University of Massachusetts Medical School
UMASS

Treatment of opioid use disorders

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Disclosures

- I have no financial conflicts to disclose
- I will review evidence based off-label use of medications

Outline

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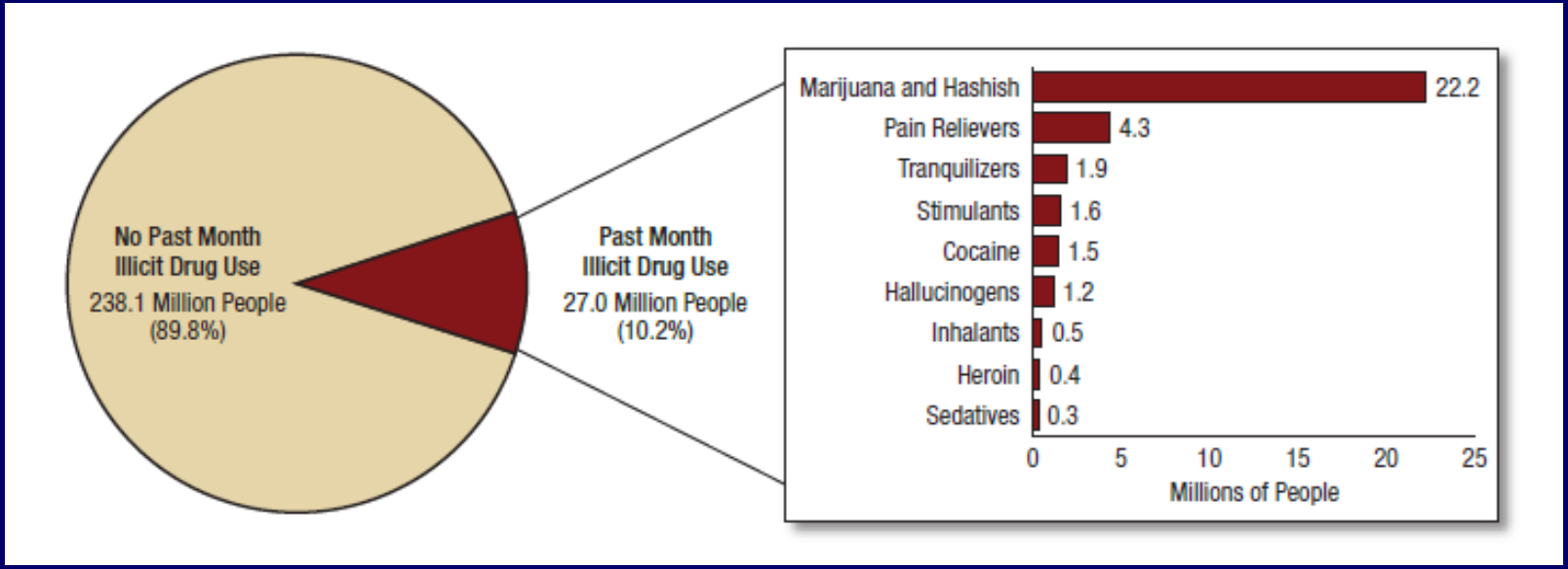
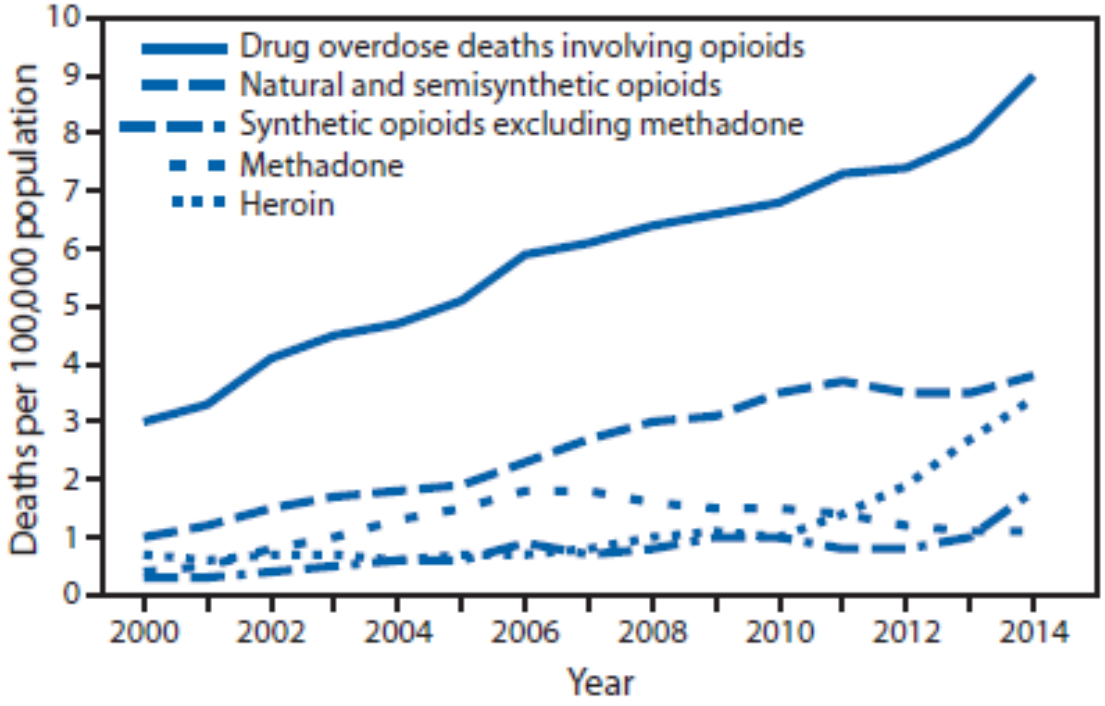
- Epidemiology
- Neurobiology
- Preventive efforts
- Treatment
- Longitudinal outcomes
- Conclusions

