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The Opioid Epidemic

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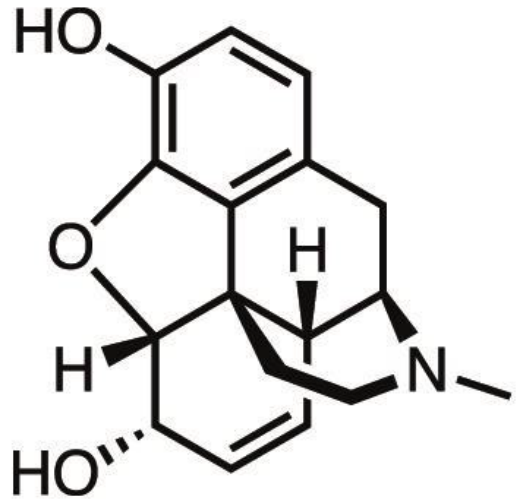
Learning Objectives

- Historical perspective on opioid prescribing and addiction
- Criteria for diagnosis of opioid use disorder
- Impact of opioid epidemic
- Treatment of opioid use disorder

Discovery of Morphine, 1806

Friedrich Wilhelm Adam Serturner, 1783-1841

Morphine is named for Morpheus, God of Sleep and Dreams



15 mg standard dose

1864:

Michael S.

- Civil War battle injury
- Morphine treated his pain

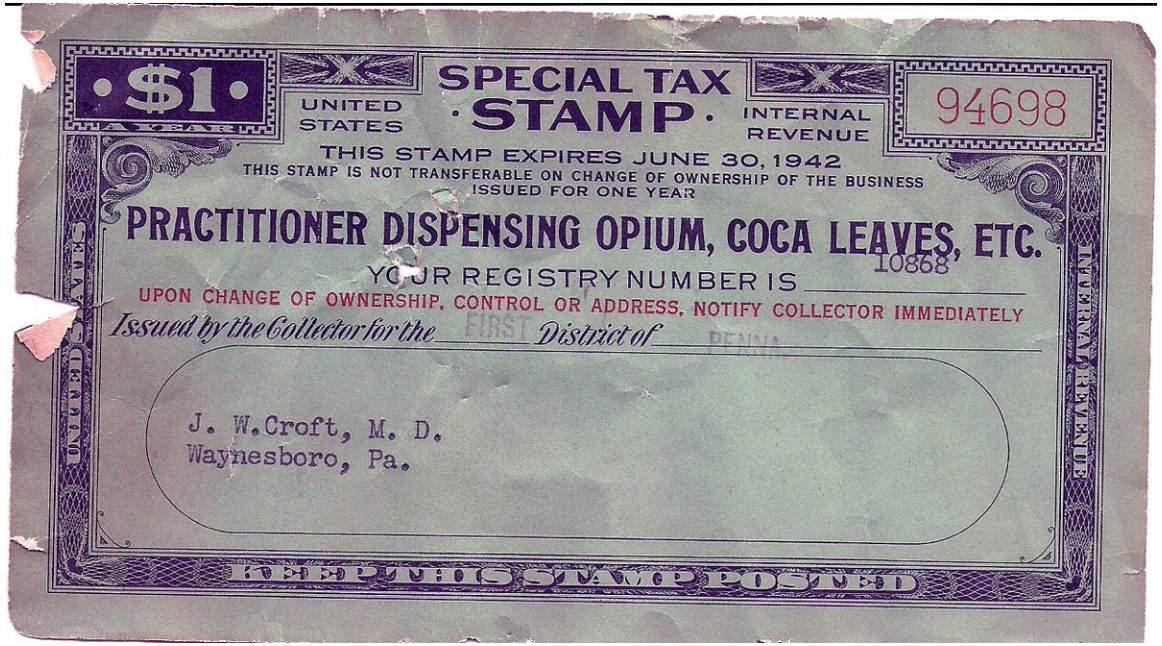
1899:

Michael S.

- Chronic cough from industrial exposure
- Di-acetylmorphine from Bayer

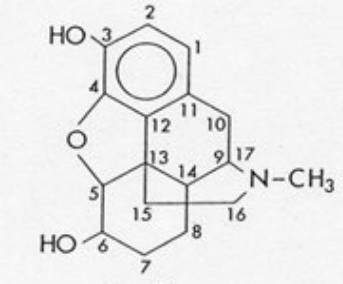
Harrison Act of 1914

- Combat addictive properties of medicinal opioids (heroin, morphine, codeine)
- Regulate nonmedical opioid use
- Made possession without prescription illegal

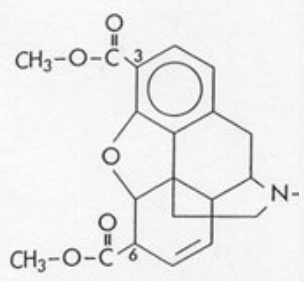


Opioids

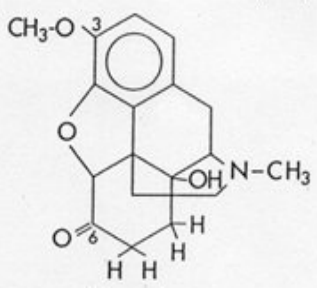
Natural and Semi-synthentic



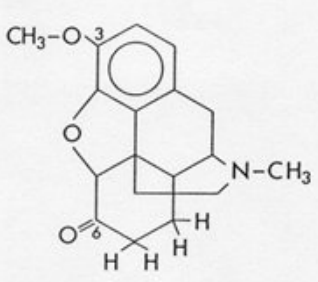
Morphine



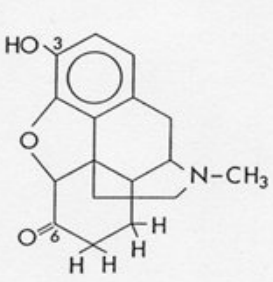
Diacetylmorphine (Heroin)



