Medication for Opioid Use Disorder: Tips for Better Outcomes

Mississippi Physician Health Program 2023 Prescriber Summit

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No Disclosures

- Todays speaker has no disclosure of real or apparent conflict related to the content of this presentation.

Objectives:

1. Discuss the opioid crisis in America.
2. Describe regulatory changes regarding medication assisted treatment for addictive disorders.
3. Describe buprenorphine for opioid replacement therapy.

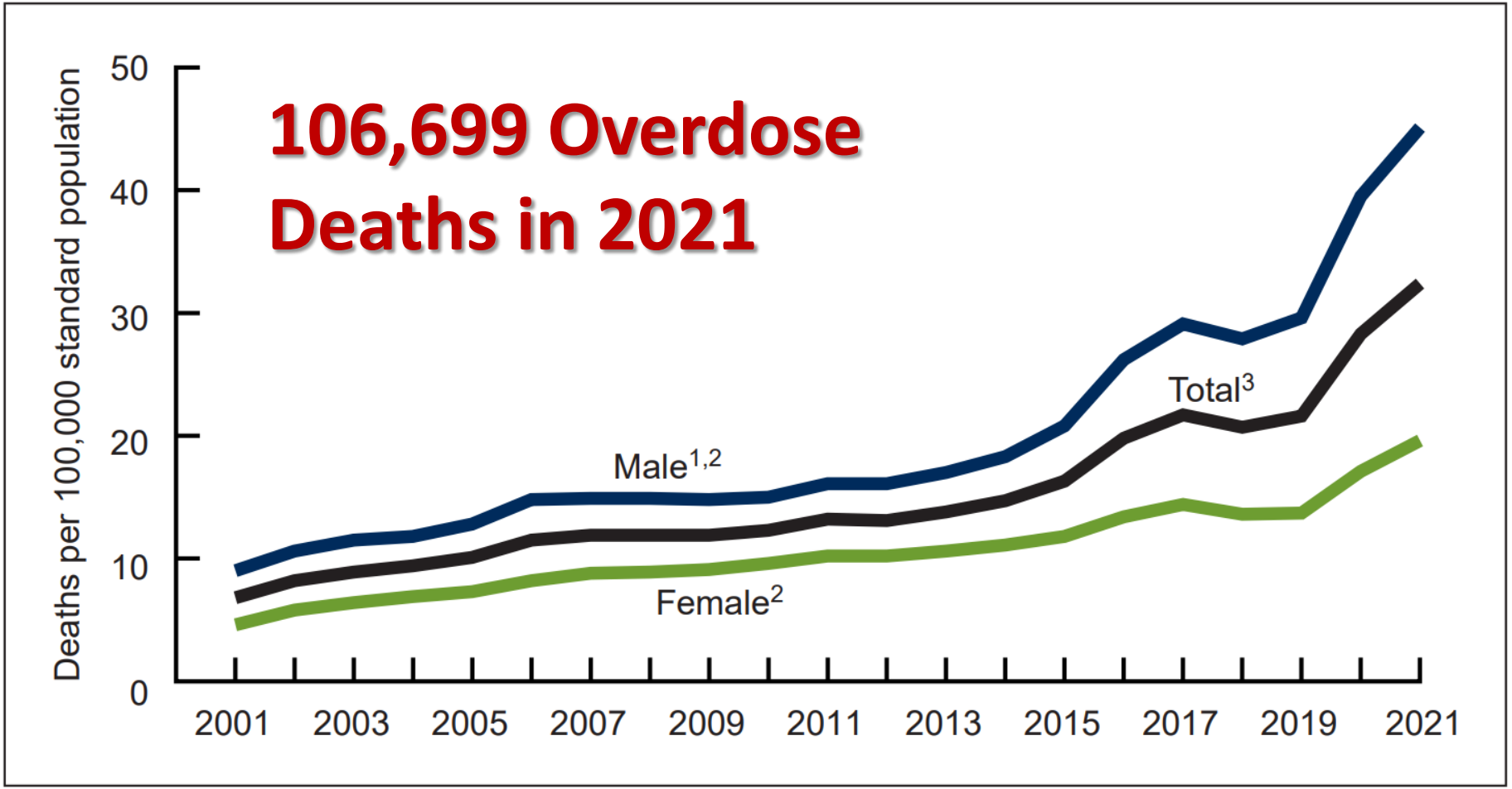
Abbreviations

- MAT = medication assisted treatment (no longer used)
- MOUD = Medications for Opioid Use Disorder (replaced MAT)
- ORT = opioid replacement therapy
- OTP = opioid treatment program
- OBT = Office Based Treatment

What are Opioids?

