

Module 1

Medications for Treating Opioid Use Disorder

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Case:

A friend asks for your advice...

- His 26-year-old niece was admitted to a detox after an opioid overdose
- Niece's substance use history:
 - Opioid use after a rotator cuff tear in high school
 - Obtained opioids from friends
 - Opioid overdose her senior year
 - After taking time off, she remained in recovery by going to narcotics anonymous (NA) and completed college
 - Recently relapsed after dating someone who was actively using opioids
 - Never treated with medications for opioid use disorder
 - No history of other drug, alcohol or tobacco use or HIV and hepatitis C

DSM-5: 11 Criteria for Substance Use Disorder

Uncontrolled use

1. Using in larger amounts or for longer than intended
2. Repeated unsuccessful efforts to cut back or control use

Use despite negative consequences

1. Social problems caused/exacerbated by use
2. Being in physically hazardous settings
3. Physical or psychological problems caused or worsened by use

More time

1. Great deal of time spent using, obtaining, recovering
2. Important things given up or reduced by use
3. Failure to fulfil major obligations due to substance use

“Biological”

1. Craving
2. Tolerance
3. Withdrawal

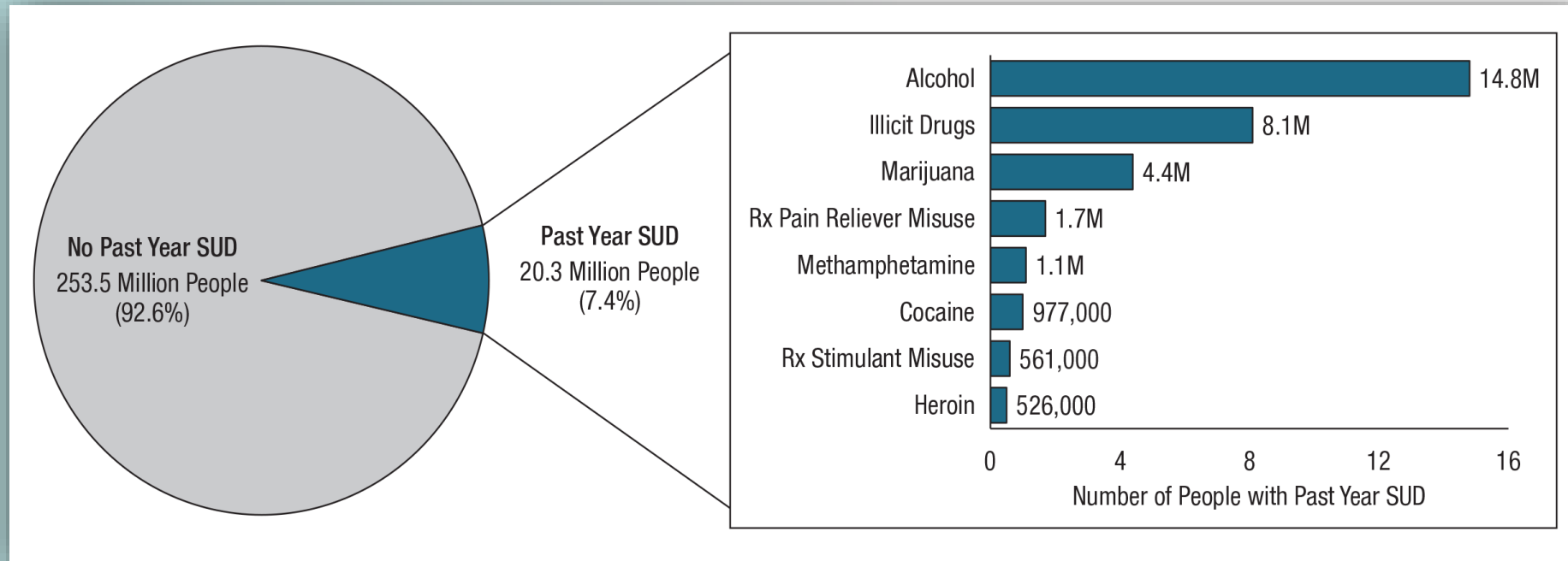
Number of symptoms

Mild: 2-4

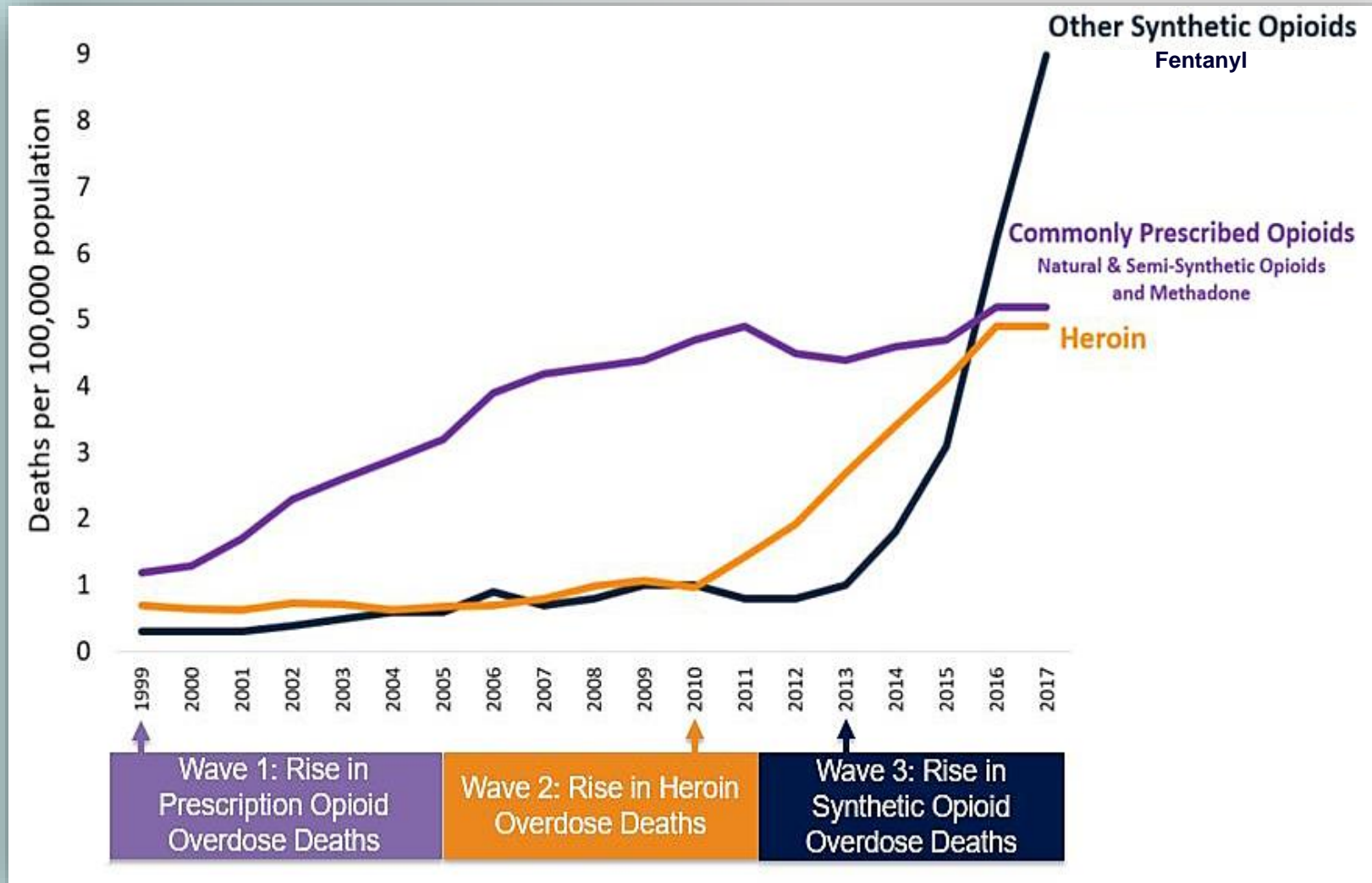
Moderate: 4-5

Severe: 6+

Past Year Substance Use Disorder



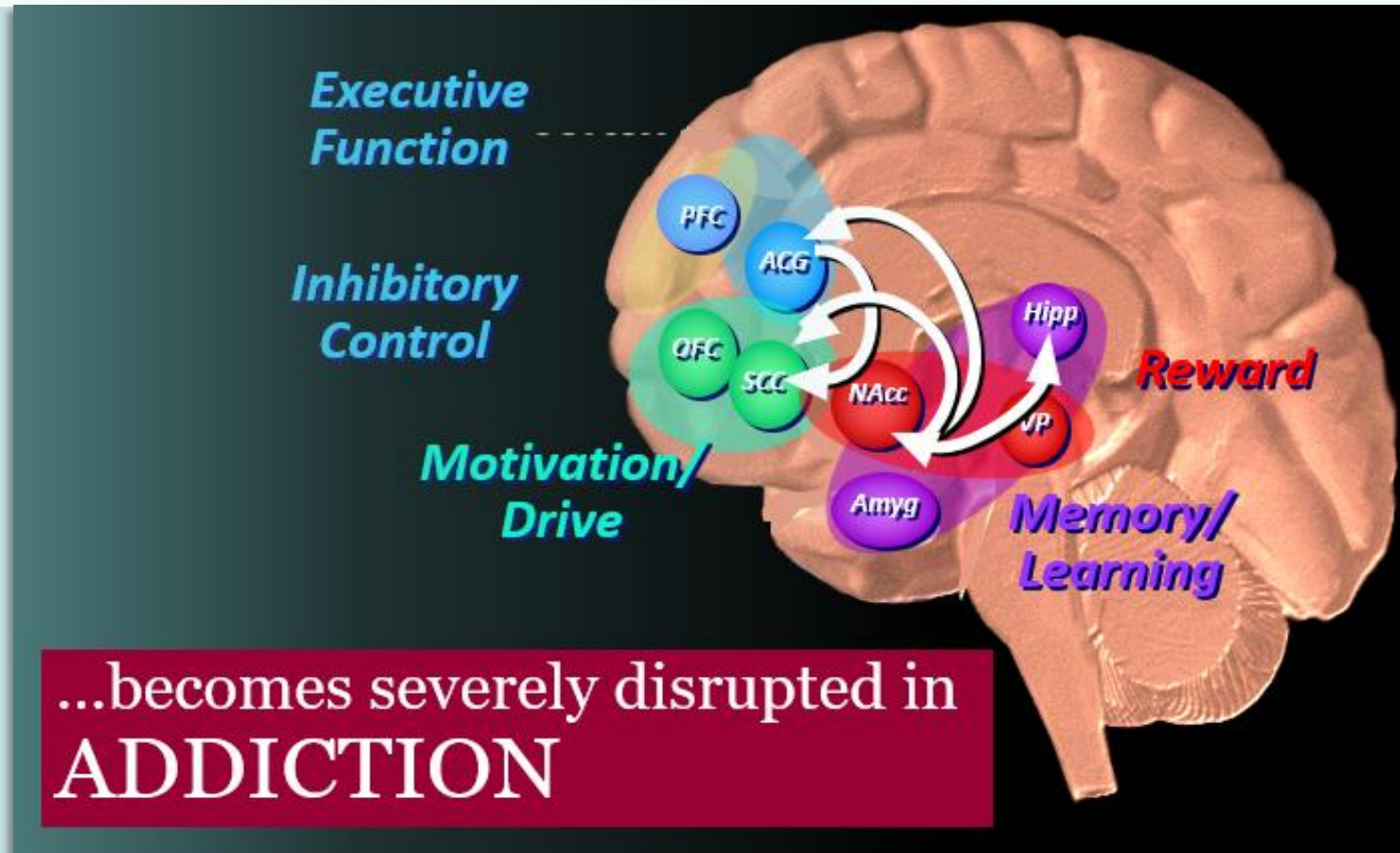
Overdoses by Specific Opioid



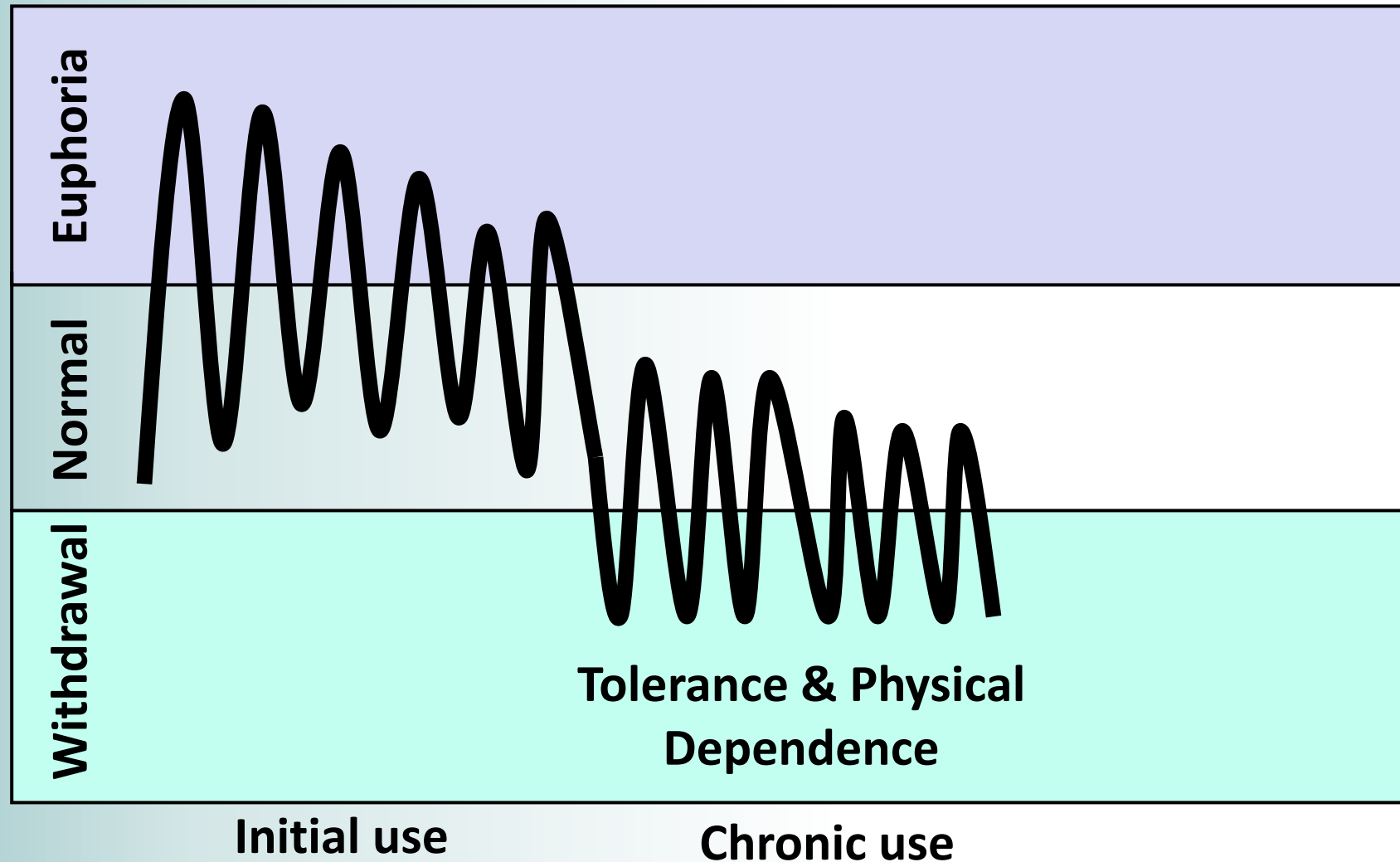
Source: Centers of Disease Control and Prevention (CDC) <https://www.cdc.gov/>

Neurobiology of Opioid Use Disorder

Fine balance in connections that normally exists between **reward, motivation/drive, learning/memory** and **inhibitory control**...



Natural History of OUD



Opioid Detoxification Outcomes

- Low rates of treatment retention
- High rates of relapse post-treatment
 - Less than 15% abstinent at 12 months
 - Increased rates of overdose due to decreased tolerance

O'Connor PG. *JAMA*. 2005;294(8):961-3.

Mattick RP, et al. *Lancet*. 1996;347(8994):97-100.

Stimmel B, et al. *JAMA*. 1977;237(12):1216-20.

Reasons for Relapse

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

Case (cont.)

