Department of
Mental Health &
Substance Abuse Services

Emerging Drug Trends

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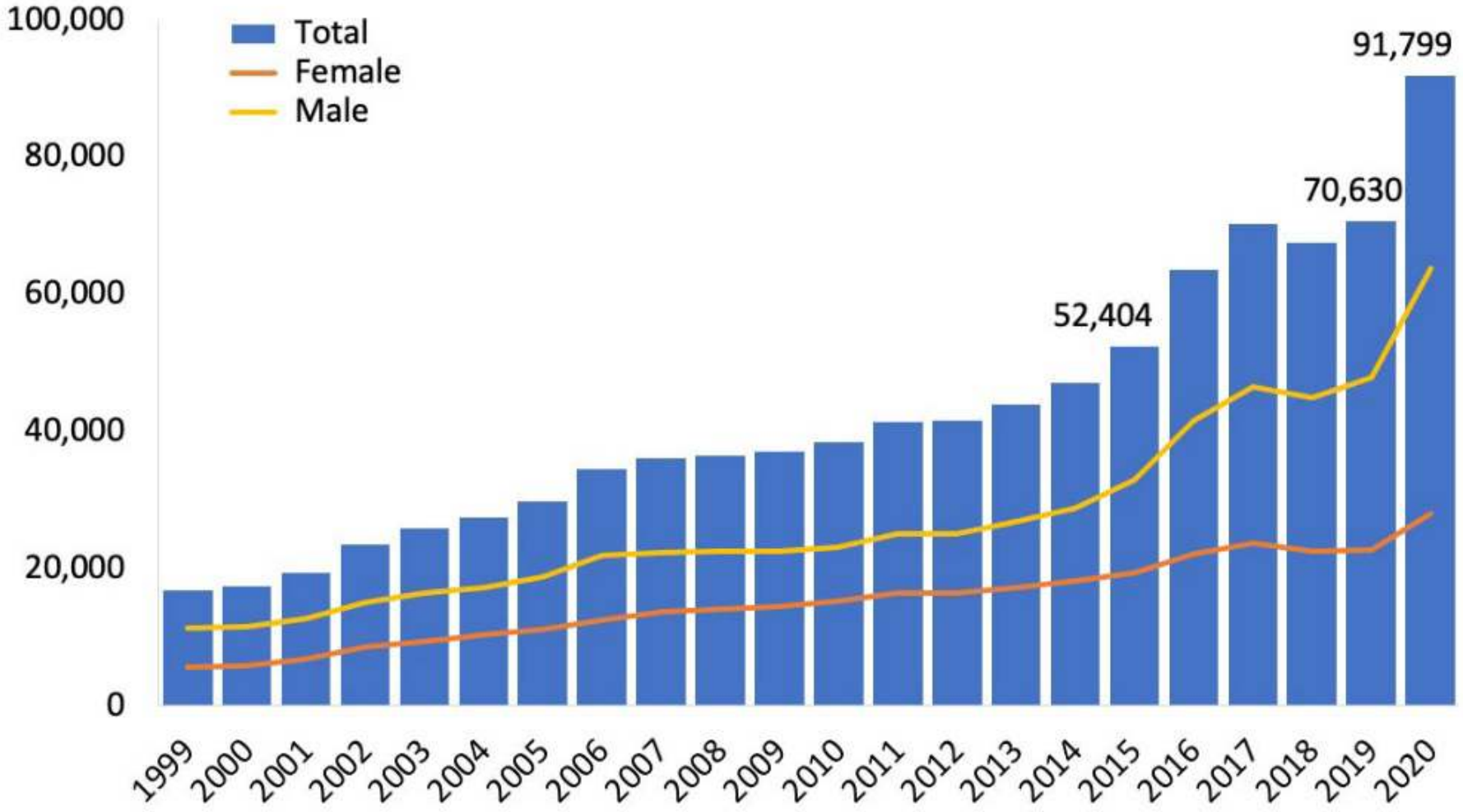
Learning Objectives

By the end of the presentation, the attendee will:

- Evaluate the trends of drug-related overdoses
- Understand the biopsychosocial mechanisms associated with addiction
- Be aware of the key findings from the National Academy's review of medications for opioid use disorder
- Compare and contrast the mechanisms of the different medications approved for opioid use disorder
- Understand the regulatory requirements for each of the medications approved for opioid use disorder

Current Trends: National

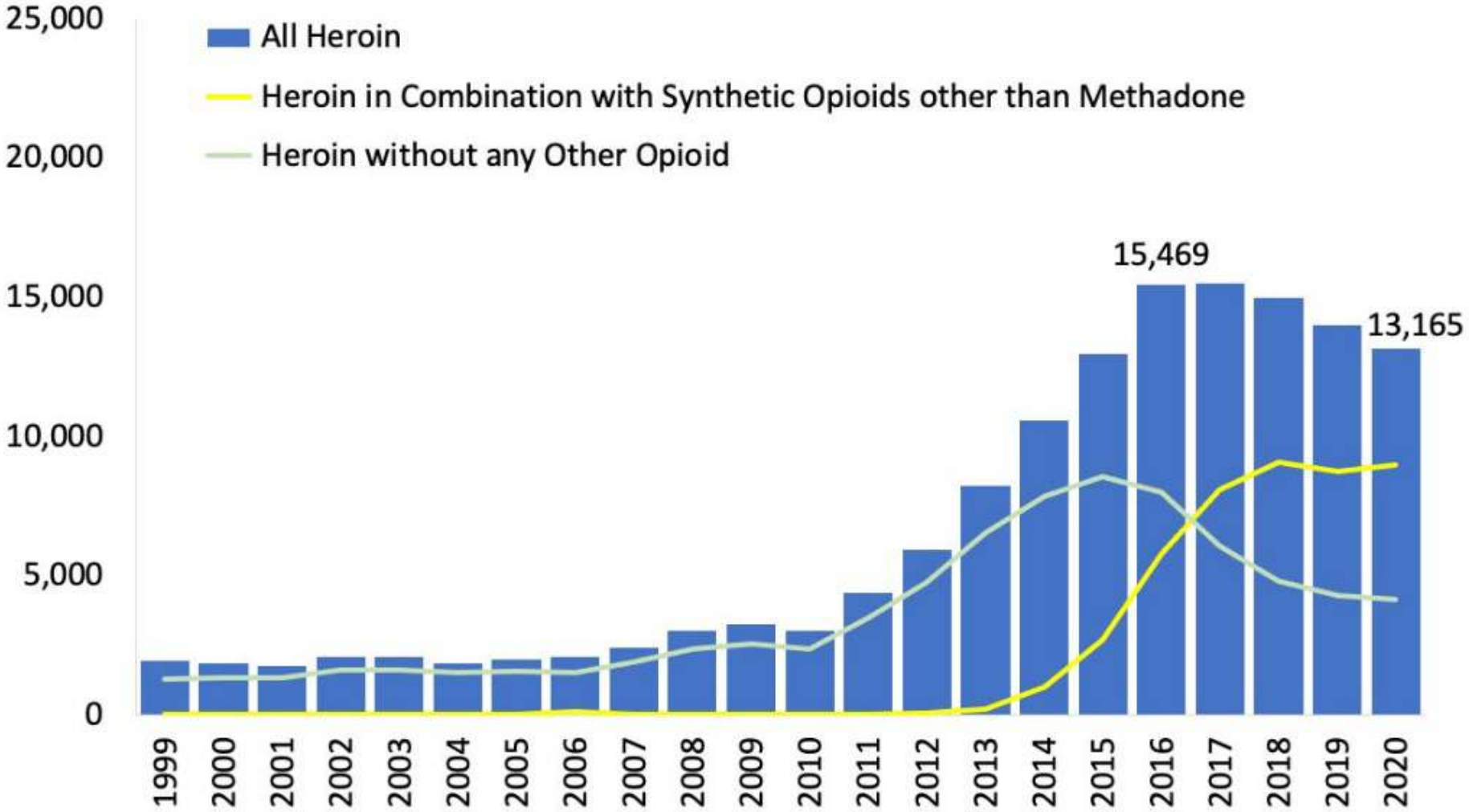
Figure 1. National Drug-Involved Overdose Deaths*
Number Among All Ages, by Gender, 1999-2020



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision.
Source: 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.

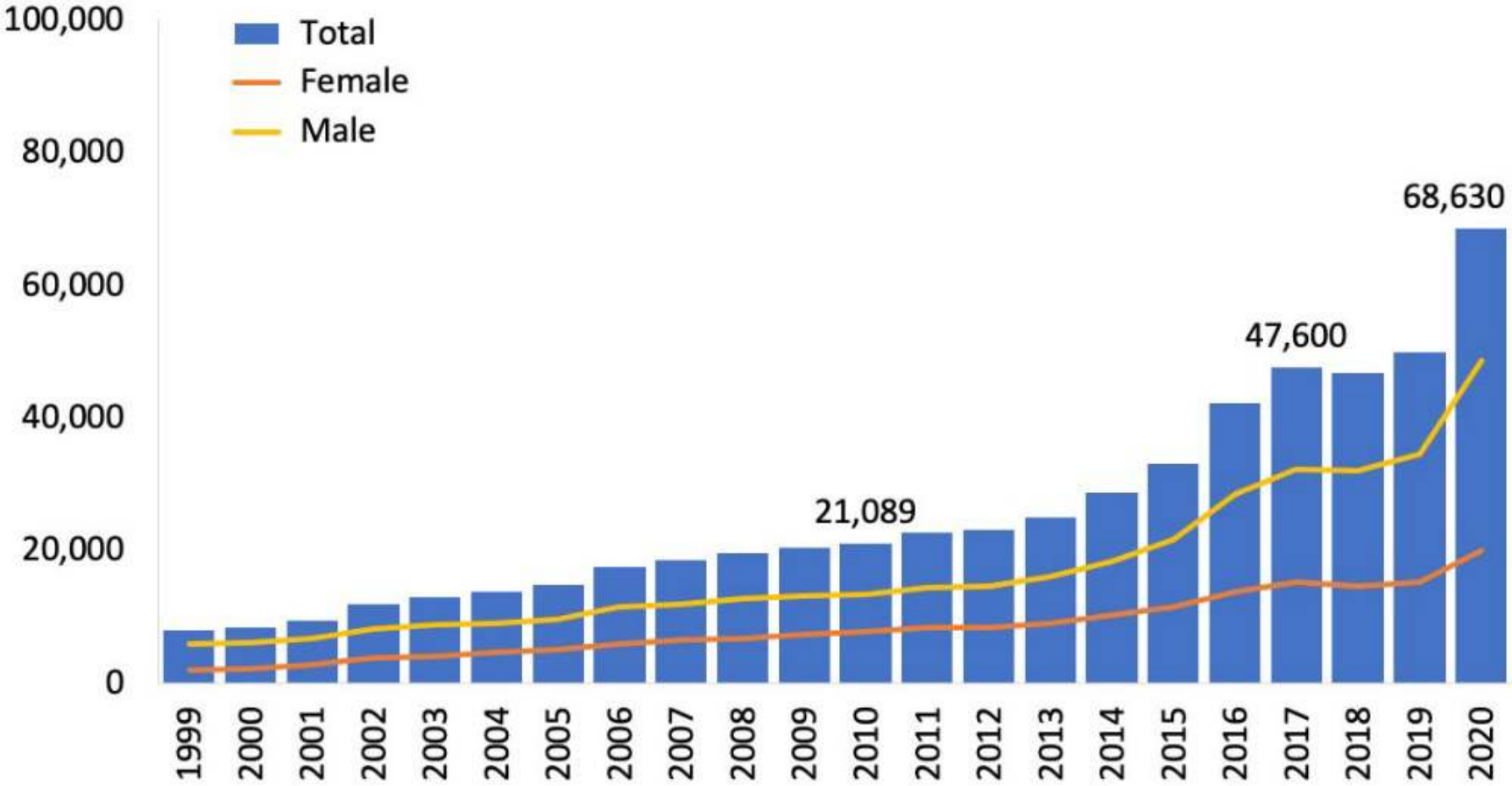
Figure 5. National Overdose Deaths Involving Heroin*, by other Opioid Involvement

