

MAT TRAINING

PROVIDERS' CLINICAL SUPPORT SYSTEM
For Medication Assisted Treatment

Management of Opioid Withdrawal and Overdose

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Frances Levin, MD is a consultant for GW Pharmaceuticals and receives study medication from US Worldmed. This activity's planning committee has determined that Dr. Levin's disclosure information poses no bias or conflict to this presentation.

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Educational Objectives

- At the conclusion of this activity participants should be able to:
 1. Gain familiarity with strategies for inpatient and outpatient opioid induction
 2. Learn how to use and rate the Clinical Opioid Withdrawal Scale (COWS)
 3. Be able to discuss the relative advantages of antagonist vs. agonist treatments, as well as medication-assisted treatments in general, for opioid dependence.

Target Audience

- The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.

Accreditation Statement

- American Academy of Addiction Psychiatry (AAAP) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

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 - Date of Release July 10, 2014
 - Date of Expiration July 10, 2017

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Opioid

- Illicit opioids: Heroin (diacetyl morphine)
- Short-acting prescription opioids: Hydromorphone (Dilaudid), Hydrocodone (Vicodin), Codeine, Meperidine (Demerol)
- Long-acting prescription opioids: Oxycodone (Oxycontin), Morphine (MS Contin), Methadone (Dolophine), Fentanyl (Duragesic)

Opioid Analgesics

Short-Acting Opioids	Dosing Frequency (Time/Day)
Hydromorphone Dilaudid	4
Hydrocodone (Vicodin), Codeine	4-6
Meperidine (Demerol) not for chronic pain	6/8
Long Acting Opioids	Durations (hrs)
Buprenorphine (Subutex, Suboxone)	8
Codeine (Codeine Contin)	12
Oxycodone (Oxycontin)	12
Morphine (Avinza, MS Contin)	12
Methadone (Dolophine)	12
Fentanyl (Duragesic)	72

American College of Physicians. Available at:
http://www.acpinternist.org/archives/2008/01/extra/pain_card.pdf.
 Accessed March 14, 2011.

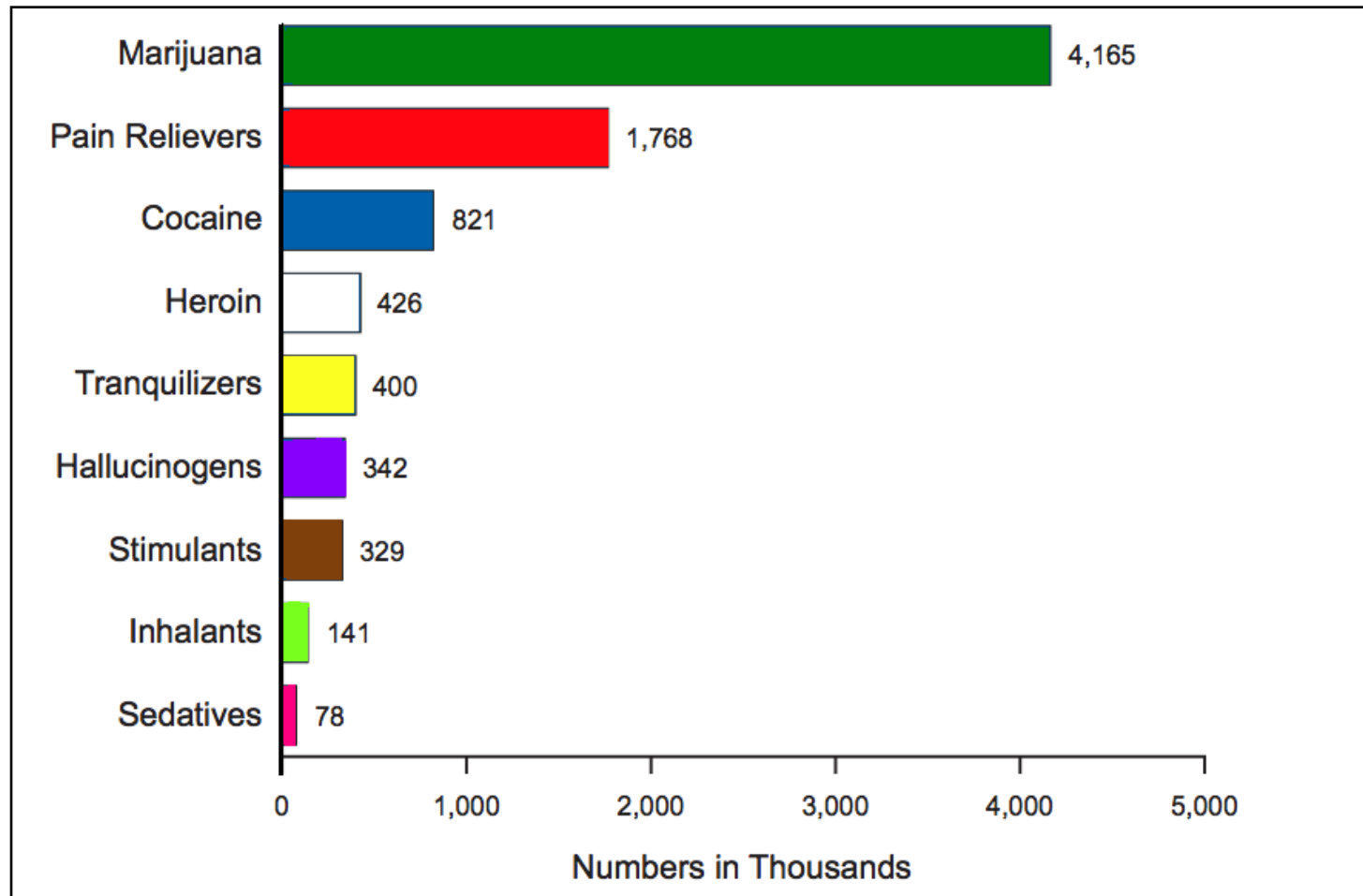
Narcotic Addiction: A Public Health Imperative

- Up to 1 million heroin users in need of treatment and nearly 2 million untreated prescription opioid addicts in the U.S. (NSDUH 2011)
- In past two decades, non-medical use and abuse of opioids has risen dramatically
- Prescription opioid abuse: more than 3 times prevalence of heroin dependence
- By 2006, number of new initiates to prescription opioid abuse exceeded those for marijuana and cocaine (NSDUH, SAMHSA)
- HCV prevalence among injecting heroin addicts: 75-95%
- Mortality: 2% (overdose deaths) - 3.5% (all causes) per year

Epidemiology of Prescription Opioid Abuse in the United States

- 5.2 million Americans (2.1% of U.S. pop.) used prescription opioids non-medically in past month (USDUH 2011)
- Prevalence: 30.4% chronic pain patients in a large (N=239) general practice reported taking extra narcotic doses (Rosser et al., 2011)
- Most common sources for misused opioids: free from friend or relative (60%), followed by obtaining prescriptions from one physician (17%) (NSDUH 2011)
- Prescription opioids are gateway drug: 17.1% of substance abusers cite pain medication as being the first substance they abused (NSDUH 2009)
- Efforts to more aggressively manage pain have resulted in sharp rises in prescribing and misuse of high-potency opioids such as hydrocodone and oxycodone

