



# **The Heroin and Fentanyl Epidemic**

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# Objectives:

- Understand the scope of the heroin and fentanyl epidemic
- Have an appreciation for how we got here and where we are headed
- Acquire an appreciation that treatment is not a “one size fits all” proposition
- Understand the evidence-based treatments for opioid use disorders

# Introduction:

- No one who tries drugs envisions that they will eventually stick a needle in their arm
- By the time these individuals come to the hospital, drug use is no longer motivated by a desire to have fun
- In true addiction, drug use is an obsession/compulsion
- Criminal behavior is often in the service of their underlying addiction

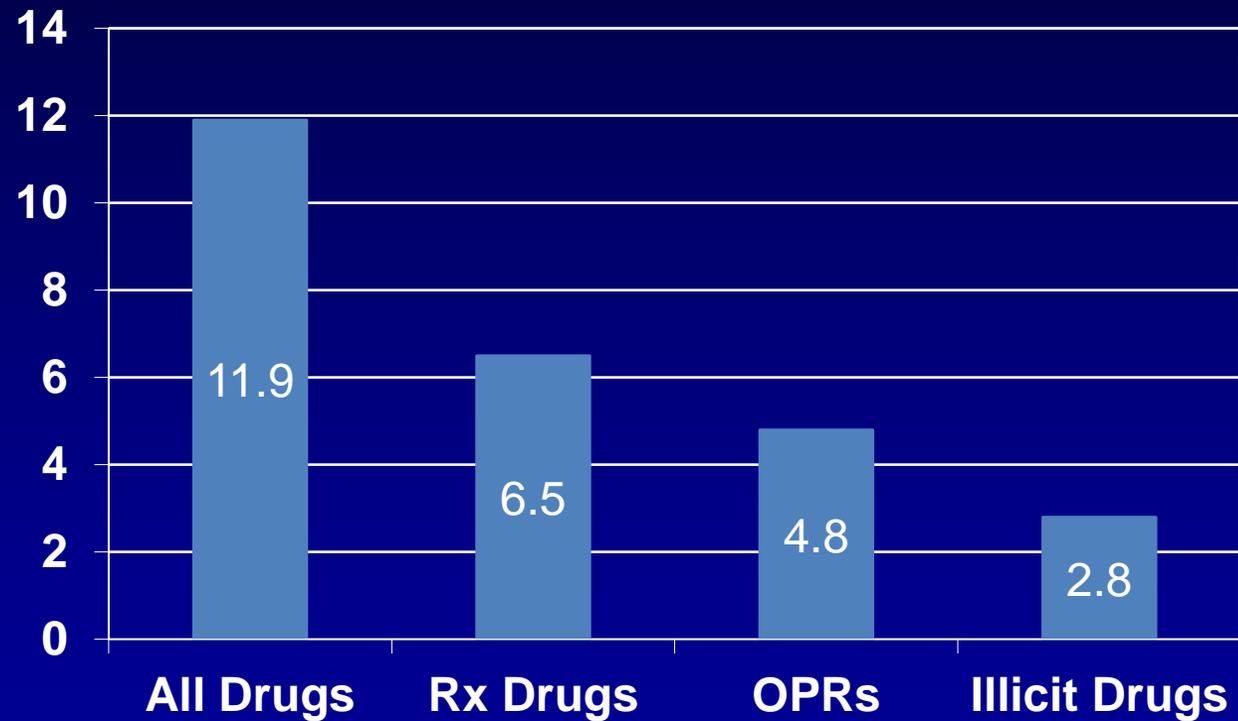
# Mortality:

- On average, addicts lose 18.3 potential years of life<sup>1</sup>
- Mortality for injection heroin users is about 2% per year<sup>2</sup>
- Roughly half of the mortality is attributable to overdose<sup>2</sup>
- Mortality rate is 6-20 times greater than that of peers who do not use drugs<sup>2</sup>