Epidemiology



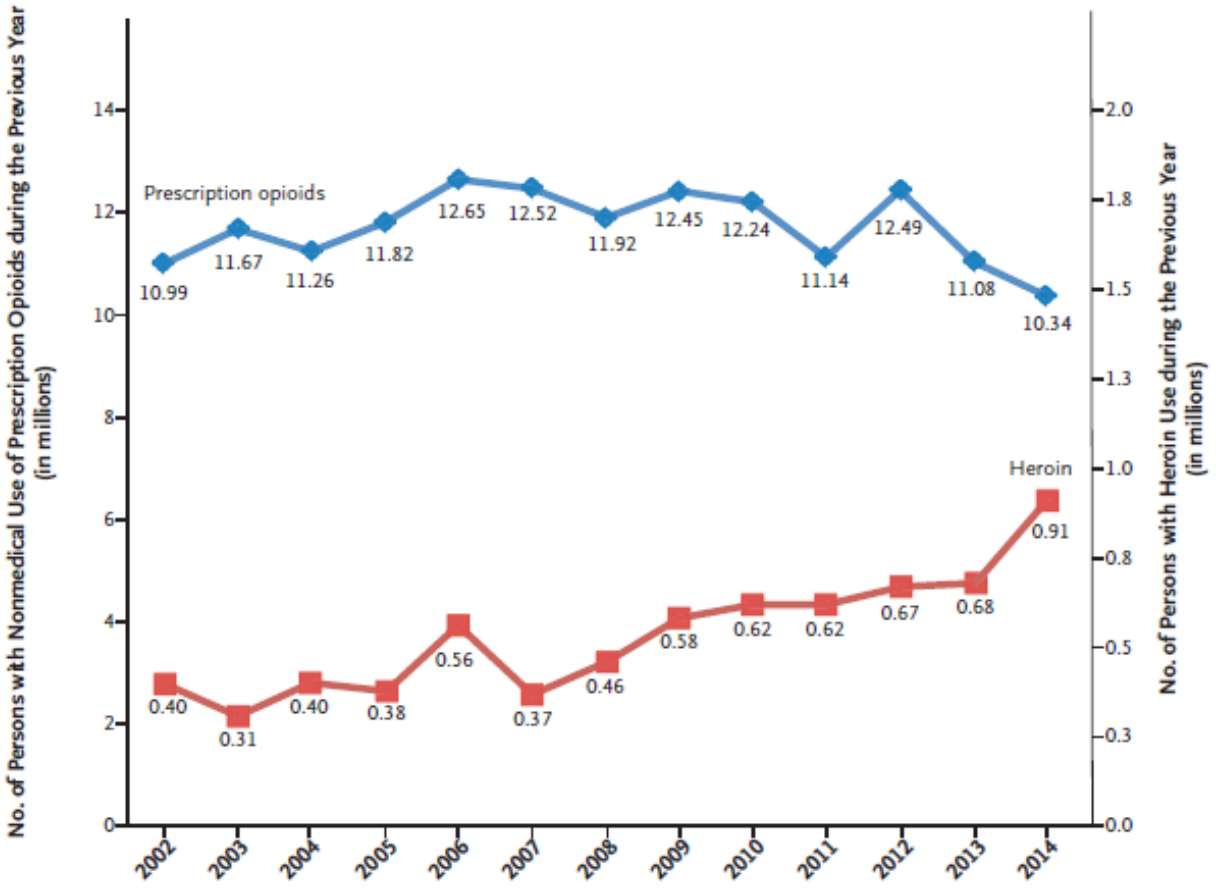
NSDUH, 2014

Drug overdose deaths involving opioids by type of opioid
United States, 2000–2014



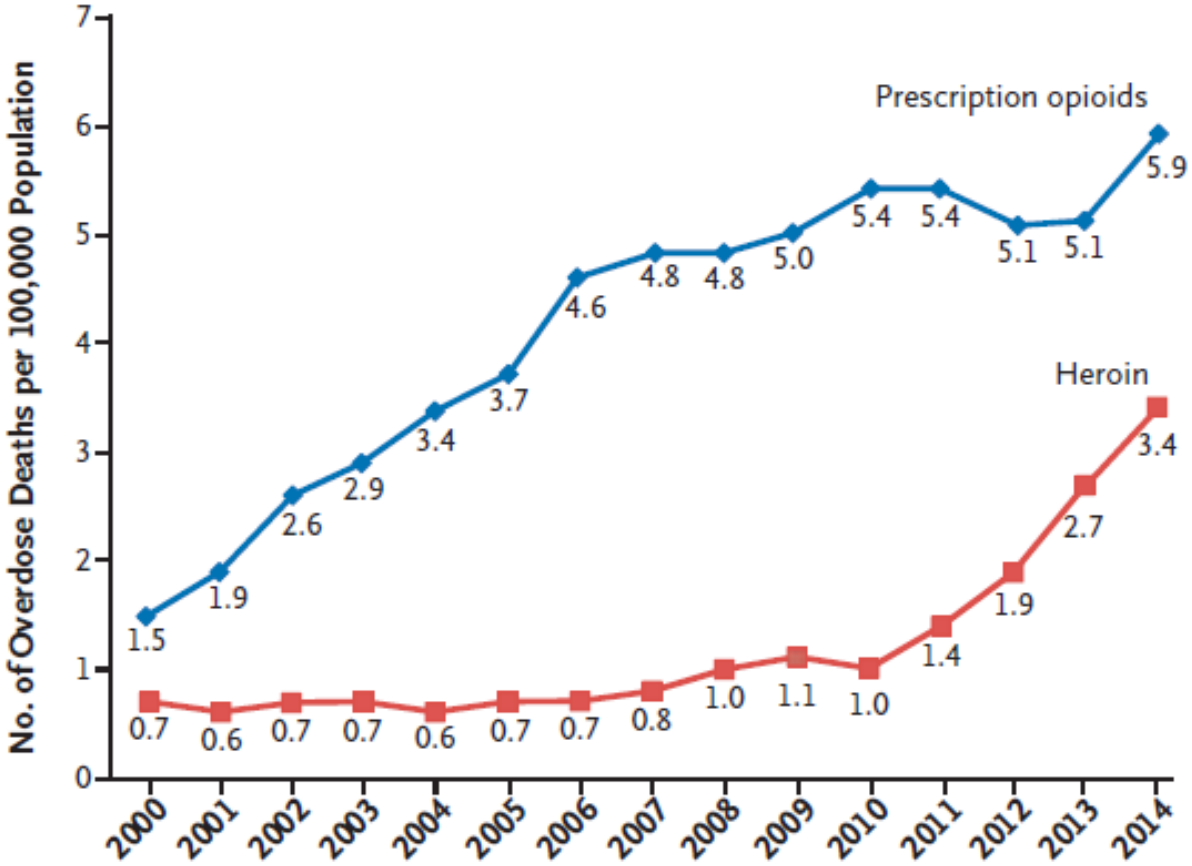
CDC, 2016

Prescription Opioids and Heroin use during the Previous Year United States, 2000–2014.

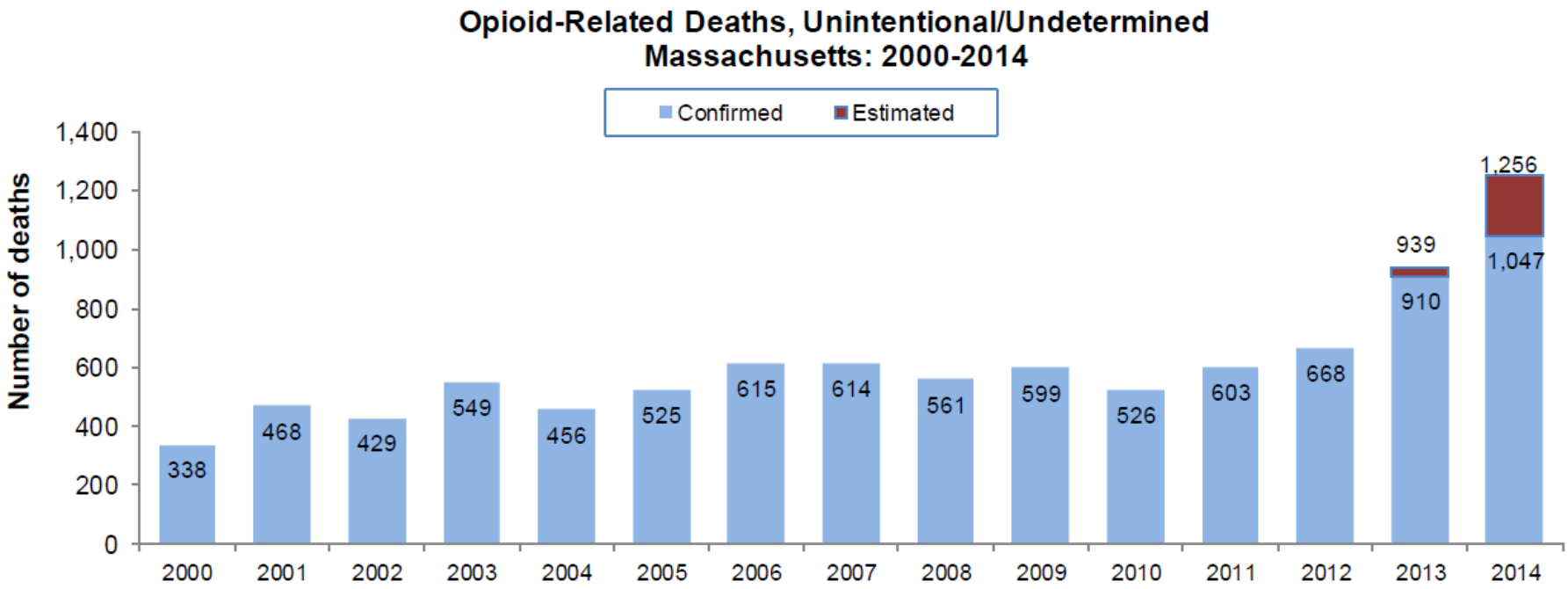


Comptom, 2016

Prescription Opioids and Heroin Drug Poisoning
United States, 2000–2014.