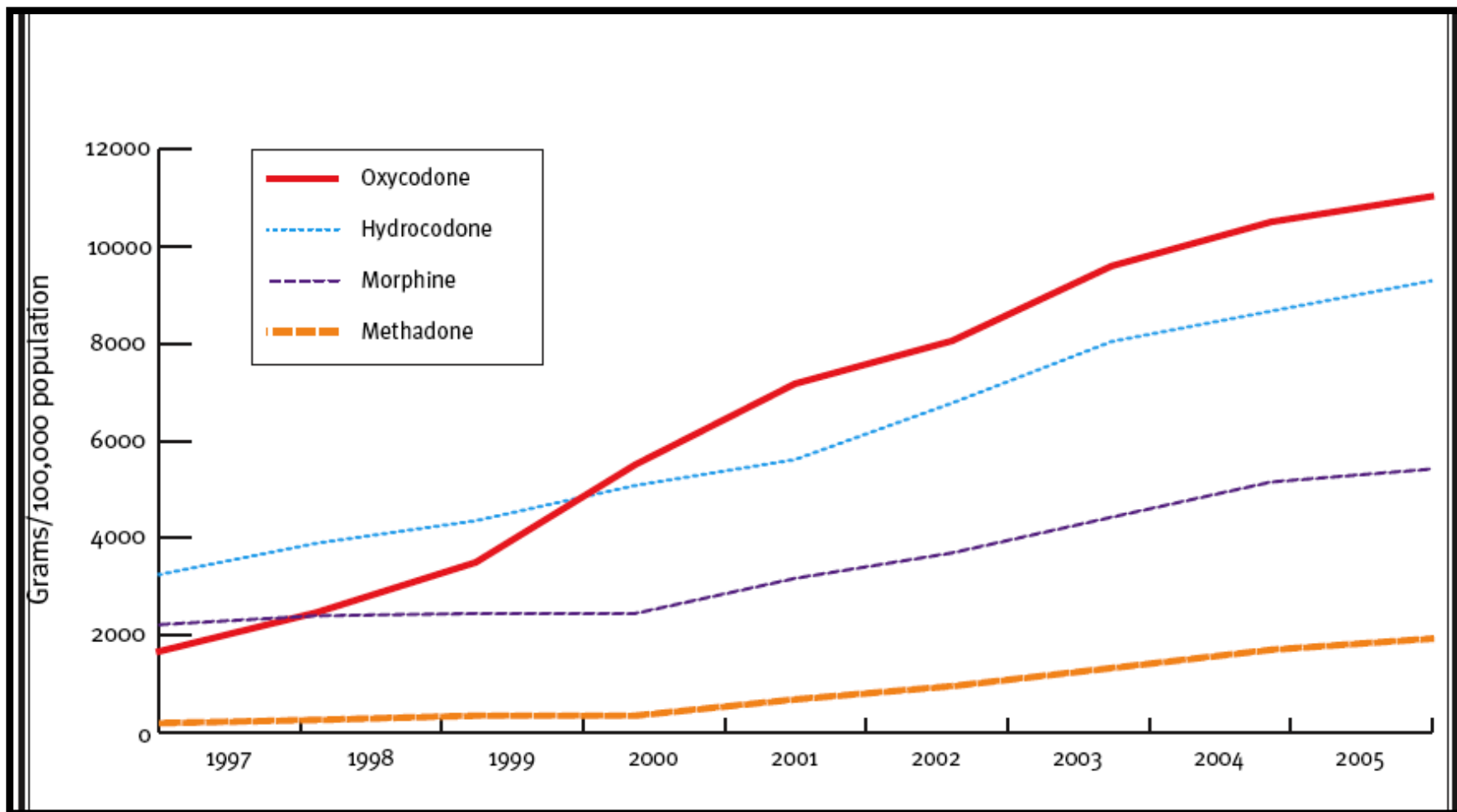
Illicit Drug Dependence or Abuse in the Past Year Among Persons Aged 12+



Opioid Prescribing Trends in the United States

- Events in late 1990s led to increased opioid prescribing: (1) state medical boards liberalized rules for prescribing for non-cancer pain (Manchikanti et al., 2010), (2) FDA approval of high-potency Oxycontin.
- Reimbursement for medical care linked to number of encounters; does not reward risk vs. benefit analyses (Gallagher and Rosenthal 2008)
- From 1997 to 2007, retail sales of oxycodone increased 866% and 1293% for methadone (Manchikanti et al., 2010)
- Physician offices: significant increase in visit rate for high-potency opioids (hydrocodone, oxycodone) (Mendelson et al., 2008).
- MD offices and EDs are important channels for abused opioids.

Prescribed Therapeutic Opioids in the U.S.



Sources for Misused Opioids

- Sources for abused prescription opioids -- Most frequent: free from friend or relative (60%), Other common source: single physician (17%) (NSDUH 2005)
- Numerous active street markets involve patients, Medicaid recipients, pharmacies (Inciardi et al. 2007)
- Physician offices: significant increase in visit rate for high-potency opioids (hydrocodone, oxycodone) (Mendelson et al., 2008).
- MD offices and EDs are important channels for abused opioids

Management of Opioid Detoxification



Signs of Physical Dependence to Opioids

- **Tolerance:** Effectiveness of drug diminishes over time, with regular daily or chronic use
- **Withdrawal:** Rebound hyperactivity of noradrenergic system. Clinically significant opioid withdrawal requires daily use of an adequate amount of an opioid for 2-3 weeks

Signs and Symptoms of Opioid Withdrawal

Early-Moderate

- Anxiety
- Craving
- Dysphoria
- Mydriasis
- Perspiration
- Piloerection
- Restlessness
- Rhinorrhea
- Yawning

Moderate-Advanced

- Abdominal cramps
- Hot or cold flashes
- Increased pulse and BP
- Insomnia
- Low-grade fever
- Muscle and bone pain
- Muscle spasms
- Mydriasis
- Nausea and vomiting

Time Frame for Opioid Withdrawal Onset

Drug	Onset of Withdrawal (hours)	Peak Effects (hours)	Most Symptoms are Over
Heroin	8-12	36-72	7-10 days
Morphine	8-12	36-72	7-10 days
Oxycodone	8-12	36-72	7-10 days
Hydromorphone	4-5	36-72	7-10 days
Fentanyl	3-5	8-12	4-5 days
Methadone	36-72	96-144	14-21 days

Treatments for Opioid Dependence

- **Residential and drug-free approach:** Detoxification is usually followed by referral to psychosocial services without pharmacologic support, but detox. also permits XR-NTX induction.
- **Agonist maintenance:** Buprenorphine/naloxone prescribed in office setting or methadone in MMT
- **Antagonist maintenance:** Oral naltrexone or monthly IM injections of extended-release naltrexone

Goals of Detoxification

- 1. Eliminate acute physiological dependence from chronic opioid use
- 2. Diminish the pain and discomfort of opioid withdrawal
- 3. Provide a safe environment for remaining abstinent during acute withdrawal
- 4. Identify and treat any concurrent medical problems
- 5. Refer patient for treatment to prevent relapse and to address family, work, and legal problems

Medication-assisted Withdrawal

- Two pharmacological strategies for detoxification:
 - (1) Agonist approach: methadone is associated with highest retention rate (80% at 6 months); buprenorphine allows for office-based treatment and retains 60% at 6 months
 - (2) Antagonist treatment: oral or injection naltrexone (XR-NTX) is incompatible with illicit opioid use; does not produce any tolerance or withdrawal

Strategies for Treating Opioid Withdrawal

- **Opioid Agonist Substitution and Taper:**
 - Methadone
 - Buprenorphine
 - Other short-acting prescription opioids
- **Methadone:** orally effective; long-acting opioid produces milder (but protracted) withdrawal syndrome
- **Buprenorphine:** approved in 2002 for detoxification and maintenance; its use as a detoxification agent is increasing

Agonist-based Opioid Detoxification

- Urine toxicology should be done to confirm presence of opioids. Heroin (as morphine) detected up to 48 hrs.
- With illicit opioids, knowledge of exact doses used is usually not available. Wait for withdrawal symptoms to appear.
- Begin with 10-20 mg methadone (relieves withdrawal but safe if habit is low) or 8-mg buprenorphine
- Observe for drowsiness or depressed respiration. Dose can be repeated in 12 hours.
- Total 24-hr dose of methadone should not exceed 40 mg
- On Day 2, repeat dose needed to stabilize patient on Day 1
- Inpatient detox usually 5-7 days; outpatient can be longer

Detoxification and Antagonist Induction

- **Ancillary medications** allow withdrawal symptoms (e.g. myalgias, insomnia) to resolve sooner
- **Combining naltrexone with clonidine:** alpha-2 agonist mitigates precipitated opioid withdrawal
- **Advantages:** reduction in detox time, ability to transition to abstinence with fewer lingering symptoms; no tolerance or withdrawal
- **Disadvantages:** poorer patient acceptance, compared with other techniques; need for intensive monitoring

Ancillary Medications: Non-Opioid Detoxification Agents

- **Alpha-2 agonists** (clonidine, guanfacine, lofexidine)
 - Reduce sympathetic hyperactivity by feedback inhibition of presynaptic neurons
- **Benzodiazepines** (e.g. clonazepam)
 - For insomnia, anxiety, muscle spasm
- **NSAIDs** (ketorolac, acetaminophen, ibuprofen)
 - For muscle and bone pain
- **Anti-emetics** (ondansetron, prochlorperazine)
- **Anti-diarrheal agents** (e.g. loperamine)
- **Hypnotic agents** (zolpidem, trazodone)

Naltrexone

- Approved by FDA in 1984 (oral) and 2010 (long-acting injectable Vivitrol)
- Blocks opioids without agonist effects; incompatible with ongoing illicit opioid abuse. No tolerance or withdrawal develops.
- Oral form taken daily (50 mg) vs. monthly (380 mg) IM injection;
- Serum level of 2 ng/ml provides effective blockade against 25 mg IV heroin effects
- Only 15.8 % of treatment facilities in U.S. report using naltrexone. (SAMHSA, 2009)

SAMHSA. National Survey of Substance Abuse Treatment Services. Data on Substance Abuse Treatment Facilities. 2009. Rockville MD: US Department of Health and Human Services; DHHS publication SMA 05-4112.

