The Opioid Epidemic – Lessons form the Trenches

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DISCLOSURES

Kevin A. Sevarino, MD, PhD has no financial relationships with an ACCME defined commercial interest relevant to the content of this presentation.

Dr. Sevarino will not discuss off-label uses of psychotropics in today's presentation

That Title?

- involved in medications development and clinical treatment of SUDs since 1989.
- former director of the Connecticut VA's OTP (methadone) and VACT Newington Campus buprenorphine clinic.
- PI or co-I on many preclinical and clinical research studies involved in SUD medication development.
- with the AAAP have been involved in the SAMHSA's PCSS Program since 2014, and worked with Drs. Chou and Weimer in development of the Pain Curriculum for the PCSS.

EDUCATIONAL OBJECTIVES

At the conclusion of this session, participants should be able to:

1. Review general concepts of addiction
2. Identify recent trends in opioid use disorders (OUDs)
3. Discuss recommended treatment of OUDs
4. Discuss how OUDs and their treatment impact the workforce.
5. Discuss how employers can impact OUDs.

What Is Addiction?

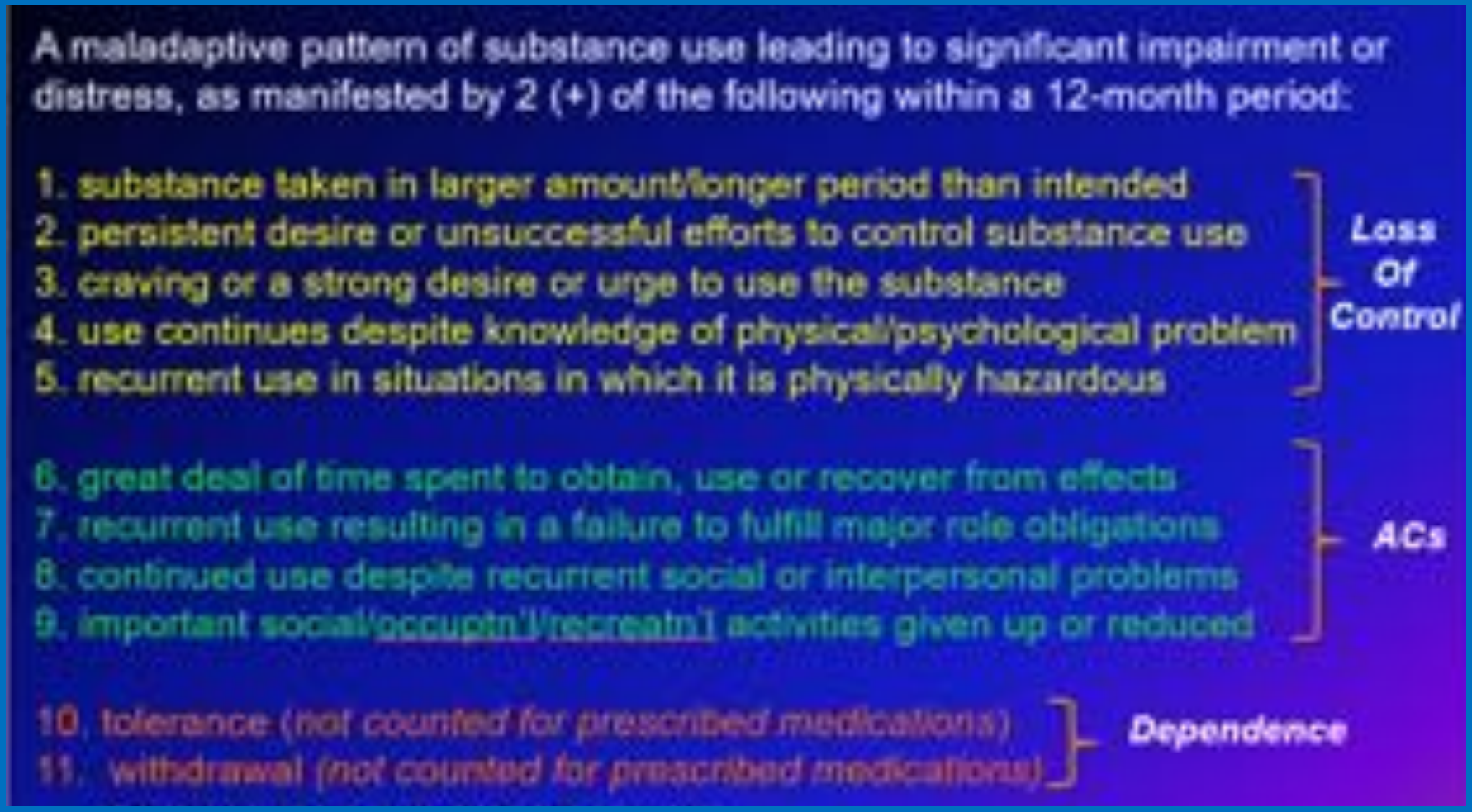
Dependence ≠ Addiction:

1. NIDA defines addiction as the “compulsive drug seeking and use, despite adverse consequences.”[1]

1. The key misunderstanding is that physiological dependence means addiction – it doesn’t, one must have loss of control and adverse consequences.

1. One can be physically dependent, run out of meds and have withdrawal, but that doesn’t mean one is an addict.

DSM-5 Definition: Substance Use Disorder



Mild 2-3; Moderate 4-5; Severe 6+

Addiction is a Brain Disease, Chronic and Relapsing

Behavioral Constructs of Substance Use Disorder (SUD) Progression

Experimentation

Addiction

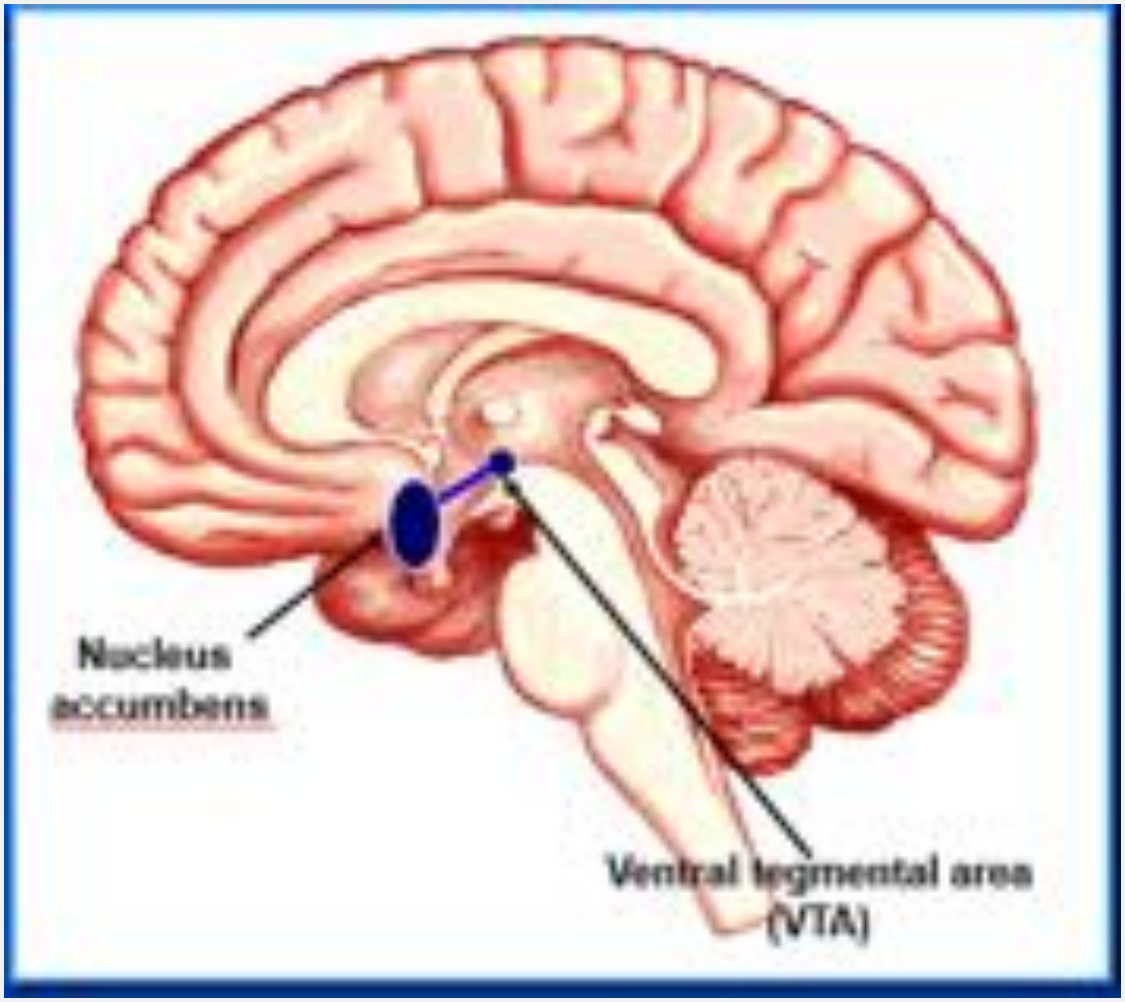
Impulse Control Disorder

Compulsive Disorder

Positive Reinforcement (Reward)

Negative Reinforcement (Avoidance)

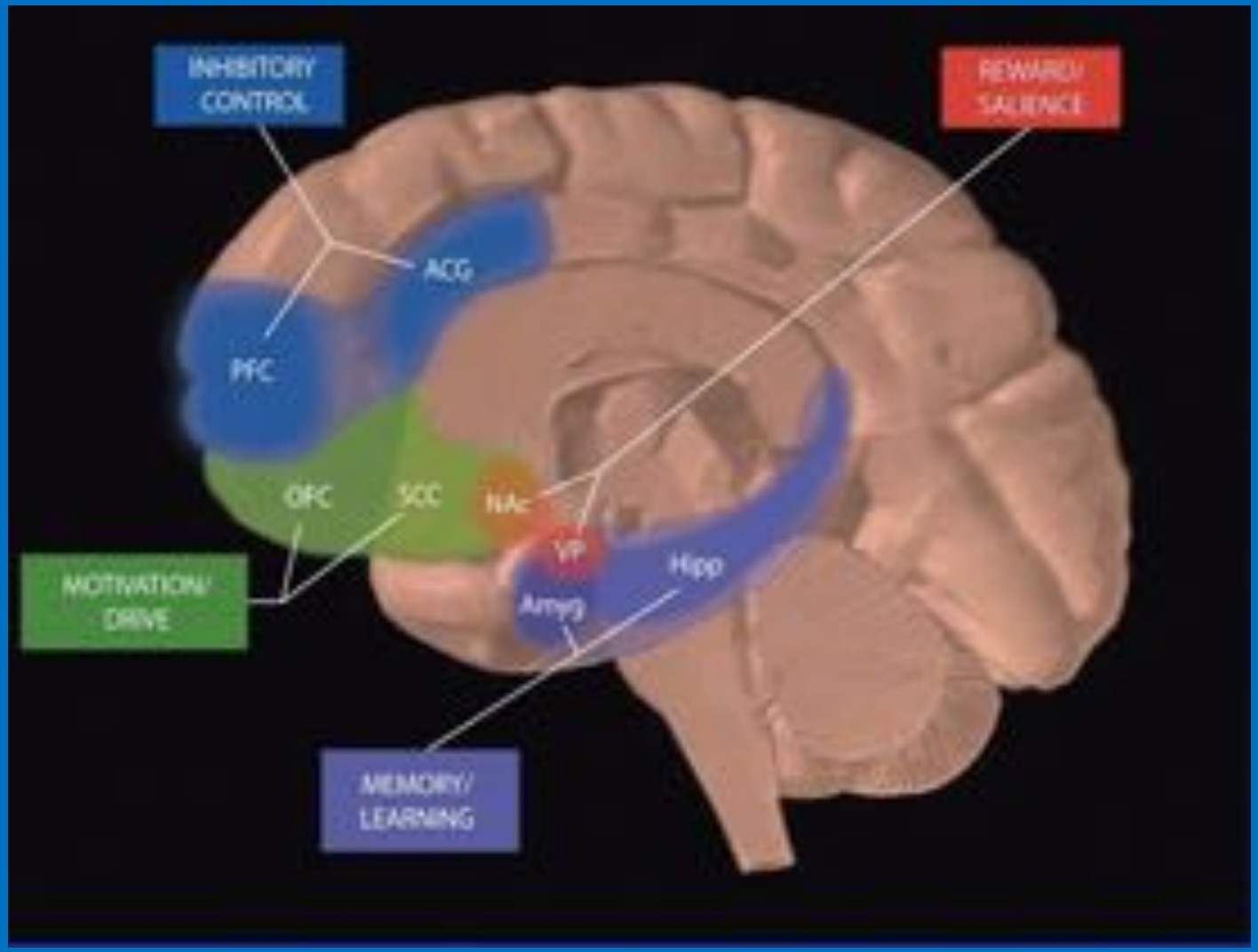
Brain Reward Pathways



- The VTA-nucleus accumbens pathway is activated by all illicit drugs and alcohol.
- This pathway is important not only in drug use disorders, but also in essential physiological behaviors such as eating, drinking, sleeping, and sex.