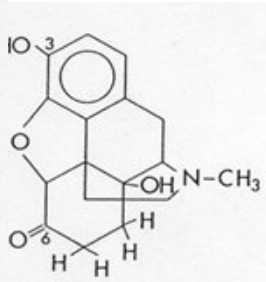
Oxycodone



Hydrocodone

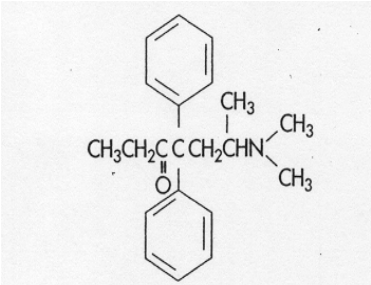


Hydromorphone

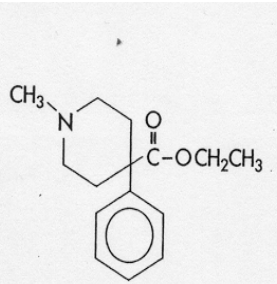


Oxymorphone

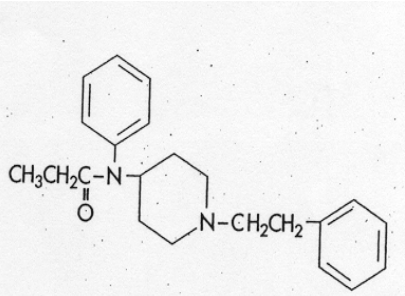
Synthetic



Methadone



Meperidine (Demerol)



Fentanyl

Buprenorphine

1974:

Michael S.

- Exposed to heroin and drugs during deployment in Vietnam
- Treated with methadone

Heroin, 1960s – 1970s

- Mostly minority communities
- Returning Vietnam vets
- Methadone approved 1972

Undertreatment of Pain

ANNALS of Internal Medicine
FEBRUARY 1973 · VOLUME 78 · NUMBER 2
Published Monthly by the American College of Physicians

Undertreatment of Medical Inpatients with Narcotic Analgesics

RICHARD M. MARKS, M.D., and EDWARD J. SACHAR, M.D., New York, New York

Structured interviews of 37 medical inpatients being treated with narcotic analgesics for pain showed that 32% of the patients were continuing to experience severe distress, despite the analgesic regimen, and another 41% were in moderate distress. Chart review suggested significant undertreatment with narcotics:

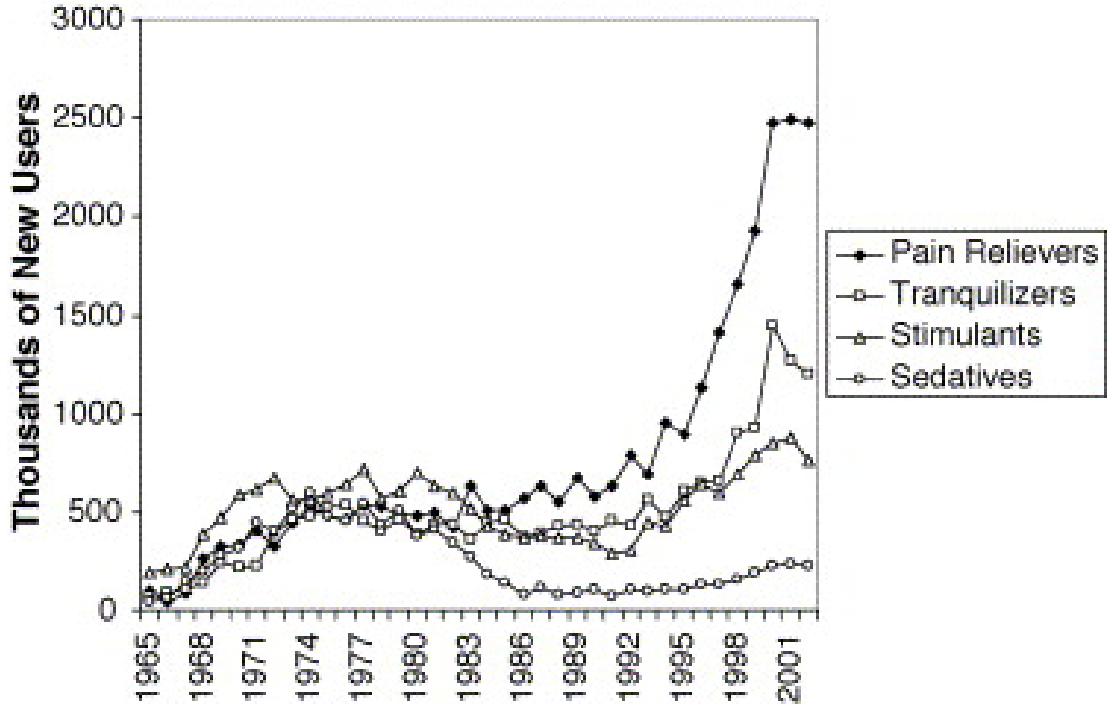
INCREASING CONCERN about the problem of drug abuse in this country, especially in relation to narcotic addiction, has developed in recent years. In this paper we draw attention to another type of drug misuse—the failure to treat patients in severe pain with adequate doses of narcotic analgesics. Our data

- 1970s-1980s
- Undertreated cancer pain

“Addiction Rare in Patients Treated with Narcotics”

January 10, 1980
N Engl J Med 1980; 302:123

Wave 1: Increase Opioid Prescribing



- 1996: Oxycontin marketed aggressively by Purdue
- 2001 Joint Commission: Pain as a 5th vital sign

