Opioids

Immersion Training in Addiction Medicine Program 2024

April 2024

Hallie Rozansky, MD
Assistant Professor of Medicine
Boston Medical Center; Chobanian & Avedisian School of Medicine

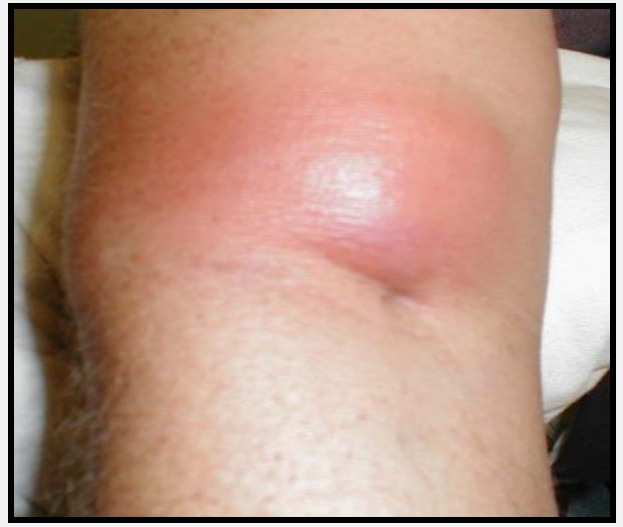
CARE Clinical Addiction Research and Education

Boston Medical Center EXCEPTIONAL CARE. WITHOUT EXCEPTION.

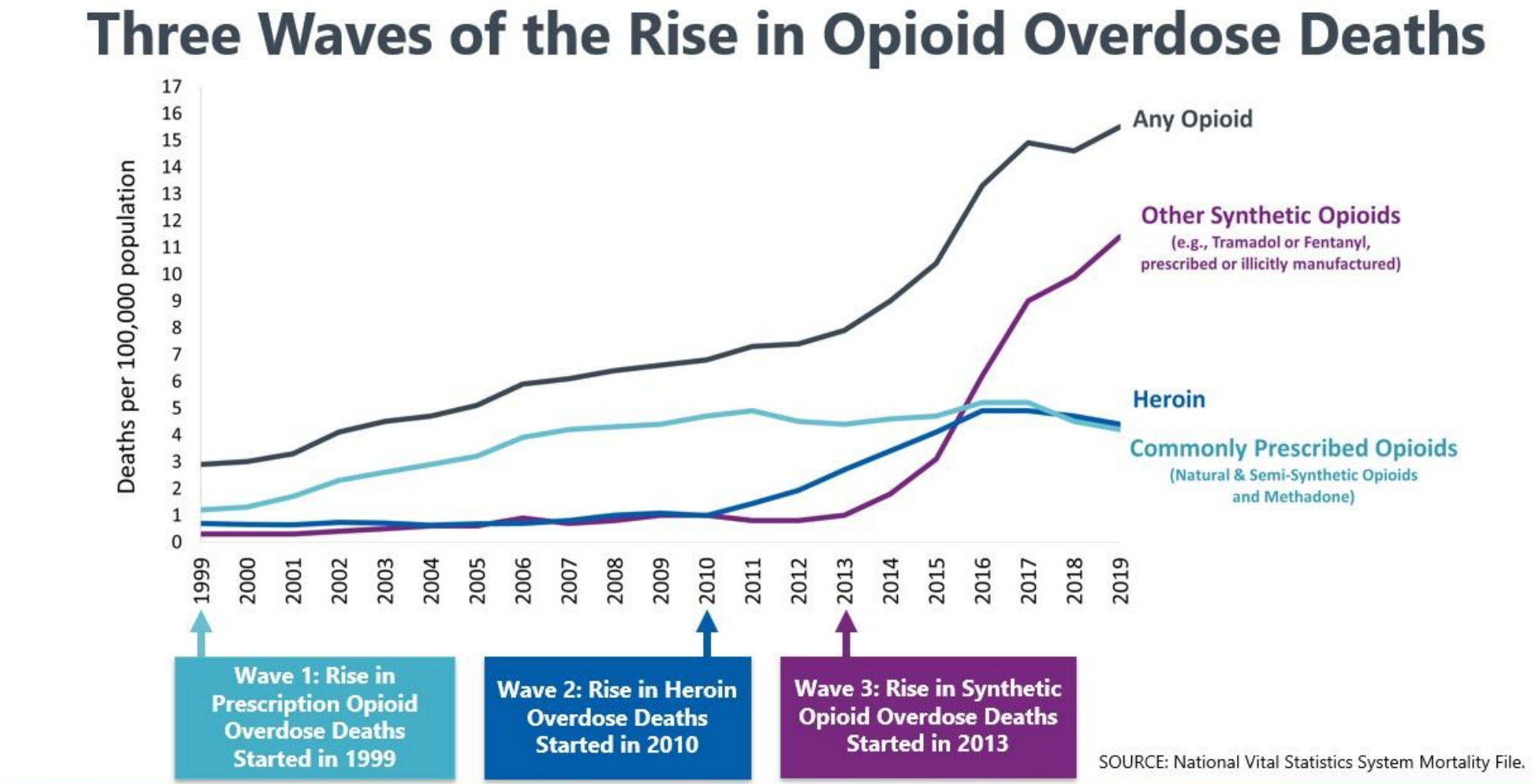
Grayken Center for Addiction Boston Medical Center

Case

- 32-year-old male brought into the Emergency Department after an “opioid overdose”
- Brisk response to naloxone; wakes up & c/o feeling “sick”
- Abscess and cellulitis in left antecubital fossa, significant tenderness with movement of the joint; T101.9
- Admitted for “drug overdose” and “cellulitis/abscess, ?septic joint”

