AETC AIDS Education & Training Center Program
Southeast Regional Conference 2023

HIV and substance use disorders: refresh and updates

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Disclosures

- *I have no disclosures.*

Learning Objectives

- *Refresh on medication for opioid use disorder and updates on DEA prescribing regulations.*
- *Update on opportunities for Addiction Medicine board certification.*
- *Update on novel substances in regional drug supply.*
- *Refresh on principals of harm reduction and what we can all do to reduce morbidity associated with IV drug use.*

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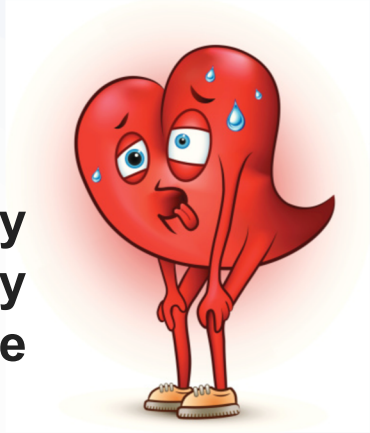
Destigmatizing substance use disorders

Addiction is a chronic brain disease that is preventable and treatable

Coronary artery disease



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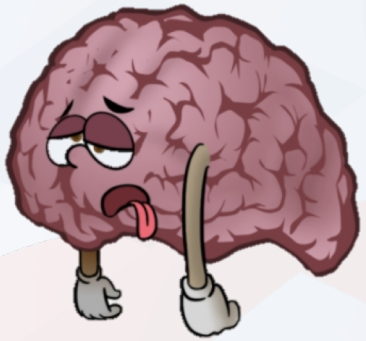


Substance use disorder

- **Prevention:** Routine assessment and early intervention when risk factors present
- **Treatment:** Medical therapies, management of co-occurring diseases, lifestyle modification, social support, and risk mitigation

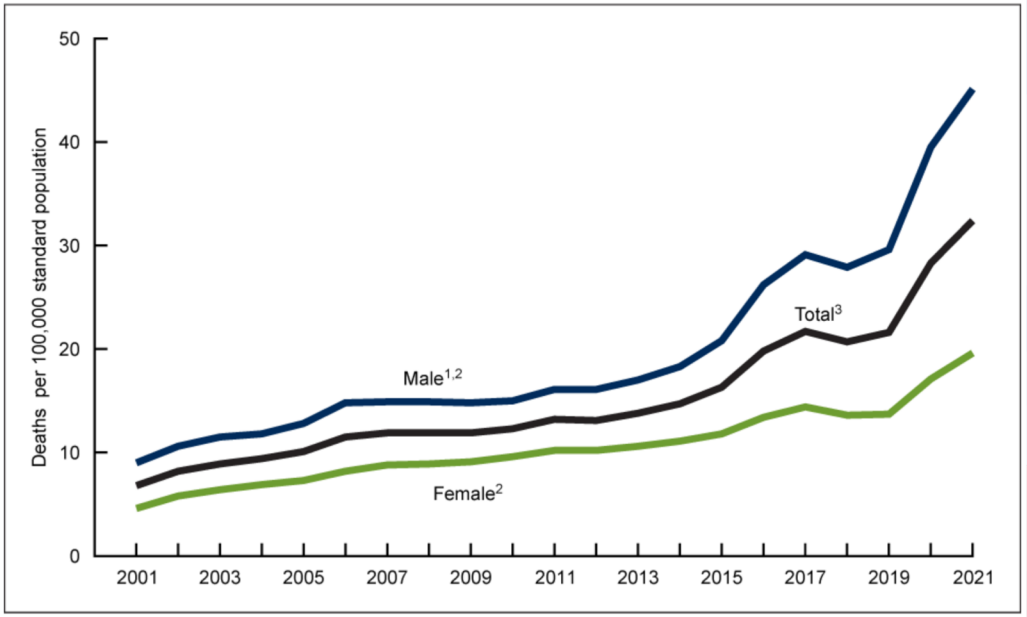
Destigmatizing substance use disorders

Language matters

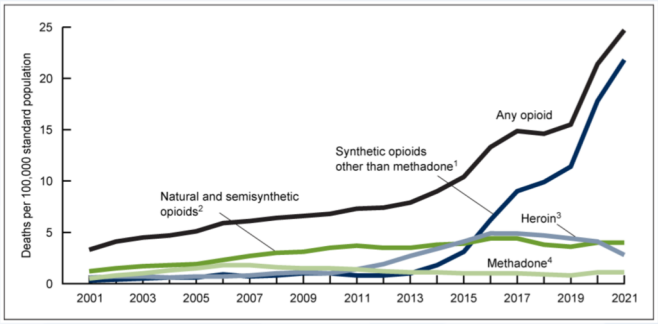
Commonly Used Term	Preferred Term	Rationale
Addict, abuser, etc.	Person with a substance use disorder	• Focuses on respect, dignity and primacy of personhood
Substance abuse	Substance use disorder	• Avoids implication of willful misconduct • Shift emphasis to chronic disease model
Opioid substitution therapy/replacement therapy	Opioid agonist therapy	• Avoids implication of "switching addiction" • Pharmacologic classification more in line with other medications (i.e., ACEi, SSRI)
Clean	Sober/abstinent	• Avoids value-laden, non-clinical terminology
Dirty or clean urine	Positive or negative urine drug screen	• Avoids value-laden, non-clinical terminology
Detox	Withdrawal management	• Chronic disease model demands shift from "one and done—you're fixed"

Brezing and Marcovitz, 2015. https://www.recoveryanswers.org/addiction-ary/

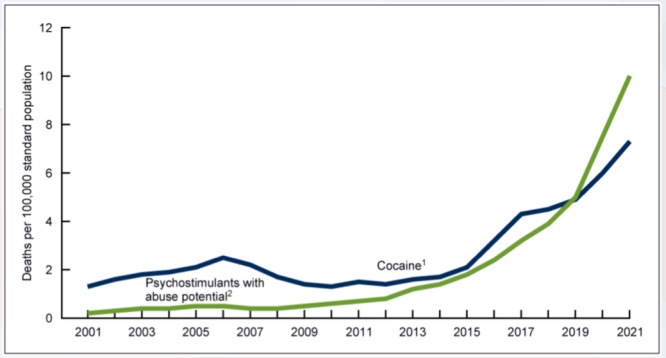
Overdose deaths : up!



