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RIOT
Rutgers Interdisciplinary Opioid Trainers

Addressing the Opioid Epidemic:

A Primer on Opioid Addiction, Overdose Management, and Medications for Opioid Use Disorder

Sponsored by a grant from the NJ Department of Human Services, Division of Mental Health & Addiction Services

Learning Objectives

As a result of participating in this session, learners will:

- Understand the factors that led to the US opioid crisis
- Know the proper uses of naloxone for overdose reversal
- Recognize the signs of opioid use disorder
- Debunk commonly held myths and beliefs about treatment for opioid use disorder
- Understand the key role of MOUD (Medications for Opioid Use Disorder) in enhancing outcomes

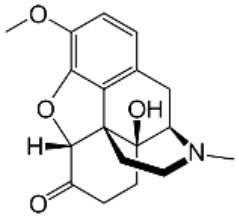
The Opioid Epidemic

Opioid Use Disorder as a Disease

Overdose Management

Medications for Opioid Use Disorder

What are Opioid Drugs and what are their Effects?



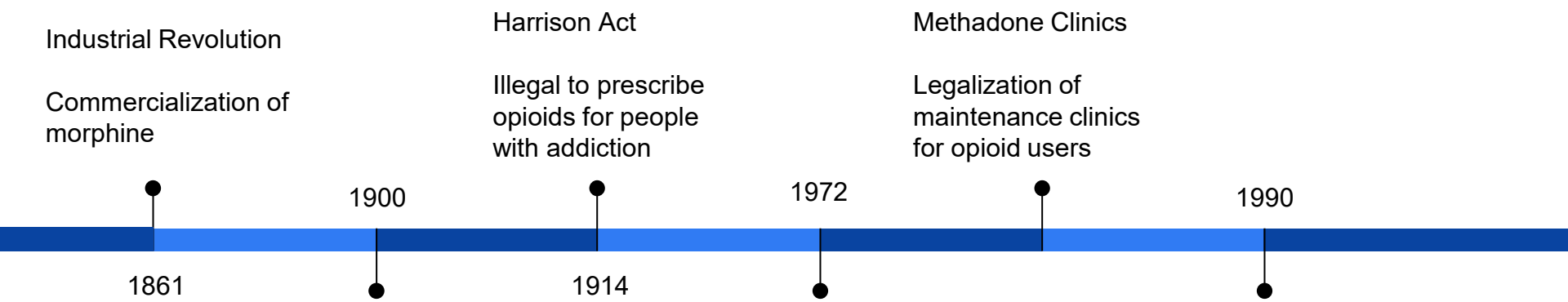
Oxycodone

- Bind to the opioid receptors; in the brain, spinal cord, and gastrointestinal tract
- Opioids are:
  - Opiate drugs (derived from opium from the poppy plant), e.g., morphine, heroin
  - Semi-synthetic and synthetic drugs (man made with chemicals), e.g., hydrocodone, oxycodone and fentanyl

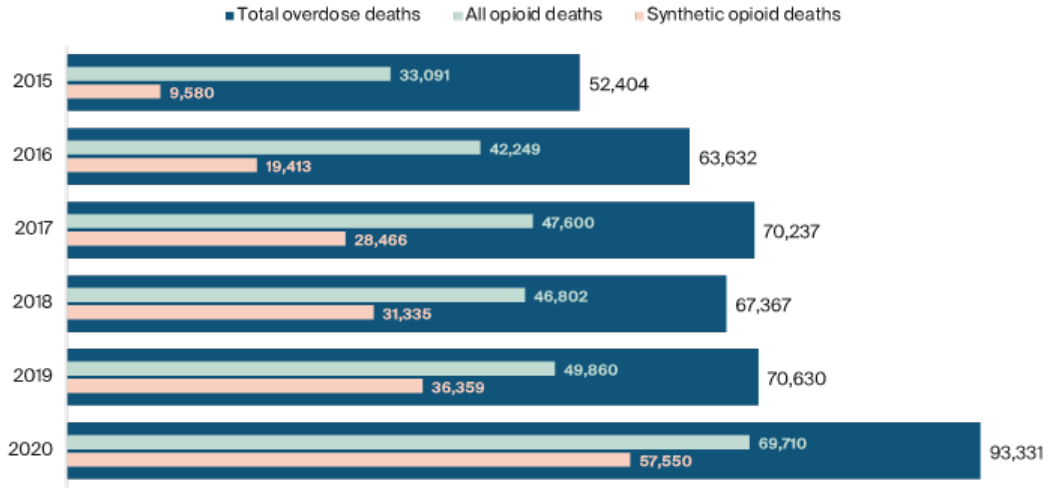
- Used to treat pain, cough
- Side effects include: euphoria, sedation, nausea, constipation, itching
- Creates tolerance, the need to take higher doses for same effect, and craving or withdrawal symptoms in its absence
- Overdose danger: respiratory depression

Source: Samhsa.gov

Not a New Problem



Record high of 93,331 drug overdose deaths in 2020



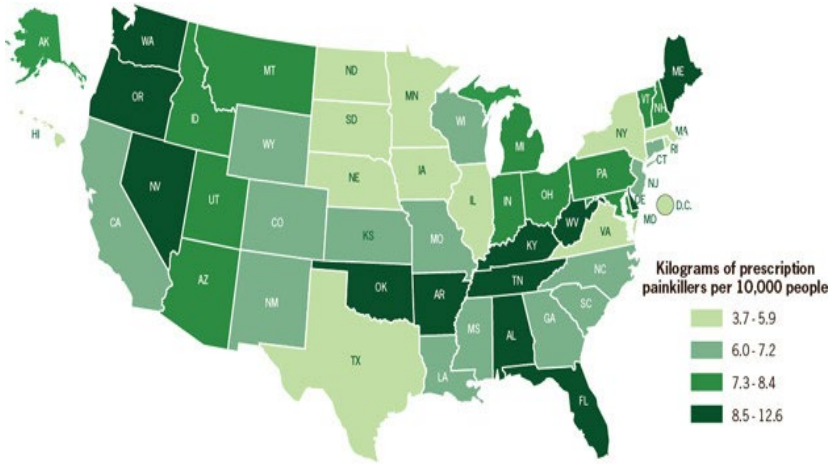
AIDS crisis peaked at 50k/ year

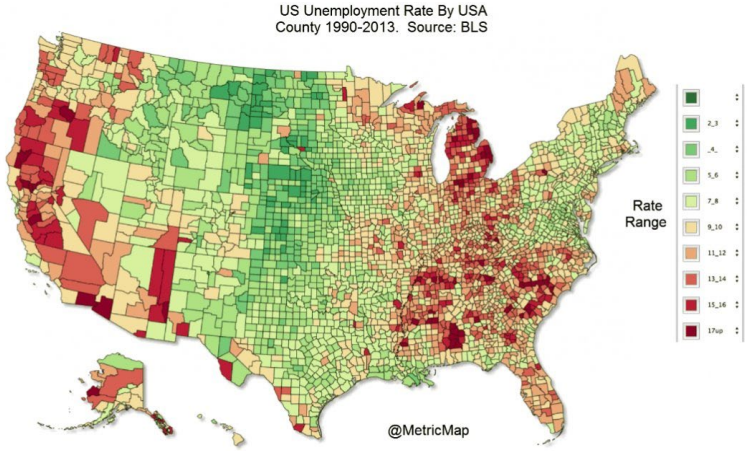
More than 60% = synthetic opioids

During 2020, 28 states saw drug overdose deaths ↑ > 30%, amid the social isolation and economic stress of the pandemic

Data: 2015–2019 — Final data from CDC WONDER; 2020 — National Vital Statistics System, Provisional Drug Overdose Death Counts.
Jesse C. Baumgartner and David C. Radley, "The Drug Overdose Mortality Toll in 2020 and Near-Term Actions for Addressing It," *To the Point* (blog), Commonwealth Fund, July 15, 2021, updated Aug. 16, 2021.