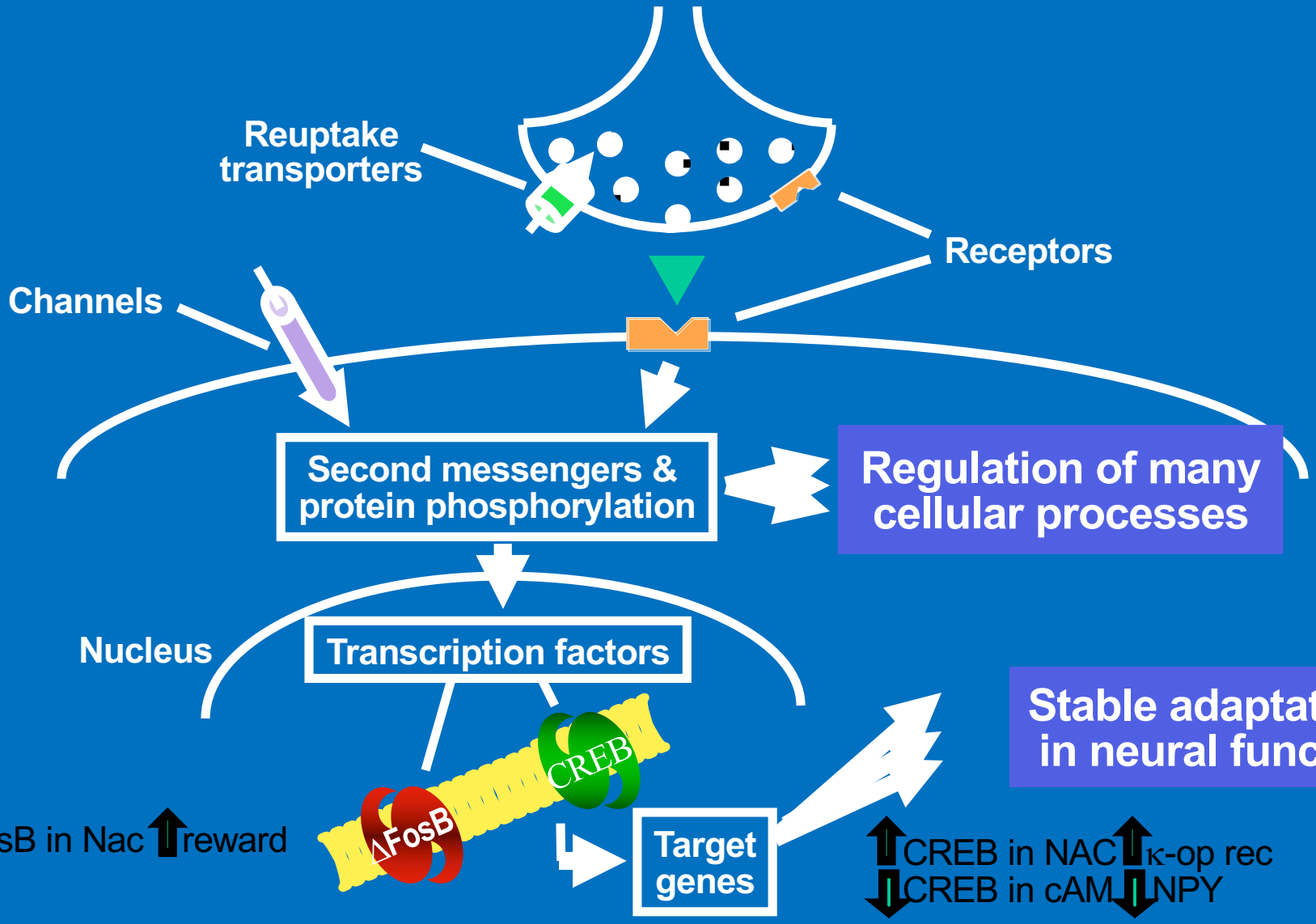
Source: Messing RO. In: Harrison's Principles of Internal Medicine. 2001:2557-2561.

Circuits Involved in Drug Use Disorder



All of these brain regions must be considered in developing strategies to effectively treat addiction.

ADDICTION CAN BE VIEWED AS DRUG-INDUCED NEURAL PLASTICITY



Heritability of SUDs

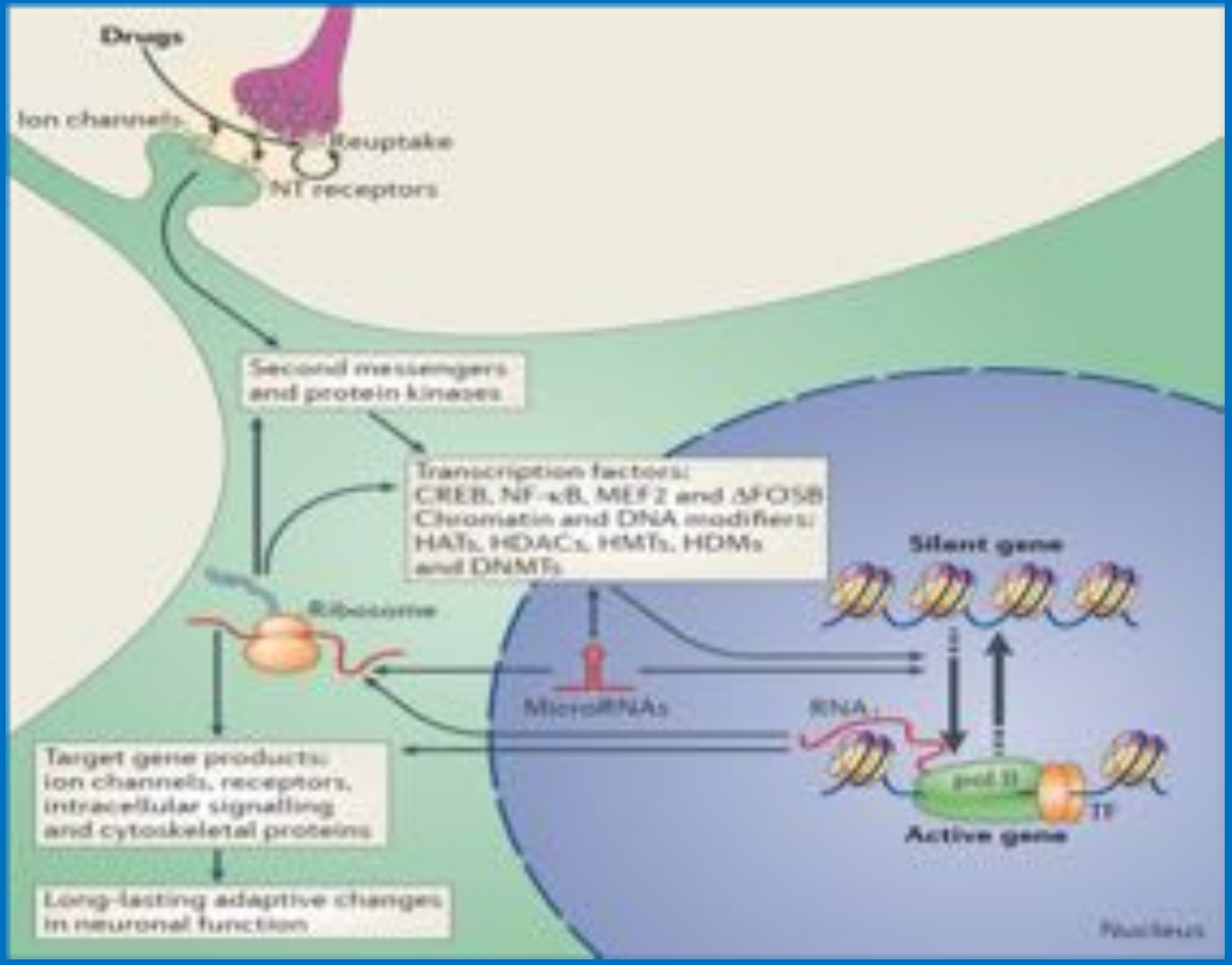
• Cocaine Dependence	0.65 - 0.79
• Nicotine Dependence	>0.60
• Alcohol Dependence	0.50 - 0.60
• Opiate Dependence	0.43

Based on Twin and Adoption Studies, summarized from Galanter and Kleber, 2015

Individual/Contextual Influences

1. Risk Taking/Novelty Seeking/Impulsivity
2. Deficient interpersonal relatedness - insecure attachment and avoidant personality
3. Peer Influence, impoverished environment, availability etc.
4. Psychopathology
   - Antisocial syndromes (CD, ASPD, aggressiveness)
   - ADHD/CD
   - Mood disorders (BPD, MDD)
   - Anxiety disorders
   - SUD (e.g. early, continuous smokers)

Epigenetics Explains Lasting Environmental Effects on Risk



Robison, A.J. and Nestler, E.J. (2011) *Nat. Rev. Neurosci.* 12:623-637.

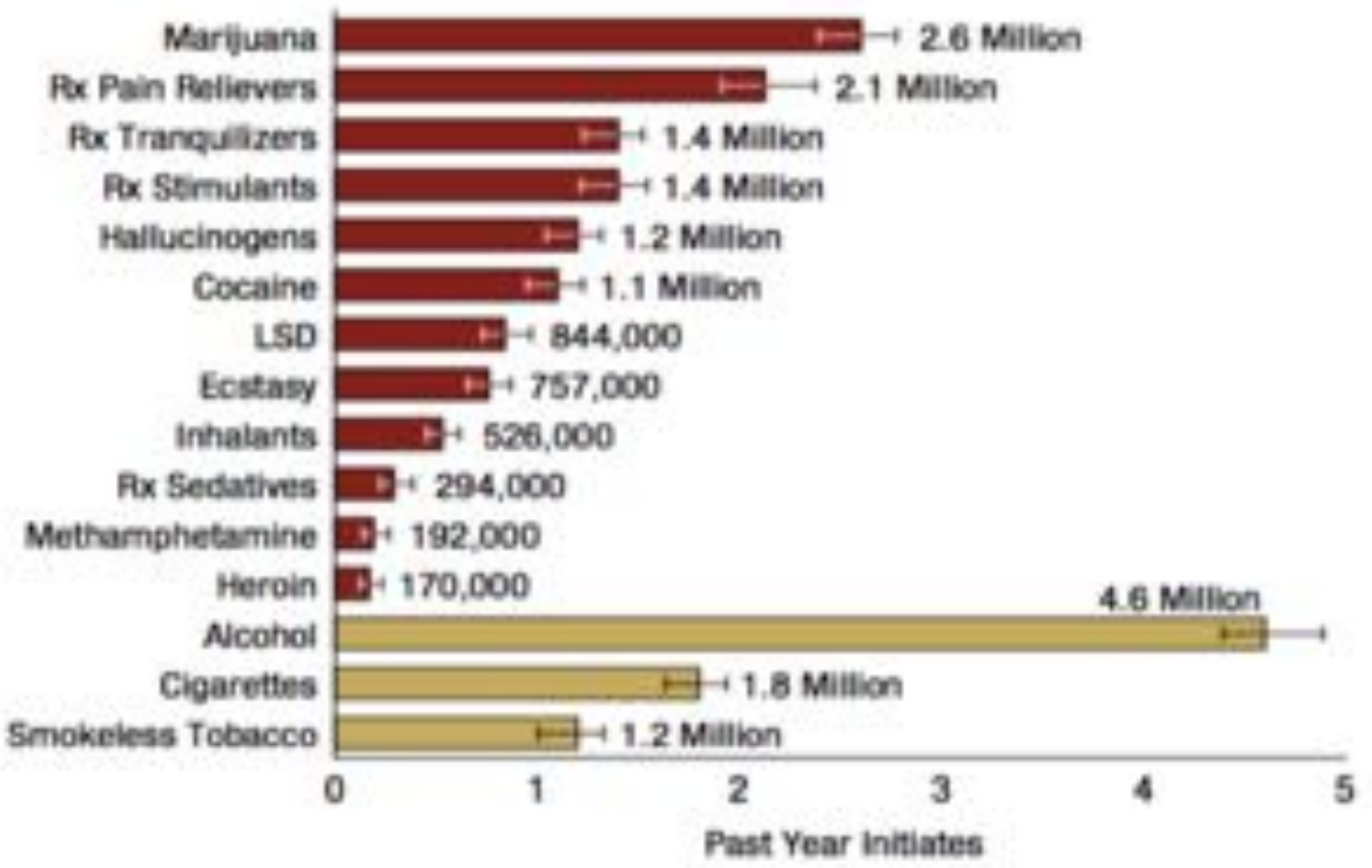
The drug-dependent state represents not just a perturbation of the homeostatic state, but the establishment of a new allostatic state, dysfunctional but stable.