Barriers to Antagonist Treatment

- Induction onto naltrexone requires abstinence for 5-7 days from heroin, 7-10 days from methadone.
- **A single day of buprenorphine as part of oral naltrexone-assisted detoxification can shorten the abstinence requirement to 12-24 hours.**
- Adherence has historically been poor with oral naltrexone.
- **Injection naltrexone avoids the need for daily adherence and improves retention.**

Naltrexone-assisted Opioid Detoxification

- *Day 1* – Ancillary meds: clonidine, clonazepam, compazine, zolpidem, trazodone
- *Day 2* – Buprenorphine 4 mg BID
- *Day 3* – Washout Day
- *Day 4* – Naltrexone 3 mg
- *Day 5* – Naltrexone 6 mg
- *Day 6* – Naltrexone 25 mg
- *Day 7* – Naltrexone 50 mg, followed by 380 mg IM (Vivitrol)
 - Alpha-2 adrenergic agents (clonidine), benzodiazepines, and sleeping agents can ameliorate withdrawal symptoms
 - Approximately 70% of patients complete inpatient induction and accept long-acting naltrexone (NTX-XR)

Safety Concerns with Naltrexone

- It is expected that 50% of patients will test the blockade. Sporadic testing 1-3 times early in course of treatment should lead to extinction.
- Repeated consecutive testing (blocked use) later in treatment heralds unblocked use; requires more frequent visits, increased therapy, monitored ingestion of oral naltrexone, etc.
- Naltrexone protects against overdose, but discontinuation poses risk because of lost tolerance.
- Consider transition onto agonist to decrease risk of overdose if patient is unable to comply with naltrexone or to stop using.

Anesthesia-assisted Opioid Detoxification

- Patient interest reflects desire for pain-free detox.
- Uses naltrexone, propofol anesthesia, ondansetron, octreotide (anti-diarrhea), clonidine, and benzodiazepines
- Heavy sedation with midazolam is alternative to general anesthesia
- Technique carries potentially serious morbidity and mortality to achieve opioid detoxification, but safer and less expensive methods are available (Collins et al., 2005, Kleber 1998)
- Withdrawal symptoms persist for days or even weeks after the procedure (Collins et al., 2005, Scherbaum et al., 1998)
- Little benefit but significant adverse effects (e.g. pulmonary edema, diabetic ketoacidosis, (Collins et al., 2005)

Buprenorphine Taper for Detoxification

- For detoxification from buprenorphine maintenance, taper is often unsuccessful, with no advantage to longer taper. Abstinence at end of taper: 44% (7 days), 30% (28 days) (Ling et al., 2009)
- For treatment of prescription opioid dependence using buprenorphine/naloxone (bup/nx) stabilization, retention and naltrexone ingestion were superior in a 4-week vs. briefer tapers (both $P=.04$) (Sigmon et al., 2013)

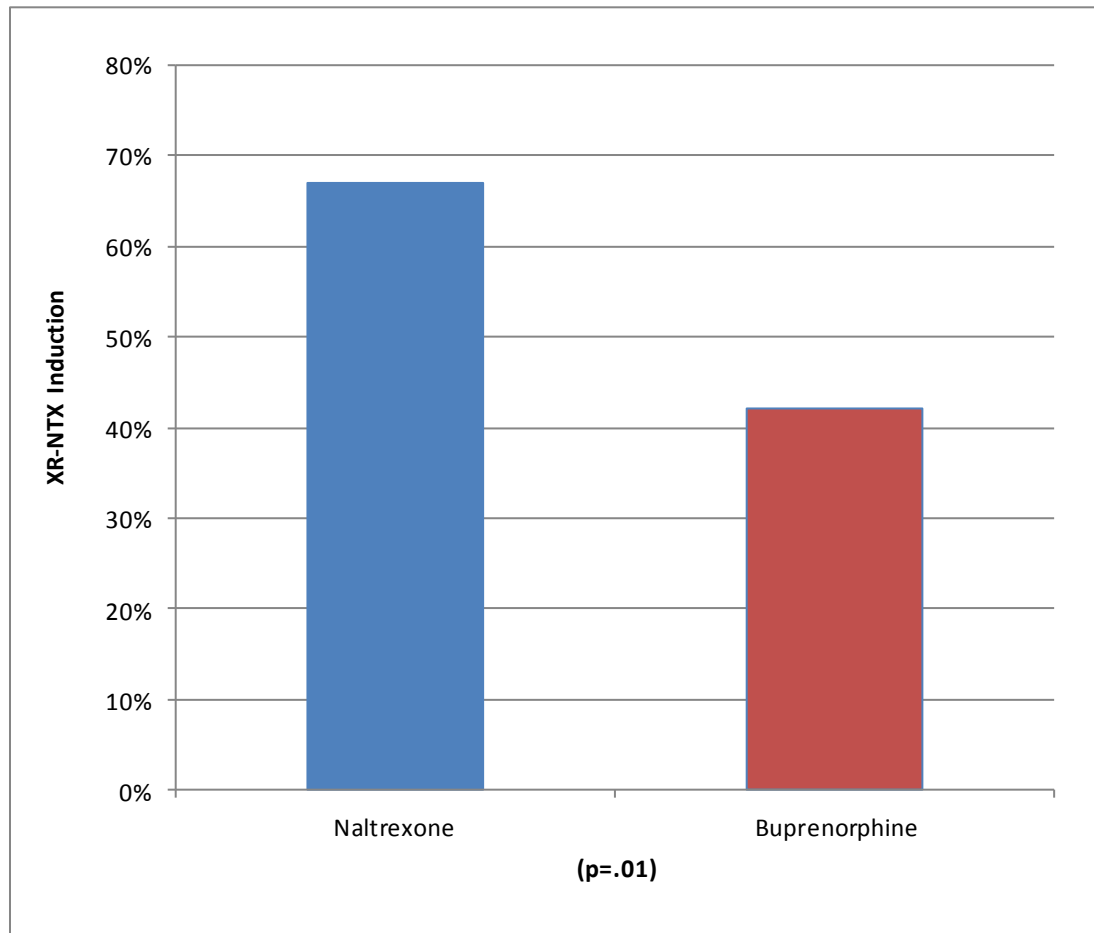
Long-acting Injectable Naltrexone Induction: Randomized Trial of Outpatient Opioid Detoxification with Naltrexone vs. Buprenorphine

- **Sample:** 100 opioid-dependent patients
- **Randomized to one of two outpatient detoxification strategies:**
 - (1) 7-day buprenorphine induction/taper (8 mg to 0 mg)
 - (2) 7-day naltrexone induction (1 mg to 25 mg) + adjunct medications (clonidine, clonazepam, prochlorperazine, zolpidem)
- Single administration of injection naltrexone given on Day 8 (naltrexone group) and on Day 15 (buprenorphine group)
- Aim: Compare injectable naltrexone induction rates between the naltrexone and buprenorphine detoxification arms