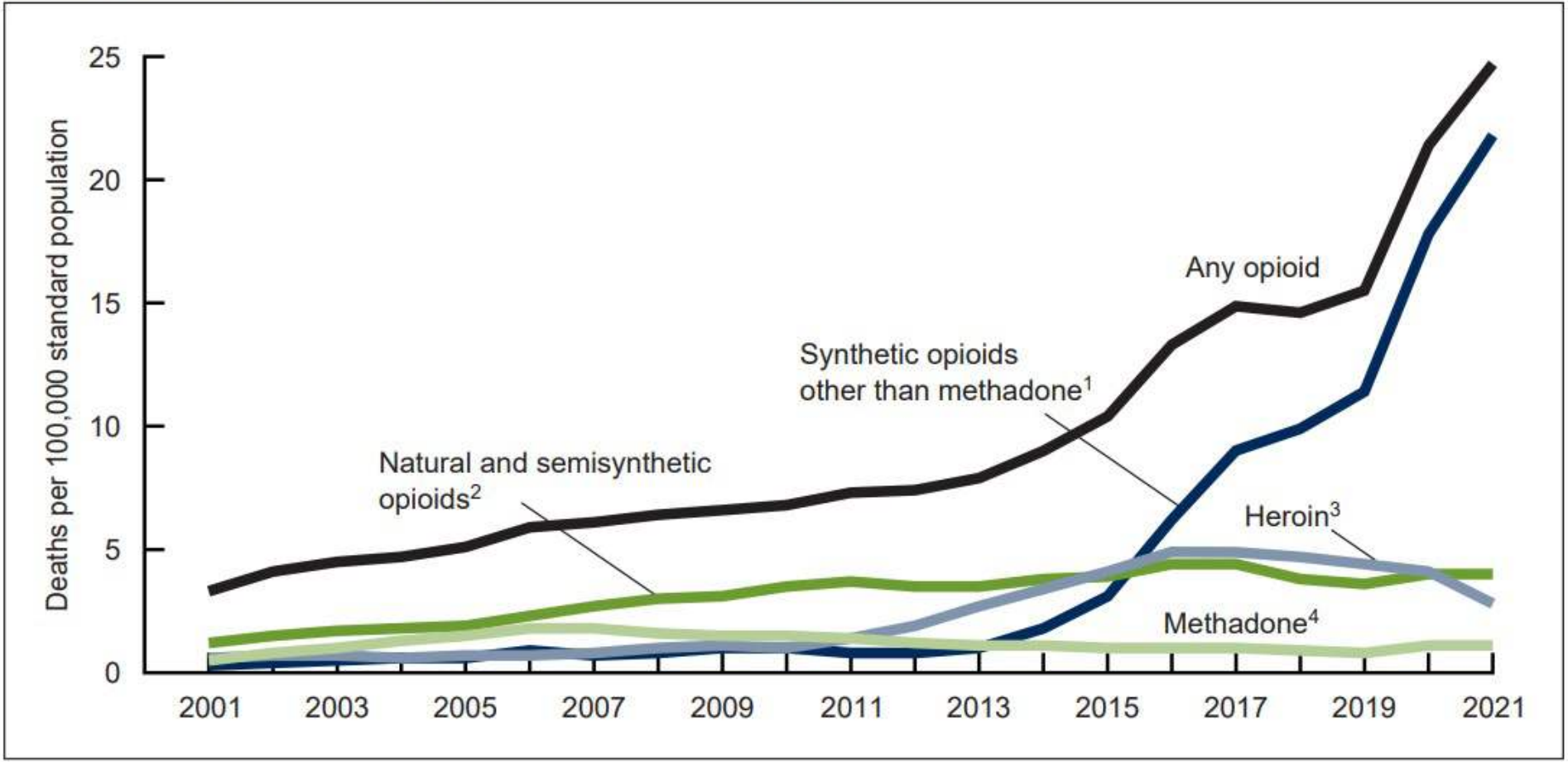
- Drugs that interact with Mu opioid receptor
  - Opiates: extracted from opium poppy (Codeine, Morphine)
  - Semi synthetic opiates: partially derived from opium poppy (Buprenorphine, Hydrocodone, Oxycodone, Heroin)
  - Synthetic opiates: not derived from opium poppy (Fentanyl, Demerol, Methadone)

