OPIOID USE DISORDER

MEDICATION ASSISTED TREATMENT

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Disclaimer

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AMA AMERICAN MEDICAL ASSOCIATION

Advocacy Resource Center

Advocating on behalf of physicians and patients at the state level

Issue brief: Reports of increases in opioid-related overdose and other concerns during COVID pandemic

***Updated May 25, 2020**

As the COVID-19 global pandemic continues, so does the nation's opioid epidemic. The AMA is greatly concerned by an increasing number of reports from national, state and local media suggesting increases in opioid-related mortality—particularly from illicitly manufactured fentanyl and fentanyl analogs. More than 20 states have reported increases in opioid-related mortality as well as ongoing concerns for those with a mental illness or substance use disorder in counties and other areas within the state. See below for select national and state examples.

THE OPIOID EPIDEMIC BY THE NUMBERS

130+
People died every day from opioid-related drug overdoses[3] (estimated)

10.3 m
People misused prescription opioids in 2018[1]

47,600
People died from overdosing on opioids[2]

2.0 million
People had an opioid use disorder in 2018[1]

81,000
People used heroin for the first time[1]

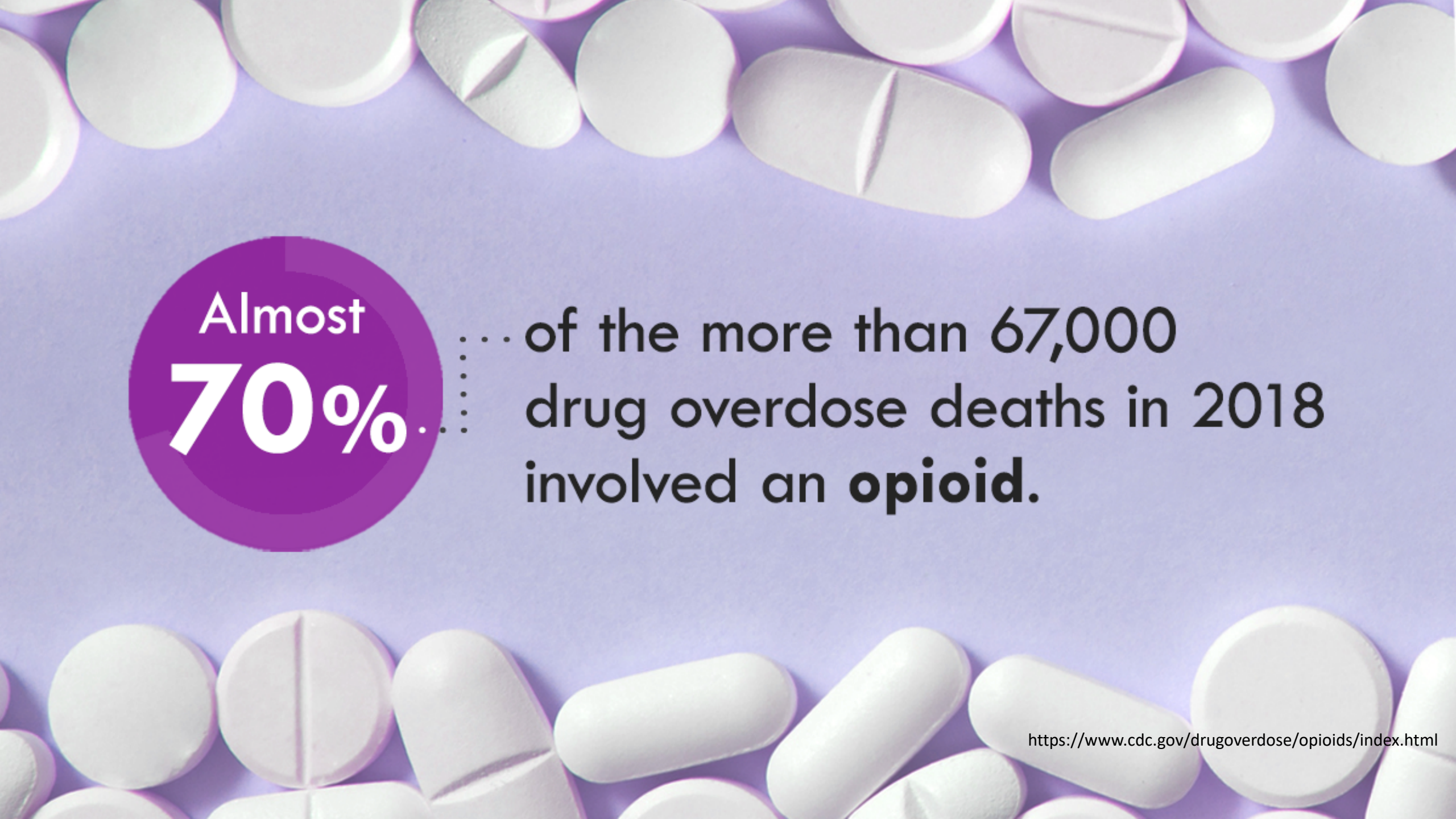
808,000
People used heroin in 2018[1]

2 million
People misused prescription opioids for the first time[1]

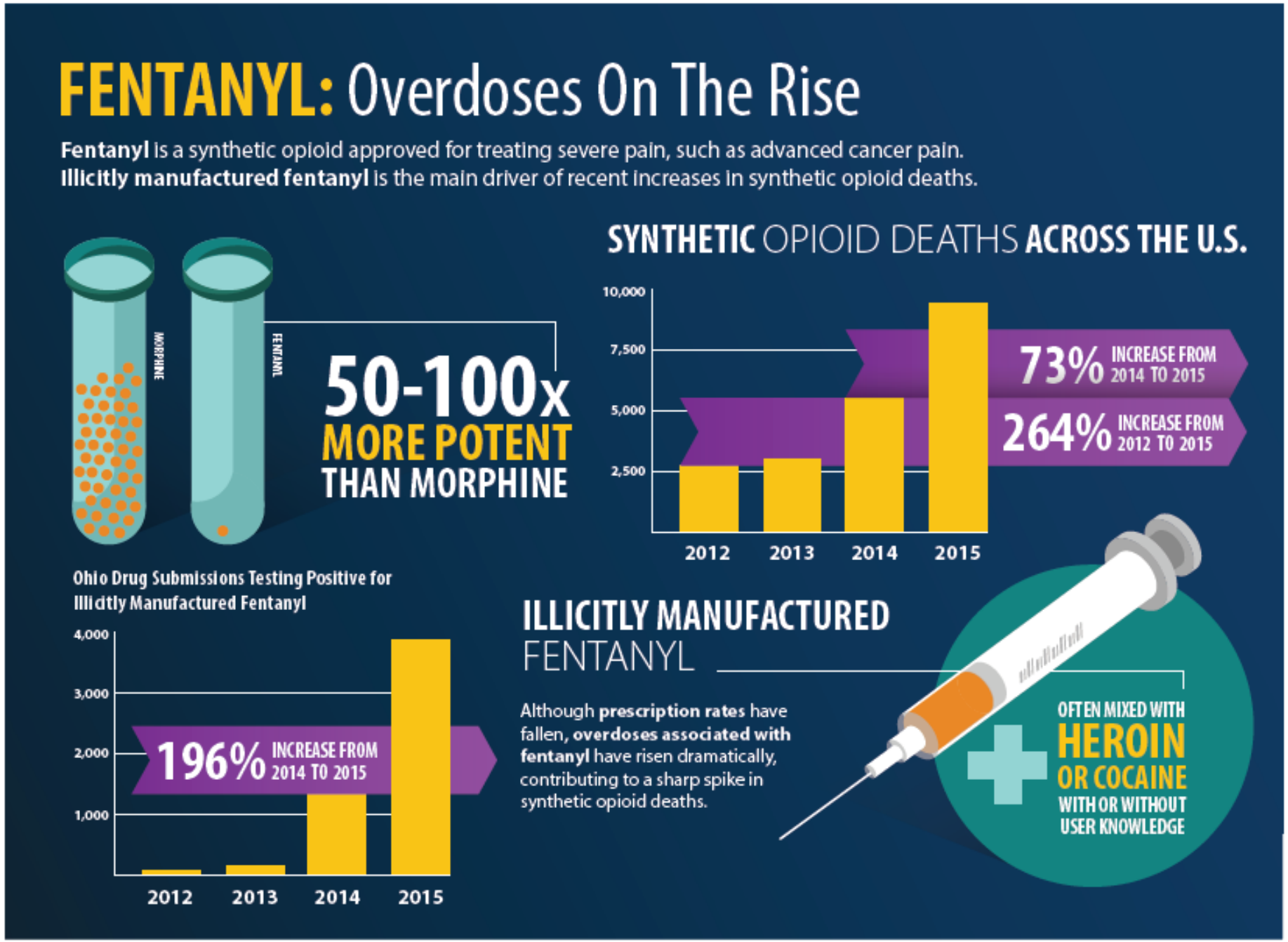
15,349
Deaths attributed to overdosing on heroin (in 12-month period ending February 2019)[2]

32,656
Deaths attributed to overdosing on synthetic opioids other than methadone (in 12-month period ending February 2019)[2]

https://www.hhs.gov/opioids/about-the-epidemic/index.html



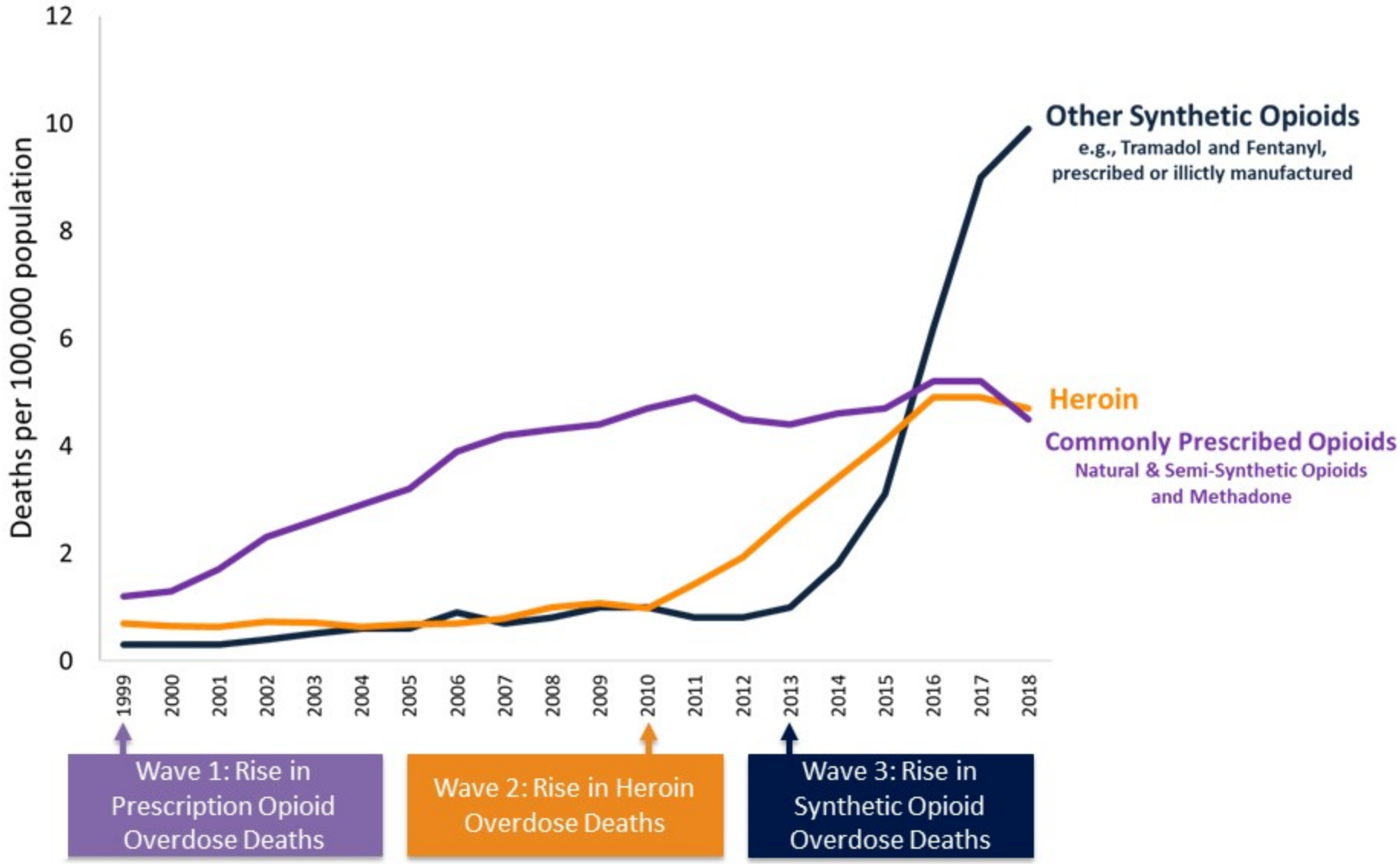
https://www.cdc.gov/drugoverdose/opioids/index.html



https://www.cdc.gov/drugoverdose/pdf/pbss/PBSS-Report-072017.pdf

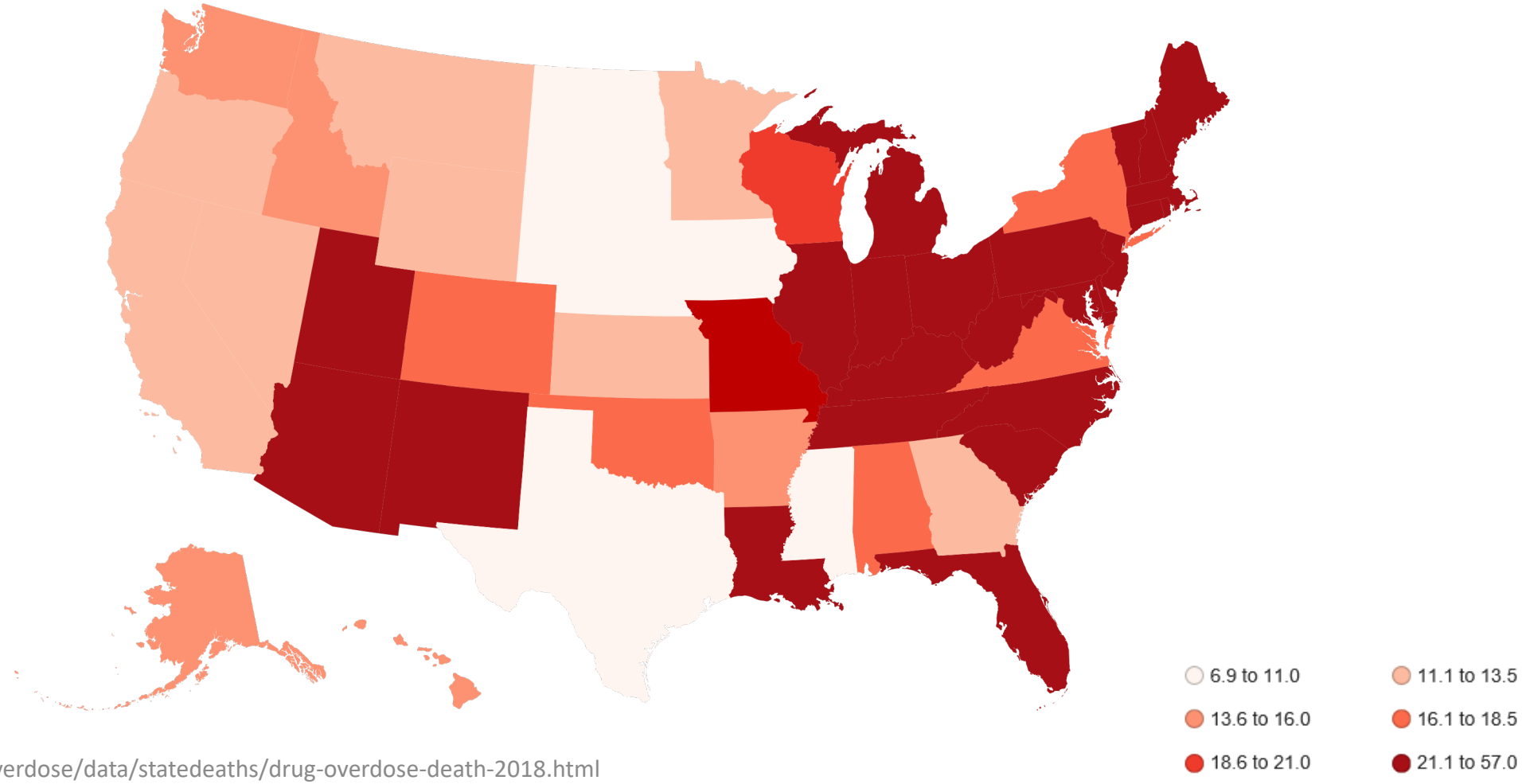
Lethal Doses

3 Waves of the Rise in Opioid Overdose Deaths



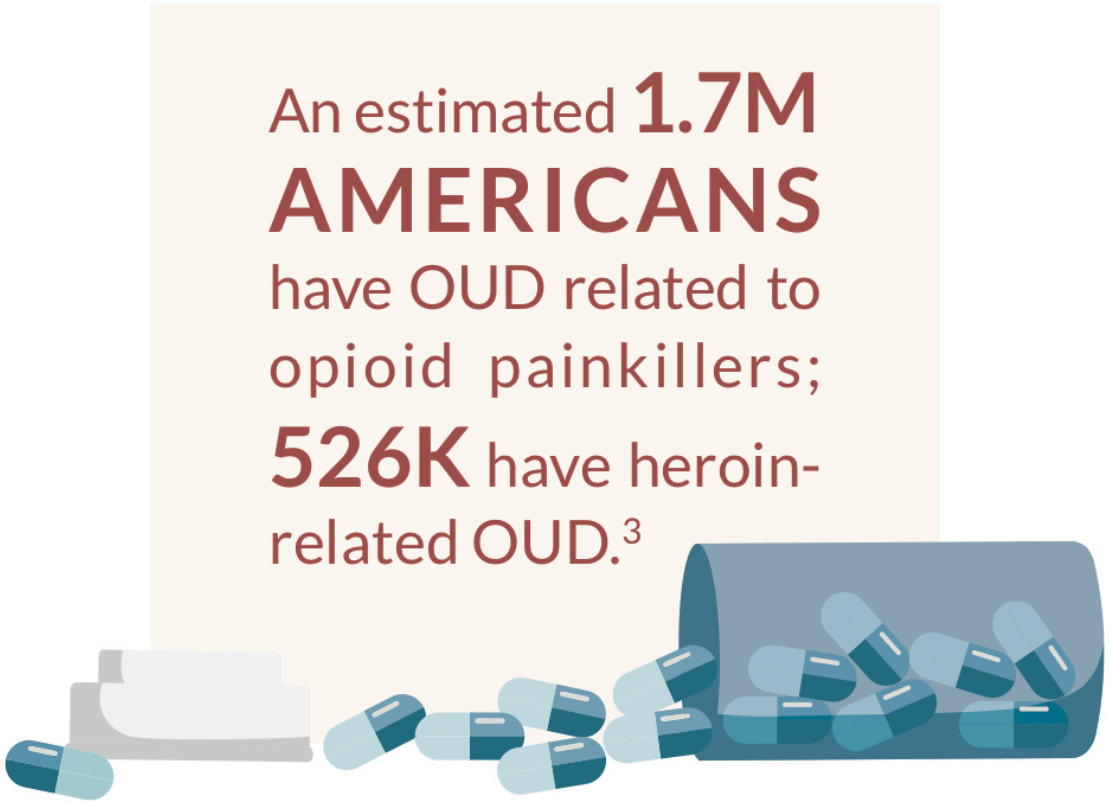
SOURCE: National Vital Statistics System Mortality File.