Number Among All Ages, 1999-2020



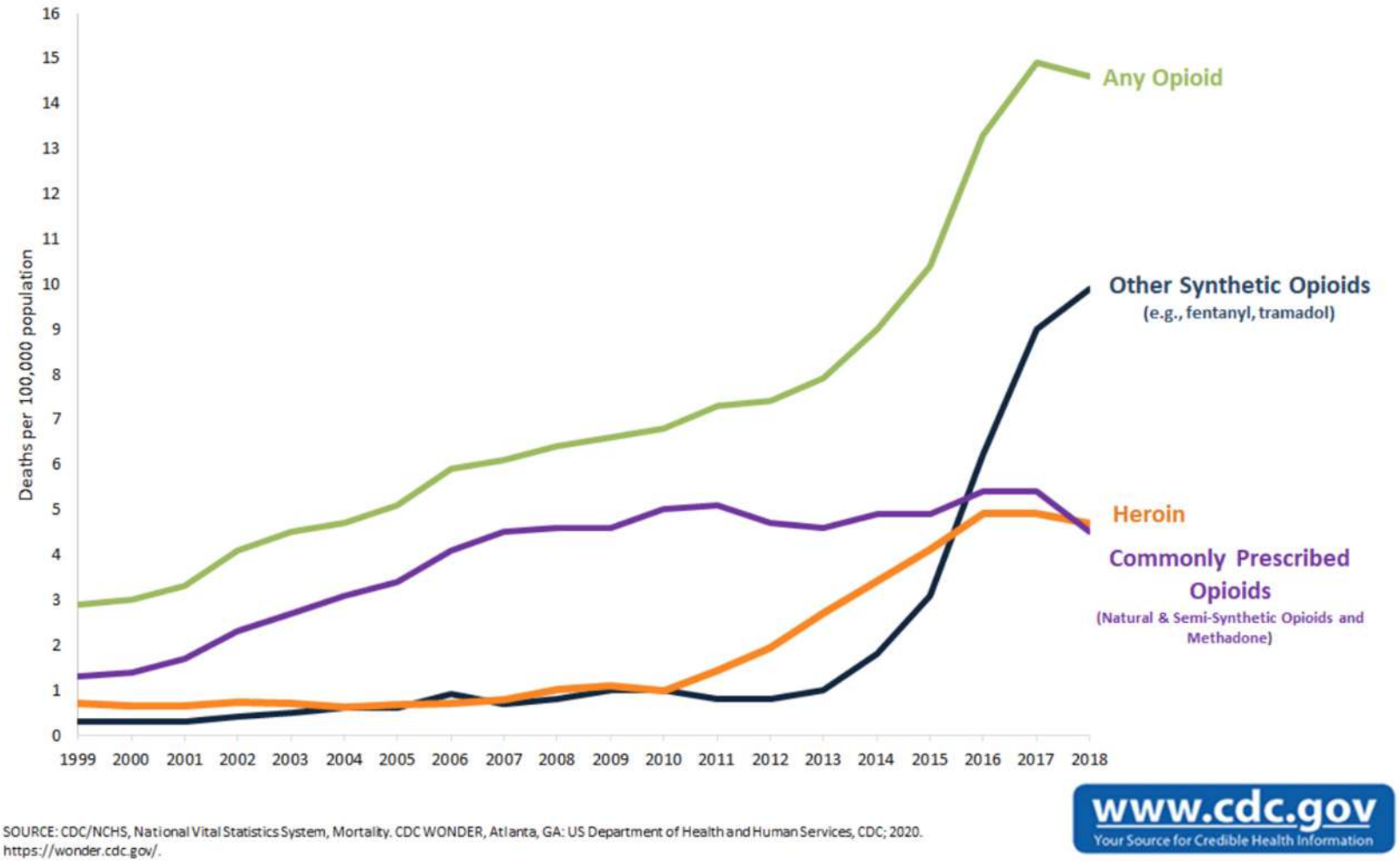
*Among deaths with drug overdose as the underlying cause, the heroin category was determined by the T40.1 ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

Figure 3. National Overdose Deaths Involving Any Opioid, Number Among All Ages, by Gender, 1999-2020



*Among deaths with drug overdose as the underlying cause, the any opioid subcategory was determined by the following ICD-10 multiple cause-of-death codes: natural and semi-synthetic opioids (T40.2), methadone (T40.3), other synthetic opioids (other than methadone) (T40.4), or heroin (T40.1). Source: 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.

National Opioid Overdose Statistics



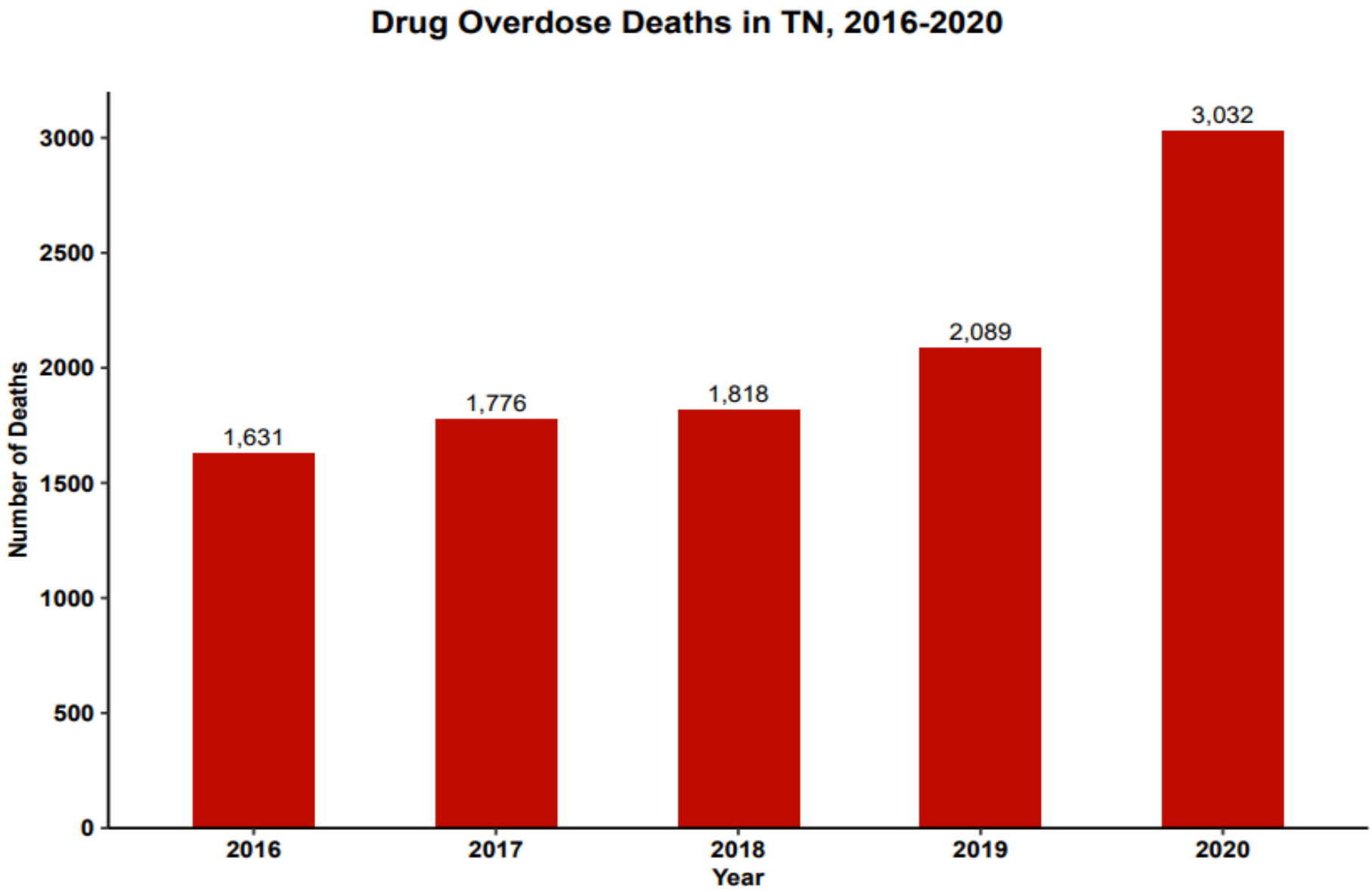
Current Trends: Tennessee

Nonfatal and Fatal Overdoses in TN

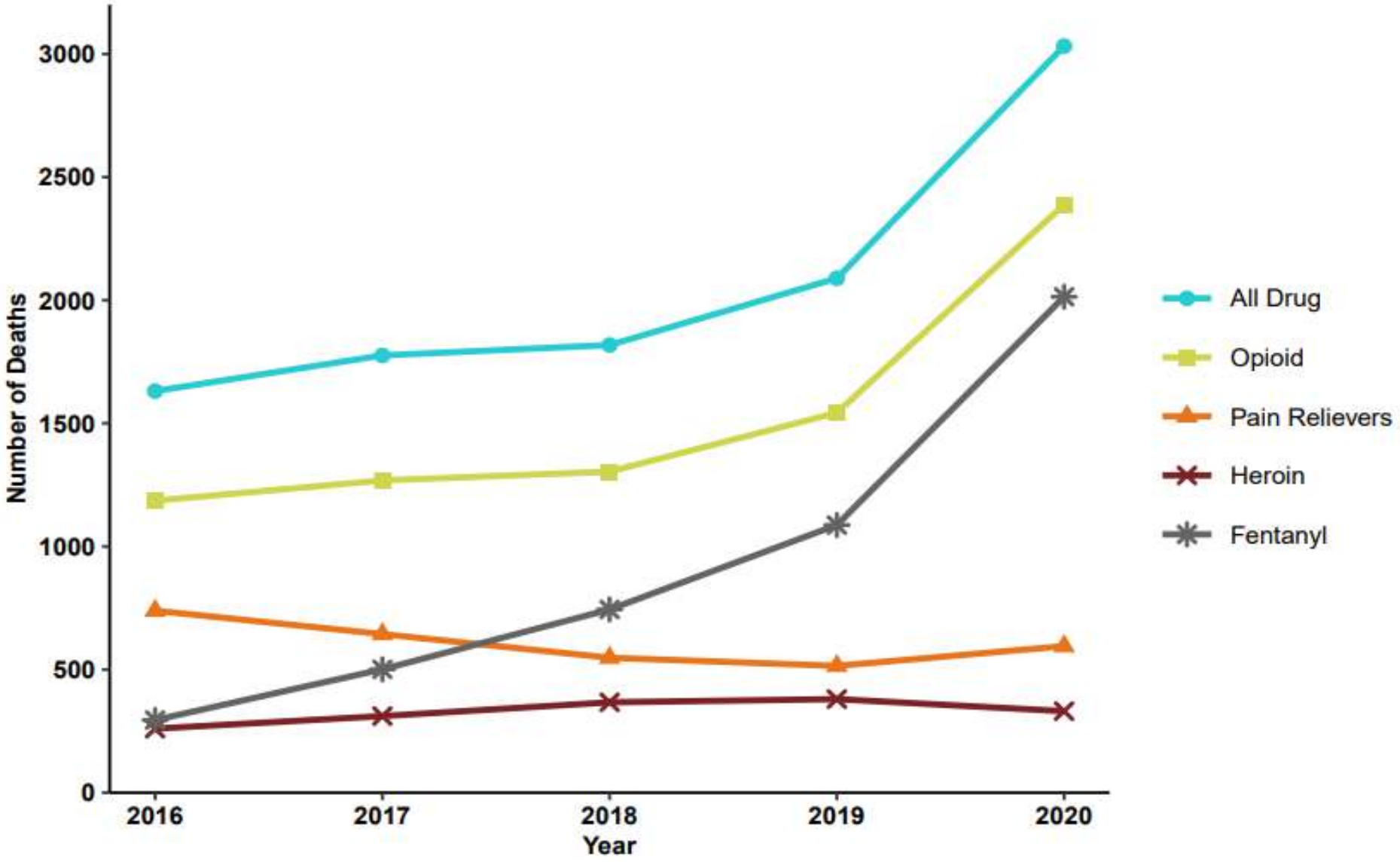
- n 2020, there were **25,796** all drug overdose hospital discharges among TN residents.
  - 7,063 (27.4%) were inpatient stays
  - 18,733 (72.6%) were outpatient visits

- 3,034 were fatal overdoses

State-level overview 2016 - 2020



Number of Overdose Deaths by Drug Type in TN, 2016-2020



Analysis by the Office of Informatics and Analytics, TDH (last updated August 26, 2021). Limited to TN residents.