Social, Economic and Cultural Issues Contribute to Substance Use Patterns

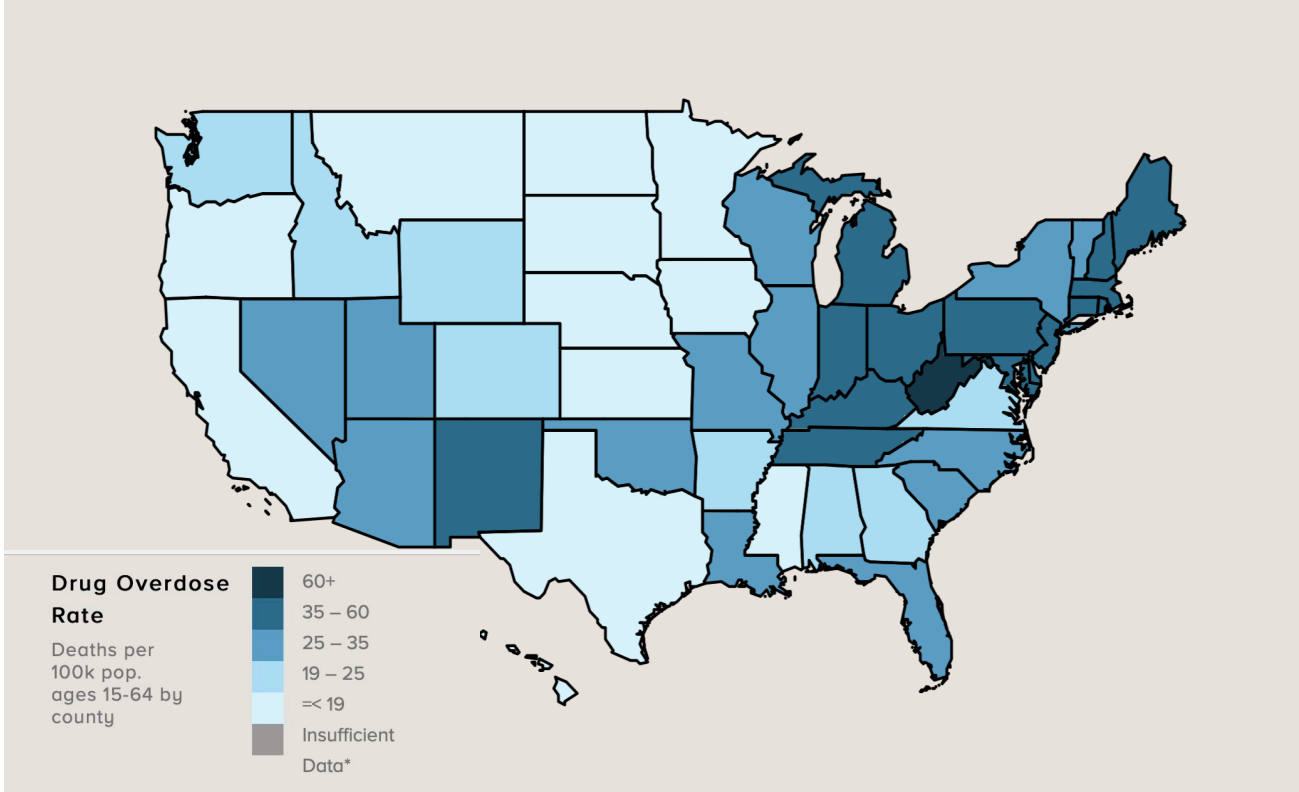




Overlap in Regions with High Opioid Pain Medication Use and Unemployment
(around 2010)

SOURCE: Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 2010

US Drug Overdoses 2015-2019



New Jersey

Second Highest Group of States with Drug Overdoses per 100k population

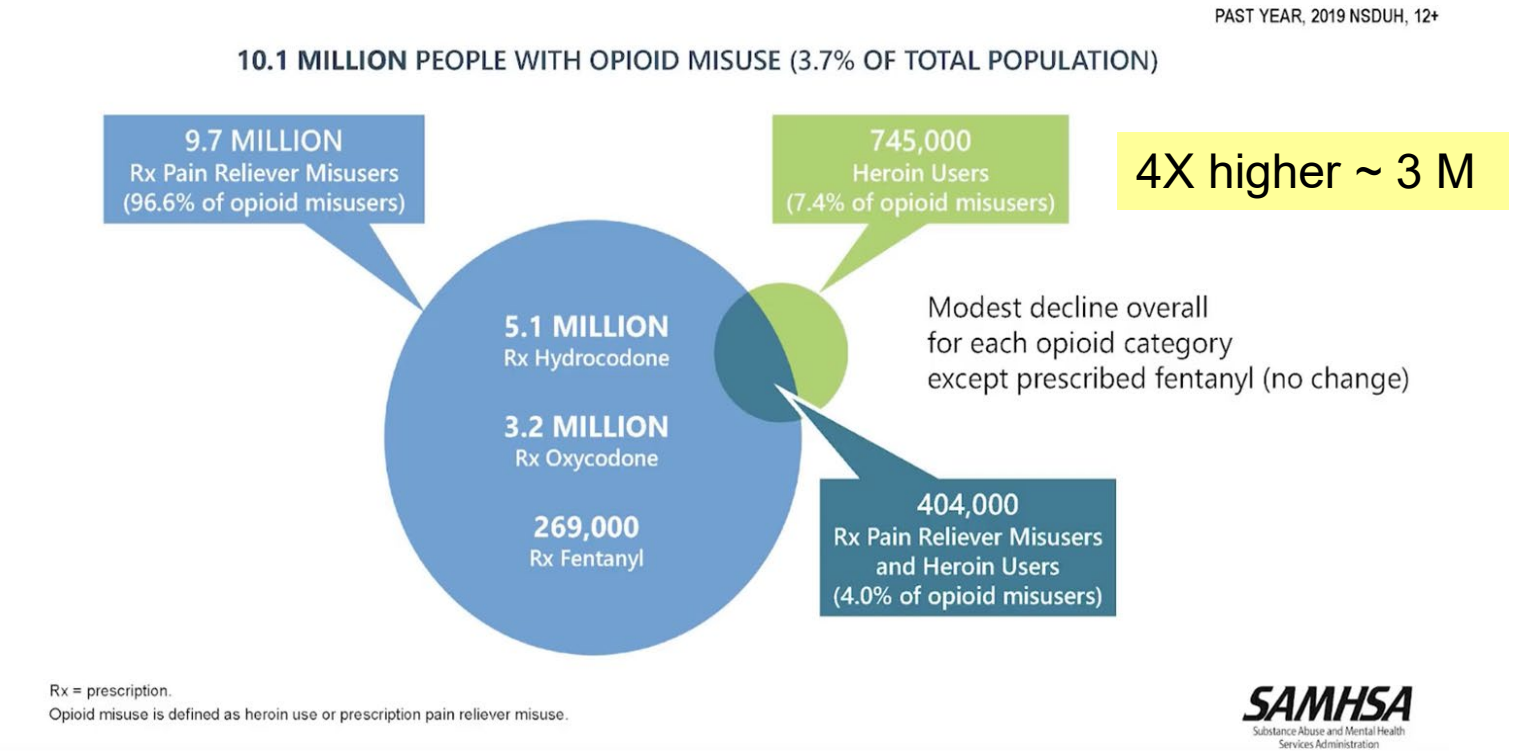
~ 11/day

~ 3000/ year

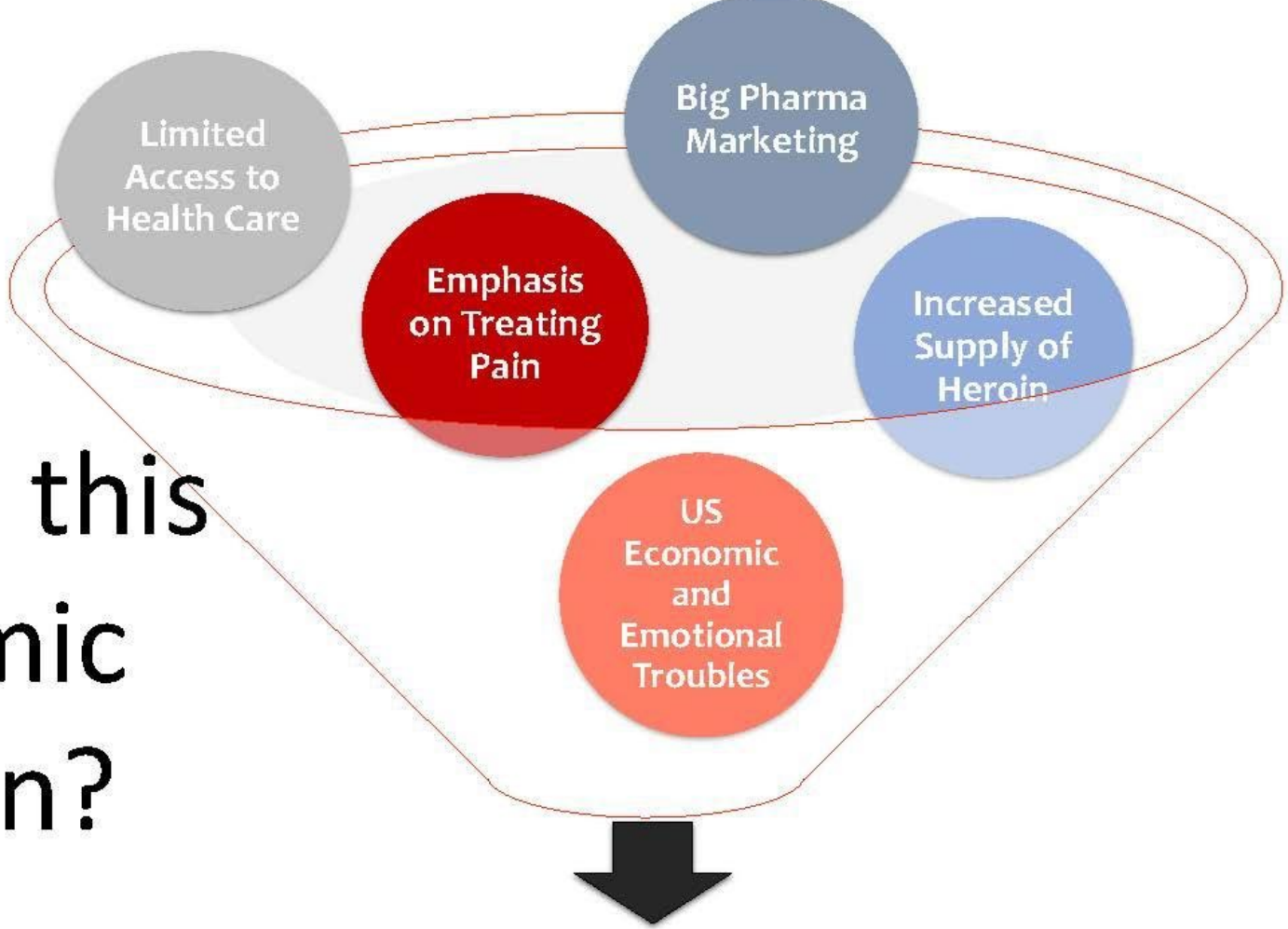
NJ OD Deaths Increasing in African Americans And 55 and Older

Still More than 10 Million People in US with Opioid Misuse

Vast Majority of those with Opioid Misuse = Prescription Pain Relievers



How did this epidemic happen?



ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug
Surveillance Program
Waltham, MA 02154 Boston University Medical Center

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

Porter & Jick, NEJM, Jan 1980

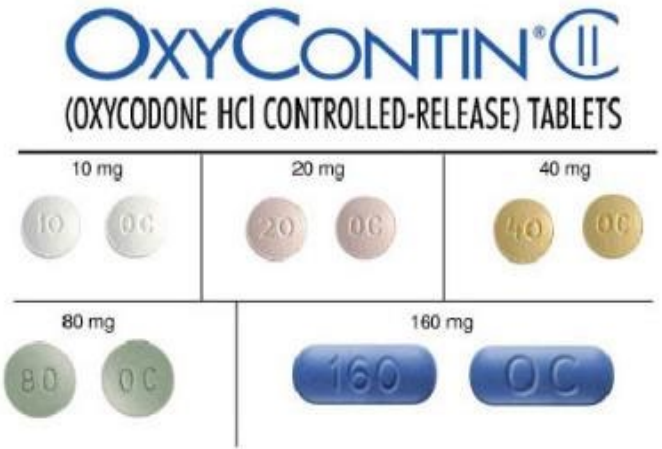
“The risk of addiction is much less than 1%”

Porter & Jick, NEJM 1980

Cited more than 900 times (Google Scholar)

Oxycodone vs Oxycontin

- **Oxycodone** (Roxycodone)
  - Immediate release
  - Acute pain
  - 4-6 hrs duration of action
  - Tabs (30mg), liquid



- **Oxycodone CR** (Oxycontin)
  - Controlled release
  - Chronic pain; already tolerant to opioids
  - 12 hrs duration of action (BID dosing)
  - Tablets (80 or 160 mg)
  - Long acting oxycodone; Delayed absorption “abuse-resistant”

Crush, sniff, and inject

Powerful high > eight hrs

Euphoria ~ heroin

Commercial Triumph, Public Health Tragedy

The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy

Art Van Zee, MD

I focus on issues surrounding the promotion and marketing of controlled drugs and their regulatory oversight. Compared with noncontrolled drugs, controlled drugs, with their potential for abuse and diversion, pose different public health risks when they are overpromoted and highly prescribed. An in-depth analysis of the promotion and marketing of OxyContin illustrates some of the associated issues.

Modifications of the promotion and marketing of controlled drugs by the pharmaceutical industry and an enhanced capacity of the Food and Drug Administration to regulate and monitor such promotion can have a positive impact on the public health. (*Am J Public Health*. 2009;99:221–227. doi: 10.2105/AJPH.2007.131714)

CONTROLLED DRUGS, WITH their potential for abuse and diversion, can pose public health risks that are different from—and more problematic than—those of uncontrolled drugs when they are overpromoted and highly prescribed. An in-depth analysis of the promotion and marketing of OxyContin (Purdue Pharma, Stamford, CT), a sustained-release oxycodone preparation, illustrates some of the key issues. When Purdue Pharma introduced OxyContin in 1996, it was aggressively marketed and highly promoted. Sales grew from $48 million in 1996 to almost $1.1 billion in 2000.[1] The high availability of OxyContin correlated with increased abuse, diversion, and addiction, and by 2004 OxyContin had become a leading drug of abuse in the United States.[2]

Under current regulations, the Food and Drug Administration (FDA) is limited in its oversight of the marketing and promotion of controlled drugs. However, fundamental changes in the promotion and marketing of controlled drugs by the pharmaceutical industry, and an enhanced capacity of the FDA to regulate and monitor such promotion, can positively affect public health.

OxyContin's commercial success did not depend on the merits of the drug compared with other available opioid preparations. The *Medical Letter on Drugs and Therapeutics* concluded in 2001 that oxycodone offered no advantage over appropriate doses of other potent opioids.[3] Randomized double-blind studies comparing OxyContin given every 12 hours with immediate-release oxycodone given 4 times daily showed comparable efficacy and safety for use with chronic back pain[4] and cancer-related pain.[5,6] Randomized double-blind studies that compared OxyContin with controlled-release morphine for cancer-related pain also found comparable efficacy and safety.[7–9] The FDA's medical review officer, in evaluating the efficacy of OxyContin in Purdue's 1995 new drug application, concluded that OxyContin had not been shown to have a significant advantage over conventional, immediate-release oxycodone taken 4 times daily other than a reduction in frequency of dosing.[10] In a review of the medical literature, Chou et al. made similar conclusions.[11]

The promotion and marketing of OxyContin occurred during a recent trend in the liberalization of the use of opioids in the treatment of pain, particularly for chronic non–cancer-related pain. Purdue pursued an "aggressive" campaign to promote the use of opioids in general and OxyContin in particular.[1,12–17] In 2001 alone, the company spent $200 million[18] in an array of approaches to market and promote OxyContin.

PROMOTION OF OXYCONTIN

From 1996 to 2001, Purdue conducted more than 40 national pain-management and speaker-training conferences at resorts in Florida, Arizona, and California. More than 5000 physicians, pharmacists, and nurses attended these all-expenses-paid symposia, where they were recruited and trained for Purdue's national speaker bureau.[19–22] It is well documented that this type of pharmaceutical company symposium influences physicians' prescribing,

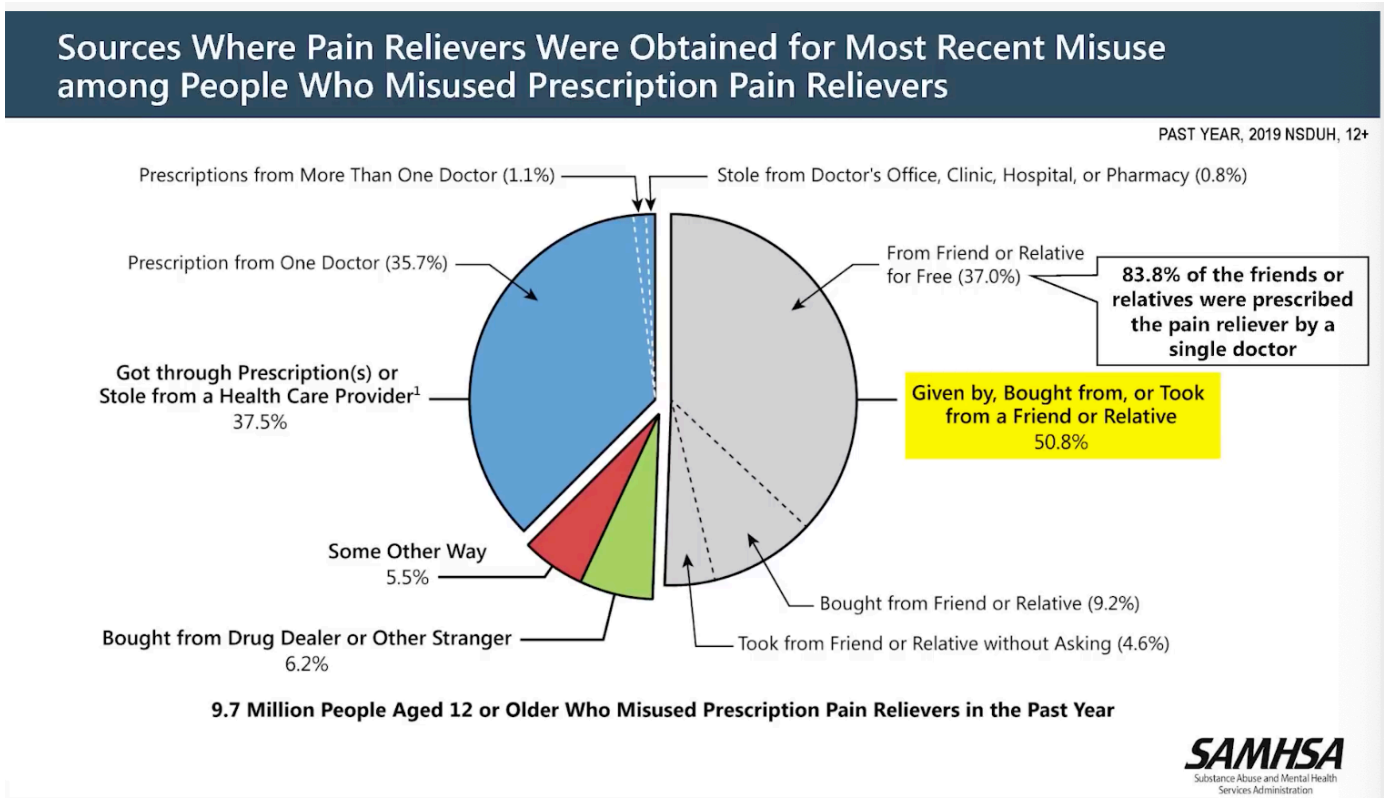
$ 1 Billion sales within 5 years of FDA approval