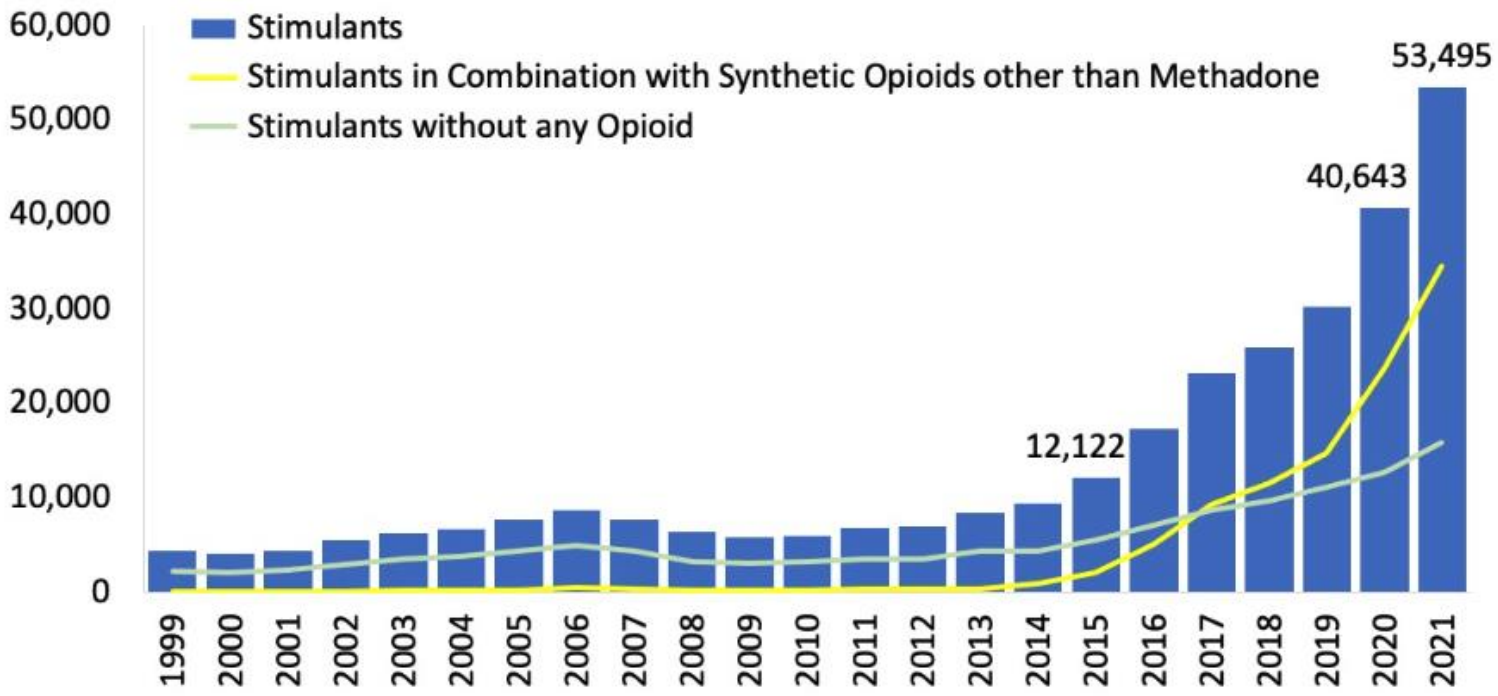


Since 1999, opioid overdose epidemic described in "waves"



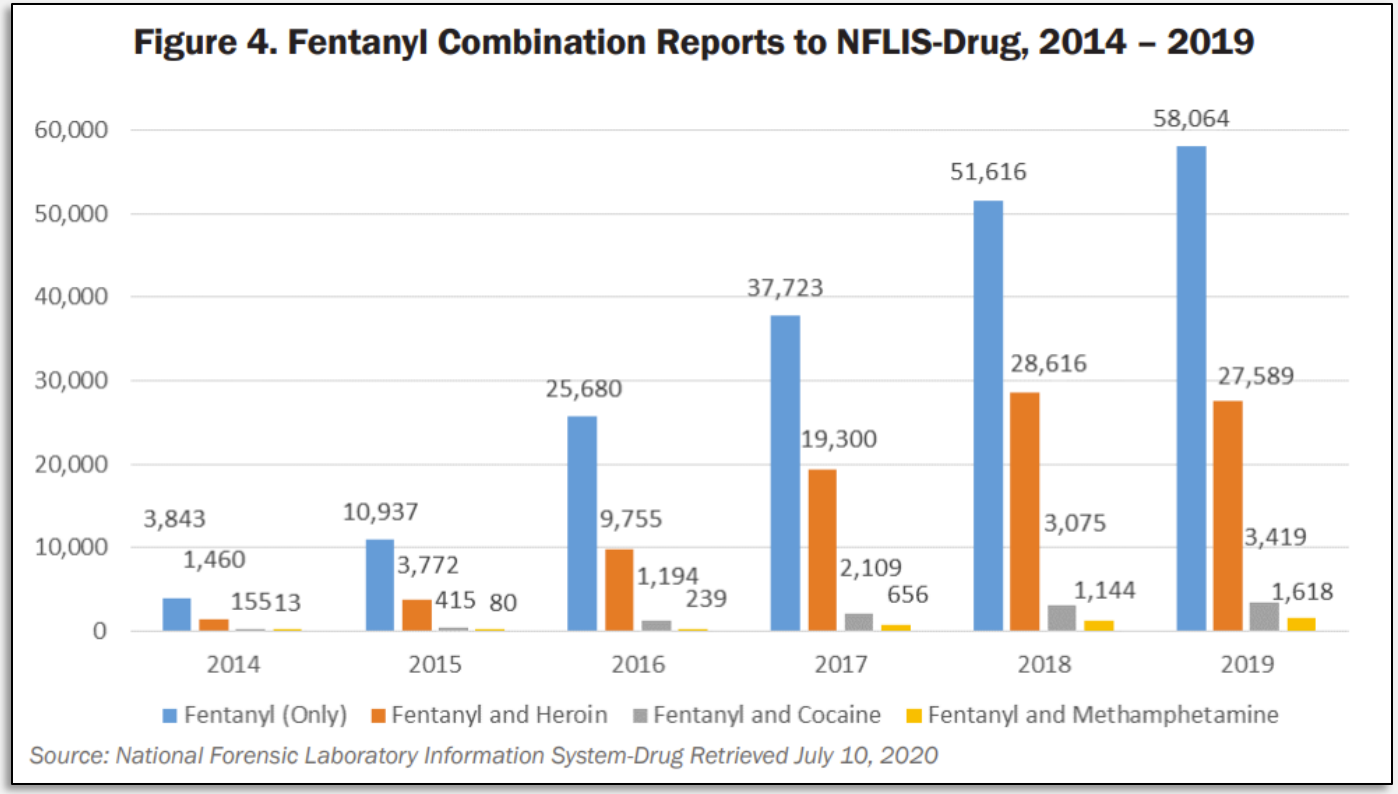
“Fourth wave” – stimulant-involved deaths

Figure 6. National Overdose Deaths Involving Stimulants (Cocaine and Psychostimulants*), by Opioid Involvement, Number Among All Ages, 1999-2021



*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the T43.6 ICD-10 multiple cause-of-death code. Abbreviated to *psychostimulants* in the bar chart above.
Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

