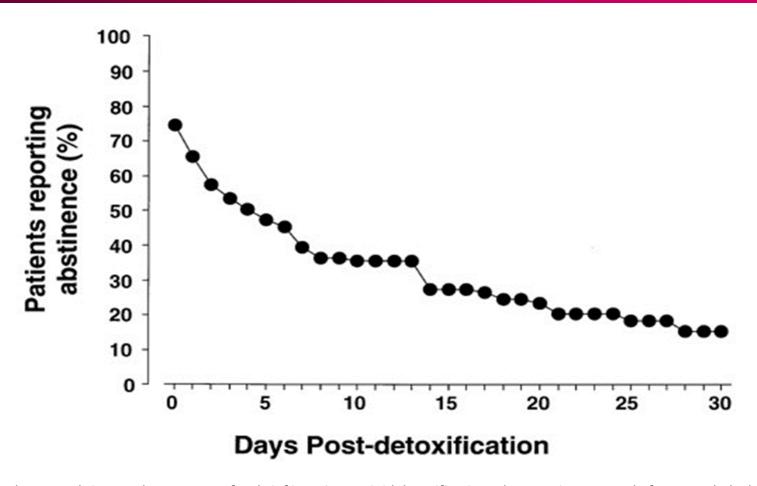
### Contra Costa County, CA

#### Bridge Buprenorphine Pilot:

- Treated abstinence withdrawal and naloxone precipitated withdrawal
- Precipitated withdrawal rate <1%</li>
- 25% of patients retained in treatment at 30 days
- CA policy change: buprenorphine no longer requires calling medical direction as of 2023



#### **Detoxification Doesn't Last**



Chutuape, M et al. One-, three-, and six-month outcomes after brief inpatient opioid detoxification. The American Journal of Drug and Alcohol Abuse. Vol 27:1, 2001.

## Medications for Opioid Use Disorder (MOUD)

#### Methadone **Buprenorphine ± Naloxone Naltrexone**

Full mu (opioid) receptor agonist



Oral (often solution)

Partial mu receptor agonist





Sublingual (tab, film), IV, IM, subcutaneous injection, transdermal patch Mu receptor antagonist (blocker)



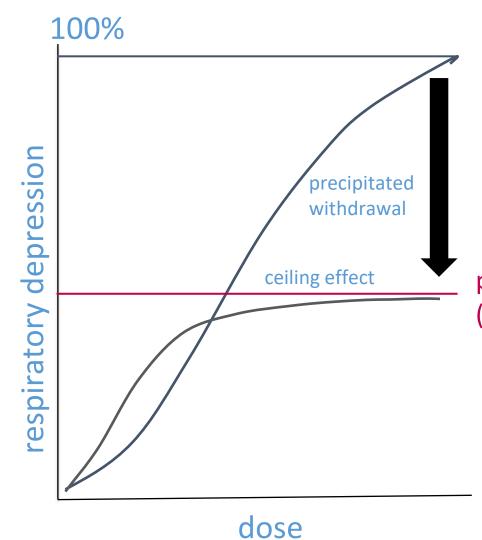
Intramuscular injection (extended release) or Oral

Ex: "Vivitrol," "ReVia"