Michigan Hit Hard



https://www.cdc.gov/drugoverdose/data/statedeaths/drug-overdose-death-2018.html

Opioid Use Disorder



- Data: Dept of Health & Human Services 2018
- Probably higher, but difficult to ascertain.
  - Self-report unreliable
  - Periods of remission and relapse common

U.S. Department of Health and Human Services Substance Abuse and Mental Health Services Administration Center for Substance Abuse Treatment, TIP #63, Publication No. PEP20-02-01-006 First released 2018. Revised 2019 and 2020

Addiction

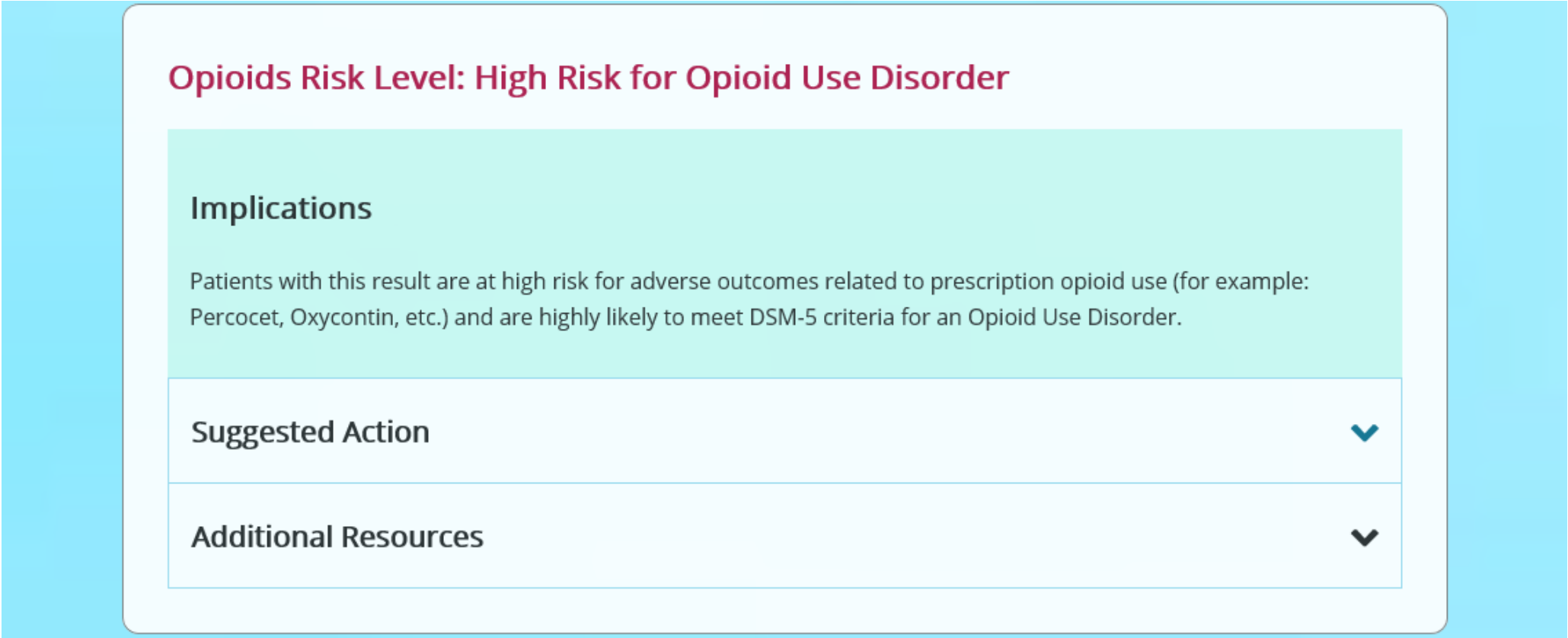
- American Society of Addiction Medicine (ASAM): “Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual’s life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.”
- Obsession or compulsion to use a drug despite an inability to control it, resulting in negative consequences

Single Item Screen

- How many times in the past year have you used an illegal drug or prescription medication for non-medical reasons?
- Sensitivity 85.1%, Specificity 88.6% for identifying a substance use disorder
- Any use is considered positive and further eval warranted
  - Consider Modified ASSIST or
  - TAPS Tool (Tobacco, Alcohol, Prescription Medications, and Other Substances Use)

McNeely, et al, J Gen Intern Med, 2015;30(12):1757-1764

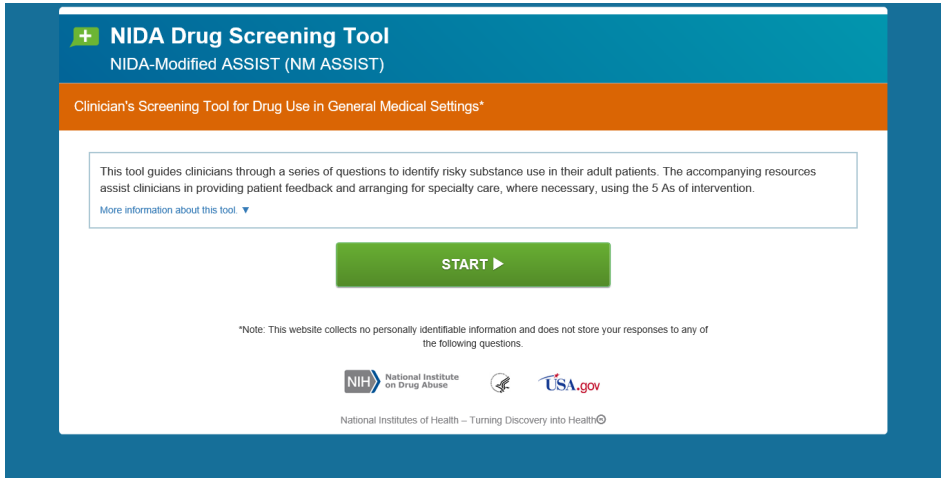
National Institute on Drug Abuse (NIDA): TAPS Tool



https://www.drugabuse.gov/taps/#/

Screening for Opioid Use Disorder

- No validated screening tools for OUD specifically
- NIDA Modified ASSIST good, but cumbersome. Can be completed online.



https://www.drugabuse.gov/nmassist/

DSM-5 Opioid Use Disorder

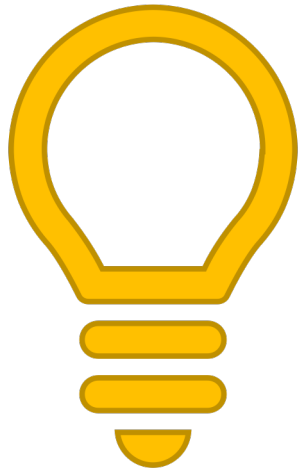
Broad Domain	DSM-5 Diagnostic Criteria
CONTROL	Opioids are taken in larger amounts or over longer periods than intended
	Desire or unsuccessful attempts to cut down or control opioid use
	A great deal of time spent obtaining, using, or recovering from opioids
CRAVINGS	Craving, or a strong desire or urge to use opioids
CONSEQUENCES	Failure to fulfill major role obligations as a result of opioid use
	Continued opioid use despite social or interpersonal problems
	Diminished, social, occupational, or recreational activities due to opioid use
	Recurrent opioid use in physically hazardous situations
	Continued opioid us despite physical of psychological problems
COMPULSION	Tolerance
	Withdrawal

2-3 Mild
4-5 Moderate
6+ Severe

Opioid Withdrawal Symptoms

- Lacrimation
- Rhinorrhea
- Yawning
- Restlessness
- Insomnia
- Dilated pupils
- Piloerection
- Myalgias
- Arthralgias
- Abdominal cramping
- Nausea/Vomiting/Diarrhea
- Autonomic Instability: tachycardia, tachypnea, HTN/hypotension, fever
- Anxiety/Dysphoria

People with opioid addiction don’t steal to get high, they steal to avoid getting sick.



COWS Clinical Opiate Withdrawal Scale

Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9.

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 Pulse rate 80 or below 1 Pulse rate 81-100 2 Pulse rate 101-120 4 Pulse rate greater than 120	GI Upset: *over last 1/2 hour* 0 No GI symptoms 1 Stomach cramps 2 Nausea or loose stool 3 Vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 No report of chills or flushing 1 Subjective report of chills or flushing 2 Flushed or observable moistness on face 3 Beads of sweat *on* brow or face 4 Sweat streaming off face	Tremor *observation of outstretched hands* 0 No tremor 1 Tremor can be felt, but not observed 2 Slight tremor observable 4 Gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 Able to sit still 1 Reports difficulty sifting still, but is able to do so 3 Frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	Yawning *Observation during assessment* 0 No yawning 1 Yawning once or twice during assessment 2 Yawning three or more times during assessment 4 Yawning several times/minute
Pupil size 0 Pupils pinned or normal size for room light 1 Pupils possibly larger than normal for room light 2 Pupils moderately dilated 5 Pupils so dilated that only the rim of the iris is visible	Anxiety or irritability 0 None 1 Patient reports increasing irritability or anxiousness 2 Patient obviously irritable anxious 4 Patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 Not present 1 Mild diffuse discomfort 2 Patient reports severe diffuse aching of joints/ muscles 4 Patient is rubbing joints or muscles and is unable to sit still because of discomfort	Gooseflesh skin 0 Skin is smooth 3 Piloerrection of skin can be felt or hairs standing up on arms 5 Prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 Not present 1 Nasal stuffiness or unusually moist eyes 2 Nose running or tearing 4 Nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing Assessment:_____

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

Timing

- Signs and symptoms of **withdrawal may begin 6 to 12 hours** after the last dose of a **short-acting opioid and 24 to 72 hours after cessation of methadone**
- Last 4 days for short acting opioids, up to 14 for long-acting
- Post-acute withdrawal symptoms (PAWS): fatigue, anhedonia, poor appetite, insomnia, craving. May last for months.

Schuckit, Marc A, NEJM 375:4, July 28 2016

Detoxification

- Medications: Clonidine, buprenorphine, methadone, tramadol
- Adjunctive medications: benzodiazepines, antiemetics, antidiarrheals, NSAIDs, muscle relaxers, sleep aids, gabapentin
- Typically 3-30 days

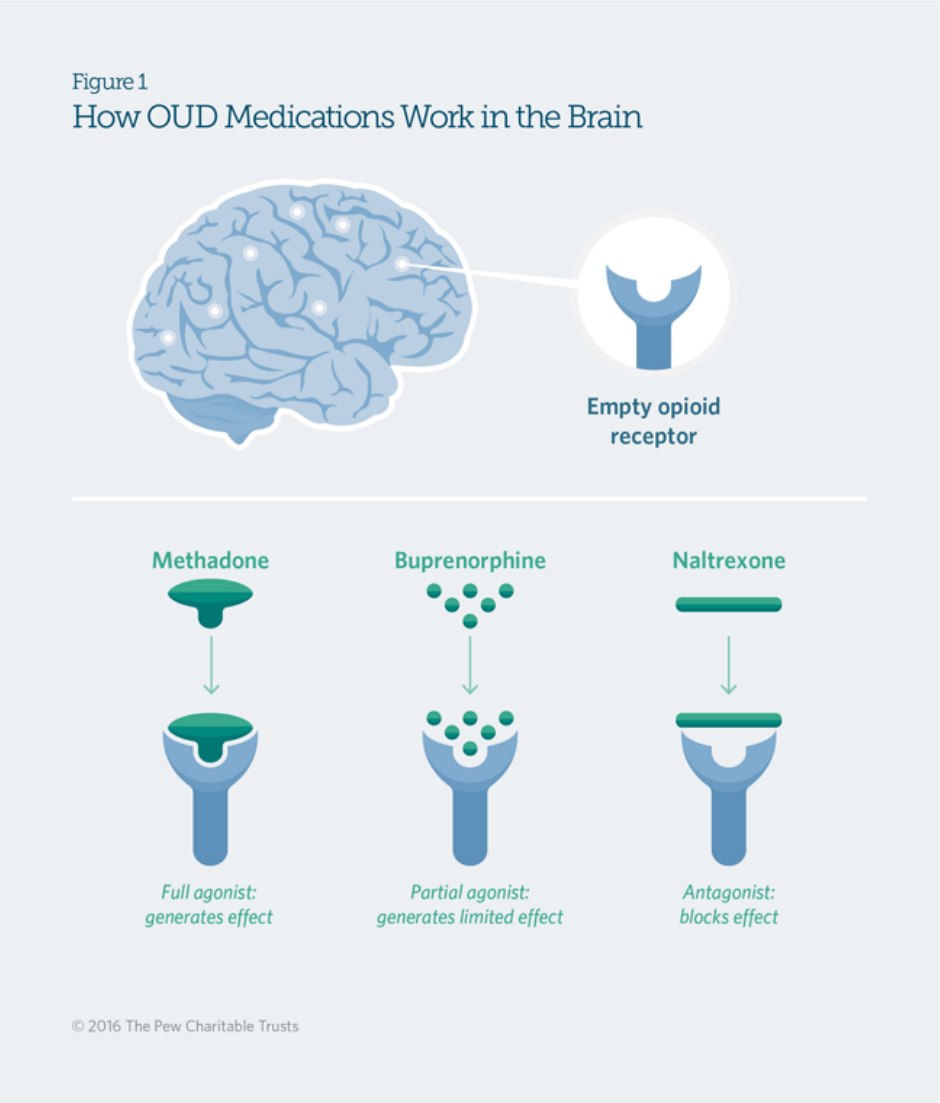
“Detoxification is good for a lot of things; staying off drugs is not one of them.”

-Walter Ling MD

Medication Assisted Treatment (MAT)

- Studies consistently show >80% patients out of detox will relapse
- Overdose risk higher after detox
- 3 FDA Approved Medications:
  - Buprenorphine: Agonist
  - Methadone: Agonist
  - Naltrexone (PO, IM): Antagonist

- **Opioid Agonists generally first line**



Wakeman, JAMA May 26,2020. Vol 323(20)

Naltrexone

- Approved by FDA in 1994
- Mechanisms:
  - Reduces cravings
  - Competitively blocks heroin and other opioids for up to 72 hours

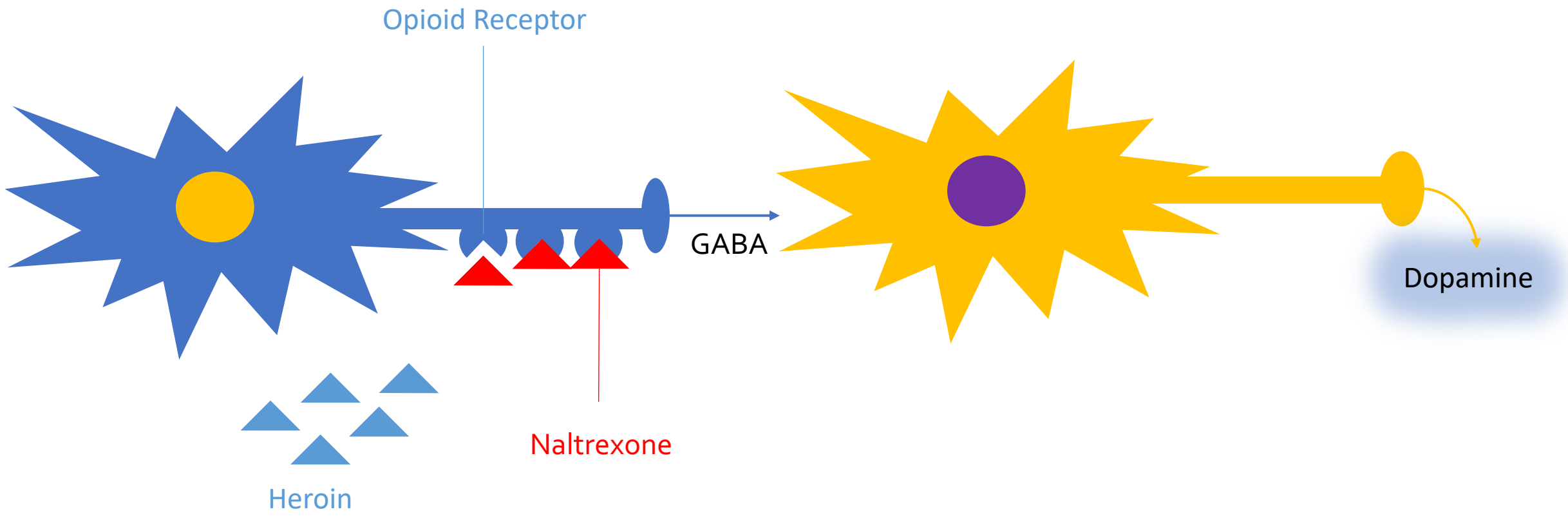
- Long acting form: Vivitrol. FDA approved for OUD 2010

Naltrexone Candidates

- Consider Vivitrol (XR-NTX) if:
  - Highly motivated and wish to be opioid free
  - Monitored patients or upon release from controlled environments (rehab, jail, prison, etc.)
  - Patient presents already opioid-free
  - Safety-sensitive occupations (driving, flying, railroad, utility, health care, etc.)
  - Structured/Sober living precludes use of agonists
  - Comorbid alcohol use disorder
  - Previous attempts with opioid agonists have gone poorly
  - Mild opioid use disorder

- Oral naltrexone is generally discouraged
  - Poor compliance
  - Increased relapse and overdose risk

Naltrexone Mechanism of Action



Ventral Tegmental Area GABA interneuron and dopamine neuron projecting to the Nucleus Accumbens