Per Koob and colleagues

Epidemiology of OUDs:

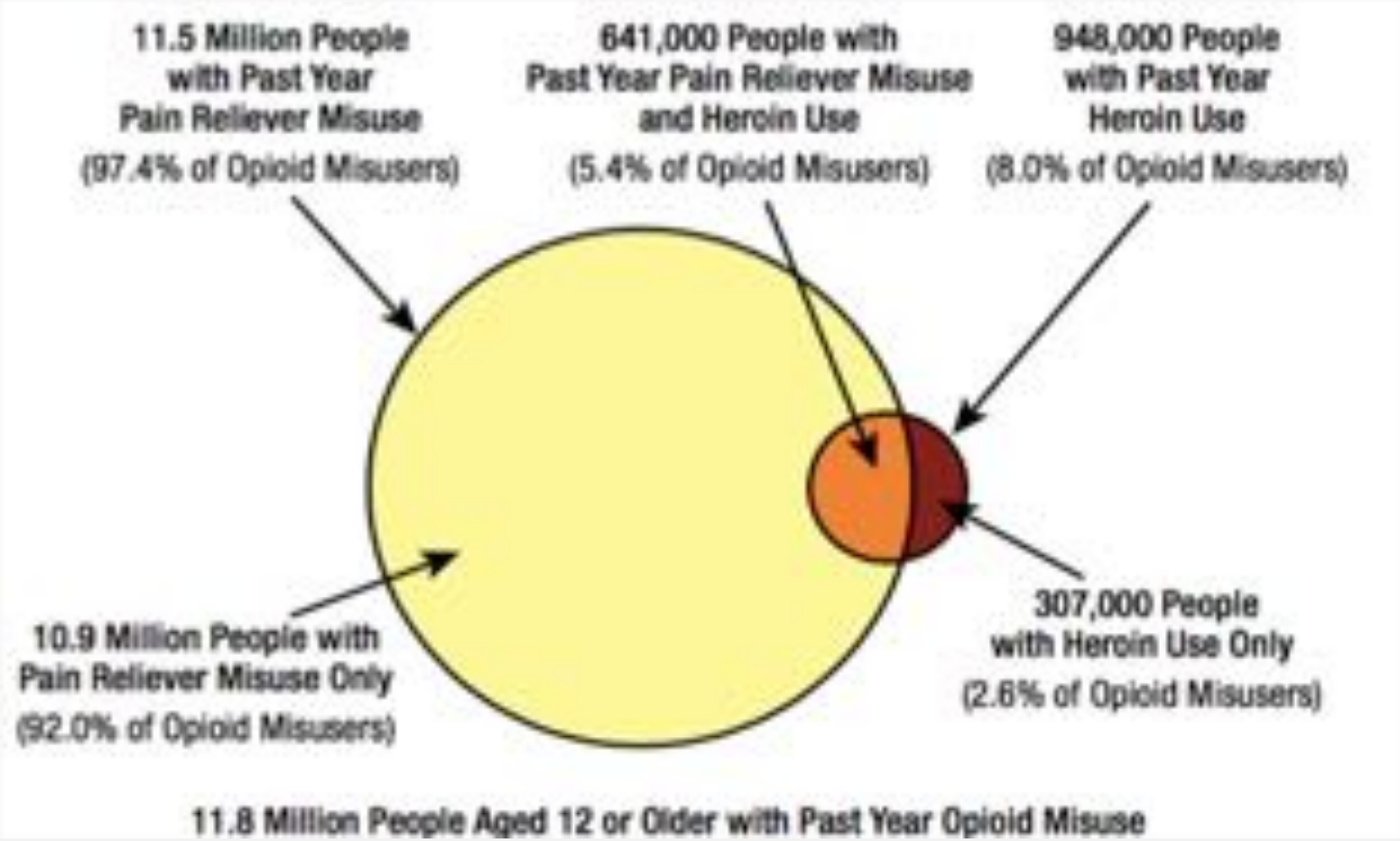
Their Impact Exceeds Their Numbers

Past Year Initiates for Specific Illicit Drugs among Persons Aged 12+: 2016



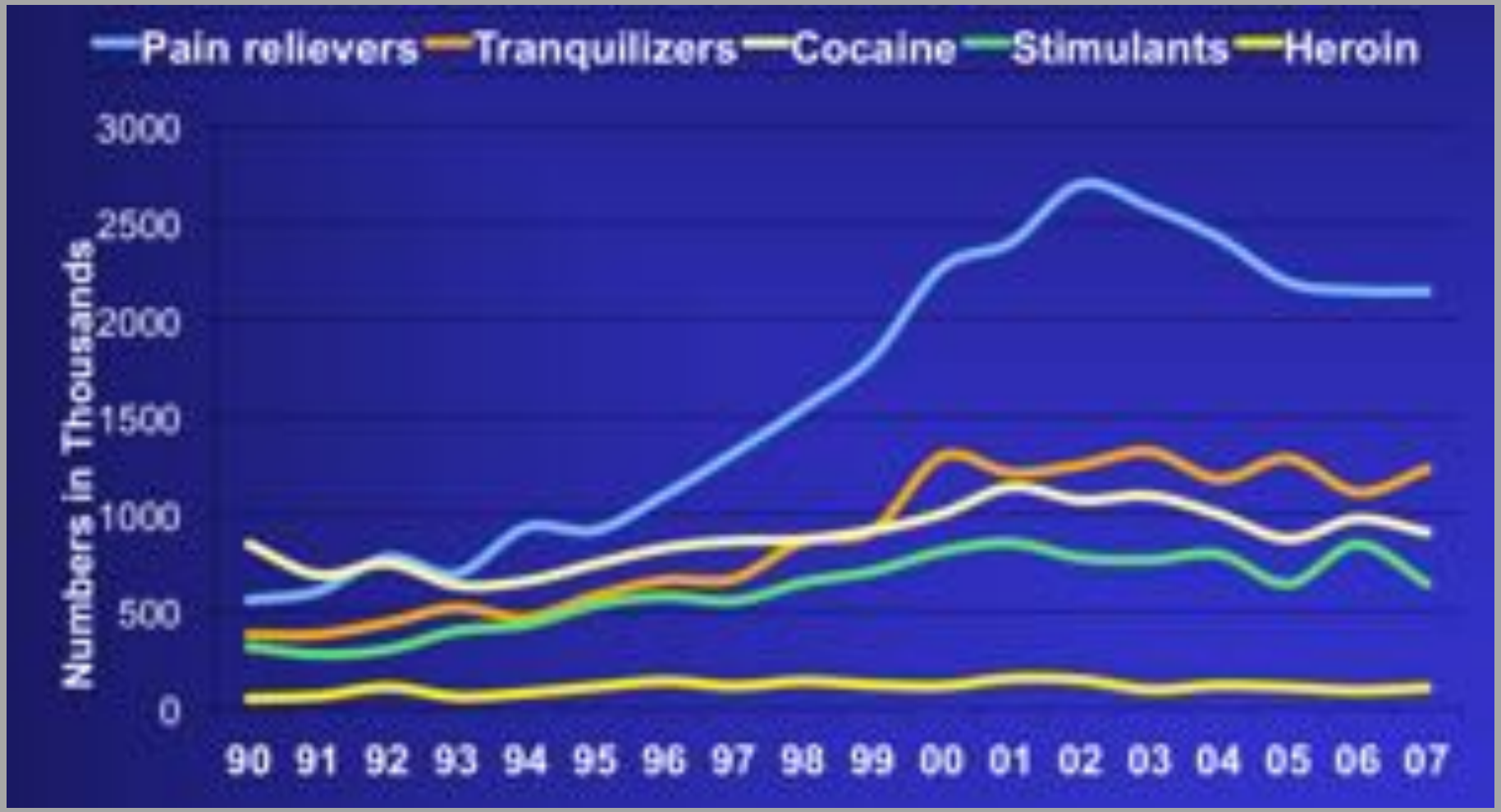
Source: SAMHSA Lipari et al.,2017, Fig. 11

NMUP Opioids far Exceeds Heroin Use in Persons Aged 12 or Older, U.S.



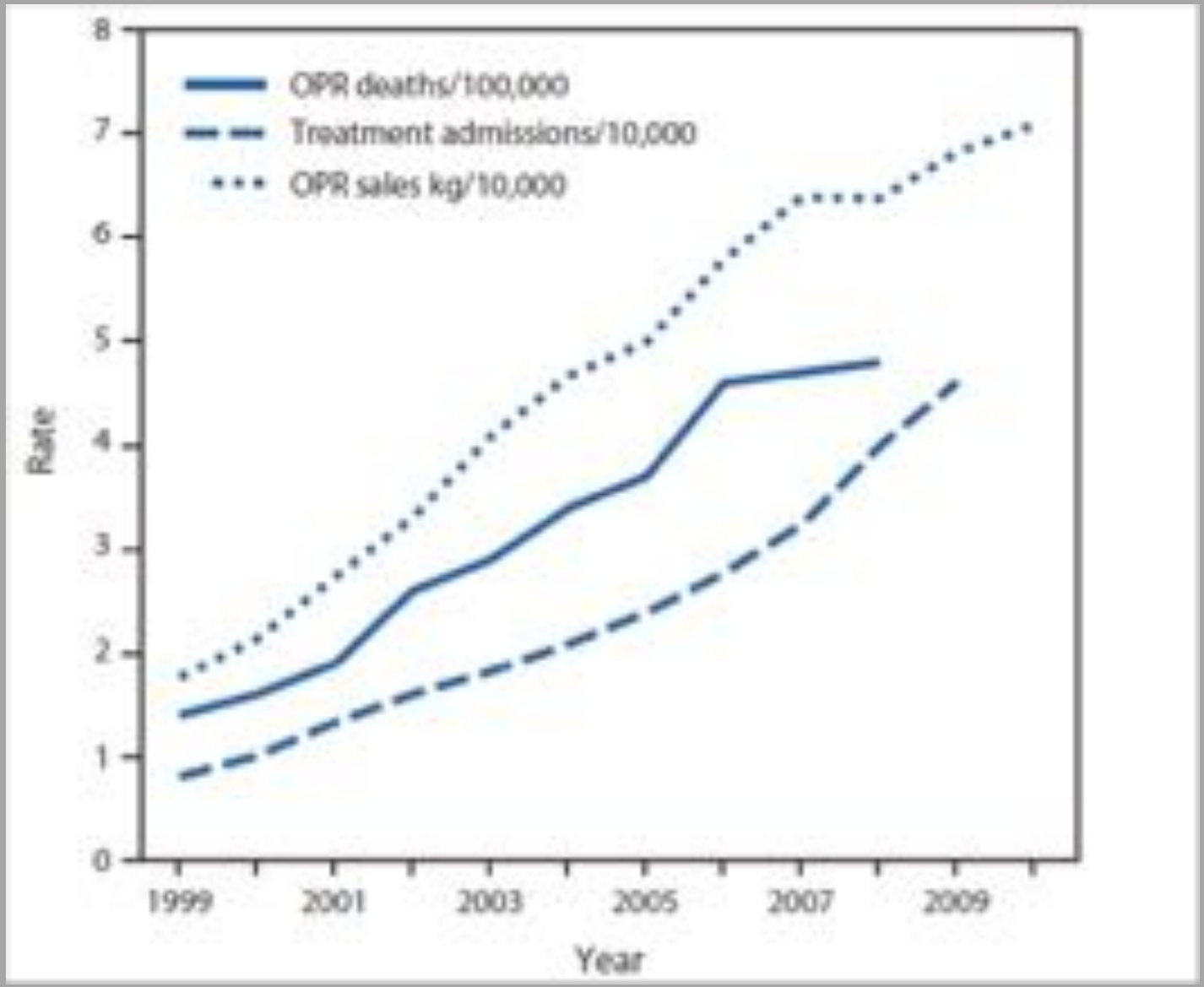
Source: NSDUH, 2017, Fig. 27

Estimated numbers of new nonmedical users in past year by type of drug, U.S., 1990-2007