Figure 1. Age-adjusted rate of drug overdose deaths, by sex: United States, 2001–2021



(https://www.cdc.gov/nchs/data/databriefs/db457.pdf)

Figure 4. Age-adjusted rate of drug overdose deaths involving opioids, by type of opioid: United States, 2001–2021



(National Center for Health Statistics, National Vital Statistics System, Mortality File)

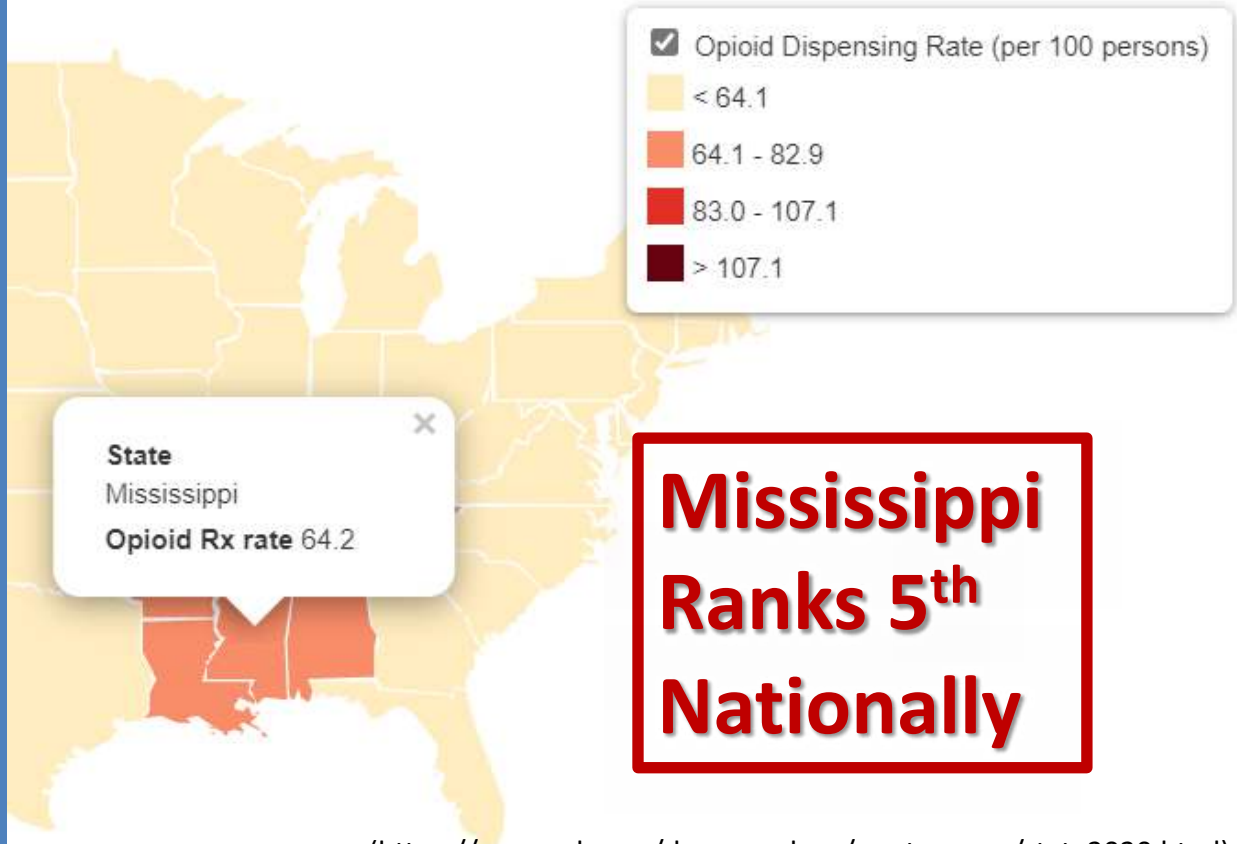
Fentanyl: Game Changer

- 20,000 deaths in 2016
  - 540% increase in 3 years
- 70,000 in 2021!!!
- 50X potency heroin
- 100X potency morphine
- Carfentanil = 10,000X potency morphine

(https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm)

(https://pmp.mbp.ms.gov/statistics/)

U.S. Opioid Dispensing Rate Maps



Mississippi Ranks 5th Nationally

(https://www.cdc.gov/drugoverdose/rxrate-maps/state2020.html)

Opioids for Chronic Non-Cancer Pain

- “No validated, reliable way exists to predict which patients will experience serious harm from opioid therapy and which patients will benefit from opioid therapy.”