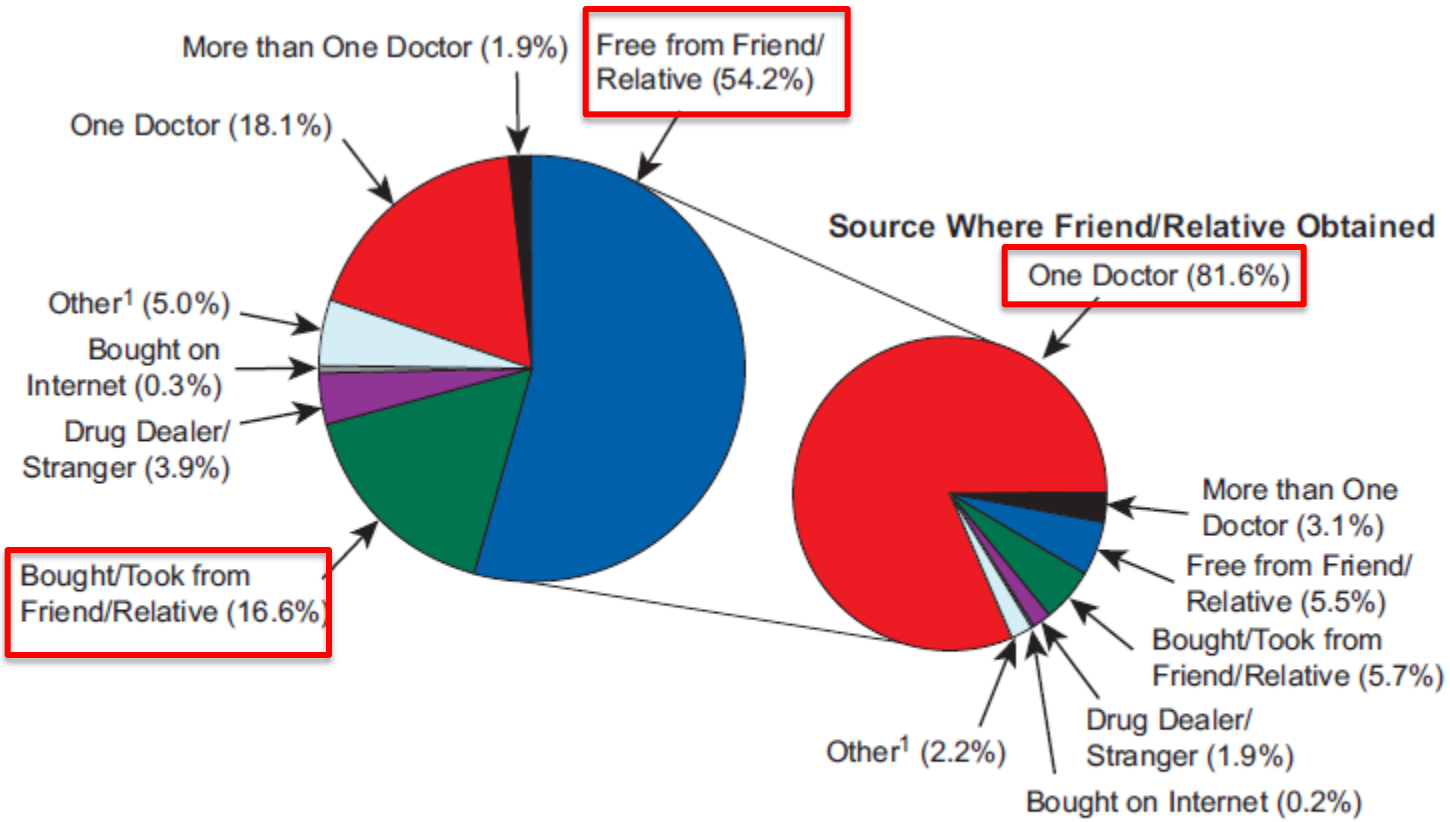


Comptom, 2016



Massachusetts Department of Public Health, 2015

Source Where Pain Killers Were Obtained
Age 12 or Older: 2010-2011

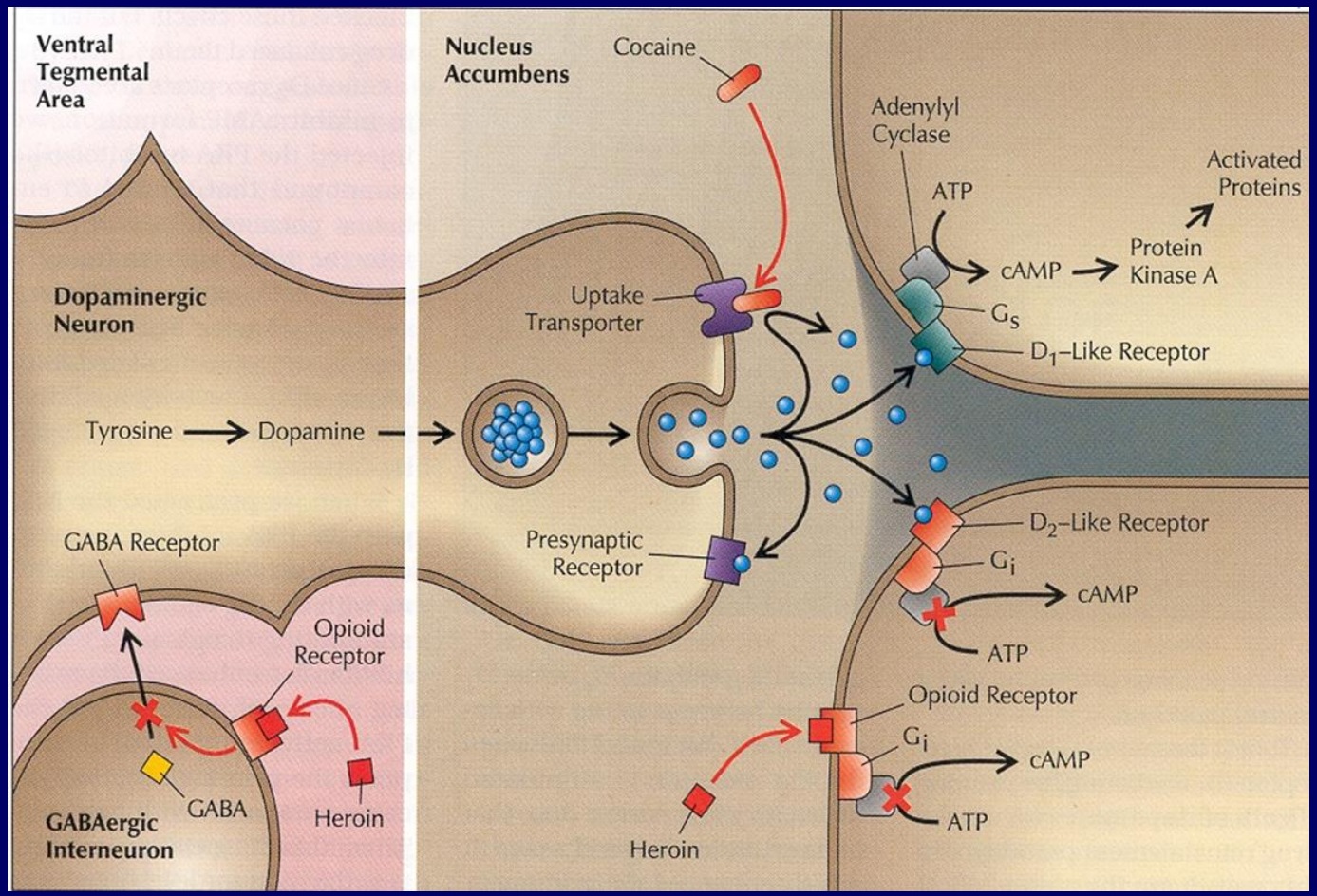


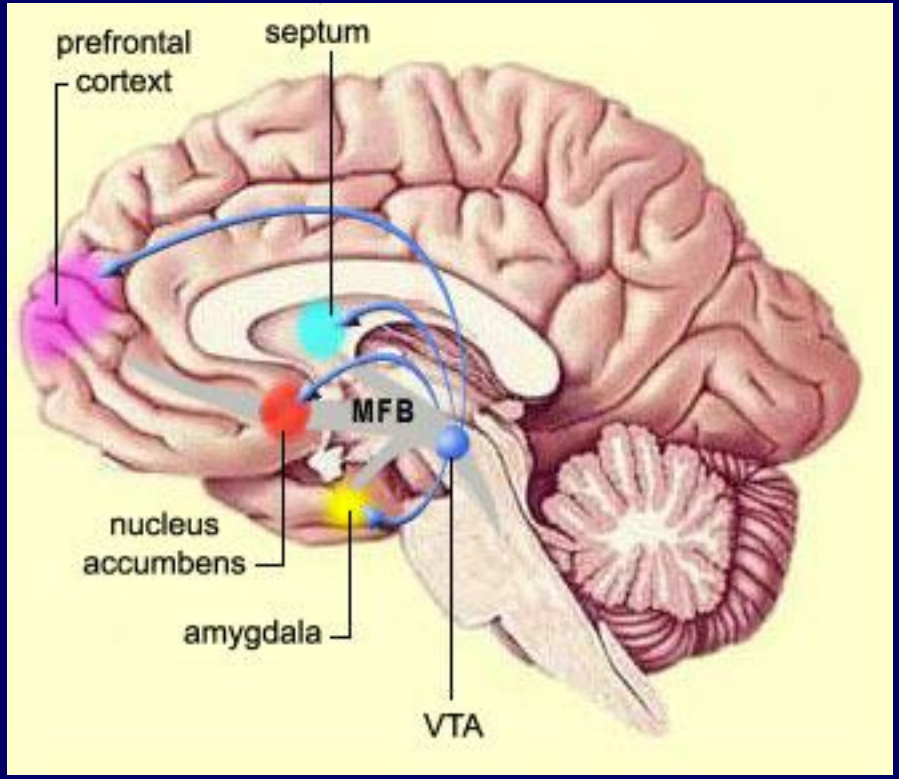
Note: The percentages do not add to 100 percent due to rounding.

[1] The Other category includes the sources "Wrote Fake Prescription," "Stole from Doctor's Office/Clinic/Hospital/Pharmacy," and "Some Other Way."


FAVORITA
ADDICTION

Neurobiology




prefrontal
cortext
septum
MFB
nucleus
accumbens
amygdala
VTA

Substance use disorders (DSM-5)

- ***Neuroadaptation:***
  - Tolerance
  - Withdrawal
- ***Cognitive distortion:***
  - Importance of substance use
  - Subjective awareness of decrease control
  - Craving or a strong desire or urge to use
- ***Behavioral dyscontrol:***
  - Obtaining, using and recovering
  - Use despite knowledge of problems
  - Using more and longer than intended

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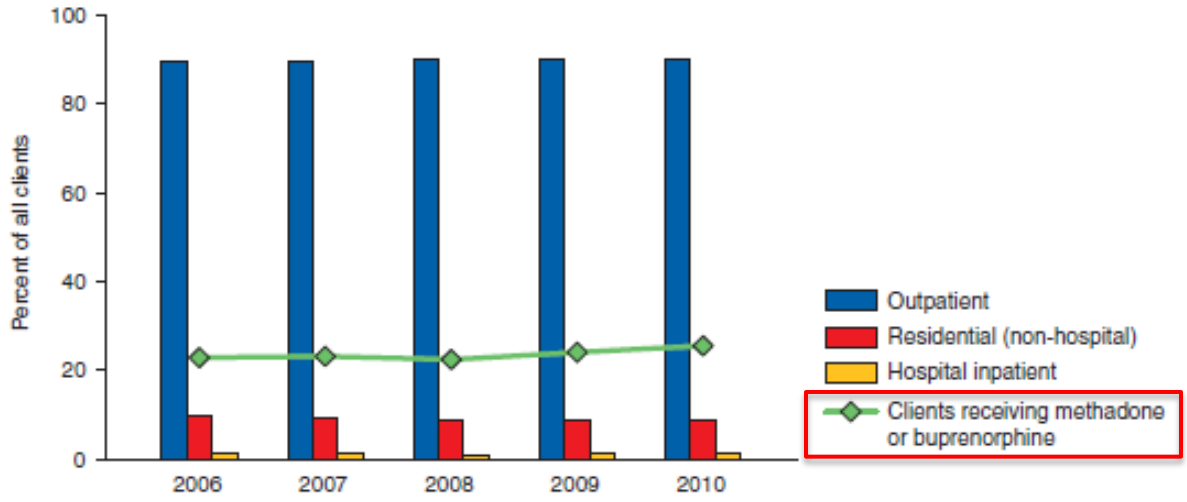
Preventive efforts

Preventive efforts

- Education of medical and nursing students on universal precautions with controlled substances
- Prescription guidelines for practicing physicians and dentists on safe pain management
- Prescription monitoring program (PMP)
- Safe storage of opioid analgesics (locked box)
- Appropriate disposal of unused opioid analgesics
- Naloxone rescue kits available (standing orders)