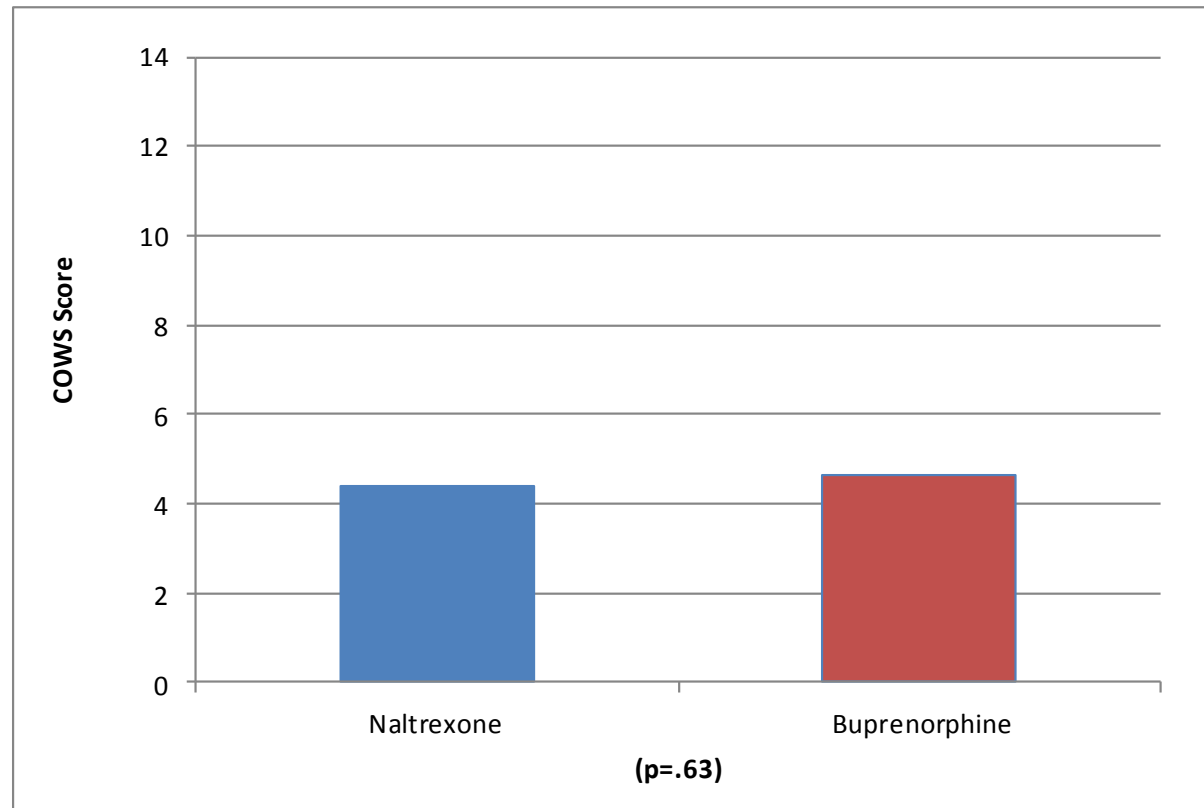
Outpatient Opioid Detoxification: Participant Demographics

	Naltrexone (n=68)	Buprenorphine (n=38)	Total (n=106)
Age (mean, SD)	37.3 (12.5)	35.1 (11.1)	36.5 (12.0)
Gender (female)	16.1%	5.2%	12.3%
Ethnicity			
Caucasian	61.7%	68.4%	64.1%
Hispanic	26.4%	18.4%	23.5%
African American	10.2%	10.5%	10.3%
Asian	1.4%	2.6%	1.8%
Heroin severity of use (mean bags of heroin day)	7.60 (4.68)	6.90 (3.85)	7.38 (4.42)
Rx severity of use (mean mg of morphine/day)	139.22 (78.34)	128.43 (63.97)	134.56 (71.72)
Rx Users	29.4%	34.2%	31.1%
IV Users	13.2%	23.6%	16.0%
IN Users	58.8%	42.1%	52.8%

Injection Naltrexone (XR-NTX) Induction



Withdrawal Symptoms during Detox. By Treatment Group



Summary of Opioid Detoxification

- In early 1900s, detoxification was considered a cure for opioid addiction; in fact, it is only the precursor to abstinence-based treatment.
- Various medications are used for opioid detoxification, including full agonists (e.g. methadone), partial opioid agonists (e.g. buprenorphine), opioid antagonists (e.g. naltrexone), alpha-2 agonists (e.g. clonidine), and adjuvant medications (e.g. clonazepam, ibuprofen) for symptomatic relief
- Within one month of discharge from detox., 80%-90% have relapsed (Smyth et al., 2010, Weiss et al., 2011).
- First weeks after detoxification carry significant risk of overdose and death
- Post- detox. pharmacological assistance with antagonist maintenance is essential: role for long-acting injectable naltrexone (Vivitrol)

Management of Opioid Overdoses



Prescription Opioid Morbidity and Mortality

- In parallel with increases in the opioid analgesic use, there has been a dramatic rise in unintentional overdose deaths (CDC 2012).
- Deaths due to opioid analgesics in US (2008): 15,000, surpassing motor vehicle accidents as cause of death in some states (Paulozzi et al., 2008)
- Immunosuppressive effects of opioids may increase morbidity from infectious diseases, autoimmune diseases, and cancer (Pergolizzi et al., 2008)
- In a study of 2112 fatal unintentional prescription opioid overdoses, methadone was associated with highest number of deaths per equi-analgesic dose sold (23.3) (Piercefield et al., 2010)

Prescription Opioid Overdoses

In 2008, there were **14,800** prescription painkiller deaths.⁴

For every **1** death there are...