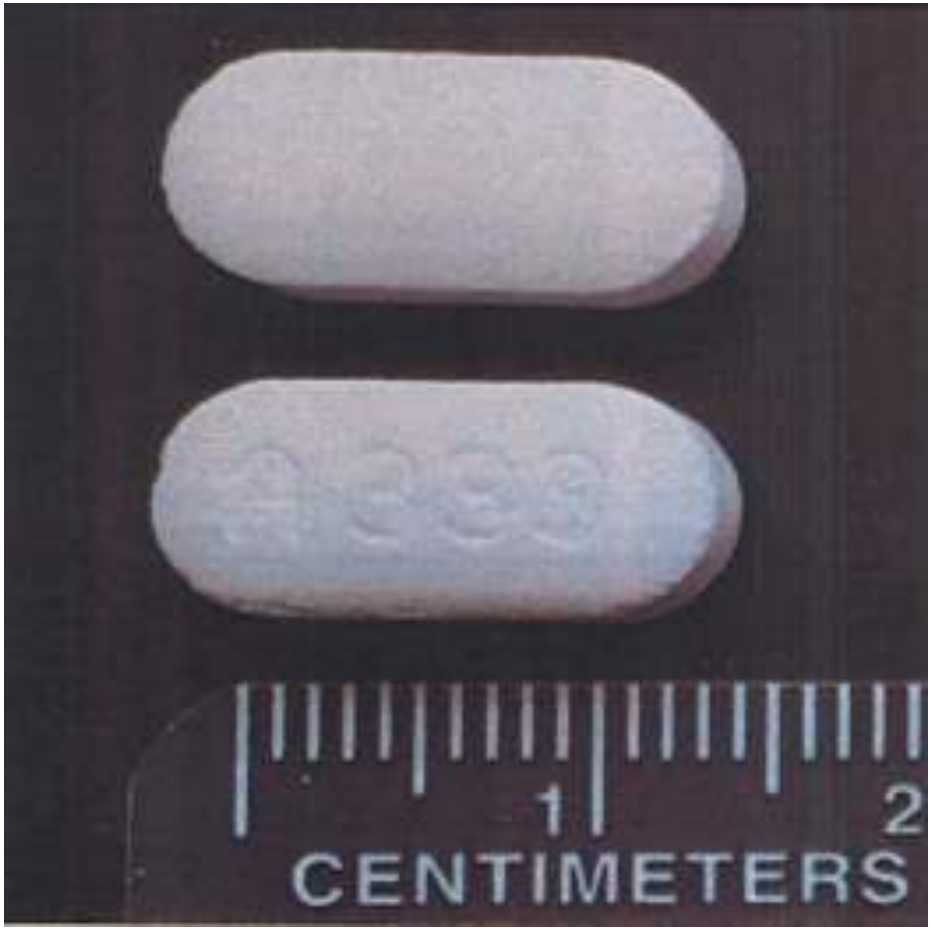
Pop Quiz – What Drug is This?

FENTANYL

Pop Quiz – What Drug is This?

FENTANYL

Pop Quiz – What Drug is This?



FENTANYL and ALPRAZOLAM

Mobile Pharmaceutical Plant

Mobile Pharmaceutical Plant

TBI has seized **12** pill presses in TN in 2017

Rainbow Fentanyl Pills

DEA HQ
@DEAHQ · **Follow**

DEA Warns of Brightly-Colored Fentanyl Used to Target Young Americans
dea.gov/press-releases...

2:42 PM · Aug 30, 2022

Emerging Trends-Xylazine and Nitazene

Xylazine

Powerful veterinary tranquilizer; not approved for human use

Commonly mixed with fentanyl; also found in combination with methamphetamine, Delta-9 THC, cocaine, alprazolam (Xanax)

Known to cause severe wounds and soft tissue infections.

Nitazene

Powerful synthetic (lab made) opioid

Common types include metonitazene, isotonitazene, protonitazene & etonitazene

Of recorded deaths in Tennessee, all of them involved other substances, most commonly fentanyl or meth

Sources: TDH, CDC, ONDCP

Emerging Drug Trends – Xylazine Basics

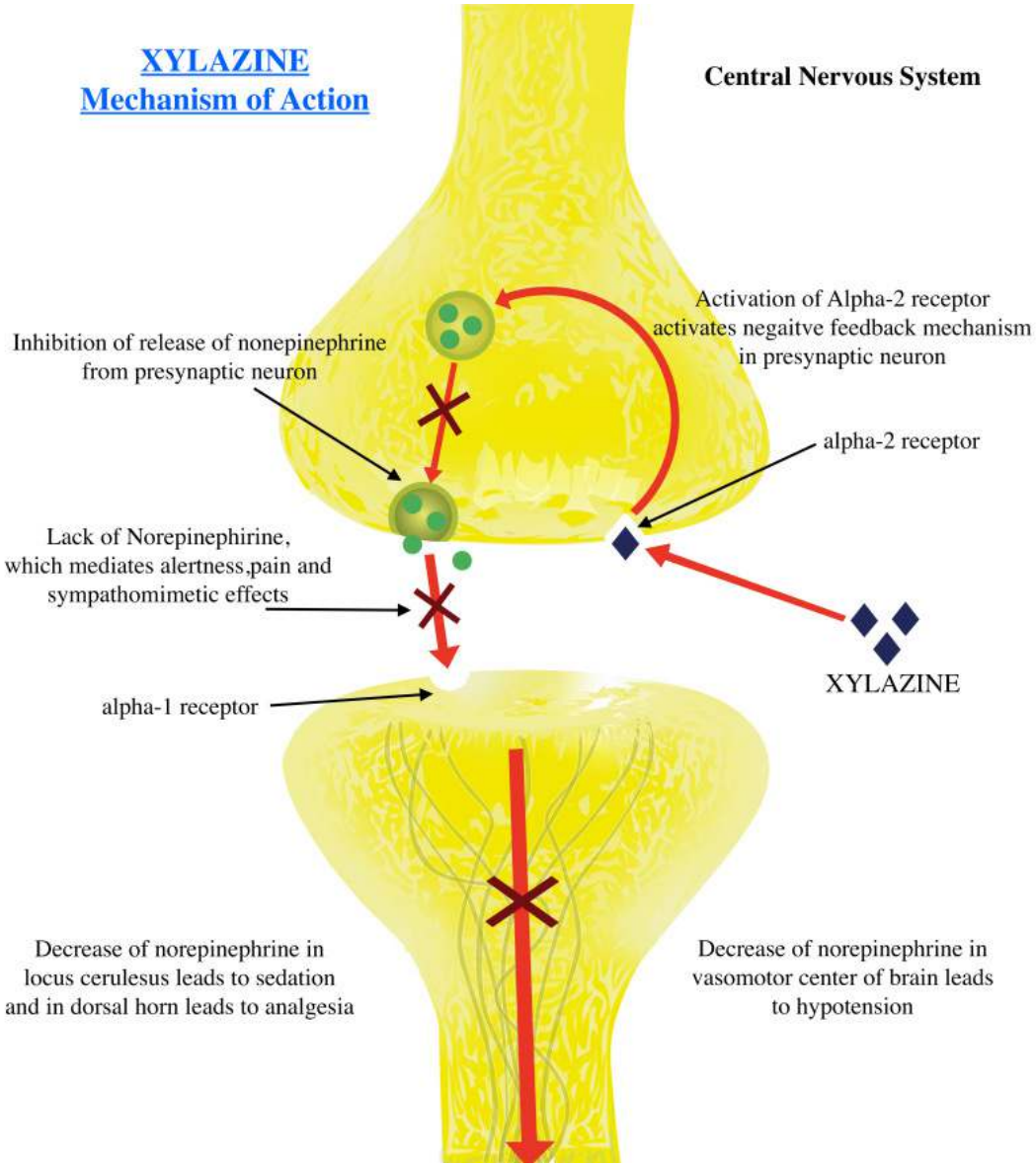
- Non-opioid veterinary tranquilizer not approved for human use
  - Sedative
  - Analgesic effects
  - Muscle relaxant properties

- Other names: “tranq” and “tranq dope”
- Routes of administration: parenteral, nasal, oral, and inhaling
- Increased xylazine prevalence as an adulterant in illicit substances (fentanyl, heroin, and cocaine)

Emerging Drug Trends – Xylazine Mechanism

- Structurally similar to phenothiazines
- Pharmacology of xylazine is well established in animal species, however human studies are limited, and effects not well known
- Alpha-2 adrenergic agonist
- May have cholinergic, serotonergic, dopaminergic, alpha-1 adrenergic, histaminergic or opiate receptor mechanisms
- Onset of action: minutes
- Length of action: ~4 hours
- Known to increase euphoric effects when added to fentanyl and “sought after” adulterant to lengthen short duration of fentanyl’s effects

Emerging Drug Trends – Xylazine Mechanism



Emerging Drug Trends – Xylazine Risks

- Not currently known to be reversed by naloxone (but still give it if suspected overdose!!)
- People often times unaware of exposure
- Repeated exposure may lead to severe, necrotic skin ulcerations requiring:
  - Complicated wound care
  - Prolonged antibiotics
  - Amputation

- Repeated exposures to xylazine leads to dependence and severe withdrawal symptoms –unable to manage with standard treatment options

Emerging Drug Trends – Xylazine Presentation

- Patient presentation may be variable:
  - Narrow pupils
  - Bradycardia
  - Hypo-or hypertension
  - Decreased level of consciousness
  - Severe, necrotic skin ulcerations/abscesses

- Unable to detect in routine urine drug screens
- Requires targeted, definitive testing methods Gas chromatography/mass spectrometry (GC/MS)
- Liquid chromatography/tandem mass spectrometry (LC/MS/MS)
- Turn around time 3-7 days
- ~3-day period of detection in urine

Emerging Drug Trends – Xylazine Skin Ulcers

- The mechanism is thought to be due to direct vasoconstricting effect on local blood vessels and the results in decreased skin perfusion
- Prolonged use can lead to decreased perfusion and impaired wound healing, leading to higher chances of infection of these ulcers and topical effect of vasoconstriction
- Excipients (impurities) found in xylazine preparations may contribute as well
- High prevalence of skin ulceration develop over various body parts irrespective of IV injection site

Emerging Drug Trends – Xylazine Skin Care

- Clean hands with soap and water or hand sanitizer before touching wounds
- Gently wash wound with soap and water or with saline at least every 2-3 days
- Put ointment on gauze & place on entire wound. Cover with more dry gauze
- Wrap wound with a bandage roll and secure with medical tape. Make sure wrap is not too tight
- Cover dressing with ACE bandage wrap or with long sleeves/pants if no other option
- Change dressing every 1-3 days. Watch for red flags

Emerging Drug Trends – Xylazine Red Flags

- Fever or chills
- Skin turns dark or black
- Skin is red, hard, & hot to touch
- Thick, smelly yellow or green drainage
- Severe or worsening pain at wound site
- Pain & decreased ability to move joint
- Pieces of tissue falling off
- Exposed bone or tendon
- New numbness

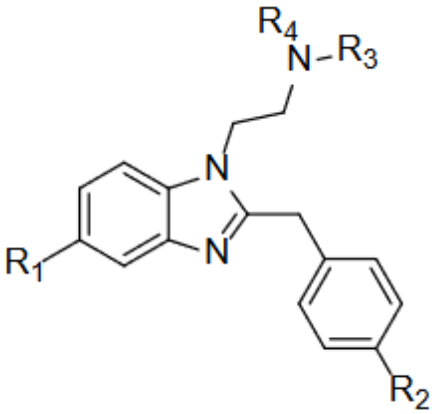
Refer to a Medical Professional!!

