Opioid Use Disorder (OUD) with a splash of COVID

Dr. David Leskowitz
Board Certified Addiction Medicine/Family Medicine

Disclosures

- Alkermes
  - Speaker for Vivitrol

Objectives

- Understand and diagnose opioid use disorder
- Understand guidelines of proper opioid prescribing
- Use of safer options to long term opioids
- Understand the role of Buprenorphine in opioid use disorder and pain management

Opioid Tolerance & Physical Dependence

- Both tolerance and physical dependence are physiological adaptations to chronic opioid exposure
- **Tolerance**
  - Increased dosage needed to produce specific effect. Develops readily for CNS and respiratory depression
- **Physical Dependence**
  - Sings and symptoms of withdrawal by abrupt opioid cessation, rapid dose reduction, administration of antagonist e.g., Narcan (Naloxone)

Addiction

- Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.
- Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

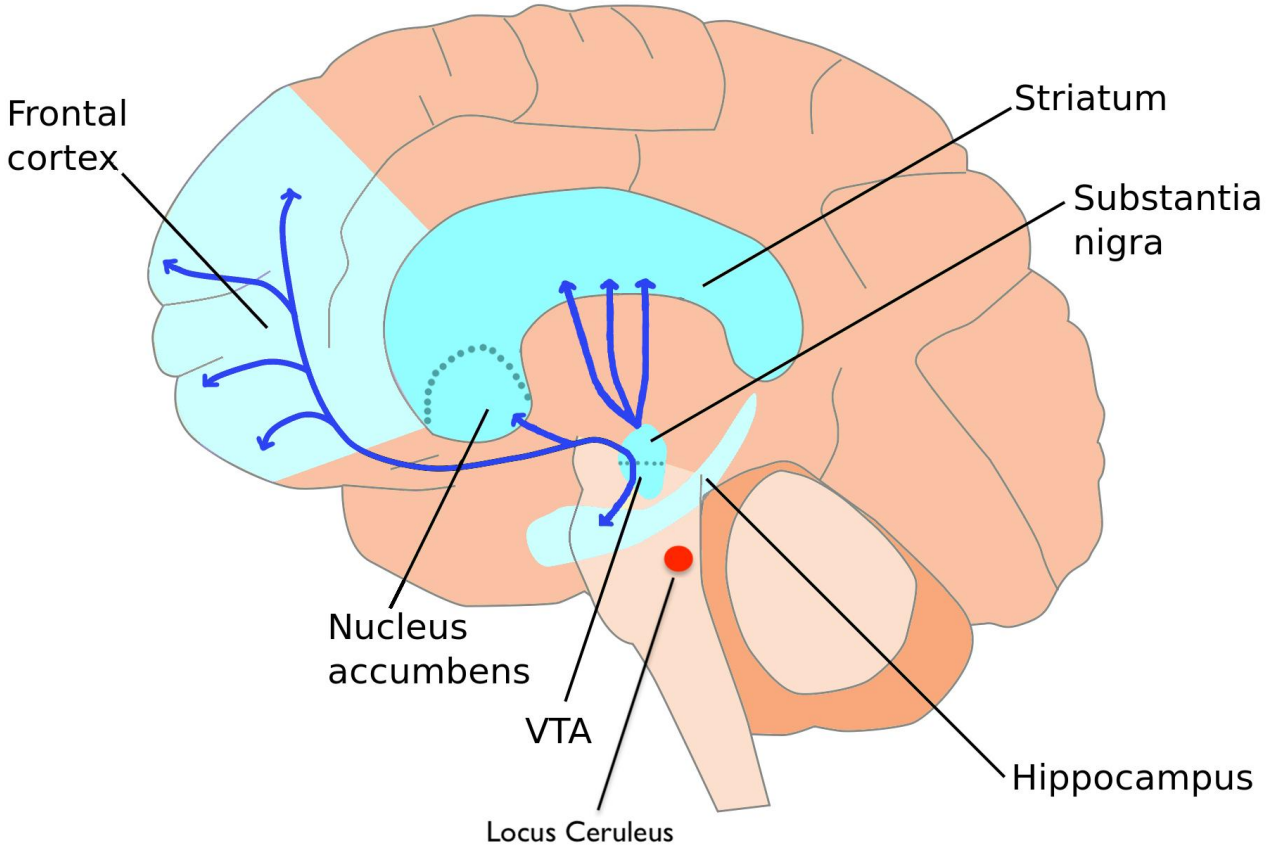
American Society of Addiction Medicine (ASAM). 2011

Neurobiology of Opioid Use Disorders

- **Opiates** are present in opium e.g., morphine, codeine, thebaine
- **Opioids** are manufactures as
  - **Semi-synthetic opioids** derived from an opiate e.g., heroin from morphine
  - **Synthetics opioids** completely synthesized to have function similar to natural opiates e.g., methadone

The Reward Pathway

- Reward/reinforcement is in part controlled by μ-receptors in the
- Reward pathway:
  - Ventral Tegmental Area (VTA)
  - Nucleus Accumbens with projections to Prefrontal Cortex
  - Dopaminergic system



Heroin and The Reward Pathway

- Heroin (di-acetyl-morphine)
  - Very lipophilic
  - Rapidly crosses the blood brain barrier in the reward pathway
- This is the reason heroin is preferred over morphine as a drug of abuse by injecting opioid users

Pharmacology

Opioid pharmacology

- Mu-opioid receptor
- G-protein coupled receptor
- Subtypes and > 100 polymorphisms to the mu-opioid receptor gene
- High affinity for beta-endorphin and enkephalins and low affinity for dynorphins
- Characterized by high affinity for morphine
- Acute changes in neuronal excitability via “disinhibition” of presynaptic release of GABA

Opioid Agonist Drug Effects

Acute Use Effects			
Euphoria	Nausea/vomiting	Miosis	Depressed respiration
Sedation	Analgesia	Itching	Decreased consciousness
Large Dose Acute Effects			
Non-responsive	Miosis	If severe anoxia Pupils may dilate	Bradycardia & hypotension
Skin cyanotic	Skeletal muscle flaccid	Pulmonary edema	Slow or absent respiration
Chronic Use Effects			
Physical dependence	Tolerance	Lethargy	Decrease bowel motility

Opioid-Induced Respiratory Depression

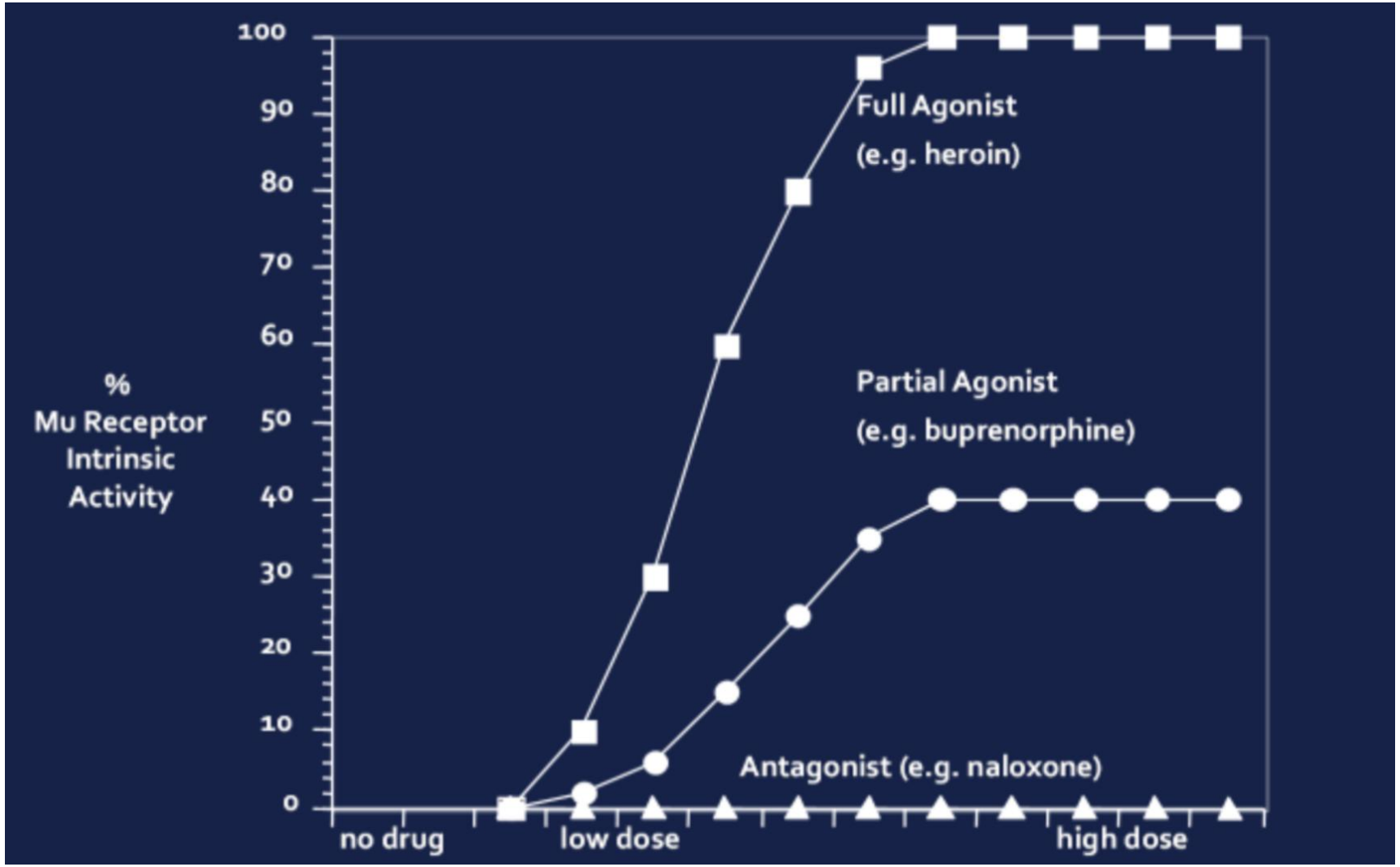
- Depression of the medullary respiratory center
- Decreased tidal volume and minute ventilation
- Right-shifted CO2 response
- Hypercapnea, hypoxia and decreased oxygen saturation
- Immediately life threatening
- Sedation occurs before significant respiratory depression and therefore is a warning sign

Dahan a et al. *Anesthesiology*. 2010.

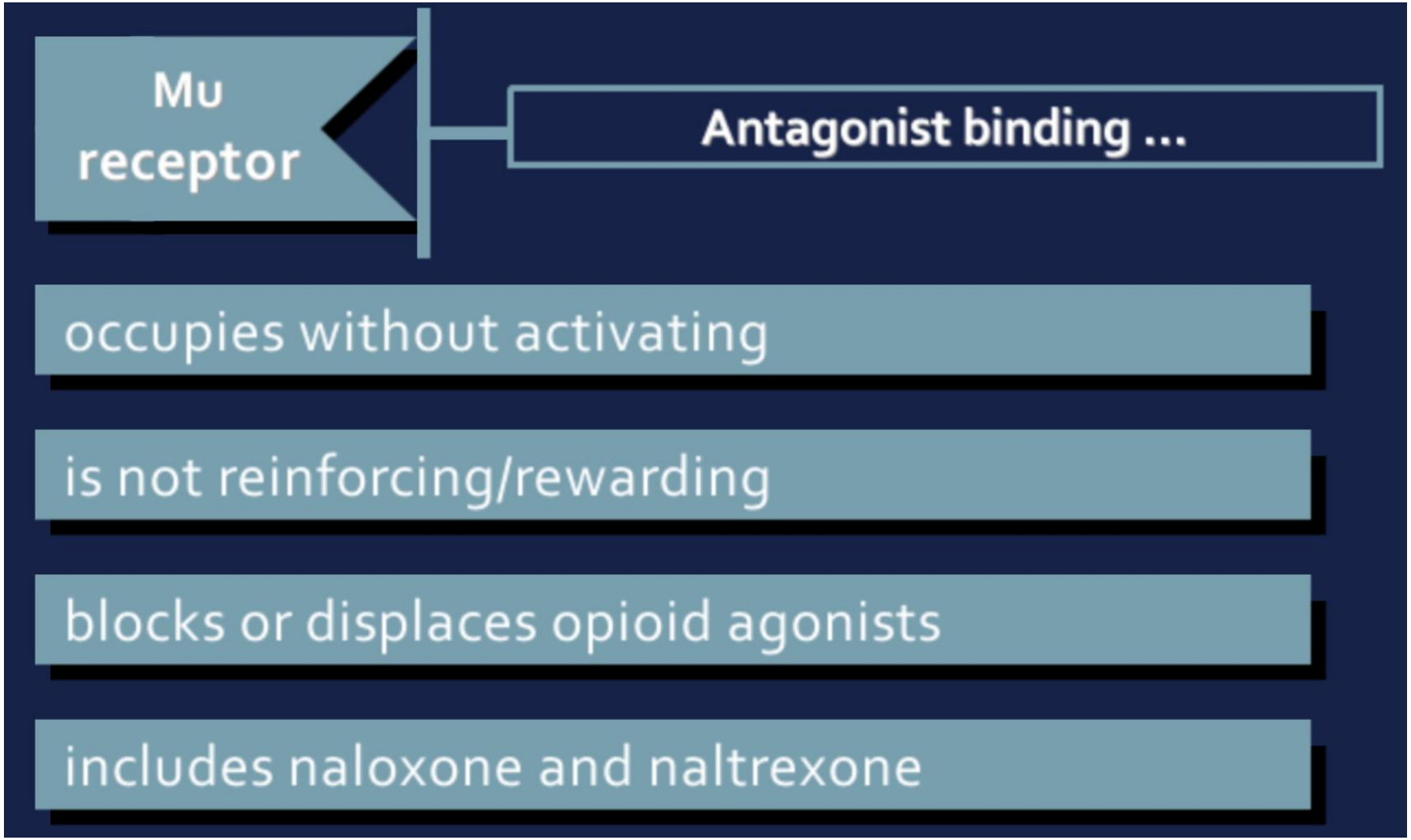
Opioid Characteristics that Increase Euphoria (reward)

- **Route of administration**
  - Faster route has a greater abuse potential
    - Injecting IV > Smoking > Injecting SQ > Oral/Intranasal
- **Drug half life**
  - Shorter half-life a greater abuse potential
    - Heroin > Methadone
- **Lipophilicity faster across blood brain barrier**
  - Higher lipophilicity has a greater abuse potential
    - Heroin > Morphine > Methadone