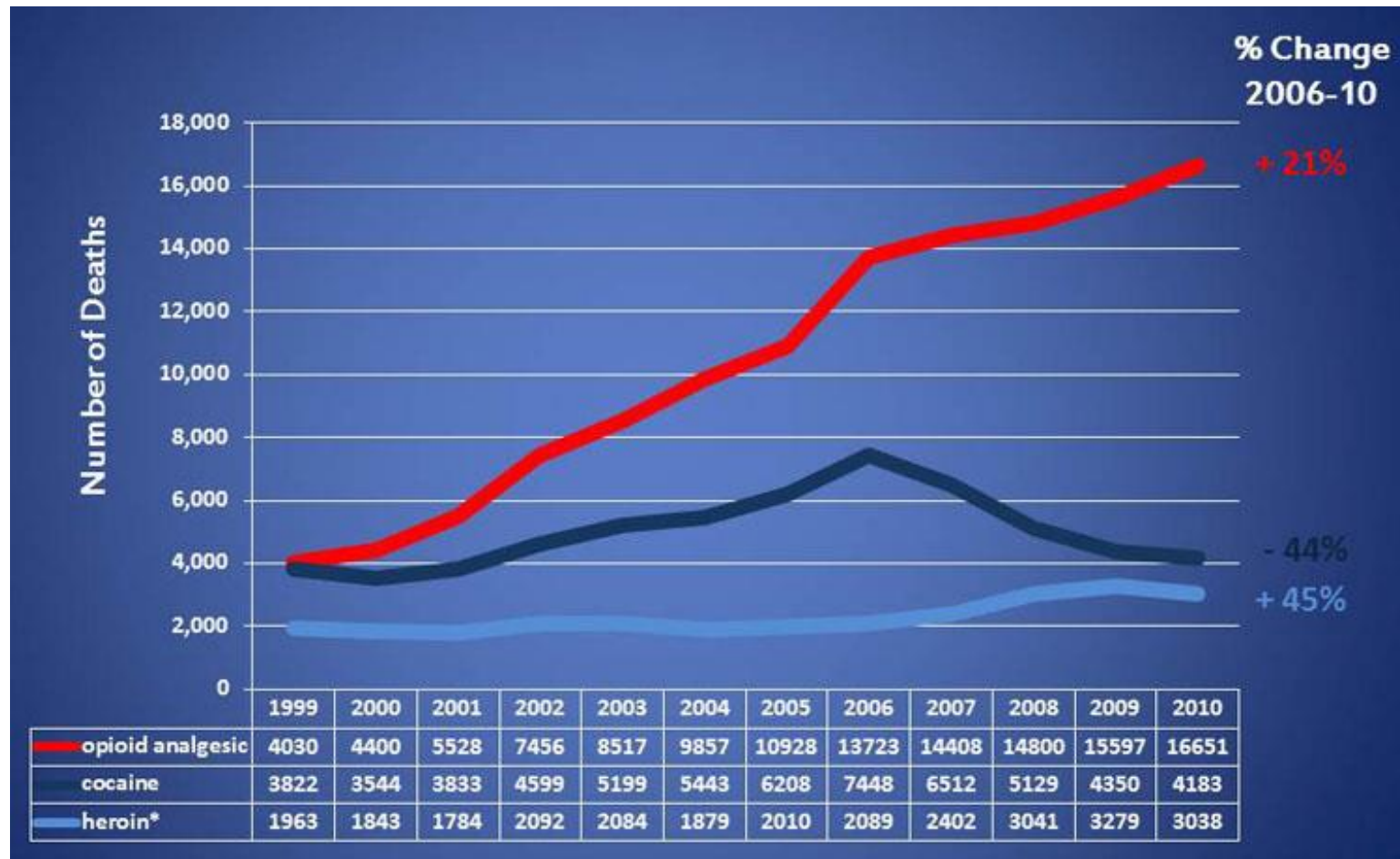
10 treatment admissions for abuse⁵

32 emergency dept visits for misuse or abuse⁶

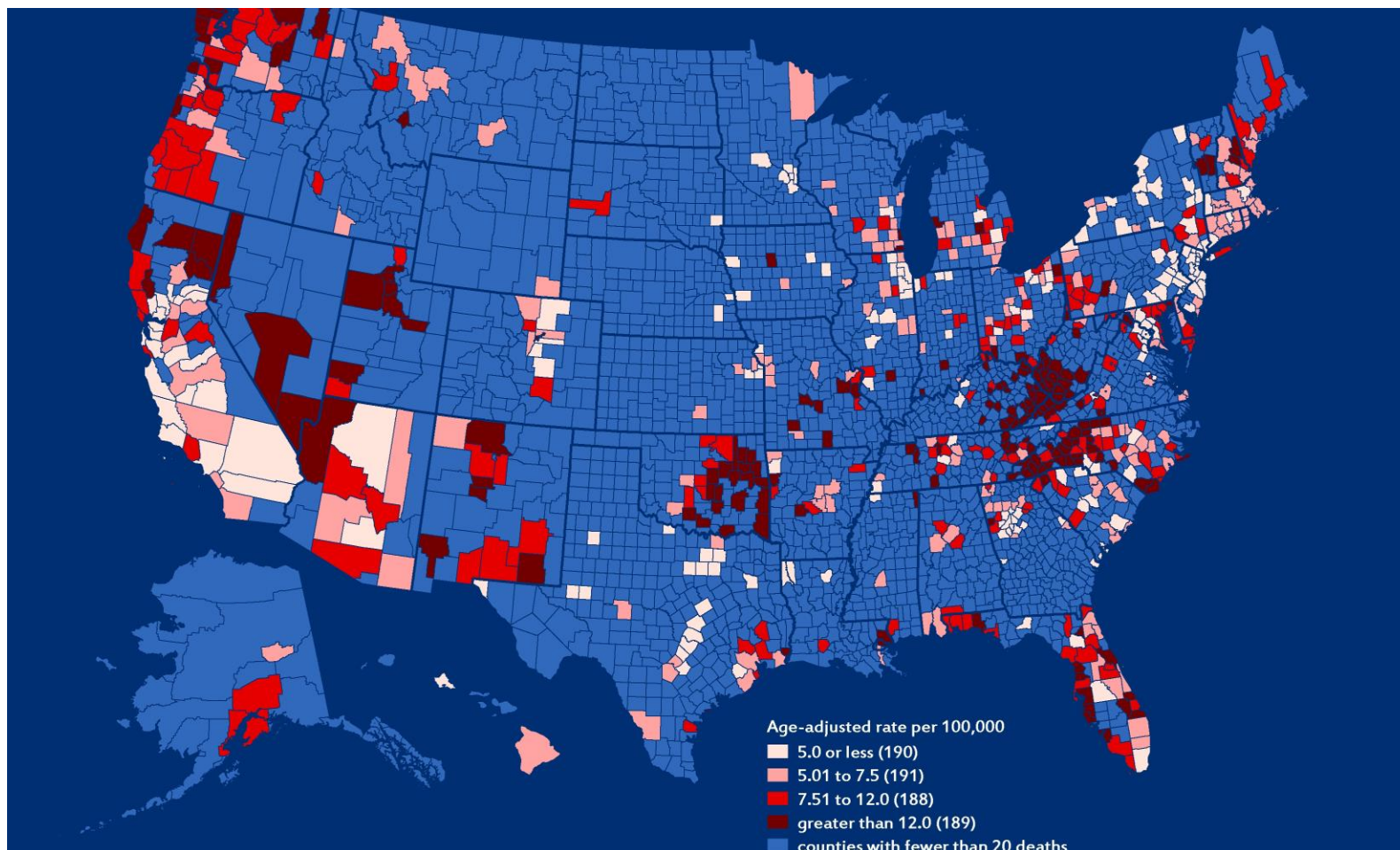
130 people who abuse or are dependent⁷

825 nonmedical users⁷

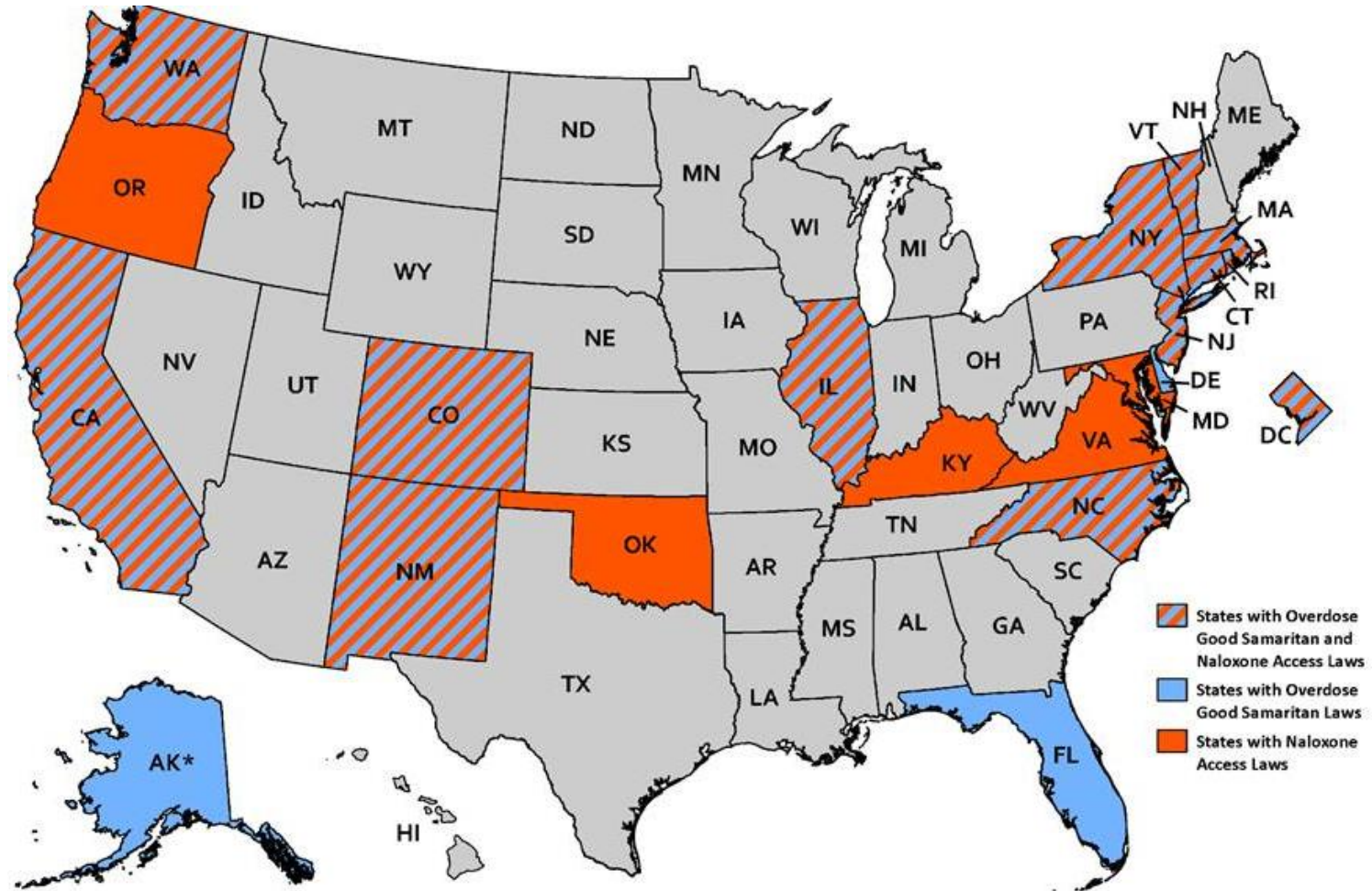
Overdose Deaths in the U.S., 1999-2010



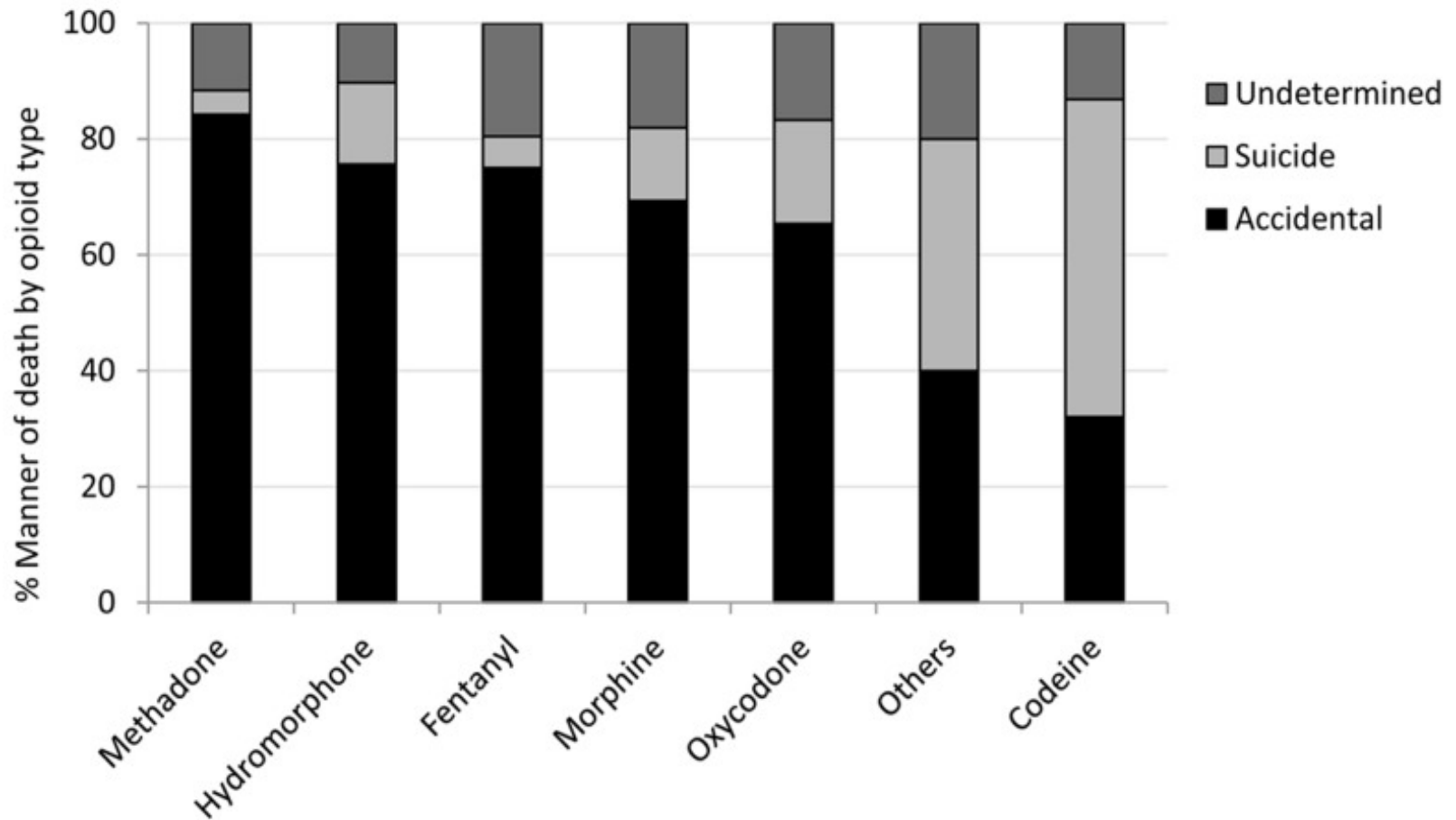
Drug Poisoning Deaths Involving Heroin and Other Opioid Drugs, by County, 2006-2010



States with Naloxone Access and Overdose Good Samaritan Laws, as of January 2014



Opioid-Related Deaths in Ontario, 2006-2008 (N=1359)



Madadi et al. 2013

Scope of the Problem

- Drug overdose is a major cause of injury and death worldwide
- Among opioid users worldwide, most common cause of death is drug overdose (Degenhardt et al., 2011)
- Since 2003, opioid analgesics account for more deaths by overdose than cocaine and heroin combined (CDC, MMWR, January 13, 2012/ 61(01): 10-13.)
- In the U.S., single leading cause of injury-related mortality in 2008 was poisoning, nearly 90% of which was attributed to legal and illegal drugs (Warner et al., 2011)

Opioid Overdose: Who is at Risk?

- Individuals at risk for overdose include those:
 - with a previous history of overdose (Darke et al., 2007, Wines et al., 2007)
 - recently discharged from detoxification programs (Strang et al., 2003; Wines et al., 2007)
 - initiating or ending opioid maintenance therapy (Degenhardt et al., 2009)
 - recreational users of prescription opioids (Centers for Disease Control and Prevention, CDC Vital Signs, November 2011; Warner et al. 2011)
 - recently released from prison (Seaman et al., 1998; Wakeman et al., 2009)

Overdose: What and Where?

- Among unintentional opioid overdose deaths in NYC 2005-2019 (N=2649), 75% overdosed in a home, 10% in an institution, and the remaining in a public indoor setting or outdoors (Siegler et al., 2013)
- Methadone carries highest risk of accidental opioid overdoses
- Buprenorphine alone is not associated with overdose risk; if injected and/or combined with alcohol or benzodiazepines, fatal overdose can occur