(CDC Clinical Practice Guideline for Prescribing Opioids for Pain–United States,2022. https://www.cdc.gov/opioids/patients/guideline.html)

Adverse Selection: Opioid Use

- Patients with mental health and substance abuse co-morbidities are more likely to receive chronic opioid therapy than patients who lack these risk factors.

(Sullivan, *Pain*, 2010)

Addiction:
Primary, Chronic Brain Disease

- "Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death."

(ASAM Public Policy Statement, 2011)

Effectiveness of MOUD

- Transmucosal buprenorphine:
  - Improves treatment retention
  - Reduces opioid use
  - Associated with decreased mortality in individuals with OUD

1. CDC Clinical Practice Guideline for Prescribing Opioids for Pain–United States,2022. https://www.cdc.gov/opioids/patients/guideline.html)
2. Substance Abuse and Mental Health Services Administration. TIP 63: Medications for Opioid Use Disorder. https://www.samhsa.gov/resource/ebp/tip-63-medications-opioid-use-disorder.

“Replacing One Drug for Another”

- Would you say the same thing about nicotine patches compared to smoking?

Historical Timeline for Buprenorphine Regulations:

- 1981: Buprenorphine is first synthesized in England.
- 1985: The U.S. Food and Drug Administration (FDA) approves buprenorphine for use as an injectable analgesic.
- 1995: The World Health Organization (WHO) recommends buprenorphine as a treatment for opioid dependence.
- 2000: The Drug Addiction Treatment Act (DATA 2000) is passed by Congress, allowing qualified physicians to prescribe buprenorphine for the treatment of opioid dependence in an office-based setting – Required “X - waiver”.
- 2002: The FDA approves the first buprenorphine product for opioid dependence treatment: Subutex (buprenorphine HCl sublingual tablet).

Historical Timeline for Buprenorphine Regulations:

- 2003: The FDA approves a second buprenorphine product for opioid dependence treatment: Suboxone (buprenorphine HCl/naloxone HCl dihydrate sublingual tablet).
- 2006: The Comprehensive Addiction and Recovery Act (CARA) is signed into law, expanding access to medication-assisted treatment (MAT) for opioid addiction, including buprenorphine.
- 2016: The final rule of the Comprehensive Addiction and Recovery Act (CARA) is issued by the Department of Health and Human Services, raising the patient limit for qualified physicians to prescribe buprenorphine from 100 to 275 patients.
- 2021: The Department of Health and Human Services removes the requirement for buprenorphine prescribers to undergo training and certification, effectively eliminating the "X-waiver" requirement for prescribing buprenorphine.

Consolidated Appropriations Act, 2023

- Signed into law December 29, 2022
- **Section 1262**: Removes requirement for DEA X-Waiver
  - Removes maximum limit for number of patients being treated with buprenorphine by a provider
  - Any provider with DEA Schedule III authority may prescribe buprenorphine for opioid use disorder

(https://www.congress.gov/bill/117th-congress/house-bill/2617)

Consolidated Appropriations Act, 2023

- **Section 1263**, known as the Medication Access and Training Expansion (MATE) Act:
  - Requires new or renewing DEA registrants, as of June 27, 2023, to have completed a total of at least 8 hours of training on opioid or other substance use disorders.

(https://www.congress.gov/bill/117th-congress/house-bill/2617)

MAT: Medication Assisted Treatment

- FDA approved medications for:
  - **Tobacco Use Disorder**:
    OTC nicotine replacement formulations;
    Varenicline; Bupropion.
  - **Alcohol Use Disorder**:
    Acamprosate, Naltrexone; Disulfuram.
  - **Opioid Use Disorder**:
    buprenorphine; methadone; Naltrexone.
    (https://www.samhsa.gov/medication-assisted-treatment)

Naltrexone

- To treat alcohol/opioid addiction
- Blocks effects of opioids
- Lasts;
  - 1-2 days(PO)
  - 30 days(IM)
- Formulations:
  - Vivitrol (360mg IM)
  - Revia (50 mg PO)