Age-adjusted rate of drug overdose deaths, 2001-2021



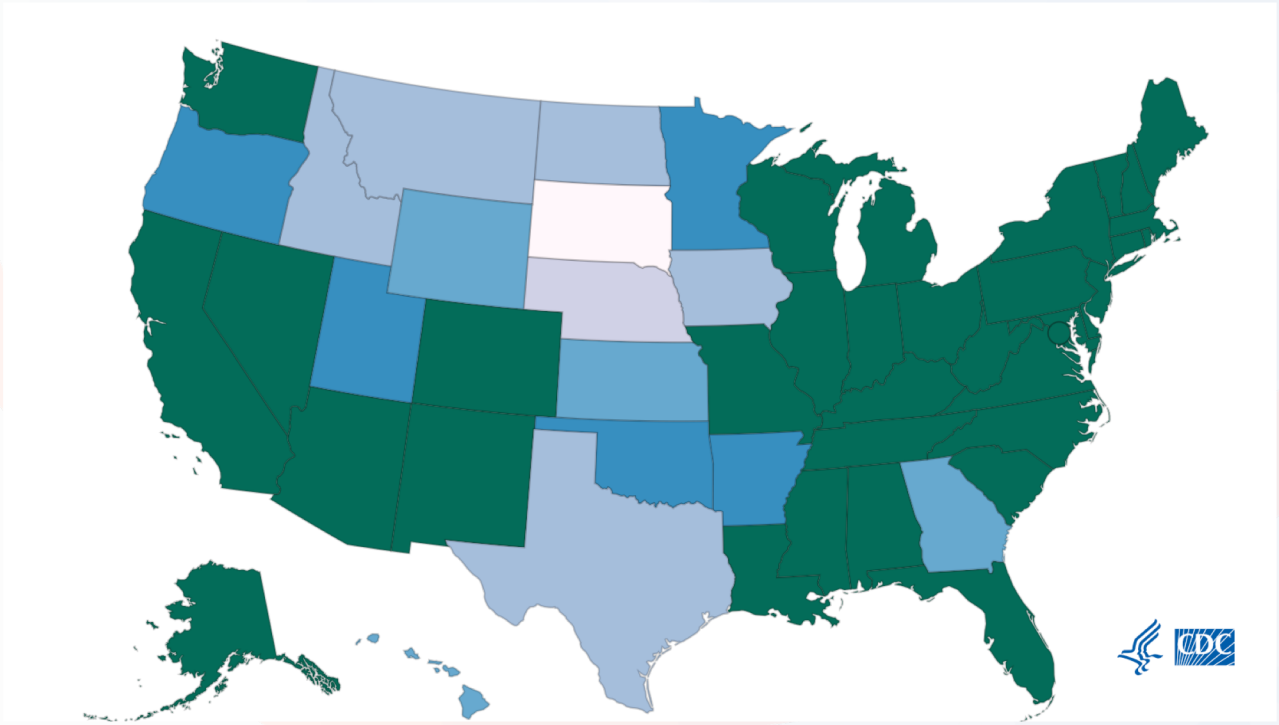
Age-adjusted rate of drug overdose deaths involving opioids, 2001-2021



Age-adjusted rate of drug overdose deaths involving stimulants, 2001-2021

CDC: https://www.cdc.gov/nchs/products/databriefs/db457.htm#:~:text=System%2C%20Mortality%20File.-,Summary,increased%20from%2017.1%20to%2019.6.

Overdose deaths : up! In the Southeast!



Age-adjusted rates of overdose deaths by state, US 2020

CDC: https://www.cdc.gov/drugoverdose/deaths/2020.html

Treatment for Opioid Use Disorder: MOUD

FDA approved medications for treatment of opioid use disorder

	Methadone	**Buprenorphine** (sublingual or subcutaneous)	**Naltrexone** (IM)
Mechanism of Action	Full agonist on opioid receptor	Partial agonist on the opioid receptor	Antagonist on opioid receptor
Dosing	80 mg – 100 mg (usual dose)	4 – 32 mg	380 mg depot injection
Advantages	• Provided in a highly structured supervised setting where additional services can be provided on-site and diversion is unlikely • May be effective for individuals who have not benefited sufficiently from partial agonists	• Improved safety due to partial agonism • Availability in office-based settings	• No addictive potential or diversion risk • Available in office-based settings • Option for individuals seeking to avoid any opioids

Treatment for Opioid Use Disorder: buprenorphine

Key properties of buprenorphine:

- Partial agonist at opioid receptor
  - Safety
- High affinity binding
  - Overdose protection; tricky to start
- Long-half life
  - Symptom stability; feasible administration

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Efficacy of buprenorphine:

- Blockade of short-acting opioids
- 8 mg required for withdrawal; 16 mg required for blockade
- Little change in tolerance over time
- Maintenance therapy outperformed even long tapers
- 50% reduced mortality, less overdose, increased retention, improved health and social functioning

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Shift from abstinence goal to "rehabilitation"
Considered first-line, alongside methadone

Buprenorphine: MAT and MATE

Consolidated Appropriations Act of 2023 (12/29/2022)

Included:

Mainstreaming Addiction Treatment (MAT) and Medication Access and Training Expansion (MATE) Acts

MAT Act:

- A DATA-Waiver registration is no longer required to treat patients with buprenorphine for opioid use disorder.
- Going forward, all prescriptions for buprenorphine only require a standard DEA registration number.
- There are no longer any limits or patient caps on the number of patients a prescriber may treat for opioid use disorder with buprenorphine.
- The Act does not impact existing state laws or regulations that may be applicable.