- Sedative drugs and/or alcohol are frequently involved in fatal poisonings with prescription opioids (Hakkinen et al., 2012)

Strategies to Prevent Overdoses

- Education of patients and families of risk of overdose, heightened in the post-detox. period or when opioids are combined with alcohol, benzodiazepines, other sedative-hypnotic drugs (Darke et al., 2006)
- Education of providers on safe opioid prescribing
- Methadone maintenance is most effective proven method of reducing overdose mortality (Sporer 2003)
- Provision of naloxone to injection drug users (Galea et al., 2006)

Naloxone: A Potential Solution

- Naloxone is a potent, short-acting opioid antagonist
- Naloxone is effective in both preventing and reversing opioid agonist effects, including respiratory depression, which is the primary cause of death due to opioid overdose (White and Irvine 1999); approved by FDA in 1971 for overdose treatment..
- Antagonist effects of naloxone are evident within 5 min following administration
- Duration of antagonism at commonly prescribed doses (0.4-0.8 mg)
- It is relatively ineffective orally; typically given IV, IM, SQ, and intranasally (Kerr et al., 2009, Merlin et al., 2010)

Naloxone: the “Pros” I

- UN’s central drug policy-making body, Commission on Narcotic Drugs, approved resolution in March 2012 to promote measures to prevent drug overdose.
- ONDCP Director Gil Kerlikowske endorsed need to train public health and safety personnel to recognize drug overdose and administer life-saving techniques and medications, including naloxone
- “Good Samaritan Laws” have been enacted in several states (e.g. NM, NY), allowing naloxone distribution to “lay savers” and providing “immunity to doctors who administer naloxone to others” (Burris et al., 2009)

Naloxone: the “Pros” II

- Most opioid users (64-97%) report that they have witnessed at least one overdose (Lagu et al., 2006, Tracy et al., 2005), so opportunity for rescue exists.
- Opioid overdoses typically do not occur instantaneously
- Majority of witnessed overdoses occur in presence of a friend (70%), acquaintance (14%), or partner (10%; Strang et al., 2000)

Naloxone: the “Cons”