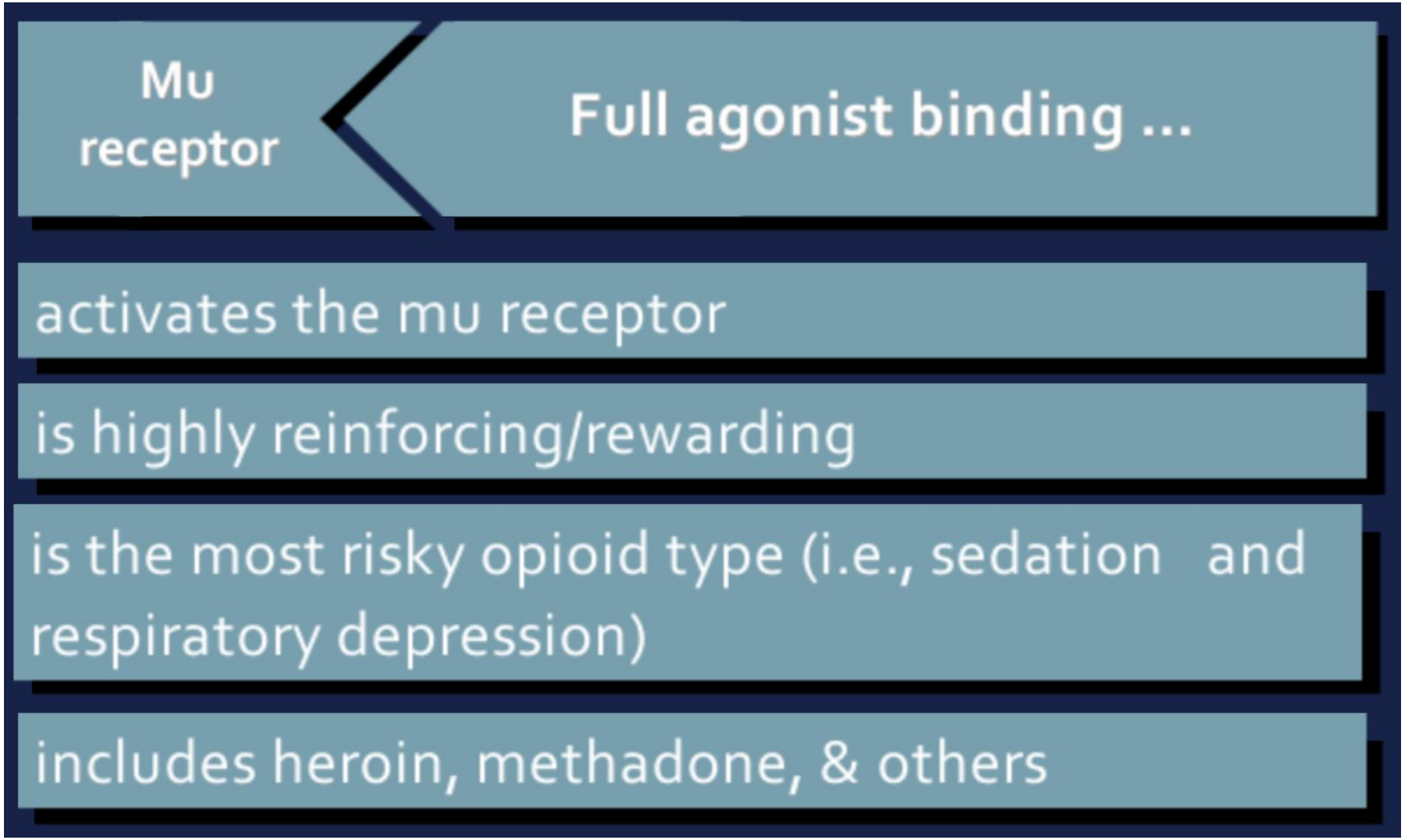
Opioid Agonists and Antagonists



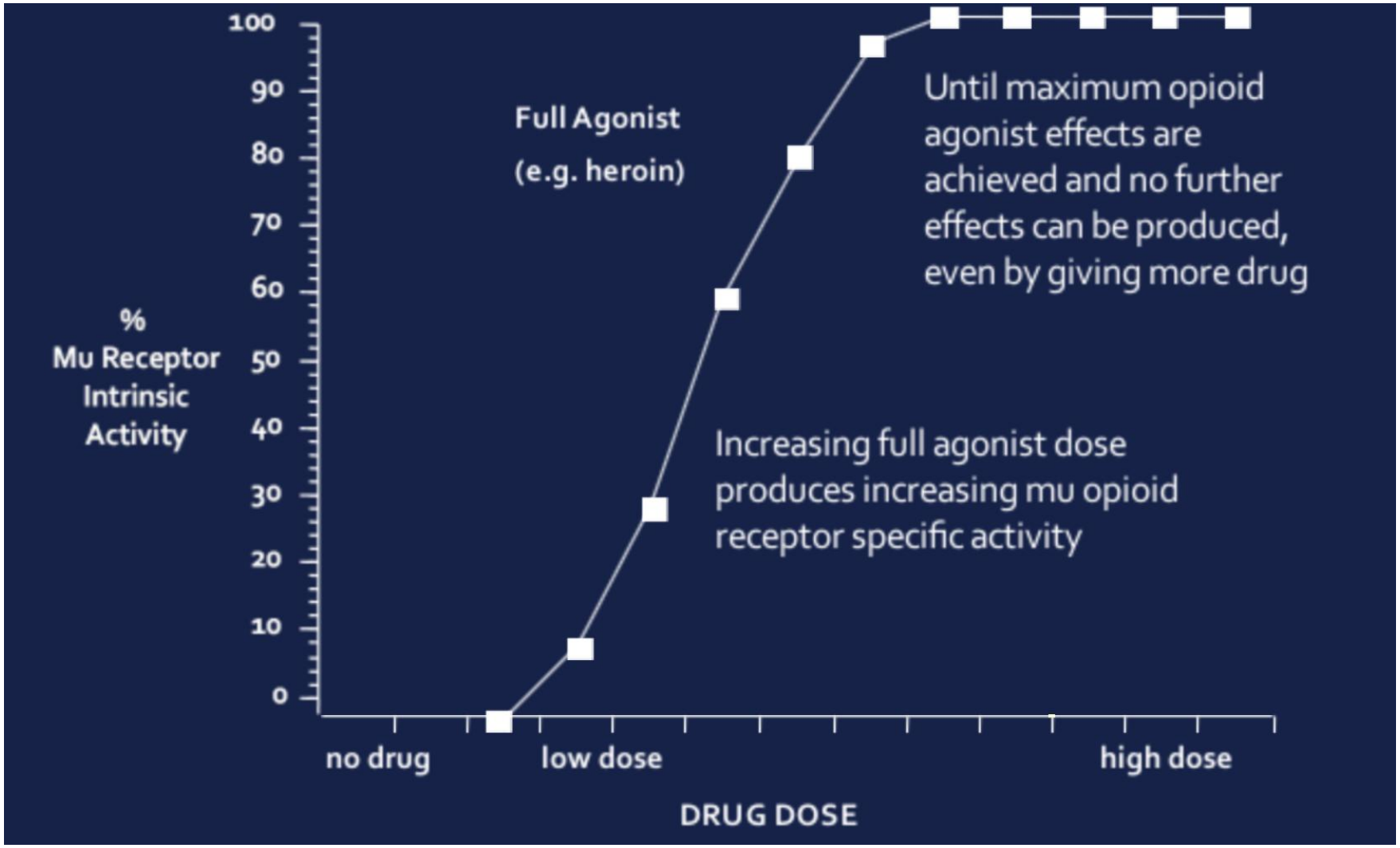
Full Opioid Antagonist



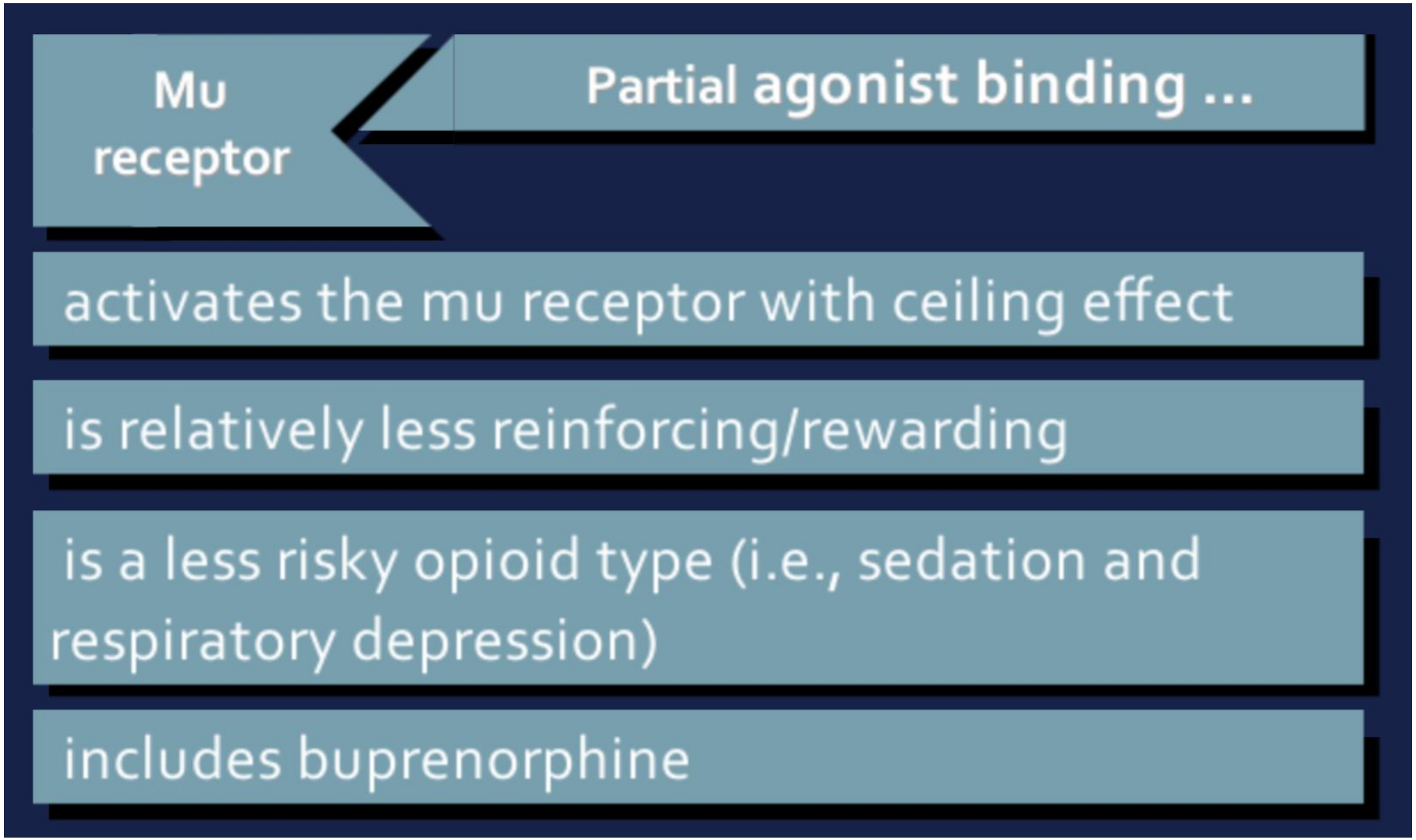
Full Opioid Agonists



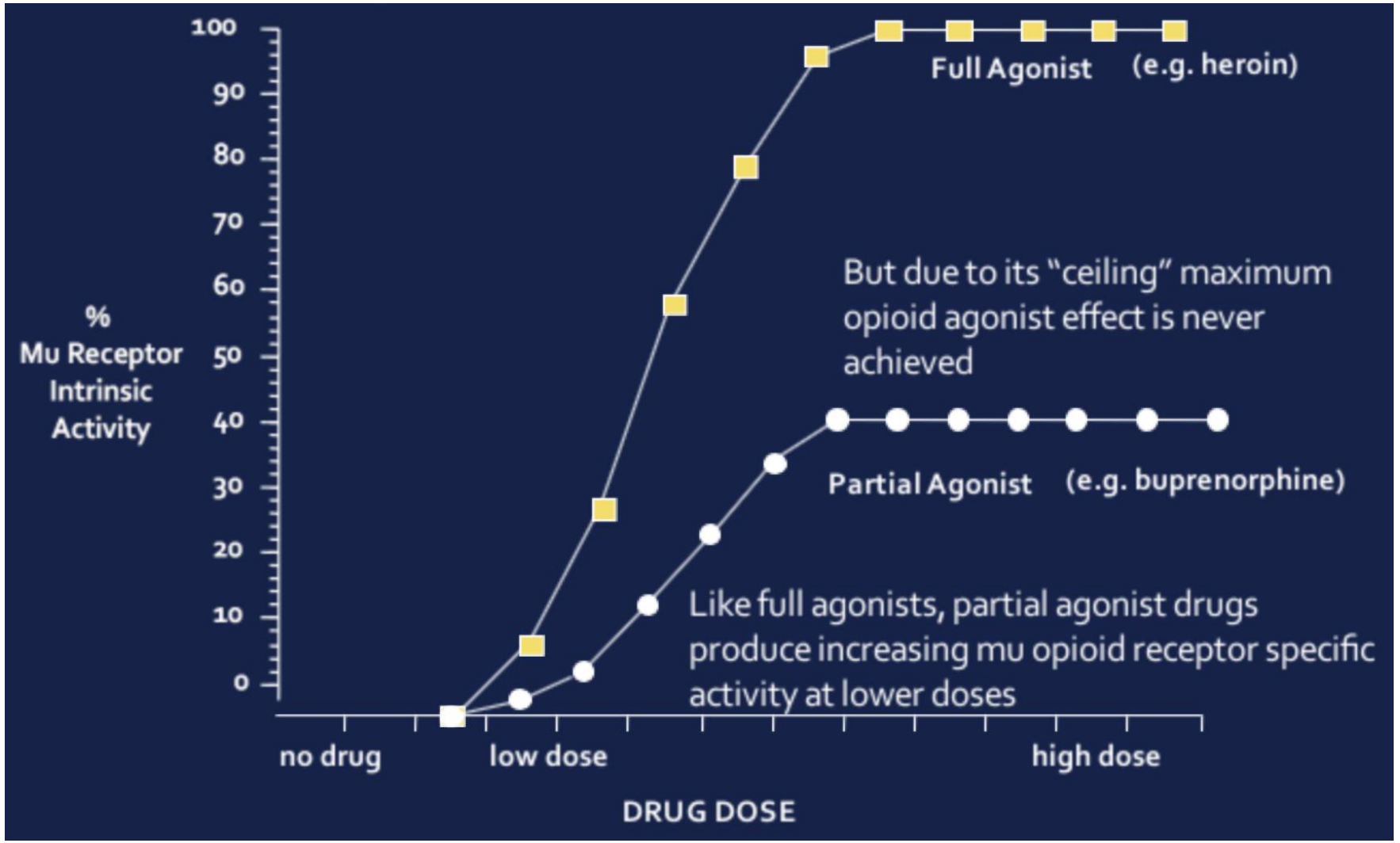
Full Agonist Activity Levels



Partial Opioid Agonists

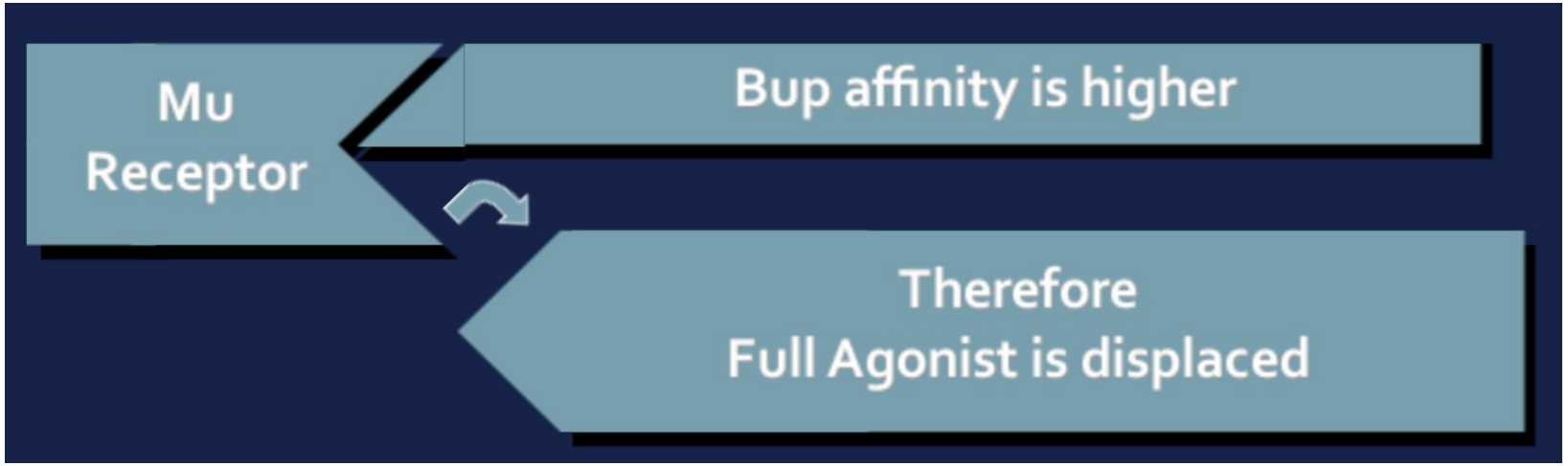


Partial Agonist Activity Levels



Receptor Affinity

- Affinity is the strength with which a drug physically binds to a receptor
  - Buprenorphine's affinity is very strong and it will displace full agonists like heroin and methadone
  - Note: receptor binding strength (strong or weak), is NOT the same as receptor activation (agonist or antagonist)



Receptor Dissociation

- Dissociation is the speed (fast or slow) of disengagement our uncoupling of a drug from the receptor
  - Buprenorphine's dissociation is slow
  - Therefore Buprenorphine stays on the receptor a long time and blocks heroin or methadone from binding