#### Buprenorphine

#### Buprenorphine:

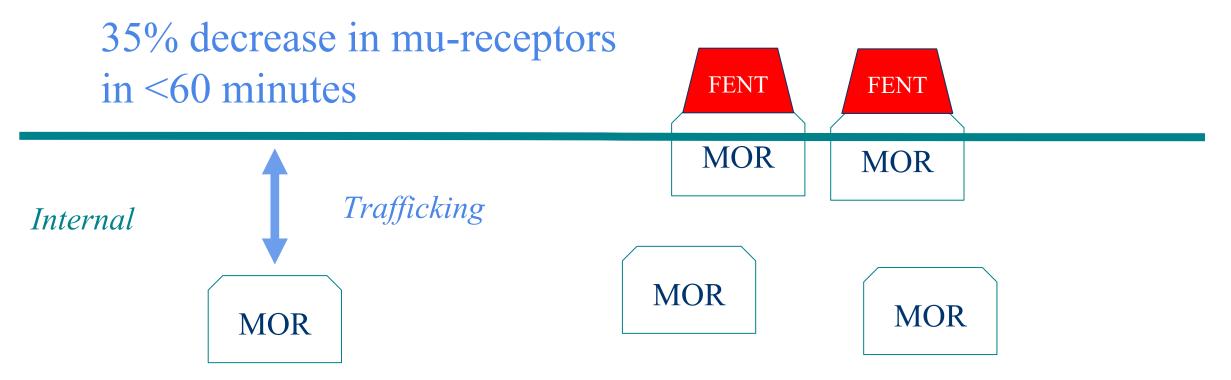
- Safely and effectively treats
   withdrawal, craving, & overdose
- Partial agonist
  - Ceiling effect:
    - Respiratory depression
    - Sedation
  - No ceiling effect:
    - Analgesia
- High affinity
  - Blocks other opioids
  - Displaces other opioids
- Long acting
  - Half-life ~ 24-36 Hours



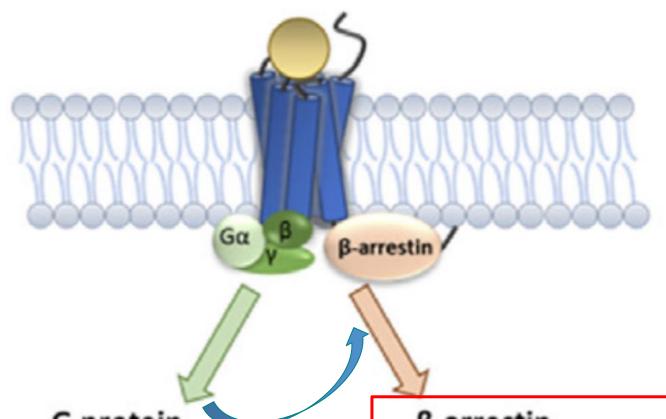
full agonist
(e.g. morphine,
methadone,
heroin,
fentanyl,
hydrocodone)

partial agonist (buprenorphine)

#### Fentanyl rapidly induces profound tolerance



MOR internalization & decreased MOR signal amplification result in <u>tolerance</u> & <u>desensitization</u>



**G** protein

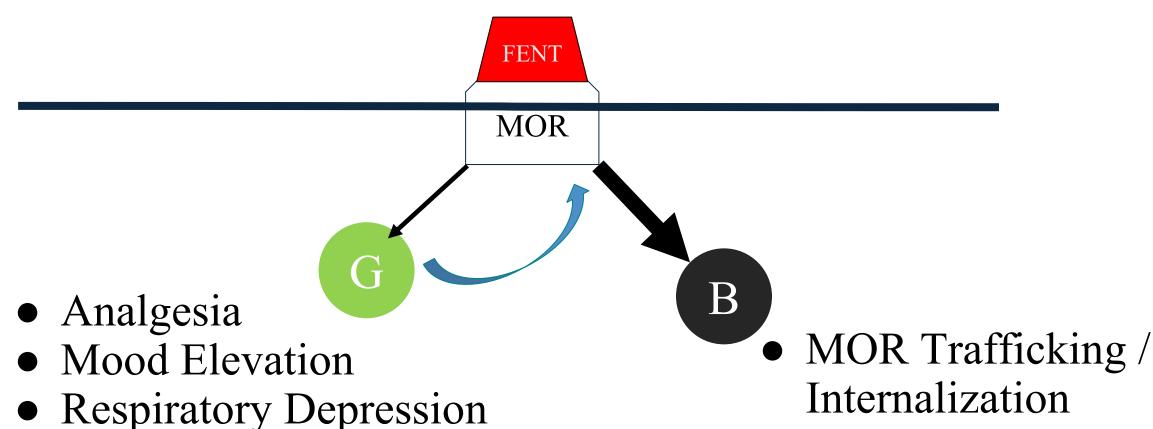
Analgesia
Respiratory depression
Constipation
Other adverse effects