Medication Access and Training Expansion (MATE) Act

- Requires a one-time, eight-hour training requirement for all Drug Enforcement Administration (DEA)-registered practitioners on the treatment and management of patients with opioid or other substance use disorders.

Medication access and training expansion (MATE) act

- **Required of all DEA-licensed providers are the time of new license application or renewal**
- **Regardless of whether provider plans to prescribe buprenorphine or other opioids**
- **Deadline: time of license renewal starting in 6/27/2023**
- **Training does not have to take place in one setting**

- Past trainings on the treatment and management of patients with opioid or other substance use disorders can count towards a practitioner meeting this requirement.
- Past DATA-Waiver trainings count towards a DEA registrant's 8-hour training requirement.
- Trainings can occur in a variety of formats, including classroom settings, seminars at professional society meetings, or virtual offerings.

Buprenorphine formulations

Brand Name/ Formulation	Administration	Advantages	Disadvantages	Comments
Subutex Buprenorphine monotherapy	Sublingual daily or split dosing	• Easy, patient-directed administration	• Higher misuse and diversion potential	• Currently recommended formulation for pregnant patients
Suboxone Buprenorphine/ naloxone	Sublingual daily or split dosing	• Easy, patient-directed administration • Lower misuse and diversion potential		• Recommended for treatment of OUD
Sublocade Long-acting SQ injection	Subcutaneous injection to abdomen every 26-28 days	• No diversion potential • Gradual taper minimizes withdrawal symptoms	• Expensive • Pain at injection site • ”Lump” persists for duration of depot	• Not used for pain management

Starting buprenorphine: Precipitated Withdrawal

Buprenorphine is a *high-affinity*, *partial agonist* at the opioid receptor.

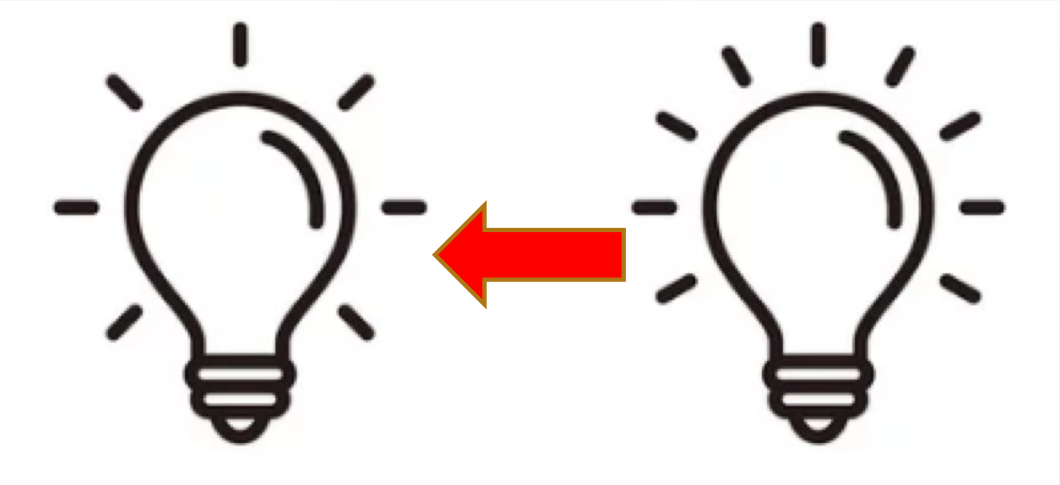
Buprenorphine: partial agonist
- Low risk for overdose*

Full agonist opioids
- High risk for overdose

Starting buprenorphine: Precipitated Withdrawal

Buprenorphine is a *high-affinity*, *partial agonist* at the opioid receptor.

Precipitated withdrawal: Buprenorphine will displace full agonist opioids and rapidly "dim the lightbulb"– felt by the patient as abrupt, often severe withdrawal symptoms.



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Full agonist opioids
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Starting buprenorphine: avoid precipitated withdrawal

1) Patient abstains from full agonist opioid use with target COWS > 12 (may need higher score for fentanyl)

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2) Start test dose of buprenorphine (≤2 mg) and titrate to target dose (typically 12-16 mg TDD)

Buprenorphine formulations: sublingual

- Taking suboxone:
  - Sublingual application preferred (buccal administration also works). Do not swallow, chew, or take with water.
  - Avoid smoking and acidic beverages (coffee, juice, soda) prior to administration.
  - Wet mouth with water prior to administration.
  - May take 15-20 minutes to fully dissolve. Films dissolve faster than tablets.
  - Advise patients to avoid sipping water while dose is dissolving.

Sublocade

1 | SUBLOCADE Administration[1]

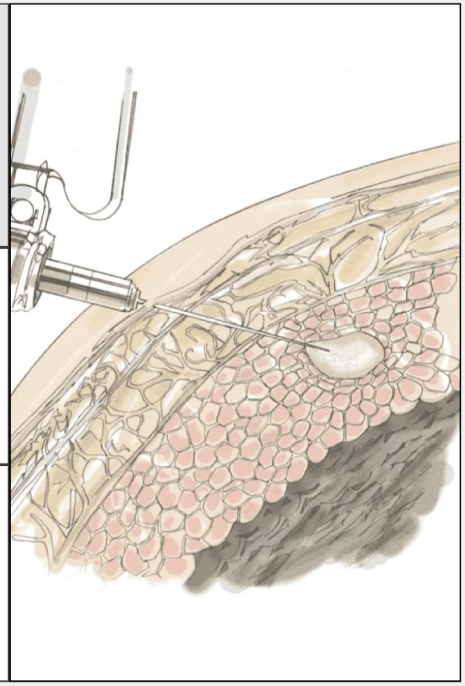
SUBLOCADE is administered as an injection into the abdominal subcutaneous tissue (total volume: 0.5 mL for 100 mg and 1.5 mL for 300 mg)

2 | Depot Formation[1]

SUBLOCADE is injected as a liquid, and upon contact with body fluids, the ATRIGEL® delivery system forms a solid depot containing buprenorphine