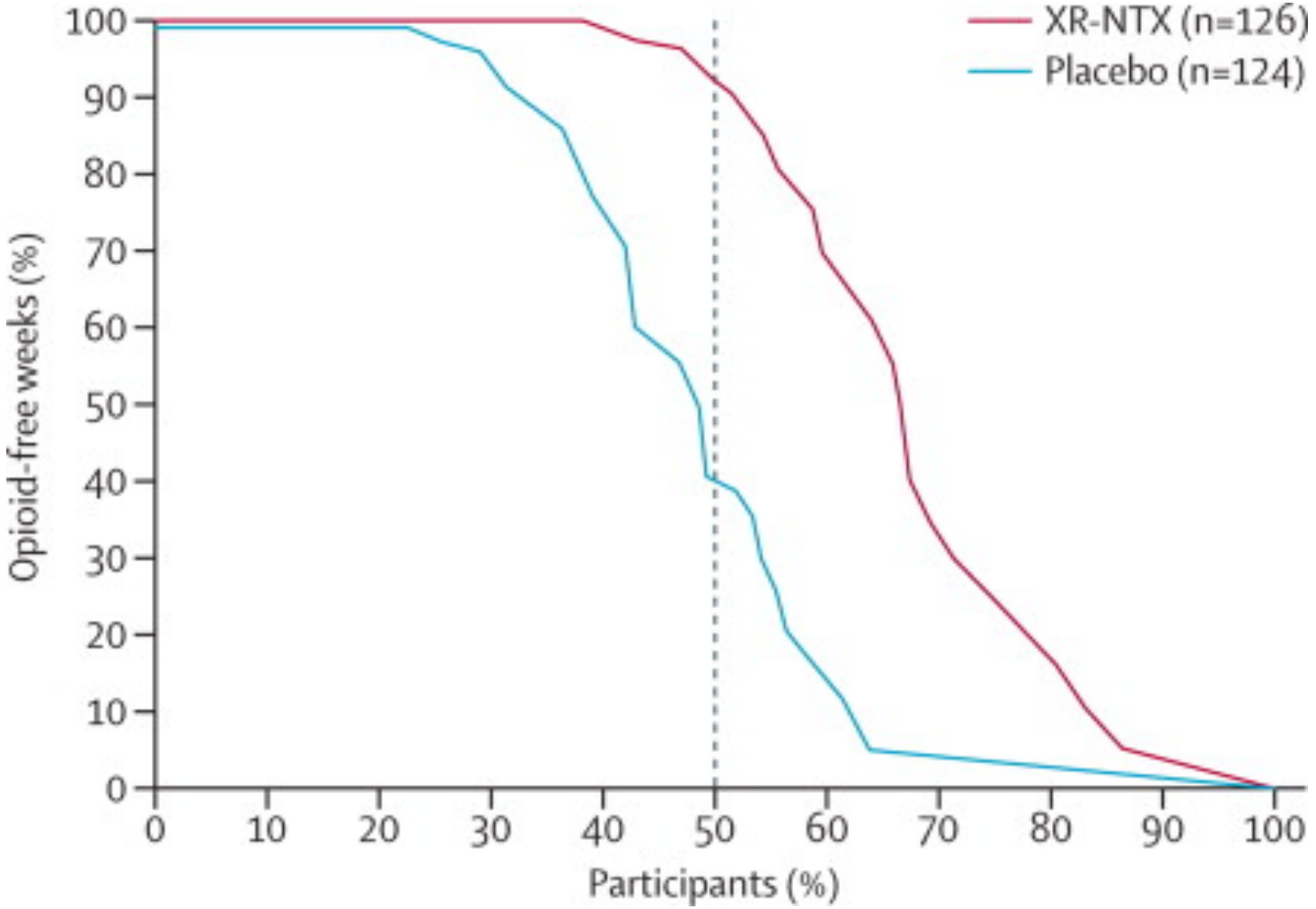
XR-NTX Superior to Placebo

- Krupitsky, et al, 2011
- N=250
- Randomized, double blind, placebo controlled
- 6 month follow up

- Median proportion of weeks of confirmed abstinence from opioids was 90% in XR-NTX group vs 35% in placebo group

Krupitsky, et al, Lancet Vol 377(9776), April 30 2011, pp 1506-1513

XR-NTX Superior to Placebo



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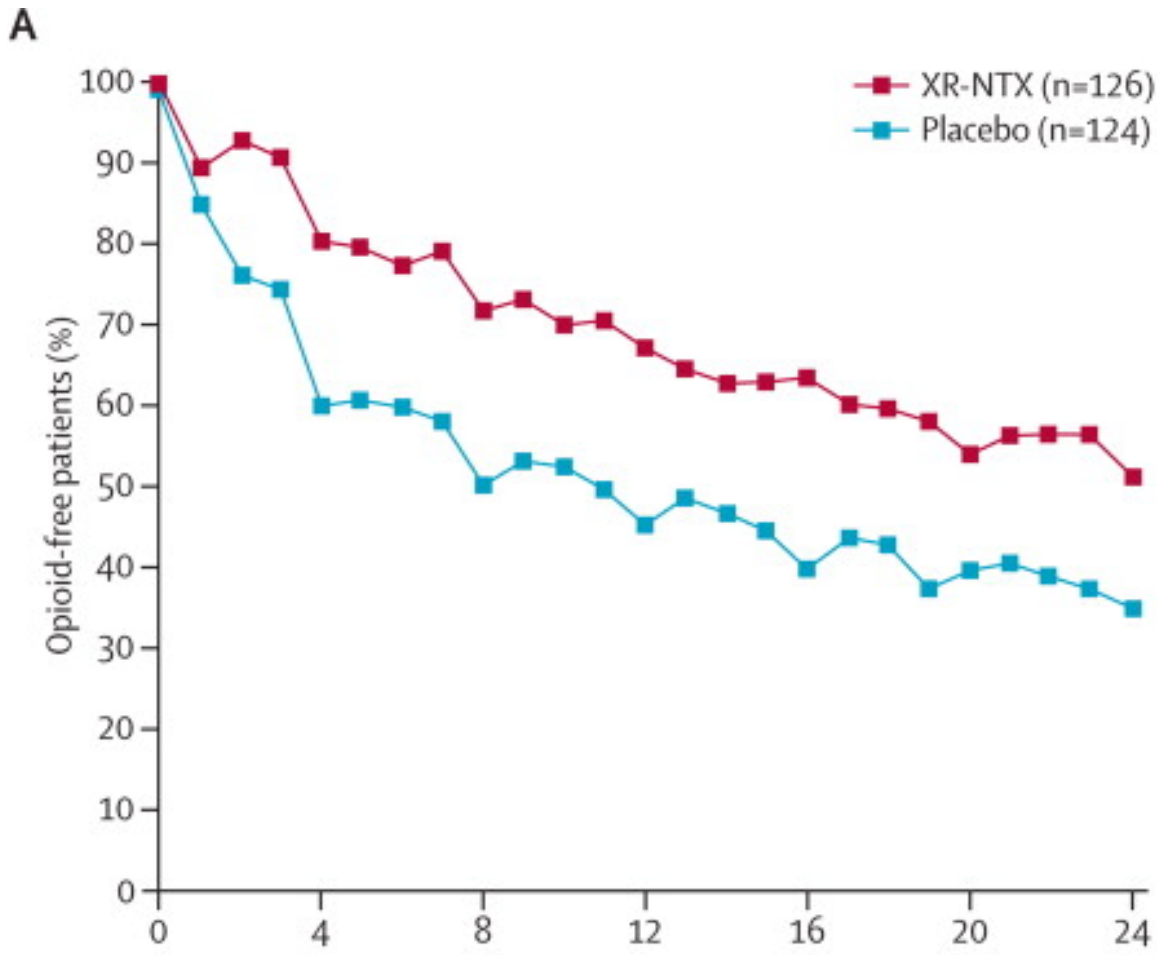
XR-NTX Superior to Placebo



Krupitsky, et al, Lancet Vol 377(9776), April 30 2011, pp 1506-1513

XR-NTX Not Inferior to Buprenorphine*

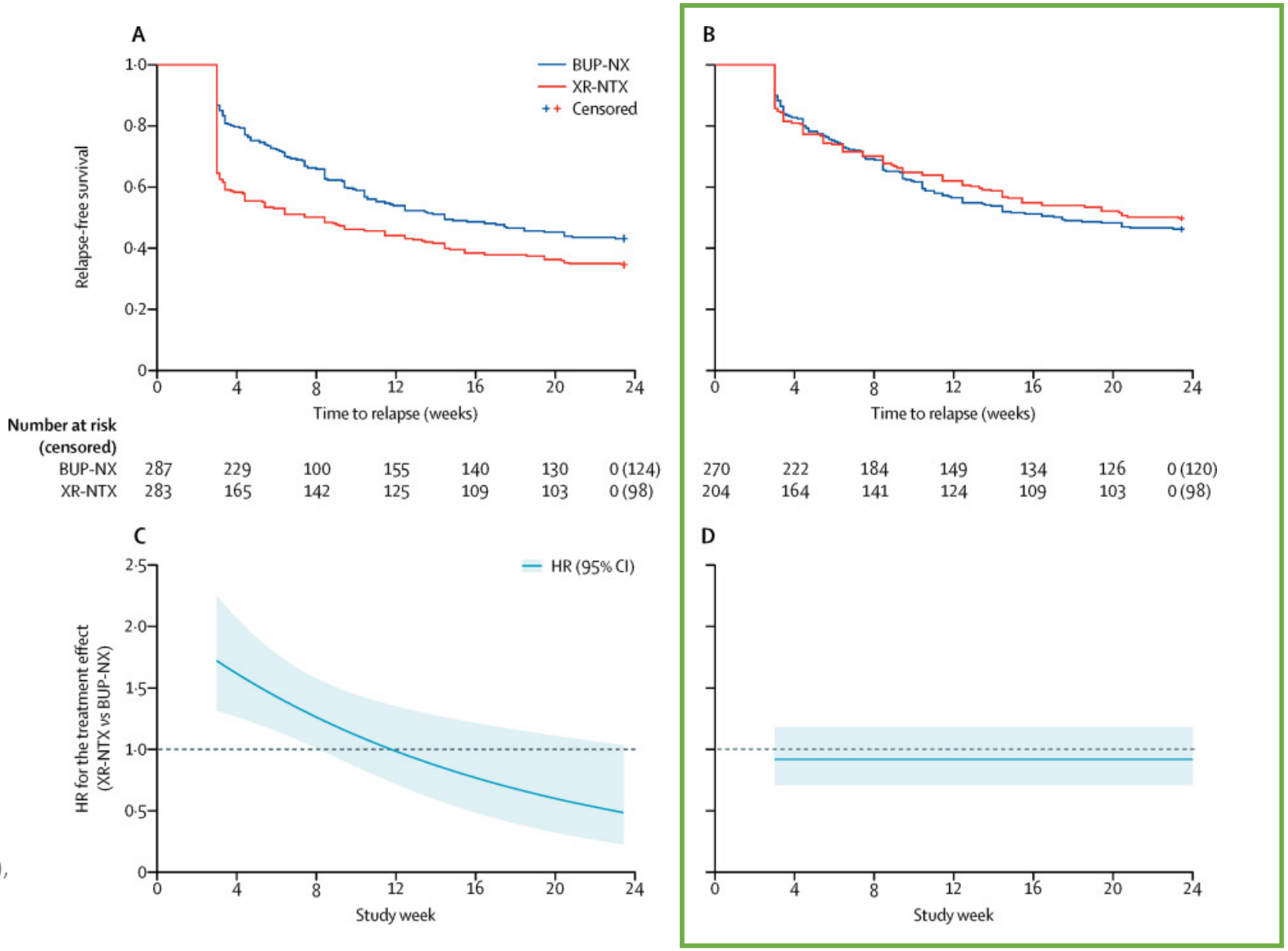
- Lee, et al. 2018
- N = 570
- Randomized to buprenorphine vs XR-NTX
- Followed 6 months

- Intention to treat group HR for relapse 1.36
- All early relapses due to XR-NTX induction failures
- Among those successfully induced (n=474), no significant difference between buprenorphine and XR-NTX

Lee, et al, Lancet, vol 391(10118), 2018, pp 309-318

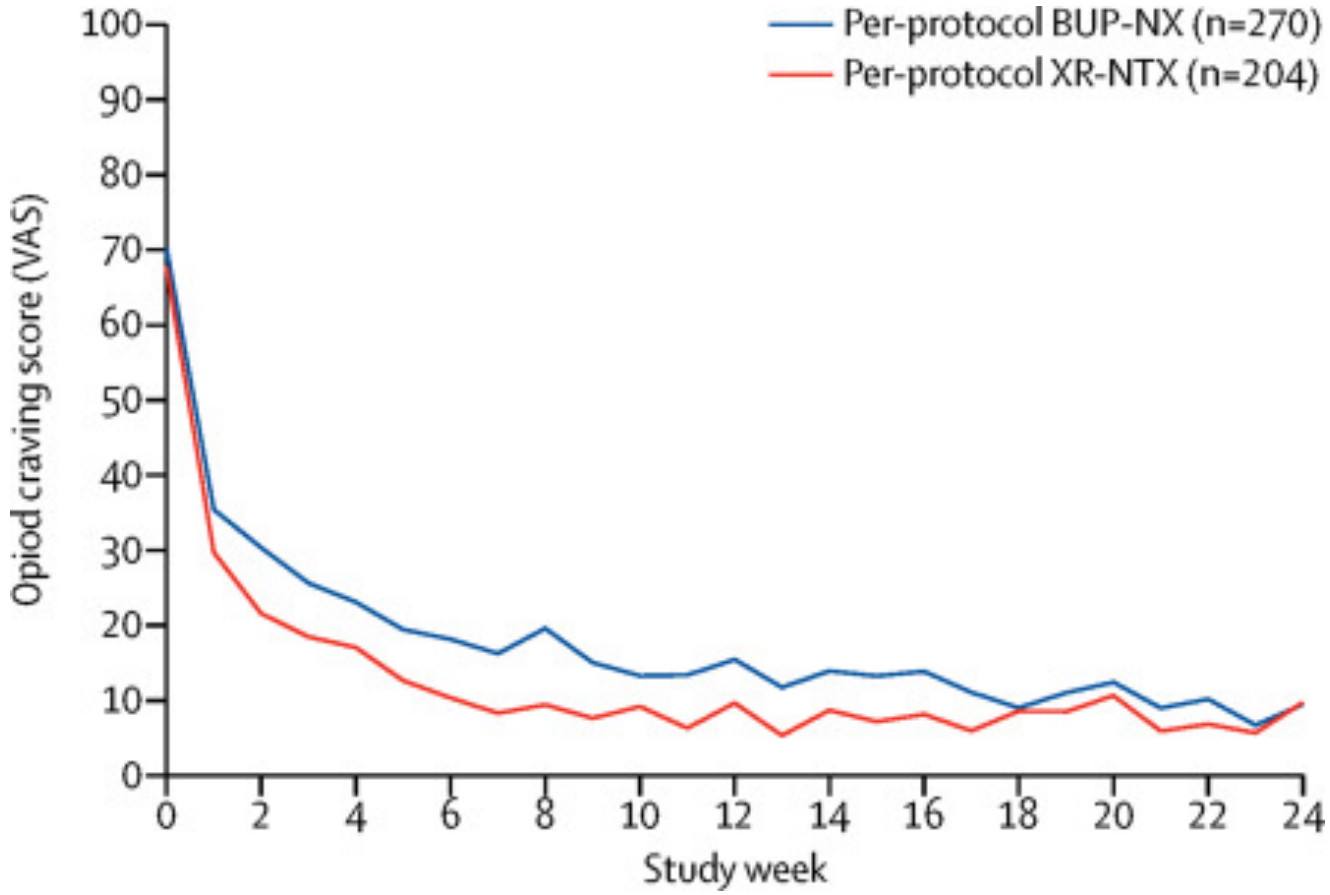
Intention to Treat

Successfully Induced



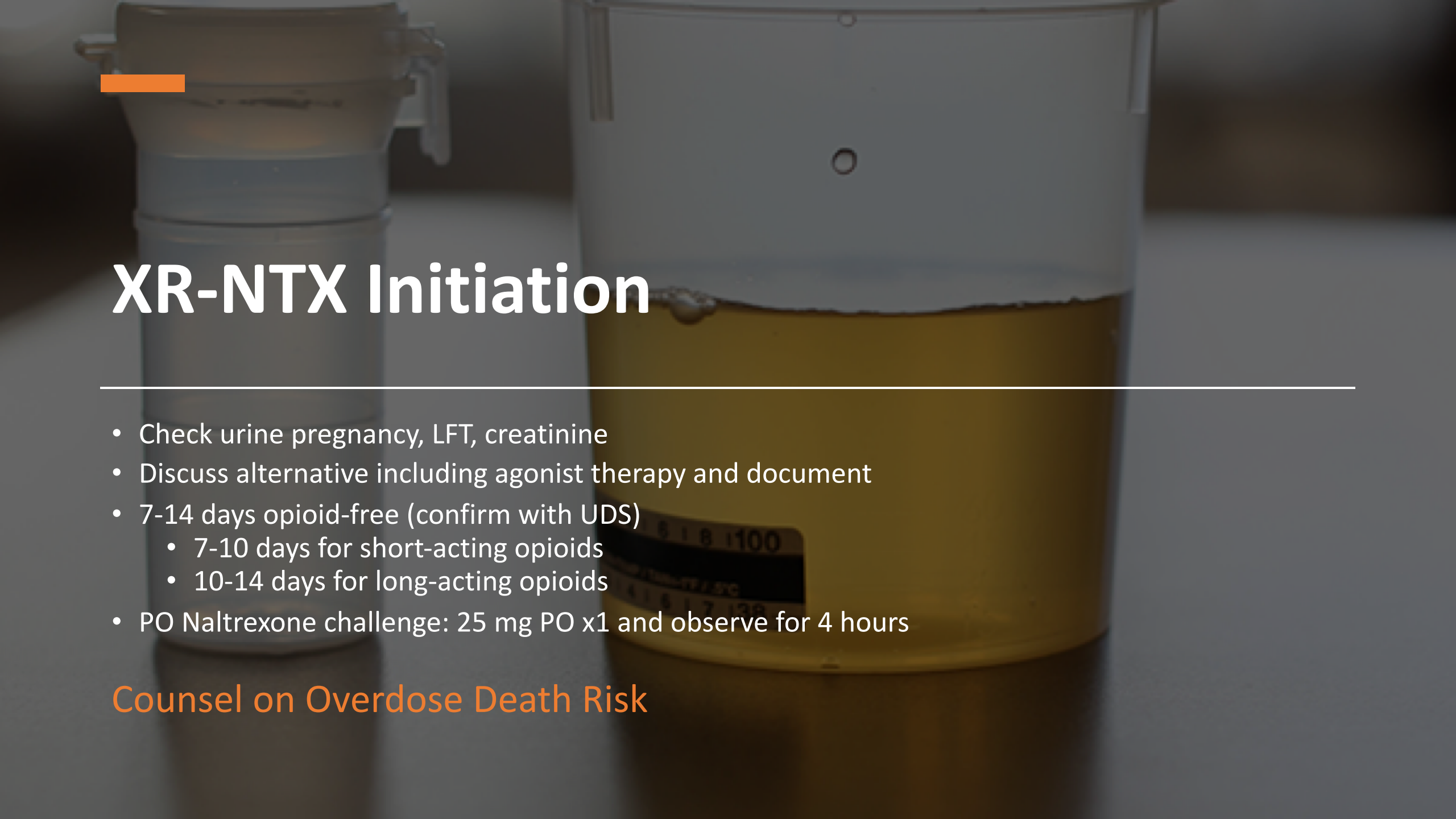
Lee, et al, Lancet, vol 391(10118), 2018, pp 309-318

Cravings Similar



Initially favored XR-NTX, but converged by 24 weeks

Lee, et al, Lancet, vol 391(10118), 2018, pp 309-318



XR-NTX Initiation

- Check urine pregnancy, LFT, creatinine
- Discuss alternative including agonist therapy and document
- 7-14 days opioid-free (confirm with UDS)
  - 7-10 days for short-acting opioids
  - 10-14 days for long-acting opioids
- PO Naltrexone challenge: 25 mg PO x1 and observe for 4 hours

Counsel on Overdose Death Risk

Naltrexone - Contraindications

CONTRAINDICATED

- Acute hepatitis / liver failure
- Pregnancy? (Data too limited to deem safe)
- Conditions requiring opioid pain medications
- Coagulopathy (XR-NTX)

CAUTION

- Caution if renal or hepatic impairment
- Caution with pre-existing severe depression

Naltrexone – Side Effects

Only 1/50 patients discontinue naltrexone due to side effects (Cochrane Review 2010)