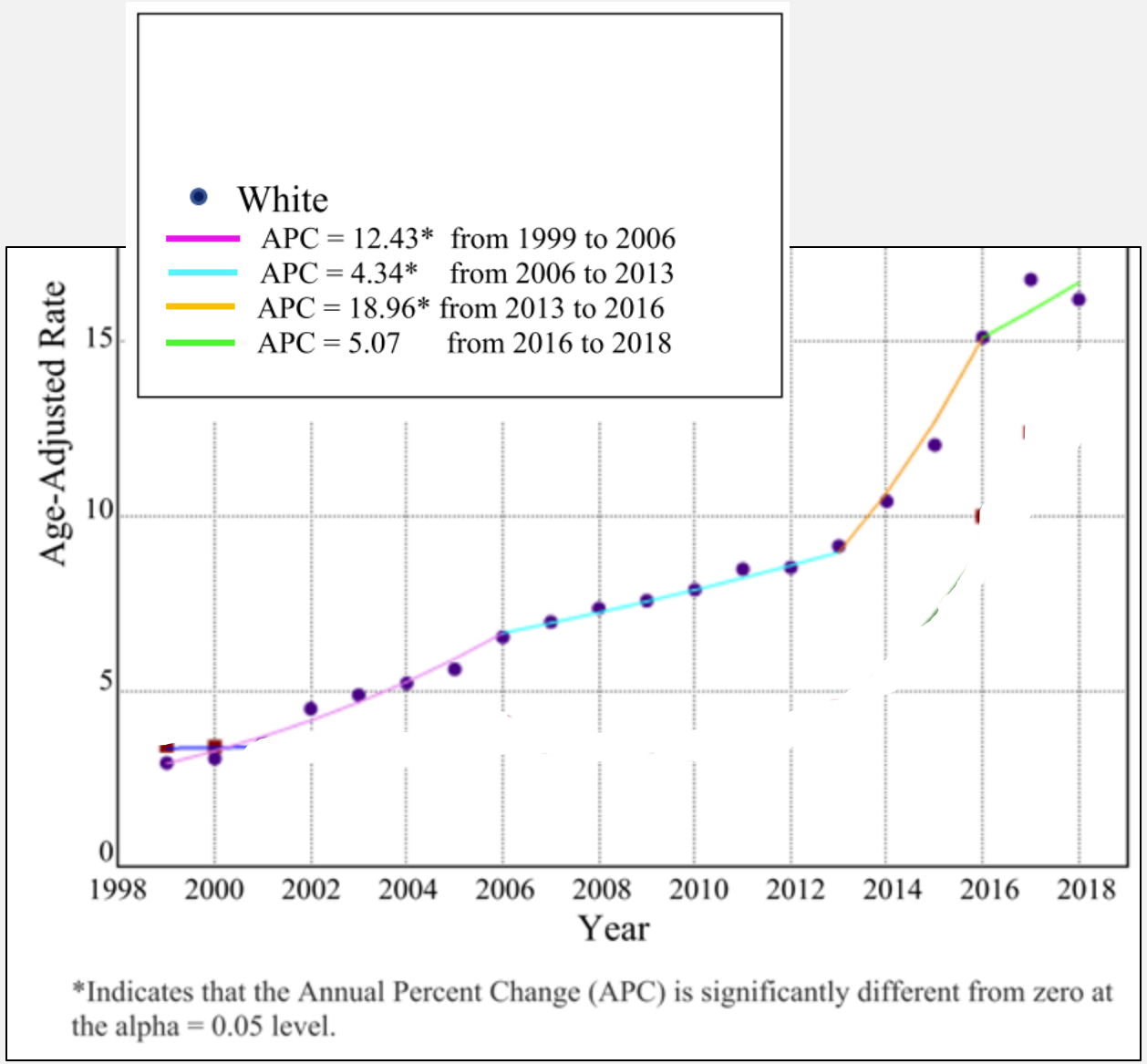
Street opioid supply is unregulated & evolving



Sample	ID	Suspected	Laboratory Detected Substances
	13157	Fentanyl	Fentanyl (10) Xylazine (7) 4-ANPP (trace)
	13156	Fentanyl	Fentanyl (10) Cocaine HCL (trace) 4-ANPP (1) Phenethyl-4-ANPP (trace)
	13155	Fentanyl	Fentanyl (10) Methamphetamine (1) Paracetamol (Acetaminophen) (2) Caffeine (1) 4-ANPP (1)
	13154	UK	Buprenorphine (10) Nicotine (trace)
	13153	M30 Pill (Percocet, Perc30)	Fentanyl (10) Para-fluorofentanyl (10) Paracetamol (Acetaminophen) (295) para-Fluoro-4-ANPP (3)

DEA National Drug Threat Assessment. March 2021
Streetcheck.Org

Disparities in opioid overdose deaths



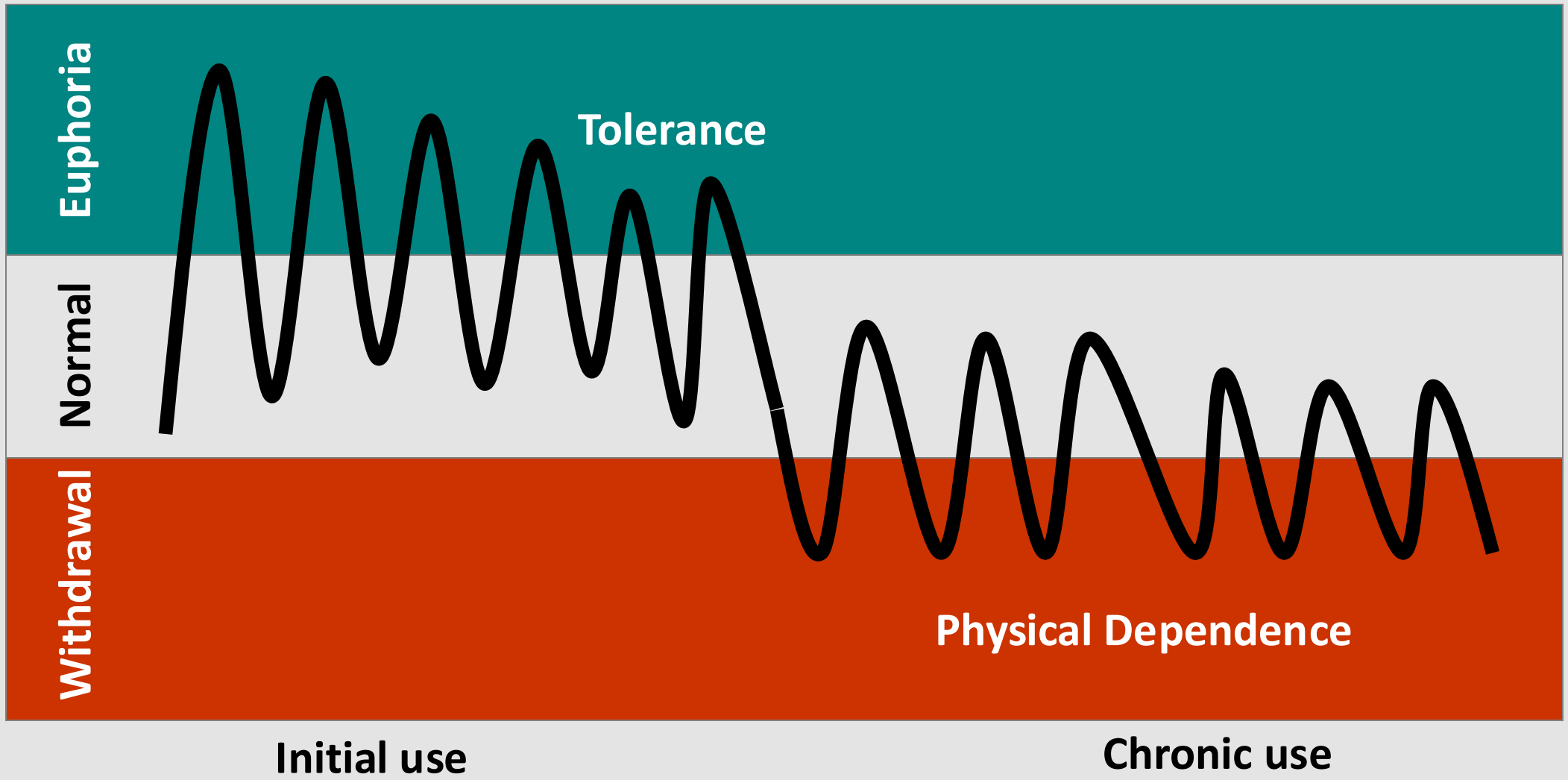
Furr-Holden D et al. *Addiction.* 2020

- White Americans with multiple periods of acceleration 1999 to 2016 with decrease rate of change 2016 to 2018
- Black Americans: low rate of change 1999-2012 followed by **rapid acceleration** (intro of street fentanyl)
- From 2013–2018 average annual precent change significantly higher in Black Americans than White Americans
- Opioid crisis response has focused on white, middle-class, suburban and rural users; the impact in Black American communities has been underrecognized