3 | Continuous Release[1]

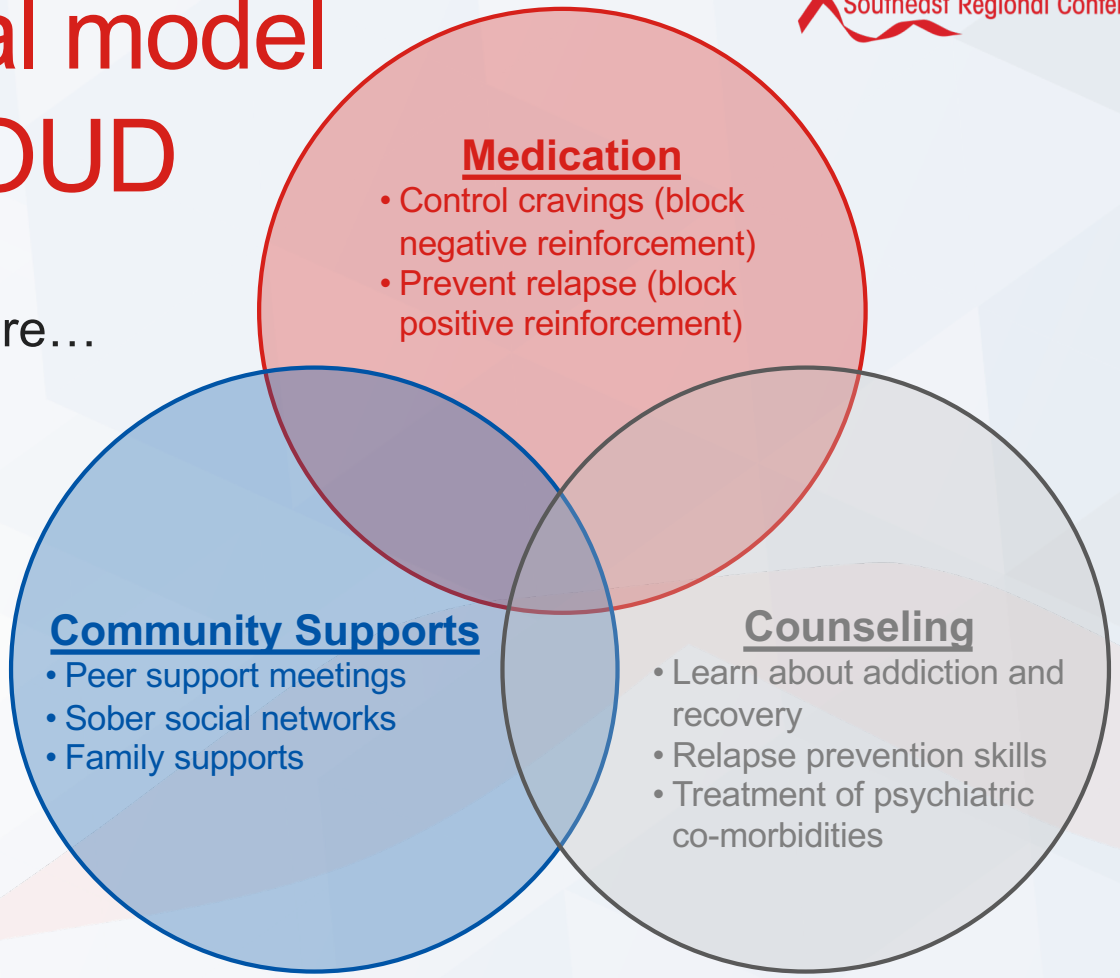
After initial formation of the depot, buprenorphine is released via diffusion from, and the biodegradation of, the depot



https://www.sublocadehcp.com/dosing-administration
https://www.anthc.org/wp-content/uploads/2022/02/Didactic_Injectable-buprenorphine_2.10.22.pdf

Bio-psycho-social model for treatment of OUD

MOUD is just part of the picture…



Stimulant use disorders: MAT

agent	dose range	outcome	population	studies	notes
D-amphetamine; MAS-ER*	up to 60 mg/day; up to 80 mg/day	~12 wks; better retention, less cocaine-pos urine vs PBO	median n = 33; CUD, with some comorbidities (ADHD, OUD)	6 from 2001 to 2016; summary in Brandt et al. Addiction 2021	corroborated by recent meta-analysis, Tardelli et al. 2020
modafinil	up to 400 mg/day	8-12 wks; only for non-AUD (3-wk abst, less cocaine-pos urine)	median n = 59; CUD	5 from 2009 to 2015; summary in Brandt et al. (id)	poor adherence; one study showed discordant effects in men and women
bupropion-naltrexone	450 mg/day ER + 380 mg ER q3wks	12 wks; 13.6% had "response" (3 neg meth-pos urines out of 4)	n = 403 (stage 1); n = 225 (stage 2)	Trivedi et al. NEJM 2021	very high retention, unclear PO adherence
mirtazapine	up to 30 mg/day	36 wks; RR ~0.7 for meth-pos urine at 12+ wks follow-up	n = 120; MUD in MSM and TGW	Coffin et al. JAMA Psych 2020	finding despite ~25% adherence; less risky sexual behavior, better sleep/dep
topiramate*	200-300 mg/day (over 8 wks)	~12 wks; more abst and less cocaine-pos urine	median n = 58; CUD often with AUD/OUD	5 from 2004-2014; summary in Brandt et al. (id)	low adherence in later trials
doxazosin	8 mg/day (over 4 wks)	12 wks; 35% reduction in cocaine-pos urine vs PBO	n = 76, CUD with ADRa1d AT and DbH TT phenotypes; n = 35, CUD	Shorter et al. AJDAA 2020; Shorter et al. DAD 2013	promising pharmacogenetics
disulfiram	250 mg/day	~12 wks; meta-analysis with worse retention; less reported use	median n = 58; CUD often with OUD	4 from 2004 to 2014; summary in Brandt et al.	may be affected by low DbH phenotype; possible sex-based discordant responses

Brandt et al., Addiction, 2021; ASAM Principles of Addiction Medicine, 6th Ed, 2019.