Compton 2006 *Drug Alc Depend* 81:103-107

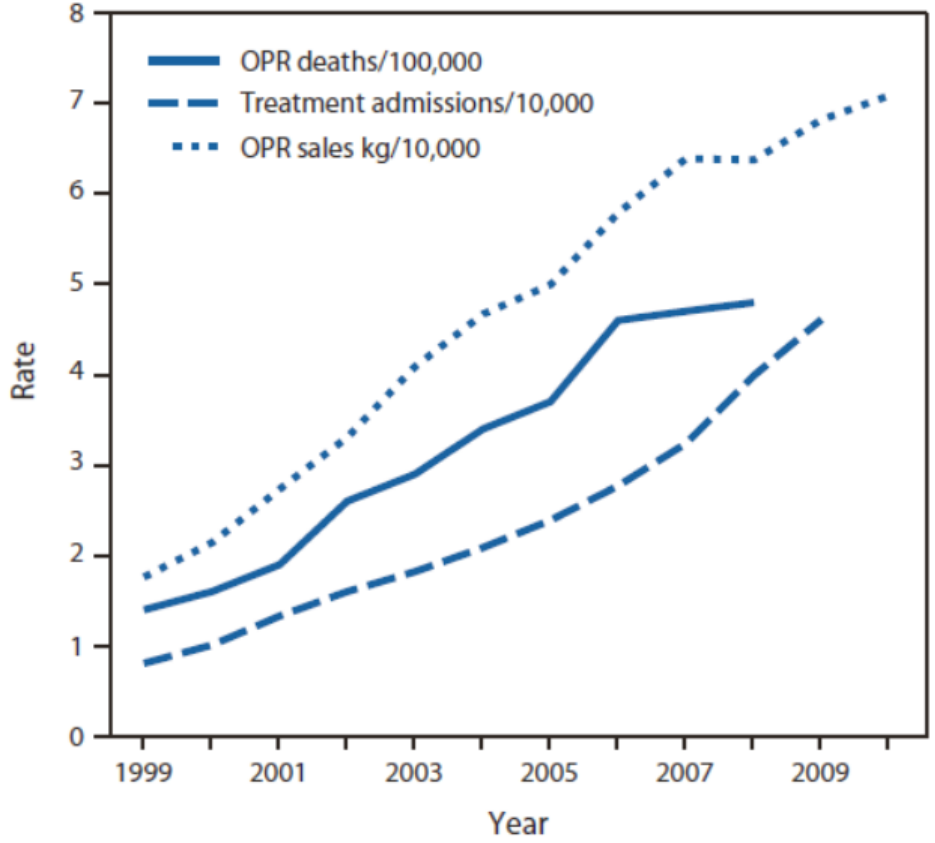
1997:

Michael S.

- Chronic back pain from construction accident
- Disabled
- Prescribed OxyContin to help with pain

Parallel Rise in Opioid Prescriptions, Addiction, and Overdose

FIGURE 2. Rates* of opioid pain reliever (OPR) overdose death, OPR treatment admissions, and kilograms of OPR sold --- United States, 1999--2010

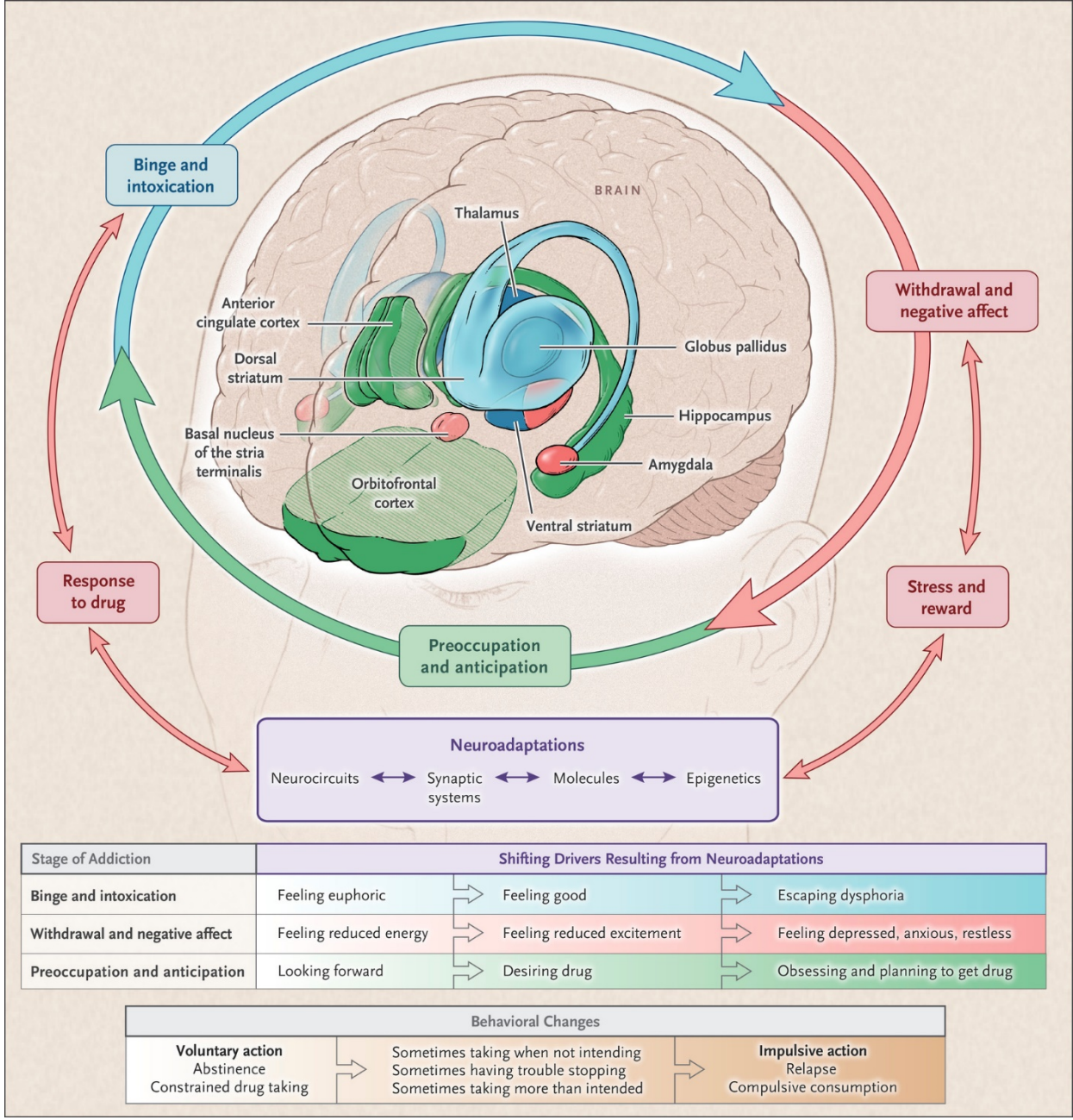


* Age-adjusted rates per 100,000 population for OPR deaths, crude rates per 10,000 population for OPR abuse treatment admissions, and crude rates per 10,000 population for kilograms of OPR sold.