Case continued

- Substance use history
  - Daily heroin/fentanyl use
  - Intranasal use for 6 months → IV for 7 years
  - 10 lifetime overdoses
  - Has gone to detox 40 times, never treated with meds; was in recovery x2 years via NA, relapsed 2 months ago
  - No other drug, alcohol or tobacco use
- HIV and hepatitis C negative
- Unemployed electrician
- Lives with wife (in recovery) and 2 young children
- **Now complaining of severe elbow pain and opioid withdrawal**
  - **How will you assess and treat him?**

Natural history of opioid use disorder



Alford DP. http://www.bumc.bu.edu/care/

Complex patient/provider experience with inpatient treatment of OUD

- Study conducted on the inpatient medical service of a public urban teaching hospital

- Qualitative analysis on the interactions with patients with OUD and their medical teams identified **4 common themes**

Merrill JO, et al. *J Gen Intern Med.* 2002

Provider perspective

1. Physician fear of deception

Physicians question the "legitimacy" of need for opioid analgesics ("drug-seeking" patient vs. legitimate need).

"All of us go through a little bit of a hitch every time we are requested to prescribe narcotics for our patients....Are they trying to get more out of me than they really should have? The last thing I want to do is over-dose them or reinforce this behavior (of) trying to coax more drugs out of you."

-Senior Medical Resident

Merrill JO, et al. *J Gen Intern Med*. 2002

Patient perspective

2. No standard approach

The evaluation and treatment of pain and withdrawal is extremely variable among physicians and from patient to patient. There is no common approach nor are there clearly articulated standards.

"The last time, they took me to the operating room, put me to sleep, gave me pain meds, and I was in and out in two days.. . .This crew was hard! It's like the Civil War. 'He's a trooper, get out the saw'. . ."

-Patient w/ Multiple Encounters

Merrill JO, et al. *J Gen Intern Med*. 2002

Patient perspective

3. Avoidance

Physicians focused primarily on familiar acute medical problems and evaded more uncertain areas of assessing or intervening in the underlying addiction problem- particularly issues of pain and withdrawal.

<u>Patient/Resident Dialogue</u>

Resident: “Good Morning”
Patient: “I’m in terrible pain.”
Resident: “This is Dr. Attending, who will take care of you.”
Patient: “I’m in terrible pain.”
Attending: “We’re going to look at your foot.”
Patient: “I’m in terrible pain.”
Resident: “Did his dressing get changed?”
Patient: “Please don’t hurt me.”

Merrill JO, et al. *J Gen Intern Med*. 2002

Patient perspective

4. Patient fear of mistreatment

Patients are fearful they will be punished for their drug use by poor medical care.

"I mentioned that I would need methadone, and I heard one of them chuckle. . .in a negative, condescending way. You're very sensitive because you expect problems getting adequate pain management because you have a history of drug abuse. . .He showed me that he was actually in the opposite corner, across the ring from me."

-Patient

Merrill JO, et al. *J Gen Intern Med*. 2002

Inpatient treatment goals

- Prevent/treat acute opioid withdrawal
  - Inadequate treatment may prevent full treatment of medical/surgical condition
- Don't expect to cure OUD during hospitalization
  - Withholding opioids will not cure patient's OUD
  - Administering opioids will not worsen patient's OUD
- Initiate addiction treatment referral
- Diagnose and treat medical illness
  - Growing evidence that medications for OUD (MOUD) facilitates the treatment of other serious complications of OUD, e.g., endocarditis and osteomyelitis (Jo Y, et al. *Addiction*. 2021)

Opioid withdrawal assessment

Grade	Symptoms / Signs
0	Anxiety, Drug Craving

Clinical Opiate Withdrawal Scale (COWS): *pulse, sweating, restlessness & anxiety, pupil size, aches, runny nose & tearing, GI sx, tremor, yawning, gooseflesh* (score 5-12 mild, 13-24 mod, 25-36 mod severe, 36-48 severe)

Inpatient treatment of opioid withdrawal

Methadone

- Start w/ **20** mg po
- Reassess q 2-3 h, give additional **5-10** mg until withdrawal signs abate
- Don't exceed **40** mg/24 hrs
- Use caution in pts with cirrhosis or long QT

Buprenorphine

- **Traditional** induction:
  - Start with **2-4** mg SL; reassess q 2-3 h, give additional **2-4** mg until withdrawal signs abate
  - Don't exceed **16** mg/24 hrs
- **Low-dose** induction: 0.5 mg SL, 20 mcg/hr TD patch, 150-450 mcg buccal)

- "Authorized hospital staff [may] administer narcotic drugs in a hospital to maintain or detoxify a person as an incidental adjunct to medical or surgical treatment of conditions other than addiction" *(Code of Federal Regulations title 21, up to date as of 4/20/2023)*
- Monitor for response and CNS and respiratory depression
- Give same dose (or higher, as needed) daily including day of discharge
- **Cannot give a methadone prescription at time of discharge; needs clinic**
- **Can give a buprenorphine prescription at time of discharge**

Peterkin A et al. *Med Clin N Am.* 2022
Sokolski E et al. *J Addict Med*. 2023
Cohen SM et al. *J Addict Med.* 2022

Pain management in patients taking methadone or buprenorphine

- Patients with OUD are more sensitive to painful stimuli
- Continue methadone or buprenorphine throughout pain management or perioperative period
- Treat pain with analgesics on top of the patients daily MOUD
- Opioid analgesic requirements are often higher due to increased pain sensitivity and opioid cross tolerance
- Ineffective pain management can result in disengagement of care

Hickey T et al. *Med Clin N Am.* 2022
Veazie S et al. *J Gen Intern Med.* 2020
Kohan L et al. *Reg Anesth Pain Med.* 2021
Alford DP, Compton P, Samet JH. *Ann Intern Med* 2006

Case continued

Hospital course

- Elbow c/w septic joint; ortho does a washout, + for staph aureus; started on IV vanc
- Pain management: received PO & IV hydromorphone PRN
- Opioid withdrawal management: methadone 40 mg daily during hospitalization
- He did not want to remain on MOUD (methadone or buprenorphine) at time of discharge

6 months later

- He presents to your primary care clinic requesting referral to “detox” for his opioid use disorder
- He has been using heroin/fentanyl since the day he left the hospital

Opioid detoxification outcomes

- Low rates of retention in treatment

- High rates of relapse post-treatment
  - < 50% abstinent at 6 months
  - < 15% abstinent at 12 months