COMMON

- Nausea
- Fatigue
- Somnolence

RARE BUT SERIOUS

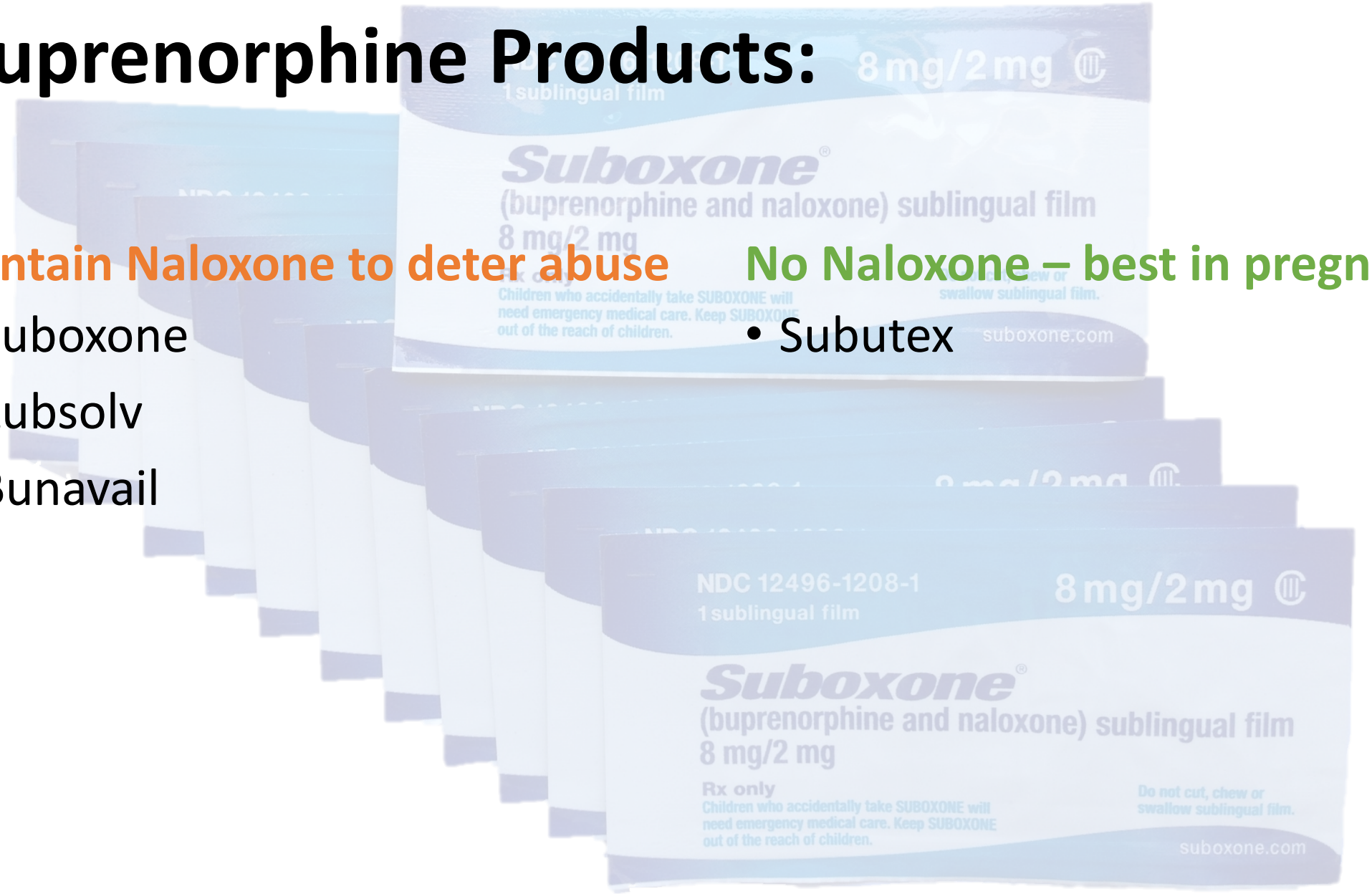
- Opioid pain medication ineffective for up to 72 hours from last dose
- Precipitated Withdrawal
- Liver toxicity
- Depression
- Suicidal ideation

Vivitrol: precipitated withdrawal, depression/SI, injection site reactions including tissue necrosis, cellulitis, abscess, anaphylaxis, cholecystitis, hepatic injury, eosinophilic pneumonia, decreased platelet count – all rare

Naltrexone - Monitoring

- Liver enzymes periodically
- Mood/SI
- Medical alert bracelet, card or dog-tags

Buprenorphine Products:



Contain Naloxone to deter abuse

- Suboxone
- Zubsolv
- Bunavail

No Naloxone – best in pregnancy

- Subutex

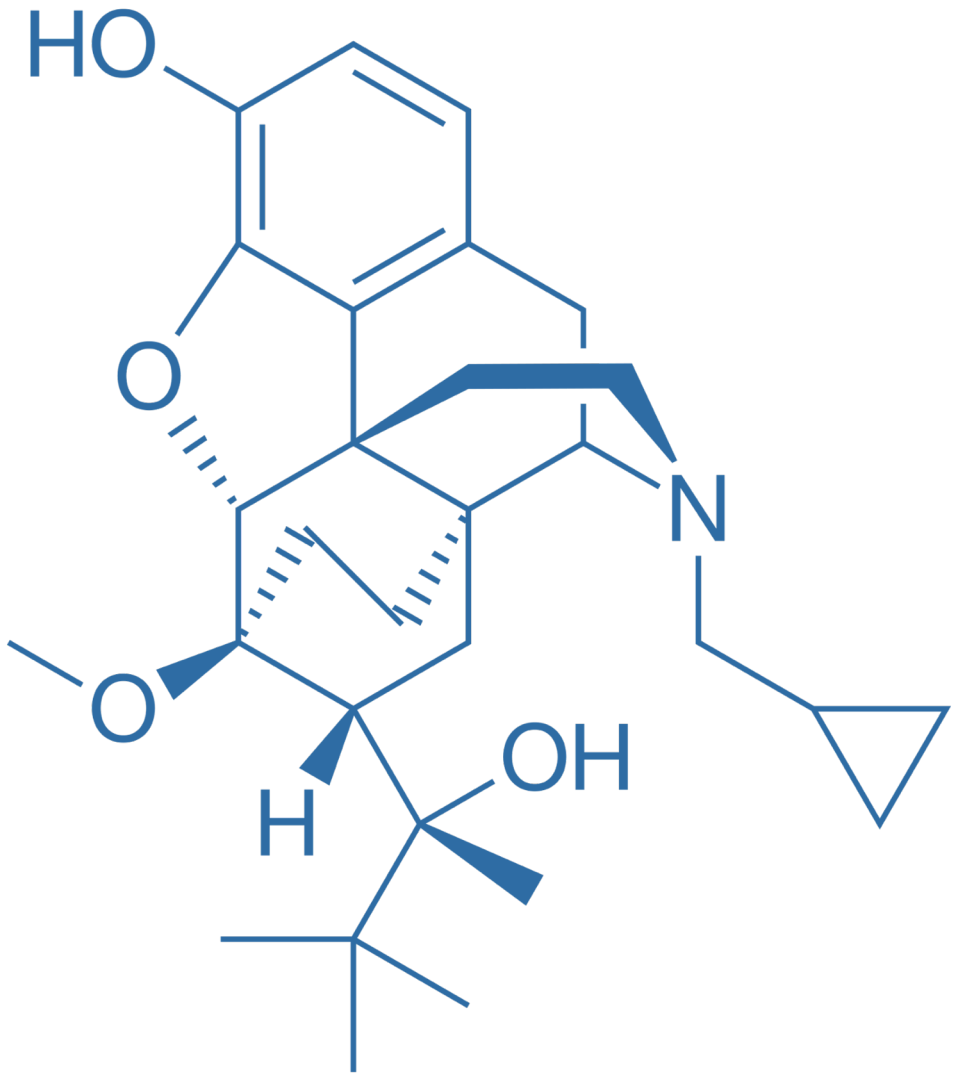
Evidence-Based Benefits of Buprenorphine

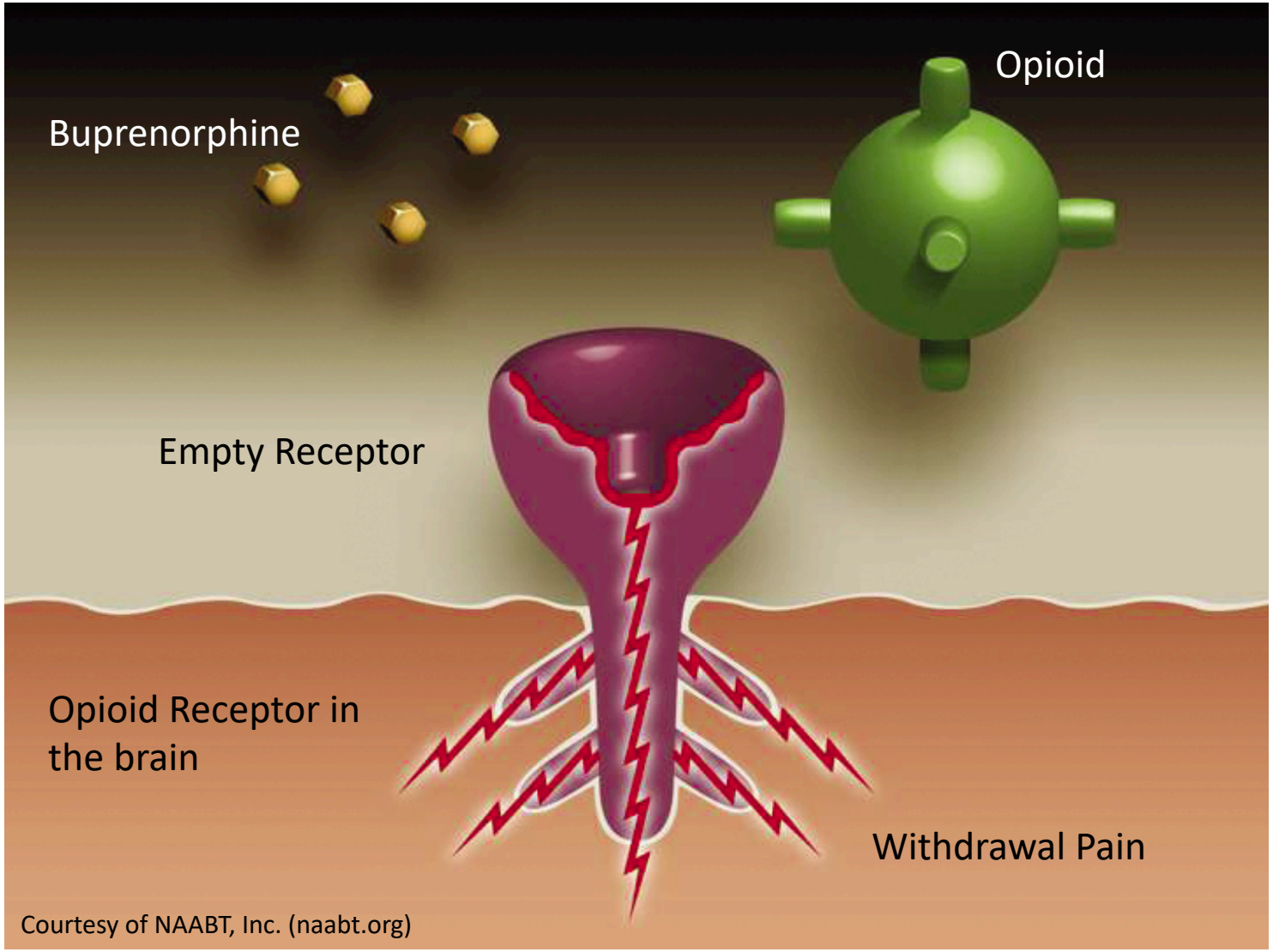
- Improve retention in treatment
- Reduce use of illicit opioids
- Reduces ER visits and acute care hospitalizations
- Reduce overdose and all-cause mortality

Wakeman, JAMA, May 26, 2020. Vol 323(20)

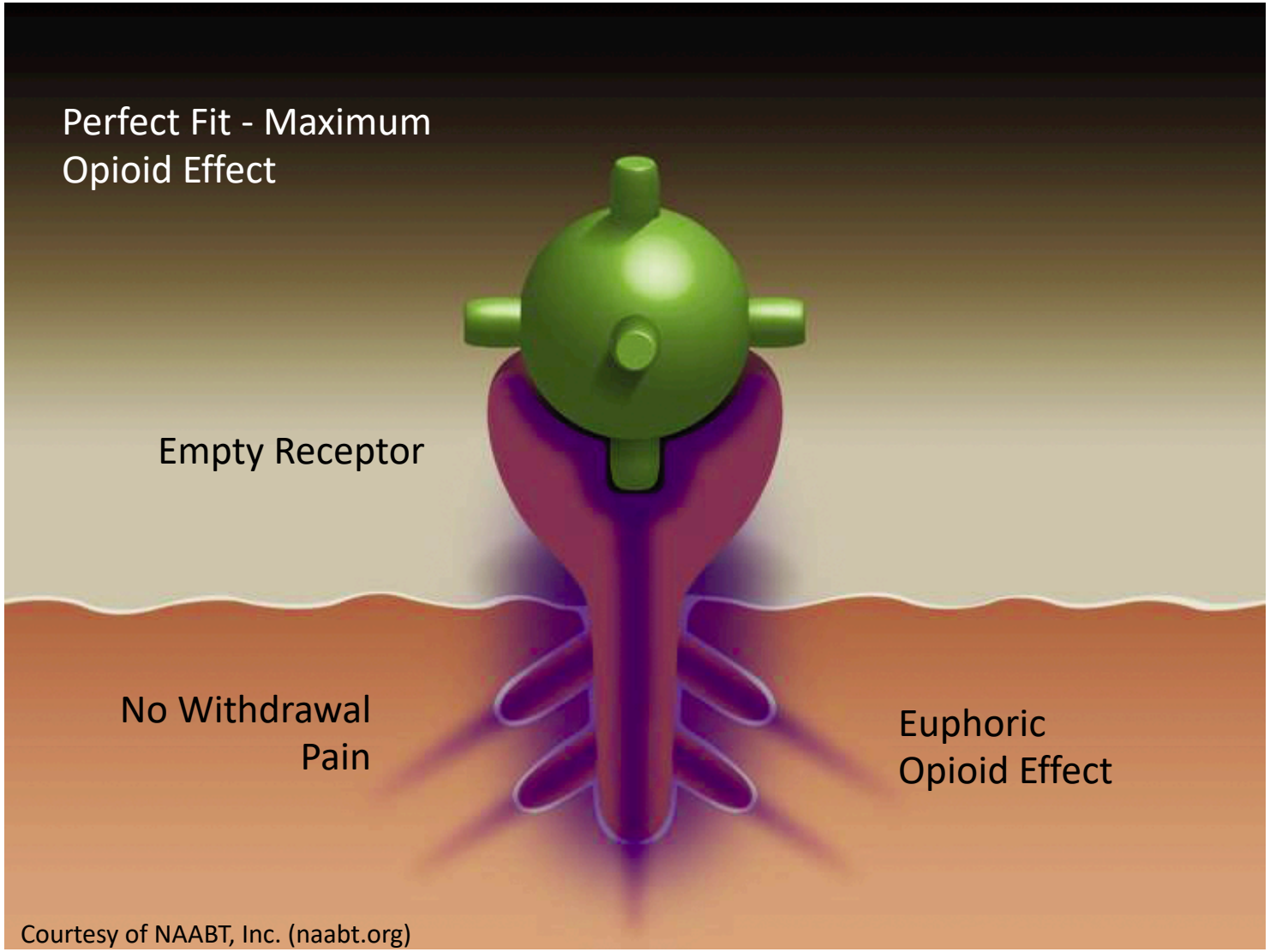
Buprenorphine Mechanism of Action

- Partial Opioid Agonist
- High mu-opioid receptor affinity
- Binds tightly but activates partially
- Less respiratory depression / lower overdose risk
- Less euphoria
- Helps curb cravings
- Blunts effects of illicit opioids