Marketed aggressively to PCPs for non-cancer pain

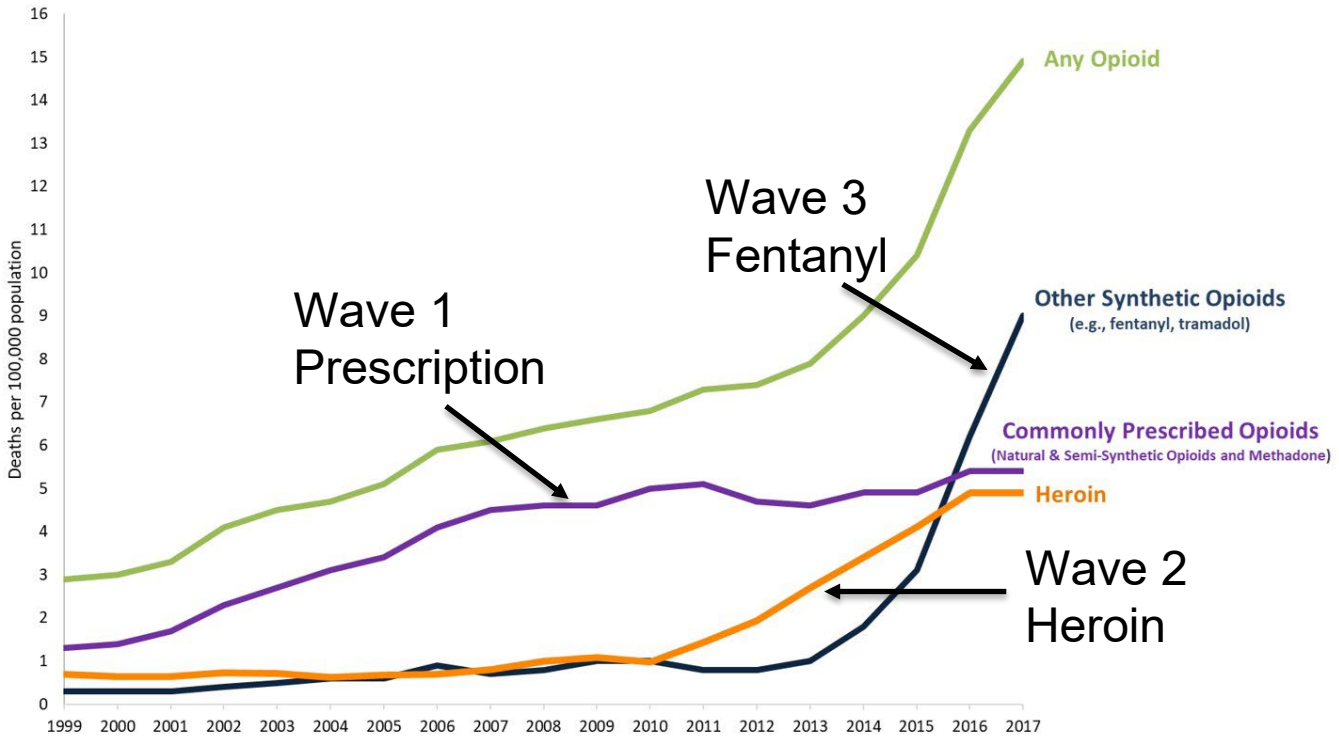
Purdue sued by 48 states for fueling the crisis

What is the most common way(s) that individuals who abuse prescription opioids obtain them?

Most get Prescription Opioids from Family/Friends



Overdose Death Rates Involving Opioids, by Type, United States, 2000-2017

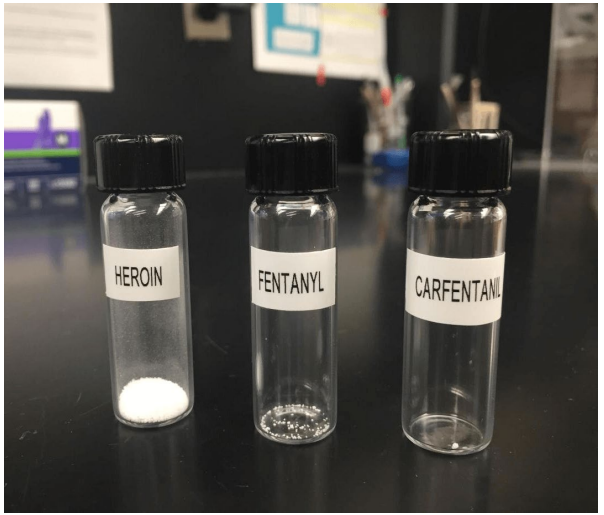


SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2018. https://wonder.cdc.gov/.

www.cdc.gov
Your Source for Credible Health Information

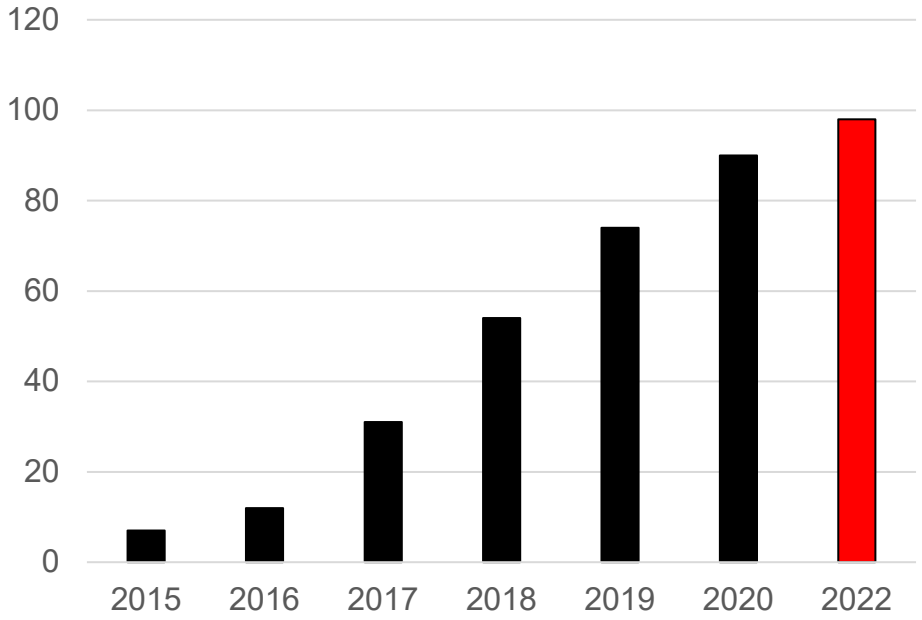
Fentanyl = U.S. Cannot Control Supply

- Schedule II synthetic opioid
- 100 times stronger than morphine
- Well suited for the internet age
- Cheap, mass-produced
- Innovations in “cooking” from precursors
- Easy to ship (tiny amount)
- Encrypted online/ monetary services
- Counterfeit pills, cocaine supply
- Lack of international controls on precursors



Pardo et al., RAND Corp, 2019

Fentanyl Increasing in Heroin and Pills in NJ



Suspected Heroin Submissions Containing Fentanyl
(98% in 2022 in NJ)