#### **B-arrestin**

**Desensitisation** – Decreased MOR signal amplification

Trafficking – MOR internalization

#### Fentanyl is a biased agonist



Constipation

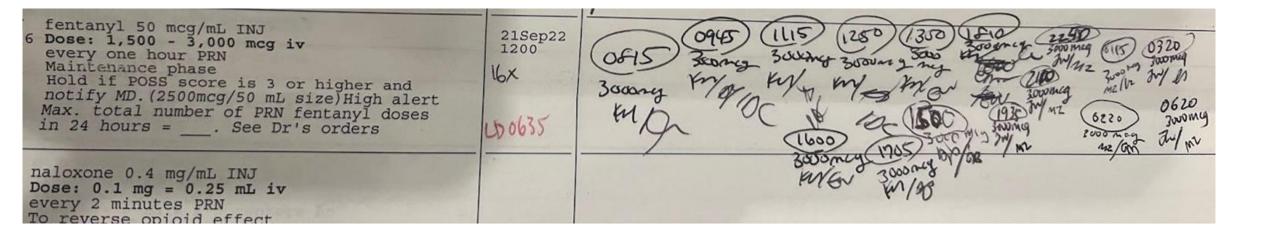
• Other Adverse Effects

- Desensitization
  - Hyperalgesia

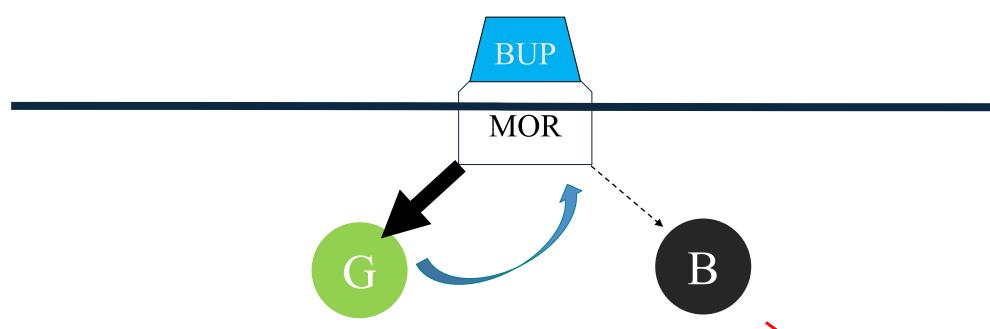


### What is high opioid tolerance?

- 1. Countries who use full agonists for OUD treatment use 1200 MME/day
- 2. Typical person who uses fentanyl- "2 grams per day"
- 3. Community-based lab testing estimates of street fentanyl purity ~20%
- 4. 2 grams=2 million micrograms x 0.2=~400,000 mcg/day
- 5. Example of Vancouver General Hospital's full agonist protocol:
  - a. Fentanyl 200-400 mcg IV q5 minutes to comfort, then 50-100% of that dose q 1 hour prn
  - b. Typical dose fentanyl 2000-4000 mcg IV q1 hour prn