- **Increased rates of overdose due to decreased tolerance**

O'Connor PG *JAMA* 2005
Mattick RP, Hall WD. *Lancet* 1996
Stimmel B et al. *JAMA* 1977

Reasons for relapse

- Protracted abstinence syndrome due to derangement of endogenous opioid receptor system
    - Generalized malaise, fatigue, insomnia
    - Poor tolerance to stress and pain
    - Opioid craving
- Conditioned cues (triggers)
- Priming with small dose of drug

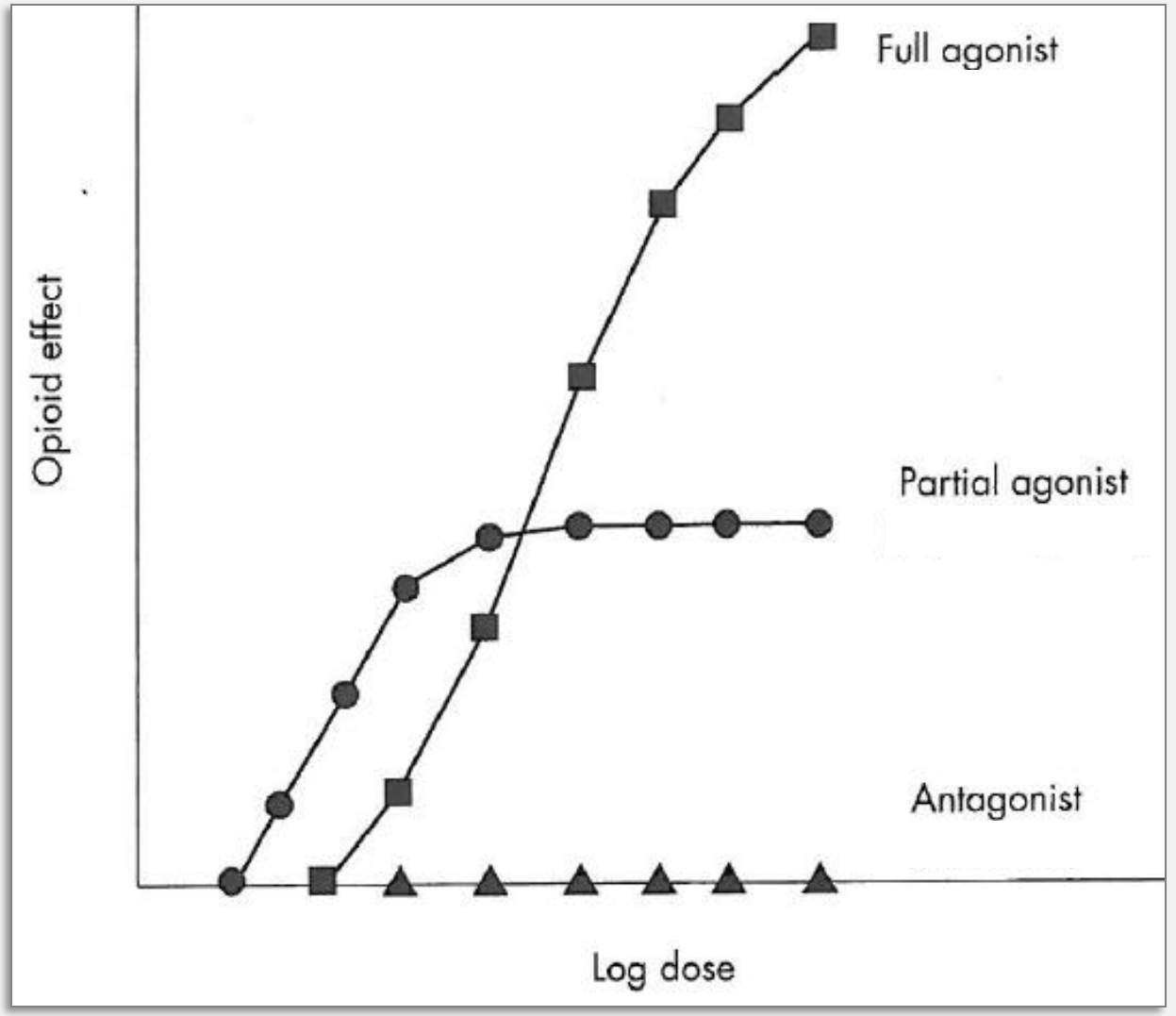
Medications for OUD (MOUD) treatment

Goals

- Suppress opioid withdrawal*
- Mu opioid receptor blockade
- Alleviate craving
- Normalize brain changes

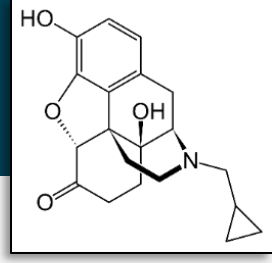
Options

- ***Opioid Agonist Therapy (OAT)**
  - **Methadone** (full agonist)
  - **Buprenorphine** (partial agonist)
- **Naltrexone** (full antagonist)



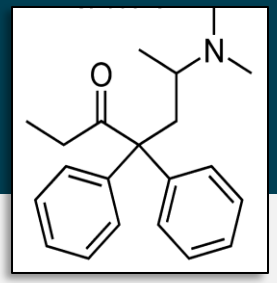
Peterkin A et al. *Med Clin N Am.* 2022

Naltrexone



- Pure opioid antagonist (must be opioid-free for 7-10 days beforehand)
- Oral naltrexone (daily)
  - Well-tolerated, safe, duration of action 24-48 hours
  - Not statistically significant compared to placebo due to poor retention (Minozzi S et al. 2011); more effective when legally mandated
- Injectable IM XR naltrexone (monthly)
  - In-office injection, administered by provider
  - Increased abstinence (90% vs 35% *[Krupitsy E, et al. Lancet, 2011]*)
  - Poor retention (40% at 3 months, <10% at 6 months *[Cousins SJ et al. J Sub Abuse Treat 2016]*)
- Risk: loss of tolerance to opioids

Methadone



- Full opioid agonist
  - PO onset of action 30-60 minutes; reaches steady state in 3-5 days
  - Duration of action 24-36 hours to treat OUD
  - Dosing for OUD
    - 20-40 mg for acute withdrawal
    - > 80 mg for craving, “opioid blockade”
    - Higher doses in fentanyl era
- Opioid Treatment Programs
  - Highly structured
  - Observed daily → “Take homes”

Buresh et al. 2022. J Subst Abuse Treatment. https://doi.org/10.1016/j.jsat.2022.108832.
Volkow 2021. World Psychiatry.