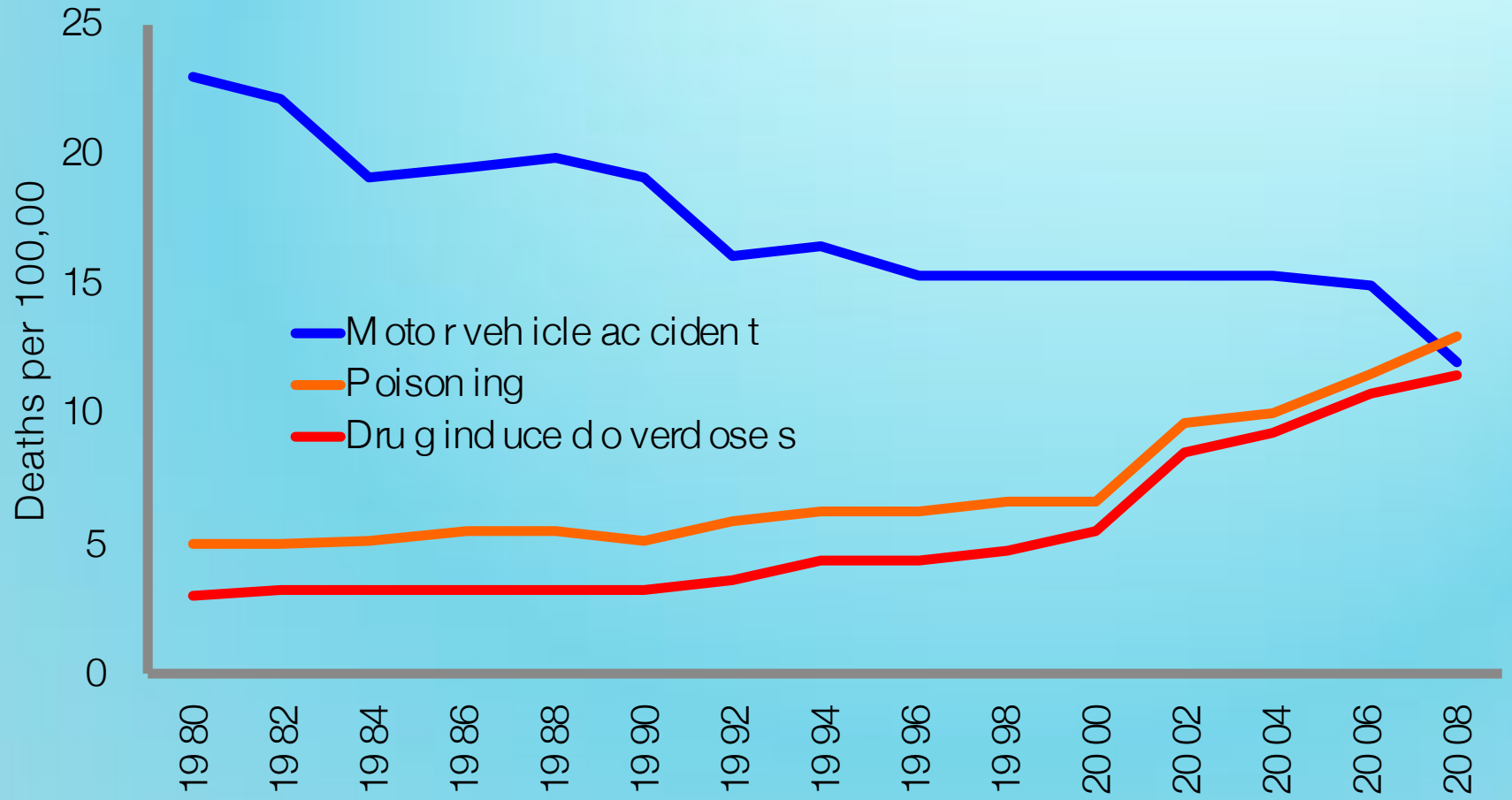
Source: SAMHSA NSDUH, 2006 and 2007

Overdose Deaths Paralleled Opioid Medication Prescribing



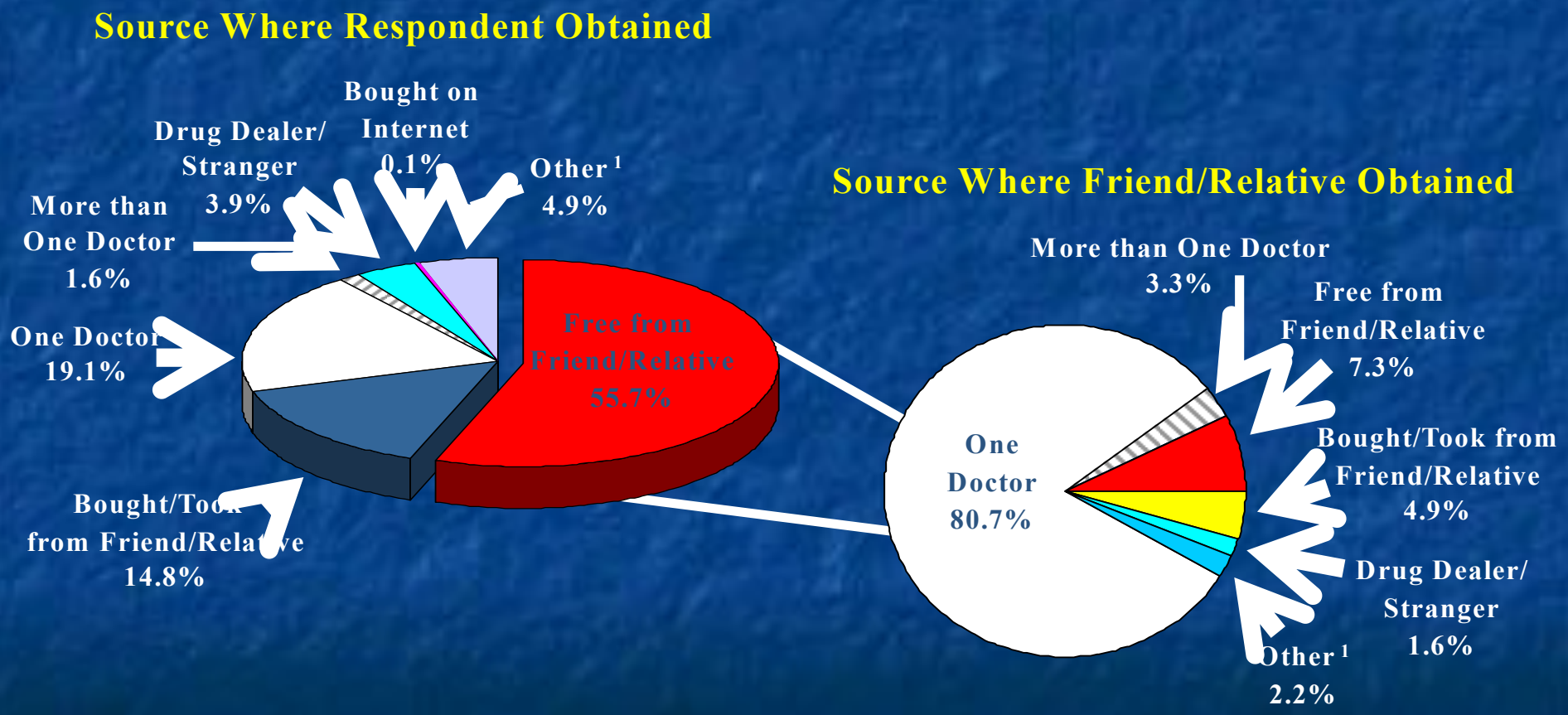
Source: MMWR, 11/4/11; 60: 1487-1492

Drug Overdoses now the Leading Cause of Accidental Death



In 2017, 115 people die each day of opioid overdose, a number estimated to rise to 131 in 2018 (USDHH 2018)

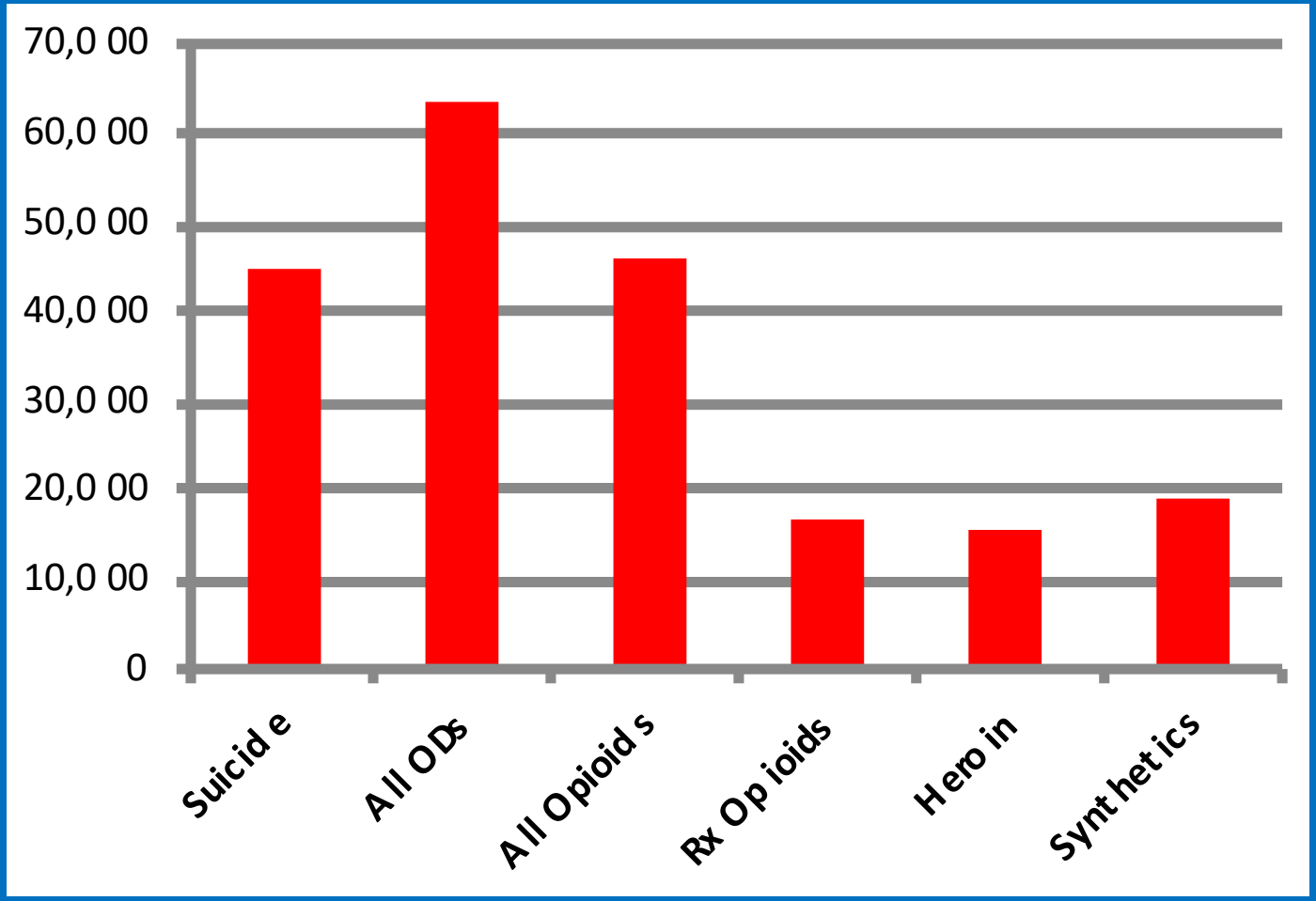
Source Where Pain Relievers Were Obtained for Most Recent Nonmedical Use among Past Year Users Aged 12 or Older: 2006



Note: Totals may not sum to 100% because of rounding or because suppressed estimates are not shown.

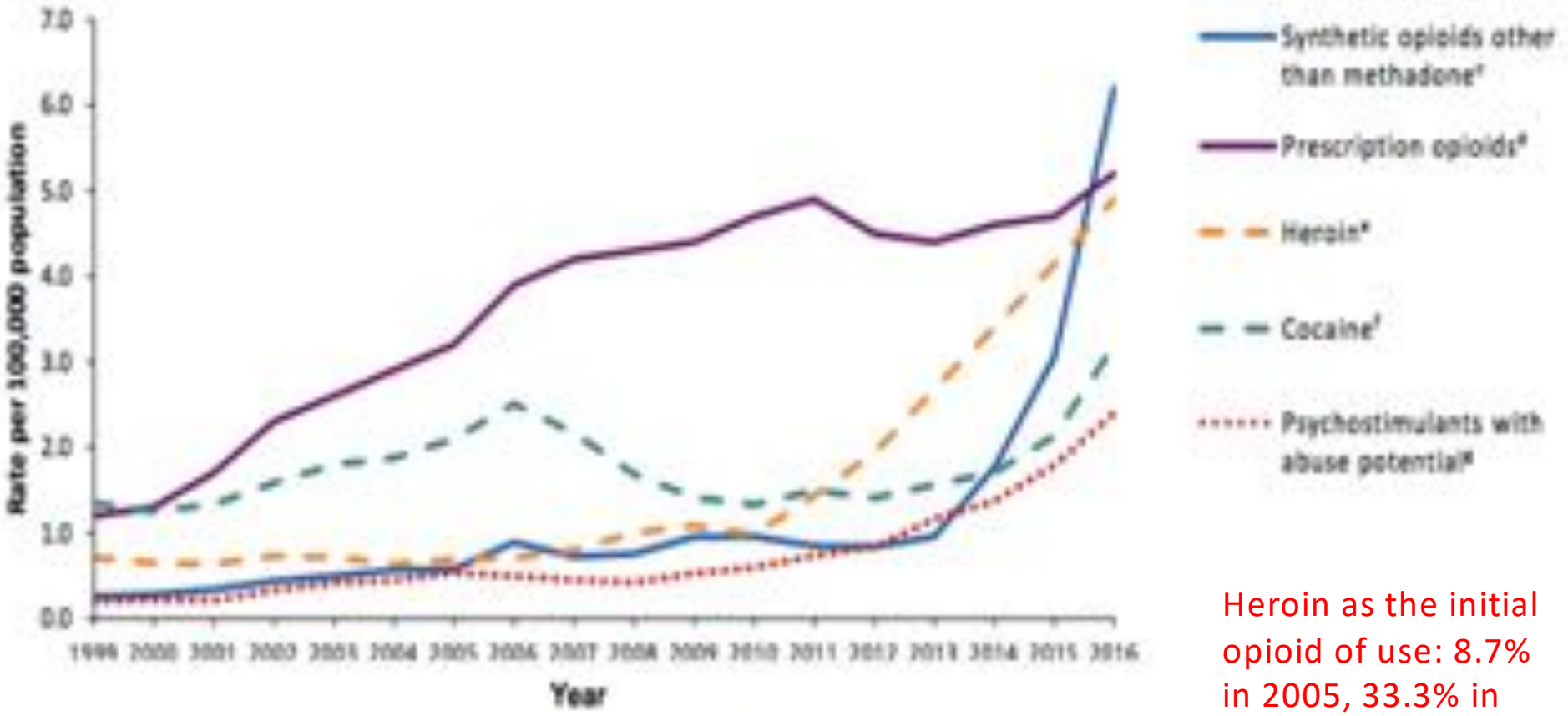
[1] The Other category includes the sources: "Wrote Fake Prescription," "Stole from Doctor's Office/Clinic/Hospital/Pharmacy," and "Some Other Way."