#### Buprenorphine only has partial Beta-arrestin activity

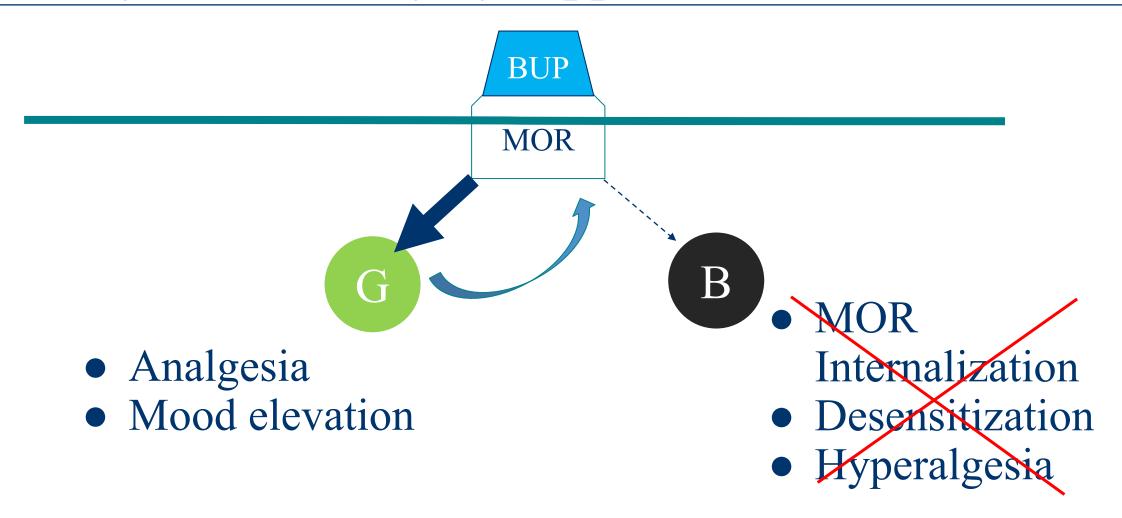


- Analgesia
- Mood elevation

- MOR
   Internalization
- Desensitization
- Hyperalgesia

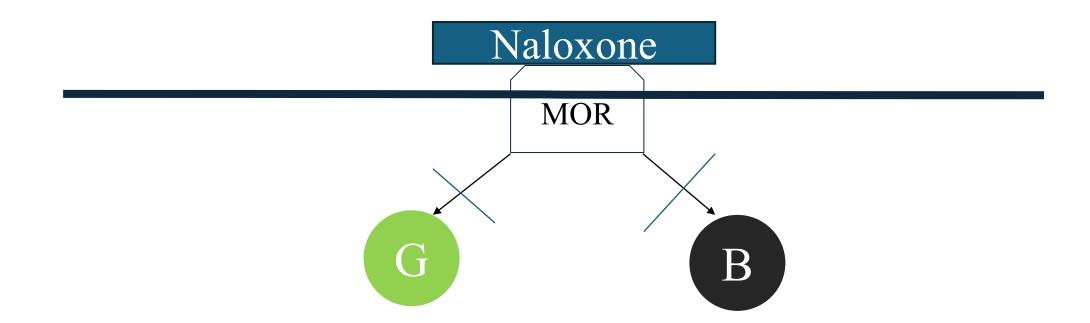
Virk MS, Arttamangkul S, Birdsong WT, Williams JT. Buprenorphine is a weak partial agonist that inhibits opioid receptor desensitization. J Neurosci. 2009 Jun 3;29(22)

## Buprenorphine is a biased agonist that promotes recovery of sensitivity by suppression of Beta-arrestin



Pedersen MF, Wróbel TM, Märcher-Rørsted E, Pedersen DS, Møller TC, Gabriele F, Pedersen H, Matosiuk D, Foster SR, Bouvier M, Bräuner-Osborne H. Biased agonism of clinically approved μ-opioid receptor agonists and TRV130 is not controlled by binding and signaling kinetics. Neuropharmacology. 2020 Apr:166:107718