Extensive research on effectiveness

A Medical Treatment for Diacetylmorphine (Heroin) Addiction

A Clinical Trial With Methadone Hydrochloride

JAMA 1965

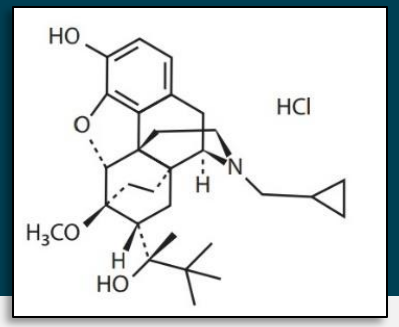
Vincent P. Dole, MD, and Marie Nyswander, MD

- Increases treatment retention
- Decreases illicit opioid use
- Decreases hepatitis and HIV seroconversion
- Decreases mortality
- Decreases criminal activity
- Increases employment
- Improves birth outcomes

Methadone maintenance limitations

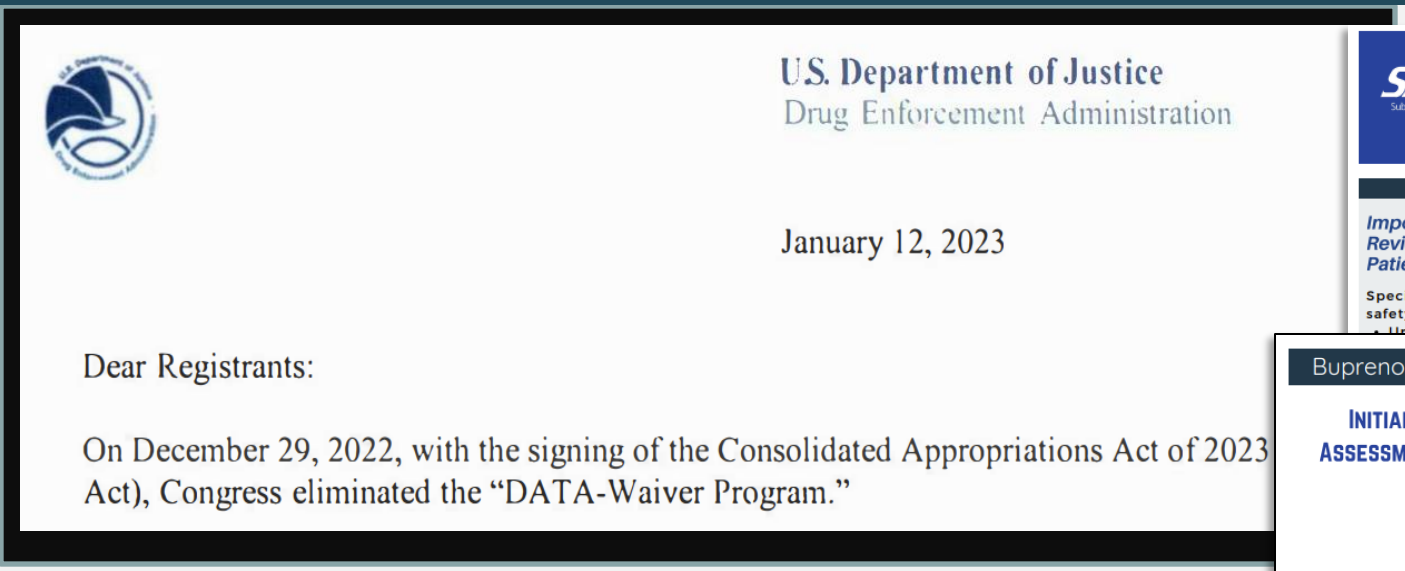
- Highly regulated - *Narcotic Addict Treatment Act 1974*
- Limited access
- Inconvenient and highly punitive
- Mixes stable and unstable patients
- Lack of privacy
- No ability to “graduate” from program
- **Stigma**

Buprenorphine



- Mu-opioid receptor partial agonist
  - Ceiling effect on CNS and respiratory depression
- Kappa-opioid receptor antagonist
  - Antidepressant and anxiolytic effects
- Formulations:
  - Sublingual tab or film (+/- naloxone)
  - Weekly & monthly SQ injections (*administered by healthcare provider*)
- FDA approved 2002 as schedule III – up to 5 refills

Buprenorphine

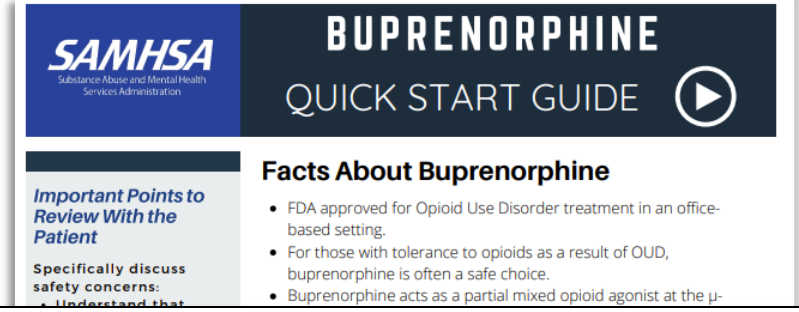


U.S. Department of Justice
Drug Enforcement Administration

January 12, 2023

Dear Registrants:

On December 29, 2022, with the signing of the Consolidated Appropriations Act of 2023 Act), Congress eliminated the "DATA-Waiver Program."



SAMHSA
Substance Abuse and Mental Health Services Administration

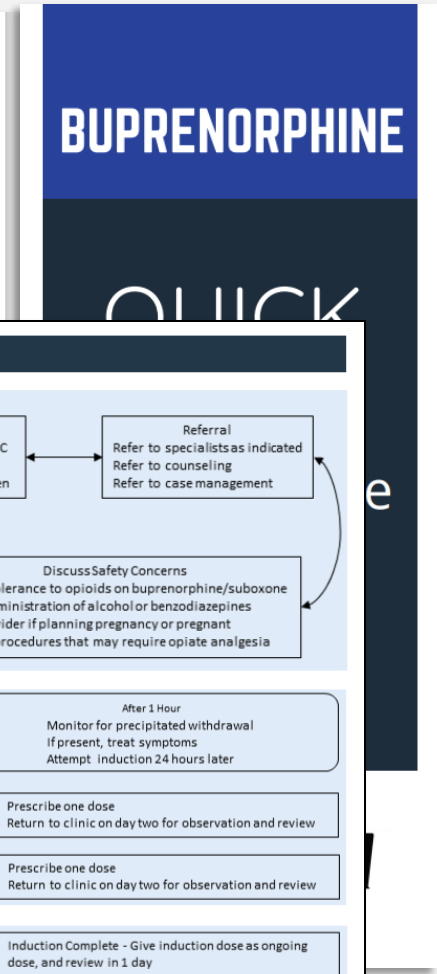
BUPRENORPHINE
QUICK START GUIDE

Important Points to Review With the Patient

Specifically discuss safety concerns:

Facts About Buprenorphine

- FDA approved for Opioid Use Disorder treatment in an office-based setting.
- For those with tolerance to opioids as a result of OUD, buprenorphine is often a safe choice.
- Buprenorphine acts as a partial mixed opioid agonist at the μ-



BUPRENORPHINE

QUICK

Buprenorphine Quick Start Guide for In Office Induction

INITIAL ASSESSMENT

History and Physical
Concurrent medical issues and substance use
Medication history (with review of the PDMP)
Allergies
Mental health status and social history
Social history

Lab Workup
CBC, CMP, HIV, hepatitis A, B & C
Urine drug testing, and
consider pregnancy & STD screen

Referral
Refer to specialists as indicated
Refer to counseling
Refer to case management