Treatment

Patients in Treatment, by type of care received: 2006-2010



SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, National Survey of Substance Abuse Treatment Services (N-SSATS), 2006-2010.

- The proportion of all clients receiving methadone was 22 to 25 percent between 2006 and 2010.
- The proportion of clients receiving buprenorphine was 1 percent or less from 2006 to 2008, but increased to 2 percent in 2009 and 2010.

Substance Abuse Treatment Services

1. Detoxification / stabilization units
2. Inpatient acute hospitalization
3. Nonhospital residential rehabilitation
4. Partial day hospital / intensive outpatient program (IOP)
5. Outpatient treatment / office-based

Psychosocial treatments

1. Drug Counseling
2. Cognitive Behavioral Therapy
3. Relapse prevention
4. Mindfulness
5. Contingency Management
6. Twelve Steps facilitation
7. Motivational Enhancement Therapy
8. Self-help groups

Use of Medications

Managed withdrawal

- In-patient stabilization units
- Reduce opioid withdrawal symptoms
- Transition off daily opioid use
- Evaluate and treat comorbid medical and psychiatric problems
- Usually 4-5 days → needs follow-up

Managed withdrawal

- Methadone
- Clonidine
- Buprenorphine

Medication assisted treatment (MAT)

- Outpatient settings
- Suppress opioid withdrawal symptoms
- Suppress craving for opioids
- Stop opioid use and relapse
- Adjust daily dose to avoid sedation

Medication assisted treatment (MAT)