- **Legal Barriers:**
 - Since naloxone is classified as prescription drug by FDA, question of liability for both prescriber and drug user who uses naloxone on another person
 - Empirical data is lacking on effectiveness of naloxone programs in reducing fatal overdoses, as well as complications of non-fatal overdoses
- **Resistance by Medical Personnel:**
 - In survey (N=327) of health care providers, most (56%) felt training drug users in naloxone would not be effective (Tobin et al., 2005)
 - Among health providers, 37% would not consider prescribing naloxone to at-risk heroin users (Coffin et al., 2003)

Naloxone: the “Cons” II

- **Adverse Events:**
 - Cardiac complications and pulmonary edema have been reported to occur within 10 min after administration to intoxicated patients (Osterwalder 1996)
 - Side effects of administration during opioid overdose are common: confusion (32%), headache (20%), nausea/vomiting (9%), aggression (8%), but serious complications such as seizure (4%) are rare (Buajordet et al., 2004)
 - Because half-life of naloxone is shorter than that of heroin, recurrence of respiratory depression could emerge if victim is left unattended after initial dose of naloxone

Naloxone: the “Cons” III

- **Resistance by Drug Users:**
 - Common reasons cited by drug users for failing to call, or delaying a call, for medical assistance during an overdose: fear of police involvement or feeling they could handle event themselves (Tracy et al., 2005; Worthington et al., 2006)
 - Among those who had received naloxone in the past, 82% reported it was extremely unpleasant (Seal et al., 2003), suggested that previous exposure may be deterrent to naloxone use
 - Yet majority of users (79%) said they would want to receive naloxone if they overdosed, and larger majority (87%) would participate in training to receive naloxone (Seal et al., 2003)

Current Data on Naloxone Distribution Programs

- Of 53,032 individuals who had received take-home naloxone at 48 U.S. programs surveyed, 10,171 overdose reversals were reported (CDC 2012)
- Rates of successful reversal if naloxone is given: 83-96% (Piper et al., 2008, Wagner et al., 2010, Yokell et al., 2011)
- Pilot study conducted at Harm Reduction Coalition in NYC found only 50% of drug users had called 911 during witnessed overdoses; many had attempted ineffectual interventions such as salt water injections (18.6%) or milk administration (11.9%) (Jones et al., 2014, in press)
- Overdose training increased participants' ability to identify opioid overdose ($p < 0.05$) and scenarios where naloxone administration was indicated ($p < 0.05$)

Conclusions

- Opioid overdose is an increasingly common cause of death, yet could be easily treated with available opioid antagonists
- Individuals recently released from controlled environments (e.g. detox units, prisons) are an especially vulnerable group for both overdose and death
- In most cases, a single administration of naloxone is sufficient to reverse an opioid overdose
- Approaches to minimizing risk of opioid overdose include physician education on prescribing of opioid analgesics and benzodiazepines, prescription of take-home naloxone, Good Samaritan laws, and further research on efficacy of naloxone distribution programs

References

American College of Physicians. Available at:

http://www.acpinternist.org/archives/2008/01/extra/pain_card.pdf. Accessed March 14, 2011.

Buajordet I, Naess AC, Jacobsen D, Brørs O. (2004). Adverse events after naloxone treatment of episodes of suspected acute opioid overdose. *European Journal of Emergency Medicine*, 11(1):19-23.

Burris S, Davis C. (2009). Assessing social risks prior to commencement of a clinical trial: due diligence or ethical inflation? *American Journal of Bioethics*, 9(11):48-54.

CDC, 2012. CDC grand rounds: prescription drug overdoses - a U.S. epidemic. *MMWR Morbidity and mortality weekly report*, January 13, 2012/ 61(01), 10-13.

CDC, 2011. Prescription painkiller overdoses in the U.S. Accessed June 24, 2014:

<http://www.cdc.gov/features/vitalsigns/painkilleroverdoses/>

CDC, 2012. QuickStats: Number of Deaths From Poisoning,* Drug Poisoning,† and Drug Poisoning Involving Opioid Analgesics § — United States, 1999–2010. Accessed on March 29, 2013:

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6212a7.htm>

Centers for Disease Control and Prevention (CDC). Policy Impact: Prescription Painkiller Overdoses.

Available online at <http://www.cdc.gov/homeandrecreationalsafety/rxbrief/>.

CDC, 2013. *MMWR* 62(3), November 22, 2013. Accessed on July 1, 2014:

http://www.cdph.ca.gov/programs/Documents/CDC_MMWR_11-22-2013.pdf

Centers for Disease Control and Prevention (CDC). Vital Signs. Available online at

<http://www.cdc.gov/VitalSigns/PainkillerOverdoses/index.html>

Coffin PO, Fuller C, Vadnai L, Blaney S, Galea S, Vlahov D. (2003). Preliminary evidence of health care provider support for naloxone prescription as overdose fatality prevention strategy in New York City. *Journal of Urban Health*, 80(2):288-90.

References

- Collins ED, Kleber HD, Whittington RA, Heitler NE. (2005). Anesthesia-assisted vs buprenorphine- or clonidine-assisted heroin detoxification and naltrexone induction: a randomized trial. *JAMA*, 294(8):903-13.
- Darke S, Duflou J, Kaye S. (2007). Comparative toxicology of fatal heroin overdose cases and morphine positive homicide victims. *Addiction* 102(11): 1793-7.
- Darke S, Duflou J, Torok M. (2010). A reduction in blood morphine concentrations amongst heroin overdose fatalities associated with a sustained reduction in street heroin purity. *Forensic Science International*, 198(1-3):118-20.
- Degenhardt L, Bucello C, Mathers B, Briegleb C, Ali H, Hickman M, McLaren J. (2011). Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. *Addiction*, 106(1):32-51.
- Degenhardt L, Randall D, Hall W, Law M, Butler T, Burns L. (2009). Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: risk factors and lives saved. *Drug and Alcohol Dependence*, 105(1-2):9-15.
- Forensic Sci Int*. 2010 May 20;198(1-3):118-20. doi: 10.1016/j.forsciint.2010.01.015. Epub 2010 Feb 16.
- Galea S, Worthington N, Piper TM, Nandi VV, Curtis M, Rosenthal DM. (2006). Provision of naloxone to injection drug users as an overdose prevention strategy: early evidence from a pilot study in New York City. *Addictive Behaviors*, 31(5):907-12.
- Gallagher RM, Rosenthal LJ. (2008). Chronic pain and opiates: balancing pain control and risks in long-term opioid treatment. *Archives of Physical Medicine and Rehabilitation*, 89(3 Suppl 1):S77-82.
- Häkkinen M1, Launiainen T, Vuori E, Ojanperä I. (2012). Comparison of fatal poisonings by prescription opioids. *Forensic Science International*, 222(1-3):327-31.

References

- Inciardi JA, Surratt HL, Kurtz SP, Cicero TJ. (2007). Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. *Pain Medicine*, 8(2):171-83.
- Jones JD, Roux P, Stancliff S, Matthews W, Comer SD. (2014). Brief overdose education can significantly increase accurate recognition of opioid overdose among heroin users. *Int J Drug Policy* 25(1): 166-70.
- Kerr D, Kelly AM, Dietze P, Jolley D, Barger B. (2009). Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose. *Addiction*, 104(12):2067-74.
- Kleber HD. (1998). Ultrarapid opiate detoxification. *Addiction*, 93(11):1629-33.
- Lagu T, Anderson BJ, Stein M. (2006) Overdoses among friends: Drug users are willing to administer naloxone to others. *Journal of Substance Abuse Treatment*, 30(2):129-33.
- Ling W, Hillhouse M, Domier C, Doraimani G, Hunter J, Thomas C, Jenkins J, Hasson A, Annon J, Saxon A, Selzer J, Boverman J, Bilangi R. (2009). Buprenorphine tapering schedule and illicit opioid use. *Addiction*, 104(2):356-65.
- Madadi P, Hildebrandt D, Lauwers AE, Koren G. (2013). Characteristics of opioid-users whose death was related to opioid-toxicity: a population-based study in Ontario, Canada. *PLoS One* 8(4):e60600.
- Manchikanti L, Fellows B, Ailinani H, Pampati V. (2010). Therapeutic use, abuse, and nonmedical use of opioids: a ten-year perspective. *Pain Physician*, 13(5):401-35.
- Mendelson J, Flower K, Pletcher MJ, Galloway GP. (2008). Addiction to prescription opioids: characteristics of the emerging epidemic and treatment with buprenorphine. *Experimental and clinical psychopharmacology*, 16(5):435-41