Emerging Drug Trends – Xylazine Scheduling

- **Tenn. Code Ann. § 39-17-456 (Public Chapter 412 of 2023)**
- (a) t is an offense to knowingly possess xylazine.
- (b) t is an offense to knowingly manufacture, deliver, or sell xylazine.
- (c) t is an offense to knowingly possess xylazine with intent to manufacture, deliver, or sell xylazine.
- (d) Notwithstanding subsections (a) – (c):
  - (1) t is not an offense to possess, manufacture, deliver, or sell xylazine in the course of legitimate veterinary practice; and
  - (2) t is not an offense to possess xylazine pursuant to a valid prescription from a licensed veterinarian;
- (e) As used in this section, "xylazine" means xylazine and any salt, sulfate, isomer, homologue, analog, or other preparation of xylazine, and any salt, sulfate, isomer, compound, derivative, precursor, homologue, analog, or other preparation thereof that is substantially chemically equivalent or identical to xylazine.
- (f) A violation of subsection (a) is a Class A misdemeanor; and
- (g) A violation of subsection (b) or (c) is a Class C felony.

Emerging Drug Trends – Nitazenes

- Also known as benzimidazole-opioids. dentified nitazenes are Schedule controlled substances
- Act on opioid receptors and behave similarly to other opioid agonists
- Overdoses associated with nitazenes are likely to respond to naloxone



	R_1	R_2	R_3	R_4
metonitazene	NO_2	OCH_3	CH_2CH_3	CH_2CH_3
metodesnitazene	H	OCH_3	CH_2CH_3	CH_2CH_3
etonitazene	NO_2	OCH_2CH_3	CH_2CH_3	CH_2CH_3
etodesnitazene	H	OCH_2CH_3	CH_2CH_3	CH_2CH_3
protonitazene	NO_2	$OCH_2CH_2CH_3$	CH_2CH_3	CH_2CH_3
butonitazene	NO_2	$OCH_2CH_2CH_2CH_3$	CH_2CH_3	CH_2CH_3
isotonitazene	NO_2	$OCH(CH_3)_2$	CH_2CH_3	CH_2CH_3
clonitazene	NO_2	Cl	CH_2CH_3	CH_2CH_3
flunitazene	NO_2	F	CH_2CH_3	CH_2CH_3
etonitazpyne	NO_2	OCH_2CH_3	$-CH_2CH_2CH_2CH_2-$	
etonitazepipne	NO_2	OCH_2CH_3	$-CH_2CH_2CH_2CH_2CH_2-$	

Emerging Drug Trends – Nitazenes

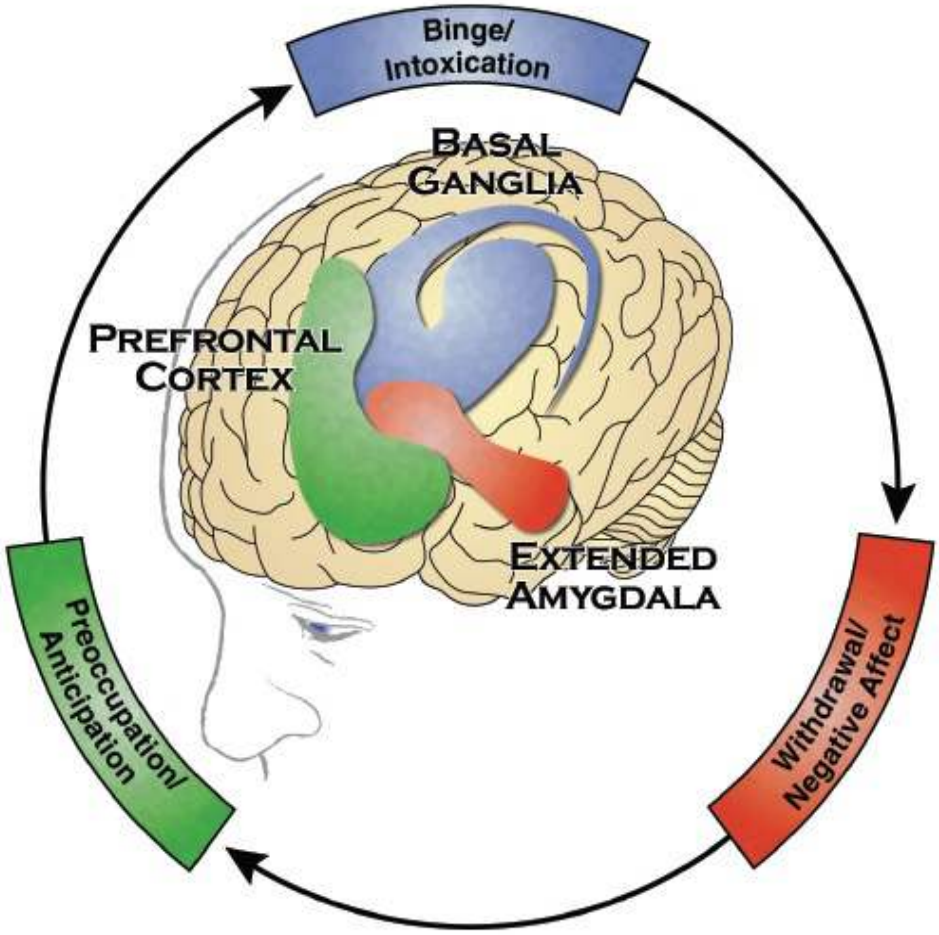
- Old things are new again. Originally developed in the 1950s but has never been marketed for approved use.
- Not commonly tested for, and prevalence is increasing.
- Reports can be conflicting but many nitazenes are thought to be more potent than fentanyl.

Pathophysiology and Treatment of Opioid Use Disorder

Pathophysiology – Cycle of Addiction

REWARD

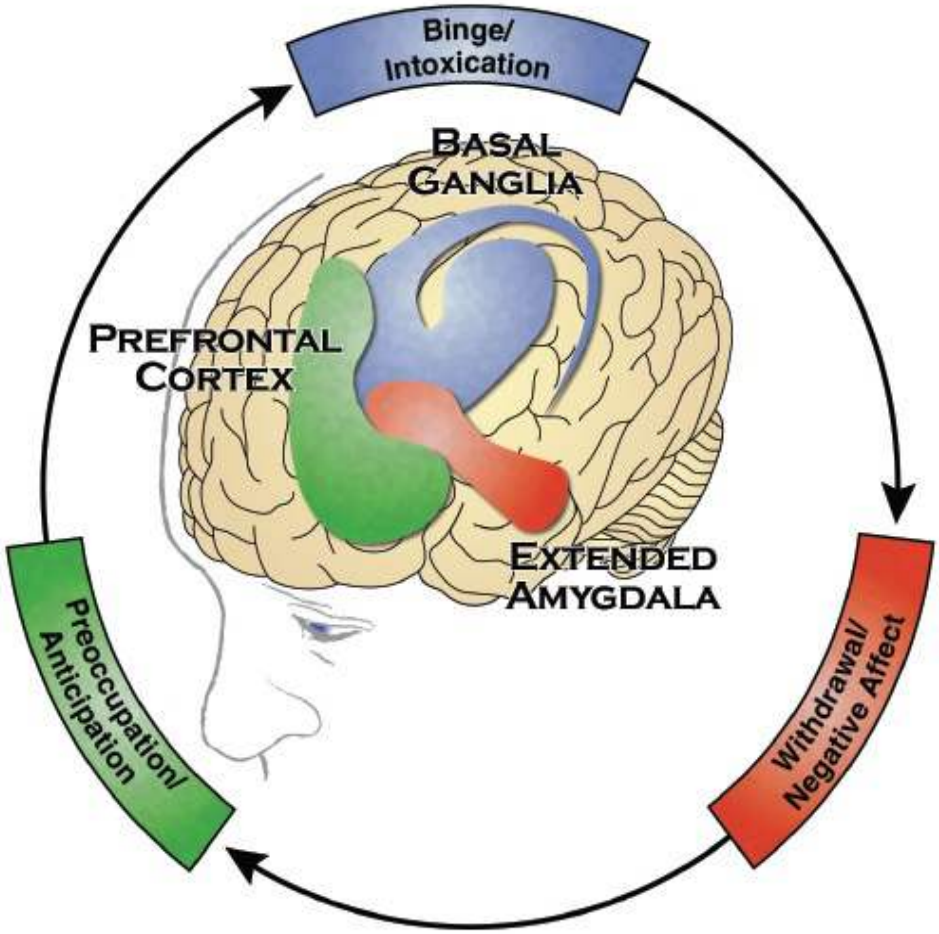
- Dopamine is stimulated to a low to moderate level (*within the physiologic range*) by water, food, meaningful social interactions, sex, and parenting
- Dopamine is stimulated to a moderate to very high level (in the super-physiologic or pharmacologic range) by dopamine surge (or intoxicating) drugs like opioids, stimulants, cannabinoids



Pathophysiology – Cycle of Addiction

WITHDRAWAL

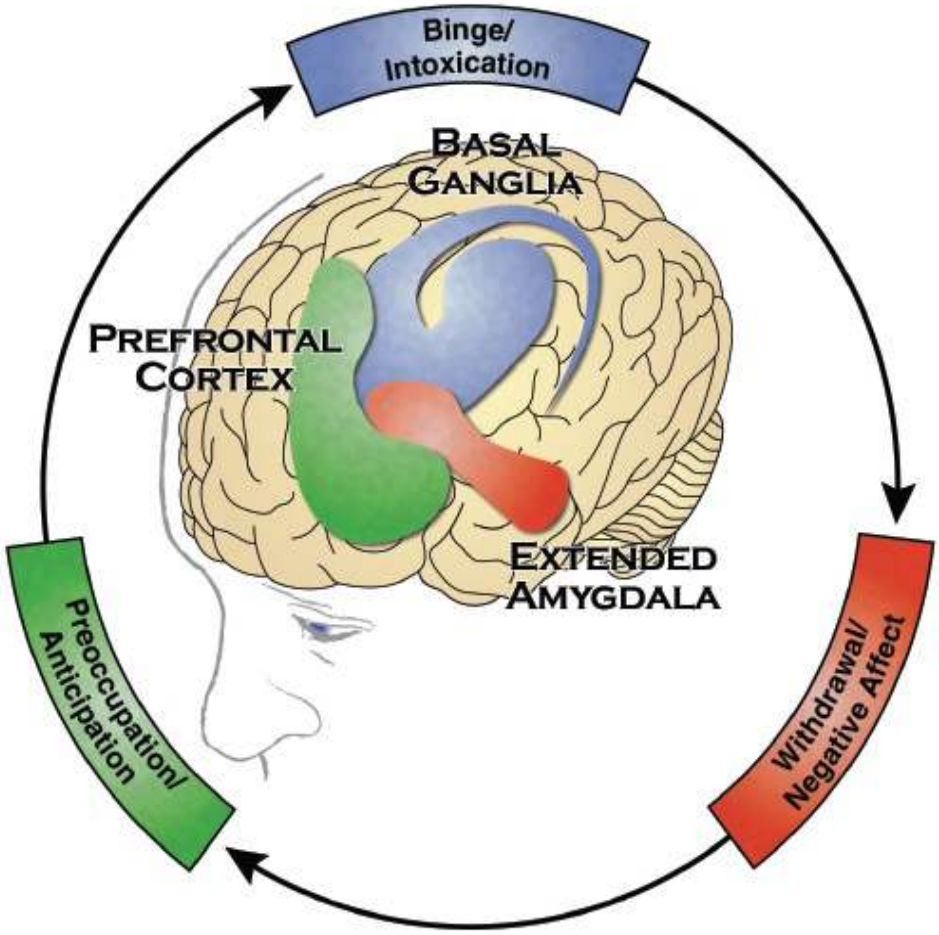
- Modulates negative emotions
  - Unease
  - Anxiety
  - Irritability
- Fight or flight response
- Conducts the release of norepinephrine and corticotropin releasing hormone causing stress and inhibits dopamine