Acute Opioid Withdrawal

Grade	Symptoms / Signs
0	Anxiety, Drug Craving
1	Yawning, Sweating, Runny nose, Tearing eyes, Restlessness Insomnia
2	Dilated pupils, Gooseflesh, Muscle twitching & shaking, Muscle & Joint aches, Loss of appetite
3	Nausea, extreme restlessness, elevated blood pressure, Heart rate > 100, Fever
4	Vomiting / dehydration, Diarrhea, Abdominal cramps, Curled-up body position

Clinical Opiate Withdrawal Scale (COWS):
Pulse, sweating, restlessness & anxiety, pupil size, aches, runny nose & tearing, GI symptoms, tremor, yawing, gooseflesh

5-12: mild
13-24: moderate
25-36: moderately severe
> 36: severe

Determinants of Withdrawal Risk

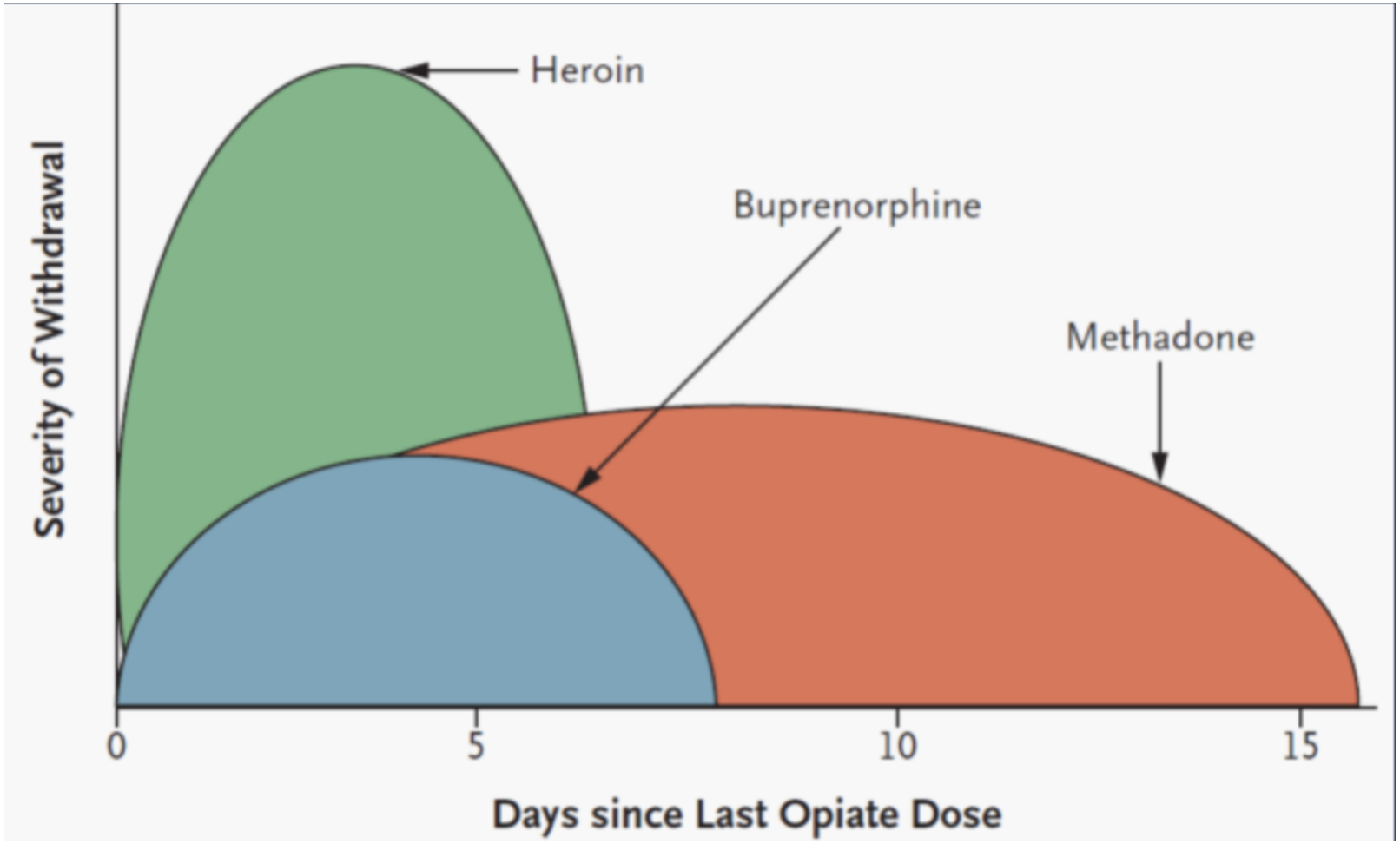
- Exposure to steady state level of medication
  - Neuro-adaptation to opioids
- Higher intensity withdrawal from
  - Higher steady state levels
  - Longer term exposure
  - Faster rate of medication clearance
    - Long vs. short half life agents

Spontaneous Acute Opioid Withdrawal

- Develops spontaneously in physically opioid dependent person suddenly stops, or markedly decreases the opioid.
- Severity is usually less with long half-life type of opioids
- Duration depends upon half-life of opioid used

	Onset	Peak	Duration
Heroin	4-6 hours	~ 3 days	4-7 days
Methadone	1-2 days	~ 7 days	12-14 days

Spontaneous Acute Opioid Withdrawal



Kosten, O'Connor. *NEJM*. 2003

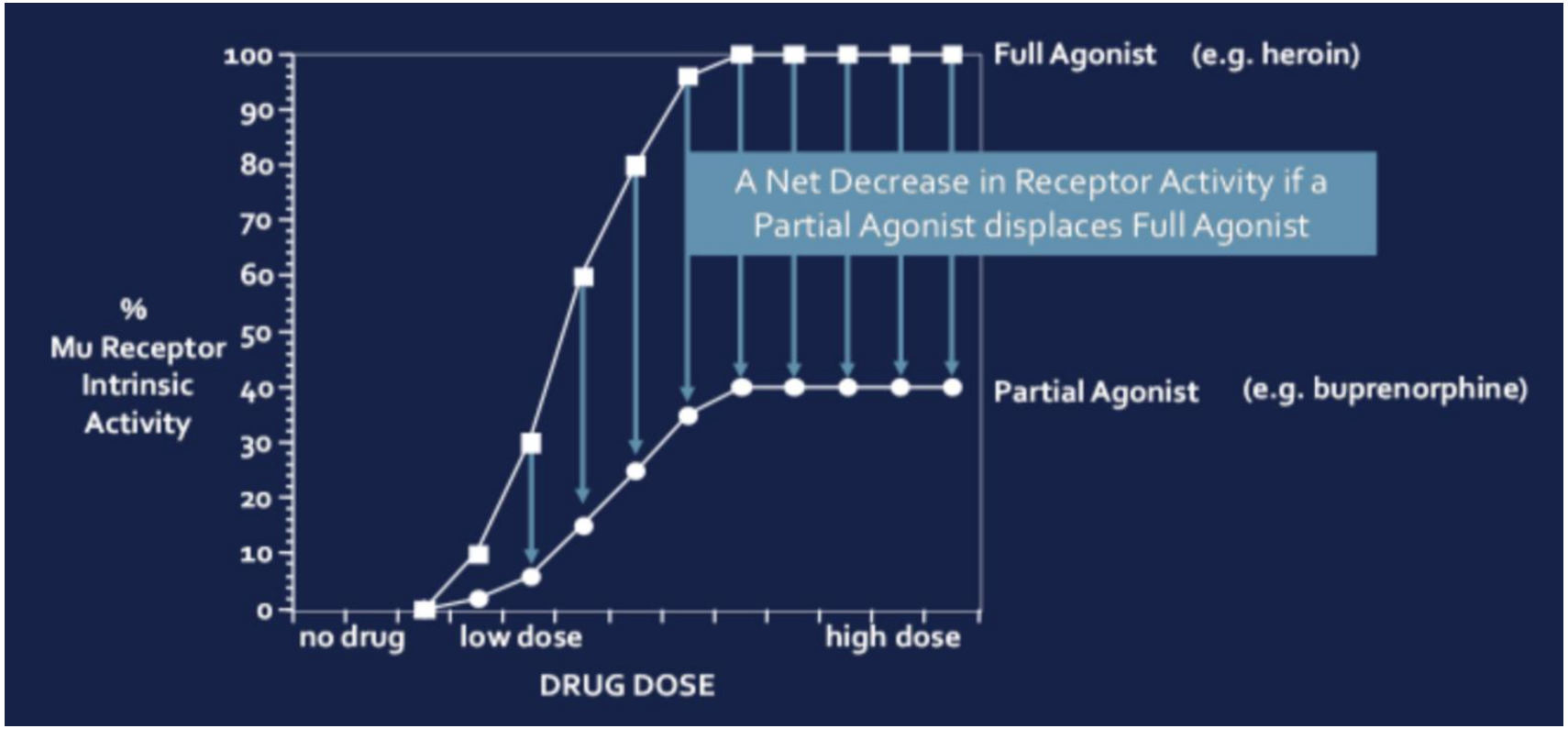
Precipitated Acute Opioid Withdrawal

- Precipitated in a physically opioid dependent person by administration of either
- An opioid antagonists drug (e.g., naloxone, naltrexone) or
- An opioid partial agonist drug (e.g., buprenorphine)
- Qualitatively similar to spontaneous withdrawal but faster onset
- Duration depends upon half-life of opioid used

	Onset	Peak	Duration
Naloxone	Minutes	Minutes	~ 20 minutes
Naltrexone	Minutes	Minutes	1-2 days
Buprenorphine	Minutes	Minutes	1-2 days

Precipitated Acute Opioid Withdrawal

- Buprenorphine will precipitate withdrawal when it displaces full agonists off the mu receptors



Treatment

Never judge, takes all those that comes before you!

HARM

Medically supervised withdrawal ”opioid detoxification”

- Low rates of retention in treatment
- High rates of relapse post-treatment
  - < 50% abstinent at 6 months
  - < 15% abstinent at 12 months
- ”Detox” is not treatment, it is just the start of treatment
- Increased rates of overdose due to decreased tolerance

O’Connor PG et al. *JAMA*. 2005.
Mattick RP, Hall WD et al. *Lancet*. 1996.
Stimmel B et al. *JAMA.* 1977.

Reasons for Relapse post detox

- Protracted abstinence syndrome (chronic withdrawal_
  - Generalized malaise, fatigue, insomnia
  - Poor tolerance to stress and pain
  - Opioid craving
- Conditioned cues (triggers)
- Priming with small dose of drug

Why use medications? Because they work….

- 80-89% relapse to drug use without medication assisted treatment (MAT)
- Increased treatment retention
- 80% decreases in drug use and crime
- 70% decrease all cause death rate

NIH Consensus Statement et al. *JAMA.* 1998.

Medication Assisted Treatment (MAT)

- "**All** Treatments Work for **Some** People/Patients."

- No One Treatment Works for **All** People/Patients."

Alan I. Leshner Ph.D

Former Director NIDA

Medication Assisted Treatment (MAT)

- Goals
  - Alleviate signs/symptoms of physical withdrawal
  - Opioid receptor blockade
  - Diminish and alleviate drug craving
  - Normalize and stabilize perturbed brain neurochemistry
- Options
  - Opioid antagonist
    - Naltrexone (full opioid antagonist)
  - Opioid agonist
    - Methadone (full opioid agonist)
    - Buprenorphine (partial opioid agonist)

Naltrexone

- Pure opioid antagonist
- Blocks opioids without agonist effects
  - Serum level of 2ng/ml blocks 25mg IV heroin effects
- No tolerance or physical dependence (withdrawal) develops
- Prevents impulsive drug use
- Protects against overdose, but discontinuation poses higher risk because of lost tolerance

Oral Naltrexone Efficacy

- Oral Naltrexone
  - Duration of action 24-48 hours
  - FDA approved in 1984
- 10 RCTs ~ 700 participants to naltrexone alone or with psychosocial therapy compared with psychosocial therapy alone or placebo
  - No clear benefit in treatment retention or relapse at follow up
- Benefit in highly motivated patients
  - Impaired physicians > 80% abstinence at 18 months

Cochrane Database of Systematic Reviews. 2006.

Oral Naltrexone Safety

- Naltrexone has the capacity to cause hepatocellular injury when given in excessive doses
- Naltrexone does not appear to be hepatotoxic at the recommended doses
- Contraindicated in hepatitis or liver failure

Injectable Naltrexone Dosing

- Monthly XR-NTX 380mg for opioid dependence
- IM injection (w/customized needle) once/month
- FDA approved 2010
- Patients must be opioid free for a minimum of 7-10 days before treatment

Sigmon S et al. *American Journal of Drug and Alcohol abuse.* 2012.

Methadone Maintenance Treatment

- Highly regulated – *Narcotic Addict Treatment Act 1974*
  - Created Opioid Treatment Programs (OTPs)
  - Separate system not involving primary care or pharmacists
- Treatment (methadone dispensing) for opioid use disorder limited to licensed OTPs
- It is illegal for a physician to prescribe methadone for the treatment of opioid use disorders in an office-based practice

Methadone Maintenance in OTP

- Highly structured
  - Daily nursing assessment
  - Weekly individual and/or group counseling
  - Random supervised drug testing
  - Psychiatric services
  - Medical services
  - Methadone dosing
    - Observed daily → ”take homes” based on stability and time in treatment. Max: 27 take homes. Varies by state, county and individual clinic.

Methadone Maintenance Treatment Benefits

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

Methadone Maintenance Treatment Limitations

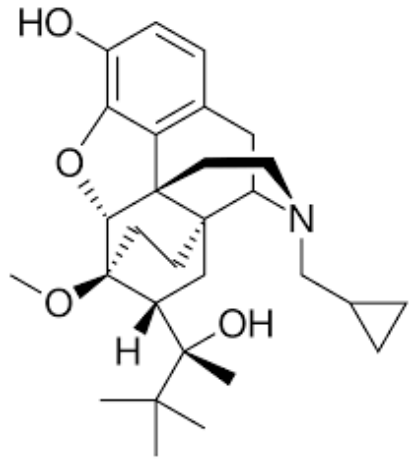
- Limited access
- Inconvenient and highly punitive
- Mixes stable and unstable patients
- Lack of privacy
- No ability to “graduate” from program
- Stigma

Methadone Safety

- Long, variable, unpredictable half-life
  - Serum t ½ 20-120 hours
- QTc prolongation, risk of torsades de pointes
  - Generally does related; > 100mg daily
  - Multifactorial; ↓ K; ↓ Mg, other drugs ↑ QTc
  - CYP450: 3A4, 2D6 interactions
  - QTc > 500 msec > Torsades de Pointes

Wedam E et al. *JAMA Internal Medicine.* 2007.

Buprenorphine



- Partial mu-opioid agonist
- Schedule III (*vs. Methadone: schedule II*)
- **Metabolism**
  - In liver with N-dealkylation by cytochrome P450 3A4 enzyme system into an active metabolite norbuprenorphine
    - Norbuprenorphine undergoes further glucuronidation
- **Elimination**
  - Excreted in feces (70%) and urine (30%)
    - Mean elimination half-life = 37 hours
  - Commercial screening urine drug test for parent compound and metabolite
  - Does NOT show as opiate positive on standard screen

Cytochrome P450 3A4 interactions

- Buprenorphine is metabolized by CYP3A4. Clinically significant drug/drug interactions are uncommon
- Elevated Buprenorphine levels have bene reported with co-administration of atazanavir/ritonavir
- Decreased buprenorphine levels have been reported with co-administration of rifampin

McCace-Katz et al. *The American Journal of Addictions.* 2009.