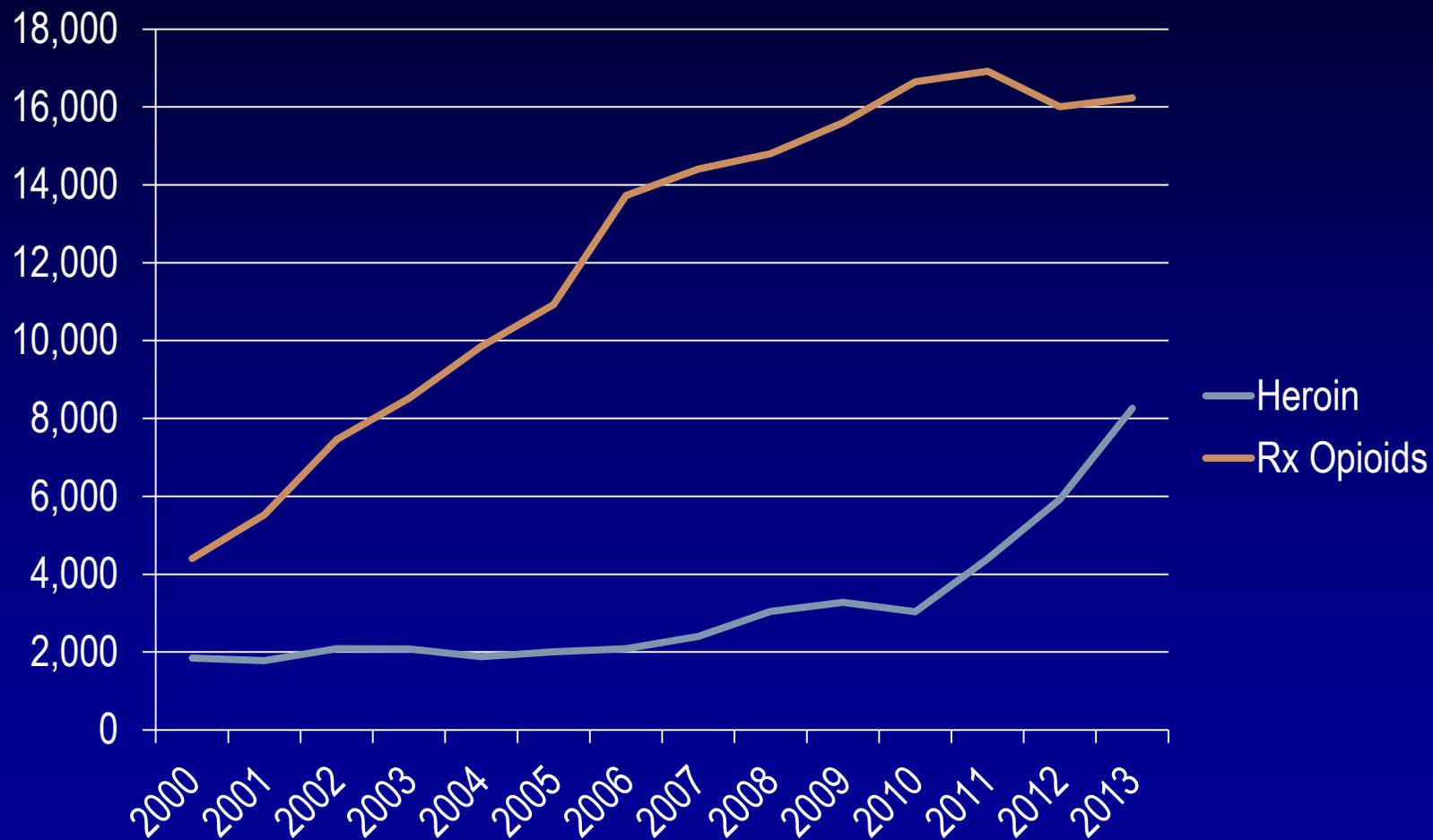
<sup>1</sup>Smyth B, et al. *Preventive Medicine* 2007; 44(4): 369-374

<sup>2</sup>Sporer KA, et al. *Ann Int Med* 1999; 130: 584-590

# U.S. Drug Overdose Death Rates, 2008:



# Rx Opioid vs Heroin ODs:



CDC: Drug-poisoning deaths involving heroin: United States, 2000-2013. NCHS Data Brief, 190, March 2015

# The Current Epidemic:

## Heroin & Fentanyl Overdose Deaths in Cuyahoga County





# Opioid & Vietnam War Fatalities

## Vietnam War

- **1968: Deadliest year of the war resulted in 16,899 deaths**
- **During the 10 deadliest years of the Vietnam war (1963-72) 58,004 soldiers died.**

## Opioids

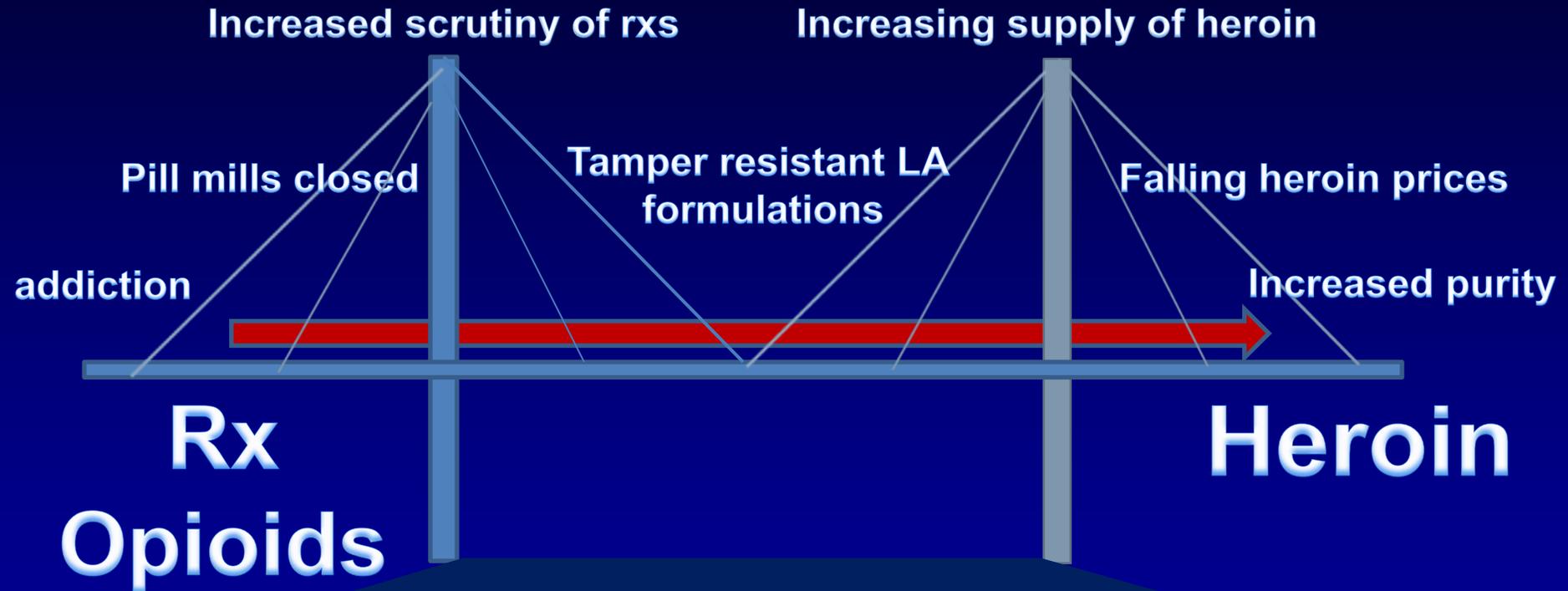
- **2013: 16,235 US citizens died from prescription opioid OD and another 8,257 died from heroin OD<sup>2</sup>. Total= 24, 492**
- **During the 10yrs spanning 2004 through 2013, more than 145,000 people in the US died from prescription opioid ODs, and another 36,000 died from heroin ODs. Total=181,000**