Some options for your friend's niece

- Residential treatment
- Outpatient behavioral treatment
- Narcotics Anonymous (NA)
- Overdose prevention education and naloxone prescription
- **Medications for Opioid Use Disorder (MOUD)**

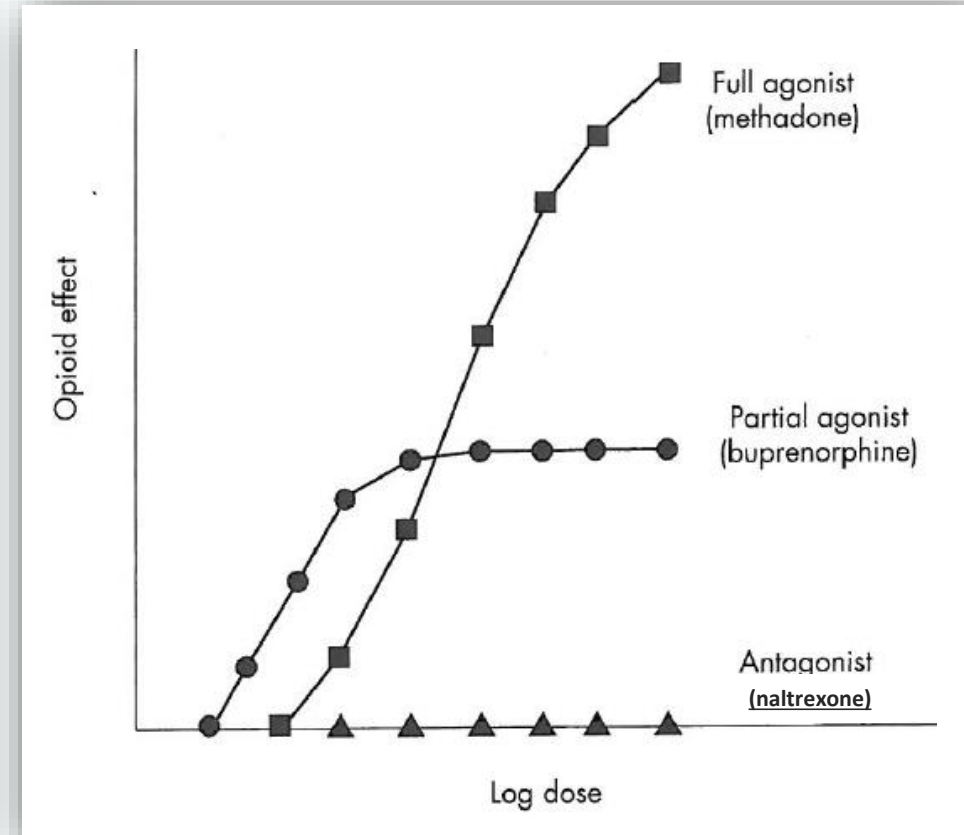
Medications for OUD (MOUD)

Goals

- Alleviate opioid withdrawal
- Create opioid blockade
- Alleviate drug craving

Options

- Opioid antagonist therapy
 - **Naltrexone**
- Opioid agonist therapy
 - **Methadone** (full agonist)
 - **Buprenorphine** (partial agonist)



Naltrexone

- Mu-opioid receptor antagonist
- Not a controlled substance
- No special restrictions on prescribing
- No misuse potential, no street value, no physical dependence
- Oral (Duration of action: 24-48 hours)
- Intramuscular extended-release (Duration of action: 1 month)
- Patients physically dependent on an opioid must be opioid free for a minimum of 7-10 days before starting naltrexone treatment
- Both formulations also approved for treating alcohol use disorder

Naltrexone

- Adherence and outcomes better with extended-release (intramuscular) than oral formulation
- Efficacy
 - Opioid blockade
 - Reduced opioid craving
 - Increased abstinence from illicit opioid use
 - Neither formulation shown to have mortality benefit
- Difficulty getting started in a patient with physical dependence
- Lower adherence and retention due to no re-enforcing effects
- No withdrawal when discontinued as opposed to opioid agonist treatment (i.e., methadone and buprenorphine)

Johansson BA, et al. *Addiction*. 2006;101:491-503.

Krupitsky E, et al. *Lancet*. 2011;377:1506-1513.