#### Naloxone completely blocks Beta-arrestin



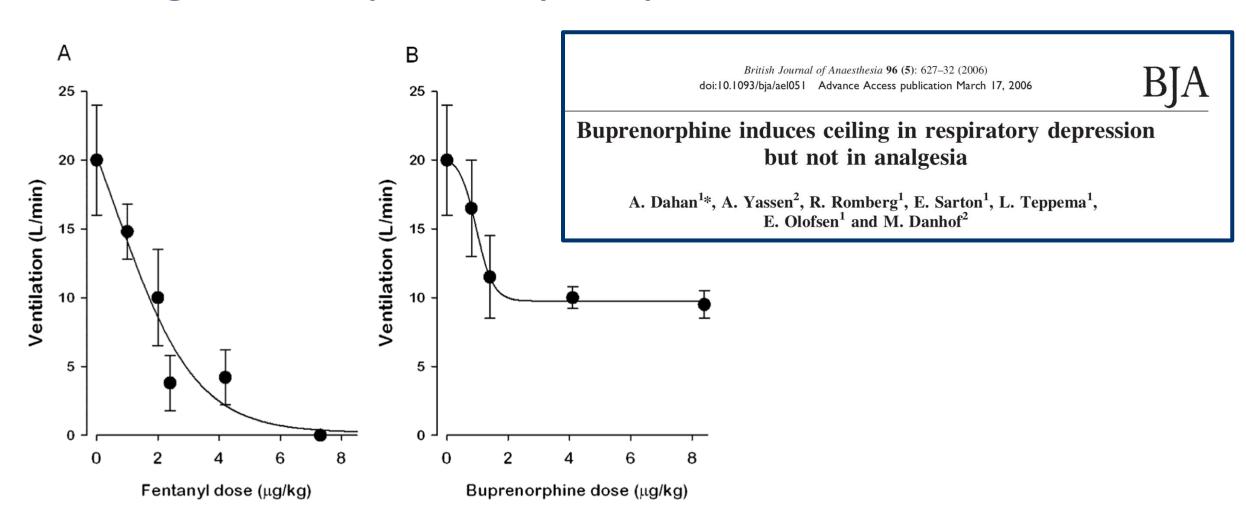
## Blockade of beta arrestin activity triggers more rapid Mu receptor traffic to membrane surface

Díaz, A., et al. "Regulation of  $\mu$ -opioid receptors, G-protein-coupled receptor kinases and  $\beta$ -arrestin 2 in the rat brain after chronic opioid receptor antagonism." *Neuroscience* 112.2 (2002): 345-353.

Bohn, Laura M., et al. "μ-Opioid receptor desensitization by β-arrestin-2 determines morphine tolerance but not dependence." Nature 408.6813 (2000): 720-723.



### Ceiling on Respiratory Depression



Dahan et al., 2006.

#### High dose is safe



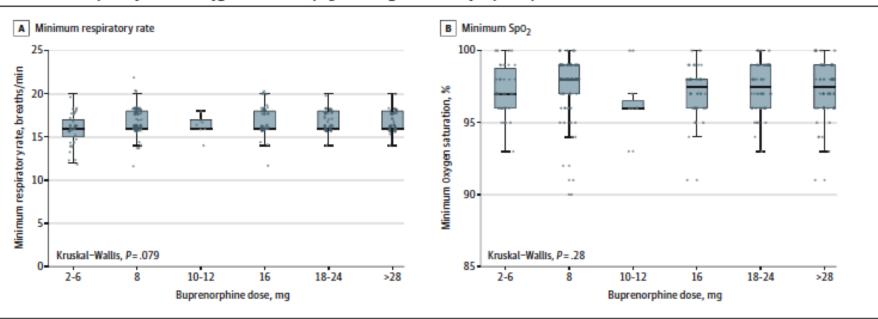


Original Investigation | Substance Use and Addiction

#### 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 (SpO2) 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% Cls. Kruskal-Wallis test compares distributions of respiratory rate and oxygen saturation across buprenorphine dose categories.