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Need: increased number of providers trained in Addiction Medicine

Most Doctors Are Ill-Equipped to Deal With the Opioid Epidemic. Few Medical Schools Teach Addiction.

PUBLIC HEALTH

Aspiring Doctors Seek Advanced Training In Addiction Medicine

npr

21 million Americans suffer from addiction. Just 3,000 physicians are specially trained to treat them.

Susan Scutti, Special to AAMCNews

December 18, 2019

AAMC

https://www.nytimes.com/2018/09/10/health/addiction-medical-schools-treatment.html

Options for Addiction Medicine certification

- Complete a fellowship
- Practice Pathway: available through 2025

Addiction Medicine

General Requirements

- **Medical License** – An unrestricted and currently valid license(s) to practice medicine in a State, the District of Columbia, a Territory, Commonwealth, or possession of the United States or in a Province of Canada is required. If the applicant has licenses in multiple states, no license may be restricted, revoked, or suspended or currently under such notice.
- **Medical Degree** – Graduation from a medical school in the United States which at the time of the applicant's graduation was accredited by the Liaison Committee on Medical Education, a school of osteopathic medicine approved by the American Osteopathic Association, an accredited medical school in Canada, or from a medical school located outside the United States and Canada that is deemed satisfactory to the Board is required.
- **ABMS Member Board Certification** – Primary board certification is a core requirement. The Practice Pathway requires current ABMS member board certification. The ACGME-Accredited Fellowship pathway offers limited exceptions to the ABMS member board requirement. Please review the board certification requirements for each pathway.

American Board of Preventive Medicine

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AM I ELIGIBLE?

Addiction Medicine

Question:

Have you completed two years and 1920 hours of Addiction Medicine practice within the last five years?

Practice hours must include a minimum of 25% (or 480 hours) of direct patient care in Addiction Medicine. Practice must consist of broad-based professional activity with significant responsibility in the subspecialty. Practice time need not be continuous, however, all practice time must have occurred in the five-year period preceding June 30 of the application year.

Yes

No

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Practice Activity ?	1920 hours (must span at least 24 months of the past 60 months). Documentation of Addiction Medicine teaching, research and administration activities as well as clinical care or prevention of, or treatment of, individuals who are at risk for or have a substance use disorder may be considered.

Direct Patient Care Activity	A minimum of 25% (or 480 hours) of practice must be in direct patient care. Practice outside of direct patient care, such as teaching, research, and administration activities may count for a combined maximum of 75% (or 1440 hours).
General Practice Activity Limit	Only 480 hours (25% of practice activity) can count towards the practice activity requirement.

*by June 30 of year of application.

Application requirements

- CV
- Board certification verification
- Practice and training verification
- Fellowship verification (if using credit from a fellowship)
- One letter of reference

Direct Patient Care Practice Activity Menu

Type of Activity	Practice Activity information
Addiction Counseling: Individual, Group and Family	Provide a detailed description of the type of counseling and/or behavioral therapies offered by you in your practice. May Include the number of patients treated through individual, group or family counseling per week in your practice.
Assessment/Diagnosis of Addiction and Substance-related Disorders	Provide a detailed description of how you assess/diagnosis Addiction and Substance-related disorders in your practice activities, including the assessment tools or skills used. Your description may include an explanation of the treatments and or therapies that may be offered. Include the average number of patients assessed or diagnosed you may assess/diagnose per week.
Assessment/Diagnosis of Intoxication	Describe methods or tools you use in your practice to assess and diagnose intoxication. Include any assessment protocols or tools used. Include the average number of patients are assessed or treated per week in your practice.
Assessment/Diagnosis of Withdrawal	Provide a detailed description of you assess or diagnoses a patient in withdrawal. Descriptions may include the number of patients treated per week and any ongoing care provided.
Assessment/Management of Dual Diagnosis	Describe the assessment and/or treatment methods used in your practice. The average number of patients assessed/managed with dual diagnosis may be included.
Brief Intervention	Describe your practice activities in which you engage patients showing risking substance use behaviors. Provide the average number of patients that your practice may engage in a brief intervention.
Management of Mild to Moderate Withdrawal	Provide a detailed description of your management of patients in mild to moderate withdrawal, including any assessment protocols used. Descriptions may include the type of treatments and/or therapies offered, including the average number of patients managed per week.
Management of Mild to Moderate Intoxication	Provide a detailed description of your management of patients with mild to moderate intoxication. Explain the assessment tools or skills used in your practice. Descriptions may include the type of treatments and/or therapies offered, including the average number of patients managed per week.
Management of Psychiatric Complications	Describe the treatments and therapies used to treat patients experiencing psychiatric complications related to addiction and other substance-related disorders. The number of patients on average per week may be included.

Direct Patient Care Practice Activity Menu continued

Type of Activity	Practice Activity information
Management of Severe or Complex Intoxication	Provide a detailed description of how you manage patients during a severe or complex intoxication. Include assessment and diagnostic activities and the average number of patients presenting per week.
Management of Severe or Complex Withdrawal	Describe how you manage patients during a severe or complex withdrawal. Include assessment and/or protocols used. A description of the treatments and therapies offered and the average number of patients treated per week may be included.
Medication Management of Addiction	Provide a detailed description of the type of counseling and/or behavioral therapies offered. This includes providing detail about prescribing buprenorphine to patients and whether the applicant provides separate subspecialty-level addiction treatment for addiction (for example, detoxing patients from alcohol as well as opioids, or treating addiction in patients who do not use opioids).
Prevention Services	Describe the evidence-informed interventions used in your practice to prevent the unhealthy use of alcohol, tobacco, nicotine and other substances.
Referral	Describe in detail how you evaluate a patient to determine if a referral is made? On average how many patients do you refer for additional treatment or therapies per week?
Screening	Provide a detailed description of the screening tools you use in your practice to identify patients with risky substance use behaviors. Describe the average number of patients that are included in the screening process per week.
Screening/Referral for Dual Diagnosis	Please describe the screening methods and the referrals used by you in your practice to screen and refer patients with a dual diagnosis. Include the average number of patients screened or referred for a dual diagnosis per week.
Other	The activity type of "Other" is often used by Physicians to describe a General Practice. This type of hour classification may count towards the General practice maximum limit of 480 hours. Other may also be used to cover Addiction Medicine activities that are not reflected in the dropdown menu.