Annual Deaths from Drug Overdose and Suicide in United States



Sources: CDC 2018 and https://afsp.org/about-suicide/suicide-statistics/

Age-adjusted rates of Overdose Deaths, U.S.



Heroin as the initial opioid of use: 8.7% in 2005, 33.3% in 2015.

Source: CDC, 2018, Fig. 2.B

Cicero et al. (2017) Addict. Behav. 74: 63

How Do We Treat OUDs?

Recent Guidelines

- 2017: CDC Guideline for prescribing Opioids for Chronic Pain, accessed at https://www.cdc.gov/drugoverdose/prescribing/guideline.html
- 2015: The American Society of Addiction Medicine National Practice Guideline for the use of medications in the treatment of addiction involving opioid use. *J Addict Med* **9:** 358-367.
- 2018 Bruneau J et al. Management of opioid use disorders: a national clinical practice guideline. *CMAJ* **190:** E247-257.

ASAM PLACEMENT CRITERIA

LEVELS OF OF CARE	I. OUTPT	II. INTENSIVE OUTPT	III. MED MON INPT	IV. MED MGD INPT
CRITERIA				
Withdrawal	no risk	minimal	some risk	severe risk
Medical Complications	no risk	manageable	medical monitoring required	24-hr acute med. care required
Psych/Behav Complications	no risk	mild severity	moderate	24-hr psych. & addiction Tx required
Readiness For Change	cooperative	cooperative but requires structure	high resist., needs 24-hr motivating	
Relapse Potential	maintains abstinence	more symptoms, needs close monitoring	unable to control use in outpt care	
Recovery Environment	supportive	less support, w/ structure can cope	danger to recovery, logistical incapacity for outpt	

Treatment Settings for SUDs

ASAM Criteria Aim to Use the Least Restrictive Settings Possible

- 12 Step Meetings
- Outpatient Individual and Group Treatment
- Intensive Outpatient Programs
- Residential Rehabilitation Programs
- Inpatient Medical Units

Locations Where Past Year Substance Use Treatment Was Received among Persons Aged 12 or Older: 2013

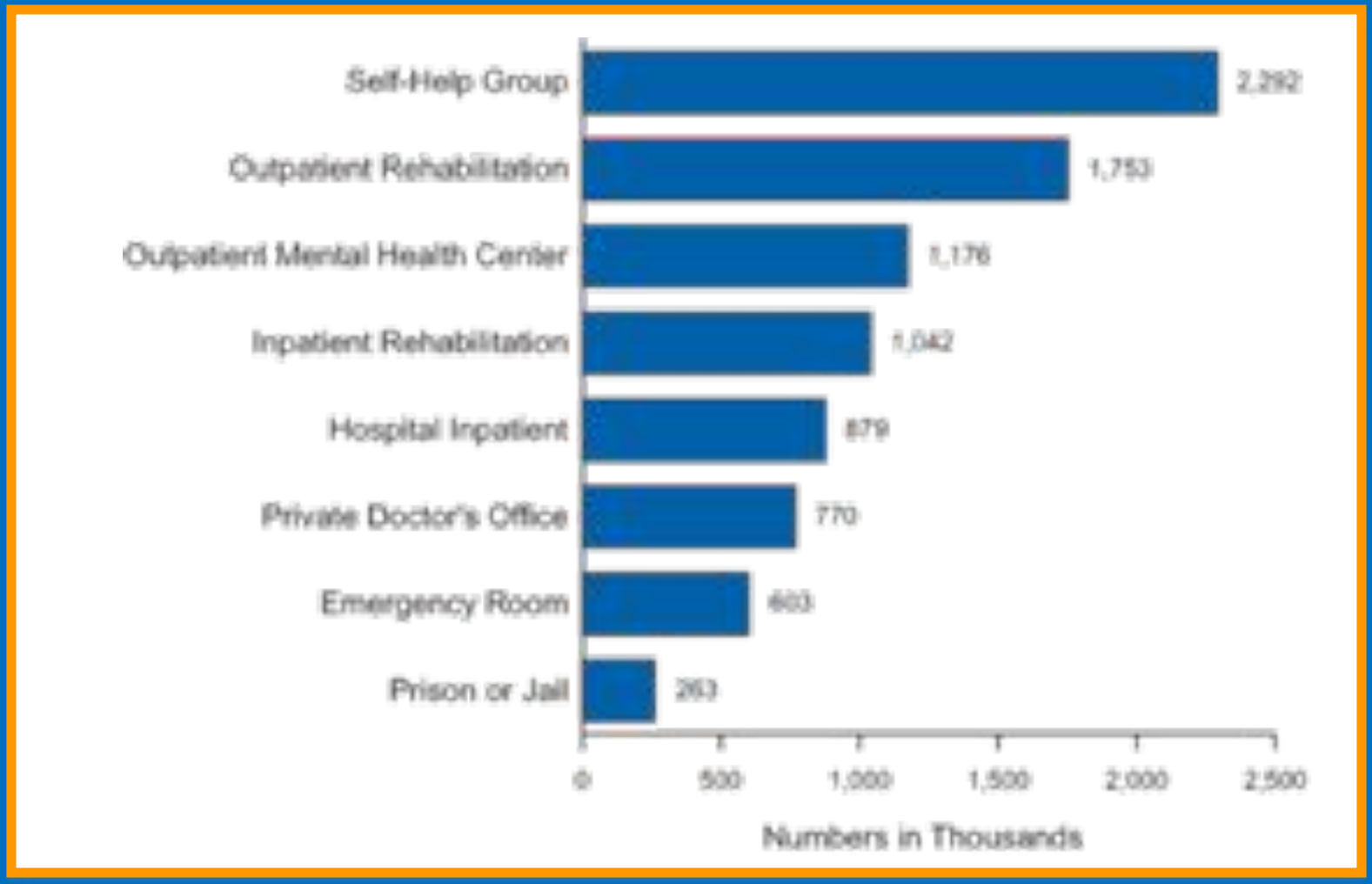
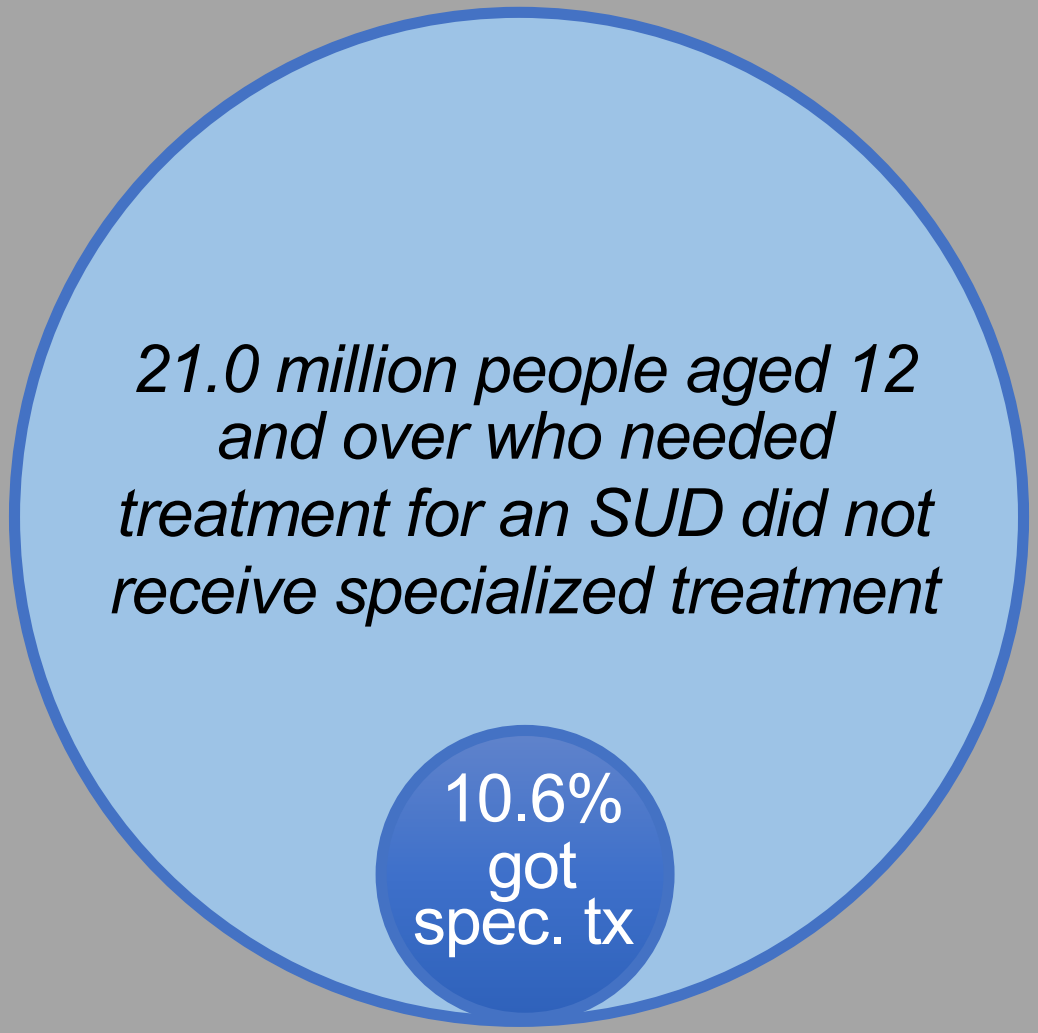


Figure 7.7 NSDUH 2014

The Challenge



Data from SAMSHA NSDUH 2017

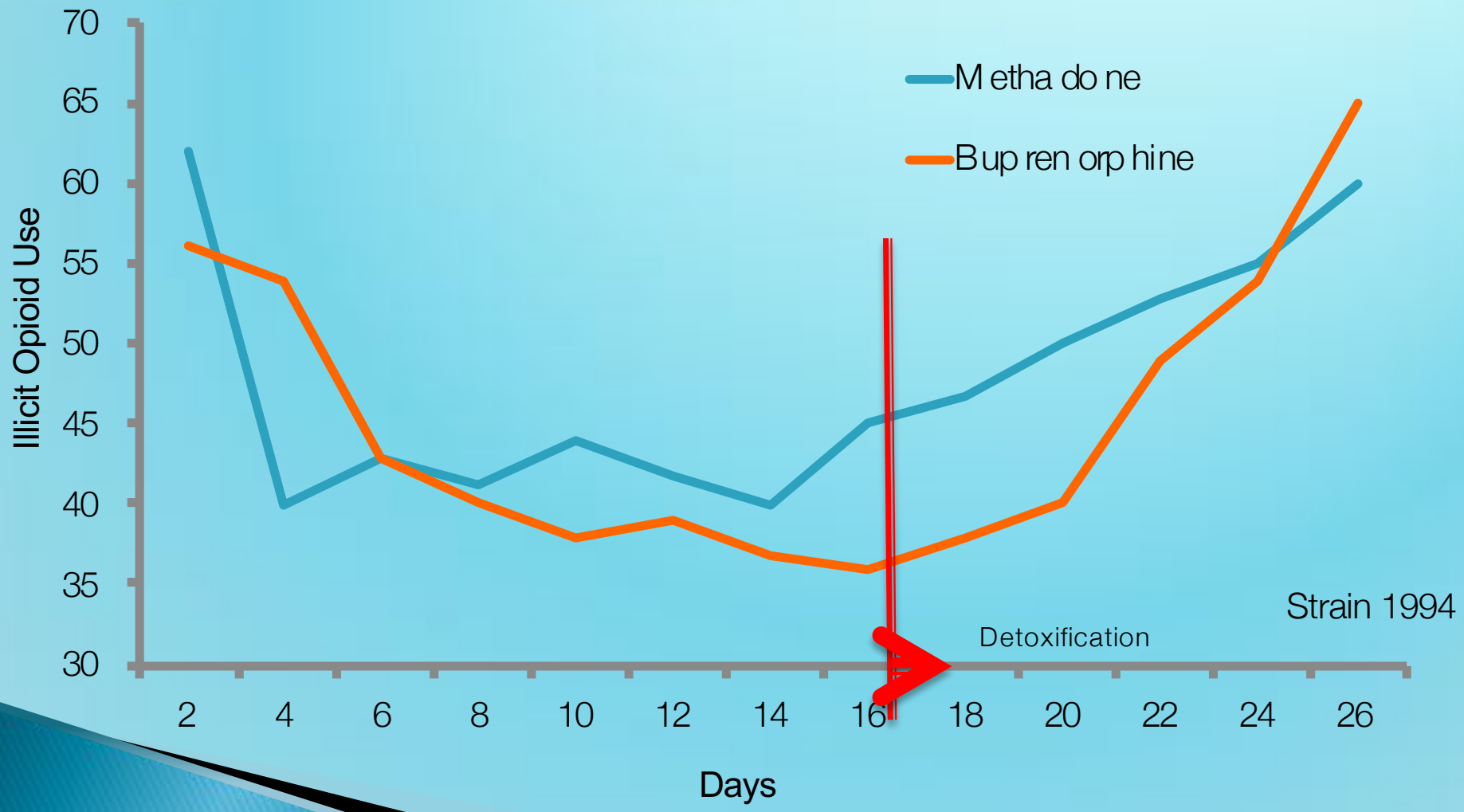
Standard of Care for Treatment of OUD

- Screen for and Identify those with OUD – includes EDs, PCP offices etc.
- If an OUD is identified, options for MAT to be discussed and made be available
- Detoxification alone is NOT TREATMENT
- Goal - reduce the huge harm now caused by OUD, including #1 cause of accidental death in those 15 – 50 AND improve lives of those with OUD.