(SAMHSA)

Narcan Nasal Spray

- Opioid receptor antagonist
- Temporarily reverses an opioid overdose
- Effects last 30-60 minutes
- Many formulations;
  - Injectible 1mg/mL ($)
  - Narcan Nasal Spray ($$)
  - Evzio 2mg auto-injector ($$$)
- Indicated for: H/O OD; SUD; >50MME, or concurrent BZOs
- Approved by FDA for OTC use on March 29, 2023

Naltrexone versus Naloxone

Naloxone:	Naltrexone:

• IV/IM/intranasal
• Onset: IV = 1-2 minutes
• Duration: 30-60 minutes
• Uses:
  ➢ Emergent OD reversal
  ➢ Combined with Buprenorphine (Suboxone)
	• PO/IM
	• Onset: 30-60 minutes
	• Duration:
	  ➢ Oral: 24-48 hrs
	  ➢ IM: 30 days
	• Uses: Addiction(opioids/EtOH)

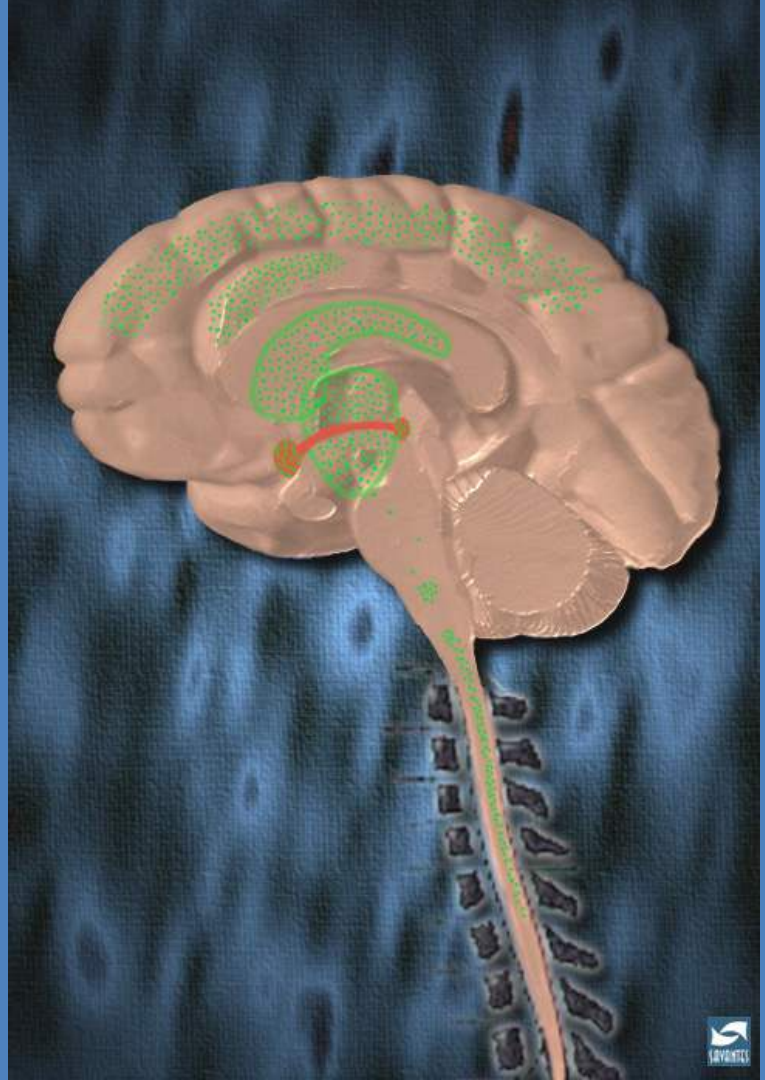
(SAMHSA)

Other Meds for Opioid Withdrawal

- Clonidine
  - PO or transdermal
  - 0.1–0.3 mg every 6–8 hours
  - Maximum dose of 1.2 mg/day
- Benzodiazepines for anxiety(inpatient)
- Loperamide for diarrhea
- Acetaminophen/NSAIDS for pain
- Ondansetron or other agents for nausea

(ASAM National Practice Guideline, 2015)

- Opioid binding sites (green)
- Reward Pathway (orange)