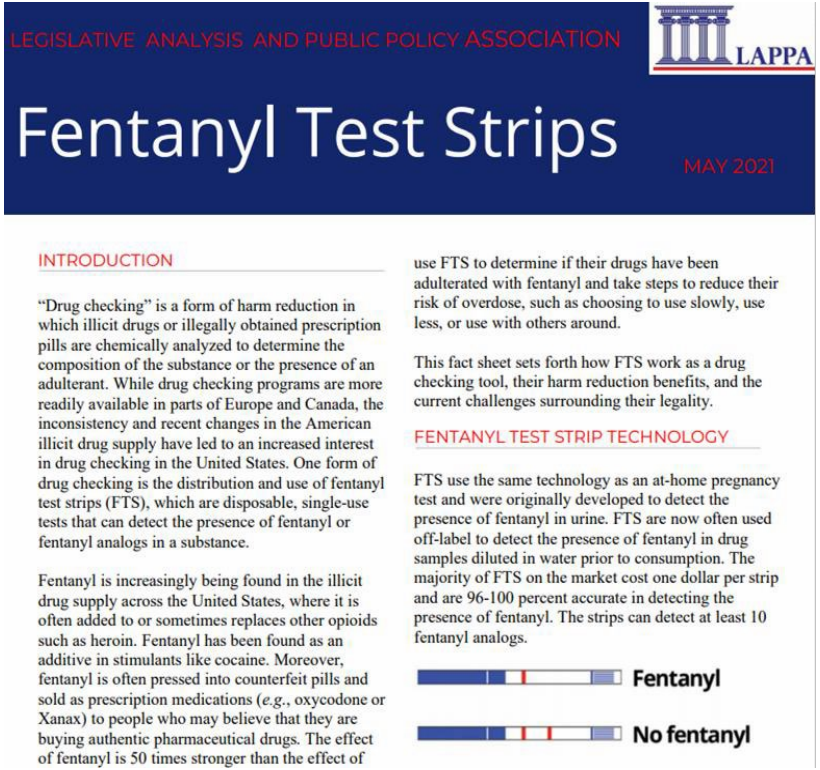
15-20 types of fentanyl analogs by 2017

Fentanyl in 21% of pills seized by law enforcement

Office of Drug Monitoring & Analysis
Fentanyl Trends in New Jersey

January 1, 2015 – December 31, 2020

•Step 1: Put a small amount (at least 10mg) of your drugs aside in a clean, dry container.
•Step 2: Add water to the container and mix together.
Please note: For most drugs, you need ½ teaspoon of water. If you are testing methamphetamines, use1 full teaspoon.[4]
•Step 3: Place the wavy end of the test strip down in the water and let it absorb for about 15 seconds.
•Step 4: Take the strip out of the water and place it on a flat surface for 2 to 5 minutes.



LEGISLATIVE ANALYSIS AND PUBLIC POLICY ASSOCIATION

LAPPA

Fentanyl Test Strips

MAY 2021

INTRODUCTION

"Drug checking" is a form of harm reduction in which illicit drugs or illegally obtained prescription pills are chemically analyzed to determine the composition of the substance or the presence of an adulterant. While drug checking programs are more readily available in parts of Europe and Canada, the inconsistency and recent changes in the American illicit drug supply have led to an increased interest in drug checking in the United States. One form of drug checking is the distribution and use of fentanyl test strips (FTS), which are disposable, single-use tests that can detect the presence of fentanyl or fentanyl analogs in a substance.

Fentanyl is increasingly being found in the illicit drug supply across the United States, where it is often added to or sometimes replaces other opioids such as heroin. Fentanyl has been found as an additive in stimulants like cocaine. Moreover, fentanyl is often pressed into counterfeit pills and sold as prescription medications (*e.g.*, oxycodone or Xanax) to people who may believe that they are buying authentic pharmaceutical drugs. The effect of fentanyl is 50 times stronger than the effect of

use FTS to determine if their drugs have been adulterated with fentanyl and take steps to reduce their risk of overdose, such as choosing to use slowly, use less, or use with others around.

This fact sheet sets forth how FTS work as a drug checking tool, their harm reduction benefits, and the current challenges surrounding their legality.

FENTANYL TEST STRIP TECHNOLOGY

FTS use the same technology as an at-home pregnancy test and were originally developed to detect the presence of fentanyl in urine. FTS are now often used off-label to detect the presence of fentanyl in drug samples diluted in water prior to consumption. The majority of FTS on the market cost one dollar per strip and are 96-100 percent accurate in detecting the presence of fentanyl. The strips can detect at least 10 fentanyl analogs.

Fentanyl

No fentanyl

Changing Patterns

Xylazine

- Veterinary tranquilizer (Rompun)
- Not controlled substance
- Similar to antipsychotic (Chlorpromazine)
- Potentiates high- raises risk of OD
- Causes skin necrosis
- “tranq” or “tranq dope”

Fentanyl Sudden Death

- Worse hypoxia (lack oxygen)
- Hypothermia (low body termperature)
- Chest Wall Rigidity (no breathing)

Cocaine and Stimulant ODs

- Increasingly, especially in Northeast

The Opioid Epidemic

Opioid Use Disorder as a Disease

Overdose Management

Medications for Opioid Use Disorder

Substance Use Disorders = Chronic Medical Conditions

- ✓ Genetic susceptibility
- ✓ Chronic pathophysiologic/functional changes
- ✓ Risk factors influenced by choices
- ✓ Similar treatment goals & strategies
- ✓ Similar clinical outcomes

Addiction is a brain disease

Risk Factors for Opioid Use Disorder

- 10-20% of opioid users at risk (licit/illicit)

- **Higher Risk**
  - Co-occurring psychiatric (Depression / Attention deficit disorder)
  - Family history substance use
  - Prior substance use disorder
  - Men > women
  - Native Americans
  - Trauma exposure

DSM 5 Criteria for Substance Use Disorder

- **Loss of Control**
  - Larger amounts, longer time
  - Inability to cutback
  - More time spent, getting, using, recovering
  - Activities given up to use
  - Craving
- **Physiologic**
  - Tolerance
  - Withdrawal
- **Consequences**
  - Hazardous use
  - Social or interpersonal problems related to use
  - Neglected major roles to use
  - Continued use after significant problems

2-3 = mild
4-5 = moderate
6+ = severe

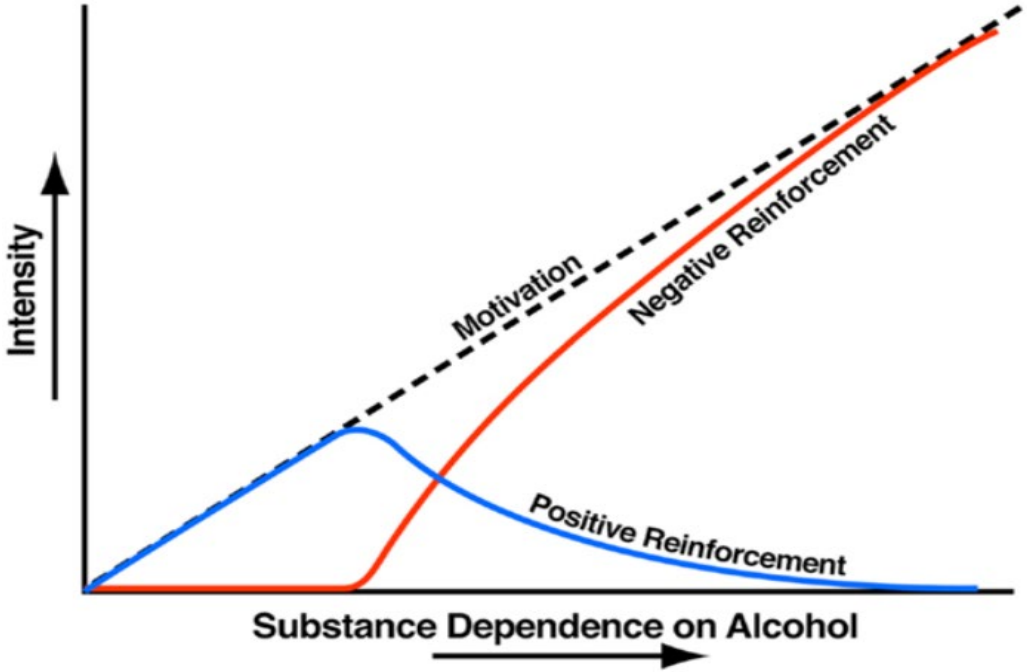
A substance use disorder is defined as having 2 or more of these symptoms in the past year.

Tolerance and withdrawal alone don't necessarily imply a disorder.

Severity is related by the number of symptoms.

Why Do People Use / Seek Drugs?