Research, Training, Administration

Practice Activity Menu

Type of Activity	Practice Activity information
Research, Administrative or Training responsibilities within Medical and Professional Organizations	Acceptable examples include American Society of Addiction Medicine, American College of Academic Addition Medicine, AMA, AOA, Advanced Studies in Medicine, American Psychiatric Association, etc., or state and local medical societies.
Volunteer activities that include Administration, Research or Administrative duties.	Participation in uncompensated activities of social significance, such as volunteer work at community health agencies, volunteer services on a board of directors for a healthcare agency, or volunteer work with schools, Planned Parenthood, Boy Scouts, etc.
Clinical Contributions	Clinical contributions such as developing a unique model for addiction treatment or advancing the knowledge base of addiction medicine.
Political or Legislative Involvement	Political or legislative involvement, grassroots or other lobbying, holding elected or appointed public office, serving as a committee member in the political process to further the goals of addiction medicine or ASAM, and/ or testifying before local, state, or federal legislative bodies to further the goals of addiction medicine.
Administrative Appointments	Administrative appointments such as a position of authority within a hospital, hospital committee, or substance abuse treatment program; boards of substance abuse treatment programs; and federal or state departments of alcoholism and/or drug abuse
Published Work	Published writings in peer-reviewed journals and/or books, or chapters of books, written for the education of professionals.
Teaching or Educational Contributions	Teaching contributions, such as appointment to medical school faculty in substance abuse teaching, volunteer teaching of alcoholism and drug abuse information to patients in publicly funded treatment or education programs, or presentations of formal lectures in the substance abuse field to physicians and/or healthcare providers in the addiction field, on a consistent basis
Screening/Referral for Dual Diagnosis	Please describe the screening methods and the referrals used by you in your practice to screen and refer patients with a dual diagnosis. Include the average number of patients screened or referred for a dual diagnosis per week.

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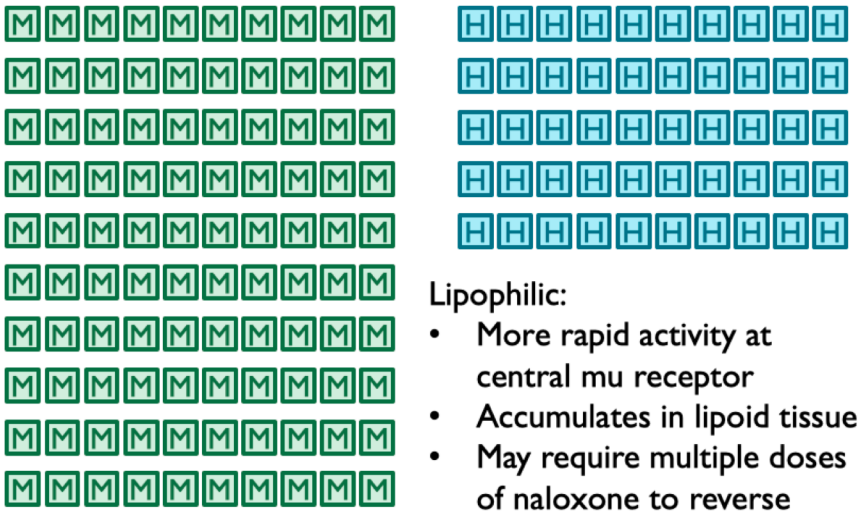
High potency synthetic opioids (HPSO)

Fentanyl F
100X more potent than morphine M
50X more potent than heroin H



Lipophilic:

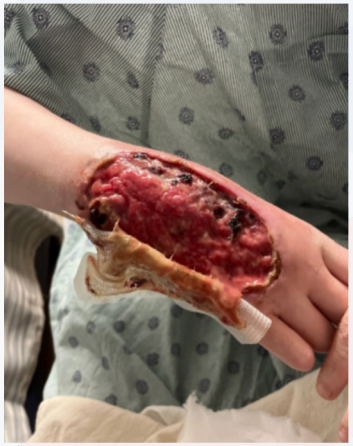
- More rapid activity at central mu receptor
- Accumulates in lipoid tissue
- May require multiple doses of naloxone to reverse
- May complicated buprenorphine induction

Carfentanyl C
100X more potent than fentanyl F

- Developed for use in veterinary medicine (anesthetic for large animals)
- Not included in standard epidemiology reports such as SAMHSA's National Survey on Drug Use and Health

Emerging threat: xylazine

- Non-narcotic pharmaceutical intended for veterinarian use
- Street name: Tranq
- Chemically resembles phenothiazines, tricyclic antidepressants, and clonidine
- Potentiates euphoric effects of opioids
- Causes central nervous system depression
- NOT reversed by naloxone (no known antidote)
- Associated with severe skin/soft tissue necrosis
  - Potentially mediated by vasoconstriction



(U) Figure 1. DEA Forensic Laboratory Identifications of Xylazine by Region

Region	2020	2021	Percent Increase
Northeast	346	556	61%
South	198	580	193%
Midwest	110	118	7%
West	77	163	112%