Buprenorphine Formulations

- Approved for moderate to severe OUDs, can be used OFF LABEL for pain
  - Sublingual forms (tablets and films)
  - **“Combo”** (buprenorphine/naloxone)
  - **”Mono”** (Buprenorphine only) generic tablets only
- Approved for pain and NOT OUDs
  - Parenteral form
  - Transdermal Patch (7-day)

Sublingual Use & Bioavailability

- Sublingual tablets/film strip must be held under tongue for several minutes to dissolve
  - Instruct to:
    - Not talk
    - Keep dissolving liquid under tongue
    - Don’t swallow till entire tablet dissolved
    - Considerable variability between patients in Bup Bioavailability of tablets/film strip
    - Buccal film – able to talk and swallow

Purpose of Naloxone in “Combo”

- Naloxone has limited bioavailability orally or sublingually, but is active parenterally, e.g., injected SQ, IM or IV
- The combo product, if crushed, dissolved and injected the:
  - Naloxone may cause initial withdrawal if the person is physically opioid dependent
    - Decreasing diversion and misuse
  - Naloxone will block, or attenuate, the opioid agonist effect of the buprenorphine
    - Therefore safer if diverted

Comer S et. al. *Addiction.* 2010.

Buprenorphine/Naloxone Bioavailability

- If dissolved sublingually
  - Buprenorphine is active
  - Naloxone is not active
- If swallowed
  - Buprenorphine not active (minimal oral bioavailability)
  - Naloxone not active (no oral bioavailability)
- If injected
  - Buprenorphine active, but
  - Naloxone active x 20 minutes so attenuates the parenteral “rush”

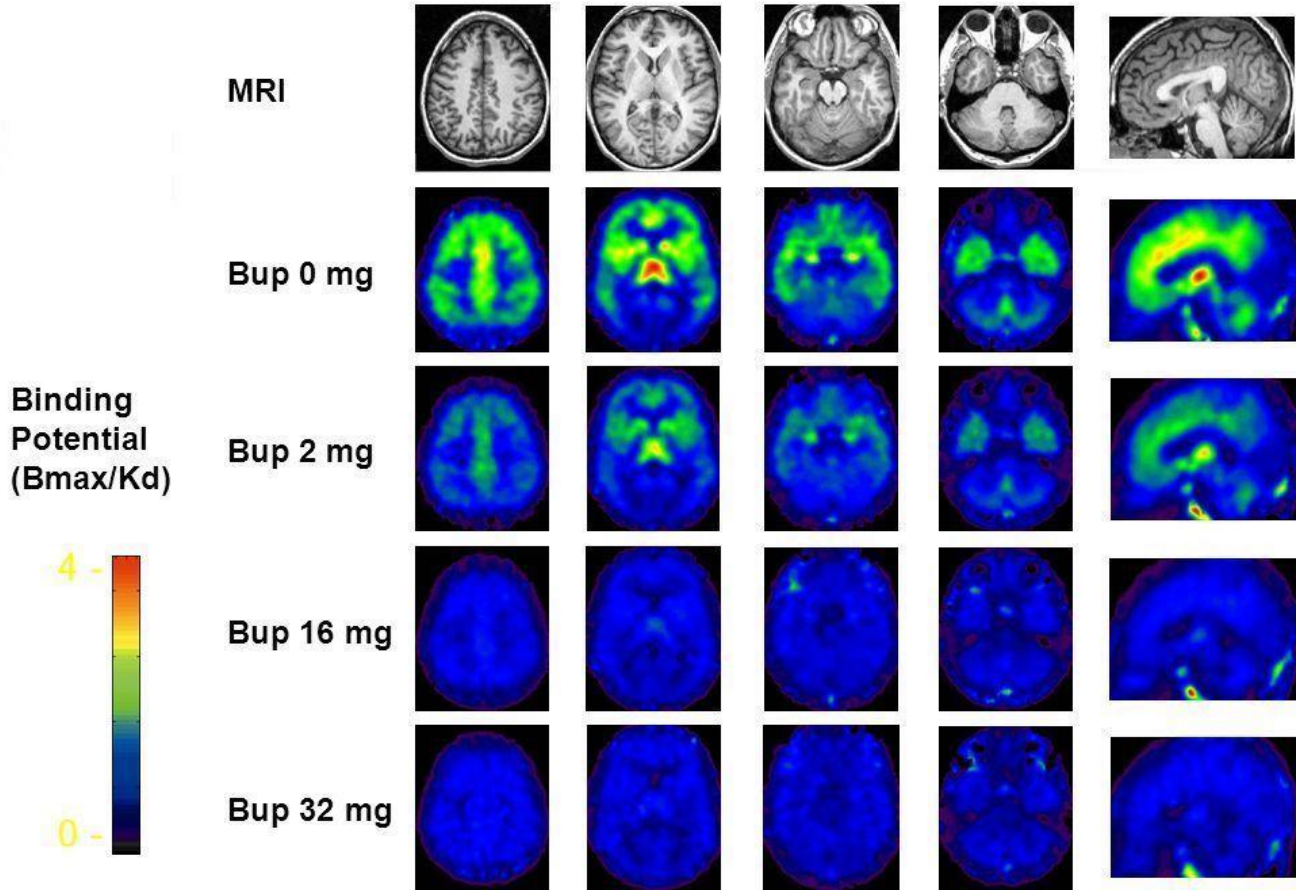
- Not time released so tablets/film strip can be split

  (splitting tablets or film is considered “off-label” use)

How Does Buprenorphine Work?

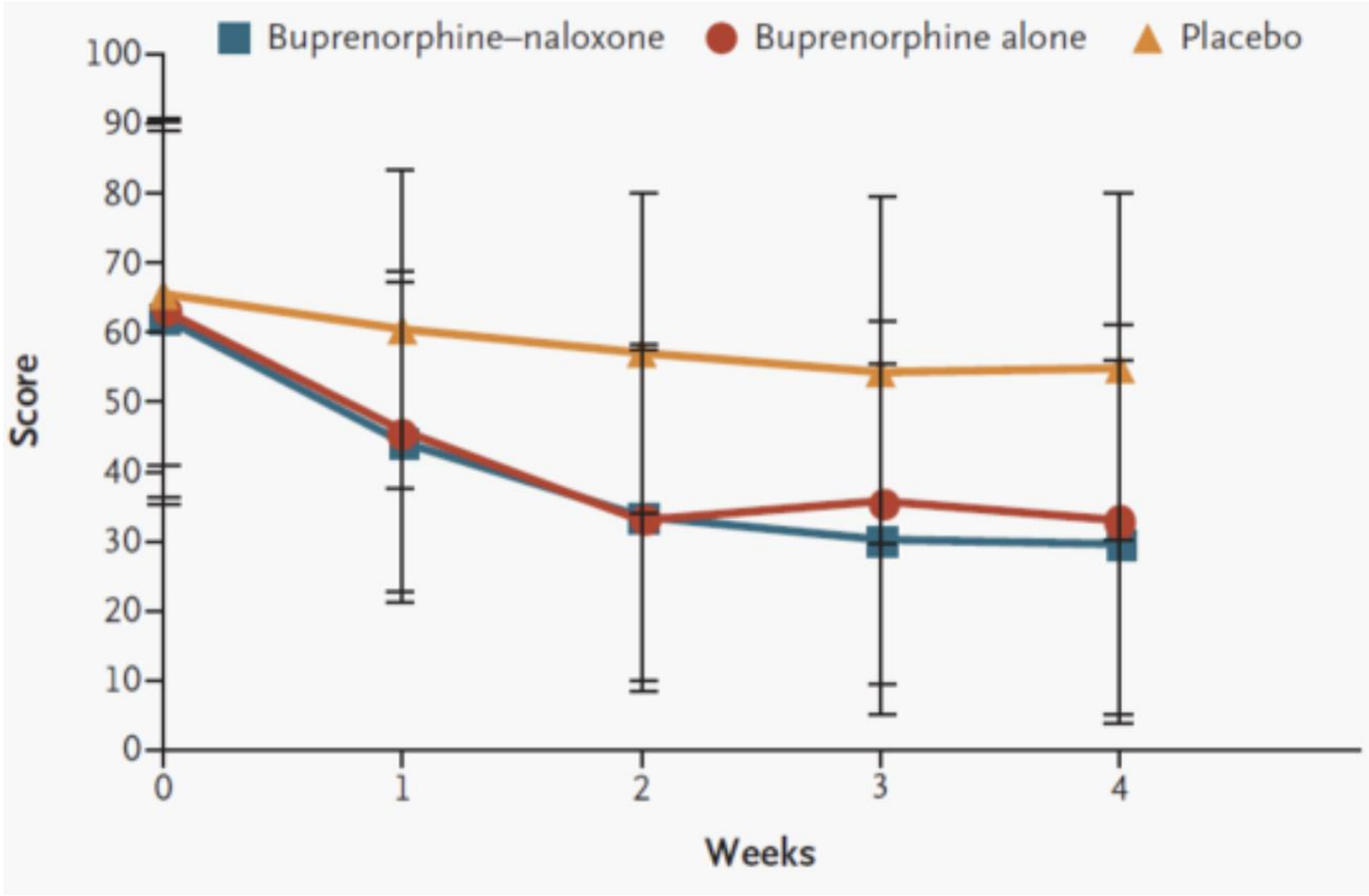
- Buprenorphine may reduce the effects of other opioids taken due to its high affinity for, and slow dissociation from, the mu receptor
- However, buprenorphine is unlikely to block *ALL* effects from an opioid taken after initiation of buprenorphine treatment
- This is because the availability of mu receptors is a dynamic process; while effects may be less, they are not likely to be completely eliminated

Effects of Buprenorphine Dose on mu opioid receptor availability in subjects



Zubieta et al. *Neuropsychopharmacology.* 2000; 23:326-334.

Buprenorphine Decreases Opioid Craving



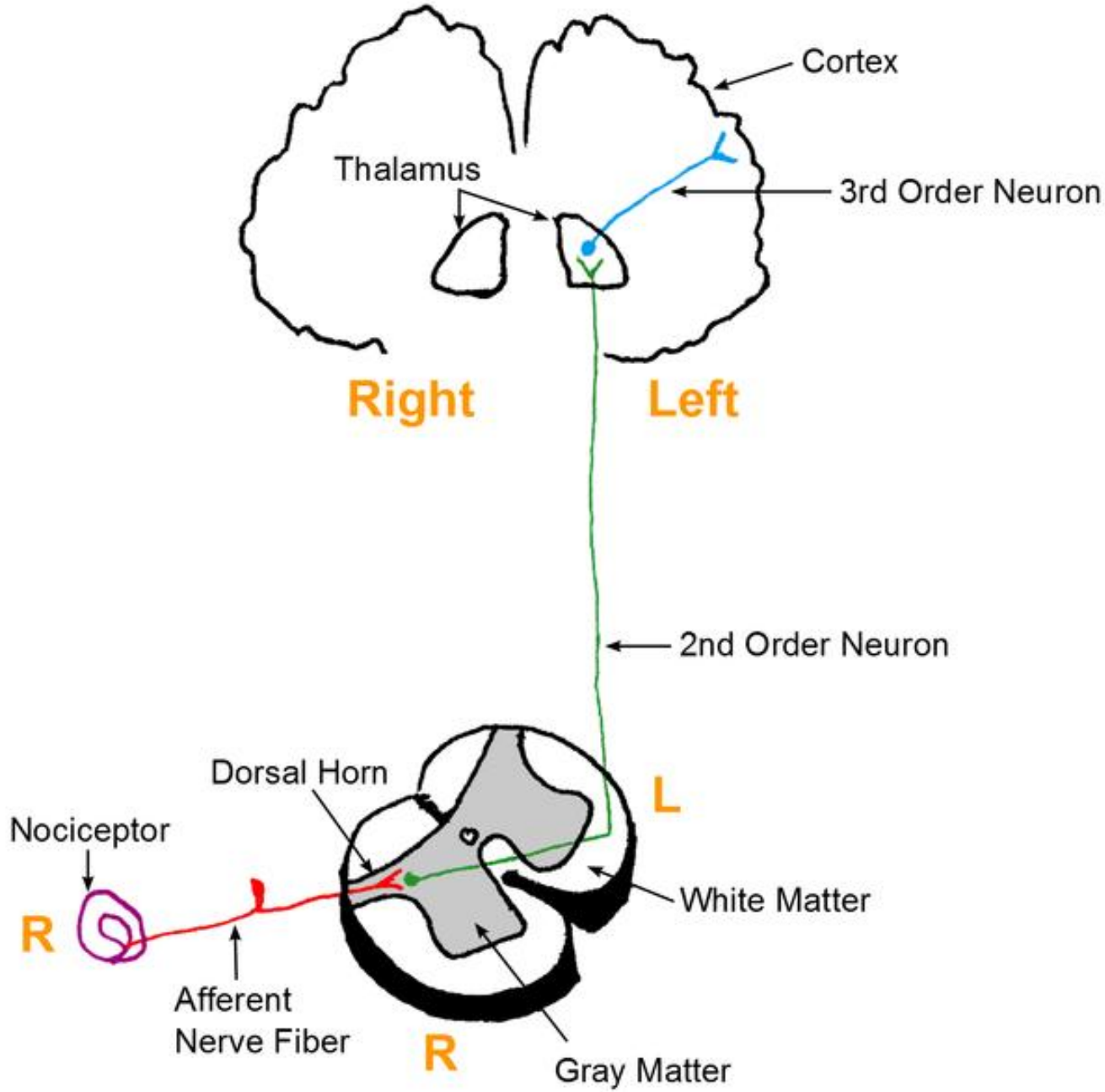
Fudala P et al. *NEJM*. 2003.

Medication Comparison

	Methadone	Buprenorphine	ER Naltrexone
Pharmacology	Full agonist	Partial agonist	Full antagonist
Dosing	Daily (but duration often longer)	Daily	*q4wks*
Setting	Specialty licensed OTP	Office-based or OTP, requires "X" waiver	Any medical setting, requires injection
Induction	No time restriction; start low, go slow	Mild-mod withdrawal: > 8-12 hrs after last opioid	>7 days after last opioid
Adherence	Intrinsically reinforcing	Intrinsically reinforcing	Long acting

Pain

- Pain is a subjective experience with two complementary aspects:
  - One is a localized sensation in a particular body part
  - The other is an unpleasant quality of varying severity commonly associated with behaviors directed at relieving or terminating the experience.


Cortex
Thalamus
3rd Order Neuron
Right
Left
2nd Order Neuron
Dorsal Horn
L
Nociceptor
White Matter
R
Afferent
Nerve Fiber
R
Gray Matter

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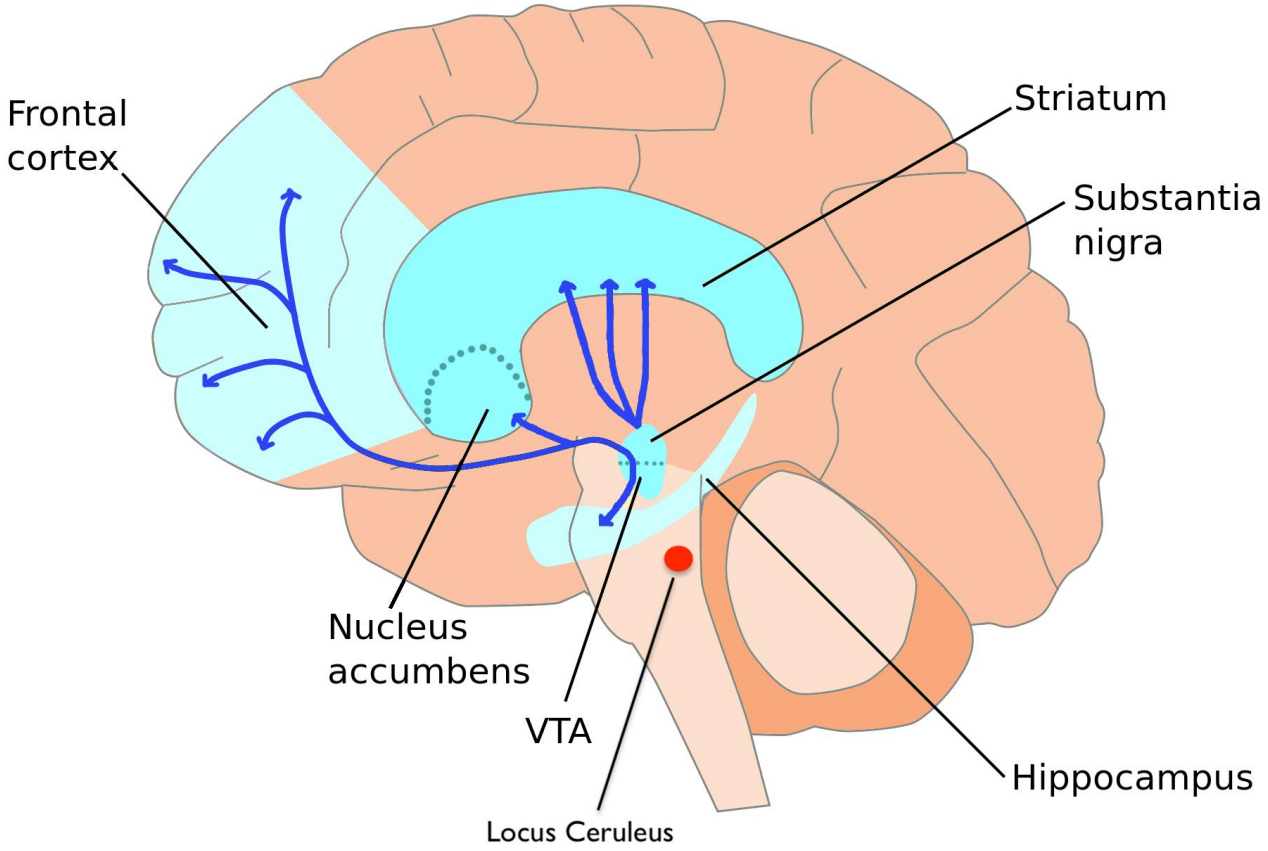

Heroin and The Reward Pathway

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- This is the reason heroin is preferred over morphine as a drug of abuse by injecting opioid users

Cancer pain use

- **Metastatic Bone Pain** – MCC of pain in cancer patients, caused by stretching of the periosteum
- **Visceral pain** (internal organ pain) - pain fibers around organs are activated.
- **Neuropathic pain** in cancer patients is often not caused by the cancer itself; instead, it may be a side effect of treatment
  - Chemotherapy can cause a painful sensory neuropathy
  - Targeted radiation used to treat cancer can also cause neuropathic pain
- **Headaches** - Parenchymal brain tissue has no pain receptors; pain is generated when vessels and/or the meninges are stretched by a mass

Duloxetine

Brand name: Cymbalta

Antidepressant and Nerve pain medication

It can treat depression, anxiety, diabetic peripheral neuropathy, fibromyalgia, and chronic muscle or bone pain.