Theoretical Framework for Understanding Addiction and Motivation for Alcohol/Drug Seeking Over the Lifetime



Positive Reinforcement

- Pleasurable Experience

Negative Reinforcement

- Drug withdrawal
- Depression
- Abuse/ Trauma
- Neglect/Poverty
- Social Deprivation

Koob 2013

The Opioid Epidemic

Opioid Use Disorder as a Disease

Overdose Management

Medications for Opioid Use Disorder

Opioid Intoxication

- Euphoria (“high”)
- Constricted pupils
- Slowed breathing
- Low body temperature
- Vomiting
- Constipation
- Drowsiness
- Decreased awareness

Opioid Overdose

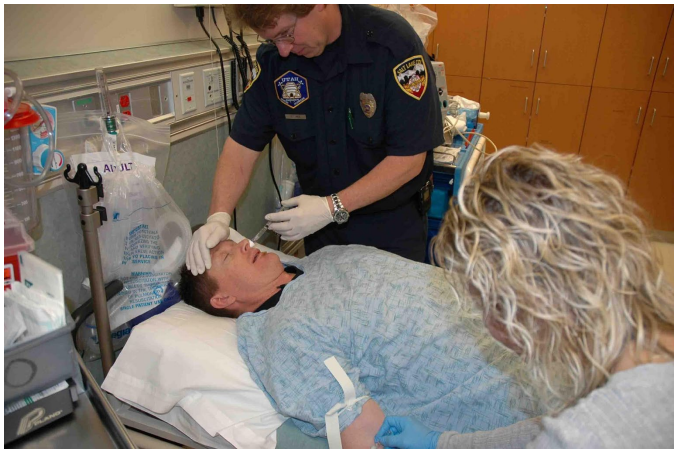
- Nonresponsive
- Pinpoint pupils
- **No respiration**
- Low blood pressure
- Slow heartbeat
- Coma
- Cyanotic
- Flaccid muscles

Opioid Overdose

- Cause of death = respiratory depression
- ~7 non-fatal OD for every fatal OD
- Risks
  - Higher Dose (>50 MME)
  - Recent abstinence (detox, jail)
  - Combination with sedatives (alcohol/ benzodiazepine)
  - Injection User
  - Medical: HIV, liver disease
  - Depression
  - People in household possess

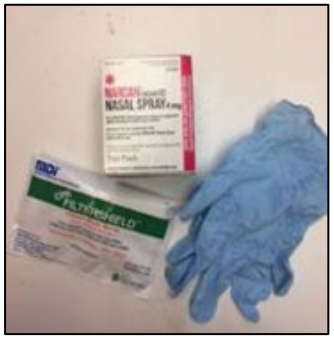
OD Reversal

- Management: Opioid antagonist, naloxone (Narcan)
  - Call 911
  - Rescue treatment
- Intranasal



Naloxone Access

- Free trainings & kits in NJ



Contact Kelley Hamilton, MPH, CHES
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Rutgers Robert Wood Johnson Medical School

- Individuals can obtain at pharmacies without a prescription
  - Approx. $50-150
  - May be covered by insurance
  - Availability varies by pharmacy

Opioid Withdrawal

Not life threatening

- Anxiety
- Yawning
- Sweating
- Tearing
- Runny nose
- Pupils widen (dilate)
- “Goosebumps” / muscle twitching
- Nausea / vomiting
- Diarrhea and abdominal cramps
- Muscle / bone pain

The Opioid Epidemic

Opioid Use Disorder as a Disease

Overdose Management

Medications for Opioid Use Disorder

Recovery is Bio-Psycho-Social-Spiritual

• Biological	Withdrawal, craving, medical conditions
• Psychological	Depression, trauma, coping
• Social	Friends, environment, relationship
• Spiritual	Hope, purpose, altruism, forgiveness

MOUD Saves Lives

Medications for Opioid Use Disorder (MOUD)

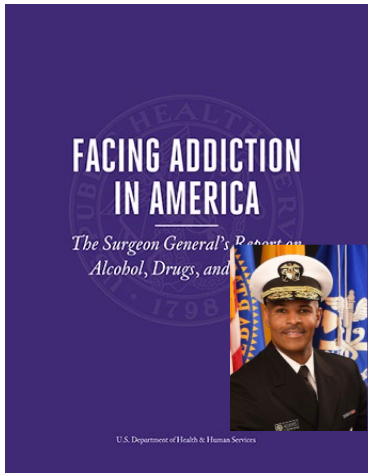
- Buprenorphine (Suboxone)
- Methadone
- Extended Release Naltrexone (Vivitrol)

Increases Treatment Retention

Saves Lives (Reduces Overdose Deaths)

Rationale for MOUD

- Detoxification and maintenance
- Prevents or lessens withdrawal
- Reduces use (negative urine drug screen)
- More substance free days/weeks
- Reduces crime, infection, HIV
- **Greater treatment retention (fewer dropouts) and reduced rate of death**



Surgeon General's Report 2016

JEROME M. ADAMS, M.D., M.P.H.
Vice Admiral, U.S. Public Health Service Surgeon General

Medication (MOUD) combined with psychosocial therapies and community-based recovery supports is the **gold standard** for treating opioid addiction.

- Counseling Only/ Abstinence only model is Not recommended
- MOUD are substantially more effective than abstinence-based treatment

Only **13%** of eligible patients with OUD receive treatment with MOUD

Krawczyk et al., 2022

Barriers to MOUD Access

- Personal
  - Stigma, Misinformation & Beliefs
- Provider Level
  - Stigma, Misinformation & Beliefs
  - Lack of Education
- Systems Level
  - Stigma, Misinformation & Beliefs
  - Lack of / Limited Insurance Coverage

Opioid Use Disorder- Variable Course over 42 Months

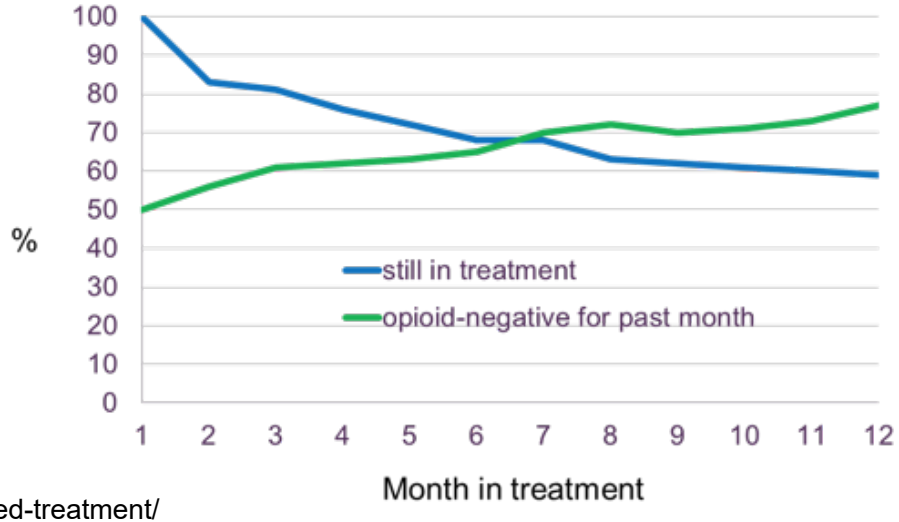
Abstinence in the Past Month

Most people with OUD have alternating periods of abstinence and use

Weiss, Drug Alcohol Dep, 2015

Treatment Retention and Decreased Illicit Opioid Use on MOUD

Buprenorphine promotes retention, and those who remain in treatment become more likely over time to abstain from other opioids

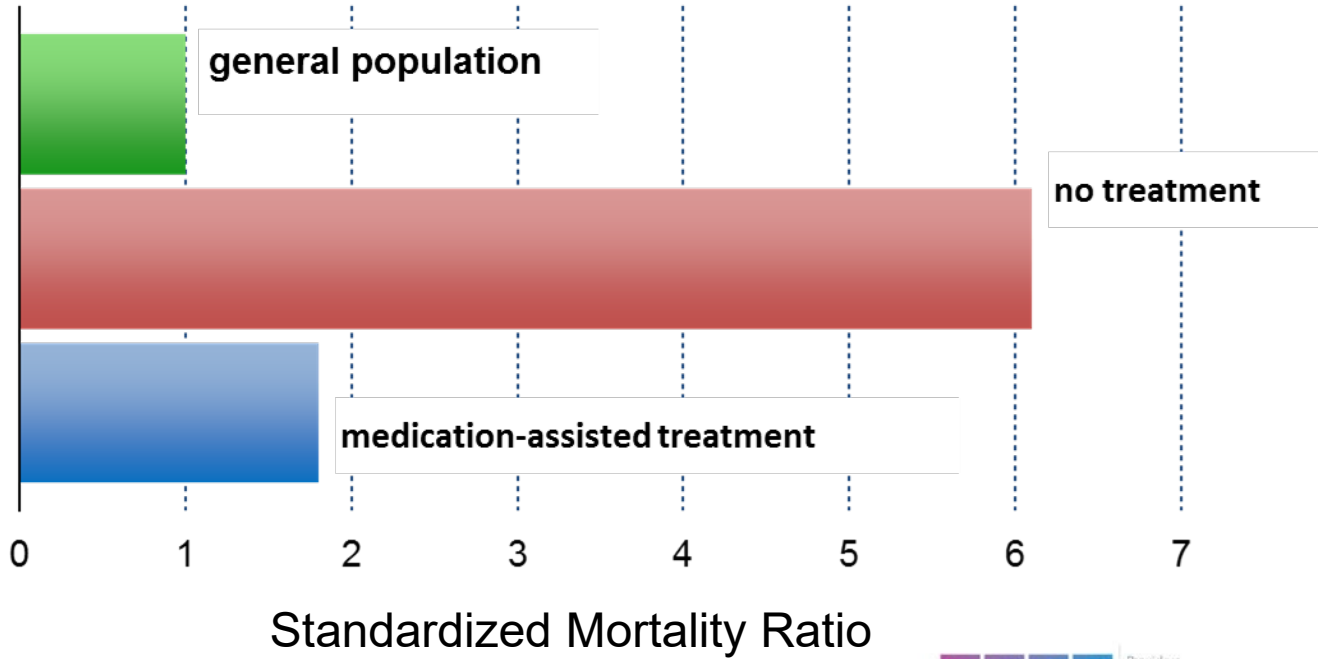


Kakko et al, 2003
Soeffing et al., 2009

From PCSS Waiver Training, 2019.
https://pcssnow.org/medication-assisted-treatment/