Source: DEA

(U) Figure 2. Number of Xylazine-Positive Overdose Deaths by Region

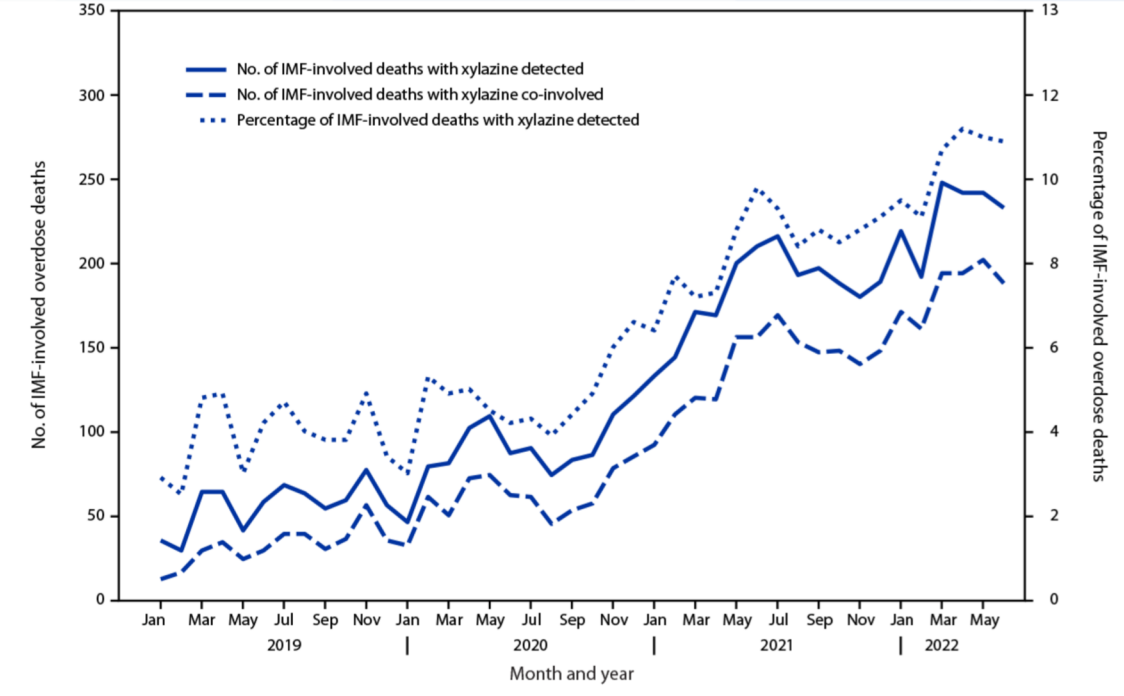
Region	2020	2021	Percent Increase
Northeast	631	1,281	103%
South	116	1,423	1,127%
Midwest	57	351	516%
West	4	34	750%

Source: DEA

Source: DEA (https://www.dea.gov/sites/default/files/2022-12/The%20Growing%20Threat%20of%20Xylazine%20and%20its%20Mixture%20with%20Illicit%20Drugs.pdf)
Photo: American Academy of Dermatology (https://www.aad.org/dw/dw-insights-and-inquiries/archive/2022/xylazine-potential-for-loss-of-life-and-limb)

HPSO and xylazine

Number/percentage of overdose deaths involving IMF and xylazine



Xylazine associated skin injury
(NEJM, Gupta et al. 2023)

CDC;
https://www.cdc.gov/mmwr/volumes/72/wr/mm7226a4.htm#:~:text=In%202022%2C%20provisional%20data%20indicated,(IMFs)%20(1).

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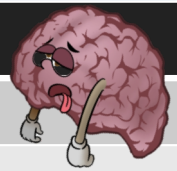
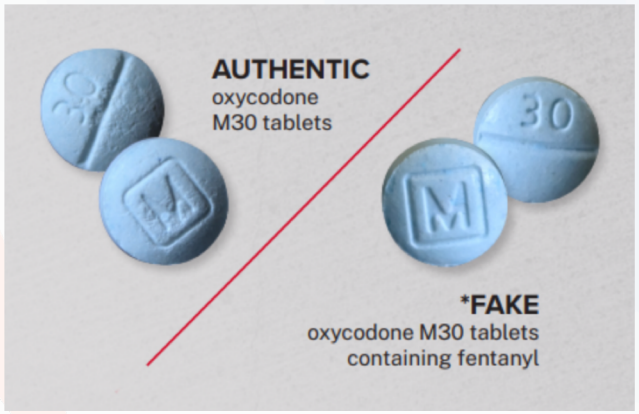
Harm reduction: patient education

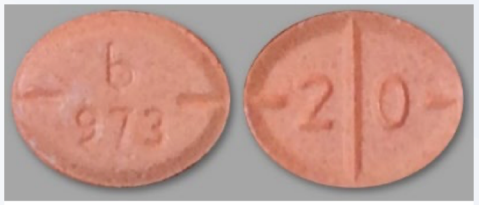
Harm Reduction: practical strategies and steps to reduce negative disease outcomes

Coronary Artery Disease	Substance Use Disorder
Decrease tobacco use	Overdose education and prevention
Diet and exercise	Naloxone prescription
Treat hypertension, diabetes, hyperlipidemia	Never use alone
Maybe low-dose aspirin	Safe injection education
Pacemaker or defibrillator placement in advanced disease	Syringe exchange resources
	Testing for HIV and viral hepatitis
	PrEP/vaccination for HAV/HBV