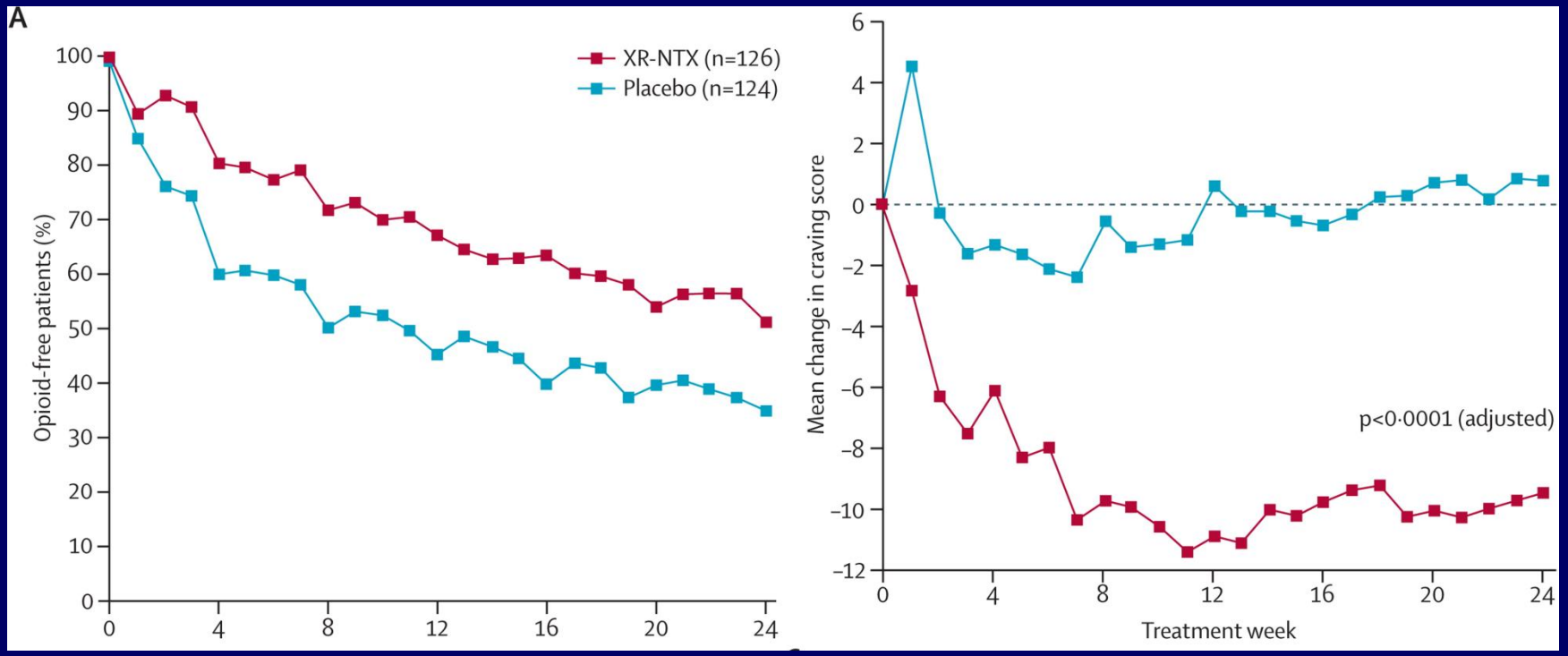
- Naltrexone
- Methadone
- Buprenorphine + Naloxone

Naltrexone

- *Indications:* Severe opioid use disorder
- *Mechanism:* Opiate receptor antagonist
- *Efficacy:* Oral is good in high motivated.
- *Implementation:* 50-100 mg/per day; LFT's
- *Side effects :* nausea, headache, anxiety, OD
- *Compliance*: Improved with naltrexone depot (IM)

(Comer, 2006; Krupitsky, 2011)

Naltrexone Depot



Krupitsky, 2011

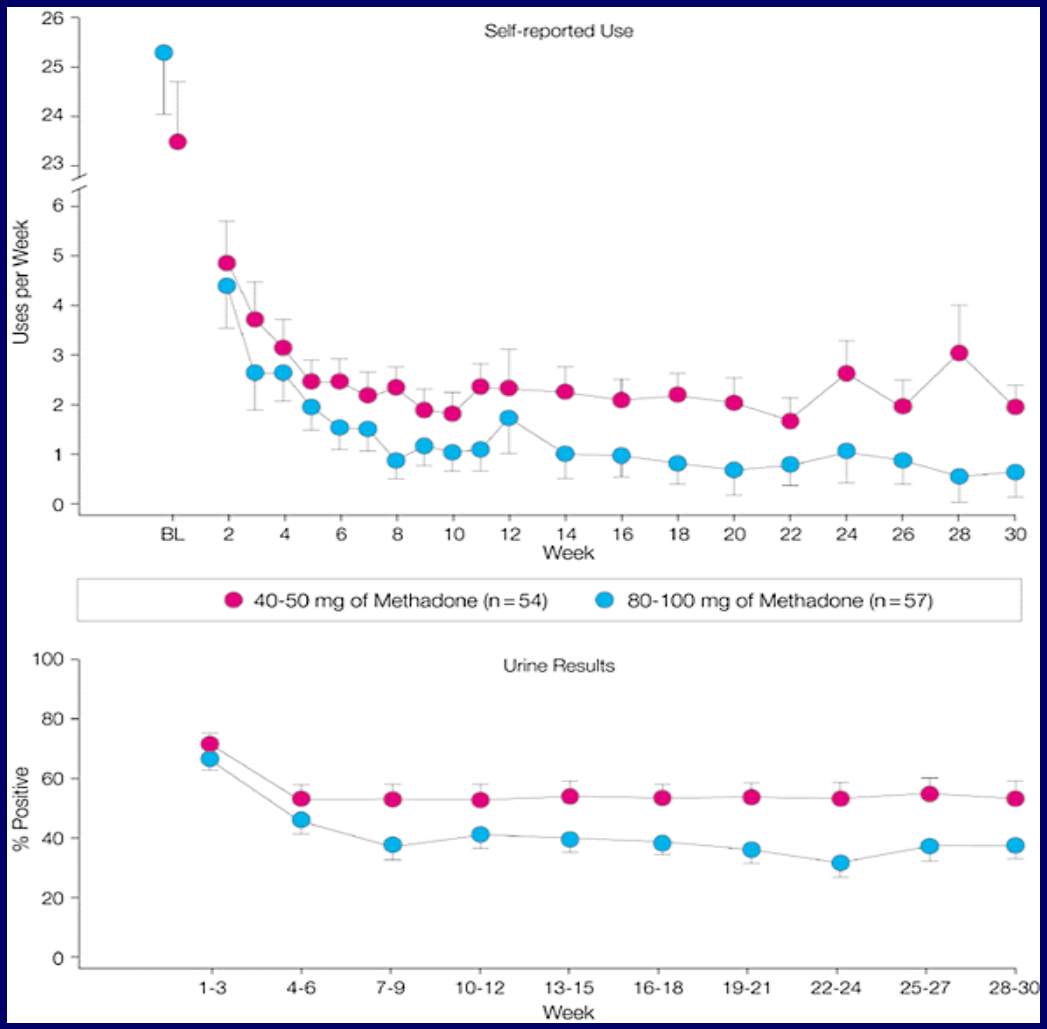
Methadone

- *Indications:* Severe opiate use disorder
- *Mechanism:* Full opiate receptor agonist.
- *Efficacy:* 70-80 % retention in OTP.
- *Implementation:* Start at 25-30mg and built-up dose until opiate free urines.
- *Side effects :* sedation
- *Interactions:* benzodiazepine – alcohol.

Methadone

- Age >18 or 2 documented failures of detox.
- One year history of severe opiate use disorder
- Exceptions:
  - Pregnancy
  - Release from prison
  - History of previous treatment.