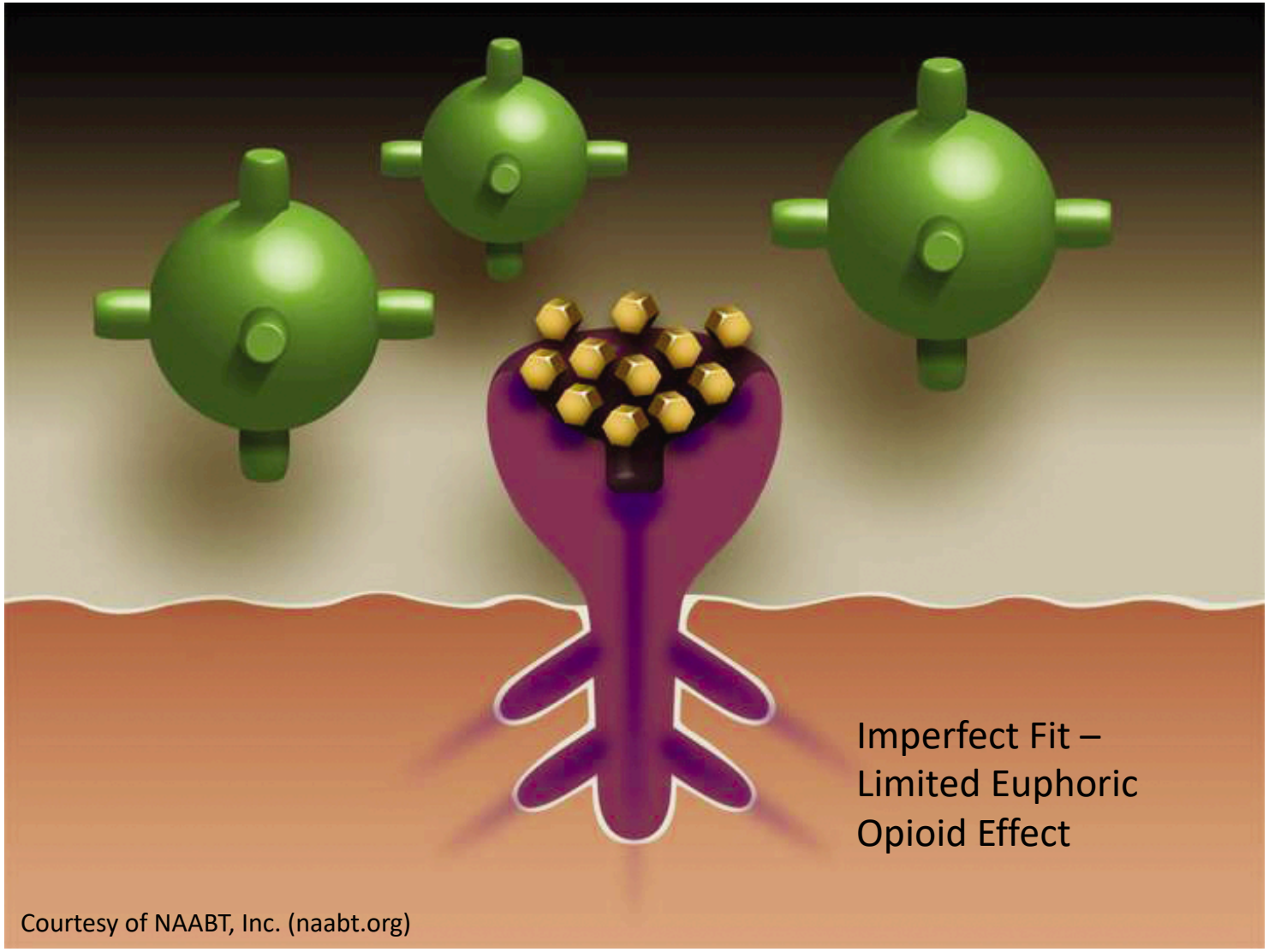




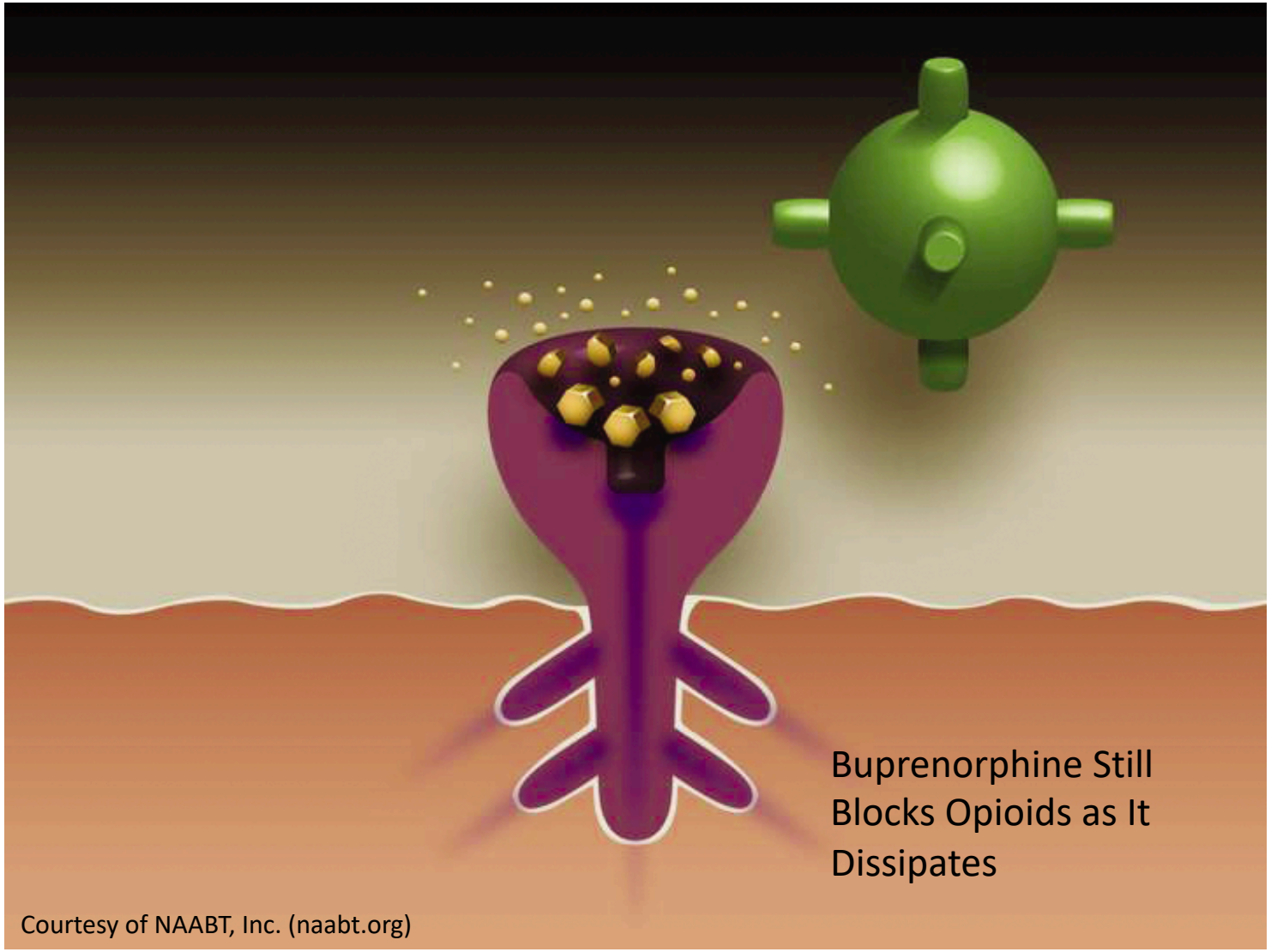
Opioid receptor unsatisfied -- Withdrawal. As someone becomes “tolerant” to opioids their opioid receptors become less sensitive. More opioids are then required to produce the same effect. Once “physically dependent” the body can no longer manufacture enough natural opioids to keep up with this increased demand. Whenever there is an insufficient amount of opioid receptors activated, the body feels pain. This is withdrawal.



Opioid receptor satisfied with a full-agonist opioid. The strong opioid effect of heroin and painkillers stops the withdrawal for a period of time (4-24 hours). Initially, euphoric effects can be felt. However, after prolonged use, tolerance and physical dependence can develop. Now, instead of producing a euphoric effect, the opioids are primarily just preventing withdrawal symptoms.

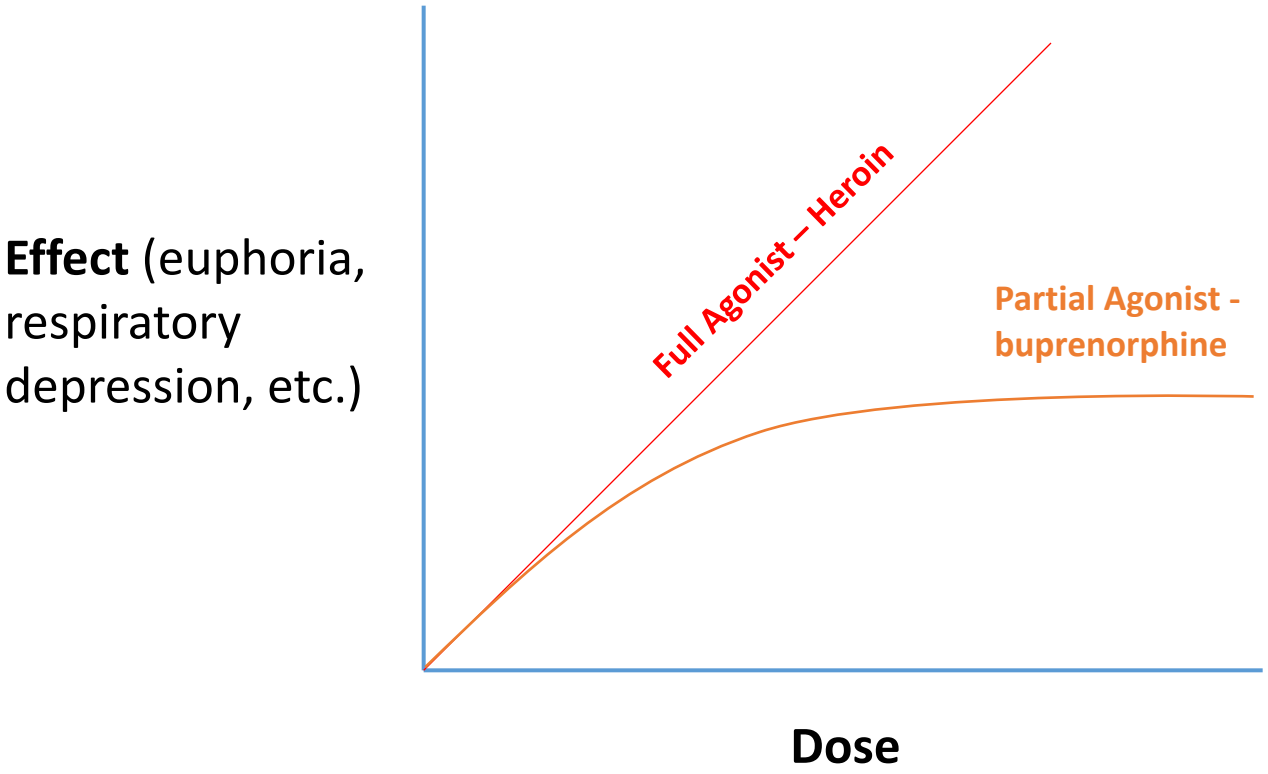


Opioids replaced and blocked by buprenorphine. Buprenorphine competes with the *full agonist opioids* for the receptor. Since buprenorphine has a higher *affinity* (stronger binding ability) it expels existing opioids and blocks others from attaching. As a *partial agonist*, the buprenorphine has a limited opioid effect, enough to stop withdrawal but not enough to cause intense euphoria.



Over time (24-72 hours) buprenorphine dissipates, but still creates a limited opioid effect (enough to prevent withdrawal) and continues to block other opioids from attaching to the opioid receptors.

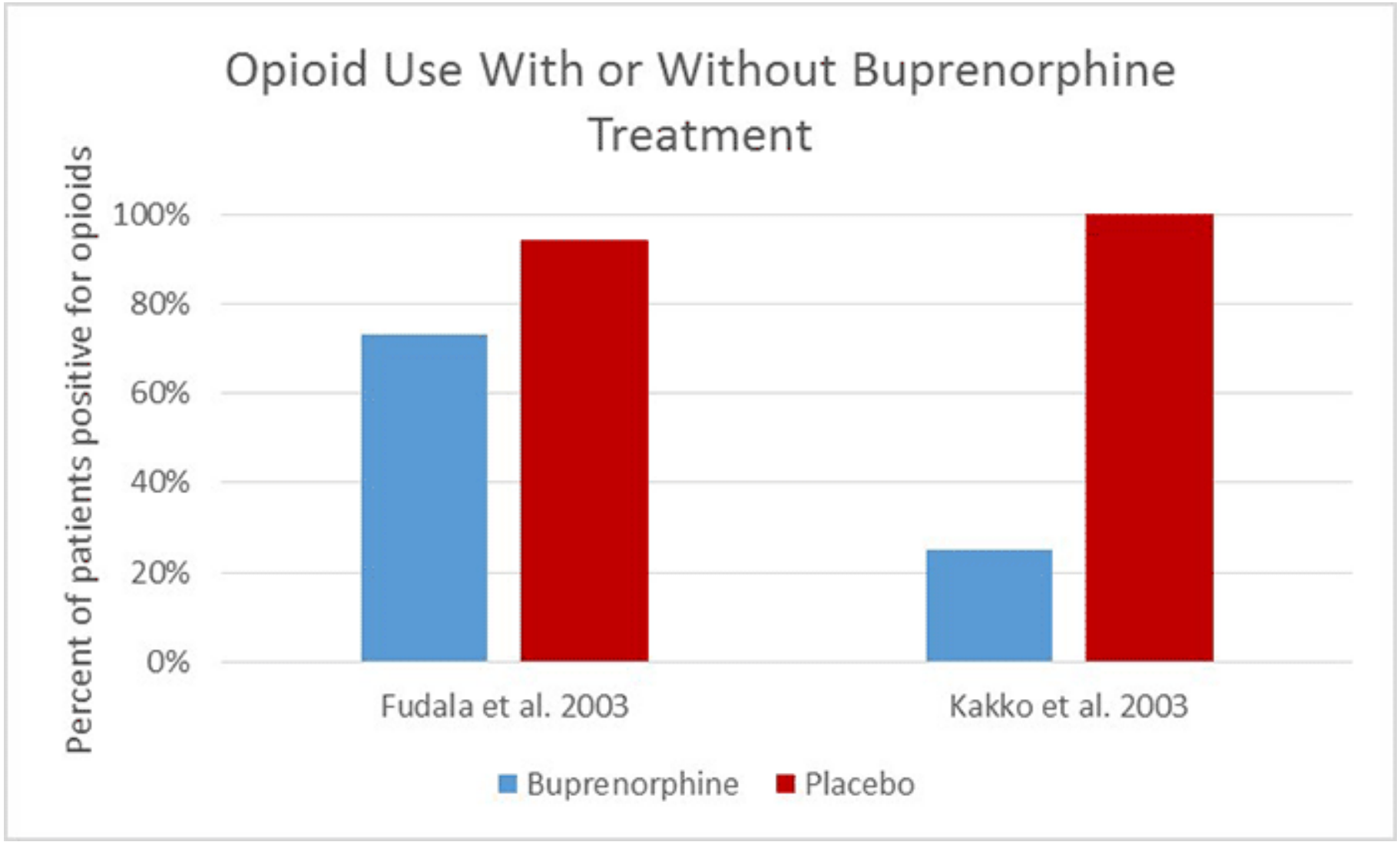
Buprenorphine Mechanism of Action



Buprenorphine – Cochrane Review 2014

- 31 RCT's including 5430 patients (Mattick et al, 2014)
- Buprenorphine superior to placebo in retaining patients in treatment at any dose, and superior to placebo at producing negative urine drug screens at doses of 16mg or more.

	RR for retention in treatment	95% CI
Bup 2-6 mg	1.5	1.19 to 1.88
Bup 7-15 mg	1.74	1.06 to 2.87
Bup 16+ mg	1.82	1.15 to 2.90

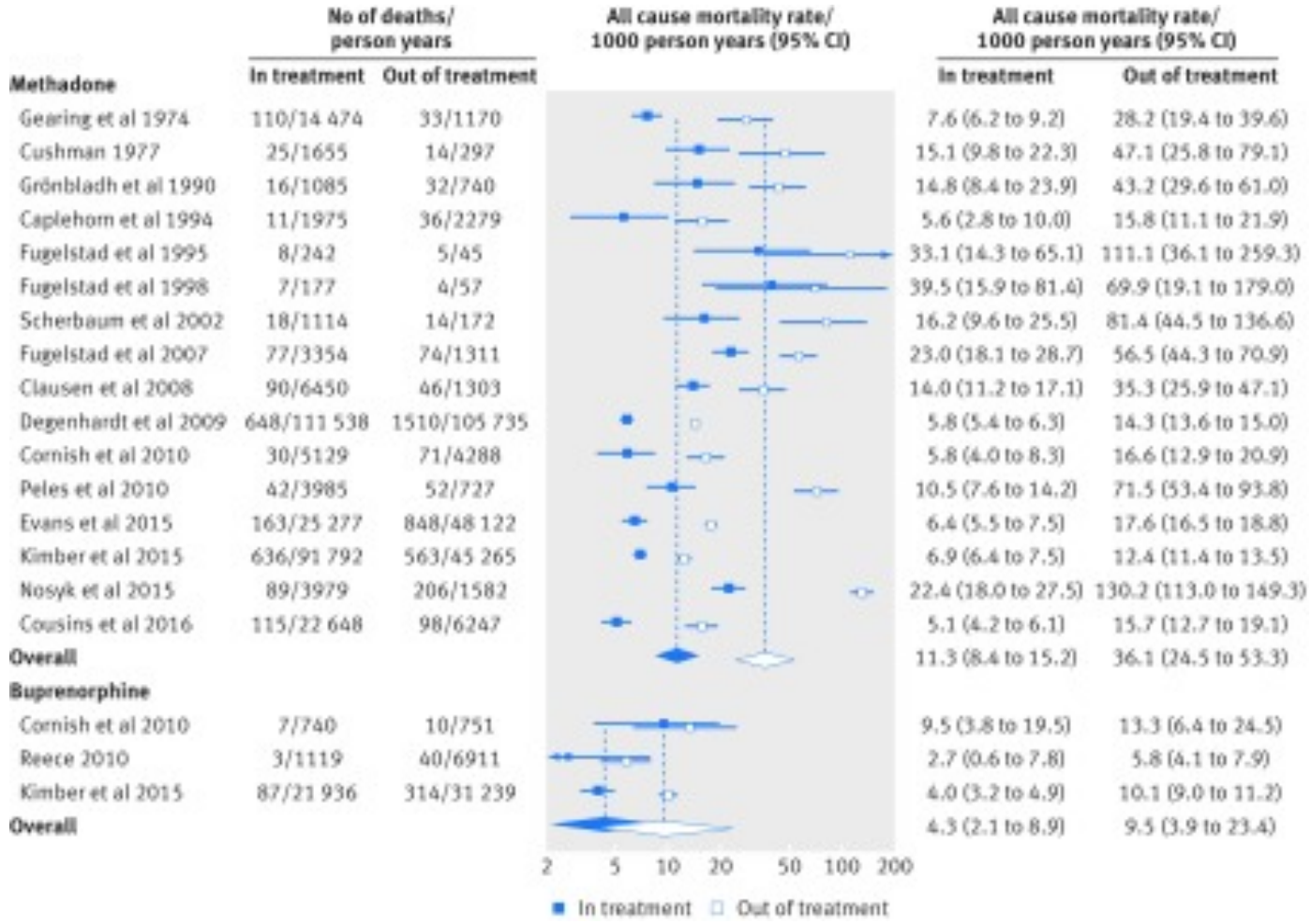


https://www.drugabuse.gov/publications/research-reports/medications-to-treat-opioid-addiction/efficacy-medications-opioid-use-disorder

Studies included in Cochrane meta-analysis

Buprenorphine Reduces Mortality

- 2017 Meta-analysis showed buprenorphine cuts mortality in HALF
  - 15,831 patients over 1.1-4.5 years
  - Mortality rate 4.3 and 9.5 / 1000 person years with and w/o buprenorphine
  - Unadjusted RR 2.2 (1.34-3.61)



	No of deaths/ person years		All cause mortality rate/ 1000 person years (95% CI)	
Methadone	In treatment	Out of treatment	In treatment	Out of treatment
Gearing et al 1974	110/14 474	33/1170	7.6 (6.2 to 9.2)	28.2 (19.4 to 39.6)
Cushman 1977	25/1655	14/297	15.1 (9.8 to 22.3)	47.1 (25.8 to 79.1)
Grönbladh et al 1990	16/1085	32/740	14.8 (8.4 to 23.9)	43.2 (29.6 to 61.0)
Caplehorn et al 1994	11/1975	36/2279	5.6 (2.8 to 10.0)	15.8 (11.1 to 21.9)
Fugelstad et al 1995	8/242	5/45	33.1 (14.3 to 65.1)	111.1 (36.1 to 259.3)
Fugelstad et al 1998	7/177	4/57	39.5 (15.9 to 81.4)	69.9 (19.1 to 179.0)
Scherbaum et al 2002	18/1114	14/172	16.2 (9.6 to 25.5)	81.4 (44.5 to 136.6)
Fugelstad et al 2007	77/3354	74/1311	23.0 (18.1 to 28.7)	56.5 (44.3 to 70.9)
Clausen et al 2008	90/6450	46/1303	14.0 (11.2 to 17.1)	35.3 (25.9 to 47.1)
Degenhardt et al 2009	648/111 538	1510/105 735	5.8 (5.4 to 6.3)	14.3 (13.6 to 15.0)
Cornish et al 2010	30/5129	71/4288	5.8 (4.0 to 8.3)	16.6 (12.9 to 20.9)
Peles et al 2010	42/3985	52/727	10.5 (7.6 to 14.2)	71.5 (53.4 to 93.8)
Evans et al 2015	163/25 277	848/48 122	6.4 (5.5 to 7.5)	17.6 (16.5 to 18.8)
Kimber et al 2015	636/91 792	563/45 265	6.9 (6.4 to 7.5)	12.4 (11.4 to 13.5)
Nosyk et al 2015	89/3979	206/1582	22.4 (18.0 to 27.5)	130.2 (113.0 to 149.3)
Cousins et al 2016	115/22 648	98/6247	5.1 (4.2 to 6.1)	15.7 (12.7 to 19.1)
Overall			11.3 (8.4 to 15.2)	36.1 (24.5 to 53.3)
Buprenorphine				
Cornish et al 2010	7/740	10/751	9.5 (3.8 to 19.5)	13.3 (6.4 to 24.5)
Reece 2010	3/1119	40/6911	2.7 (0.6 to 7.8)	5.8 (4.1 to 7.9)
Kimber et al 2015	87/21 936	314/31 239	4.0 (3.2 to 4.9)	10.1 (9.0 to 11.2)
Overall			4.3 (2.1 to 8.9)	9.5 (3.9 to 23.4)

Lordo et al, BMJ 2017 Apr 26;357:j1550.