Brands: Irenka and Cymbalta

Availability: Prescription needed

Pregnancy: Consult a doctor

Alcohol: Interactions can occur

side effects | interactions | warnin

For informational purposes only. Consult your local medical

Cancer pain

- **Spinal cord compression** occurs in roughly 2% to 5% of cancer patients. A tumor produces edema, inflammation, and mechanical compression, with direct neural injury to the cord, as well as vascular damage and impairment of oxygenation
- Pain due to surgery for cancer
  - Pain after Thoracotomy
  - Pain after Mastectomy

PRE-EXISTING PAINFUL CONDITIONS

- Ten percent of people with cancer pain have a pre-existing painful condition such as :
  - degenerative arthritis
  - diabetic peripheral neuropathy.
- Always ask about this in your history:
  - “Do you have any painful conditions that existed before cancer?”
  - Not every type of pain a cancer patient has is cancer related.

Pain treatment in cancer patients – Plan use

- The first step in treating cancer pain is to **ask patients what their goals and expectations are in terms of pain control**.
- Some patients would like you to be more aggressive, some less so.
- When developing your treatment plan, target each of the pain generators.
- Your treatment plan may include a mixture of:
  - Nonopioids
  - Opioids
  - Injections
  - Radiation
  - surgery.

Buprenorphine for treating cancer pain

- Many patients with cancer experience moderate to severe pain that requires treatment with strong analgesics.
- Buprenorphine, fentanyl and morphine are examples of strong opioids used for cancer pain relief.
- However, strong opioids are ineffective as pain treatment in all patients and are not well-tolerated by all patients.

Cochrane Review -2015

- **Buprenorphine for treating cancer pain**
  - To assess the effectiveness and tolerability of buprenorphine for pain in adults and children with cancer.
  - This Cochrane review identified 19 relevant studies including a total of 1421 patients that examined 16 different intervention comparisons.
  - Of the studies that compared buprenorphine to another drug, **11 studies performed comparative analyses between the randomised groups,** and five studies found that buprenorphine was superior to the comparison treatment.
  - Based on the available evidence, it is difficult to say where buprenorphine fits in the treatment of cancer pain with strong opioids.
  - Palliative care patients are often heterogeneous and complex, so having a number of analgesics available that can be given differently increases patient and prescriber choice.

Case Study

- A 57-year-old woman with breast cancer diagnosed 2 years ago presents to the emergency department with back pain and some mild weakness in her legs. An MRI performed in the emergency department shows a thoracic metastatic tumor, which is causing compression of the cord at T8. On a visual analog scale, she rates her pain level as 10 out of 10. The woman begins receiving intravenous (IV) Dilaudid 2 mg every 2 hours and IV Solu-Medrol. Four hours later, she rates her pain as 8 out of 10.
- What is the next step in treating this patient?

Case Study

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- What is the next step in treating this patient?
- The patient is admitted to the hospital
- Emergent radiation treatment begins.
- By the end of treatment, the patient is no longer receiving IV narcotics and using a minimal amount of hydrocodone orally for pain as needed.

Kevin: 40 yo Male
Trasnsitioning from SAO

- Social History
  - Utility worker who works outdoors most of the year
  - Smoker, 20 pack yers history
- Medical Hx
  - Chronic Low back pain due to physical demands and repetitive motion of his job
  - Undergoing chiropractic treatments and physical therapy
  - ORT (Opioid Risk Tool) Score = 5

Kevin: 40 yo Male
Trasnsitioning from SAO

- Treatment Hx
  - OTC IBU 200mg QID, increasing over a period of 2 yrs to 800mg QID. Pain level reduced, but not to a satisfactory level
  - At 800mg QID experiencing GERD issues which were treated with Esmoprazole 20mg QD
  - Transitioned to oxycodone/APAP 5mg/325mg q6h prn
  - Pain level improved; over time, dose needed to be increased to oxycodone/APAP 10mg/325mg q4h.
  - Now on 6 tablets oxycodone/APAP 10mg/325mg per day (90MME)
  - **Buprenorphine might be a good choice for Kevin**

Buprenorphine

- Increased efficacy, patients on disolvable oral formulation experienced at least 50% reduction in pain at week 12 according to Balbuca study
- Pain reduction- down from 7 to 3
- Half life – long (12h) allows for twice daily dosing
- Consistent Dose – patient can be maintained at optimal dose with leittle change once pain control achieved
- Low dose of buprenorphine needed for pain mgmt (mcg vs mg of oxycodone)
- Decreased need of rescue medication.
- **Respiratory effect** - No respiratory deression at doses used for pain mgmt
- Tolerabilty – established tolerapbility in opioid expreienced patients

Legislation

Drug Addiction Treatment Act (DATA) of 2000

- Signed by President Clinton in October 2000
- Allows prescription of an opioid to an opioid addicted person for the treatment of addiction, with certain restrictions.
- Prior to this Act, only licensed methadone treatment programs

DATA 2000, obtaining Buprenorphine waiver

- MD/DO must have 8 hours of training in opioid by AMA, AAAP, ASAM, AOA, APA
- PA/NP must complete an additional 16 hours of training
- Providers must submit notification to Secretary of HHS of intent to prescribe and obtain a new DEA number. The regular DEA is retained for other scheduled substances. The new “X” DEA is used only for buprenorphine prescriptions.

DATA 2000, restrictions: Medication allowed

- Drug must be approved by FDA for use in treating addiction
- Medication must be DEA schedule III, IV, or V (*Methadone is schedule II*)
- Buprenorphine and Buprenorphine/naloxone sublingual tablets and film strips approved October 2002, are schedule III, and are the only the only medications fitting these restrictions

DATA 2000, restrictions: number of patients

- 30 patients per provider during the first year of the waiver
- After the first year 100 patients per provider – a new waiver must be obtained
- Patient remains on your census until the last prescription has run out
- Hospitalized patients with a primary diagnosis of other than opioid dependence can be ordered buprenorphine by a non-waivered provider

Questions?

10 min break

MAT from Primary Care to Federally Qualified Healthcare Center

With a splash of COVID-19

AN ESTIMATED 97 MILLION ADULTS IN THE UNITED STATES ARE OVERWEIGHT OR OBESE

WEIGHT MANAGEMENT IN PRIMARY CARE

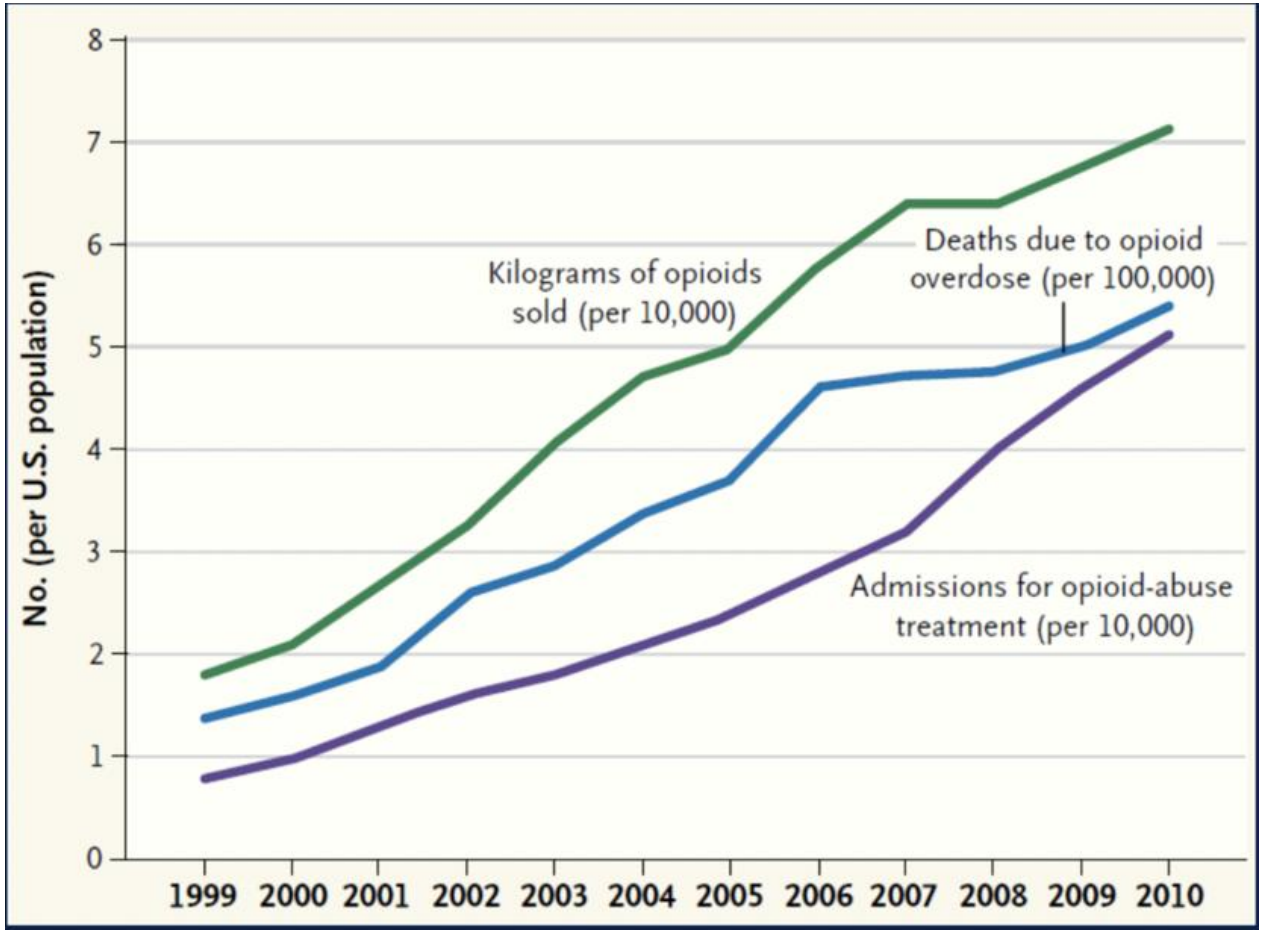
BAYER
PHARMACEUTICAL PRODUCTS.

Send for samples and Literature to

FARBENFABRIKEN OF ELBERFELD CO.

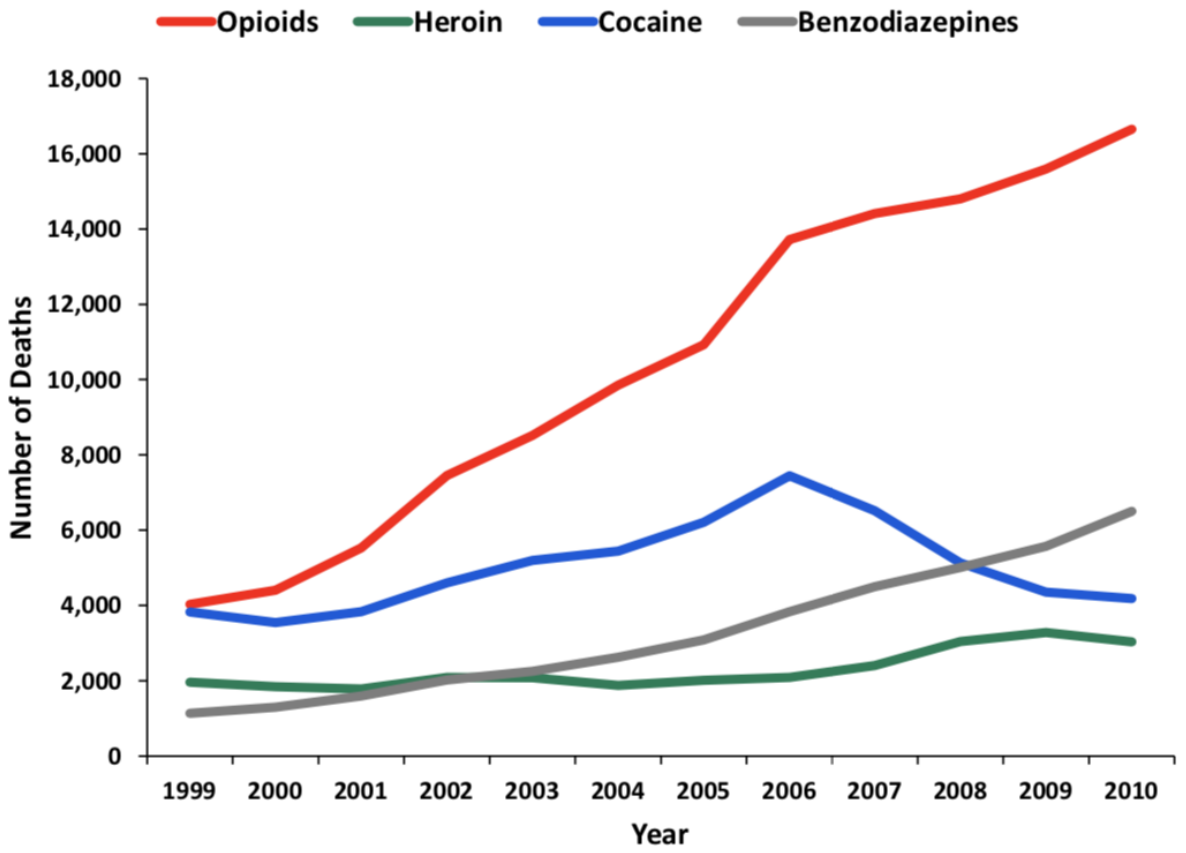
40 STONE STREET, NEW YORK.