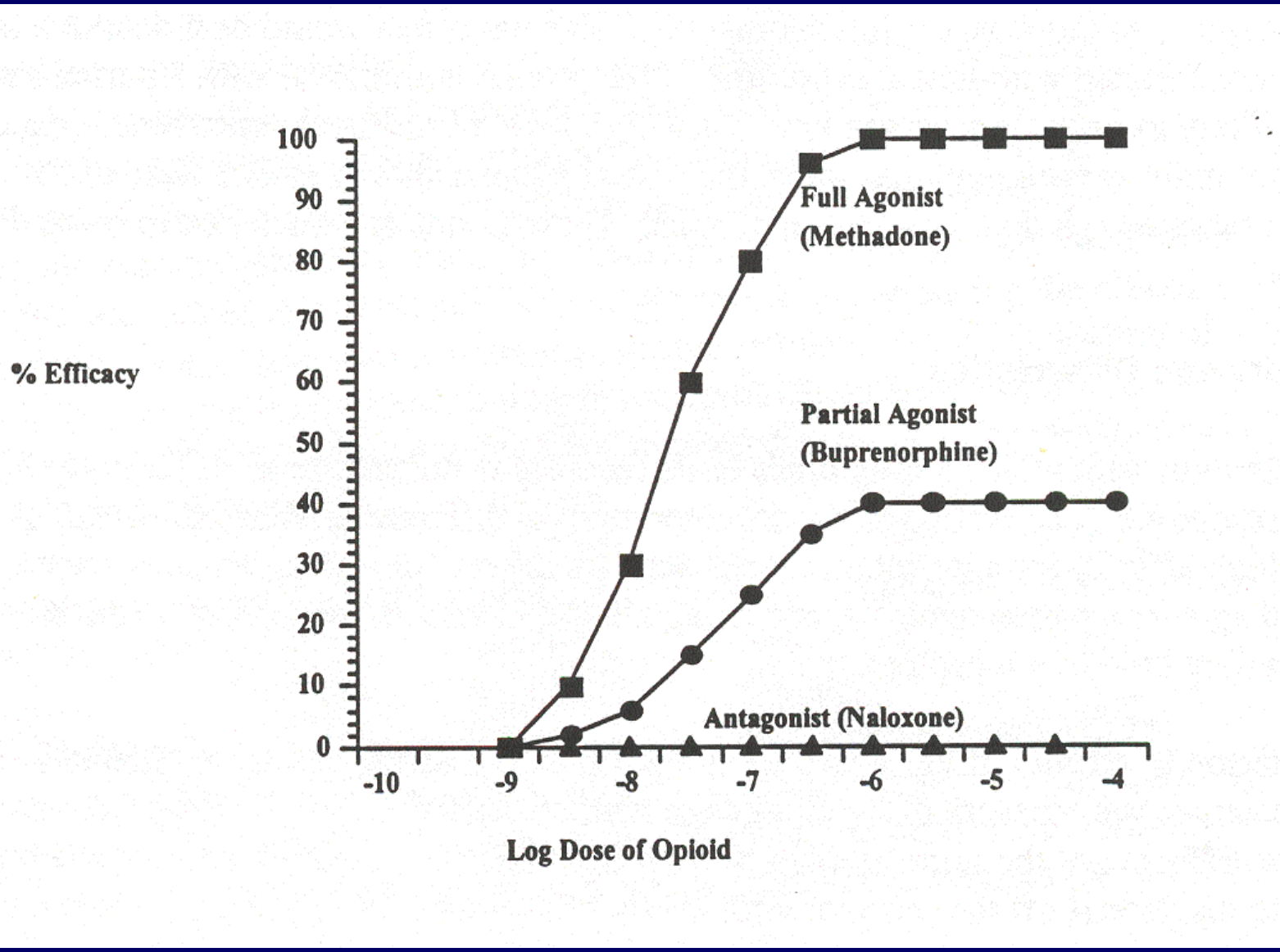
Methadone dose: illicit opioid use



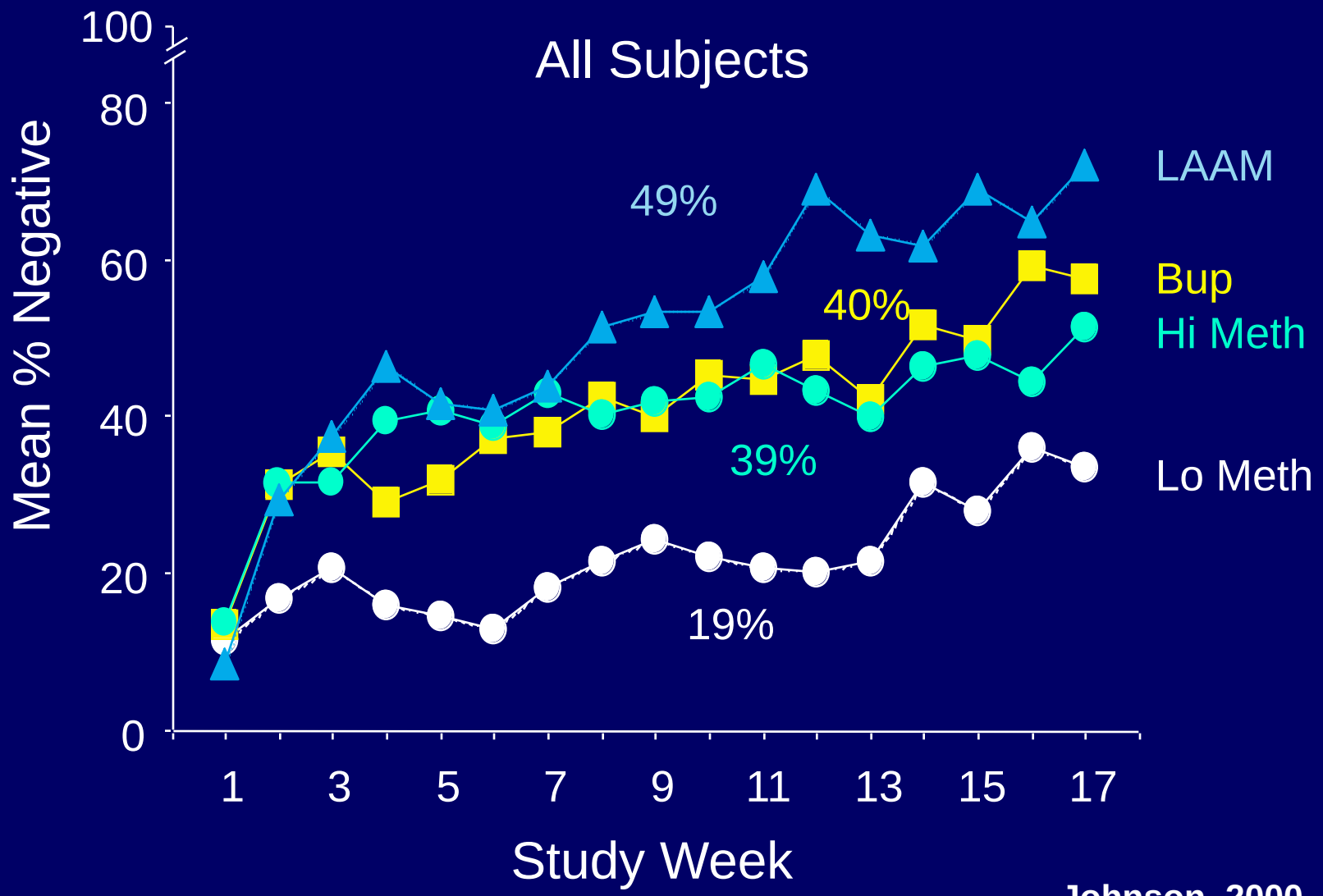
Strain, 1999

Buprenorphine

- Partial opiate receptor agonist
- Combination tablet /film 4:1 (Bup/naloxone)
- Sublingual administration
- High affinity and slow dissociation
- Office based opiate use treatment
- Death associated with IV use and with benzodiazepines