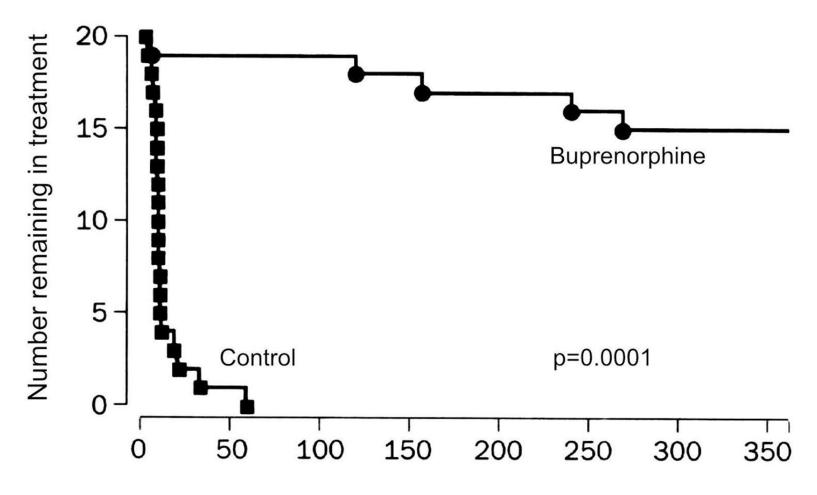
#### **NNT by Buprenorphine Dose**

NNT	<b>Buprenorphine Dose</b>
1 in 4	using low dose buprenorphine (2 to 6 mg)
1 in 3	using medium dose buprenorphine (7 to 16 mg)
1 in 2	using high dose buprenorphine (≥ 16 mg)

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



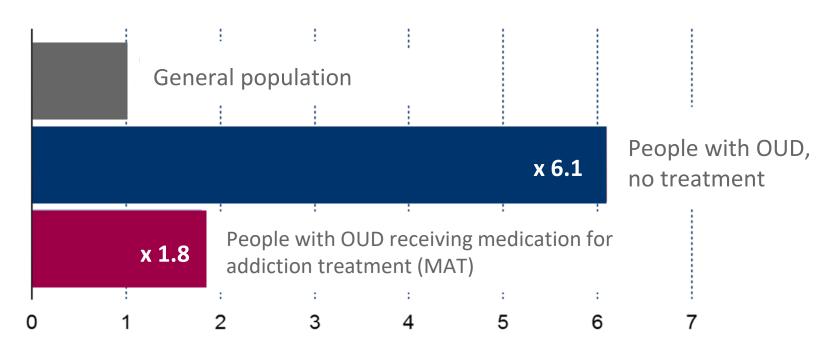
#### **Buprenorphine Improves Retention**



Time from randomization (days)

#### **Buprenorphine Saves Lives**

Mortality Risk Compared to the General Population

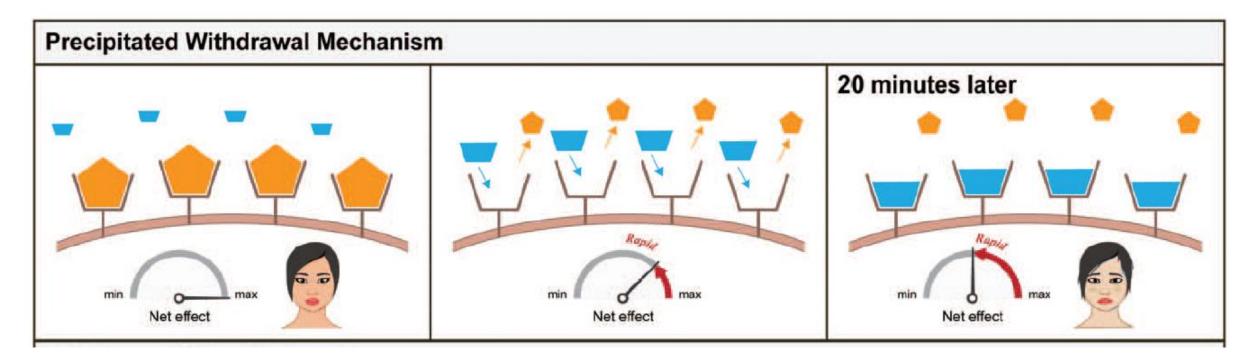


Standardized Mortality Ratio

## Number Needed to Treat (NNT)

Aspirin in STEMI	42 to save a life
Warfarin in Afib	25 to prevent a stroke
Steroids in COPD	10 to prevent tx failure
Defibrillation in Cardiac Arrest	2.5 to save a life
Buprenorphine in Opioid Use Disorder	<b>2</b> to retain in treatment

#### **Precipitated withdrawal**



- A rough patient experience and patients talk to each other!
- A rough provider experience don't want to lose trust!