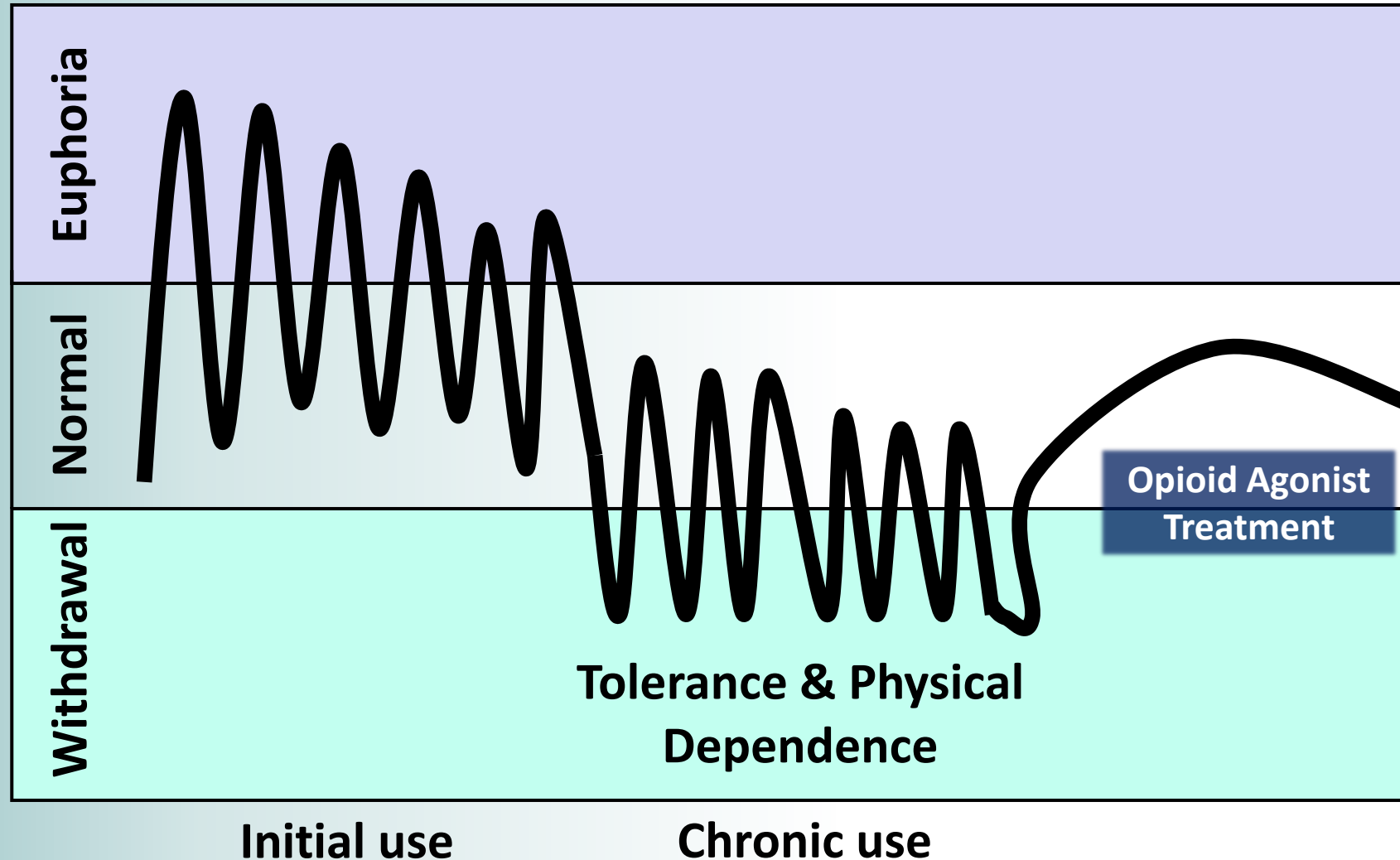
Sullivan MA, et al. *Am J Psychiatry*. 2019;176:129-137.

Lee JD, et al. *Lancet*. 2018;391:309-318.

Jarvis BP, et al. *Addiction*. 2018;113:1188-1209.

Opioid Agonist Treatment (OAT)

Methadone
Buprenorphine



Methadone

- Synthetic mu-opioid receptor agonist
- Slow onset of action; long variable elimination $\frac{1}{2}$ life
- DEA schedule II controlled substance
- Oral: Duration of action
 - 24-36 hours to treat OUD
 - 6-8 hours to treat pain
- For treating OUD: only dispensed through government-licensed/regulated opioid treatment programs **NOT prescribed** in an office-based setting

Opioid Treatment Programs (OTP)

- Methadone dosing
 - Observed daily \Rightarrow “Take homes”
- Daily nursing assessment
- Individual and/or group counseling
- Drug testing
- Psychiatric services
- Medical services

Methadone Efficacy

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

Mattick RP, et al. *Cochrane Database Syst Rev.* 2009;3.