Provide Patient Education
Treatment goals and medication education
Side-effects
How to store medication at home
Patient should update provider with new medications or other changes
Establish open communication

Discuss Safety Concerns
Altered tolerance to opioids on buprenorphine/suboxone
No co-administration of alcohol or benzodiazepines
Alert provider if planning pregnancy or pregnant
Planned procedures that may require opiate analgesia

DAY ONE (INDUCTION)

Last opioid use >6-12 hours ago → Moderate Withdrawal (COWS >12) → **Give First Dose of Buprenorphine/Naloxone (2 – 4mg)** → After 1 Hour: Monitor for precipitated withdrawal; If present, treat symptoms; Attempt induction 24 hours later

2 – 4 Hours Later

No → Give further 2 – 4mg dose → Withdrawal Symptoms Relieved? → Yes → Prescribe one dose; Return to clinic on day two for observation and review

2 – 4 Hours Later

No → Give further 2 – 4mg dose, up to 8mg total → Withdrawal Symptoms Relieved? → Yes → Prescribe one dose; Return to clinic on day two for observation and review

DAY TWO

No → Give day 1 dose and additional 2 – 4mg up to 16mg total → Adequate symptom relief achieved After induction? → Yes → Induction Complete - Give induction dose as ongoing dose, and review in 1 day

2 – 4 Hours Later

No → Give further 2 – 4mg dose, up to 16mg → Withdrawal Symptoms Relieved? → Yes → Induction Complete - Give induction dose as ongoing dose, and review in 1 day

MAINTENANCE

No → Consider further 2 – 4mg dose, up to 16mg → Patient Stable On Current Dose? → Yes → Continue once daily dosing with regular review

Perform monthly urinary drug screens, and check PDMP regularly. Ensure on-going attendance at counseling and support groups. When patient stable on medication, assess readiness for take-home dosing

- Waiver no longer required
- No limits on number of patients that a prescriber may treat for OUD with buprenorphine

Buprenorphine efficacy summary

Studies (RCT) show buprenorphine (**16-24 mg**) more effective than placebo and equally effective to moderate doses (80 mg) of methadone on primary outcomes of:

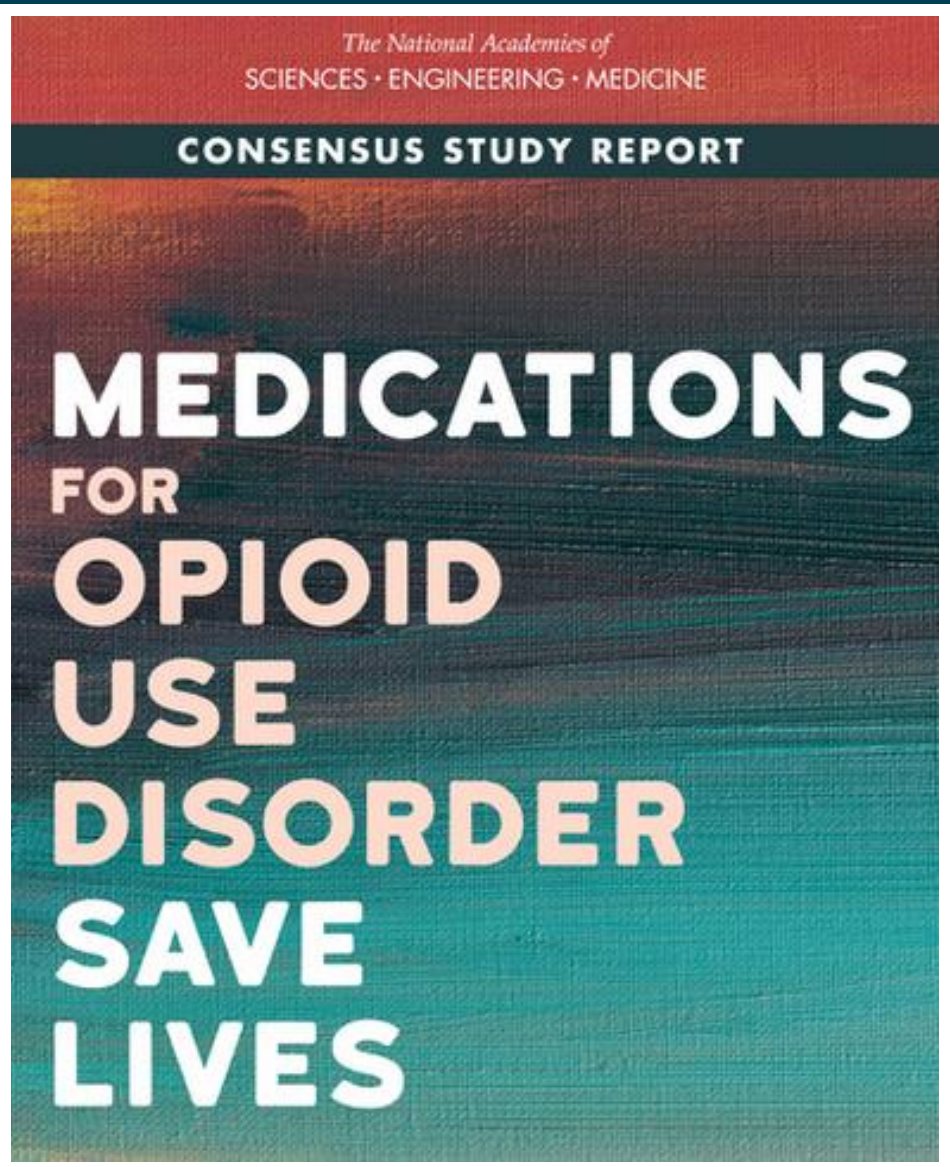
- Retention in treatment
- Abstinence from illicit opioid use
- Decreased opioid craving
- Decreased mortality
- Improved occupational stability
- Improved psychosocial outcomes

Johnson et al. *NEJM* 2000
Fudala PJ et al. *NEJM* 2003
Kakko J et al. *Lancet* 2003
Sordo L et al. *BMJ* 2017
Mattick RP et al. *Conchrane Syst Rev* 2014
Parran TV et al. *Drug Alcohol Depend* 2010

Buprenorphine limitations

- Access limited (but improving)
- Less structured than methadone maintenance – may not be a good fit for some patients
- Can cause precipitated withdrawal if given “too early” after use of a full opioid agonist
  - Low-dose initiations used more frequently today in order to mitigate this risk

Barriers to use of MOUD



- Delay between OUD onset and MOUD receipt 4-7 years
- Stigma toward individuals with OUD and the medications to treat it; perpetuated by some mutual support organizations
- Inadequate education of health professionals
- Black patients more affected by these factors than White patients - less than half the odds of initiating MOUD

National Academies of Sciences, Engineering, and Medicine. 2019. The National Academies Press.