MMWR November 4, 2011
60(43);1487-1492

Addiction Is a Brain Disease

- Drugs hijack brain reward circuits
- Develop tolerance and withdrawal
- Learned behavior “Habit”



Stage of Addiction	Shifting Drivers Resulting from Neuroadaptations		
Binge and intoxication	Feeling euphoric	Feeling good	Escaping dysphoria
Withdrawal and negative affect	Feeling reduced energy	Feeling reduced excitement	Feeling depressed, anxious, restless
Preoccupation and anticipation	Looking forward	Desiring drug	Obsessing and planning to get drug

Behavioral Changes		
Voluntary action Abstinence Constrained drug taking	Sometimes taking when not intending Sometimes having trouble stopping Sometimes taking more than intended	**Impulsive action** Relapse Compulsive consumption

Volkow, *N Engl J Med* 2016; 374:363-371
Lewis, *N Engl J Med* 2018; 379:1551-1560

What Is Opioid Use Disorder? DSM-V criteria

- ❑ Use in larger amounts or over a longer period than intended
- ❑ Unsuccessful efforts to cut down/persistent use
- ❑ A great deal of time spent getting, using, or recovering from use
- ❑ Craving, or a strong desire to use
- ❑ Recurrent use resulting in failure to fulfill major obligations at work, school, or home
- ❑ Continued use despite social or interpersonal problems caused by use

What Is Opioid Use Disorder? (Continued)

- ❑ Social, work, recreational activities given up or reduced
- ❑ Use in situations in which it is physically hazardous
- ❑ Continued use despite physical or psychological harm
- ❑ Withdrawal
  - ❑ Classic withdrawal
  - ❑ Opioids relieve withdrawal symptoms
- ❑ Tolerance
  - ❑ Need for increased amount to achieve same effect
  - ❑ Decreased effect with same amount

2 or more in 12 months; 2-3=mild, 4-5=moderate, 6 or more=severe

Pill Mills

A small number of physicians prescribed an outsized number of pills.

Prescription Drug Monitoring Programs

- State based - – to “catch” the patients who are “doctor shopping”
- 2000s
  - 2010: 27 states
  - 2018: 49 states
- Law enforcement aggressively pursue prescribers
- Shut down pill mills

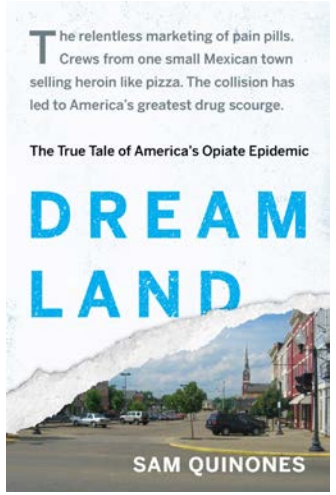
2010:

Michael S.

- Unemployed coal miner
- When OxyContin supply cut off, started buying heroin
- Injects 3-4 times daily
- Two overdoses
- Girlfriend works as a nurse
- Watches kids when girlfriend works

Wave 2: Heroin

- Import from Mexican cartels
  - Marketing directly to suburban white customers
- Heroin deaths on the rise



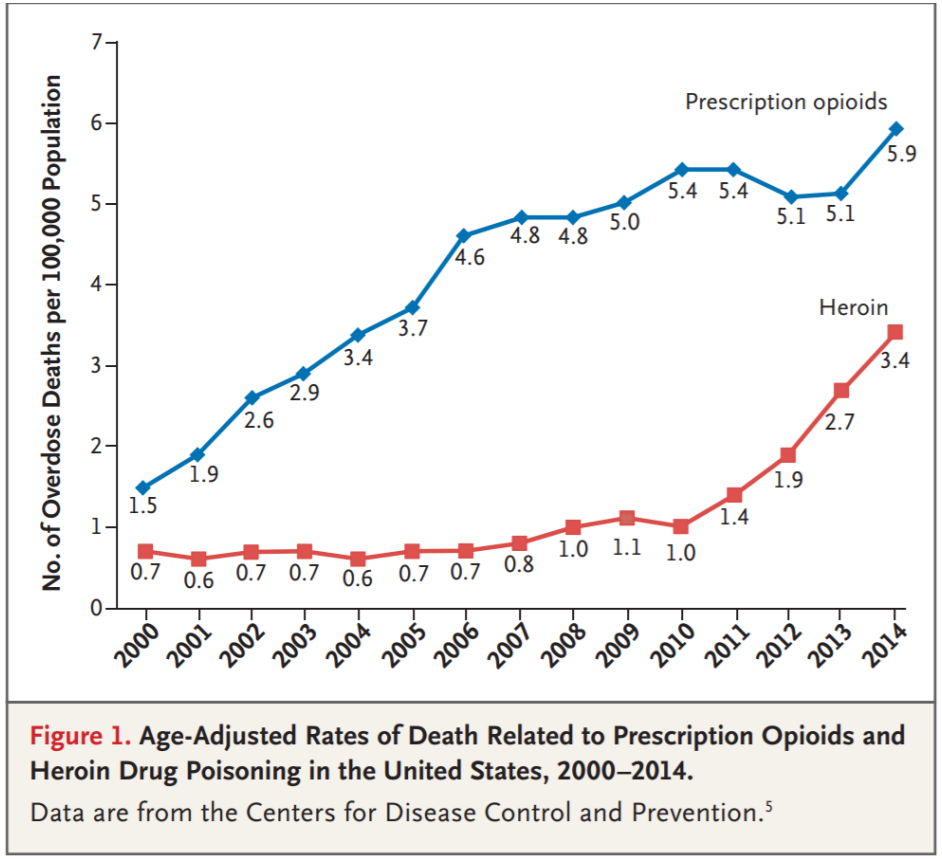
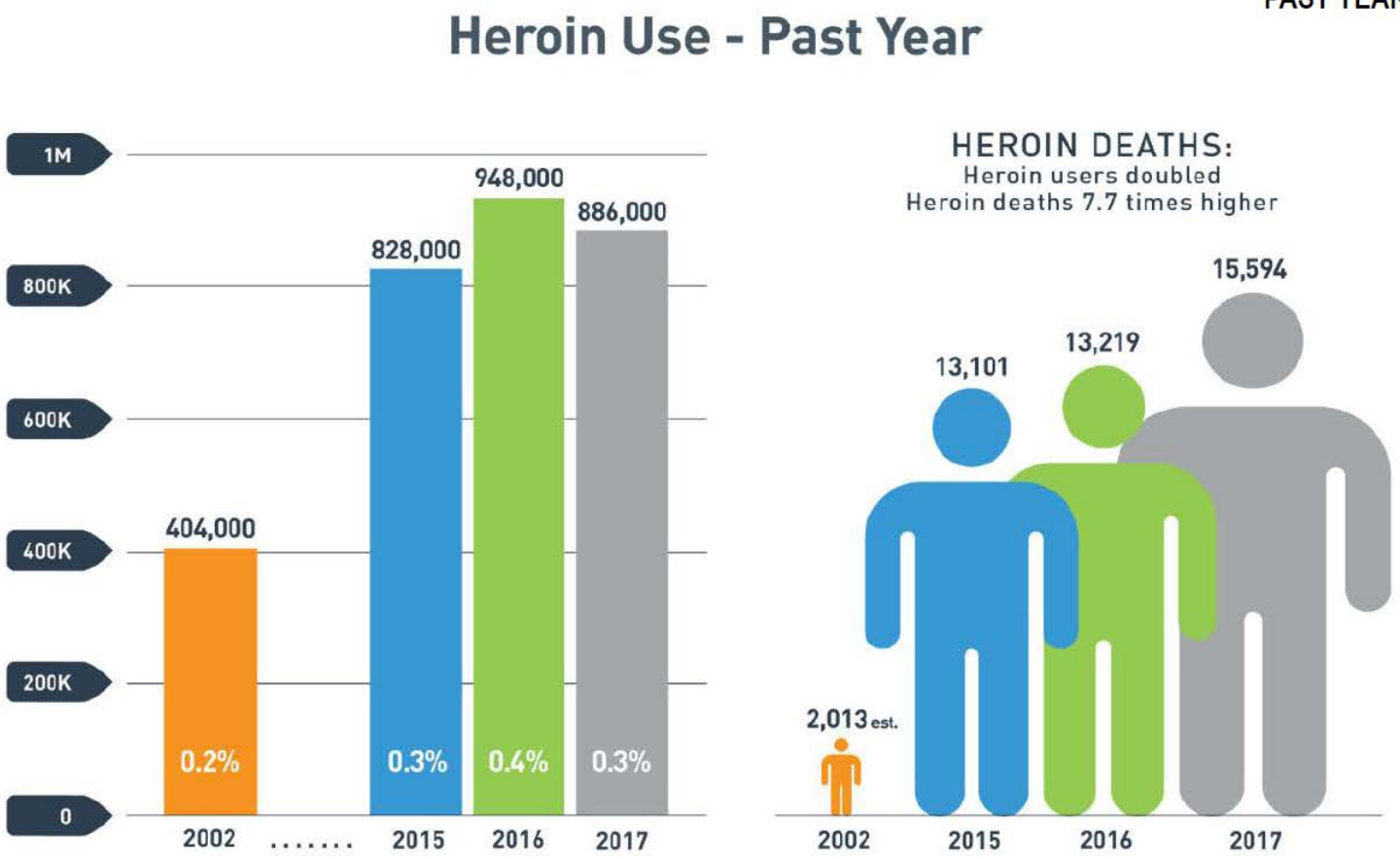