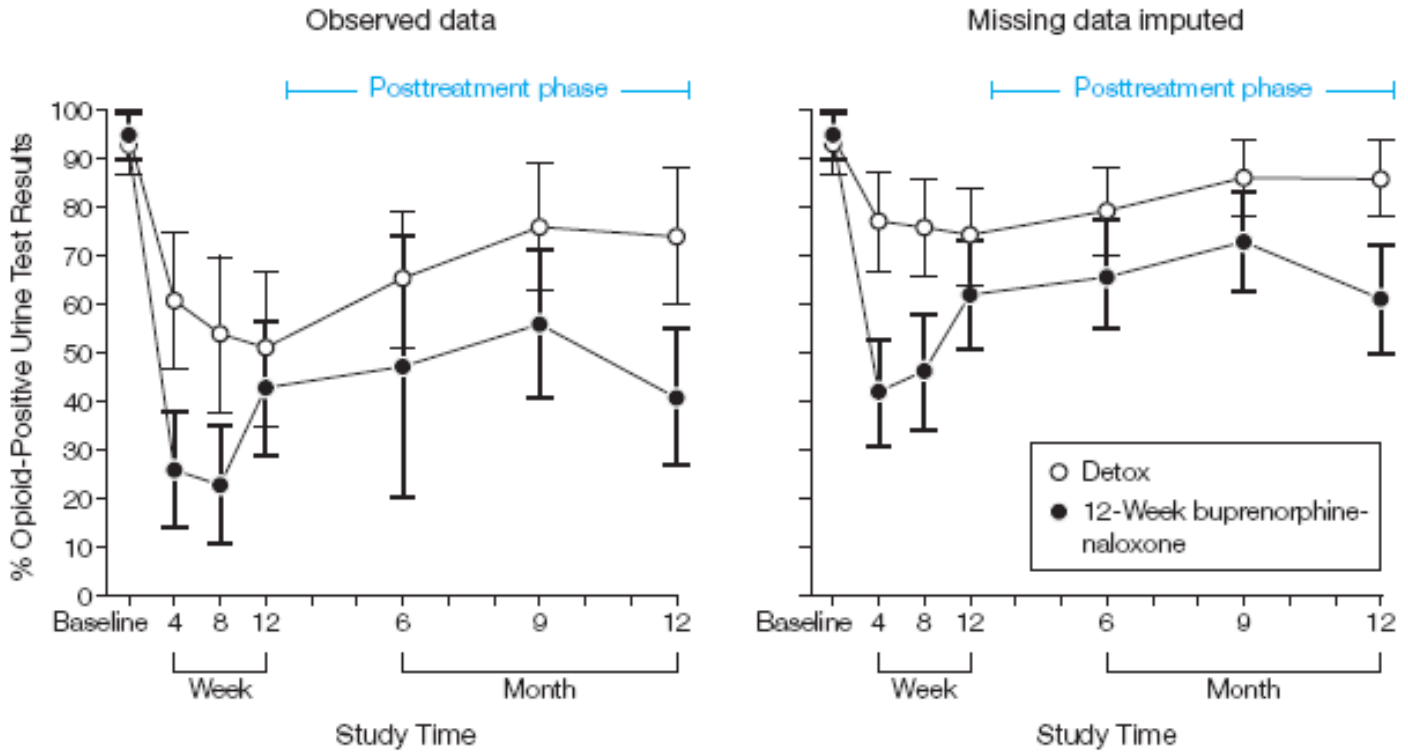

% Efficacy
100
90
80
70
60
50
40
30
20
10
0
-10
-9
-8
-7
-6
-5
-4
Full Agonist
(Methadone)
Partial Agonist
(Buprenorphine)
Antagonist (Naloxone)
Log Dose of Opioid

Buprenorphine, Methadone, LAAM: Opioid Urines



Johnson, 2000

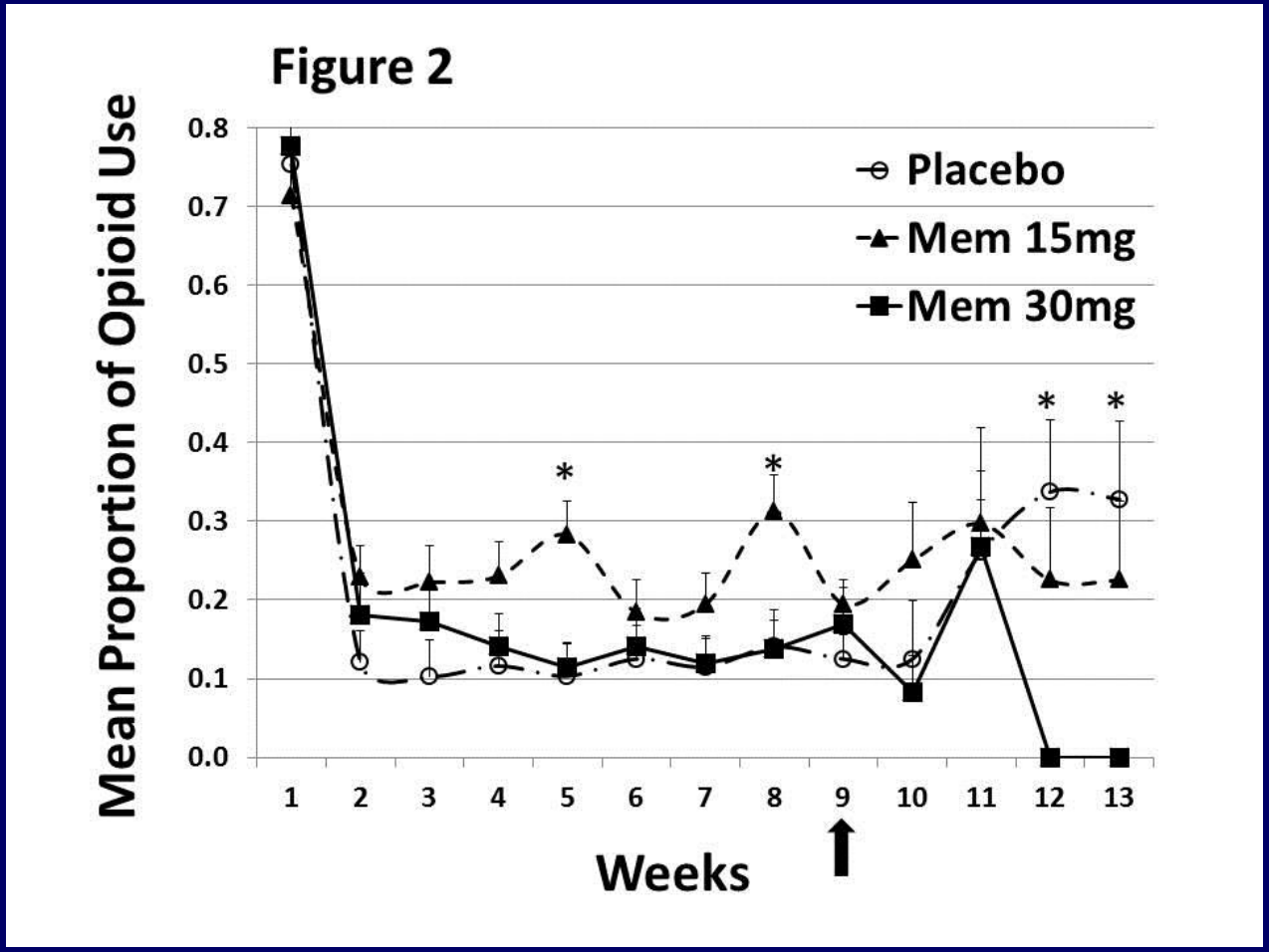
Treatment of opioid dependent youth



Detox indicates detoxification group. Error bars indicate 95% confidence intervals.
[a]12-Week buprenorphine-naloxone group.