Prescription Opioid Trends: 1999-2010



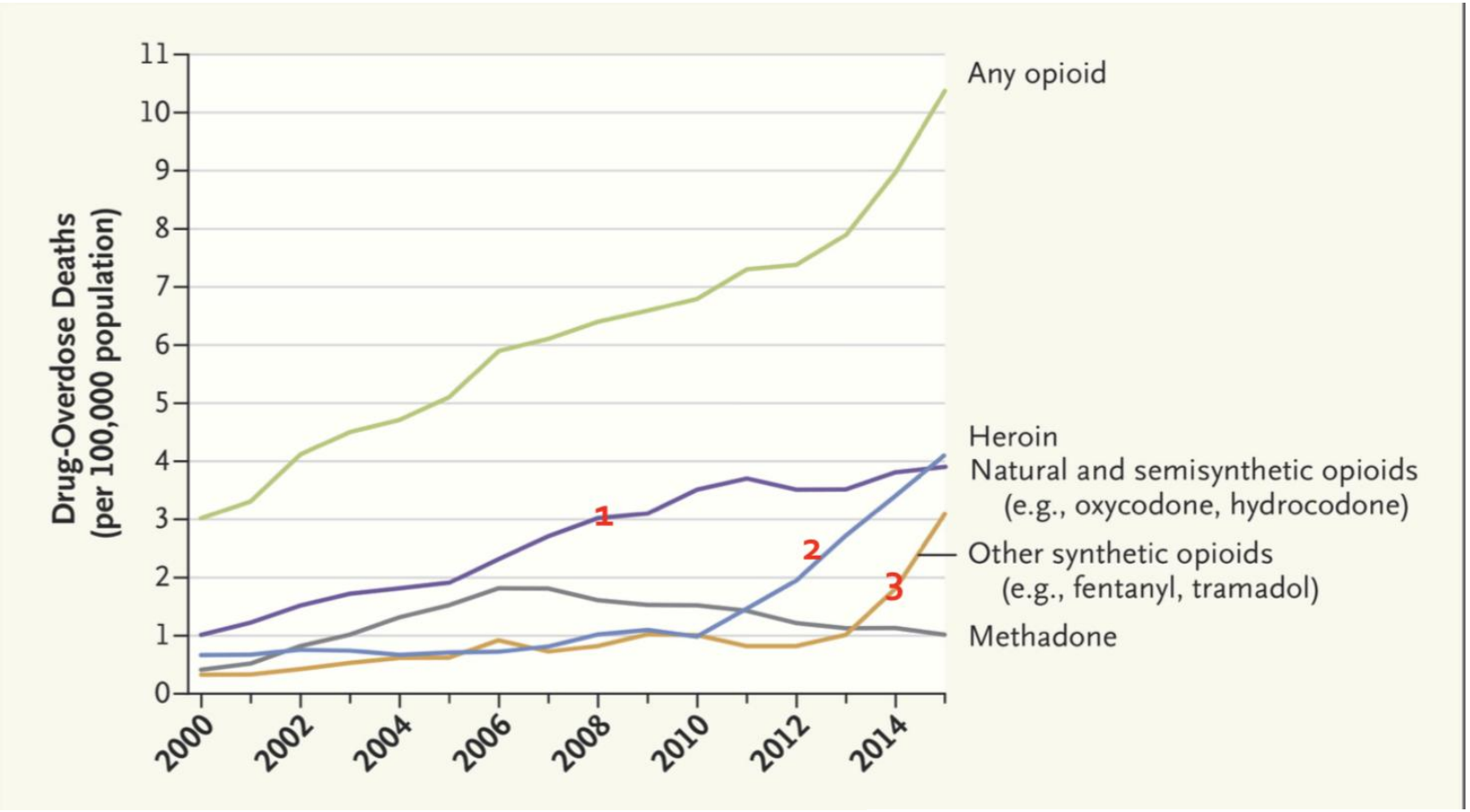
National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System of the DEA; Treatment Episode Data Set

Drug Overdose Deaths by Major Drug Type, United States, 1999-2010



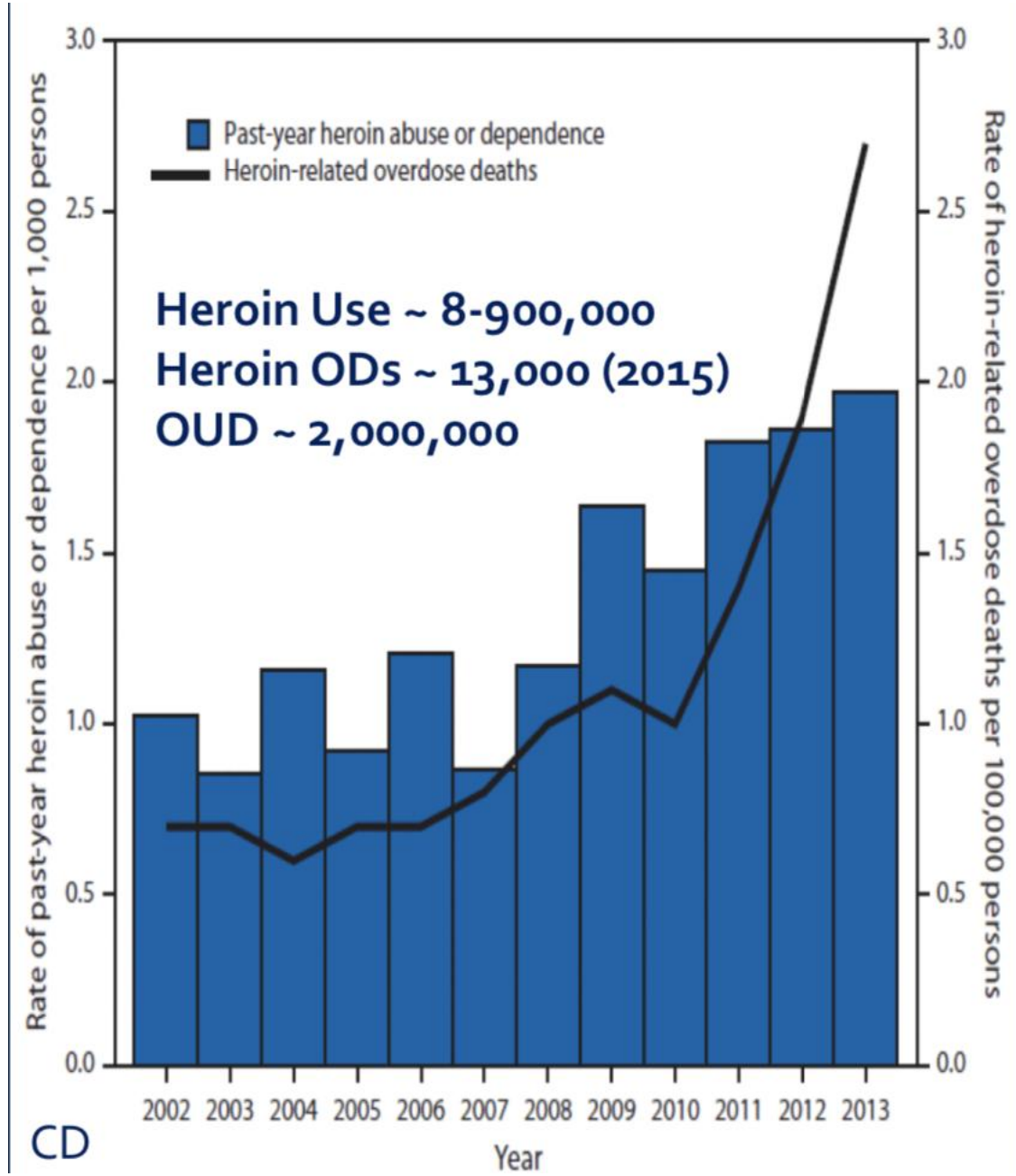
CDC, National Center for Health Statistics, National Vital Statistics System, CDC Wonder. Updated with 2010 mortality data.

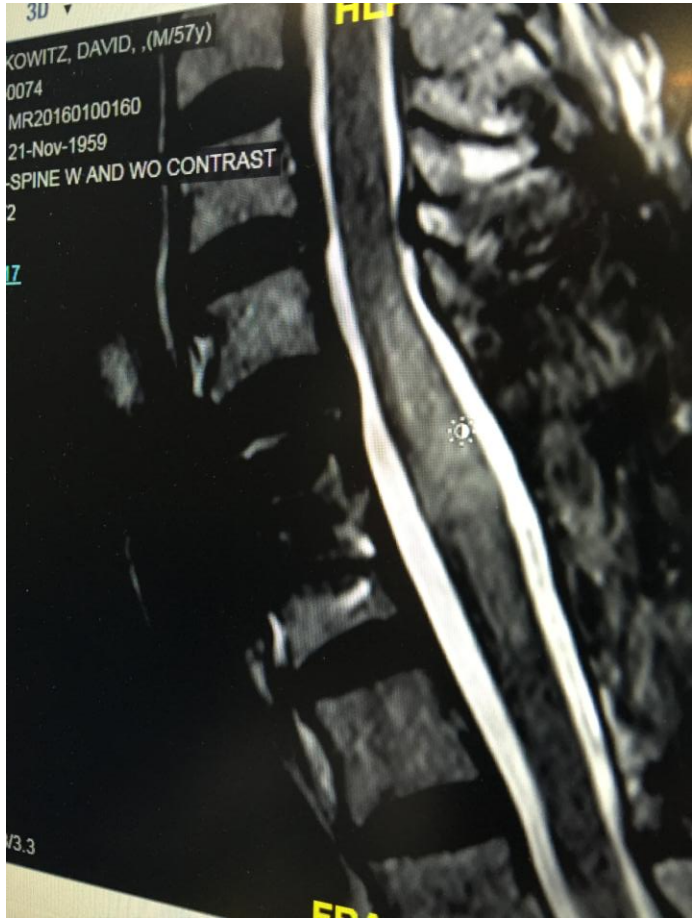
Drug-Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2014

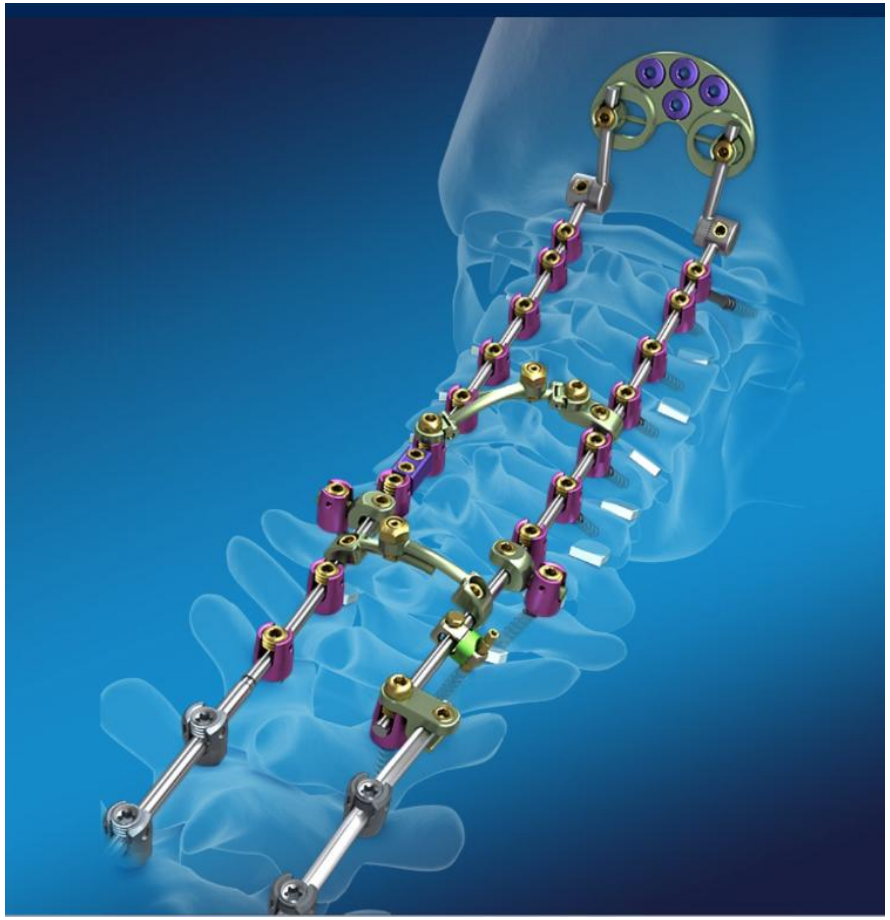


Frank RG, Pollack HA. N Engl J Med 2017;376.605-607

The NEW ENGLAND JOURNAL of MEDICINE


Past-year heroin abuse or dependence
Heroin-related overdose deaths
Heroin Use ~ 8-900,000
Heroin ODs ~ 13,000 (2015)
OUD ~ 2,000,000
Rate of past-year heroin abuse or dependence per 1,000 persons
Rate of heroin-related overdose deaths per 100,000 persons
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013
Year
CD


3D
KOWITZ, DAVID, ,(M/57y)
0074
MR20160100160
21-Nov-1959
-SPINE W AND WO CONTRAST
2
V3.3



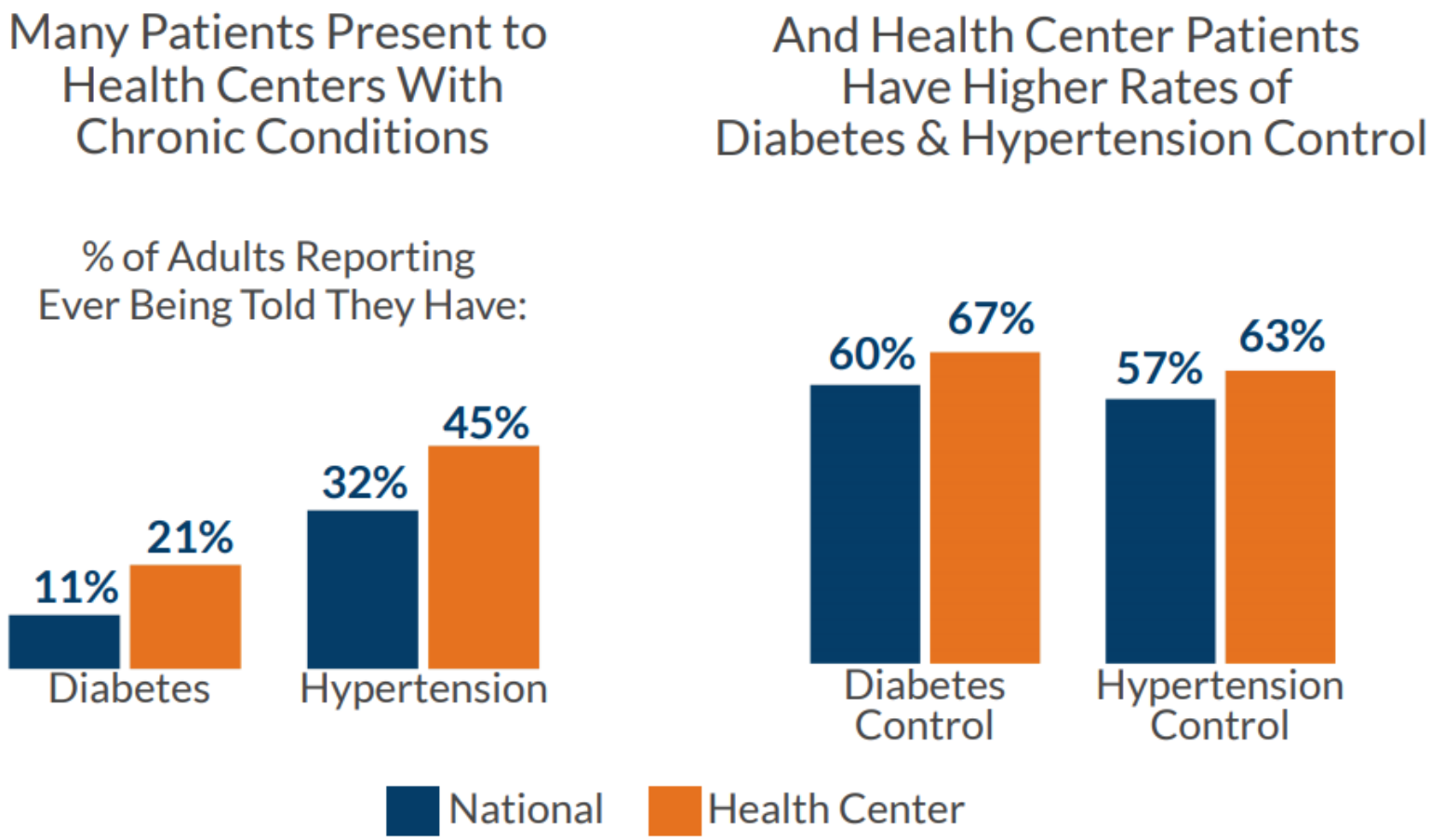
History

- 1960's: Lyndon Johnson's War on Poverty initiative opened Neighborhood Health Centers in Mound Bayou, MS and Boston
- Goal: to provide primary care to underserved rural and urban communities
- 1991: began using term FQHC
  - Added as a Medicaid and Medicare benefit
  - Precisely defined to be safety net centers like public housing or community health centers
- 2010: ACA stated FQHCs need to provide care to all people in a certain area whether they're able to pay or not