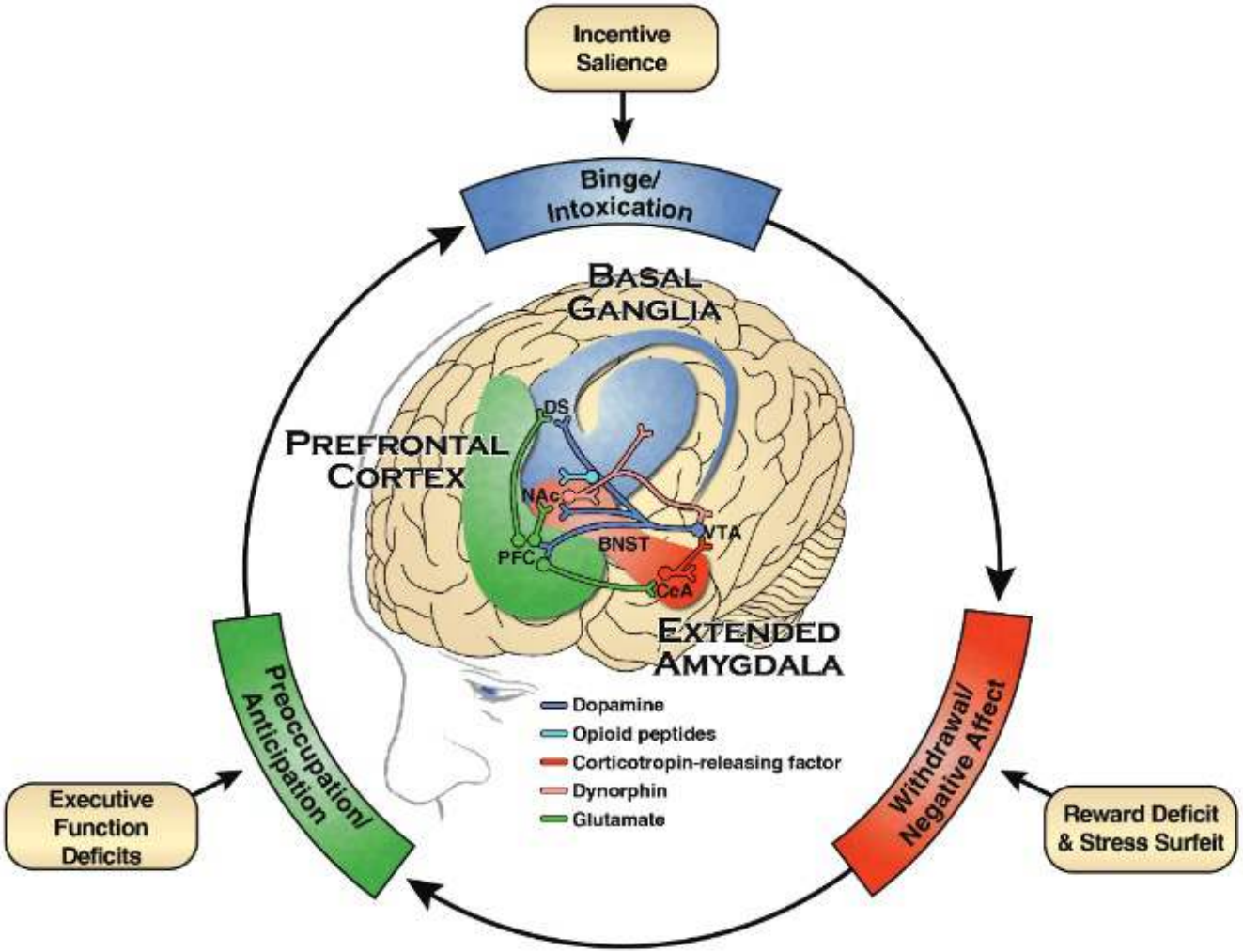
Pathophysiology – Cycle of Addiction

PREOCCUPATION/ ANTICIPATION

- Risks vs. benefits; the ability to apply understanding of consequences to certain behavior or actions
- Organization of time, money, and other responsibilities/priorities
- Over time, circuitry is rewired to prioritize drug-seeking behavior and drug use as it is 'viewed' as a life-preserving activity.



Pathophysiology – Cycle of Addiction



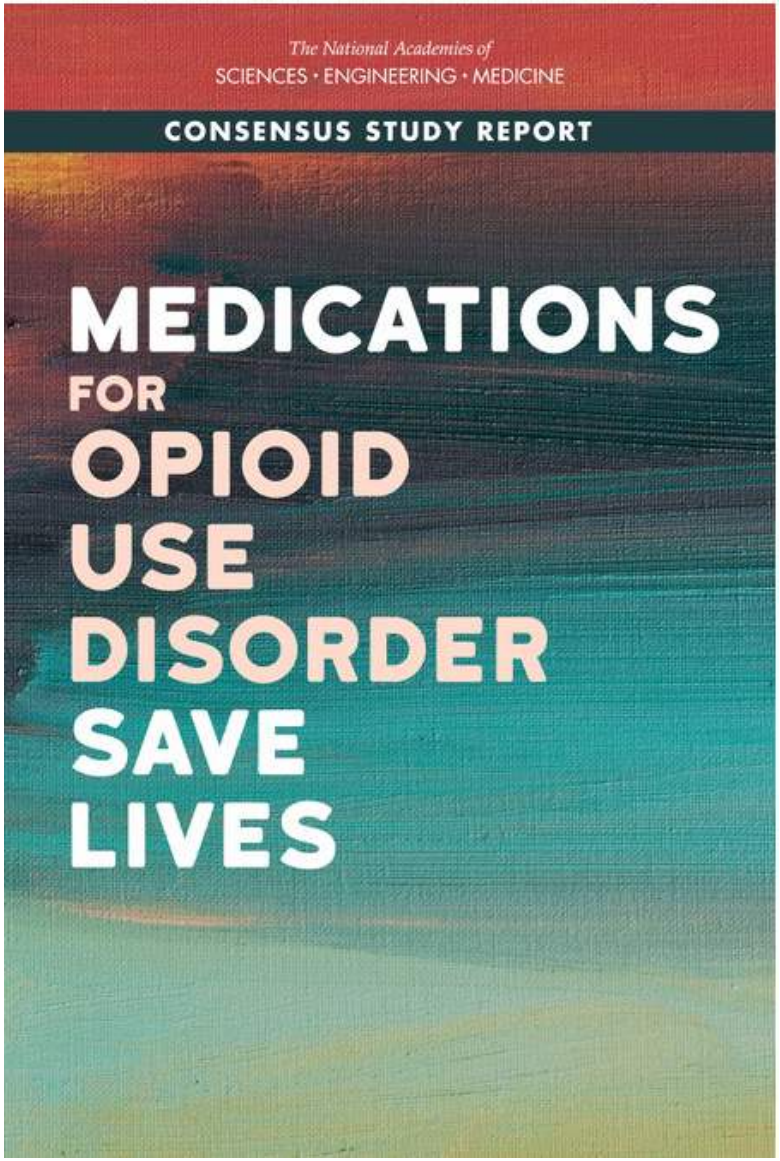
DSM-5 – Opioid Use Disorder Diagnostic Criteria

- A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. mportant social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the followings: *
    1. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
    2. A markedly diminished effect with continued use of the same amount of an opioid.
11. Withdrawal, as manifested by either of the followings: *
    1. The characteristic opioid withdrawal syndrome
    2. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

Let’s Open the Treatment Toolbox

National Academies of Sciences, Engineering, and Medicine



https://nap.nationalacademies.org/catalog/25310/medications-for-opioid-use-disorder-save-lives

National Academies of Sciences, Engineering, and Medicine

Conclusion 1:
Opioid use disorder is a treatable chronic brain disease.

OUD is a treatable chronic brain disease resulting from the changes in neural structure and function that are caused over time by repeated opioid use. The behavioral and social contexts are critically important to both its development and treatment. Stopping opioid misuse is extremely difficult. Medications are intended to normalize brain structure and function.

National Academies of Sciences, Engineering, and Medicine

Conclusion 2:
U.S. Food and Drug Administration–approved medications to treat opioid use disorder are effective and save lives.

FDA-approved medications to treat OUD—methadone, buprenorphine, and extended-release naltrexone—are effective and save lives. The most appropriate medication varies by individual and may change over time. To stem the opioid crisis, it is critical for all FDA-approved options to be available for all people with OUD. At the same time, as with all medical disorders, continued research is needed on new medications, approaches, and formulations that will expand the options for patients.

National Academies of Sciences, Engineering, and Medicine

Conclusion 3:
Long-term retention on medication to treat opioid use disorder is associated with improved outcomes.

There is evidence that retention on medication for the long term is associated with improved outcomes and that discontinuing medication often leads to relapse and overdose. There is insufficient evidence regarding how the medications compare over the long term.

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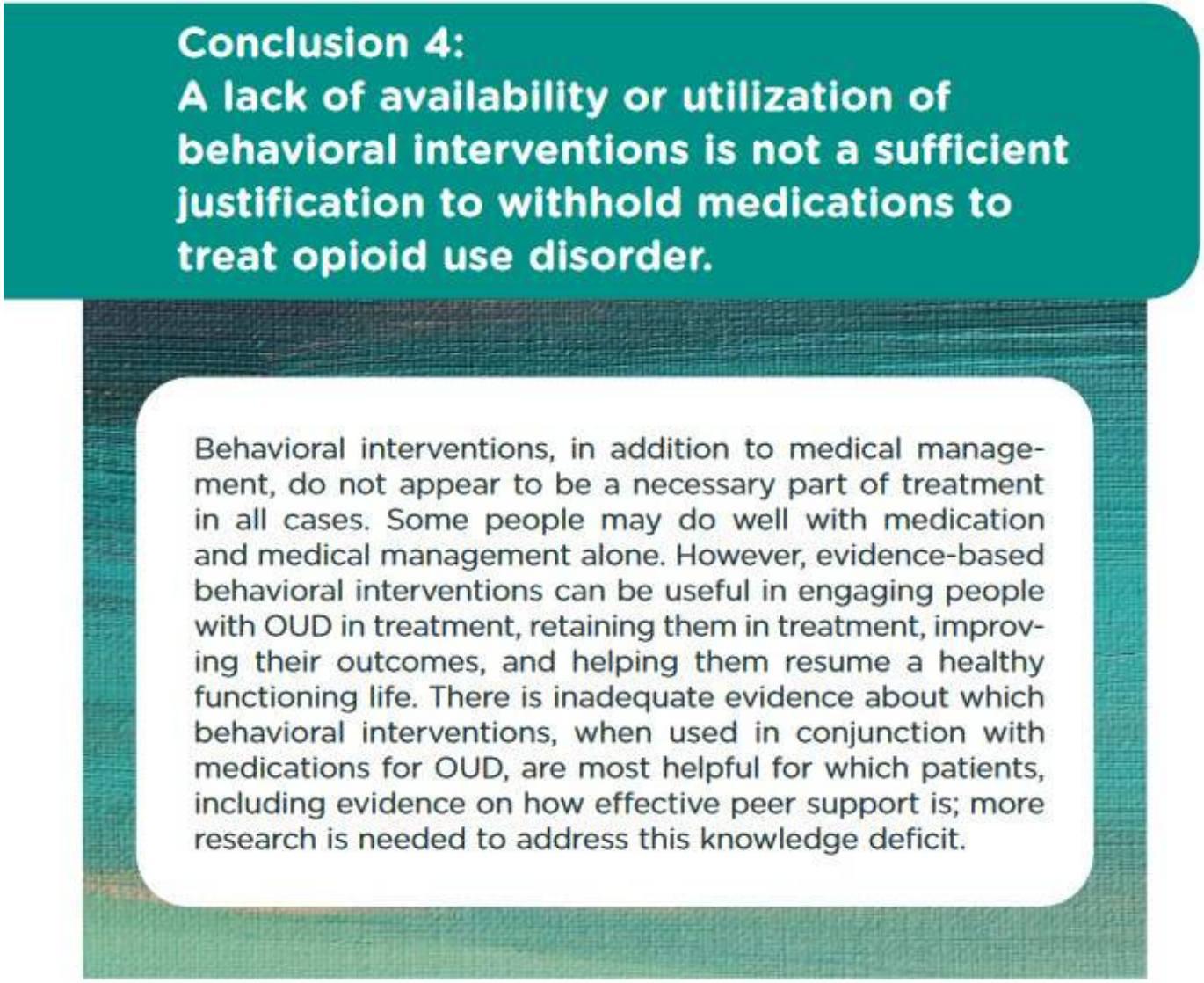


National Academies of Sciences, Engineering, and Medicine

Conclusion 5:
Most people who could benefit from medication-based treatment for opioid use disorder do not receive it, and access is inequitable across subgroups of the population.