Benefits of MOUD: Decreased Mortality

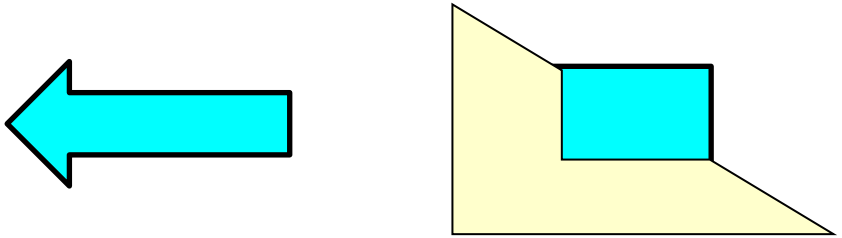
Death rates:



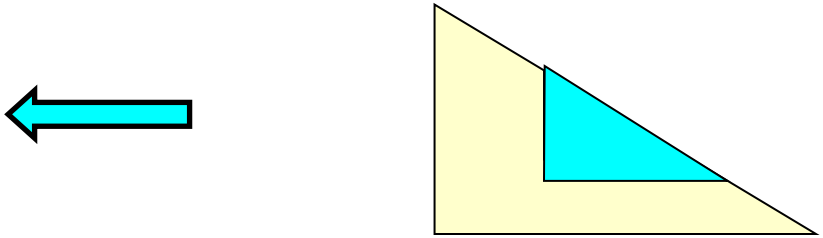
Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017

From PCSS Waiver Training, 2019.
https://pcssnow.org/medication-assisted-treatment/

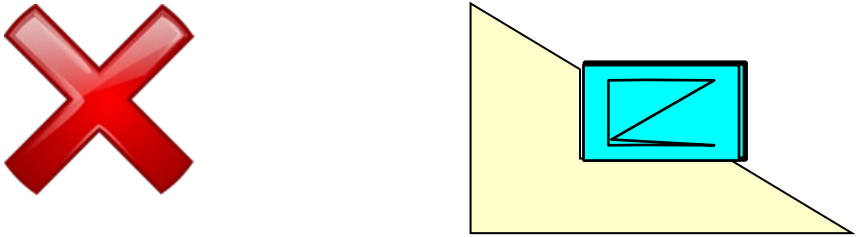
Opioid Classification (mu receptor)



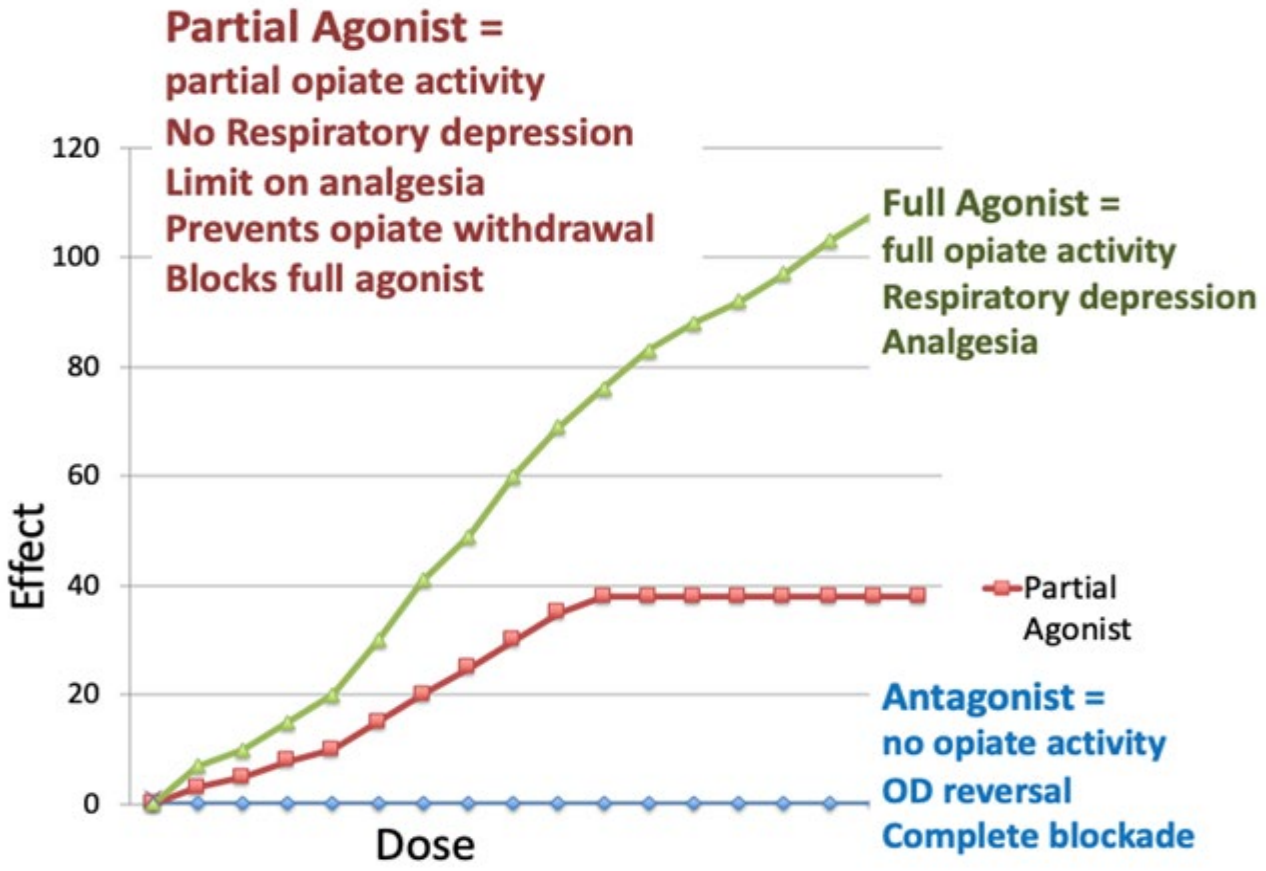
Full agonists:
- morphine
- oxycodone



Partial agonist:
- buprenorphine



Antagonists:
- naloxone
- naltrexone


Partial Agonist =
partial opiate activity
No Respiratory depression
Limit on analgesia
Prevents opiate withdrawal
Blocks full agonist
Full Agonist =
full opiate activity
Respiratory depression
Analgesia
Partial Agonist
Antagonist =
no opiate activity
OD reversal
Complete blockade
Effect
Dose
120
100
80
60
40
20
0

Buprenorphine

- Partial mu agonist with ceiling (↓ risk)
  - Lower street value
  - Lower abuse potential
  - No respiratory depression
- Long duration of action
- Strong mu affinity, Displaces other opioids
- Start first dose in mild withdrawal
- Harder induction with fentanyl (low dose)

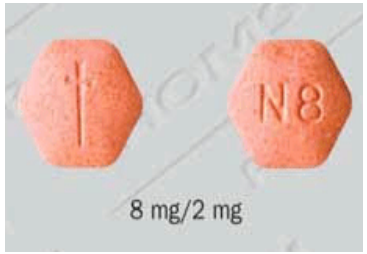
- Removal of X Waiver goes into effect June 21, 2023

  No patient limits

Buprenorphine

- Common side effects: constipation, nausea, headache, sweating, dry mouth
- FDA approved ≥ 16
- Taken sublingual (under tongue)
- **Naloxone added** to buprenorphine (↓↓ diversion)
  - When taken orally no effect
  - If crushed, snorted or injected precipitates opioid withdrawal

Suboxone (BUP:NAL)

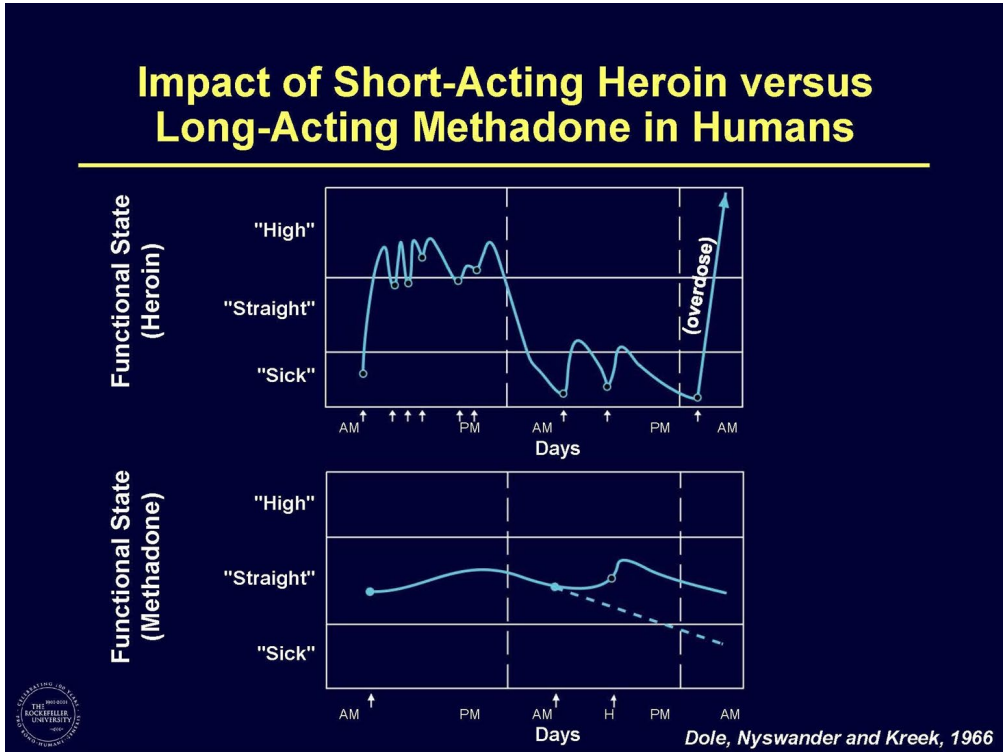


Subutex (BUP)