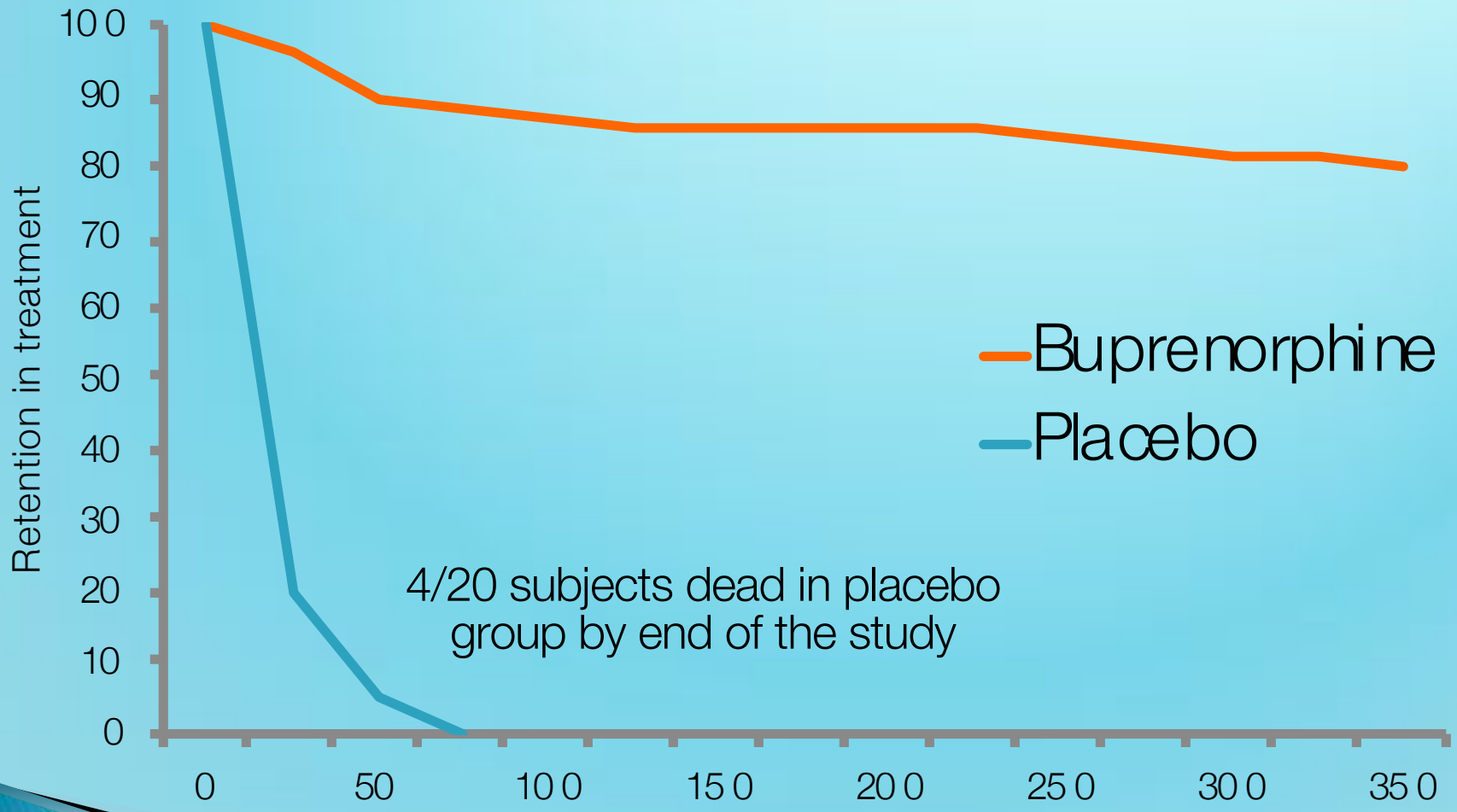
Historical Approaches to Treatment of OUDs

- Make it illegal to treat the problem (Harrison Act, 1914) i.e. they brought it on themselves.
- Force them to comply - abstinence
- Imprison them or wall them off.
- Treat them

Treatment leads to reduced illicit opioid use but relapse occurs after detoxification



Even with extensive psychosocial support, difficult to stay in treatment after detoxification compared to maintenance with buprenorphine

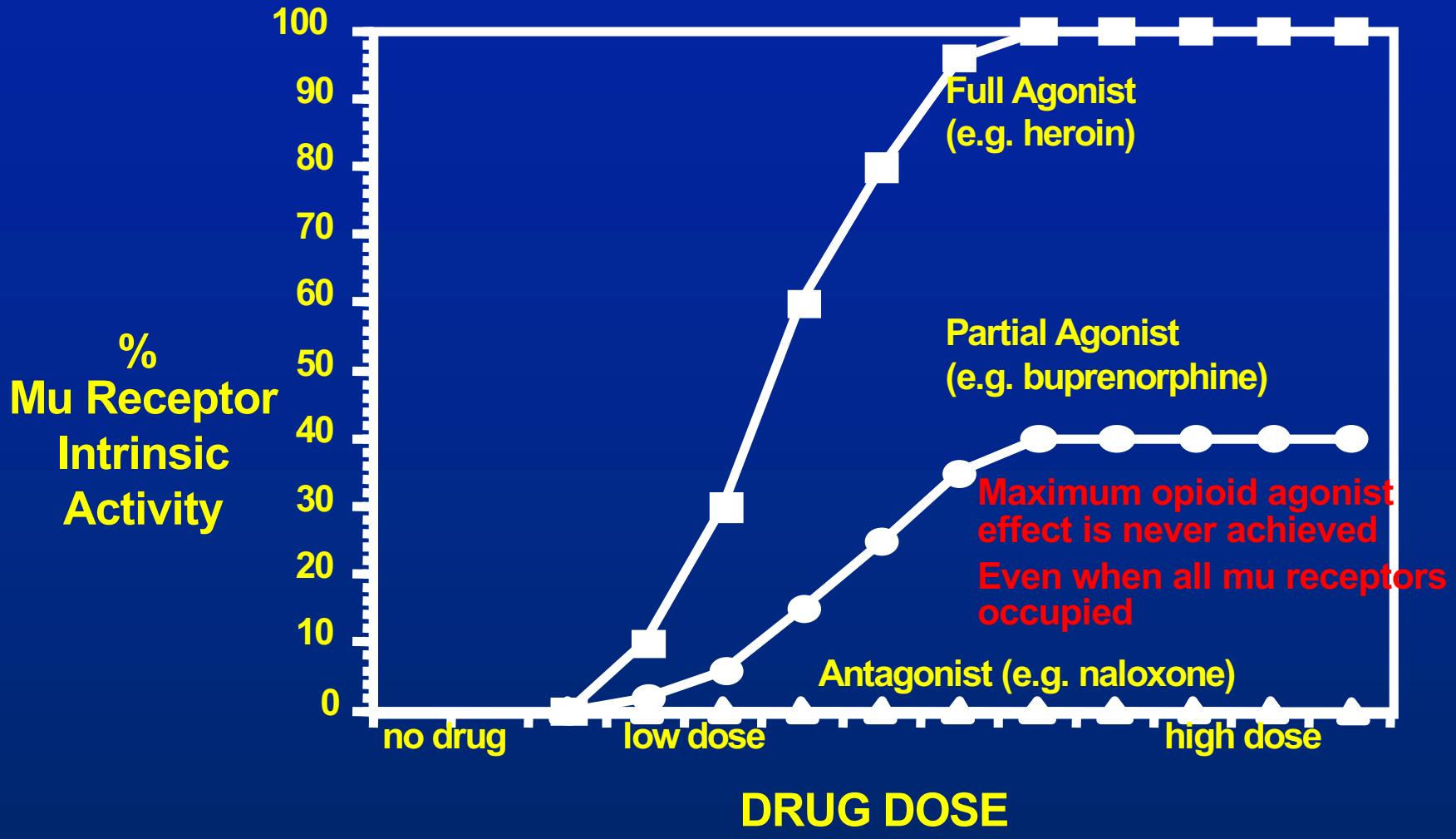


Kakko 2003

Pharmacotherapy of OUDs

- Replacement therapy vs. blockade
- Methadone 1972
- Buprenorphine 2001
- IM Naltrexone 2010 (oral 1984)

Comparison of Activity Levels



Methadone

- Methadone
  - Schedule II
  - Highly regulated
  - Narcotic Treatment Program settings
  - Approved for pregnancy
- Clear Improvement in:
  - Treatment retention (= stability and survival)
  - Reduction in contraction of HIV/HepB/HepC
  - Reduction in re-incarceration
  - Re-entry into workforce
  - Lifestyle stabilization and improved health

Ball and Ross, 1988

Buprenorphine

- Buprenorphine is a Schedule III medication approved by FDA in 2002 for treatment of opioid dependence
- It can be prescribed from office-based practices by physicians who have received a waiver from the DEA; this generally requires successful completion of an 8 hour training
- Office-based prescribing and up to 30 days prescription is an advantage to patients who fear stigma of NTPs and who do not wish to attend clinic daily to obtain medication
- Obtaining primary/mental health care and treatment of opioid dependence from one physician would improve overall health outcomes by making it easier for patients to receive the care they need in one clinical setting

Buprenorphine

- Partial opioid agonist
- Binds opioid receptors; slow to dissociate
- Dosing may be daily, every other day or three times weekly
- Tablets and rapidly dissolving film strip
- Average target dose: 8/2 to16/4 mg daily
- Use buprenorphine/naloxone (4:1) combination for opioid dependence (exception: pregnancy; use mono formulation product)
- Little effect on respiration or cardiovascular responses at high doses; but combined with other drugs can have serious AE's or death

Efficacy of Methadone vs. Buprenorphine

- Maintenance on methadone vs. buprenorphine/naloxone near equivalent in terms of treatment retention, prevention of relapse etc.
- Buprenorphine has better safety profile, and more flexible availability

Nielson et al (2016) Cochrane Database Syst Rev: CD011117
Mattick et al. (2014) Cochrane Database Syst Rev: CD002207
Sordo et al (2017) BMJ 357: 1550