Figure 1. Age-Adjusted Rates of Death Related to Prescription Opioids and Heroin Drug Poisoning in the United States, 2000–2014.
Data are from the Centers for Disease Control and Prevention.[5]

Compton, *N Engl J Med* 2016;374:154-63

Heroin Use Climbed Then Stablized

PAST YEAR, 2002 AND 2015- 2017, 12+



See table 7.2 in the 2017 NSDUH detailed tables for additional information and the 2017 CDC Mortality Data.

SAMHSA
Substance Abuse and Mental Health Services Administration

Wave 3: Fentanyl

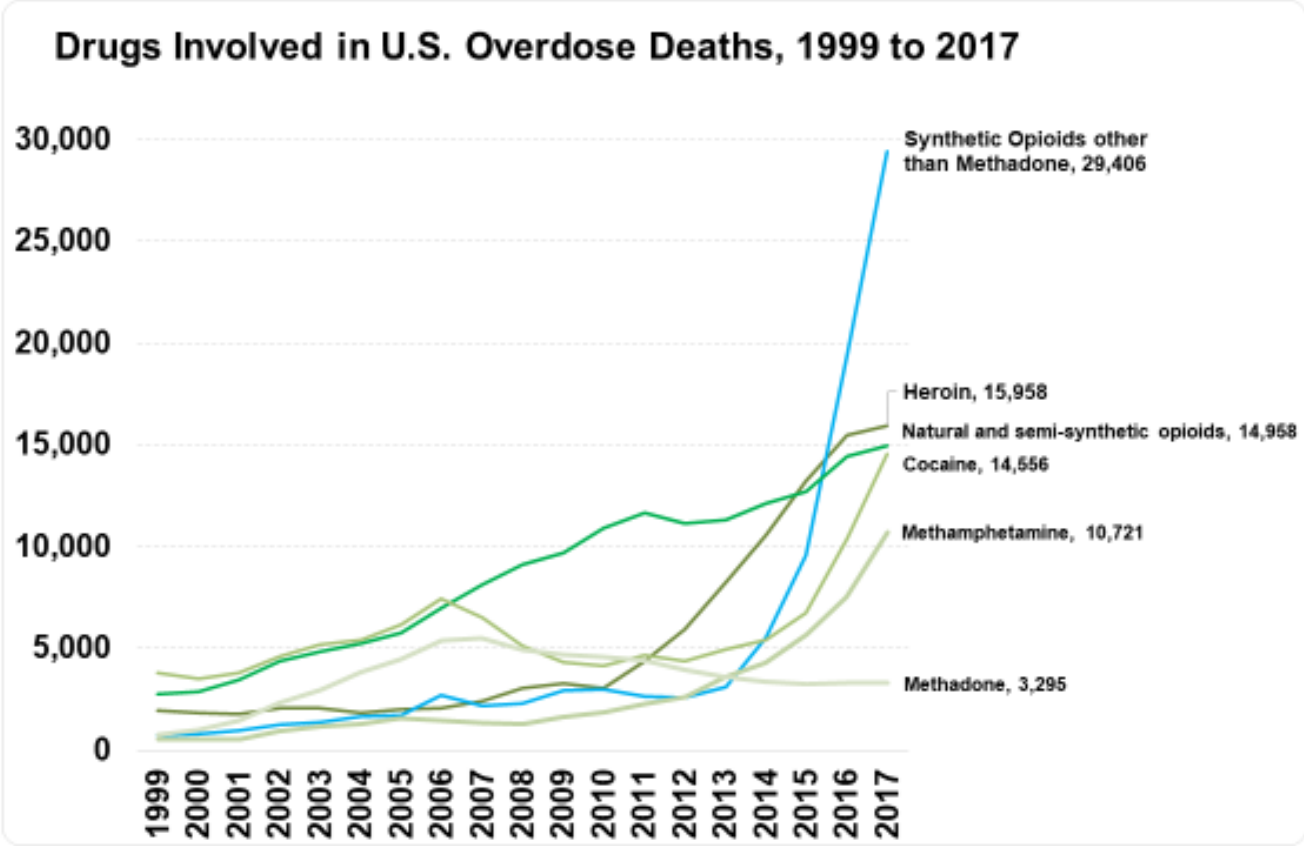
- 50 times more potent than heroin
- Manufactured in China and elsewhere
- Mixed with heroin and other drugs to increase “high”