Methadone

- Mu receptor agonist
- 50-100mg daily
- Complicated medication interactions
- Lasts a long time in body
- Side effects: constipation, sweating, sexual dysfunction, sedation
- Decades of evidence
  - Reduces and eliminates use of opioids and cocaine
  - Reduces risk of HIV
  - Reduces needle sharing and needle use
  - Reduces crime and incarceration
- Used for **opiate use disorder** only in a licensed methadone treatment facility. More take home doses since COVID

Methadone Removes Cycle of Intoxication and Withdrawal



Extended Release Naltrexone (ER-NTX)

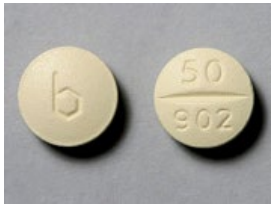
- Vivitrol
- FDA approved relapse prevention
- XR-NTX 380mg shot every 4 weeks
- Cannot start until 7 days opioid free
- Works: Greater abstinence, less craving and greater treatment retention vs placebo
- Side effects: Insomnia, injection site reaction, nausea, headache
- Can be expensive ($1500/ shot)

Opiate Antagonists

Both = Strong affinity, displace full agonist

Overdose Reversal

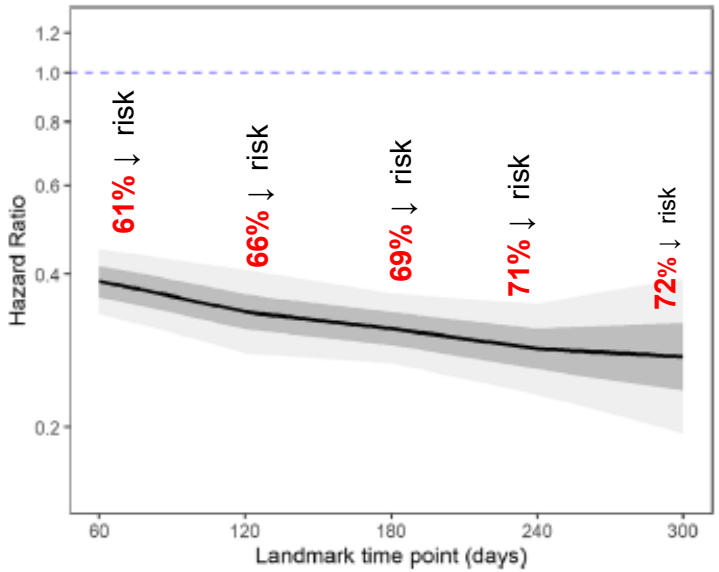
Naloxone (Narcan) – shot, intranasal



Relapse Prevention / MOUD

Naltrexone – oral or long acting injection

Longer Duration of MOUD Treatment Reduces Overdose



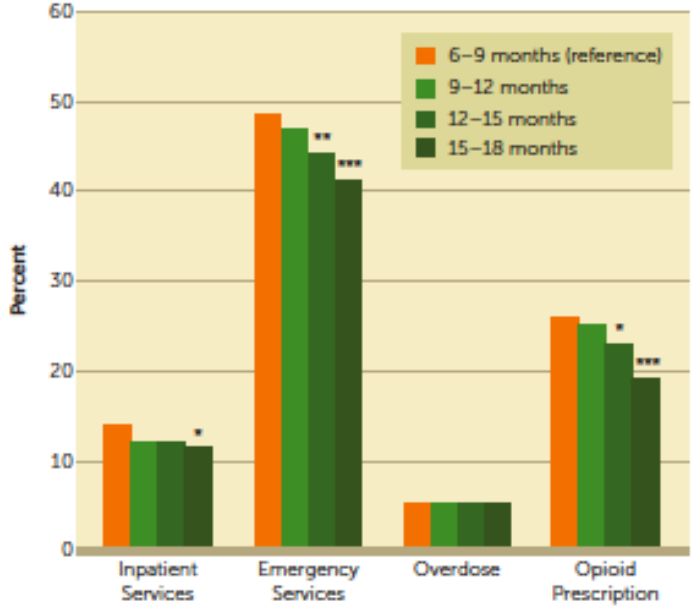
Relative hazard of OD in continued vs stopped MOUD

- 6 months MOUD, 61% less risk of OD (vs stopping)
- Every extra 60 d of MOUD treatment received, reduced risk by another 10%
- Same effect across 11 states
- Medicaid data analysis ~300k
- **Longer treatment is better**

Burns et al., Addiction 2022

Risk for Relapse Following Buprenorphine Discontinuation is High

FIGURE 3. Unadjusted 6-month outcomes following discontinuation among Medicaid beneficiaries ages 18–64 retained on buprenorphine for ≥180 days, by treatment duration cohort (2013–2017)[a]



All Groups High Risk for

- Inpatient Services
- Emergency Services
- Overdose
- Prescription of opioid (full agonist)

6 months after discontinuation

Insurance was not a factor related to duration of treatment

Williams AR et .al., AJP, 2020

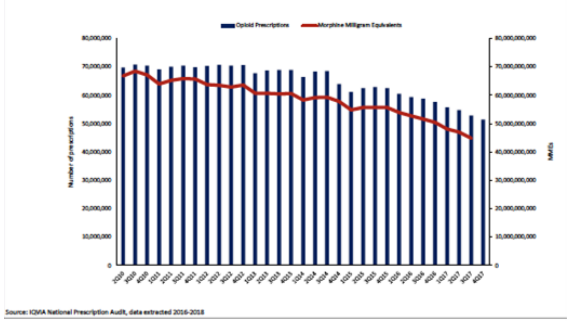
Equally Effective		
Buprenorphine-Naloxone **(Suboxone)**	**Methadone**	**ER-Naltrexone** **(Vivitrol)**
Minimal overdose risk	Best retention (better for most severe)	No abuse potential
More access (office based); rural	Easy induction	Complete opioid blockade (pain relief; Less pleasure)
Better- elderly, complex medical	Most stigma	Induction requires 7 days opioid free
Less neonatal abstinence syndrome than methadone	Less available	Expensive
Some pain relief	Complex medical interactions, long half life; cardiac heart arrthymias	Shots not available everywhere

MOUD is working if

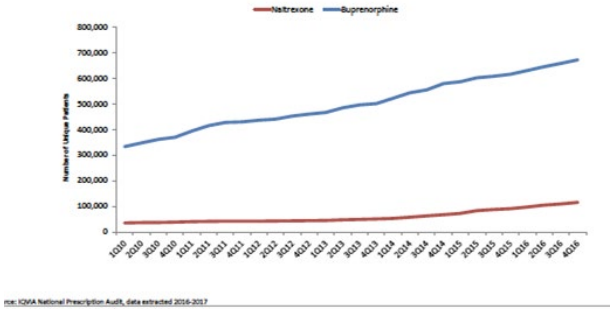
- Stops using other opioids
- Experiences no craving for opioids
- Has no opiate withdrawal symptoms
- Has no side effects from medications
- **Feels that life is no longer out of control**

US Crisis: Signs of Progress

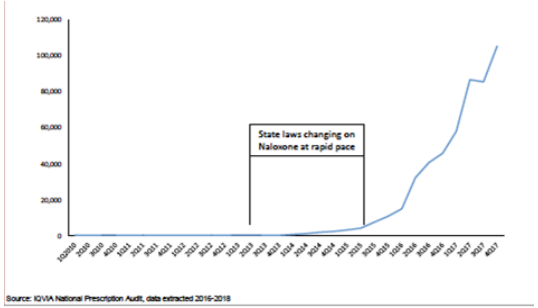
Opioid prescribing declining since 2011



Receipt of MOUD from treatment facilities and pharmacies increasing



Increase in naloxone dispensing from US pharmacies



Conclusions

- Several factors including over-prescribing led to the US Opioid Crisis
- Substance use Disorders are chronic brain diseases that warrant recognition and treatment
- Medications for Opioid Use Disorders are effective and underutilized
- 1-844-REACHNJ connects individuals to info and services

  reachnj.gov

Sponsored by a grant from the NJ Department of Human Services, Division of Mental Health & Addiction Services
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