Available evidence suggests that medication-based treatment for OUD is highly effective across all subgroups of the population, including adolescents, older persons, pregnant women, individuals with co-occurring disorders (e.g., psychiatric disorders, SUDs, infectious diseases), and all racial, sex and gender, and socioeconomic groups. However, the nature and extent of OUD in these groups appear to vary greatly, as does access to needed medications. To more widely and equitably address the opioid crisis, additional study will be required of the significance and causes of these differences as well as of the potential need for specific medication-based treatment guidelines for subpopulations.

National Academies of Sciences, Engineering, and Medicine

Conclusion 6:
Medication-based treatment is effective across all treatment settings studied to date. Withholding or failing to have available all U.S. Food and Drug Administration–approved classes of medication for the treatment of opioid use disorder in any care or criminal justice setting is denying appropriate medical treatment.

Treatment with FDA-approved medications is clearly effective in a broader range of care settings (e.g., office-based care setting, acute care, and criminal justice settings) than is currently the norm. There is no scientific evidence that justifies withholding medications from OUD patients in any setting or denying social services (e.g., housing, income supports) to individuals on medication for OUD. Therefore, to withhold treatment or deny services under these circumstances is unethical.

National Academies of Sciences, Engineering, and Medicine

Conclusion 7:
Confronting the major barriers to the use of medications to treat opioid use disorder is critical to addressing the opioid crisis.

The major barriers to the use of medications for OUD include

- High levels of misunderstanding and stigma toward drug addiction, individuals with OUD, and the medications to treat it.
- Inadequate education of the professionals responsible for working with people with OUD, including treatment providers and law enforcement and other criminal justice personnel.
- Current regulations around methadone and buprenorphine, such as waiver policies, patient limits, restrictions on settings, and other policies that are not supported by evidence or employed for other medical disorders.
- The fragmented system of care for people with OUD and current financing and payment policies.

MAT Medications

Opioid Antagonist:
Naloxone and Naltrexone

0%
Intrinsic Activity

Opioid Partial Agonist:
Buprenorphine

40%
Intrinsic Activity

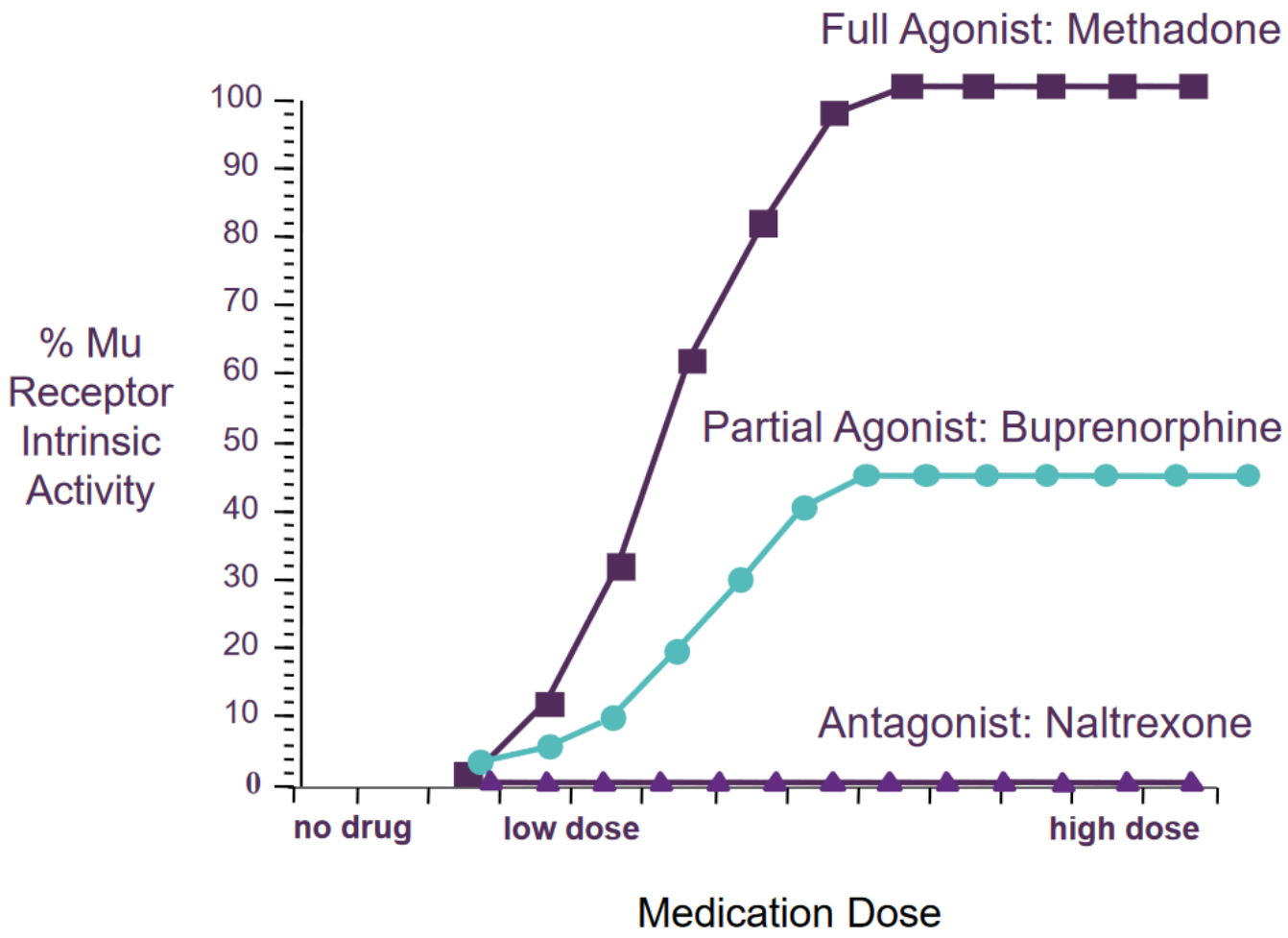
Full Opioid Agonist:
Methadone

100%
Intrinsic Activity

(Wyatt, 2017)

Medication-Assisted Treatment

- Approved medications:



Medication-Assisted Treatment (MAT)

Purpose of MAT for OUD

- Allow reestablishment of homeostasis of the reward pathways in the brain away from substances
- Restore emotional and decision-making capacities
- Control symptoms of opioid withdrawal (agonists)
- Suppress opioid cravings
- Block the reinforcing effects of ongoing opioid use
- Promote and facilitate patient engagement in recovery-oriented activities
- Coupled with behavioral interventions
  - Enhance the salience of natural, healthy rewards
  - Reduce stress reactivity and negative emotional state
  - mprove self-regulation
  - ncrease avoidance of relapse triggers

Medication-Assisted Treatment (MAT)

Goal of MAT for OUD

- Reduce mortality
  - All cause and drug-related
- Reduce associated morbidity
  - Transmission of blood-borne viruses
  - nfectious complications from V drug use
- Reduce and/or discontinue opioid use
- ncrease retention in addiction treatment
- mprove general health and well-being
- Reduce drug-related crime
- NCREASED CONNECT ONS AND POS T VE RELAT ONSH PS!!

Common Misconception with MAT

"Maintenance opioid agonists is just switching addictions and patients should not be on them long term"

- Research on maintenance treatment demonstrated:
  - Normalization of functioning
  - No euphoric, tranquilizing, or analgesic effects
  - No change in tolerance levels over time
  - Effectiveness when administered orally
  - Relief for opioid craving
  - Minimal side effects

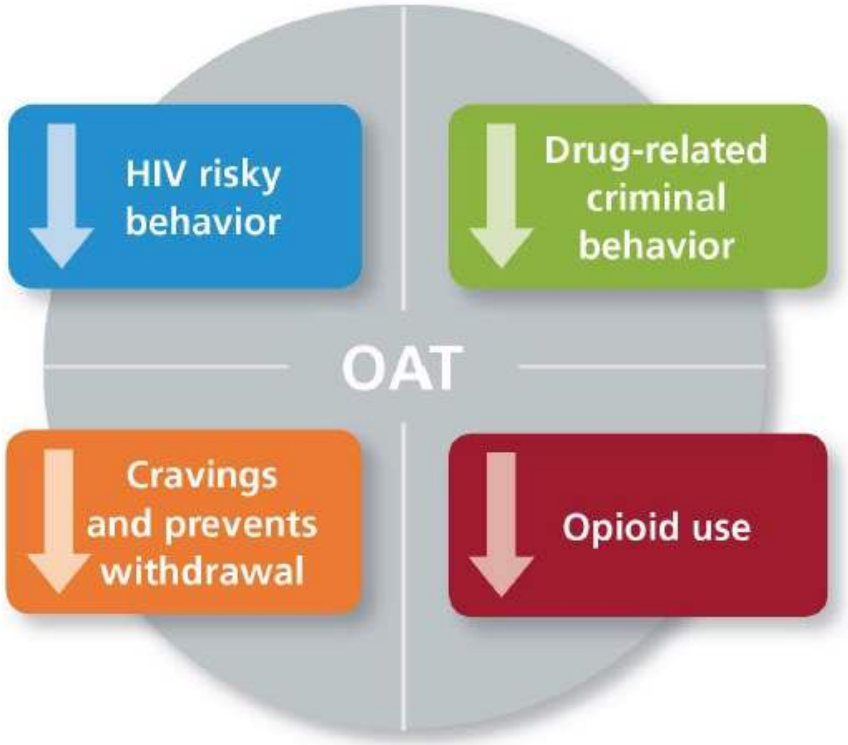
  (Refer to DSM-5 OUD Diagnostic Criteria – Symptoms of OUD are not present when using medications appropriately and are engaged in recovery)

- Research on forced tapering demonstrated
  - Significant rate of relapse
  - ncreased risk for drug overdose

Common Misconception with MAT

OUD Pharmacotherapy

Figure 7. Opioid Agonist Therapy (OAT) is considered 1st line treatment for OUD.[16]



OAT allows the patient to focus more readily on recovery activities by preventing withdrawal and reducing cravings; helps achieve long-term goal of reducing opioid use and the associated negative medical, legal, and social consequences, including death from overdose.[17,18]

VA Clinician's Guide to Identification and Management of Opioid Use Disorder. VA Academic Detailing Service 2016

Stigma

e Treatment," PCSS E. A. Salsitz and M. D. Disclosures, "Stigma in Methadone and Buprenorphine Maintenanc-Substance Use Disorder
Stop the Stigma and Expand Acces to Comprehensive Treatment," American Medical Association.
MAT Training.

MAT - Methadone

Brand Name: Dolophine, Methadone Intensol, Methadose

MOA: full opioid agonist; may also antagonize NMDA

Generally dosed daily for addiction vs every 4-8 hours for pain

Average dose: 80-120mg/day

Duration of analgesic activity: 6-8 hours

Metabolized by:

CYP2B6, CYP2C19 (major) CYP2C9, CYP2D6, CYP3A4 (major), Inhibit CYP2D6

Can cause QT prolongation, increasing risk of arrythmias

MAT- Methadone History

A Medical Treatment for Diacetylmorphine (Heroin) Addiction

A Clinical Trial With Methadone Hydrochloride

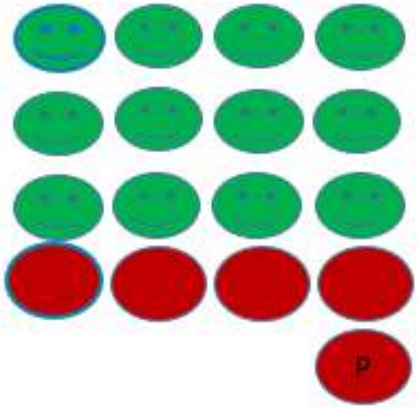
Vincent P. Dole, MD, and Marie Nyswander, MD

A group of 22 patients, previously addicted to diacetylmorphine (heroin), have been stabilized with oral methadone hydrochloride. This medication appears to have two useful effects: (1) relief of narcotic hunger, and (2) induction of sufficient tolerance to block the euphoric effect of an average illegal dose of diacetylmorphine. With this medication, and a comprehensive program of rehabilitation, patients have shown marked improvement; they have returned to school, obtained jobs, and have become reconciled with their families. Medical and psychometric tests have disclosed no signs of toxicity, apart from constipation. This treatment requires careful medical supervision and many social services. In our opinion, both the medication and the supporting program are essential.