Sordo L, et al. *BMJ.* 2017;357.

Farrell M, et al. *BMJ.* 1994;309:997.

Hser YI, et al. *Addiction.* 2016;111:695-705.

Joseph H, et al. *Mt Sinai J Med.* 2000;67:347-364.

Methadone Limitations

- Methadone can prolong the QTc interval and cause arrhythmias such as torsade de pointes
- **Opioid Treatment Programs (OTP)**
 - Limited access
 - Inconvenient, can be perceived as punitive
 - Mixes stable and unstable patients
 - Lack of privacy
 - No ability to “graduate” from program
- **Stigma** “Substituting one drug for another...I don’t believe in methadone”

Buprenorphine

- **Mu-opioid receptor partial agonist** (ceiling effect on CNS and respiratory depression)
- **Kappa-opioid receptor antagonist** (antidepressant and anxiolytic effects)
- DEA schedule III controlled substance
- Oral duration of action (24-36 hours to treat OUD; 6-8 hours to treat pain)
- Available alone and in combo with the opioid antagonist naloxone
 - Taken orally, naloxone is poorly absorbed and has no clinical effects
 - Intended to decrease IV or intranasal misuse

Buprenorphine Formulations

For **ODU** (off-label for pain)

Drug		Formulations
Buprenorphine		
	generic	2, 8 mg SL tabs
	Sublocade	100 mg SQ injection
Buprenorphine/Naloxone		
	generic	2/0.5, 8/2 mg SL tabs
	Bunavail	2.1/0.3, 4.2/0.7, 6.3/1 mg buccal film
	Suboxone	2/0.5, 4/1, 8/2, 12/3 mg SL film
	Zubsolv	1.4/0.36, 5.7/1.4 mg SL tab

For Pain NOT OUD

Drug	Formulations
Belbuca	Buccal q12h
Butrans	Transdermal 7-day patch
Buprenex	IM/IV q6h

Buprenorphine Efficacy Summary

Buprenorphine (16-24 mg) more effective than placebo and equally effective to moderate methadone doses (80 mg) on primary outcomes of:

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

Johnson RE, et al. *NEJM*. 2000;343:1290-7.

Fudala PJ, et al. *NEJM*. 2003;349:949-58.

Kakko J, et al. *Lancet*. 2003;361:662-8.

Sordo L, et al. *BMJ*. 2017;357:j1550.

Mattick RP, et al. *Conchrane Syst Rev*. 2014

Parran TV, et al. *Drug Alcohol Depend*. 2010;106:56-60.

“Overcoming My Fear of Treating OUD”

Dr. P was reluctant to obtain a waiver to prescribe buprenorphine for the treatment of OUD until her patient (Ms. L) with longstanding OUD died from an opioid overdose...

- “Caring for these patients has become the most meaningful part of my practice.”
- “Providing some sense of normalcy for patients whose lives are roiled by overdose and estrangement is the most profound therapeutic intervention I’ve engaged in as a caregiver.”
- “I did not know what Ms. L. meant all those years ago when she said that she only wished to feel normal again. I wish that I’d listened more closely. I wish that I had not been afraid.”

Primary Care–Based Models for the Treatment of Opioid Use Disorder

A Scoping Review

P. Todd Korthuis, MD, MPH; Dennis McCarty, PhD; Melissa Weimer, DO, MCR; Christina Bougatsos, MPH; Ian Blazina, MPH; Bernadette Zakher, MBBS; Sara Grusing, BS; Beth Devine, PhD, PharmD, MBA; and Roger Chou, MD

Models for integration into primary care settings across diverse health care settings

Hub and Spoke Model	Centralized intake, initial management	Coordination/integration between hub and spoke and within each primary care site
Maryland Model	Collaborative integrated prescribing model	Initial assessment and transferred to Federally Qualified Health Centers
Massachusetts Model	Nurse led within primary care settings	Team based complex care management
Medicaid Health Home	Flexible model with integrated behavioral health and primary care	Provider and community engagement and education