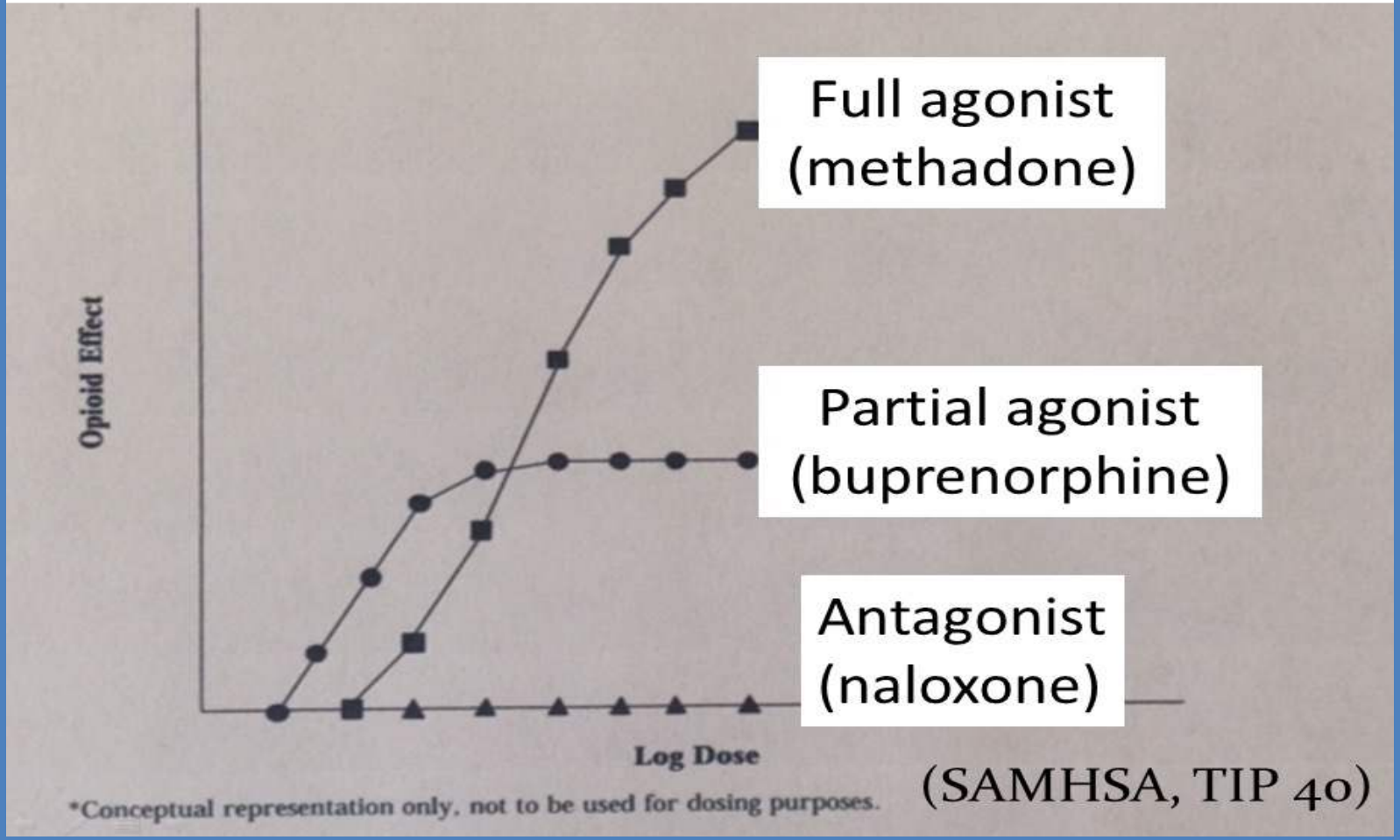


Buprenorphine Pharmacology

- Semisynthetic, partial μ-opioid agonist
- Partial agonists activate receptors, but not to the same degree as full agonists.
  - less euphoria
  - less respiratory depression
  - less sedation
- k-receptor antagonist (blocks dysphoria)

(ASAM National Practice Guideline, 2015)

Buprenorphine Ceiling Effect



(SAMHSA, TIP 40)

Buprenorphine Pharmacology

- Metabolized by the liver via cytochrome P450
- Slow rate of dissociation from mu opioid receptor
  - Long duration of action
  - Half-life of 24–60 hours (mean 37)
  - Prolonged suppression of opioid withdrawal
- Short duration of analgesia
- Maximal effects at ≤ 24mg (Suboxone)
- Highest affinity of μ-opioid receptor of any opioid