2016:

Michael S.

- Multiple nonfatal overdoses
- No treatment slots in his rural county
- Died of fentanyl overdose

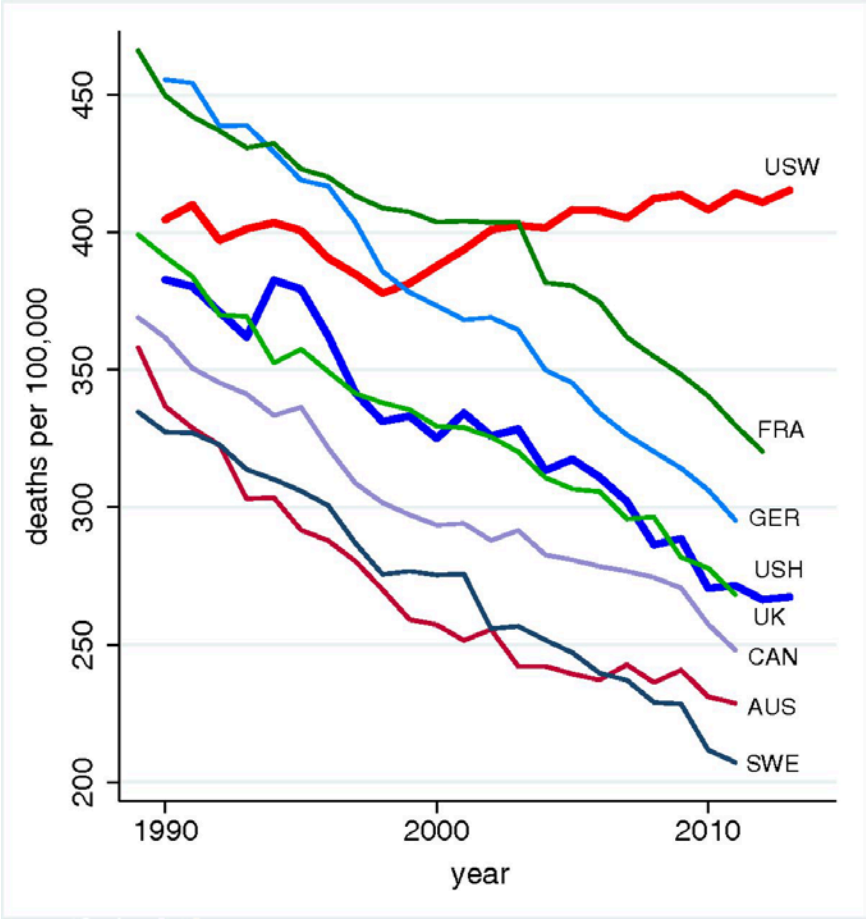
>72,000 drug overdose deaths 2017



Mortality Rates Rise for U.S. Whites

All-cause mortality, ages 45-54 for U.S. White non-Hispanics (USW), U.S. Hispanics (USH), and six comparison countries:

- France (FRA)
- Germany (GER)
- United Kingdom (UK),
- Canada (CAN)
- Australia (AUS)
- Sweden (SWE)



Deaths of Despair:
Overdose
Alcoholism
Suicide

Anne Case, and Angus Deaton PNAS 2015;112:49:15078-15083

PNAS

Impact on Families

- 2.8 million custodial grandparents raising 4.5 million children
- Increase of 7% since 2009
- Parent support groups:
  - www.palgroup.org
  - https://www.learn2cope.org/

Neonatal Withdrawal Syndrome (NOWs)

- Hyperactivity of central and autonomic nervous system and gastrointestinal tract

- 2009: 1.19/1000 live births
- 2012: 5.63/1000 live births

- Rural > Urban
  - West Virginia: 50/1000 live births

Types of Treatments:

- Medications
- Behavioral Therapies

Medication Treatments:

Full Agonists

- Methadone
- Morphine*

Partial Agonists

- Buprenorphine (Suboxone)

Antagonists

- Naltrexone (Vivitrol)

Naloxone (Narcan)

*off-label

Clinical Setting

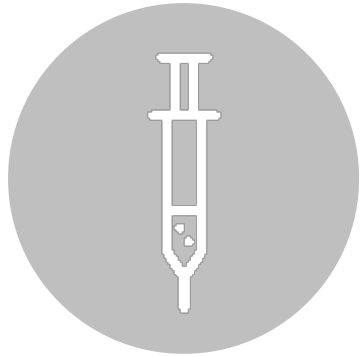
Methadone (Agonist)

- Federally licensed facility
- Daily observed dosing

Buprenorphine (Partial Agonist)