Harm reduction: patient education





Authentic Adderall

Counterfeit Adderall Containing methamphetamine

Left: Authentic Xanax
Right: Counterfeit Xanax containing fentanyl

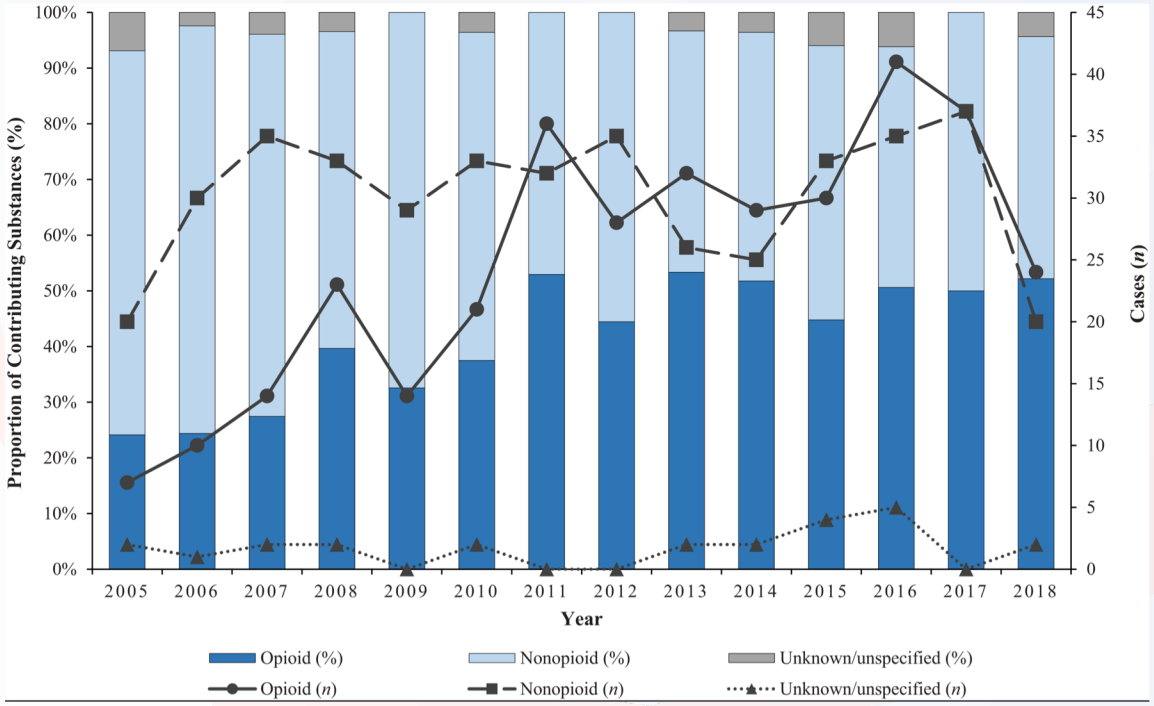
DEA.gov

- 60% of fentanyl-laced counterfeit pills now contain a potentially lethal dose of fentanyl (2 mg; 2022 data)

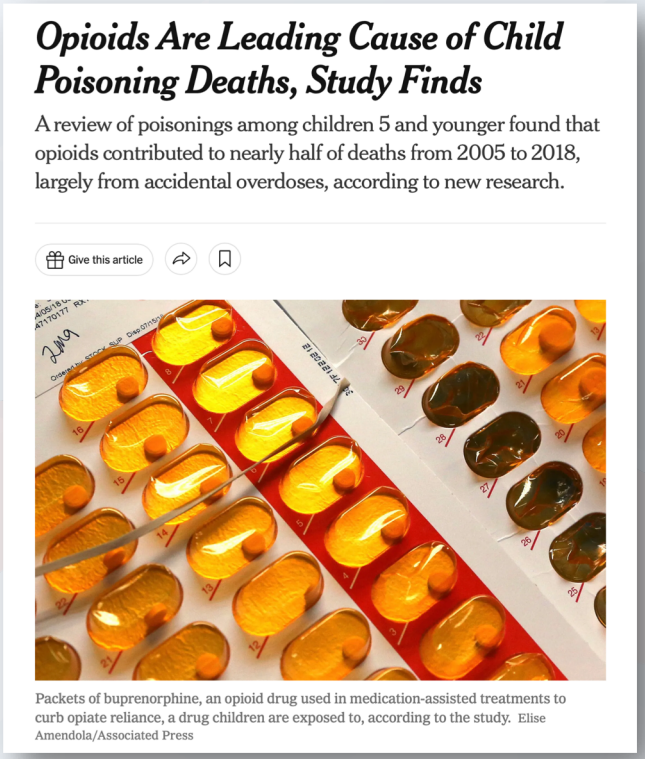
Important note

- Fentanyl is not detected on routine UDS
- Must send-out for GC/MS testing to assess for fentanyl and metabolites

Harm reduction: patient education



Gaw *et al*., Pediatrics 151(4); 2023.



Opioids Are Leading Cause of Child Poisoning Deaths, Study Finds

A review of poisonings among children 5 and younger found that opioids contributed to nearly half of deaths from 2005 to 2018, largely from accidental overdoses, according to new research.

Give this article

Packets of buprenorphine, an opioid drug used in medication-assisted treatments to curb opiate reliance, a drug children are exposed to, according to the study. Elise Amendola/Associated Press

Harm reduction: prescribe Naloxone

Per CDC:

- People who are taking high-dose opioid medications (greater or equal to 50 morphine milligram equivalents per day) prescribed by a doctor,
- People who use opioids and benzodiazepines together,
- People who use illicit opioids like heroin

Consider also:

- Prescription for any person with opioids in the house that might be accessed by another individual (including children).

Patient education for overdose:

Signs of overdose

Recognizing the signs of opioid overdose can save a life. Here are some things to look for:

- Small, constricted "pinpoint pupils"
- Falling asleep or losing consciousness
- Slow, weak, or no breathing
- Choking or gurgling sounds
- Limp body
- Cold and/or clammy skin
- Discolored skin (especially in lips and nails)

Action steps for overdose:

- Call 911 immediately
- Administer naloxone and perform CPR
- Try to keep person awake and breathing
- Lay person on their side
- Stay with the person until EMS arrives

Ensure that family/household contacts know how to administer naloxone

Patient education: never use alone

Harm reduction: good Samaritan law

- Grants civil immunity for administering naloxone to someone they reasonably believe is overdosing on an opioid
- Any person who in good faith seeks medical assistance for a person experiencing or believed to be experiencing a drug overdose shall not be arrested, charged, or prosecuted for a drug violation if the evidence of the arrest, charge, or prosecution of the drug violation resulted from seeking such medical assistance.
- Similar statement protecting persons experiencing overdose.
- No longer limited to an individual's first overdose.

Thank you to the SE AETC and YOU!

Katie D. White, MD, PhD
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