Buprenorphine > Naltrexone and/or Therapy

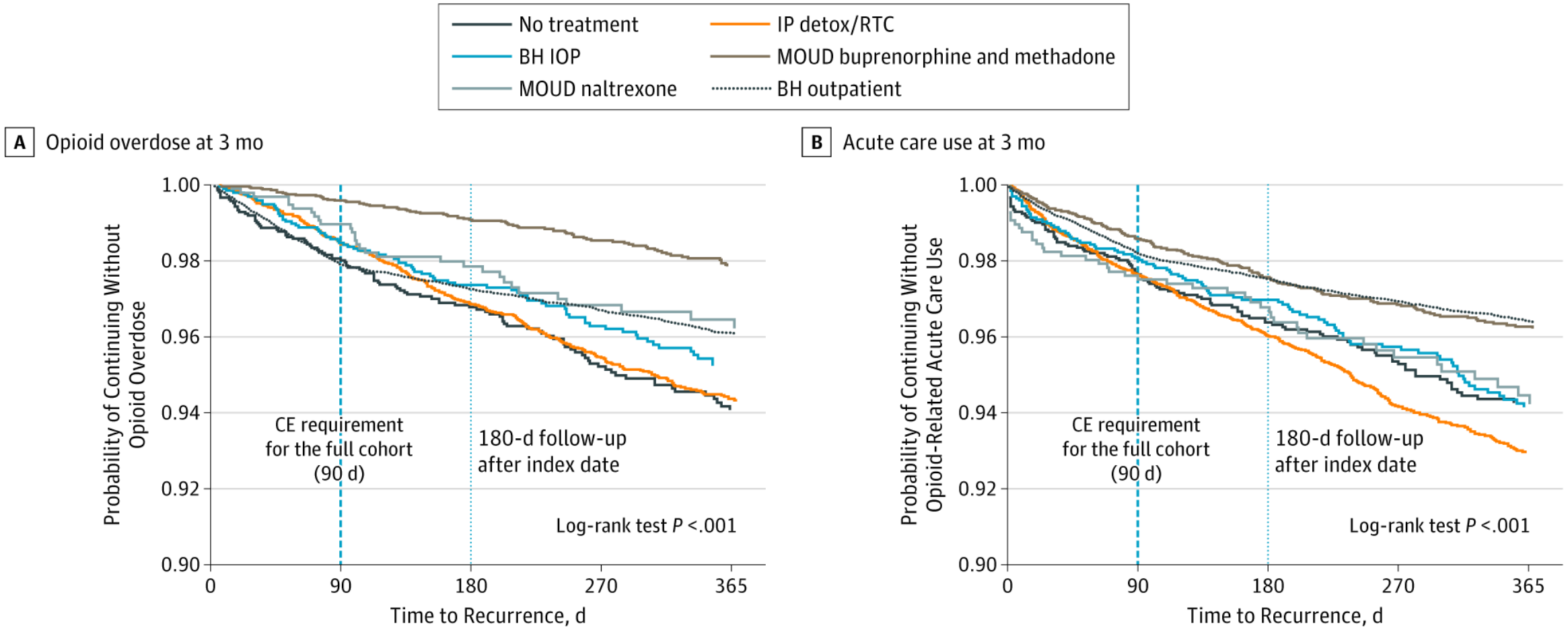
- Wakeman 2020 Retrospective Chart review
- N = 40,885
- 6 treatment pathways
  - No treatment
  - Inpatient detox or residential care
  - Intensive behavioral health
  - Agonist therapy with buprenorphine or methadone
  - Naltrexone (PO & Vivitrol combined)
  - Non-intensive behavioral health

Wakeman, S, JAMA Netw Open. 2020;3(2):e1920622.
doi:10.1001/jamanetworkopen.2019.20622

Buprenorphine > Naltrexone and/or Therapy

- Only buprenorphine & methadone were associated with decreased risk of overdose death
  - 3-Month AHR 0.24
  - 12-Month AHR 0.41
- Only buprenorphine & methadone were associated with decreased serious opioid-related acute care visits
  - 3-Month AHR 0.68
  - 12-Month AHR 0.74

Wakeman, S, JAMA Netw Open. 2020;3(2):e1920622.
doi:10.1001/jamanetworkopen.2019.20622

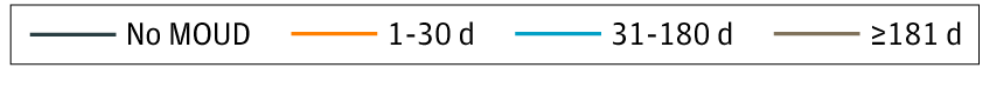


No. at risk

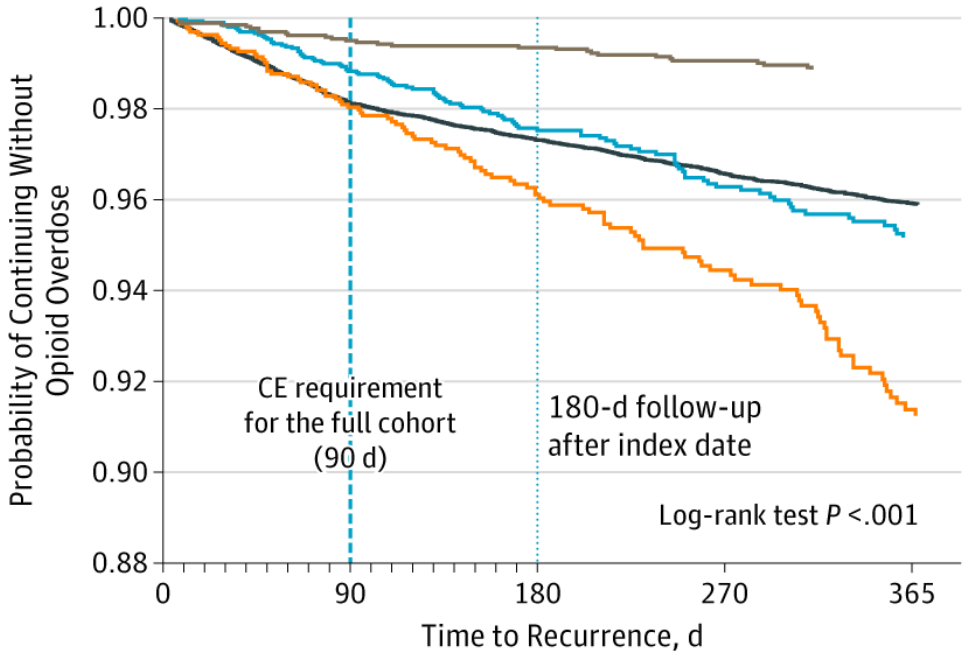
No treatment	2116	2075	1641	1248	944
IP detox/RTC	6455	6359	4911	3850	2947
BH IOP	1970	1941	1550	1237	950
MOUD buprenorphine and methadone	5123	5102	4014	3048	2282
MOUD naltrexone	963	953	743	558	421
BH outpatient	24258	23757	19950	16041	12551

No. at risk

No treatment	2116	2067	1631	1245	944
IP detox/RTC	6455	6304	4868	3786	2887
BH IOP	1970	1932	1546	1228	936
MOUD buprenorphine and methadone	5123	5051	3951	2989	2236
MOUD naltrexone	963	940	734	551	409
BH outpatient	24258	23830	19993	16059	12547

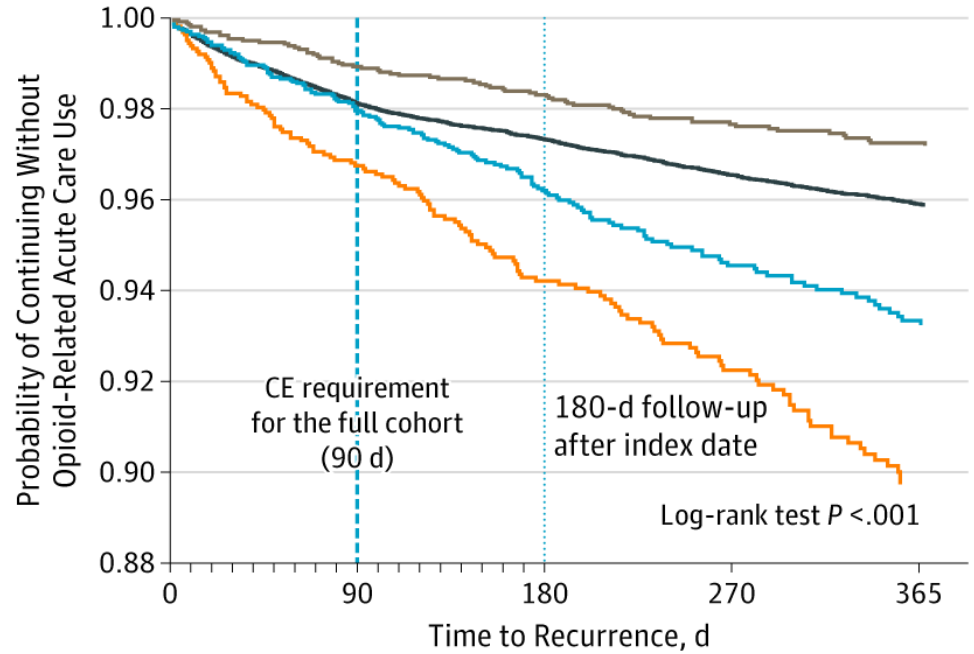


A Opioid overdose at 12 mo



No. at risk					
No MOUD	33656	33036	27017	21497	16708
MOUD					
1-30 d	1630	1599	1262	920	658
31-180 d	2990	2956	1938	1400	1047
≥181 d	2609	2596	2592	2165	1682

B Acute care use at 12 mo



No. at risk					
No MOUD	33656	33033	27013	21462	16646
MOUD					
1-30 d	1630	1578	1237	900	650
31-180 d	2990	2932	1908	1364	1016
≥181 d	2609	2581	2565	2132	1647

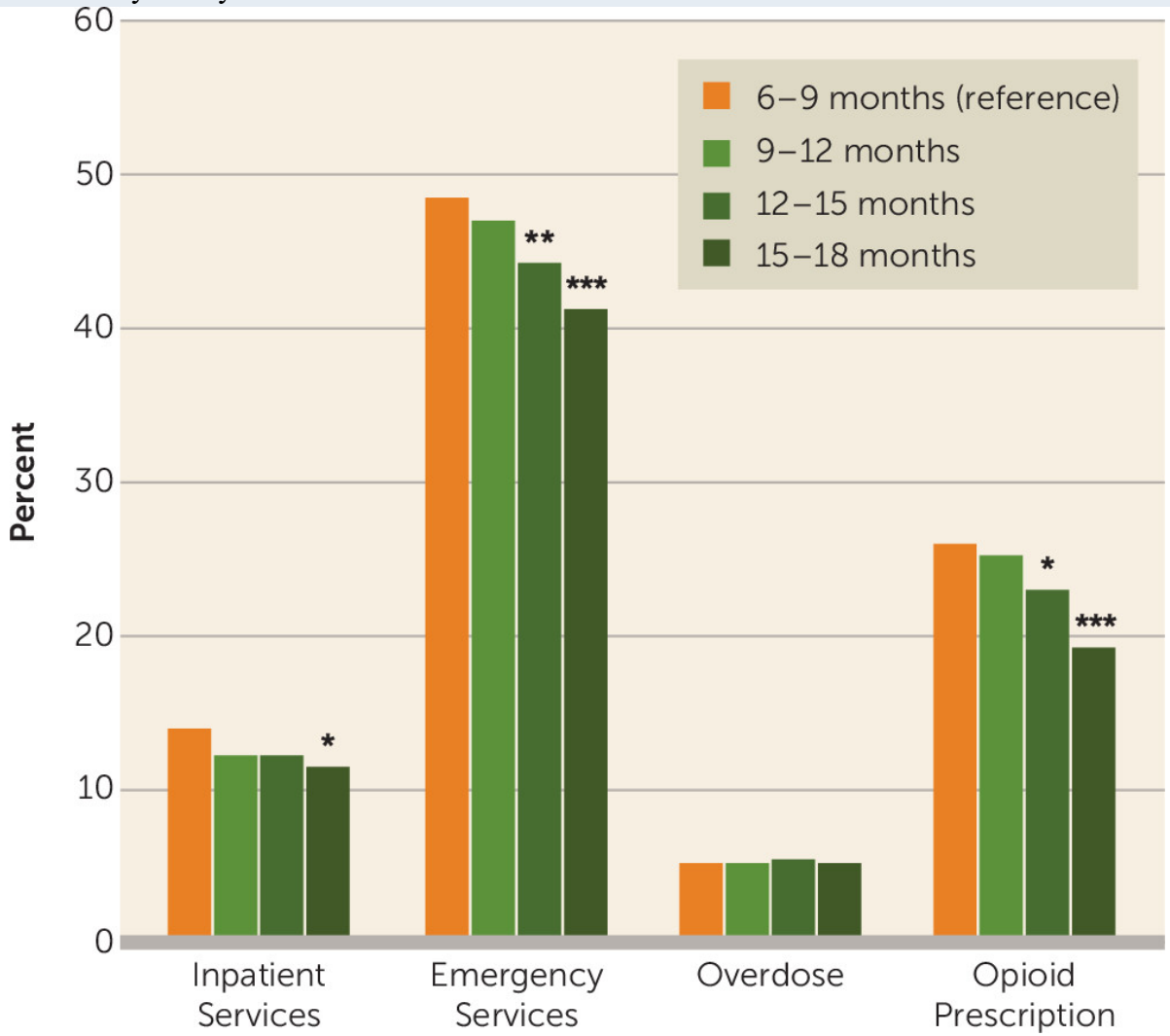
Long Term Treatment Necessary for Most

- 2019 Retrospective Longitudinal Cohort Study
- N= 8996
- Divided into 4 groups by treatment duration
  - Buprenorphine 6-9 months
  - Buprenorphine 9-12 months
  - Buprenorphine 12-15 months
  - Buprenorphine 15-18 months
- Followed for 6 months after buprenorphine discontinuation
- Significantly fewer ER visits, acute hospitalizations and opioid Rx's in the 15-18 month group
- Approximately 5% experienced overdoses (no significant difference between groups)

Willams, AR, et al, Am J Psychiatry, 2020 Feb 1;177(2):117-124.

From: Acute Care, Prescription Opioid Use, and Overdose Following Discontinuation of Long-Term Buprenorphine Treatment for Opioid Use Disorder

American Journal of Psychiatry



Willams, AR, et al, Am J Psychiatry, 2020 Feb 1;177(2):117-124.

*p<0.05. **p<0.01. ***p<0.001.

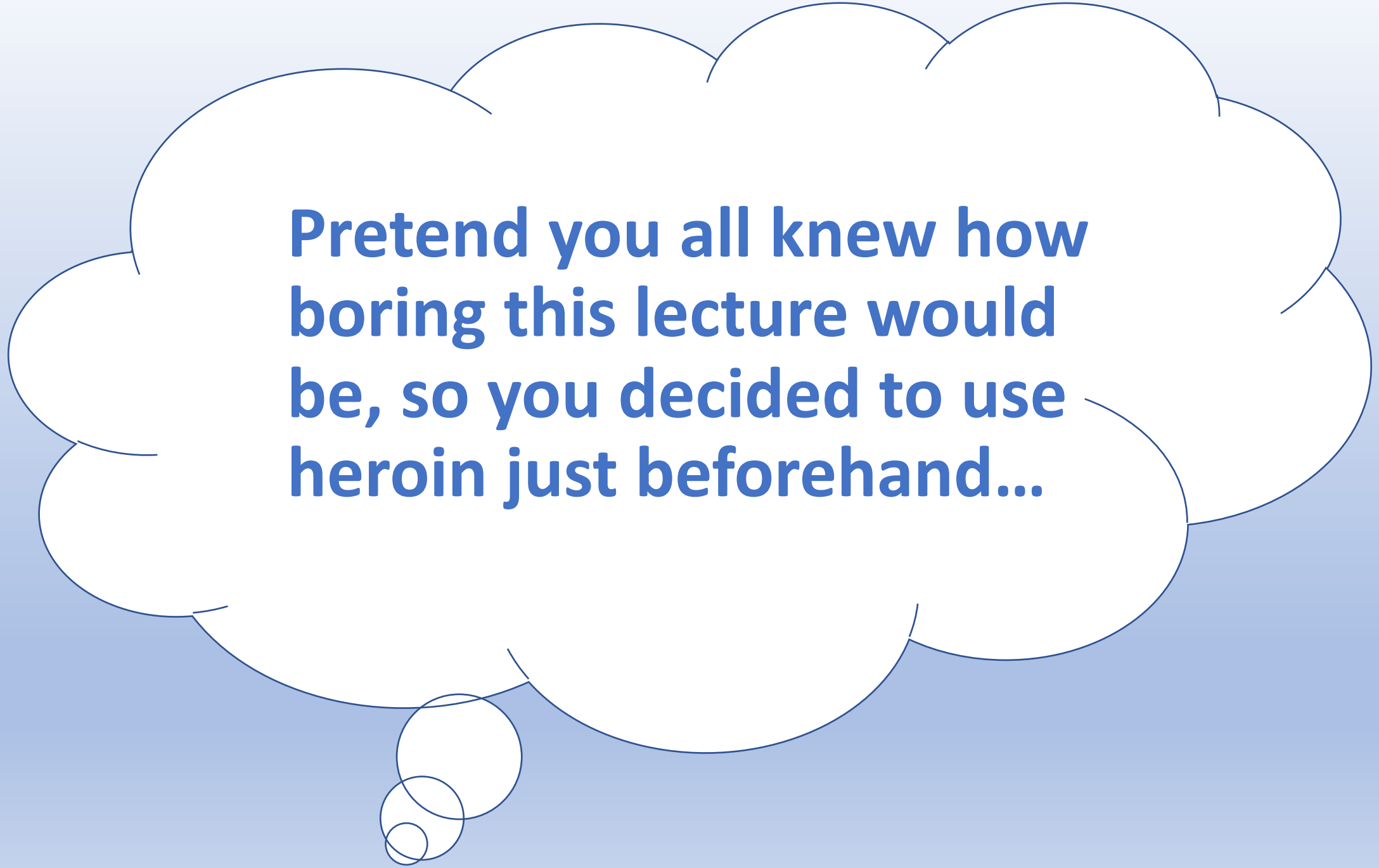
Buprenorphine Initiation Checklist

- ❑ Discuss RBSE of buprenorphine (Michigan Opioid Start Talking form)
- ❑ Treatment contract
- ❑ Detailed history including all potential drugs of abuse, treatment encounters, psychiatric conditions and social history creating barriers to recovery
- ❑ Targeted physical exam looking for signs of intoxication, withdrawal, injection, abscesses, signs of endocarditis (murmur, Janeway lesions, Osler nodes)
- ❑ Check MAPS
- ❑ Obtain UDS (illicit drugs, buprenorphine/norbuprenorphine), consider breathalyzer/ETG/CDT