Monitoring Patients on MOUD

- **Drug tests**
 - *Information on* **therapeutic adherence**
 - *Information on* **use or non-use of illicit drugs**
- **Medication counts**
 - *Information on* **medication adherence**
 - *Information concerning* **for diversion**
- **Prescription drug monitoring program**
 - *Information on* **harmful polypharmacy**
 - *Information on* **multiple provider use**

Monitoring Patients on MOUD

- **Relapse prevention**

- Educate on how to anticipate/avoid/cope with triggers (negative affect, craving/cues, social pressure)

- **Relapse management**

- After initial use (a lapse), patients may experience guilt, shame resulting in return to heavy use
- Recovery is a learning process, lapses provide valuable lessons

- **Overdose education and naloxone distribution**

- Most opioid users do not use alone
- Know risk factors such as mixing substances, unknown source of drugs
- www.prescribetoprevent.org

Managing a Patient Who Relapses

Assess the cause for relapse

– Withdrawal or craving?

- Review other medications that may interact with MOUD
- Review other illicit drug use
- Consider dose adjustment of MOUD

– Social stressors?

- Enhance behavioral therapies
- Address social determinants of health

– Negative affect?

- Assess for untreated psychiatric comorbidities

Starting MOUD Wherever Patients Present

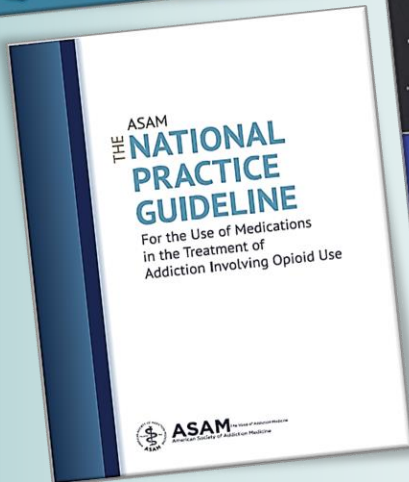
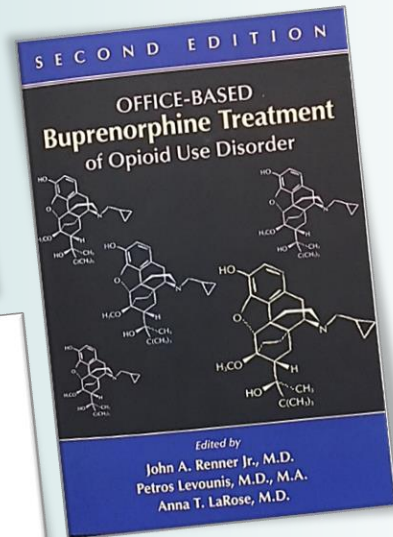
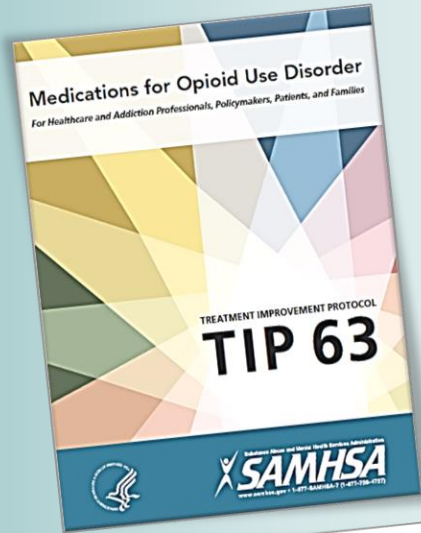
Inpatient Service (Liebschutz JM, et al. *JAMA Intern Med.* 2014;174:1369-76.)

- Compared with inpatient detoxification, initiation of and linkage to buprenorphine treatment is effective for engaging medically hospitalized patients who are not seeking addiction treatment and reduces illicit opioid use after hospitalization

Emergency Department (D'Onofrio G, et al. *JAMA.* 2015;313:1636-44.)

- ED-initiated buprenorphine treatment versus brief intervention and referral significantly increased engagement in addiction treatment and reduced self-reported illicit opioid use

Resources



- National Institute on Drug Abuse
<https://www.drugabuse.gov/>
- Substance Abuse and Mental Health Administration <https://www.samhsa.gov/>
- Centers for Disease Control and Prevention <https://www.cdc.gov/>
- American Society of Addiction Medicine <https://www.asam.org/>
- Providers Clinical Support System (PCSS) <https://pcssnow.org/>