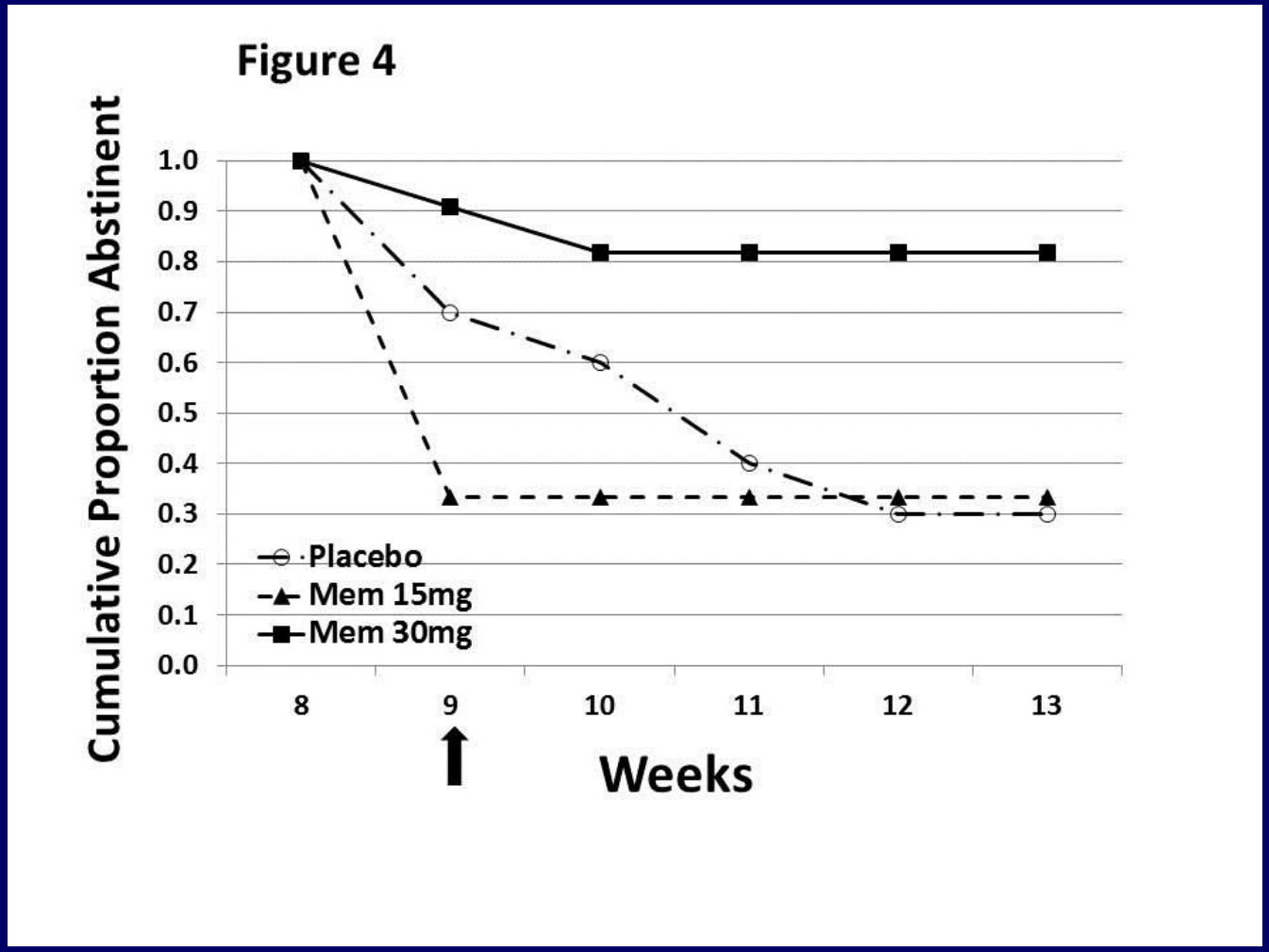
Woody, 2008

Buprenorphine with Memantine for young adults



Gonzalez, 2015

Buprenorphine and Memantine for young adults



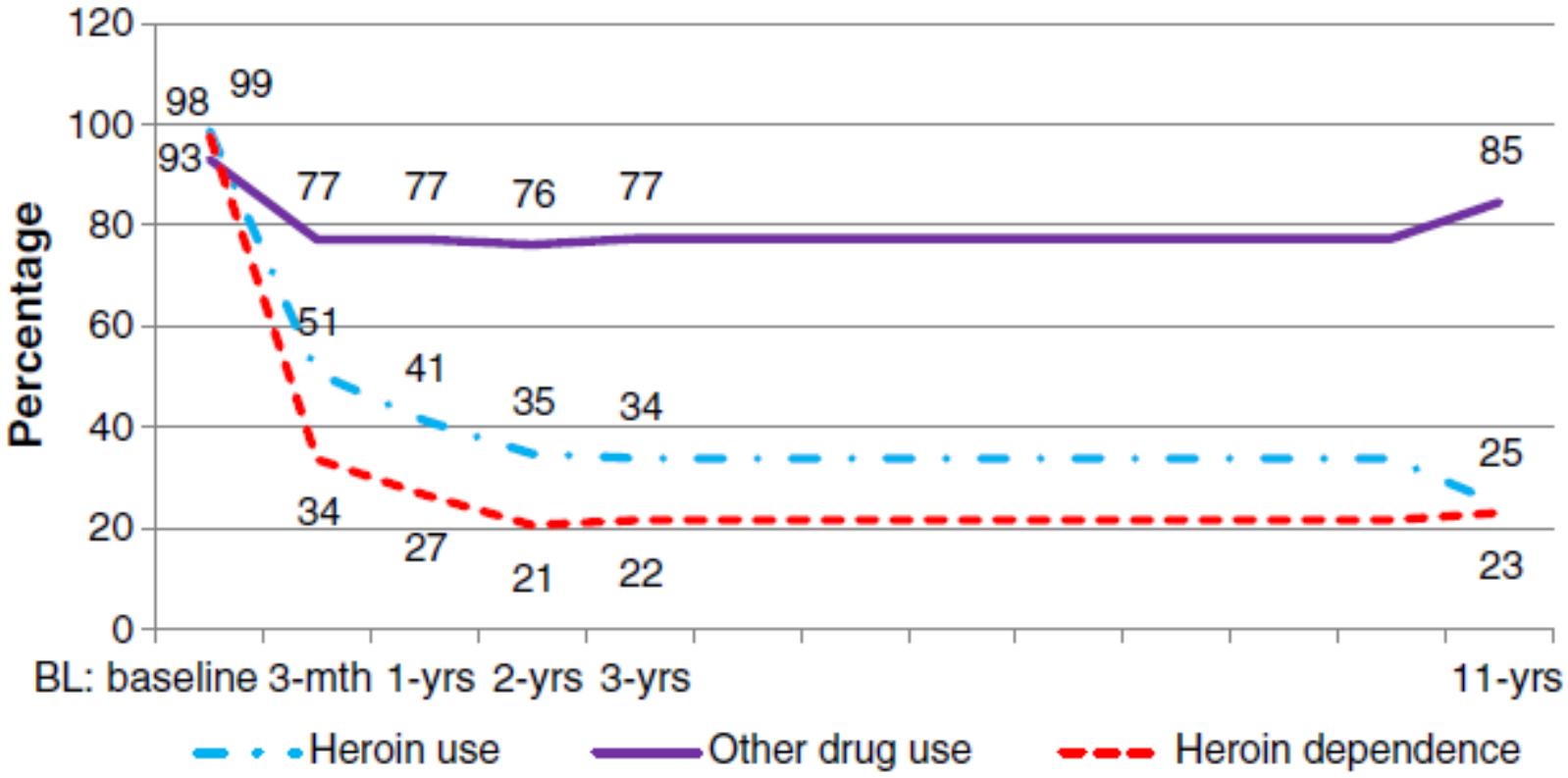
Gonzalez, 2015

Long-term outcomes

Long-term outcomes

- Reduction of mortality compared to untreated controls (Gronbladh, 1990)
- Decrease IVDU from 81% to 29% vs 82% at 1 year of those who left treatment (Ball and Ross, 1991)
- HIV seroconversion: methadone 3.5% vs active IVDU 22%

Prevalence of past month heroin use, heroin dependence and other drug use across the 11-year follow-up period



Teesson, 2015

Comorbid disorders impact

Major Depression *	1.96 (1.50 – 2.55)
Antisocial Personality	1.02 (0.70 – 1.32)
Borderline Personality	1.16 (0.91 – 1.48)
PTSD	0.81 (0.63 – 1.05)

Teesson, 2015

Treatment effect

MAT	1.11 (0.90 – 1.38)
Detoxification *	1.52 (1.20 – 1.92)
Residential Rehab *	0.59 (0.46 – 0.76)

Teesson, 2015

Conclusion

- Current opioid use epidemic is responsibility of all to help reduce.
- Education and change in prescription practices are key elements in prevention.
- Reduction of diversion and appropriate disposal is important.
- Medication - assisted treatments are effective.
- There is still need to develop effective short-term treatments.