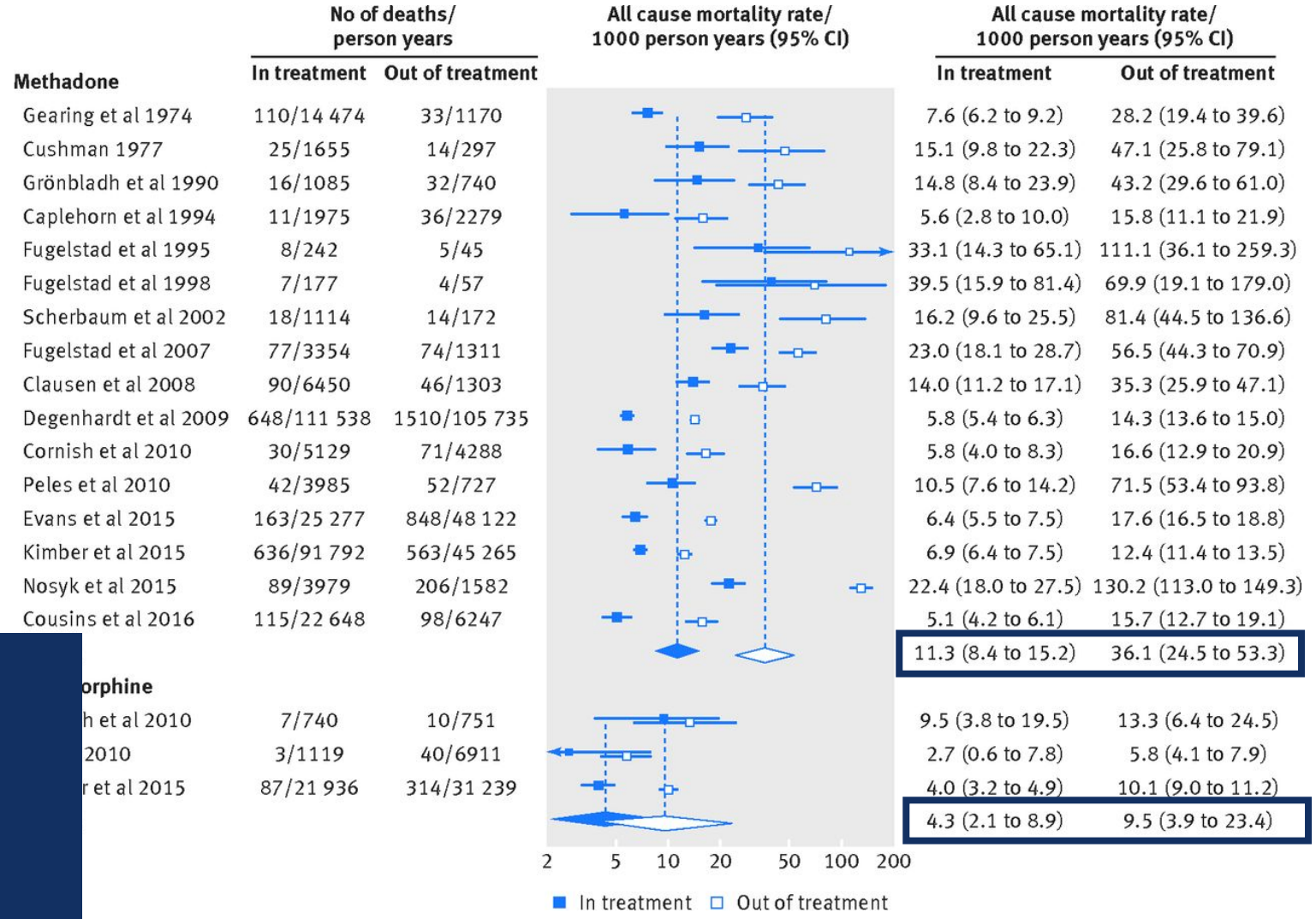
- Any outpatient setting
- DEA waiver for outpatient
- Up to 30 day supply

Naltrexone (Antagonist)



- Any licensed prescriber
- Oral (daily), injectable (4 weeks)

All Cause Mortality Rates In and Out of Methadone and Buprenorphine Treatment, 1974-2016



All Cause Mortality rates per 1000

Methadone vs. No Rx

11.3 vs. 36.1

Buprenorphine vs. No Rx

4.3 vs. 9.5

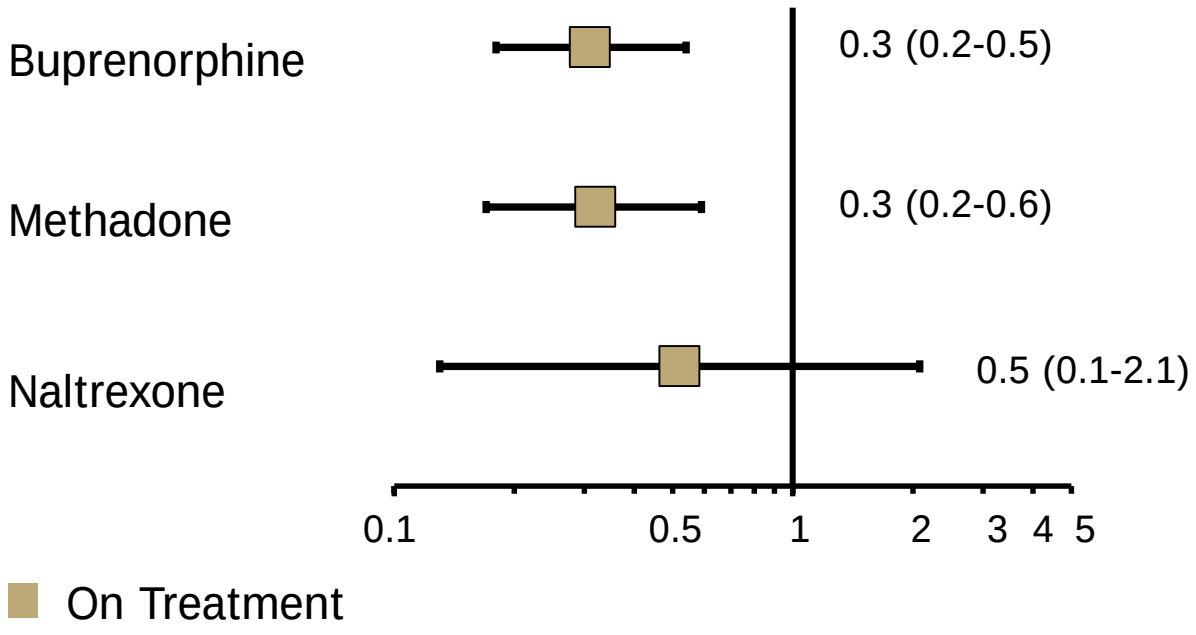
Luis Sordo et al. *BMJ* 2017;357:bmj.j1550

Massachusetts Chapter 55

Adjusted* Hazard for Opioid-Related Mortality

By Monthly Receipt of Treatment in Post-Overdose Period

N=17,568



*Adjusted for: age, sex, depression DX, anxiety DX, incarceration, detoxification, baseline opioid and benzodiazepine RX, and monthly post-overdose receipt of benzodiazepines, opioids, detoxification and short- and long-term residential treatment.