<sup>1</sup>US National Archives:

<http://www.archives.gov/research/military/vietnam-war/casualty-statistics.html>. Accessed: 03/05/2014

<sup>2</sup>CDC: Drug-poisoning deaths involving heroin: United States, 2000-2013. NCHS Data Brief, 190, March 2015

# The Transition to Heroin in Ohio...



Increasing Heroin Overdoses in Ohio:  
Understanding the Issue, Epidemiological  
Report, No. 3. April 2014

# Modern-day Path to Heroin:

- Started on oxycodone 2-3 years previously for shoulder injury sustained in car accident
- Soon realized they liked the “feeling”
- Began taking more than prescribed and running out of Rx’s early, ultimately resulting in doc refusing to write more
- Began obtaining illicitly but ultimately realized that heroin was about 10% of the cost of oxycodone

# Heroin: 1960'S vs. Now

## 1960s

- Young (avg age: 17yrs)
- Male (83%)
- First opioid was heroin (80%)
- Whites = non-whites (prior to 1980)
- Predominantly from urban environments

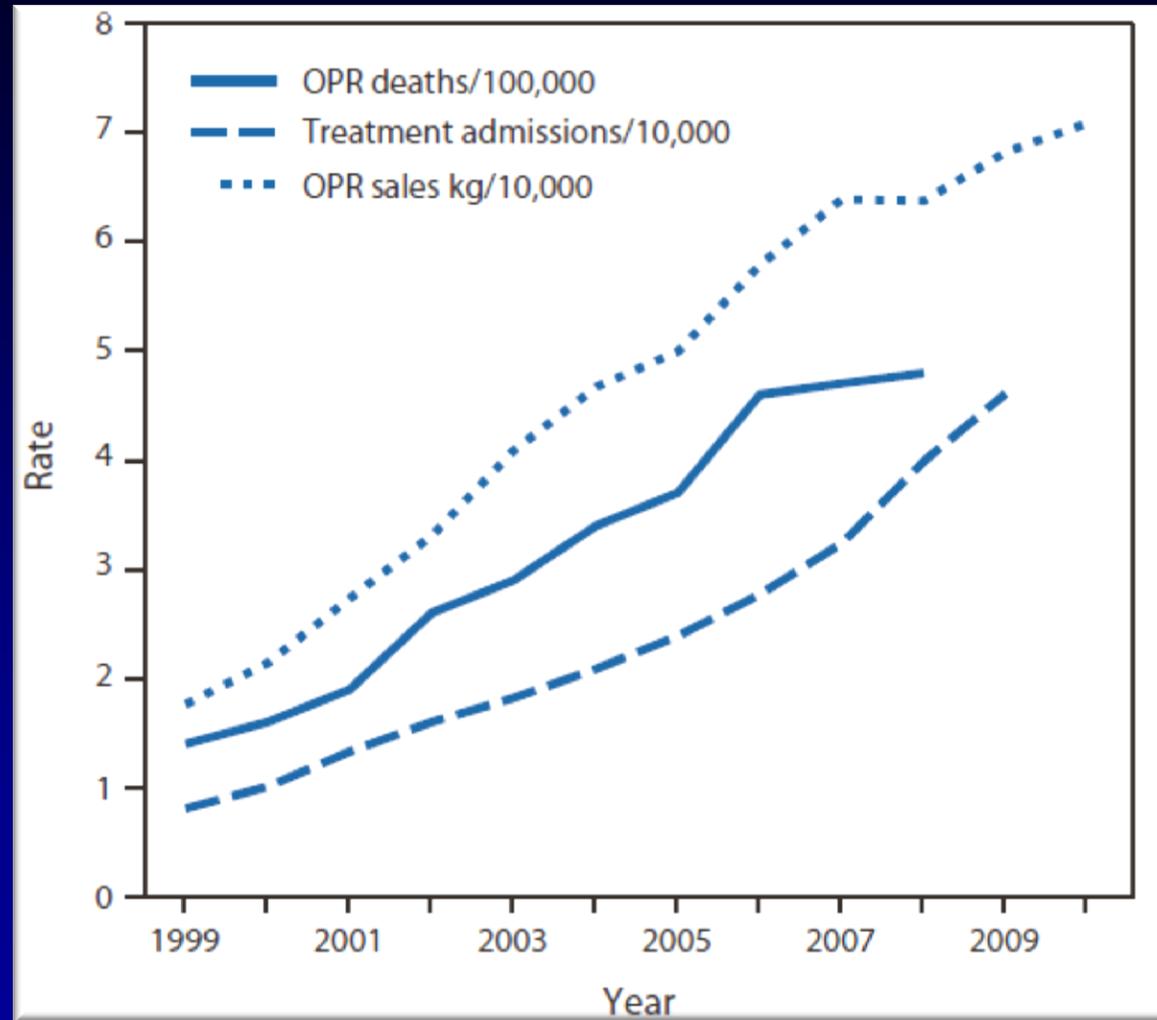
## 2010s

- Older (avg age: 23)
- Males = Females
- First opioid was Rx narcotic (75%)
- Mostly whites (90%)
- 75% from small urban or non-urban environments

# How Did We Get Here?

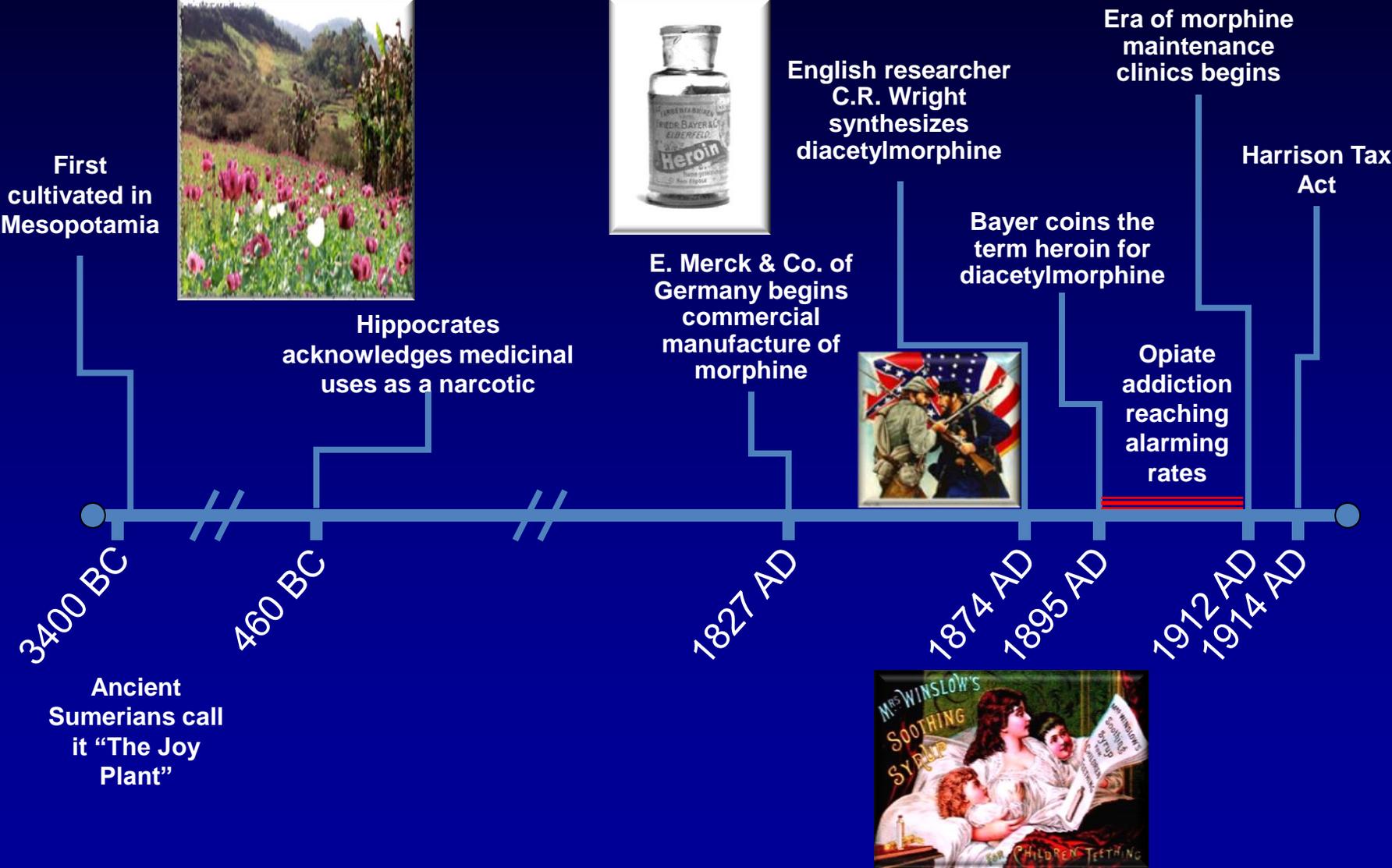
- Prior to the mid-1990's, very few doctors would have prescribed narcotics for chronic musculoskeletal pain
- Pressure by the pharmaceutical industry, regulatory agencies, and state medical boards changed the culture of pain mgmt
- “Zero” pain now seems to be the cultural expectation and is promoted by the “fifth vital sign” that is required in all medical charts