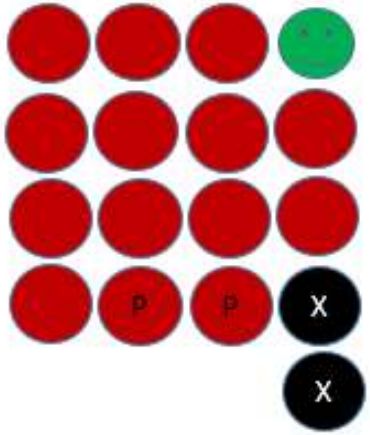
ough review of evidence available in 1957,[1] concluded that "The advisability of establishing clinics or some equivalent system to dispense opiates to addicts cannot be settled on the basis of objective facts. Any position taken is necessarily based in part on opinion, and on this question opinions are divided." With respect to previous trials of maintenance treatment, the Council found that "Assessment of the operations of the narcotic dispensaries between 1919 and 1923 is difficult because of the paucity of published material. Much of the small amount of data that is available is not sufficiently objective to be of great value in formulating any clear-cut opinion of the purpose of the clinics, the way in which they operated, or the results attained." No new studies bearing on the question

MAT- Methadone

Methadone treatment



Control group (no methadone)



According to a study evaluating methadone treatment versus control (no methadone) after 2 years, participants receiving methadone were more likely to be drug free and had fewer adverse outcomes associated with use (e.g. death, prison). P=prison; X=deceased

L. M. Gunne and L. Gronbladh, "The Swedish methadone maintenance program: a controlled study," *Drug Alcohol Depend.,* vol. 7, no. 3, pp. 249–256, Jun. 1981.

MAT- Methadone History

Federal Regulations – 21 CFR 1306.07

- (a) A practitioner may administer or dispense directly (but not prescribe) a narcotic drug listed in any schedule to a narcotic dependent person for the purpose of maintenance or detoxification treatment if the practitioner meets both of the following conditions:
  - (1) The practitioner is separately registered with DEA as a narcotic treatment program.
  - (2) The practitioner is in compliance with DEA regulations regarding treatment qualifications, security, records, and unsupervised use of the drugs pursuant to the Act.

- (b) Nothing in this section shall prohibit a physician who is not specifically registered to conduct a narcotic treatment program from administering (but not prescribing) narcotic drugs to a person for the purpose of relieving acute withdrawal symptoms when necessary while arrangements are being made for referral for treatment. Not more than one day's medication may be administered to the person or for the person's use at one time. Such emergency treatment may be carried out for not more than three days and may not be renewed or extended.

MAT- Methadone History

Federal Regulations – 21 CFR 1306.07 (continued)

- (c) This section is not intended to impose any limitations on a physician or authorized hospital staff to administer or dispense 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, or to administer or dispense narcotic drugs to persons with intractable pain in which no relief or cure is possible or none has been found after reasonable efforts.

- (d) A practitioner may administer or dispense (including prescribe) any Schedule , V, or V narcotic drug approved by the Food and Drug Administration specifically for use in maintenance or detoxification treatment to a narcotic dependent person if the practitioner complies with the requirements of §1301.28 *(DATA Waiver)* of this chapter.

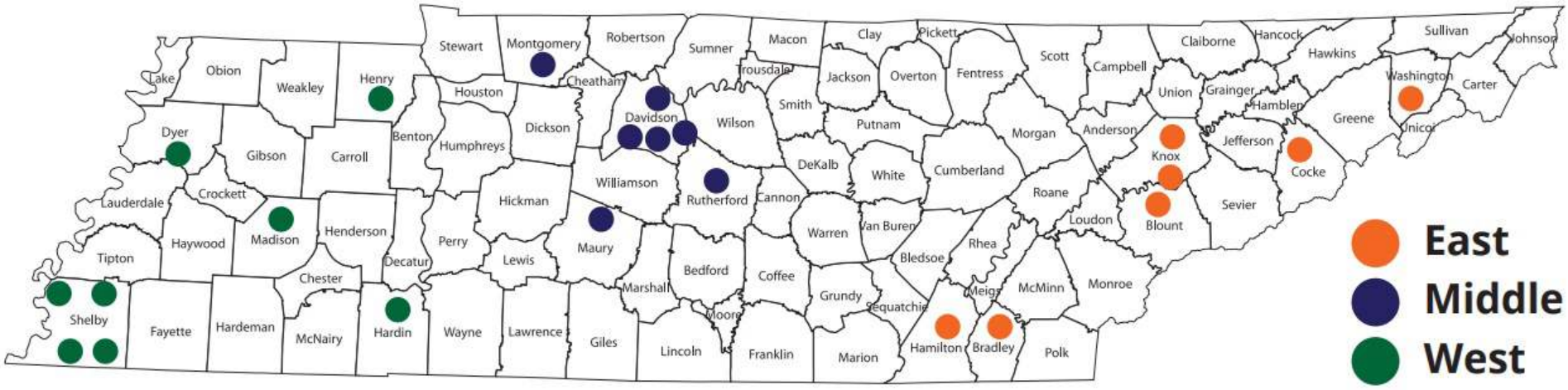
Special note: As of 2023, the DATA Waiver has been removed

MAT - Methadone

- Can only be used to treat OUD in an Opioid Treatment Program (OTP).
- OTPs are required to be federally certified by SAMHSA, separately registered by the DEA, accredited by the Joint Commission or CARF, and licensed by the TDMHSAS. A certificate of need from Health Facilities Commission is required to open a new OTP.
- Patients are initially required to attend the clinic daily to get a dose of medication, counseling, drug screens, etc. Attendance and frequency of services are decreased with time and compliance in treatment.
- Recent changes in 42 CFR Part 2 regulations will soon allow for methadone reporting in the CSMD.
  - “Reporting is permissible if it is required by the state”

MAT - Methadone

- There are currently 22 licensed OTPs in TN



MAT - Methadone

Methadone Resources

- 2015 Federal OTP Guidelines
- SAMHSA's T P 63
- American Society of Addiction Medicine's (ASAM) National Practice Guideline For the Treatment of Opioid Use Disorder

MAT - Buprenorphine

Brand Name: Subutex, Suboxone, Bunavail, Zubsolv, Sublocade

MOA: mixed-partial opioid agonist, attributing to the “ceiling effect”

Dosing: 4-24mg/day (or equivalent) with a target of 16mg/day

Metabolized by: CYP3A4

Ceiling effect can be negated by concurrent benzodiazepine or alcohol use

TN

MAT- Buprenorphine History

- Originally discovered in 1966 and was almost immediately studied for its usefulness in addiction treatment
- Landmark paper in 1979 by Donald Jasinski first published its use for addiction
- Jasinksi notes the buprenorphine ‘less toxic than methadone’ and ‘appears to have the advantage of both methadone and naltrexone but without the major disadvantage of each

MAT- Buprenorphine History

Br. J. clin. Pharmac. (1979), **7**, 287S–290S

HUMAN PHARMACOLOGY OF NARCOTIC ANTAGONISTS

DONALD R. JASINSKI

National Institute on Drug Abuse, Division of Research, Addiction Research Center, Lexington, Kentucky

1 Human studies at the Addiction Research Center enable narcotic antagonists to be classified into three subgroups: (1) nalorphine-like agents; (2) pure antagonists; and (3) morphine-like agents.

2 Six narcotic antagonists (pentazocine, nalbuphine, cyclazocine, butorphanol, propiram and buprenorphine) developed in recent years seem to have a lesser abuse potential than codeine or propoxyphene.

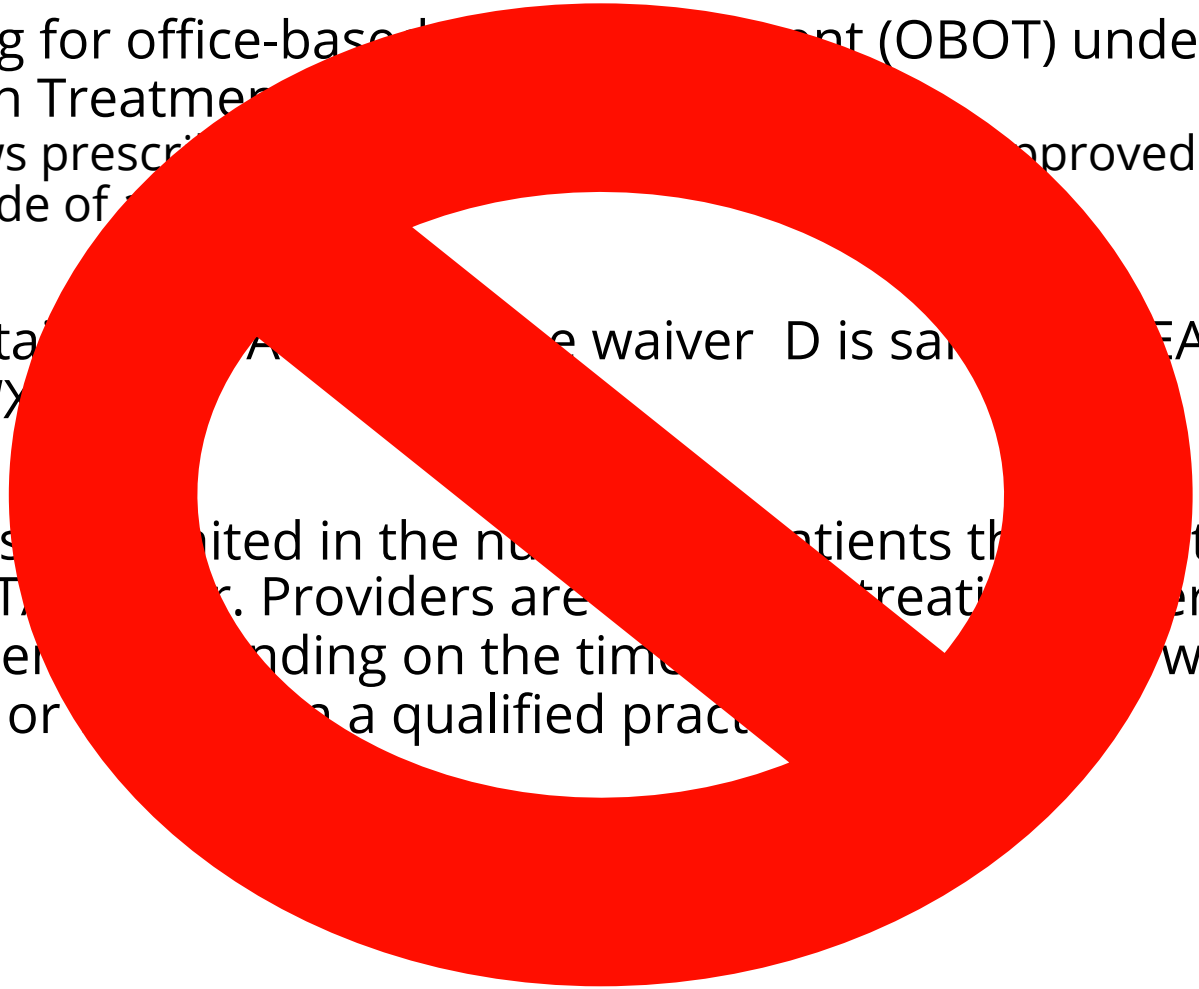
3 When adjusted for relative availability of the agents, epidemiological data shows that pentazocine is abused less than codeine or propoxyphene in the US.

4 Recent studies with buprenorphine indicate that this agent would find application both as an analgesic of low abuse potential and as a new type of drug for the treatment of addiction.