Efficacy of IM Naltrexone vs. Buprenorphine

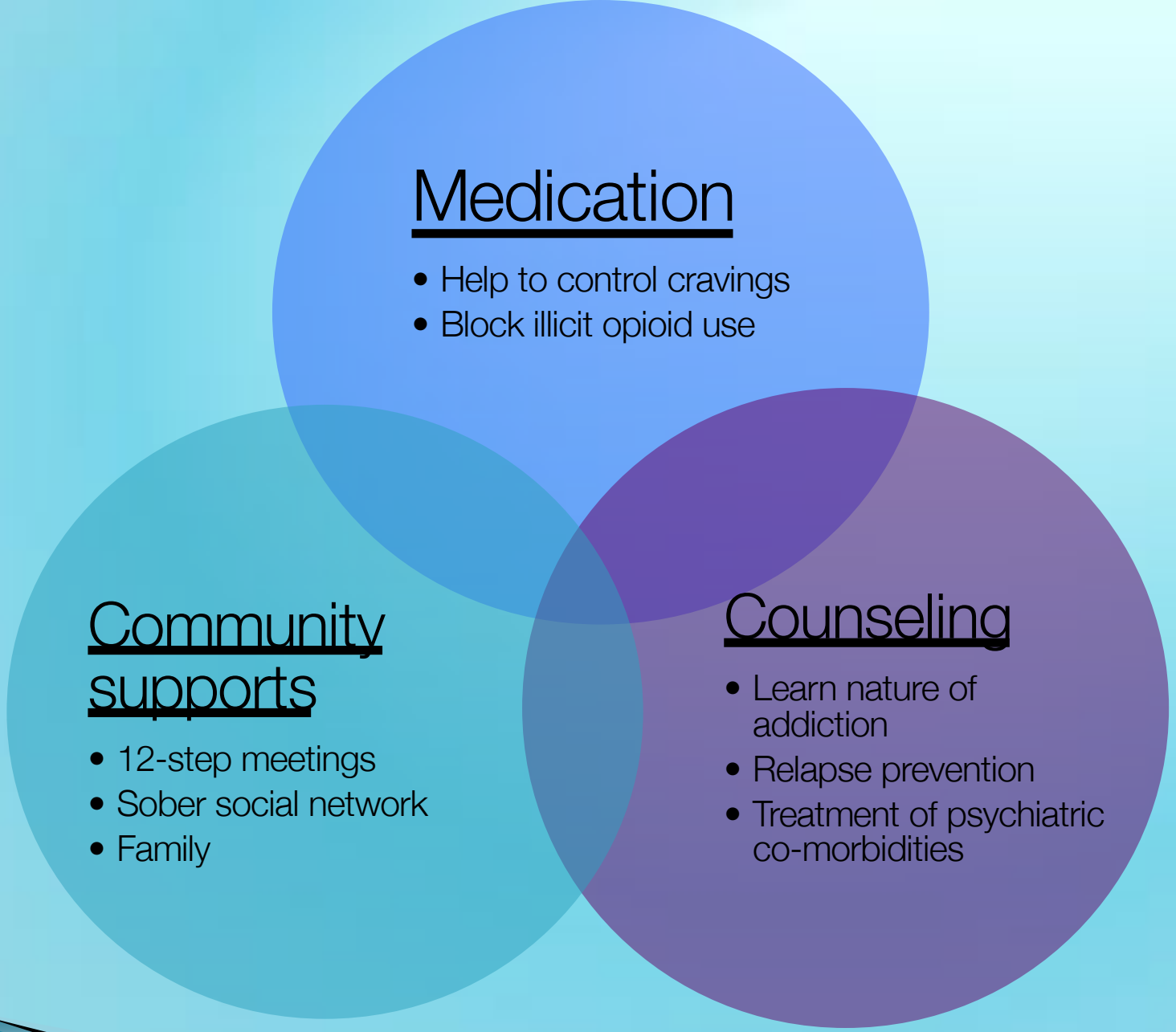
- X:BOT; *Lee et al. (2018) Lancet 391: 309-318.*
- XR-NTX (72%) harder induction than BUP-NLX (94%)
- Once initiated, equal 24 week relapse rates
- Craving lower in the XR-NTX group, no difference in overdoses

	Type of chemical	Satisfies cravings	Blocks illicit opioids
Naltrexone IM	Antagonist (no activation)	Maybe	Yes
Buprenorphine	Partial agonist (partial activation)	Yes	Yes
Methadone	Full agonist (full activation)	Yes	Yes (at higher doses)

Is the MAT patient addicted to another drug?

- *Per DSM-5 physiological dependence is not counted towards an OUD symptom if taken as prescribed; in the absence of loss of control and adverse consequences, one does not meet criteria for an OUD*
- *This has confused even health professionals, and was a main reason "dependence" was removed from the SUD vernacular.*
- *In the context of a condition defined as chronic and relapsing, and a "brain disease," the pejorative opinion against methadone and buprenorphine only exists as an extension of stigma against the person with drug-addiction.*
- *It's a war on drugs, not a war on the drug addict!*

	Heroin	Methadone	Buprenorphine
Loss of Control (Unable to stop using)			(if injected)
Cravings (Strong urges to use)			(if injected)
Compulsive (wanting to take more and more)			(if injected)
Consequences (keep using despite life getting worse)			(if injected)
Improve health, stay out of legal trouble, keep a job…..			


Medication
• Help to control cravings
• Block illicit opioid use
Community supports
• 12-step meetings
• Sober social network
• Family
Counseling
• Learn nature of addiction
• Relapse prevention
• Treatment of psychiatric co-morbidities

Abstinence-based Treatment is Ingrained in the Addiction Treatment Community

- Abandoning many hard learned lessons and rules of abstinence-based treatment is hard for many.
- The fact many people who have recovered from substance use disorders through abstinence may feel hypocritical to now embrace a different approach.
- Many still feel addiction is a volitional, moral failing that should be punished, not treated

Harm Reduction Principles

- Humanism (principles of MI, why do they do what they do)
- Pragmatism (abstinence may be unachievable)
- Individualism (what will work given strengths/stressors)
- Autonomy (patient-centered care)
- Incrementalism (emphasize the positive over the negative)
- Accountability w/o Termination (personal responsibility is not abandoned, but neither is the patient)

Hawk et al. (2017) *Harm Reduction J* **14:** 70-79

Harm Reduction Practices developed from a Public health Perspective:

- MAT
- Naloxone-overdose kits and first-responder/partner training
- Housing-First
- Meeting the patient where they are (program expansion, flexibility)
- Expansion into corrections, underserved areas

Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, Alexander GC. The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. Annual Review of Public Health. 2015; 36:559–574.

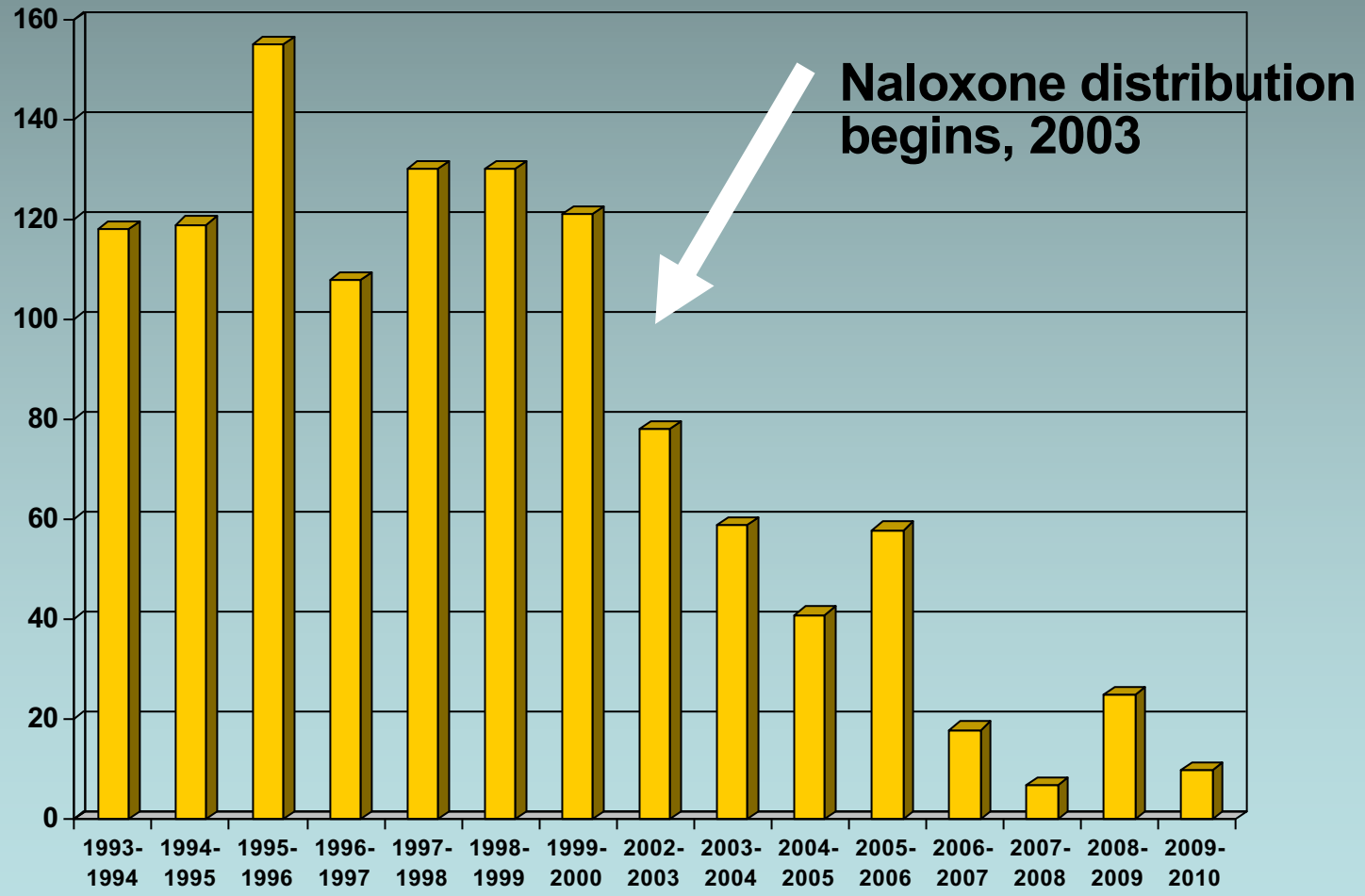
MAT and Harm Reduction:

- Reduce the spread of HIV and hepatitis B/C
- Reduce the adverse effects of OUD
- Reduce recidivism for re-incarceration
- Reduce physically and legally risky use
- Reduce social disruption

https://www.cdc.gov/hiv/rosk/ssps.html;
Kolodny et al., (2015) *Ann Rev Pub Health* 36: 559–574

Naloxone Rescue Formulations

Heroin-related Deaths, San Francisco: 1993-2010



*Data compiled from San Francisco Medical Examiner's Reports, www.sfgsa.org
**no data available for FY 2000-2001

Summary

- Any definition of addiction must include recognition of impulsive use driven by reward, compulsive use driven by avoidance of going without the substance, and its chronic, relapsing nature.
- The current epidemic of opioid use disorders has had severe societal impacts.
- Treatment of OUDs is moving from an abstinence-based approach to a harm reduction approach.

References

Ducci F, Goldman D (2012) The genetic basis of addictive disorder. Psychiatr Clin North Am 35: 495-519.

Feng J, Nestler EJ (2013) Epigenetic mechanisms of drug addiction. Curr Opin Neurobiology 23: 521-528.

Koob GF, Volkow ND (2016) Neurobiology of addiction: a neurocircuitry analysis. Lancet Psychiatry 3: 760-773.

Textbook of Substance Abuse Treatment, 5th Ed. M Galanter, HD Kleber, KT Brady, eds., American Psychiatric Publishing, Arlington, VA

USDHHS, Office of the Surgeon General, Facing Addiction in America; The Surgeon general's Spotlight on Opioids. Wash. DC, HHS, Sept. 2018