Buprenorphine Initiation Checklist

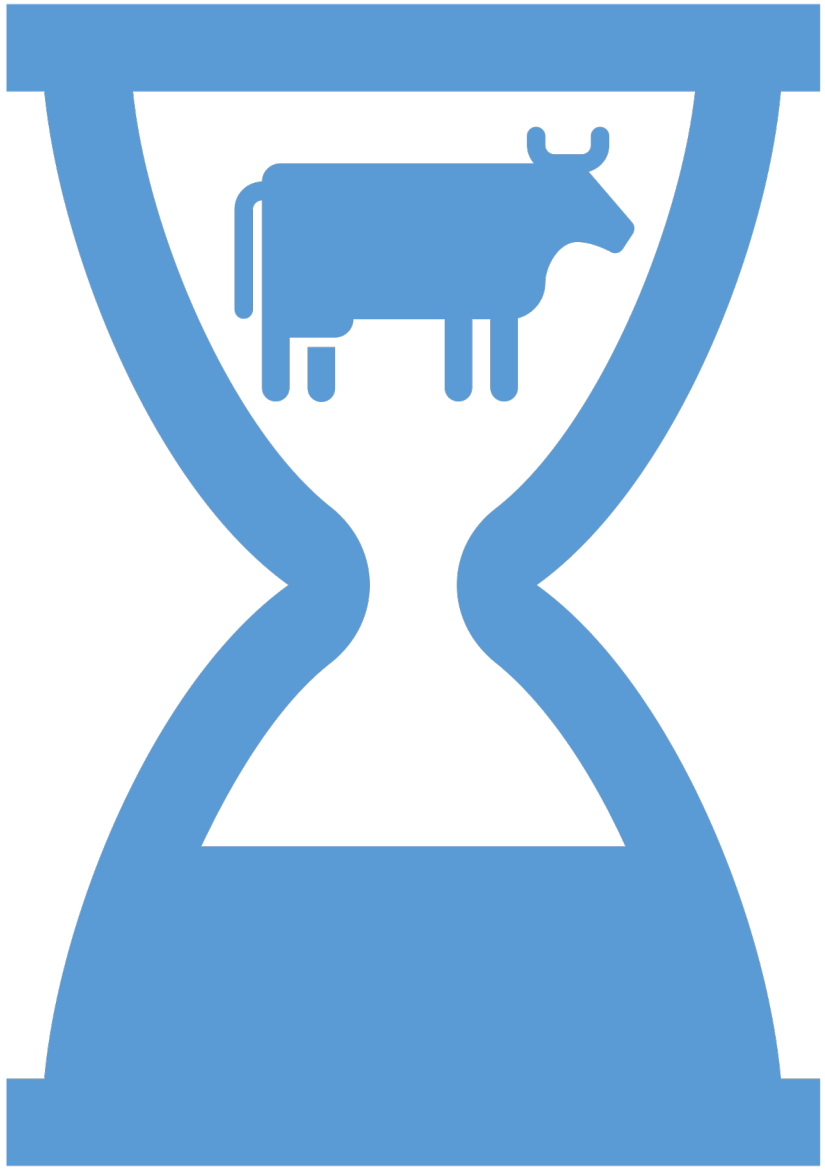
- ❑ Assess for need for inpatient treatment
- ❑ Check LFT periodically (extensive evidence it is safe, case reports likely from comorbid hepatic disease)
- ❑ Screen HIV, Hep B and Hep C
- ❑ Don’t forget to screen for pregnancy
- ❑ Schedule frequent return visits until patients are stable
- ❑ Urge patients to exercise caution in using heavy machinery and driving until they’re sure that their abilities are not compromised

What about precipitated withdrawal???


Pretend you all knew how boring this lecture would be, so you decided to use heroin just beforehand…

Avoiding Precipitated Withdrawal

- Wait until they are in withdrawal!
- COWS ≥ 10 **AND** Time Requirement
  - 16 hours for short acting opioids
  - 24 hours for most long acting opioids
  - Taper methadone until 30mg/day is WELL TOLERATED. Stop methadone and wait AT LEAST 36 hours, often 48-96 hours



Buprenorphine Induction - General

- Home induction is ok
  - Do a few office-based inductions if new to practice
  - Use Teachback to assure understanding, especially regarding precipitated withdrawal
- Must be in moderate opioid withdrawal to start
- Goal is to feel “normal.” Not high, but little withdrawal or craving
- Frequent dose adjustments may be necessary during early stabilization

Buprenorphine Induction

DAY 1:

- Start 2-4 mg
- Additional 2-4 mg every 2 hours
- Total day one dose 1 dose 8-24 mg
  - FDA 8 mg
  - Reality 16 mg average (document tolerance, lack of efficacy at lower dose)
    - Mu-opioid receptors 80-95% occupied at 16 mg/d

SUBSEQUENT DAYS:

- Day 2: total day 1 dose, given all at once.
- Additional titration as needed
- Typical maintenance doses 4-24 mg (max = 32)

Buprenorphine Induction – Special Populations

Comorbidities

- Smaller doses if:
  - Severe hepatic impairment
  - Low dose or low potency opioid dependence
  - Concurrent use of other CNS depressants
  - Concomitant strong CYP3A4 Inhibitors (some antibiotics, antifungals and antiretrovirals)

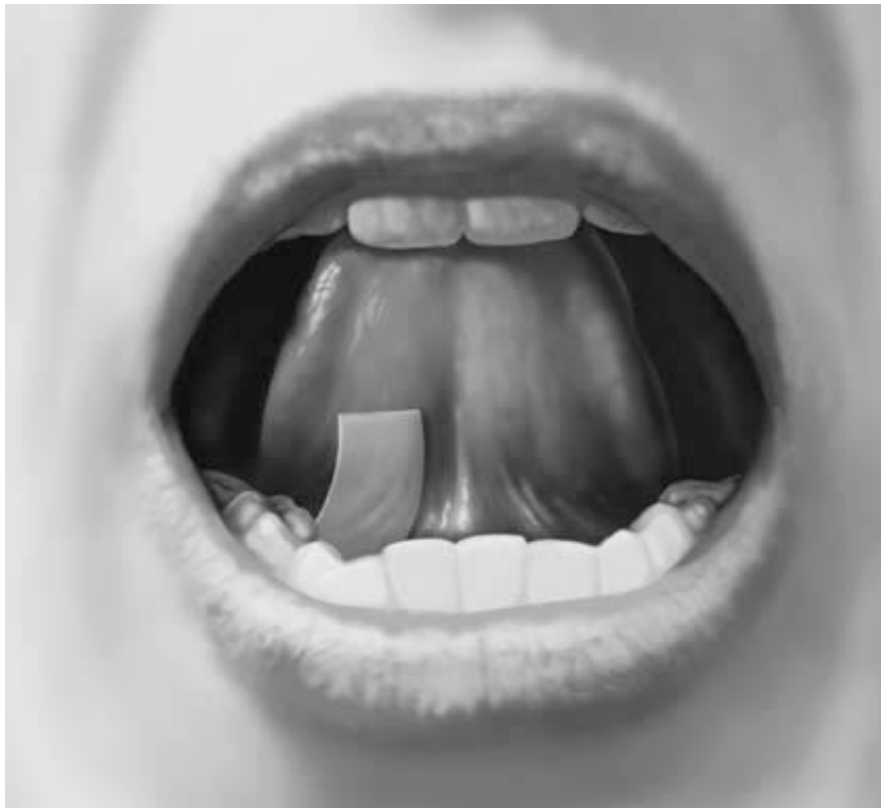
- Recommend office-based induction or residential care

Opioid-Naive

- 1 mg daily for 1 week
- Increase 1mg/d weekly until 4mg/d
- Increase 2mg/d weekly until 8 mg/d

Administration

- Sublingual
- Drink water to moisten mouth
- Do not swallow or spit out
- Avoid eating or drinking until completely dissolved (3-10 min)
- Don’t talk much
- Avoid tobacco products before dosing (vasoconstriction)



Side Effects

- Headache
- Nausea
- Dizziness
- Diaphoresis
- Pruritis
- Constipation
- Insomnia
- Somnolence
- Blurred vision
- Attention Disturbance
- Sexual Dysfunction
- Decreased blood pressure
- Adrenal suppression
- Overdose
- Withdrawal

General opioid side effects, though often less severe

Contraindications/Caution

- No Absolute Contraindications
- Caution with severe respiratory disease, other causes CNS depression, comorbid substance use disorders, strong CYP3A4 inhibitors
- Hepatic Impairment
  - Mild impairment (Child-Pugh score 5-6): no adjustment
  - Moderate impairment (Child-Pugh score 7-9): avoid combination products as decreased naloxone clearance may precipitate withdrawal
  - Severe Impairment (Child-Pugh score 10-15): avoid combination products and start at ½ normal dose, monitor titration carefully

Refer to Inpatient (Residential) Treatment

- Failing outpatient
- Recent overdose
- Comorbid substance abuse problems (alcohol, benzos, etc)
- Unstable comorbid psychiatric conditions
- Unstable comorbid medical conditions
- Unstable living situation / toxic environment
- Consider making an intake appt with the patient during their visit

Henry Ford Health System

Henry Ford Maplegrove Center

Overdose

- Lower tolerance after detox
- Lower tolerance after discontinuing naltrexone or buprenorphine
- Attempts to overcome naltrexone or buprenorphine (suboxone)
- Overdose on buprenorphine is rare given ceiling effect
  - Most involve IV misuse of buprenorphine
  - Most involve concurrent benzo or alcohol use
  - More likely if significant respiratory disease

- Keep medication locked & away from children
- In event of OD:
  - Remover film from mouth
  - Administer naloxone
  - Call 911
  - Repeat naloxone as needed
  - CPR

How to get waivered

- Eligible: Doctors, NP's, PA's (& until Oct 1, 2023: clinical nurse specialists, CNRA's, certified nurse midwives)
- Must complete training requirements (online or in person). Typically 8 hours for physicians, 24h for PA/NP
  - ASAM
  - American Psychiatric Association
  - American Osteopathic Academy of Addiction Medicine
  - Providers Clinical Support System (PCSS-MAT) – FREE - https:// pcssnow.org/medicationassisted-treatment/
- Must obtain federal waiver (DEAX number)
- https:// www.samhsa.gov/medication-assisted-treatment/training-materials-resources/ apply-for-practitioner-waiver

DATA 2000 and Counseling

- Drug Addiction Treatment Act of 2000 legislation requires that buprenorphine prescribers be able to refer patients to counseling, but making referrals is not mandatory
- Encourage Mutual Help Groups: NA, AA, SMART, Medication Assisted Recovery Services, Dharma, etc.)

“Rock bottom is the solid foundation on which I rebuilt my life.”

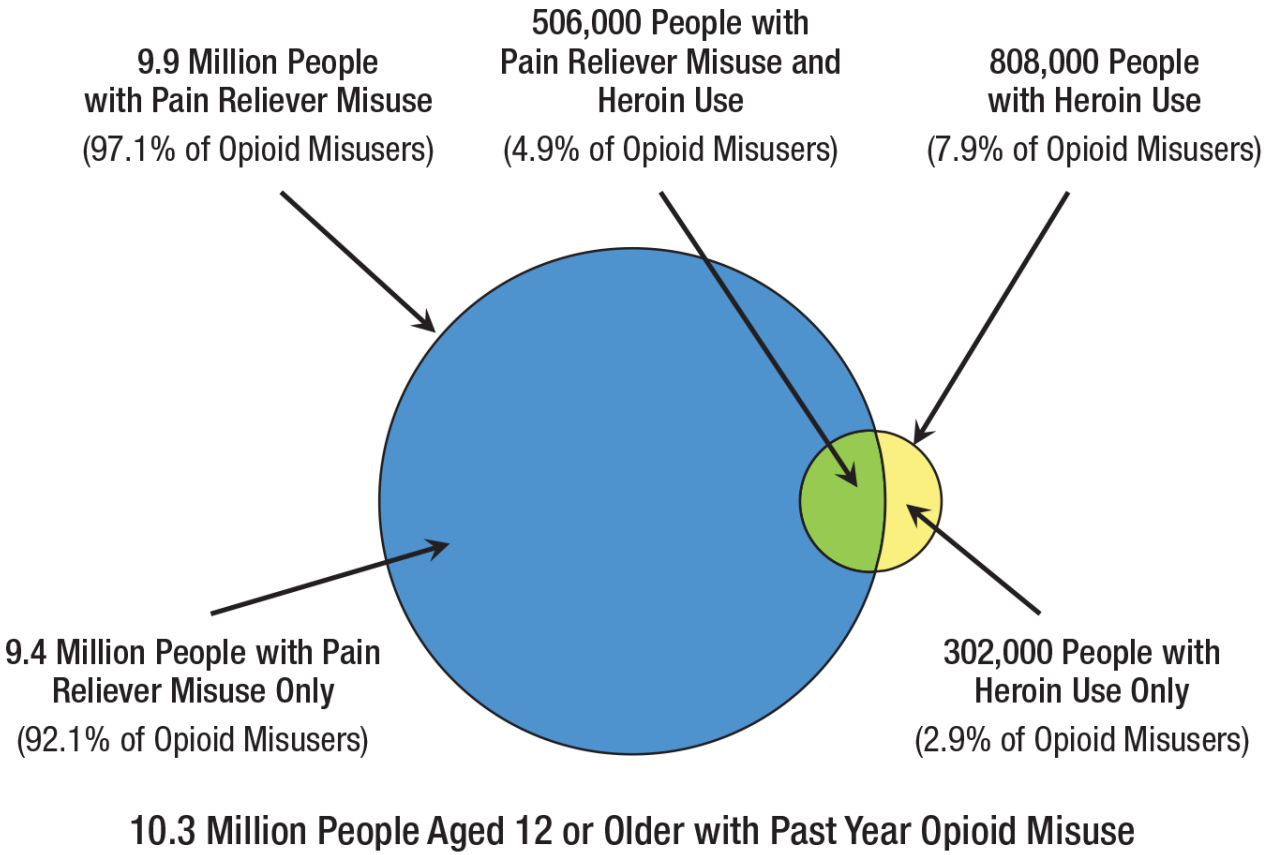
-JK Rowling

BONUS MATERIAL

- 670,367 people died of drug overdose in 2018. 184 people per day!
- 70% of these involved opioids
- OD deaths dropped 4% from 2017 – 2018
- < 35% people with OUD have received treatment in the last year
  - Many of these not offered MAT (no reliable national data)

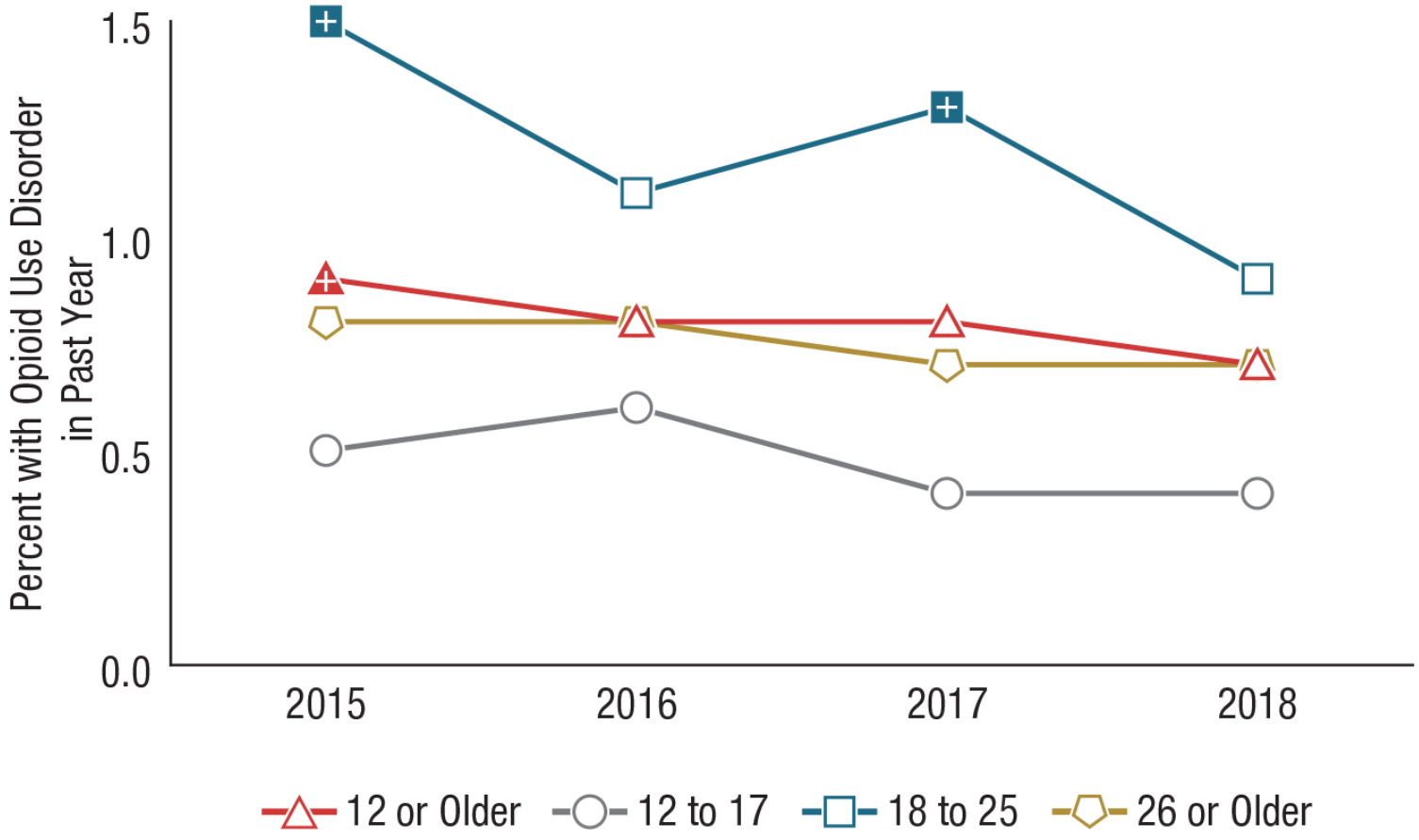
https://www.cdc.gov/drugoverdose/index.html