TN

MAT - Buprenorphine

- First drug for office-base[illegible]nt (OBOT) under the Drug Addiction Treatme[illegible]
  - Allows prescri[illegible]pproved for addiction outside of [illegible]
- Must obta[illegible]A[illegible]e waiver D is sa[illegible]EA # but begins with an "X[illegible]
- Providers [illegible]ited in the nu[illegible]atients th[illegible]treat using their DAT[illegible]r. Providers are [illegible]treati[illegible]er 30, 100, or 275, patie[illegible]nding on the time[illegible]waiver, level of training, or [illegible]a qualified pract[illegible]



MAT - Buprenorphine

- On December 29th, 2022, President Biden signed the Consolidated Appropriations Act (CAA) of 2023. The CAA incorporated the Mainstreaming Addiction Treatment Act of 2021 (MAT Act) that removes the DATA Waiver

- SAMHSA and the DEA published initial guidance on January 12th , 2023, announcing that the DATA Waiver program has ended and, effective immediately, the DATA Waiver is no longer required to prescribe buprenorphine for Opioid Use Disorder (OUD).

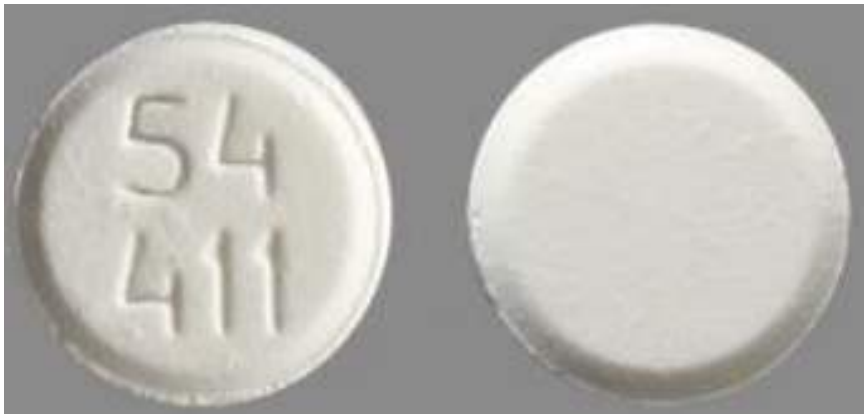
- At the federal level, buprenorphine may be prescribed like any Schedule controlled substance. At the State level, multiple restrictions still exist.

https://www.tn.gov/content/dam/tn/mentalhealth/documents/Public_Guidance_DATA_Waiver_Removal_2.27.23.pdf

MAT - Buprenorphine

Subutex – Buprenorphine
Suboxone – Buprenorphine/Naloxone

- Naloxone is added to buprenorphine as an abuse-deterrent mechanism to deter V use, although it does not deter misuse by oral route and some may still inject it.
- Although patients are frequently instructed by physicians to take partial films, the manufacturer instructs to take whole
- Currently, state law prohibits prescribing buprenorphine mono product to anyone unless they're pregnant, nursing, or allergic or have an adverse reaction to naloxone



MAT - Buprenorphine

Monthly njectable Buprenorphine (Sublocade)

- Must complete a 7-day dose adjustment with the transmucosal form of buprenorphine first
- Recommended dose is 300mg for the first two monthly injections then 100mg monthly thereafter (minimum of 26 days in between doses).
- ncludes a strict REMS program with limited distribution. A patient cannot be in possession of medication in the syringe. Fatal if used intravenously.

Buprenorphine Dispensing

2015-2019 Buprenorphine Prescription Trends

WHATS HAPPENING ACROSS TN?

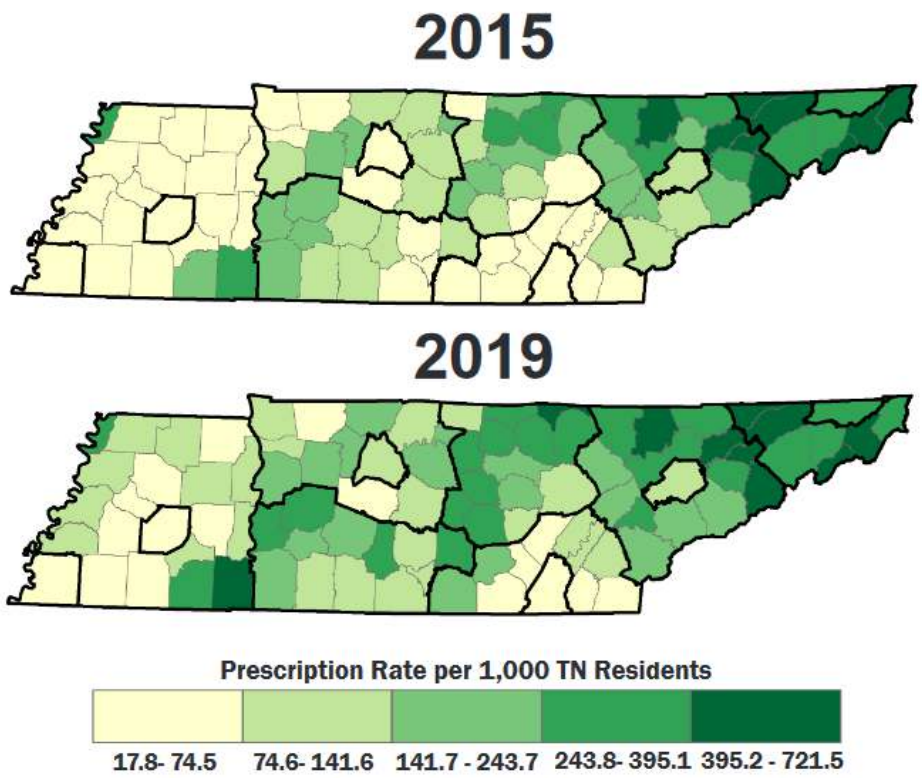
Prescription rates per 1,000 Tennessee residents for buprenorphine for MAT increased steadily from 2015 to 2019 across 78 (82%) of TN's 95 counties. The highest increase in buprenorphine prescription rates from 2015 to 2019 ocurred in:

- Coffee County
- Hickman County
- Smith County

Although prescription rates decreased in the northeast part of the state, those counties had a higher prescription rate for buprenorphine in 2015 compared to other counties.

Data Source: Tennessee Department of Health, Controlled Substance Monitoring Database. Analysis conducted by the Office of Informatics and Analytics (last updated 5/5/2020).

Rate of Buprenorphine Prescriptions for Medication-Assisted Treatment per 1,000 Population by TN County of Residence



2020 Buprenorphine Report – Tennessee Department of Health Office of Informatics and Analytics

Select Buprenorphine Laws

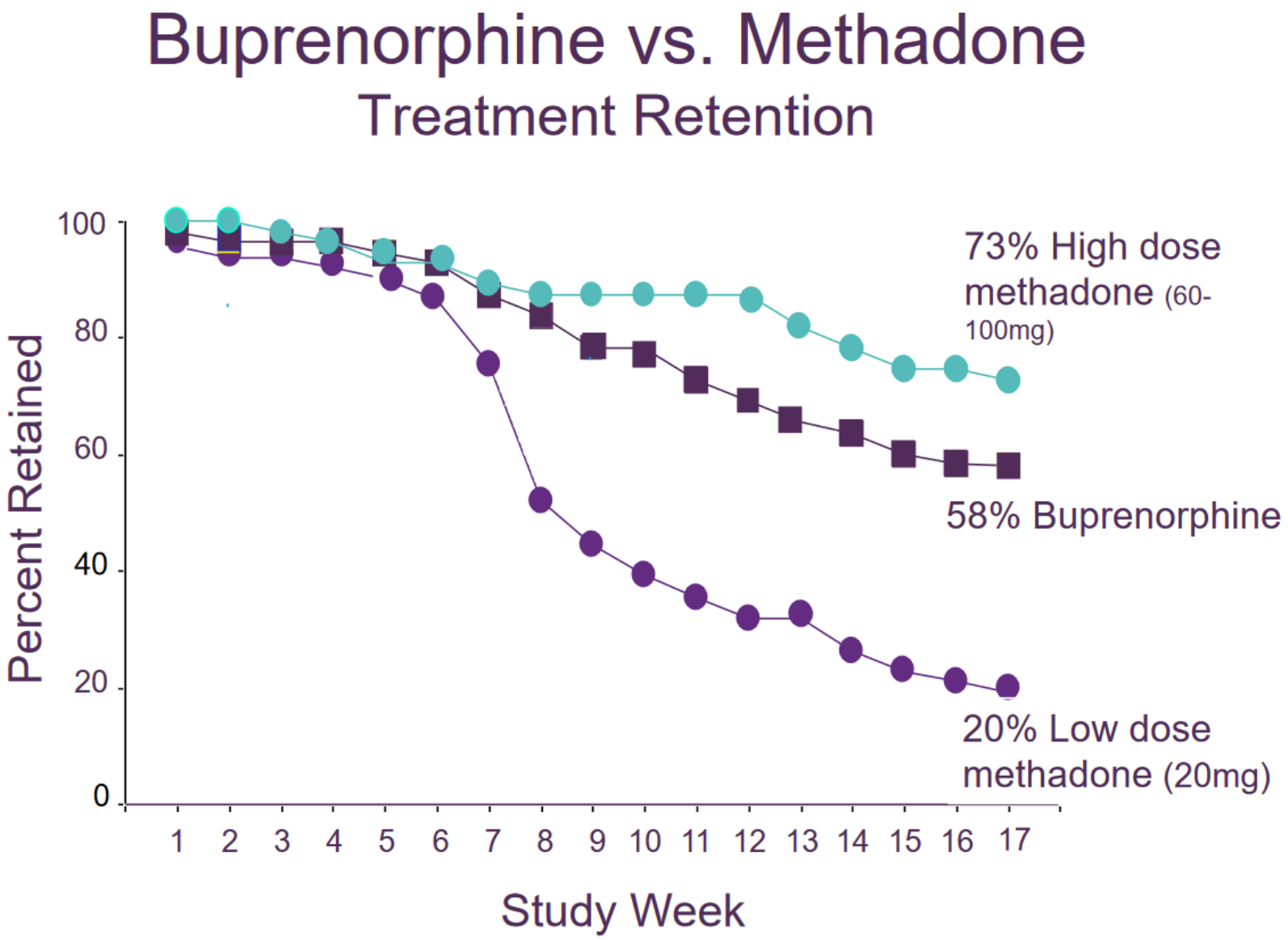
- OBOT Licensure: Facilities that prescribe buprenorphine to > 25% of its patients, or > 150 patients, require an OBOT license from TDMHSAS
- Nurse practitioners and physician assistants are restricted from prescribing buprenorphine unless it is at an OBOT, FQHC, or CMHC
- Buprenorphine prescribers cannot accept cash as payment, unless it is for a copay or coinsurance
- All TennCare enrollees must be treated by a provider that accepts TennCare
- Buprenorphine cannot be prescribed by telehealth unless it is an OBOT, FQHC, CMHC, or a provider in TennCare's BE-SMART network

MAT - Buprenorphine

Buprenorphine Resources

- Tennessee Nonresidential Buprenorphine Treatment Guidelines
- Tennessee Department of Health's 2020 Buprenorphine Report
- SAMHSA's T P 63
- American Society of Addiction Medicine's (ASAM) National Practice Guideline For the Treatment of Opioid Use Disorder

Buprenorphine vs. Methadone Comparison



MAT - Naltrexone

MOA: full opioid antagonist

Blocks euphoric effects of alcohol and any effect of opioids

No abuse potential

Tablets approved to treat alcoholism since 1995

Reduces number of heavy drinking days

May prevent a misstep from becoming a relapse

Black Box Warning: hepatoxicity

Precipitate withdrawal unless abstinent >7 days; 10 days for long acting opioids

Must counsel patient regarding the loss of tolerance while being treated with naltrexone. A relapse with an opioid dose familiar to patient prior to naltrexone may result in overdose and death

TN

MAT - Naltrexone

Vivitrol – Naltrexone njection

- Approved for alcohol and opioid dependence
- Administered as a 380mg/4mL M injection monthly. Must use included needle
- Patients must be free of opioids for 7-10 days to prevent precipitating withdrawal. Verify with UDS.
- Provides an additional challenge if acute pain management is needed = Should use regional analgesia or non-opioid pain relievers.

MAT Summary

- There has never been a more important time to use all the tools in the treatment tool belt
- Medications for opioid use disorder can help a patient stabilize and assist in the broader treatment of OUD but are not used often enough, even after an overdose event
- Buprenorphine and methadone are considered 1st line options, with naltrexone being a close second in certain settings.
- n the real world, the best treatment is the one that patients and providers agree on and the patient has access to.

QUESTIONS?

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