NSDUH – National Survey in Drug Use and Health

MMWR Morbidity and Mortality Weekly Review

Past Year Initiates Aged 12 - 49: 2016

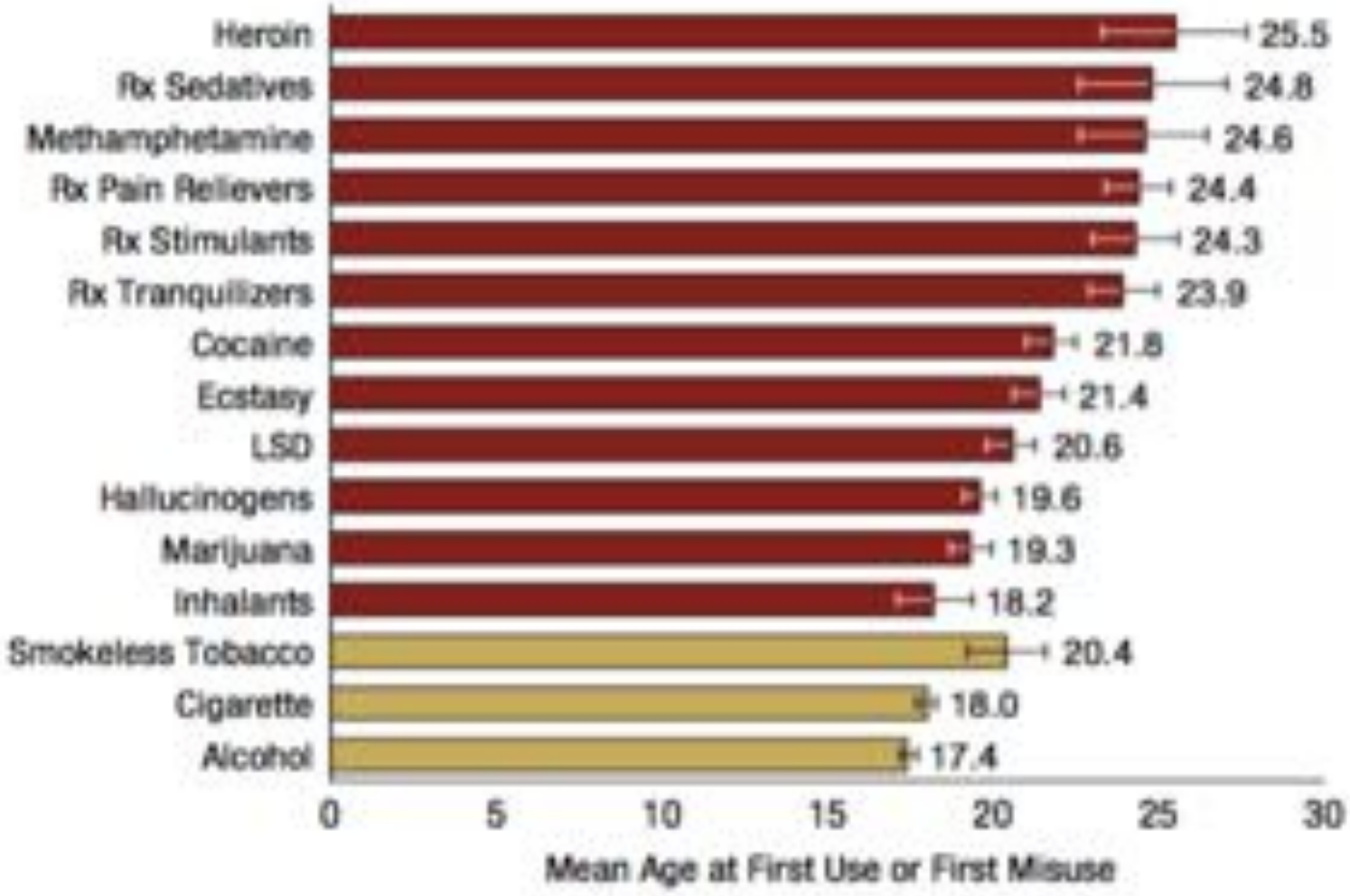


Fig 12, Lipari et al., NSDUH Data Review 2017

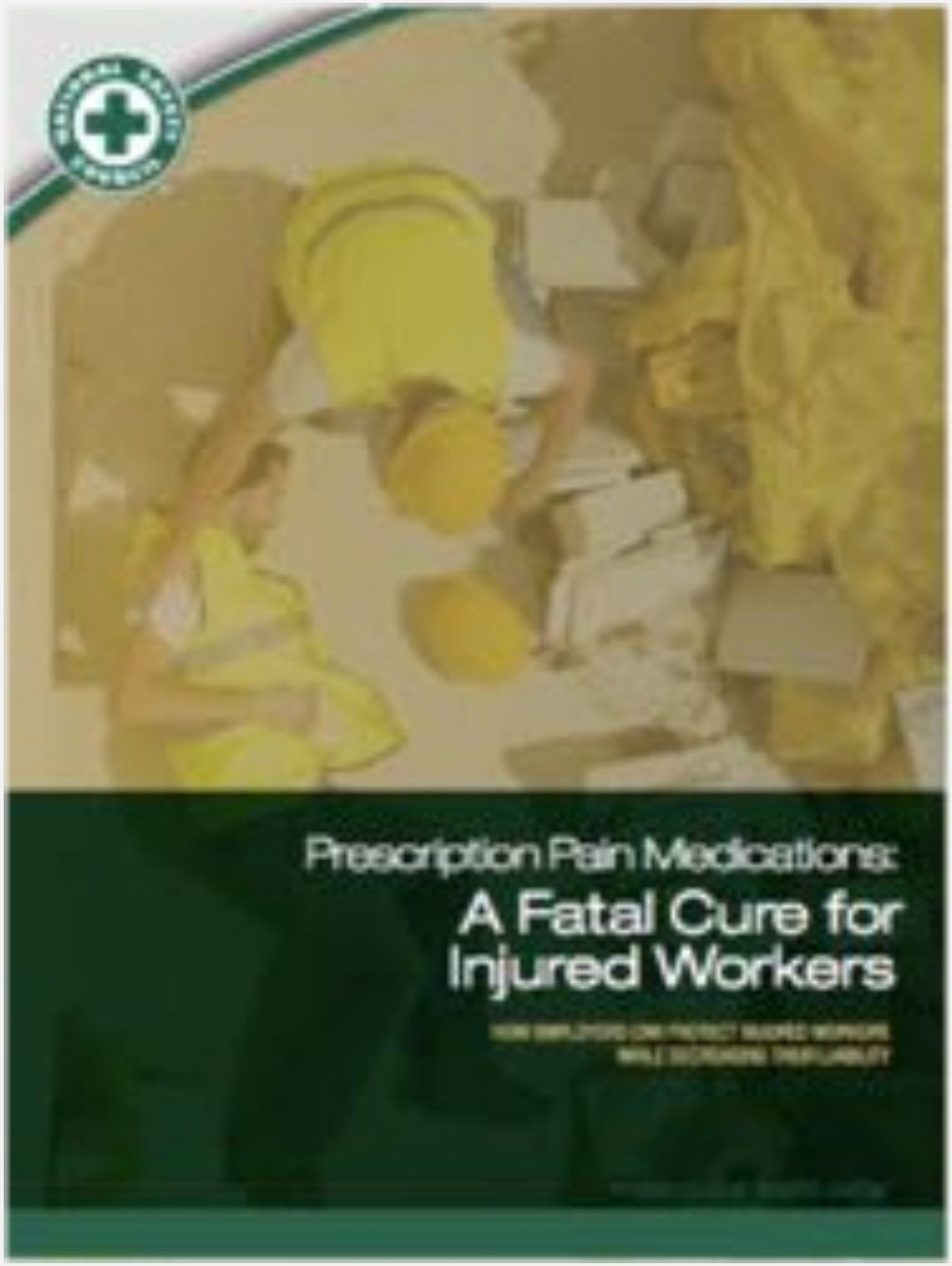
Don’t be an Ostrich!

Approximately 75% of those with an SUD are employed. https://www.samhsa.gov/workplace/toolkit/assess-workplace).

Opioid prescribing in an industrial workforce cohort doubled between 2003 and 2013 (Pensa, Galusha and Cantley (2018) *JOEM* 60: 457).

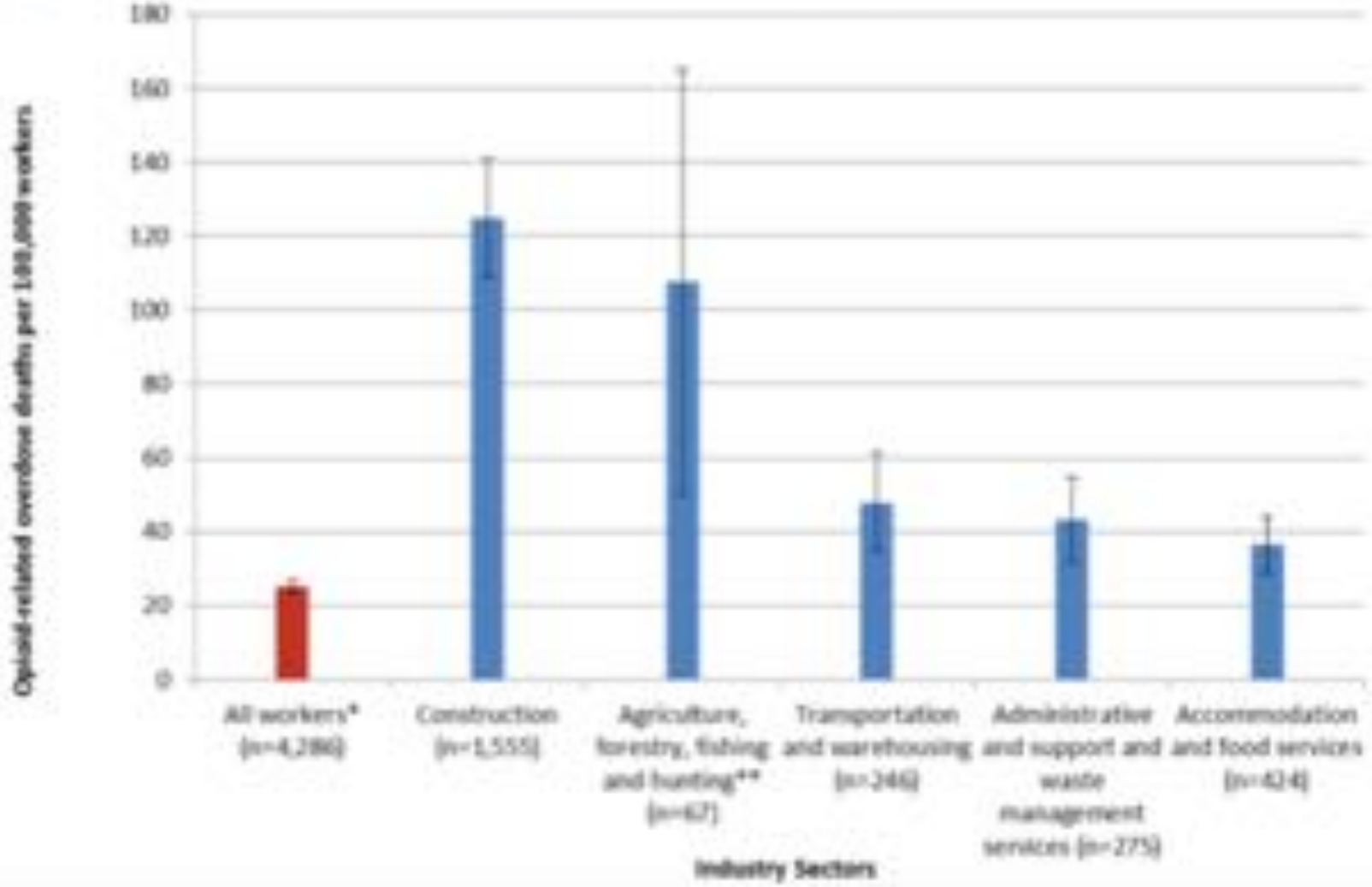
Opioids account for 29% and rising of WC prescription costs (https://blogs.cdc.gov/niosh-science-blog/2014/05/14/opioid-abuse/).

Guidelines for prescribing opioids in the workforce do not clearly address impairment other than the risk of addiction, overdose, tolerance etc. (Mai 2015)



The National Safety Council: http://safety.nsc.org/workerscomp?utm_medium=(none_&utm_source=(direct)&utm_campaign+workerscomp; also at http://www.acoem.org/PrescriptionPainMedicine.aspx

Figure 1. Industry sectors with opioid-related overdose death rates significantly higher than the average rate for all workers, Massachusetts workers, 2011-2015, n=4,302



Massachusetts Dept. of Public Health, Occupational Health Surveillance Program (2018) Opioid-related Overdose Deaths in Massachusetts by Industry and Occupation, 2011-2015; Also see MMWR (2018) 67: 925 (8/24/18).

Workplace Effects of Opioids

In the past, workplace drug testing and policies covered opiates associated with illegal use and addiction.

The widespread prescribing of opioid pain medications has been allowed through MRO review of drug screening, except in case of DOT regulated industries, where narcotic proscription is more strict.

But as we have reviewed, opioid prescribing parallels development of opioid use disorders, overdoses etc.

Opioid prescribing is directly linked to worsening course of disability (reviewed in Deyo et al. 2015).

Workplace Effects of Opioids

Opioid misuse and untreated substance use disorders are well known to reduce productivity, increase absenteeism, increase accidents on the job, reduce employee morale, and increase disability payments.

A key unanswered question is whether legal opioid use results in impairment relevant to one's job functions.

In 2014 ACOEM released practice guidelines[1] stating: "Acute or chronic opioid use is not recommended for patients who perform safety-sensitive jobs."

1: Hegmann et al., (2014) *JOEM* **56:** e46.

Workplace Effects of Opioids

Controversy exists as to whether *chronic* opioids result in impairment greater than fatigue, irritability etc. resulting form untreated pain.

Acute opioid exposure or ongoing opioid use disorder, are accepted to represent unacceptable risk of impairment.

Does MAT on buprenorphine or methadone preclude one from safety-sensitive work?

Are those on Methadone or Bup Impaired?

Meta-analyses support impairment in working memory, cognitive speed and aggressive responding for those on methadone or buprenorphine (*e.g.,* Manglione et al. (2018); Strand et al. (2013).

These studies have assessed to quality of the evidence as low, and so do not go so far as the ACOEM guidelines proscribing safety-sensitive work. They mainly focus on effects on driving ability.

Standardization of testing or specific testing of individual job performance would reduce unnecessary exclusion of employees, as well as stigma and avoidance of seeking MAT.

Workplace Policies

Testing and Screening – expand the DOT 5 UDT; worker's rights may collide with employer's policies; include a risk screening as pre-employment (SOAPP-R, ORT etc.)

Prevention – quality EAP program, educational materials, drug prevention day etc., anonymous reporting procedures; inform EEs of policies, to notify the employer if prescribed opioids

Training, see "Using naloxone to Reverse Opioid Overdose in the Workplace: Information for Employees and Workers, https://www.cdc.gov/niosh/docs/2019-101/).

Have a Clear infractions Policy – supervisors and HR take non-judgmental stance, supervisor comfortable with policy and procedures

Policy that allows outlet for treatment w/o termination, demotion etc.

?Performance testing for those on Opioids

References (2)

Deyo RA, Von Korff M, Duhrkoop D (2015) Opioids for low back pain. BMJ 350:

Hegmann et al. (2014) ACOEM Practice Guidelines: Opioids and Safety-Sensitive Work. J. Occ. Environ. Med. 7: e47-e53.

Mai J, Franklin G, Tauber G (2015) Guideline for prescribing opioids to treat pain in injured workers. Phys. Med. Rehabil. Clin. N. Am. 26: 453-465.

Manglione et al. (2018) Effects of medication assisted treatment (MAT) for opioid use disorder on functional outcomes: a systematic review. J. Subs. Abuse Treat. 89; 28-51.

Strand et al. (2013) Can patients receiving opioid maintenance safely drive? Traffic Inj. Prev. 14:26-38.

Thank You for Your Attention