Requirements

- Must be in a Health Resources & Services Admin designated underserved area
- Governed by board of directors where 51% of board uses the services of the clinic
- Offer services in addition to primary care
  - Dental
  - OB
  - Behavioral health

FQHC's are treating a sicker population and achieving better outcomes



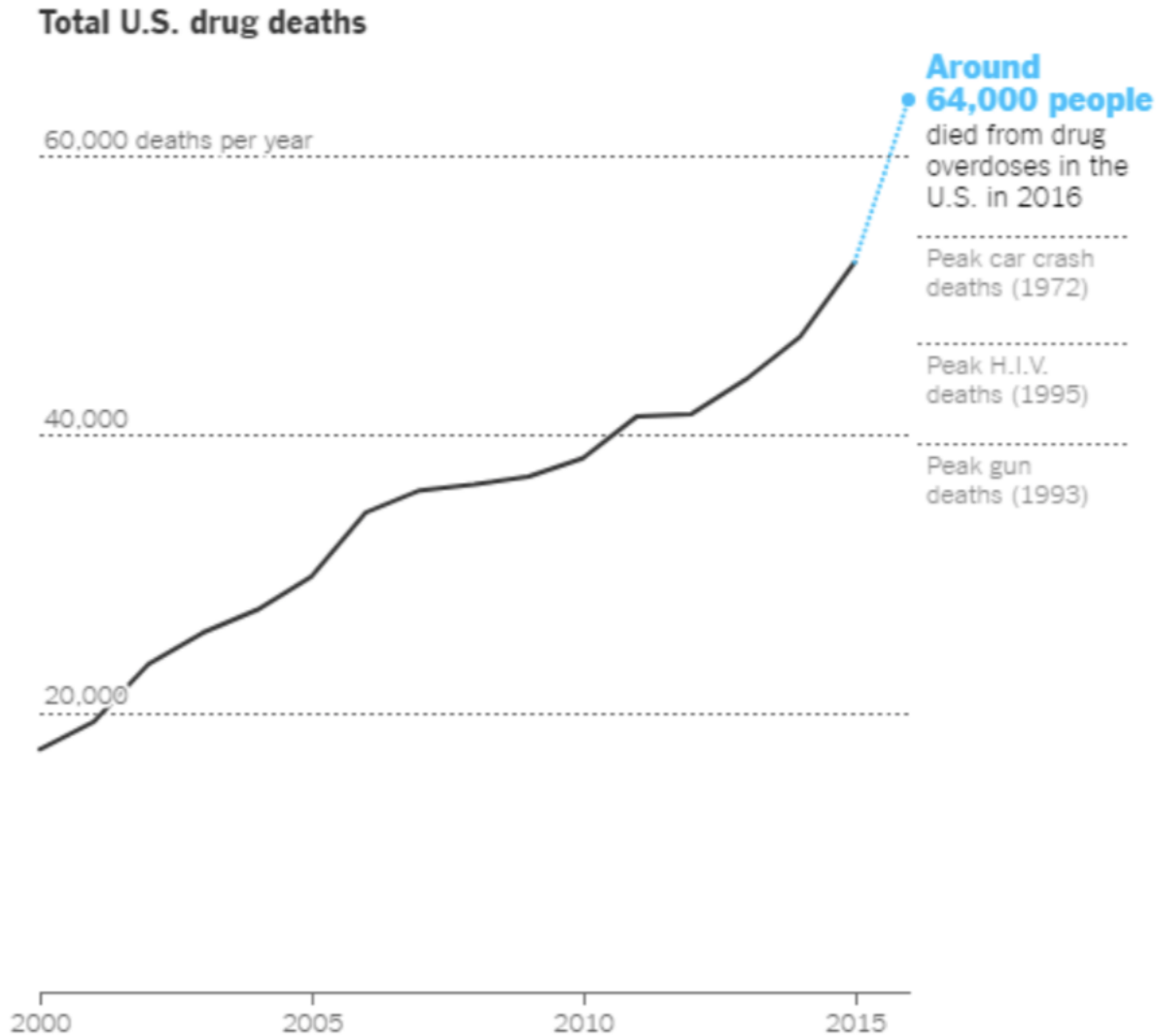
Importance of integrating MAT with primary care

- Individuals with substance use disorders have:
  - 9x greater risk of CHF
  - 12x greater risk of cirrhosis
  - 12x greater risk of PNA
- Poor adherence to DMII medications
- 54% of addiction treatment programs have no physician

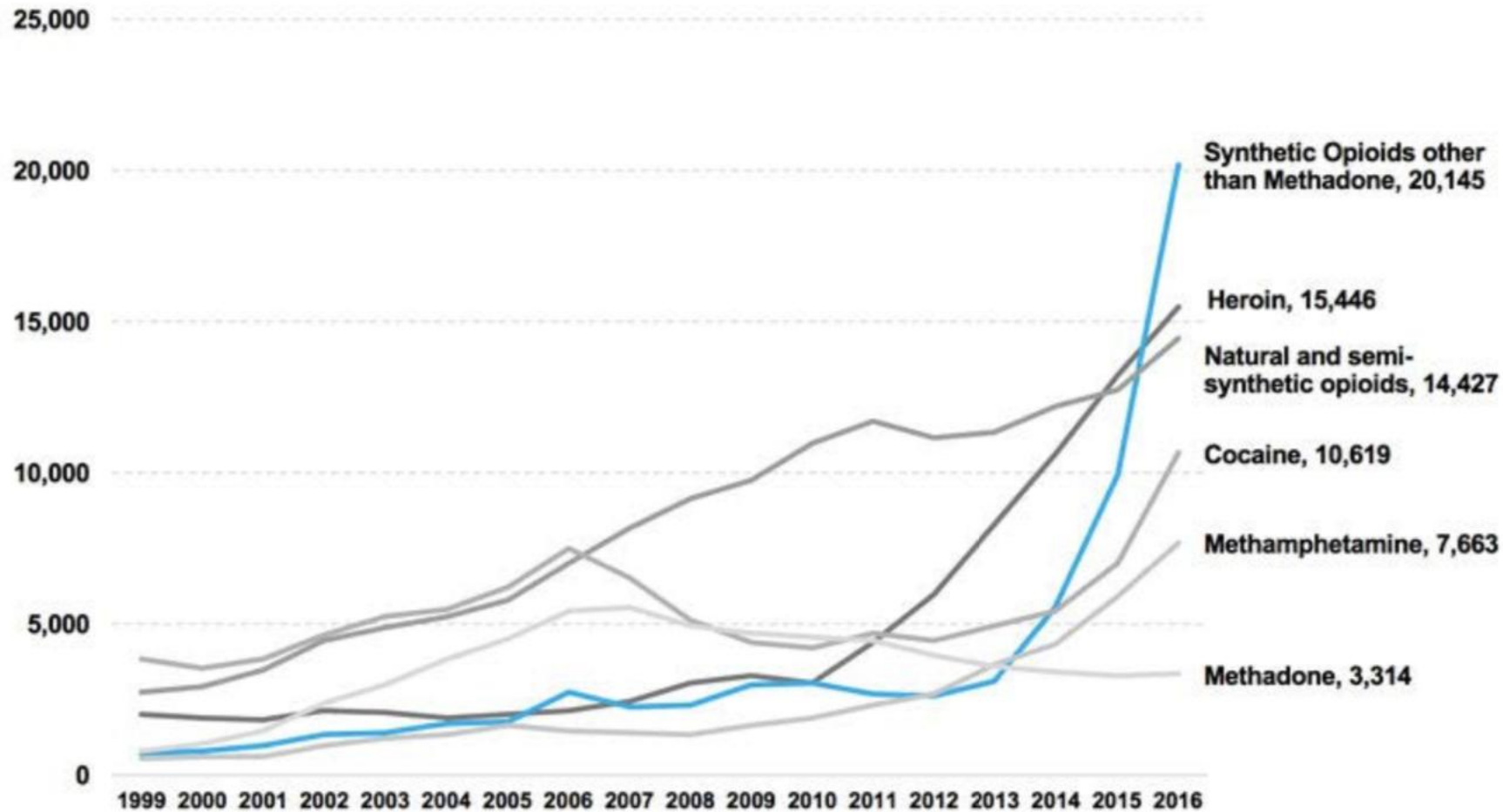
2 Minutes: $3A_4$

Synthetic opioids/fentanyl analogues/metabolites	A. All cases (N=100)	B. Acryl Fentanyl Positives (N=56)	C. Furanyl Fentanyl Positives (N=39)
Fentanyl	99 (99%)	56 (100%)	39 (100%)
Norfentanyl	64 (64%)	39 (70%)	26 (67%)
Acryl fentanyl	56 (56%)		25 (64%)
Despropionylfentanyl	46 (46%)	26 (46%)	32 (82%)
Furanyl Fentanyl	39 (39%)	25 (45%)	
Carfentanil	3 (3%)	2 (4%)	1 (2.6%)
Acetyl Fentanyl	2 (2%)	1 (2%)	1 (2.6%)
Butyryl/isobutyrylfentanyl	1 (1%)	0 (0%)	0 (0%)
Furanyl Norfentanyl	1 (1%)	1 (2%)	1 (2.6%)
U47700	1 (1%)	1 (2%)	1 (2.6%)

100 Accidental OD deaths 2017(3mos): 99% + FENTANYL Only 3 cases + HEROIN


Total U.S. drug deaths
Around 64,000 people
died from drug overdoses in the U.S. in 2016
60,000 deaths per year
40,000
20,000
Peak car crash deaths (1972)
Peak H.I.V. deaths (1995)
Peak gun deaths (1993)
2000
2005
2010
2015

Drugs Involved in U.S. Overdose Deaths, 2000 to 2016

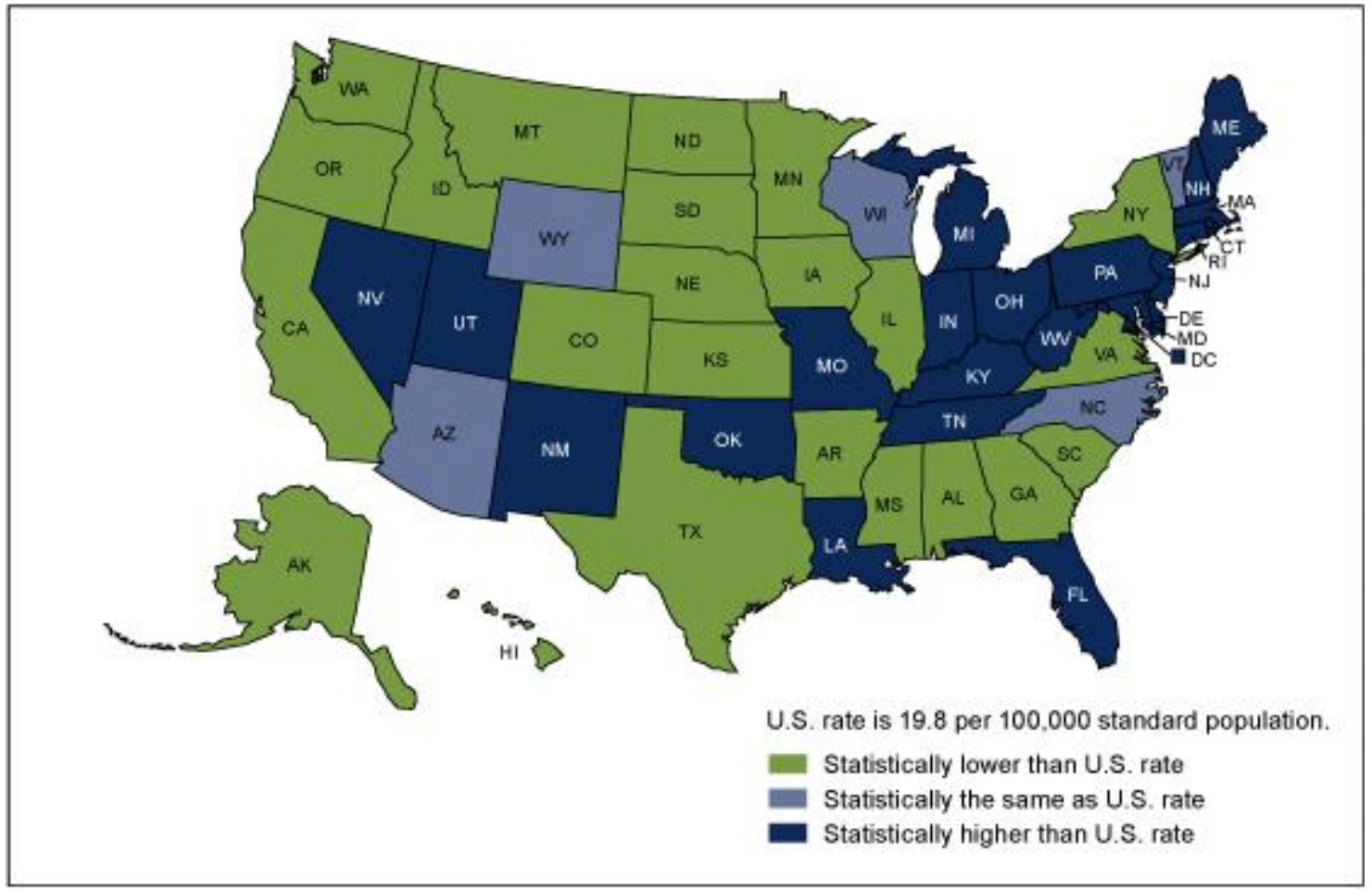


Lethal Dose

Morphine = 1X
Fentanyl = 100X
Carfentanil = 10,000X

Lethal doses of heroin compared to "synthetic" opioids.
New Hampshire State Police Forensic Lab