LaRochelle, Ann. *Int Med* 2018

Behavioral Therapies – Adjunct to Pharmacotherapy

Cognitive Based Therapy

Contingency Management

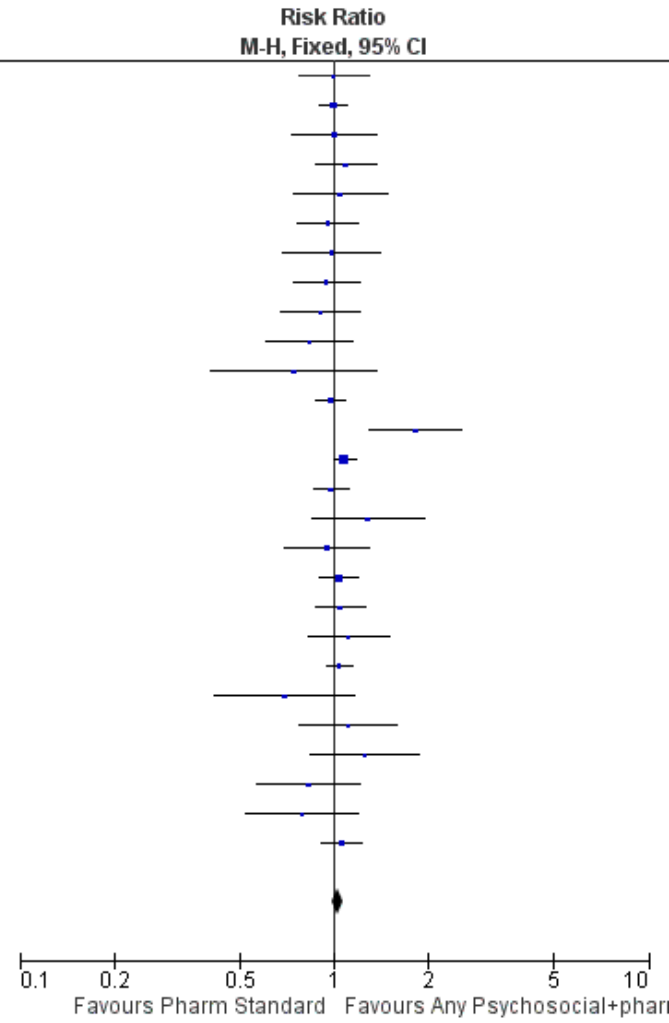
Adjuvant Psychosocial Rx/CBT

Risk Ratio: 1.03 (0.98-1.07)

Study or Subgroup	Any Psychosocial+pharm Events	Total	Pharm standard Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abrahms 1979	7	7	7	7	0.7%	1.00 [0.78, 1.29]
Avants 2004	93	108	97	112	9.1%	0.99 [0.90, 1.10]
Bickel 2008	52	90	26	45	3.3%	1.00 [0.74, 1.36]
Chawarski 2008	12	12	11	12	1.1%	1.09 [0.87, 1.36]
Chawarski 2011	16	20	13	17	1.3%	1.05 [0.74, 1.47]
Chopra 2009	60	83	28	37	3.7%	0.96 [0.76, 1.20]
Fiellin 2006	25	56	50	110	3.2%	0.98 [0.69, 1.40]
Ghitza 2008	52	76	29	40	3.6%	0.94 [0.74, 1.21]
Gross 2006	29	40	16	20	2.0%	0.91 [0.68, 1.21]
Hayes 2004	53	86	14	19	2.2%	0.84 [0.61, 1.15]
Khatami 1982	11	24	8	13	1.0%	0.74 [0.40, 1.37]
Kosten 2003	37	40	38	40	3.6%	0.97 [0.87, 1.09]
Luthar 2000	32	37	20	42	1.8%	1.82 [1.29, 2.56]
Matheson 2010	250	295	194	247	20.1%	1.08 [0.99, 1.17]
Milby 1978	51	55	18	19	2.6%	0.98 [0.86, 1.11]
Neufeld 2008	28	51	21	49	2.0%	1.28 [0.85, 1.93]
Oliveto 2005	36	70	38	70	3.6%	0.95 [0.69, 1.30]
Peirce 2006	133	198	123	190	12.0%	1.04 [0.90, 1.20]
Petry 2005	35	40	31	37	3.1%	1.04 [0.87, 1.26]
Petry 2007	45	55	14	19	2.0%	1.11 [0.83, 1.49]
Preston 2000	58	61	54	59	5.2%	1.04 [0.94, 1.14]
Rounsaville 1983	14	37	19	35	1.9%	0.70 [0.42, 1.16]
Scherbaum 2005	27	41	19	32	2.0%	1.11 [0.77, 1.59]
Silverman 2004	35	52	14	26	1.8%	1.25 [0.84, 1.87]
Stitzer 1992	16	26	20	27	1.9%	0.83 [0.57, 1.21]
Thornton 1987	14	24	17	23	1.7%	0.79 [0.52, 1.20]
Woody 1995	57	62	27	31	3.4%	1.06 [0.90, 1.23]
Total (95% CI)		**1746**		**1378**	**100.0%**	**1.03 [0.98, 1.07]**
Total events	1278		966			

Heterogeneity: $Chi^2 = 26.42$, $df = 26$ ($P = 0.44$); $I^2 = 2\%$

Test for overall effect: $Z = 1.26$ ($P = 0.21$)



Amato 2011 Cochrane Systematic Review

Key Points: OPIOIDS

- Balance between therapeutic use and addiction
- Brain adaptation
- Bending the mortality curve
- Impacts children and families
- Medication treatment saves lives

Thank You

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