Ghosh et al, 2019

### Precipitated Withdrawal is Uncommon

- 1200 patients starting buprenorphine from 28 EDs
  - most patients used fentanyl
- 9 cases of precipitated withdrawal (0.76% of participants)
- Treated precipitated withdrawal until symptoms resolved
- 86% attended follow-up MAT clinic appointment within 7 days

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

JAMA Netw Open
Published Online: March 30, 2023
2023;6;(3):e236108. doi:10.1001/jamanet-workopen.2023.6108

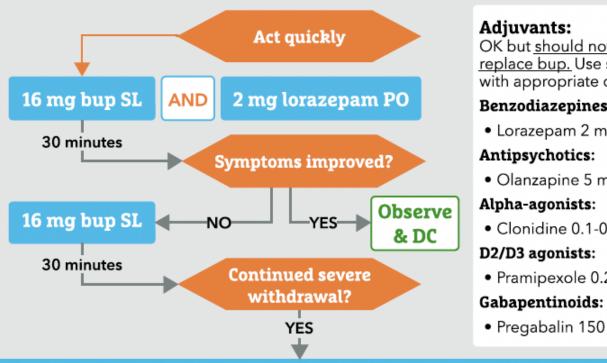
## If you do precipitate withdrawal

## Keep calm and give bup

### If You Do Precipitate Withdrawal

#### Treatment of bup precipitated withdrawal

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



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

#### Benzodiazepines:

Lorazepam 2 mg PO/IV

Olanzapine 5 mg PO/IM

Clonidine 0.1-0.3 mg PO

Pramipexole 0.25 mg PO

Pregabalin 150 mg PO

Give 16+ mg more bup.

Add a benzo.

Use adjuvant therapy.

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.

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## Common Misconceptions

"Patients should be referred to counseling before starting treatment."

"Starting someone on buprenorphine is just trading one addiction for another."

"Starting Bup in the ED takes too long."

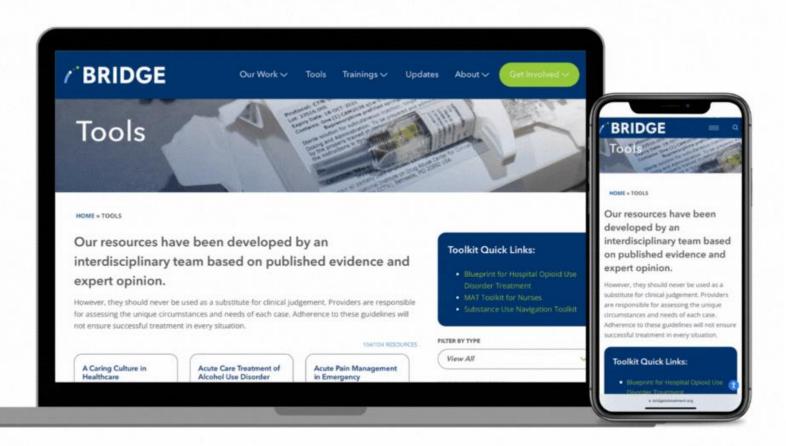
"Other patients deserve higher priority."





# Referral is not an adequate crisis response.

## Resources





#### Summary

- 1. OUD is an emergency and EMS has a crucial part to play in reducing overdose deaths.
- 2. There is evidence that prehospital bup initiation increases retention in treatment for at least 30 days, which has the potential to save lives and reduce overdose call volume.
- 3. With proper training, increased scene time is minimal, bup is cheap to stock and safe to give, and the benefits of EMS MOUD outweigh the risks and challenges of administration

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