Past Year Opioid Misuse among People Aged 12 or Older: 2018



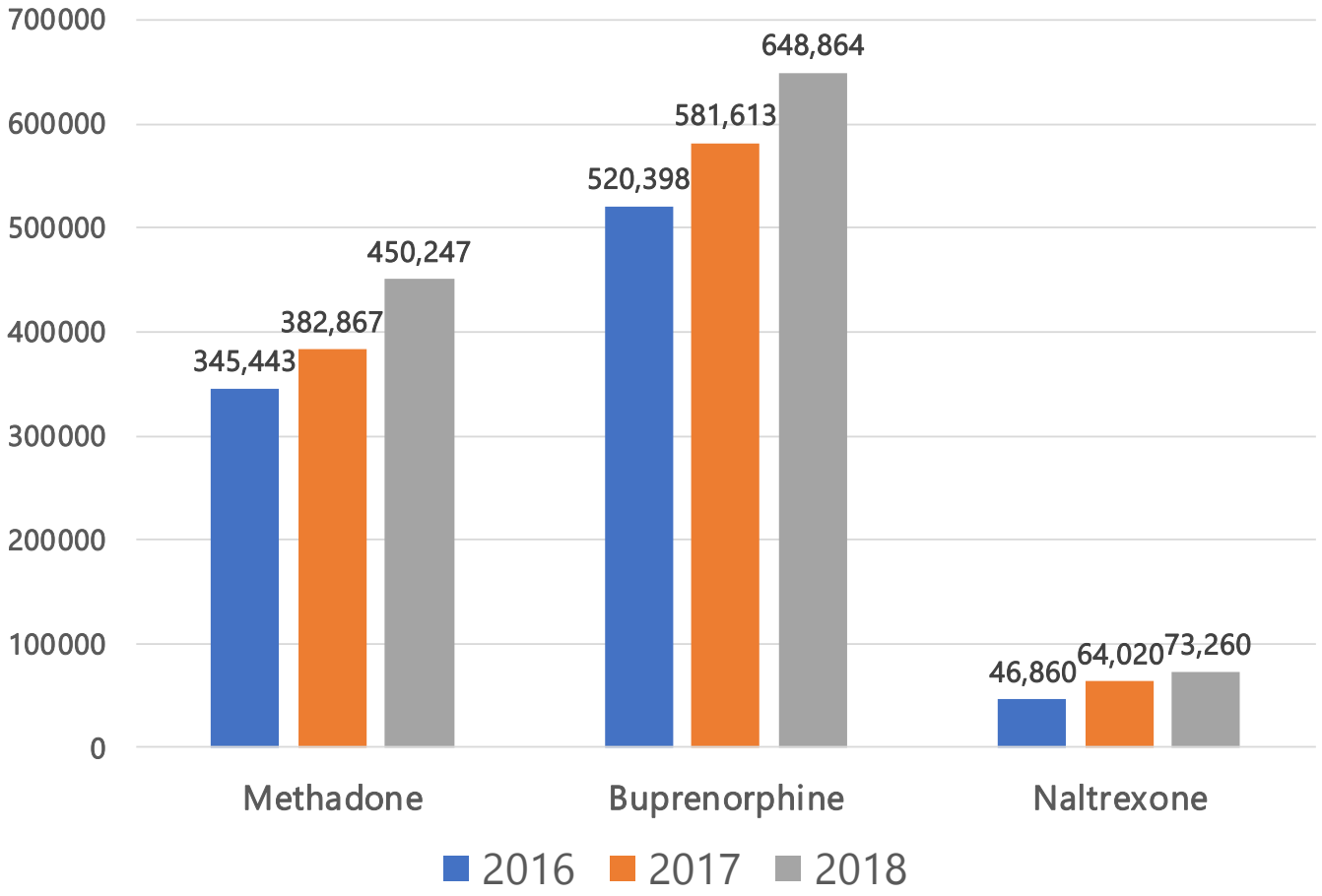
Note: The percentages do not add to 100 percent due to rounding.

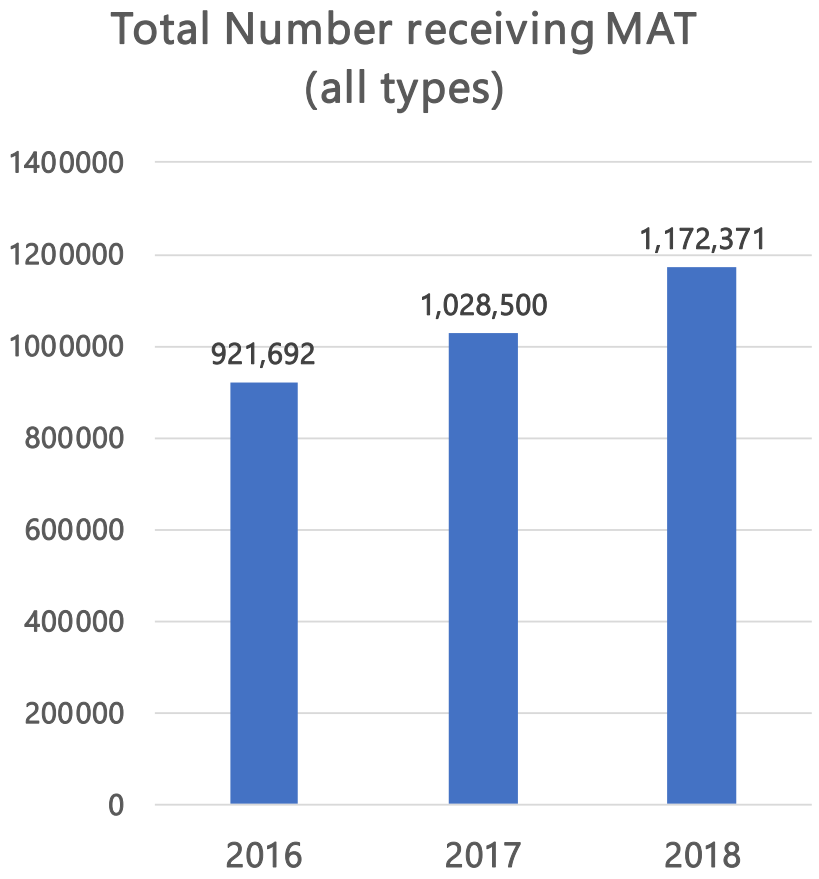
Young Adults Hit Hardest



2018 NSDUH Annual National Report.
https://www.samhsa.gov/data/report/2018-nsduh-annual-national-report

No. of Individuals Receiving MAT for OUD





2018 NSDUH Annual National Report. https://www.samhsa.gov/data/report/2018-nsduh-annual-national-report

National Academies of Sciences, Engineering & Medicine Consensus Study Report 2019

- Opioid Use Disorder is a treatable chronic brain disease resulting from the changes in neural structure and function that are caused over time by repeated opioid use
- Medications are intended to normalize brain structure and function.
- 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
- Buprenorphine and Methadone reduce mortality by ~ 50%

Medications for Opioid Use Disorder Save Lives, National Academies of Sciences, Engineering and Medicine Consensus Study Report, 2019

Buprenorphine – Cochrane Review 2014

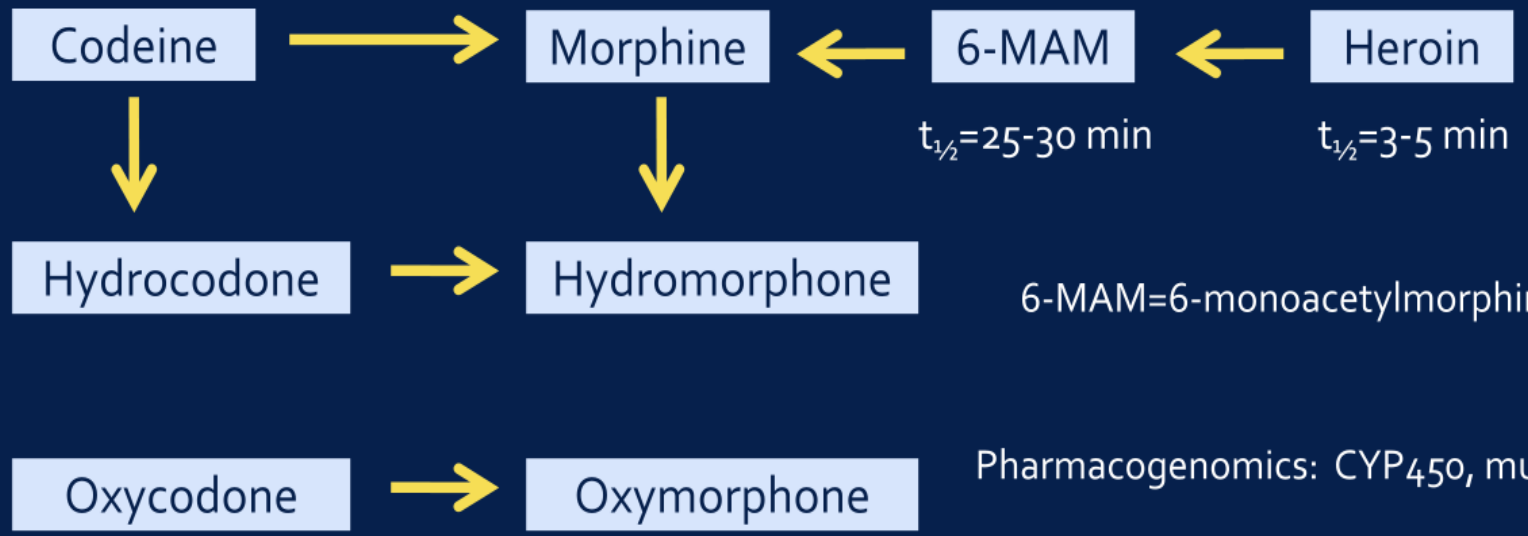
- Cochrane Review Authors concluded:

"Future trials involving placebo (or indeed short-term maintenance where people are terminated from treatment after a few weeks of intervention) should consider the ethical implications of providing substandard (i.e., placebo or short-term treatment), given the strength of the available evidence."

Understand Your Drug Screens!

- Most ELISA's only detect morphine
- Morphine is a metabolite of codeine and heroin
- Will NOT detect methadone, buprenorphine, fentanyl (most of our "heroin" is fentanyl)
- Variable results with hydrocodone and oxycodone
- Poppy seeds
- Naltrexone can give false + oxycodone
- Unisom, diphenhydramine and verapamil may give false + methadone
- Dextromethorphan, quinolones, rifampin, verapamil may cause false + opioids
- Must test for buprenorphine & norbuprenorphine during maintenance

Examples of Metabolism of Opioids



6-MAM=6-monoacetylmorphine

Pharmacogenomics: CYP450, mu opioid SNPs

Methadone, Fentanyl, Oxymorphone, Hydromorphone
Do Not Metabolize to other Opioid Analgesics

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* Ed 4. 2010.

Benzos Often Missed

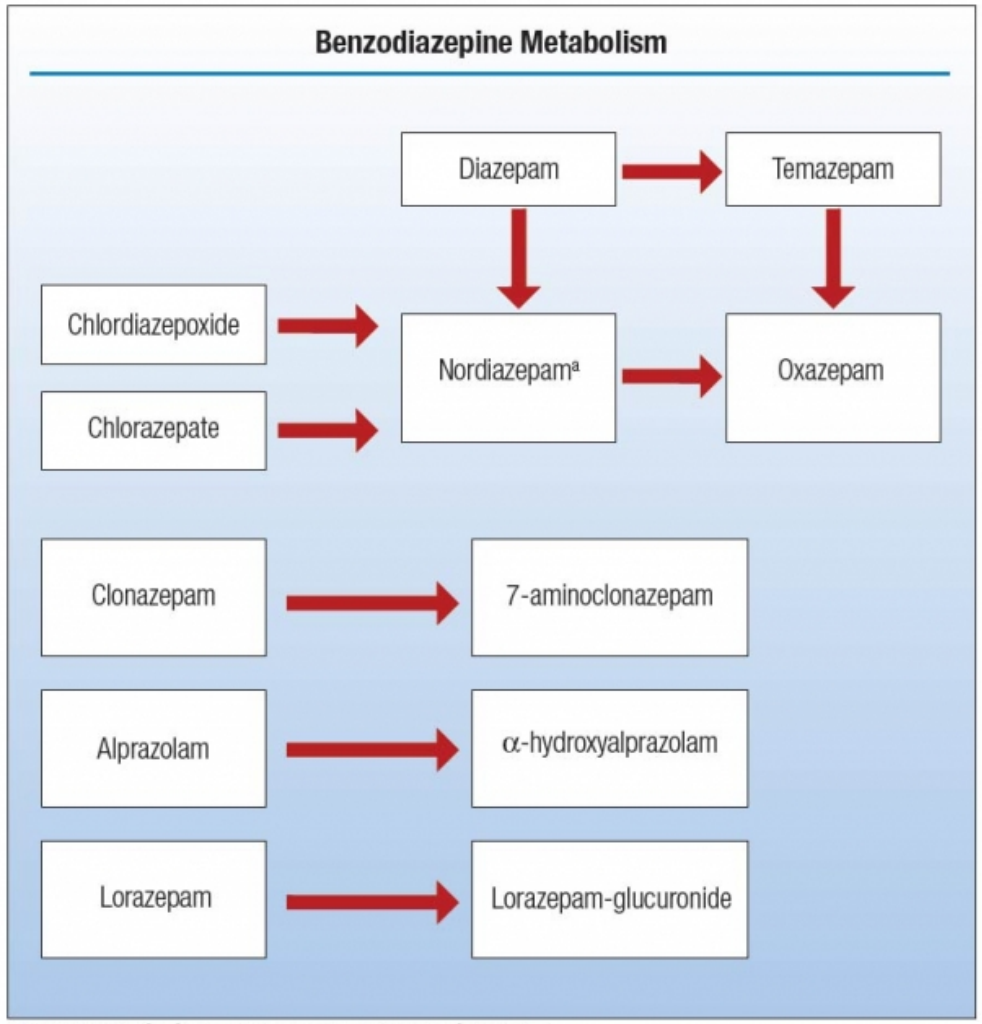


Figure 1: Illustrations of benzodiazepine metabolism.
Arrows indicate metabolic pathways
[a]Nordiazepam is also a metabolite of halazepam, medazepam, prazepam, and tetrazepam

- Most ELISA tests recognize Oxazepam or nordiazepam
- Many false negatives
  - Clonazepam
  - Alprazolam
  - Lorazepam
- High concentrations yield enough cross reactivity to sometimes be positive
- Need GCMS

https://www.practicalpainmanagement.com/treatments/addiction-medicine/drug-monitoring-screening/demystifying-benzodiazepine-urine-drug

FINAL THOUGHTS

- OUD is a chronic disease with remission and relapse. Continuing care is key
- Relapse and OD death rates are high
- Many roads to recovery. Treatment must be individualized
- Detoxification is rarely sufficient and may increase overdose risk
- MAT improves retention in treatment, reduces illicit opioid use & reduces overdose and all-cause mortality
- MAT provides time for change & healing necessary for recovery
- Counseling is important, but not a prerequisite of MAT
- MAT should only be discontinued when the patient is ready
- Drug screening may inform care but should not be punitive
- Vivitrol should be encouraged if buprenorphine is discontinued
- Buprenorphine should be re-started if there is a relapse or increased cravings
- EVERYONE should have an Rx for naloxone

References

- **Centers for Disease Control and Prevention (CDC): Opioid Overdose**

https://www.cdc.gov/drugoverdose/opioids/

- **National Institute on Drug Abuse (NIDA) – Drug Screening Tool: NM ASSIST**
  https://archives.drugabuse.gov/nmassist/
- **Substance Abuse and Mental Health Services Administration**

https://www.samhsa.gov/

- **Tobacco, Alcohol, Prescription Medication, and Other Substance Use Tool (TAPS)**

https://www.drugabuse.gov/taps/#/

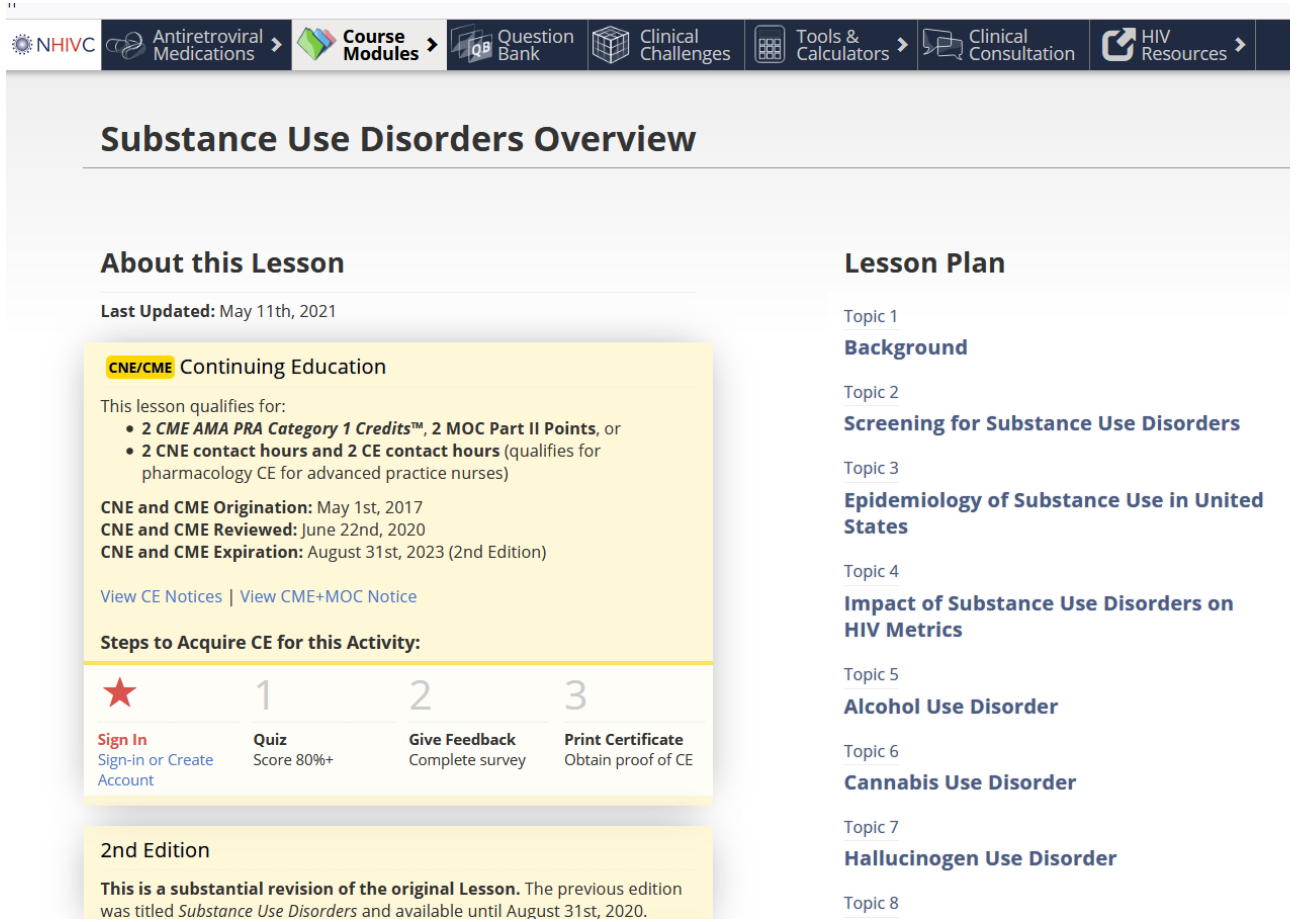
- **US Department of Health and Human Services: National Opioid Crisis - Help and Resources**

https://www.hhs.gov/opioids/

National Curriculum Modules

- **Course Module 2 Basic HIV Primary Care, Lesson 7 – Substance Use Disorders**

https://www.hiv.uw.edu/custom/primary-care/substance-use-disorders



Questions?

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Questions answered within 24 – 48 hours

WAYNE STATE
School of Medicine

AIDS Research and Education Center