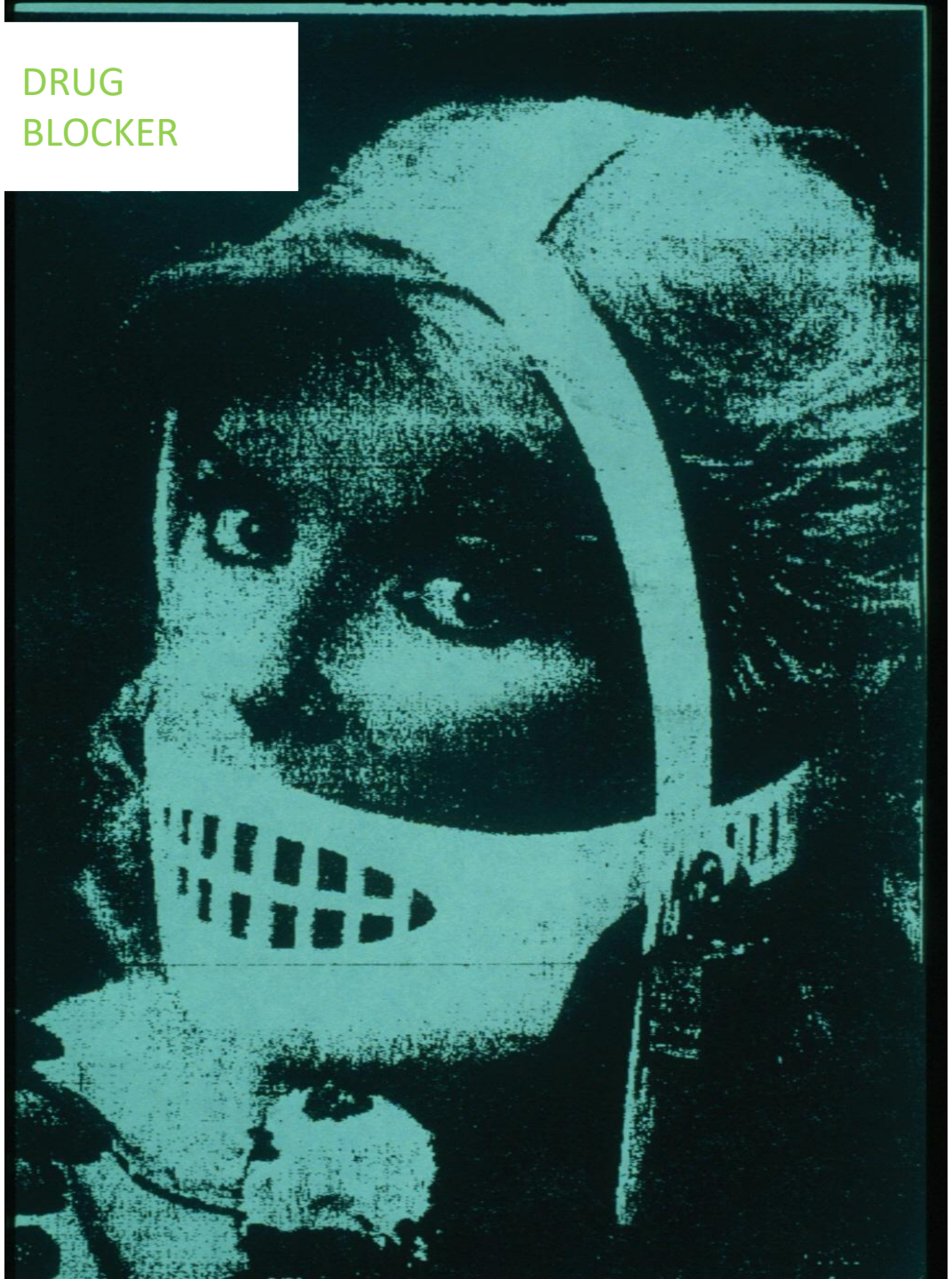
Drug Overdose Deaths - 2016

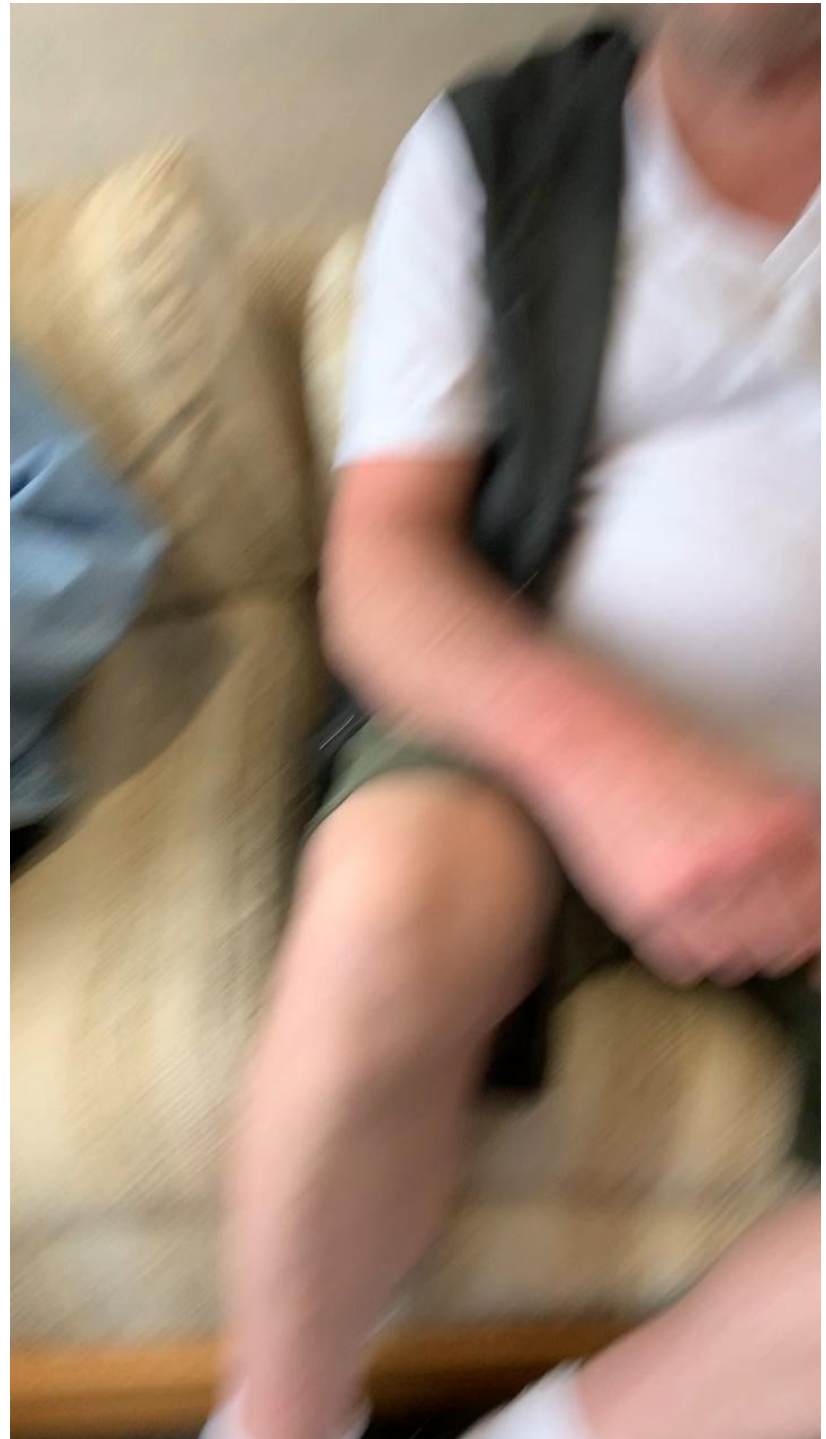


Hedegaard et al. Drug Overdose Deaths in the United States, 1999-2016. NCHS Data Brief No. 294. December 2017.

WHIZZINATOR

DRUG
BLOCKER

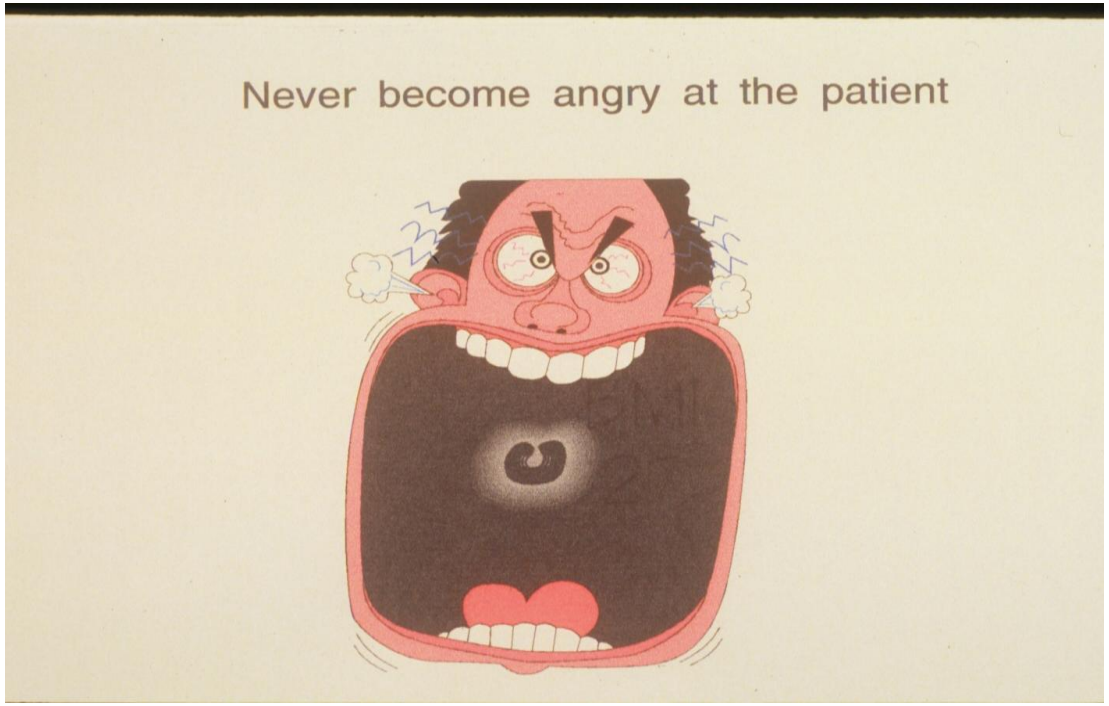




Fill Date	ID	Written	Drug	Qty	Days	Prescriber	Rx #	Pharmacy	Refill	Daily Dose *	Pymt Type	PMP
03/30/2021	2	03/26/2021	Oxycodone Hcl 30 Mg Tablet	180.00	30	Es Ali	1356155	Wal (0903)	0	270.00 MME	Medicare	MI
03/29/2021	5	03/26/2021	Oxycodone Hcl 15 Mg Tablet	20.00	20	Es Ali	0375176	Woo (3706)	0	22.50 MME	Medicare	MI
03/29/2021	5	03/26/2021	Fentanyl 100 Mcg/hr Patch	40.00	30	Es Ali	0375175	Woo (3706)	0	960.00 MME	Medicare	MI
03/26/2021	5	03/26/2021	Testosterone 1.62% Gel Pump	75.00	30	Es Ali	0375010	Woo (3706)	0		Medicare	MI
03/02/2021	5	03/01/2021	Pregabalin 75 Mg Capsule	90.00	30	Es Ali	0372875	Woo (3706)	0	1.51 LME	Medicare	MI
03/02/2021	5	03/01/2021	Fentanyl 100 Mcg/hr Patch	40.00	30	Es Ali	0372874	Woo (3706)	0	960.00 MME	Medicare	MI
03/02/2021	5	03/01/2021	Oxycodone Hcl 30 Mg Tablet	180.00	30	Es Ali	0372873	Woo (3706)	0	270.00 MME	Medicare	MI
03/02/2021	5	03/01/2021	Oxycodone Hcl 15 Mg Tablet	30.00	30	Es Ali	0372872	Woo (3706)	0	22.50 MME	Medicare	MI
02/13/2021	5	02/03/2021	Pregabalin 50 Mg Capsule	90.00	30	Es Ali	0370618	Woo (3706)	0	1.01 LME	Medicare	MI
02/03/2021	5	02/03/2021	Oxycodone Hcl 15 Mg Tablet	40.00	30	Es Ali	0370619	Woo (3706)	0	30.00 MME	Medicare	MI
02/03/2021	5	02/03/2021	Fentanyl 100 Mcg/hr Patch	40.00	30	Es Ali	0370617	Woo (3706)	0	960.00 MME	Medicare	MI
02/03/2021	5	02/03/2021	Oxycodone Hcl 30 Mg Tablet	180.00	30	Es Ali	0370616	Woo (3706)	0	270.00 MME	Medicare	MI
01/14/2021	5	12/08/2020	Pregabalin 50 Mg Capsule	60.00	30	Es Ali	0365972	Woo (3706)	1	0.67 LME	Medicare	MI
01/06/2021	5	01/06/2021	Fentanyl 100 Mcg/hr Patch	40.00	30	Es Ali	0368410	Woo (3706)	0	960.00 MME	Medicare	MI
01/06/2021	5	01/06/2021	Oxycodone Hcl 30 Mg Tablet	180.00	30	Es Ali	0368409	Woo (3706)	0	270.00 MME	Medicare	MI
01/06/2021	5	01/06/2021	Oxycodone Hcl 15 Mg Tablet	50.00	30	Es Ali	0368408	Woo (3706)	0	37.50 MME	Medicare	MI

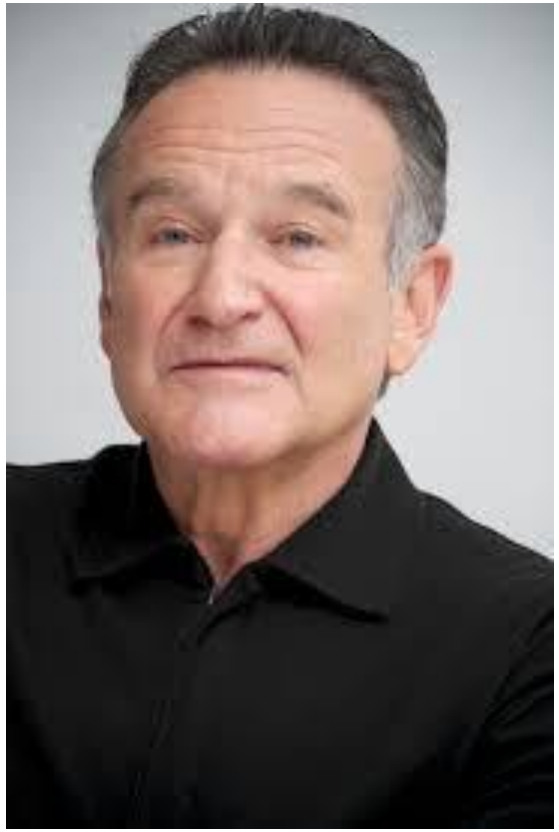
Fill Date	ID	Written	Drug	Qty	Days	Prescriber	Rx #	Pharmacy	Refill	Daily Dose *
02/12/2020	2	02/12/2020	Buprenorphine 10 Mcg/hr Patch	4.00	28	Jo Git	927214	Mil (4463)	0	0.24 mg
01/16/2020	2	01/02/2020	Buprenorphine 5 Mcg/hr Patch	3.00	21	Jo Git	921261	Mil (4463)	1	0.12 mg
01/02/2020	2	01/02/2020	Buprenorphine 5 Mcg/hr Patch	1.00	7	Jo Git	921261	Mil (4463)	0	0.12 mg
08/10/2019	4	07/31/2019	Suboxone 8 Mg-2 Mg Sl Film	10.00	5	Be Roj	3195710	Pha (9205)	0	16.00 mg
08/05/2019	4	07/31/2019	Suboxone 8 Mg-2 Mg Sl Film	10.00	5	Be Roj	3195710	Pha (9205)	0	16.00 mg
07/31/2019	4	07/31/2019	Suboxone 8 Mg-2 Mg Sl Film	10.00	5	Be Roj	3195710	Pha (9205)	0	16.00 mg
07/31/2019	4	07/30/2019	Buprenorphine-Nalox 8-2 Mg Tab	30.00	15	Da Les	3194958	Pha (9205)	0	16.00 mg
07/31/2019	4	07/30/2019	Alprazolam 1 Mg Tablet	30.00	30	Be Roj	3194852	Pha (9205)	0	2.00 LME
07/12/2019	1	07/11/2019	Buprenorphine-Nalox 4-1mg Film	42.00	14	Da Les	849318	Pon (7877)	0	12.00 mg
07/08/2019	1	07/08/2019	Buprenorphine-Nalox 4-1mg Film	21.00	7	Da Les	848683	Pon (7877)	0	12.00 mg
06/24/2019	2	06/24/2019	Buprenorphine 2 Mg Tablet Sl	42.00	14	Da Les	4001034	Pon (1034)	0	6.00 mg
06/19/2019	2	06/19/2019	Buprenorphine-Nalox 4-1mg Film	10.00	6	Da Les	4001021	Pon (1034)	0	6.67 mg
06/03/2019	1	06/03/2019	Diazepam 5 Mg Tablet	30.00	30	Ar Mar	844328	Pon (7877)	0	0.50 LME
05/23/2019	1	05/23/2019	Methadone Hcl 10 Mg Tablet	28.00	7	Ar Mar	842906	Pon (7877)	0	120.00 M
05/10/2019	1	04/16/2019	Oxycodone Hcl 15 Mg Tablet	120.00	30	Ke Ric	837419	Pon (7877)	0	90.00 MN
05/02/2019	1	05/02/2019	Methylphenidate 10 Mg Tablet	90.00	30	Ar Mar	839666	Pon (7877)	0	
04/17/2019	1	04/16/2019	Methadone Hcl 10 Mg Tablet	90.00	30	Ke Ric	837418	Pon (7877)	0	90.00 MI

- Never become angry at the patient
- Offer easier goals if necessary
- Praise even with moderate improvement
- Manage the patient’s entire care
- Encourage support groups and material
- Encourage the use of different tools



Never judge, takes all those that comes before you!

HARM



Robin Williams 1951 - 2014

Seymour Hoffman 1967 - 2014