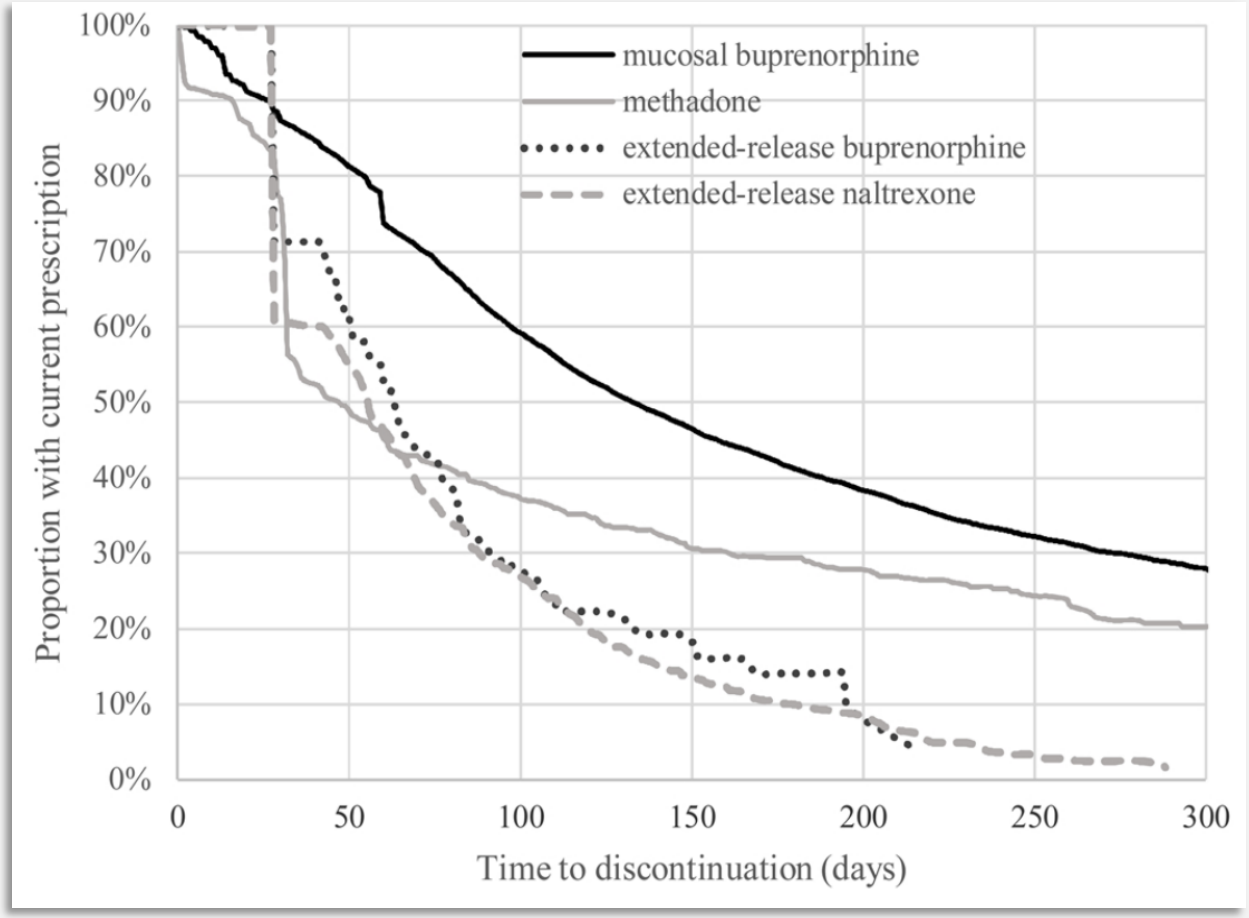
MOUD after opioid overdose

- Data from multiple Massachusetts administrative systems (2011-2015)
- Retrospective cohort of overdose survivors (N=17,568)
- For the **12 months after the index overdose only 17% received buprenorphine, 11% received methadone, and 6% received naltrexone**
- Compared with no MOUD, receipt of buprenorphine or methadone was associated with a **two-thirds reduction in death** (all-cause and opioid-related mortality)

Larochelle MR , et al. *Ann Intern Med*. 2018

Treatment retention with MOUD

- National data of commercially insured individuals
- 14,358 initiated MOUD
  - 85% SL buprenorphine
  - 8% XR naltrexone
  - 6% methadone
  - 1% XR buprenorphine
- **Treatment <u>discontinuation</u>** rates (3m)
  - 34% SL buprenorphine
  - 50% XR buprenorphine
  - 58% methadone
  - 65% XR naltrexone



Morgan JR, et al. *Drug Alcohol Depend*. 2021

Case continued

At your primary care visit

- You discuss the options of MOUD vs detox with your patient – he is amenable to starting methadone, and elects to walk in to connect with a local OTP

6 months later

- You see that he is admitted to the hospital with another injection-related abscess
- In his H&P, notes that he had trouble getting onto a methadone clinic due to long wait times; continued to use IV heroin/fentanyl
- The addiction consult team sees him & he elects to start buprenorphine inpatient

Hospital settings can provide "reachable moments" for starting MOUD wherever patients present

Inpatient Service

- Compared with detox, initiation of and linkage to buprenorphine treatment is effective for engaging hospitalized patients who are not seeking addiction treatment and reduces non-prescribed opioid use after hospitalization (Liebschutz JM et al. *JAMA Intern Med.* 2014)
- Receipt of inpatient MOUD resulted in significant reductions in LOS and readmission rates (O'Rourke BP et al. *Drug Alc Depend*. 2022)

Emergency Department

- ED-initiated buprenorphine vs brief intervention/referral significantly increased engagement in addiction treatment, and reduced self-reported non-prescribed opioid use (D'Onofrio G et al. *JAMA.* 2015)

Optimizing hospital-to-community transitions of care

- Systematic review on transitions in care from hospital to community for individuals with SUD
- 31 studies - 7 RCTs and 24 quasi-experimental designs - opioid use (n = 8), alcohol use (n = 5), or use of multiple substances (n = 18)
  - Interventions included pharmacotherapy initiation (n = 7), addiction consult services (n = 9), protocol implementation (n = 3), SBIRT (n = 2), patient navigation (n = 4), case management (n = 1), and recovery coaching (n = 3)
- Both pharmacologic and psychosocial interventions improved engagement in care and reduce hospital readmission and ED presentations

James H et al. *Drug Alc Depend* 2023

Bridge clinics: low-barrier access to MOUD

- Multiple models - outpatient hospital-based, EM-based, virtual
  - Historically provided buprenorphine, naltrexone, or other support for OUD
  - More recently, some non-OTP providers administer methadone for up to 72 hours while arranging OTP linkage (Taylor JL et al. *Drug Alc Depend*. 2022)
- Harm reduction services – overdose education, naloxone, safer injection and smoking materials, low barrier STI/hepatitis/HIV screening and treatment, PrEP/PEP, wound care, contraception, linkage to primary care
- Data on effectiveness in linking to long-term care are limited

Taylor JL, et al. *Addiction Science & Clinical Practice.* 2023 (narrative review)

Case continued

At your next primary care visit

- Reviewing the records, you see that your patient was discharged from the hospital on 8 mg SL buprenorphine BID
- He tells you he has been taking buprenorphine since discharge, with some IN fentanyl use, but significantly minimized
- Interested in discussing SQ buprenorphine in the coming months
- Appreciative for your help ☺

Thank you!