# How Did We Get Here?

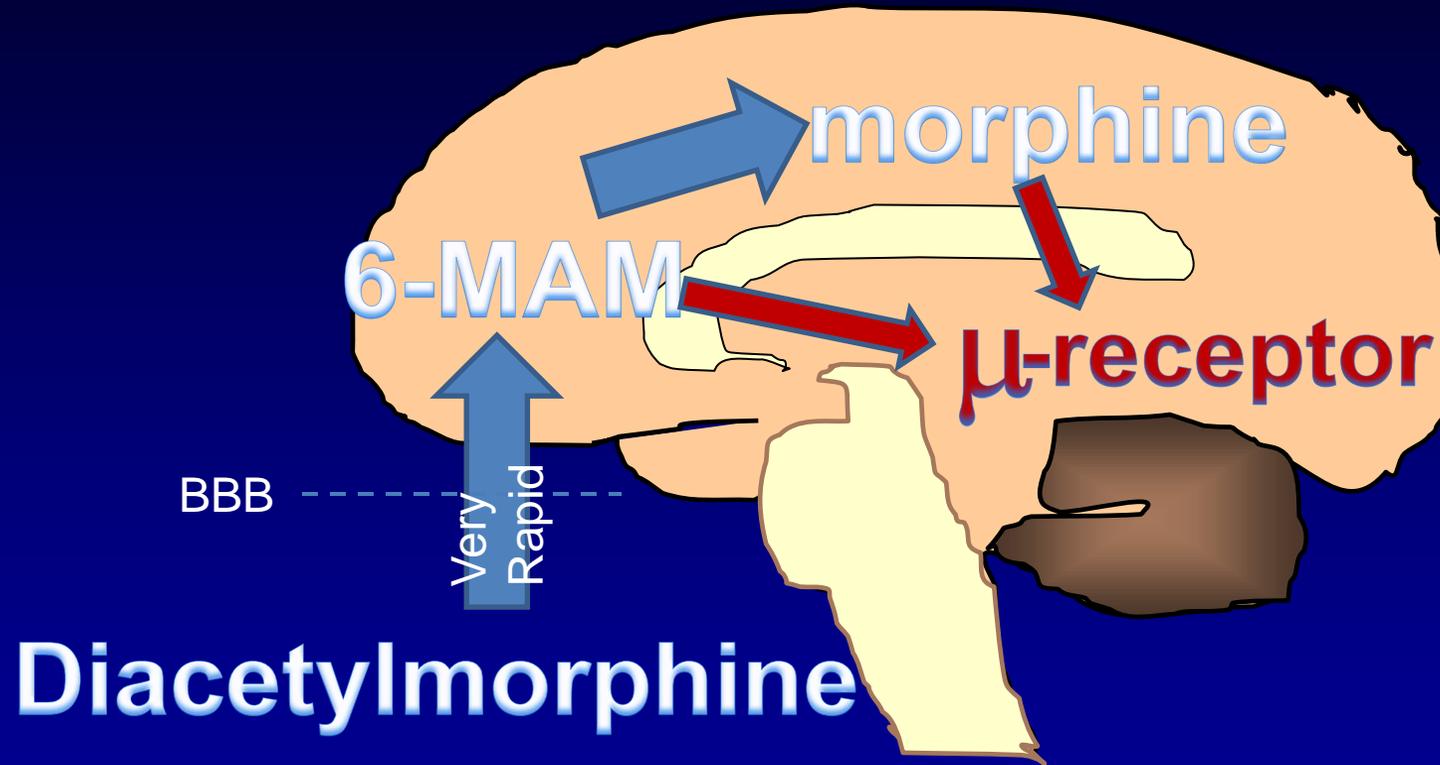


CDC. Vital Signs: Overdoses of Prescription Opioid Pain Relievers --- United States, 1999—2008, MMWR. November 4, 2011 / 60(43);1487-1492