  (ASAM National Practice Guideline, 2015)

Precipitated Opioid Withdrawal

- Occurs with buprenorphine induction prior to onset of mild to moderate opioid withdrawal
- Occurs with naltrexone/naloxone administration during opioid intoxication
- Induction:
  - Short acting opioids: 12-24 hours
  - Long acting opioids: 36-72 hours

(ASAM National Practice Guideline, 2015)

Buprenorphine Formulations: Treatment of Opioid Use Disorder

Drug	Formulation	Recommended maintenance dosage	Cost*
Monotherapy			
Buprenorphine (generic)	2- and 8-mg sublingual tablets	Target: 16 mg per day Range: 4 to 24 mg per day	$99 for 60 8-mg tablets
Probuphine	74.2-mg subdermal implants	4 implants for 6 months	$863
Combination medications			
Bunavail	2.1/0.3-, 4.2/0.7-, and 6.3/1-mg buccal films	Target: 8.4/1.4 mg per day Range: 2.1/0.3 to 12.6/2.1 mg per day	$486 for 60 4.2/0.7-mg films
Buprenorphine/ naloxone (generic)	2/0.5- and 8/2-mg sublingual tablets	Target: 16/4 mg per day Range: 4/1 to 24/6 mg per day	$205 for 60 8/2-mg tablets
Suboxone film	2/0.5-, 4/1-, 8/2-, and 12/3-mg sublingual films	Target: 16/4 mg per day Range: 4/1 to 24/6 mg per day	$468 for 60 8/2-mg films
Zubsolv	1.4/0.36-, 5.7/1.4-, 8.6/2.1-, and 11.4/2.9-mg sublingual tablets	Target: 11.4/2.9 mg per day Range: 2.9/0.71 to 17.2/4.2 mg per day	$494 for 30 11.4/ 2.9-mg tablets

*—Estimated retail cost based on information obtained from http://www.goodrx.com (accessed January 7, 2018) and http://www.drugs.com (accessed April 27, 2017).

(*Am Fam Physician.* 2018 Mar 1; 97(5):313-320)

MAT: Considerations for Acute Pain

- Buprenorphine:
  - Acute pain: NSAIDS(ketorolac)
  - Moderate pain: divided doses or extra doses of bupe
  - Elective surgery: d/c 24-36 hours before
  - Severe acute pain: high potency opioids/regional anesthesia
- Naltrexone:
  - IM: d/c 30 days before elective surgery
  - PO: d/c 72 hours before elective surgery

(ASAM National Practice Guideline, 2015)

Screening for SUD: Single Question

- “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”
- 100% sensitive
- 73.5% Specific

(Smith PC, et al., 2010)

Use PDMP to Identify:

- MME/day
- “Doctor shoppers”: Think: Opportunity for treatment!
- Dangerous combinations
- Those at highest risk of overdose
- Login - Mississippi Prescription Monitoring Program (pmpaware.net)

Urine Drug Testing (UDT): Negative Results

- Negative test does NOT:
  - R/O substance use
  - R/O out SUD
- Negative test DOES mean:
  - Targeted substance has not been used in detection window
  - Possible use below cut off level

(ASAM Consensus Document, 2017)

Point of Service UDT

- 18 panel + temperature
- Tests for buprenorphine, opiates, oxycodone, methadone, fentanyl, tramadol, and EtG.
- Cost: $2.89/cup

Diversion Strategies

- Frequent office visits (weekly in early treatment)
- Urine drug testing
- Recall visits for pill counts
- Use of PDMP
- Limiting use of Subutex (monotherapy):
  - Lactating or pregnant females
  - Naloxone allergies

(ASAM National Practice Guideline, 2015)

Patient Characteristics Associated with Successful MAT

- Substance-free, safe home environment
- Stable or controlled medical or psychiatric comorbidities
- Sporadic opioid use is not uncommon in the first few months

(ASAM National Practice Guideline, 2015)

Treatment Resources

- www.asam.org
- www.findtreatment.samhsa.gov.
- www.addictionguide.com
- www.drugabuse.gov/publications/seeking-drug-abuse-treatment-know-what-to-ask/introduction
- www.samhsa.gov
- http://www.supportprop.org/.

- Thank You!!!

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  https://www.samhsa.gov/resource/ebp/tip-63-medications-opioid-use-disorder.

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