References

- Merlin MA, Saybolt M, Kapitanyan R, Alter SM, Jeges J, Liu J, Calabrese S, Rynn KO, Perritt R, Pryor PW 2nd. (2010). Intranasal naloxone delivery is an alternative to intravenous naloxone for opioid overdoses. *American Journal of Emergency Medicine*, 28(3):296-303.
- NCHRC North Carolina Harm Reduction Coalition. (2013). Overdose prevention Law in NC. Available online at <http://www.nchrc.org/advocacy/911-good-samaritan-laws-naloxone-access-and-syringe-law-in-nc/>
- NSDUH. Substance Abuse and Mental Health Services Administration. (2011). Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-41, HHS Publication No. (SMA) 11-4658. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2011. Available online at <http://oas.samhsa.gov/NSDUH/2k10NSDUH/2k10Results.pdf>
- NSDUH. Substance Abuse and Mental Health Services Administration. (2009). Results from the 2008 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-36, HHS Publication No. SMA 09-4434). Available online at <http://www.samhsa.gov/data/NSDUH/2k8nsduh/2k8Results.htm> Accessed on September 2009, Rockville, MD.
- NSDUH. Substance Abuse and Mental Health Services Administration. (2005). Results from the 2004 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-28, DHHS Publication No. SMA 05-4062). Available online at: <http://www.samhsa.gov/data/NSDUH/2k4nsduh/2k4results/2k4Results.htm>

References

- Osterwalder JJ. (1996). Naloxone-for intoxications with intravenous heroin and heroin mixtures—harmless or hazardous? A prospective clinical study. *Journal of Toxicology*, 34(4):409-16.
- Paulozzi LJ, Xi Y. (2008). Recent changes in drug poisoning mortality in the United States by urban-rural status and by drug type. *Pharmacoepidemiology and Drug Safety*, 17(10):997-1005.
- Pergolizzi J, Böger RH, Budd K, Dahan A, Erdine S, Hans G, Kress HG, Langford R, Likar R, Raffa RB, Sacerdote P. (2008). Opioids and the management of chronic severe pain in the elderly: consensus statement of an International Expert Panel with focus on the six clinically most often used World Health Organization Step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). *Pain Practice*, 8(4):287-313.
- Piercefield E, Archer P, Kemp P, Mallonee S. (2010). Increase in unintentional medication overdose deaths: Oklahoma, 1994-2006. *American Journal of Preventive Medicine*, 39(4):357-63
- Piper TM, Stancliff S, Rudenstine S, Sherman S, Nandi V, Clear A, Galea S. (2008). Evaluation of a naloxone distribution and administration program in New York City. *Substance Use and Misuse*, 43(7):858-70.
- SAMHSA. National Survey of Substance Abuse Treatment Services. Data on Substance Abuse Treatment Facilities. 2009. Rockville MD: US Department of Health and Human Services; DHHS publication SMA 05-4112.
- Scherbaum N, Klein S, Kaube H, Kienbaum P, Peters J, Gastpar M. (1998). Alternative strategies of opiate detoxification: evaluation of the so-called ultra-rapid detoxification. *Pharmacopsychiatry*, 31(6):205-9.

References

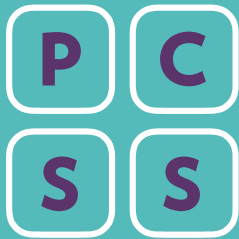
- Seal KH, Downing M, Kral AH, Singleton-Banks S, Hammond JP, Lorvick J, Ciccarone D, Edlin BR. (2003). Attitudes about prescribing take-home naloxone to injection drug users for the management of heroin overdose: a survey of street-recruited injectors in the San Francisco Bay Area. *Journal of Urban Health*, 80(2):291-301.
- Seaman SR, Brettle RP, Gore SM. (1998). Mortality from overdose among injecting drug users recently released from prison: database linkage study. *British Medical Journal*, 316(7129):426-8.
- Siegler A, Tuazon E, Bradley O'Brien D, Paone D. (2013). Unintentional opioid overdose deaths in New York City, 2005-2010: A place-based approach to reduce risk. *International Journal on Drug Policy*, S0955-3959(13)00178-3.
- Sigmon SC, Bisaga A, Nunes EV, O'Connor PG, Kosten T, Woody G. (2012). Opioid detoxification and naltrexone induction strategies: recommendations for clinical practice. *American Journal of Drug and Alcohol Abuse*, May;38(3):187-99.
- Sigmon SC, Dunn KE, Saulsgiver K, Patrick ME, Badger GJ, Heil SH, Brooklyn JR, Higgins ST. (2013). A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. *JAMA Psychiatry*, 70(12):1347-54.
- Smyth BP, Barry J, Keenan E, Ducray K. (2010). Lapse and relapse following inpatient treatment of opiate dependence. *Irish Medical Journal*, 103(6):176-9.
- Sporer KA. (2003). Strategies for prevention heroin overdose. *British Medical Journal*, 326(7386):442-4.
- Strang J, Best D, Man L, Noble A, Gossop M. (2000). Peer-initiated overdose resuscitation: fellow drug users could be mobilised to implement resuscitation. *International Journal of Drug Policy*. 11(6):437-446.

References

- Strang J, McCambridge J, Best D, Beswick T, Bearn J, Rees S, Gossop M. (2003). Loss of tolerance and overdose mortality after inpatient opiate detoxification: follow up study. *British Medical Journal*, 326(7396):959-60.
- Tobin KE, Gaasch WR, Clarke C, MacKenzie E, Latkin CA. (2005). Attitudes of Emergency Medical Service providers towards naloxone distribution programs. *Journal of Urban Health*, 82(2):296-302.
- Tracy M, Piper TM, Ompad D, Bucciarelli A, Coffin PO, Vlahov D, Galea S. (2005). Circumstances of witnessed drug overdose in New York City: implications for intervention. *Drug and Alcohol Dependence*, 79(2):181-90.
- Wagner KD, Valente TW, Casanova M, Partovi SM, Mendenhall BM, Hundley JH, Gonzalez M, Unger JB. (2010). Evaluation of an overdose prevention and response training programme for injection drug users in the Skid Row area of Los Angeles, CA. *International Journal on Drug Policy*, 21(3):186-93.
- Wakeman SE, Bowman SE, McKenzie M, Jeronimo A, Rich JD. (2009). Preventing death among the recently incarcerated: an argument for naloxone prescription before release. *Journal of Addictive Diseases*, 28(2):124-9.
- Warner M, Chen LH, Makuc DM, Anderson RN, Miniño AM. (2011). Drug poisoning deaths in the United States, 1980-2008. *NCHS Data Brief*, (81):1-8.
- Weiss RD, Potter JS, Fiellin DA, Byrne M, Connery HS, Dickinson W, Gardin J, Griffin ML, Gourevitch MN, Haller DL, Hasson AL, Huang Z, Jacobs P, Kosinski AS, Lindblad R, McCance-Katz EF, Provost SE, Selzer J, Somoza EC, Sonne SC, Ling W. (2011). Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid dependence: a 2-phase randomized controlled trial. *Archives of General Psychiatry*, 68(12):1238-46.

References

- White JM, Irvine RJ, (1999). Mechanisms of fatal opioid overdose. *Addiction*, 94(7):961-72.
- Wines JD Jr, Saitz R, Horton NJ, Lloyd-Travaglini C, Samet JH. (2007). Overdose after detoxification: a prospective study. *Drug and Alcohol Dependence*, 89(2-3):161-9.
- Worthington N, Markham Piper T, Galea S, Rosenthal D. (2006). Opiate users' knowledge about overdose prevention and naloxone in New York City: a focus group study. *Harm Reduction Journal*, 3:19.
- Yokell MA, Green TC, Bowman S, McKenzie M, Rich JD. (2011). Opioid overdose prevention and naloxone distribution in Rhode Island. *Med Health R I* 94(8): 240-2.



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Funding for this initiative was made possible (in part) by Providers' Clinical Support System for Medication Assisted Treatment (1U79TI024697) from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

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