# History of Opiates:



# What makes heroin so addictive?



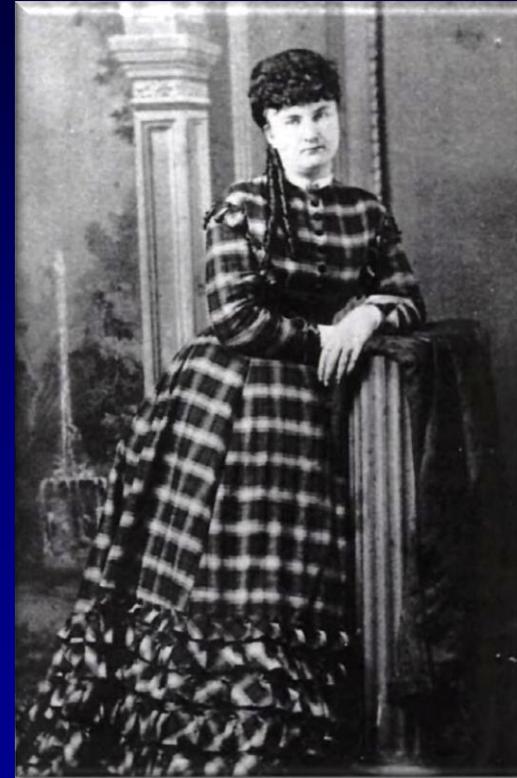
Oldendorf, 1972

Gottas A, 2013

Inturrisi et al., 1983

# The First Heroin Epidemic:

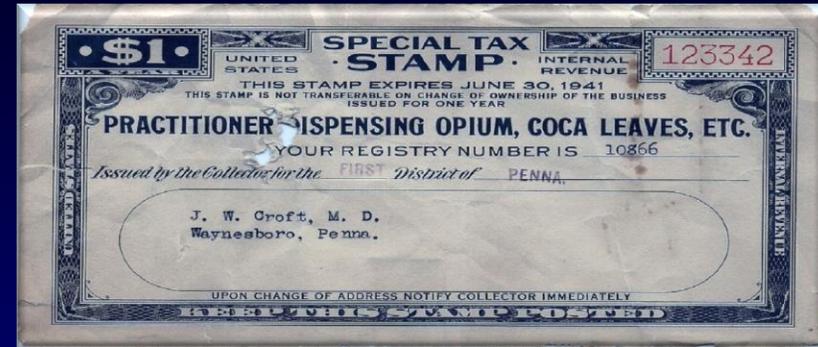
- Sharp increase in opioid addiction in late 1800s & early 1900s
- Largely secondary to OTC preparations
- Middle-upper middle class Caucasian women



Celia Ann "Mattie Blaylock", 1850-1888

# The Harrison Act of 1914:

- Technically a tax act
- Effectively forbade doctors from prescribing opiates to addicts
- In the 24yrs after its passage, more than 25,000 doctors were indicted and 3,000 were jailed



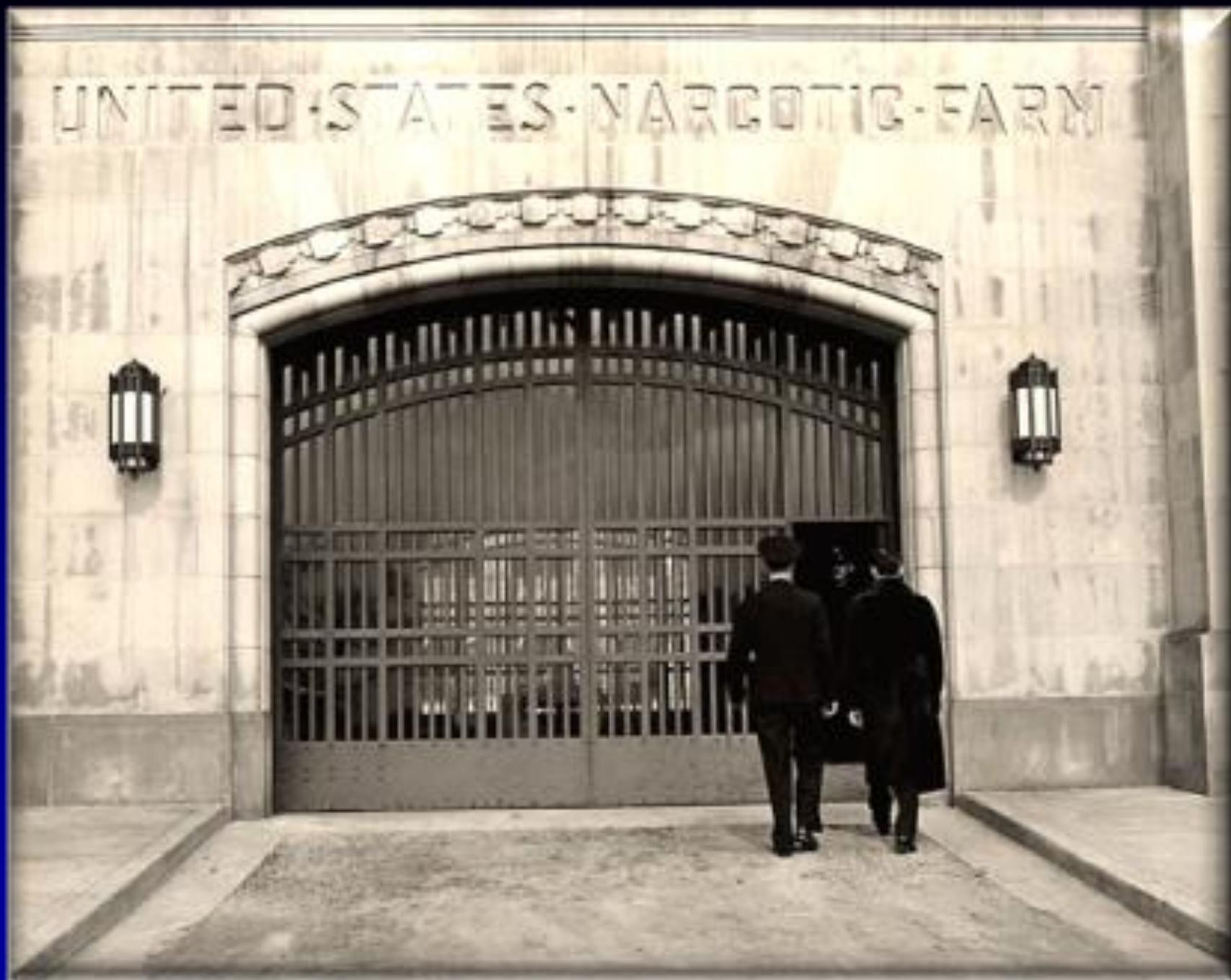
# Morphine Maintenance Clinics:

- The “clinic era,” 1912-1925
- Expanded in the wake of the Harrison Act
- 40-60 clinics around the country
- Ultimately closed secondary to government pressure
- Harry Anslinger, Commissioner of the Bureau of Narcotics called them “barrooms” for addicts

# The Federal Narcotics Farms



UNITED STATES NARCOTIC FARM



# Narcotic Farms

- U.S. Public Health Service, authorized by Congress in 1929 to establish 2 narcotic farms
- Lexington Narcotic Farm opened May 25, 1935
- First intramural research branch of NIMH
- Closed in February, 1974



# Narcotic Farms

- **Population consisted of both involuntary inmates and “voluntary” patients**
- **Variable, often short, length of stay for voluntary patients prompted passage of the “Blue Grass” law that made “habitual narcotic use” a crime that carried a sentence of one year of treatment at Lexington**

# Narcotic Farms: Outcomes

- **Several outcome studies showed that 90-96% of addicts relapsed after being treated at Lexington<sup>1,2</sup>**
- **Majority of relapses occurred within the first six months<sup>1,2</sup>**
- **Similar results were seen at Ft. Worth-- at least 9 out of 10 patients relapsed on narcotics within five years<sup>1</sup>**

<sup>1</sup>White WL. (1998). Slaying the Dragon. pp 124-125

<sup>2</sup>Hunt GH, Odoroff ME, Public Health Rep 1962

# Maintenance Treatment:



**Methadone (50-120mg) or**

**Buprenorphine (12-16mg)**

**No withdrawal symptoms**

**Receptors blocked in case of "slip"**

# Opioid Maintenance Treatment (OMT):

- **Initially conceived of as a stepping stone toward abstinence**
- **This has not, however, been the reality**
- **Only 10-20% of those who discontinue methadone are able to remain abstinent**

# Methadone Clinics:

- 1965-70: Among first 4,000 methadone patients, >98% remained in treatment for at least one year.
- 1970-73: census of 35,000 patients. One-year retention dropped to 61%
- 1975: the one-year retention rate for methadone maintenance was 59%

# Methadone Clinics

- **Until 2002—  
methadone was the  
only medication  
approved for MAT**
- **Methadone can only  
be provided to  
addicts on an  
outpatient basis by  
federally licensed  
clinics**



# Methadone Clinics

- Patients must initially come to the clinic daily to receive dose
- Relatively few clinics nationwide
- Usually located in less desirable parts of major metropolitan areas
- Associated stigma
- Attract dealers



# **An Alternative is Approved...**

- 2002: buprenorphine-naloxone was approved for MAT of opiate dependence**
- May be used in office-based settings**
- Doctors must obtain a DATA-2000 waiver in order to use this medication**
- Limited to 30 patients for the first year, 100 patients thereafter**

# Buprenorphine and MAT

- **20-year review of buprenorphine:**
  - **Improves treatment retention**
  - **Reduces illicit opioid use**
  - **Associated with improved outcomes during pregnancy**
  - **Fewer adverse outcomes than methadone in certain populations**
  - **Clearly provides greater access to care than methadone**

# Mortality (per 100,000/yr)

- **Prescription Opioids:** 4.8
- **Illicit Drugs:** 2.8
- **Methadone Maint:** 0.4-0.5
- **Buprenorphine:** 0.1

(1) Clausen et al., Drug and Alcohol Dependence 2008; 94: 151-157

(2) Caplehorn JR, et al. Subst Use Misuse 1996; 31: 177-196

(3) Bell JR, et al. Drug and Alcohol Dep 2009; 104: 73-77

# Naltrexone:

- **Blocks mu opiate receptors**
- **No abuse potential**
- **Can't be diverted**
- **Once monthly injection**

# Naltrexone:

- **Concerns:**
  - **Expensive**
  - **Logistics of giving the injection**
  - **Efficacy largely unproven**
  - **Increased risk for overdose and perhaps suicide**

# Oral Naltrexone

- **Six-month retention in treatment: 20-30%**
- **Meta-analysis<sup>(Kleber HD, 1987)</sup> of several studies involving oral naltrexone did not support its use in opiate-dependent patients**

(Minozzi S et al., 2006)

# Oral Naltrexone

- 12-month study of 81 patients treated with naltrexone: **13 overdoses** (4 fatal, representing almost 5% of the study population)
- One of the fatalities and four of the non-fatalities were intentional
- 11 out of the 13 patients who overdosed had completed or dropped out of treatment prior to the event

# Oral Naltrexone

- Longitudinal study of 12 trials (N=1,244) showed **3 times greater risk** of overdose with those on naltrexone vs those on opioid agonists **while in treatment**
- Naltrexone patients were **8 times** more likely than opioid agonist patients to overdose **after treatment**

Digiusto E et al. *Addiction* 2004; 99: 450-460.

Wolfe D et al. *Lancet* 2011; 377(9776), 1468-1470.

# Naltrexone and Overdose Risk

- The ability of naltrexone to suppress the subjective effects of heroin outlasts the ability of the medication to suppress the physiologic response <sup>1</sup>
- Supersensitivity to opioid agonists following chronic opioid antagonist treatment has been observed in laboratory studies <sup>2</sup>

<sup>1</sup>Navaratnam et al. *Drug and Alcohol Dependence* 1994; 34: 231-236.

<sup>1</sup>Schuh KJ, et al. *Psychopharmacology* 1999; 145: 162-174.

<sup>2</sup>Yoburn BC, et al. *Pharmacol Biochem Behav.* 1995 Jun-Jul; 51(2-3):535-9

<sup>2</sup>Lesscher HMB, et al. *Eur J Neurosci.* 2003;17:1006–1012.

<sup>2</sup>Sirohi S, et al. *Pharmacol Exp Ther.* 2007; 323: 701-707.

# MAT: Depot-Naltrexone

- **FDA approval based on a 24-week randomized study in Russia (N=250): XR-NTX 380 mg (N=126) vs placebo (N=124)**
  - **Primary outcome: confirmed abstinence in wks 5-24**
  - **54% of patients didn't finish the study**

Krupitsky E et al. *Lancet* 2011; 377(9776), 1506-1513.

Wolfe, D et al. *Lancet* 2011; 377(9776), 1468-1470.

# MAT: Depot-Naltrexone

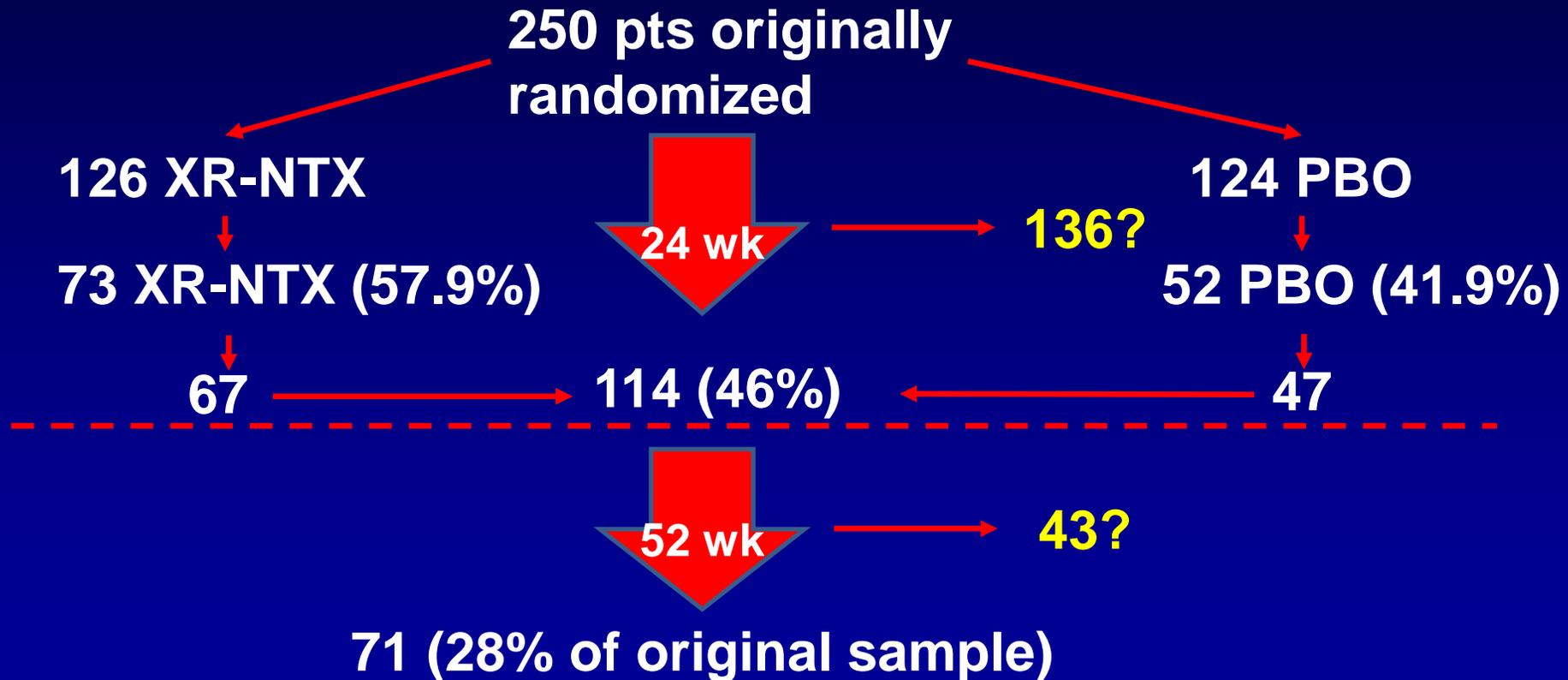
- **57.9% in the XR-NTX arm received all six injections vs 41.9% in the PBO group**
- **Primary outcome:**
  - **Median proportion of weeks confirmed abstinence: 90% in tx arm vs 35% PBO (p=0.0002)**
  - **36% of XR-NTX group reported total abstinence vs 23% in PBO group (p<0.022)**

Krupitsky E et al. *Lancet* 2011; 377(9776), 1506-1513.

Wolfe, D et al. *Lancet* 2011; 377(9776), 1468-1470.

# MAT: Depot-Naltrexone

- 52 wk open-label continuation study...



# Drug Availability:



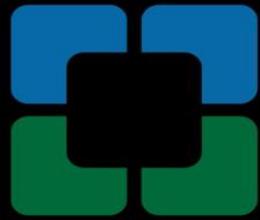
Adolescent gateway  
to addictions in the  
1980's...



Adolescent gateway  
to addictions now...

# Summary:

- Need to change unrealistic expectations regarding pain management
- Improve education about the dangers of prescription narcotics
- Decrease availability by limiting new prescriptions and through disposal of old narcotics
- Increase access to evidence-based treatments



**Cleveland Clinic**

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