

Addiction Medicine in Primary Care

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Objectives

- Upon completing this activity, participants will learn:
 - 1) The background on the establishment of addiction medicine as a subspecialty.
 - 2) How to identify and evaluate patients with opioid, alcohol and benzodiazepine use disorders.
 - 3) How to manage opioid and alcohol use disorders with medications.

Disclosures

Minor stock-holdings in pharmaceutical companies-
none relevant to current presentation.

Outline

1. Addiction Medicine as a new subspecialty
2. Background
3. Primary Care involvement in managing substance use disorders.
 - a. Why?
 - b. How?
 - a. Screening
 - b. Assessment including interpretation of drug tests
 - c. “Medication Assisted Treatment” for opioid and alcohol use disorders

Medicine Responds to Addiction

ADDICTION MEDICINE: THE NEWEST MEDICAL SUBSPECIALTY

ADM SLIDES COURTESY OF DR. KEVIN KUNZ, EXECUTIVE VP, THE
ADDICTION MEDICINE FOUNDATION

Which Organizations Are Involved?

- American Board of Addiction Medicine (ABAM)
- The Addiction Medicine Foundation (TAMF)
- American Board of Medical Specialties (ABMS)
- American Board of Preventive Medicine (ABPM)
- ACGME
- National Center for Physician Training in Addiction Medicine (NCPTAM)
- Addiction Medicine Fellowship Directors Association (AMFDA)

Incorporated August, 2007



The
**Addiction
Medicine**
Foundation
*Advancing
Medical
Practice in
Addiction
Prevention
and Treatment*



(Previously named The ABAM Foundation)

Operational Success, 2007-16

- 3,900 ABAM diplomates
- ABAM MOC: 85% enrollment
- 45+ fellowships designed, established, TAMF accredited
- Fellowship goal of 125 by 2025 on track
- \$17 Million Invested

Strategic Success

- ABMS ADM recognition announced March 2016
- ACGME program accreditation process underway
- Linkages Built
 - House of Medicine, House of Addiction Medicine
 - Government
 - Philanthropy
 - Other sectors

Impact of ABMS Recognition of ADM on Medicine and Health Care

- Addresses stigma and ignorance by the medical profession
- Addiction is recognized as preventable and treatable
- Inclusion of ADM in GME and thus into medical education
- Improved quality and access to care
- True parity for patients and physicians

Benefit to Patients, Families, and Public Health

ADM: A Specialized Field of Medicine

Training-ACGME

ABAMF
Residencies

Standards
& Procedures

Core
Competencies

Certification-ABMS

Maintenance of
Certifications

Exam

Standards
& Procedures

Candidates
& Diplomates

ABAM Foundation

ABAM

ABMS, ABPM



- American Board of Medical Specialties
 - Recognition of Addiction Medicine announced March 2016
 - Addiction Medicine is a multispecialty subspecialty
- American Board of Preventive Medicine
 - Administrative sponsoring board for Addiction Medicine



Background

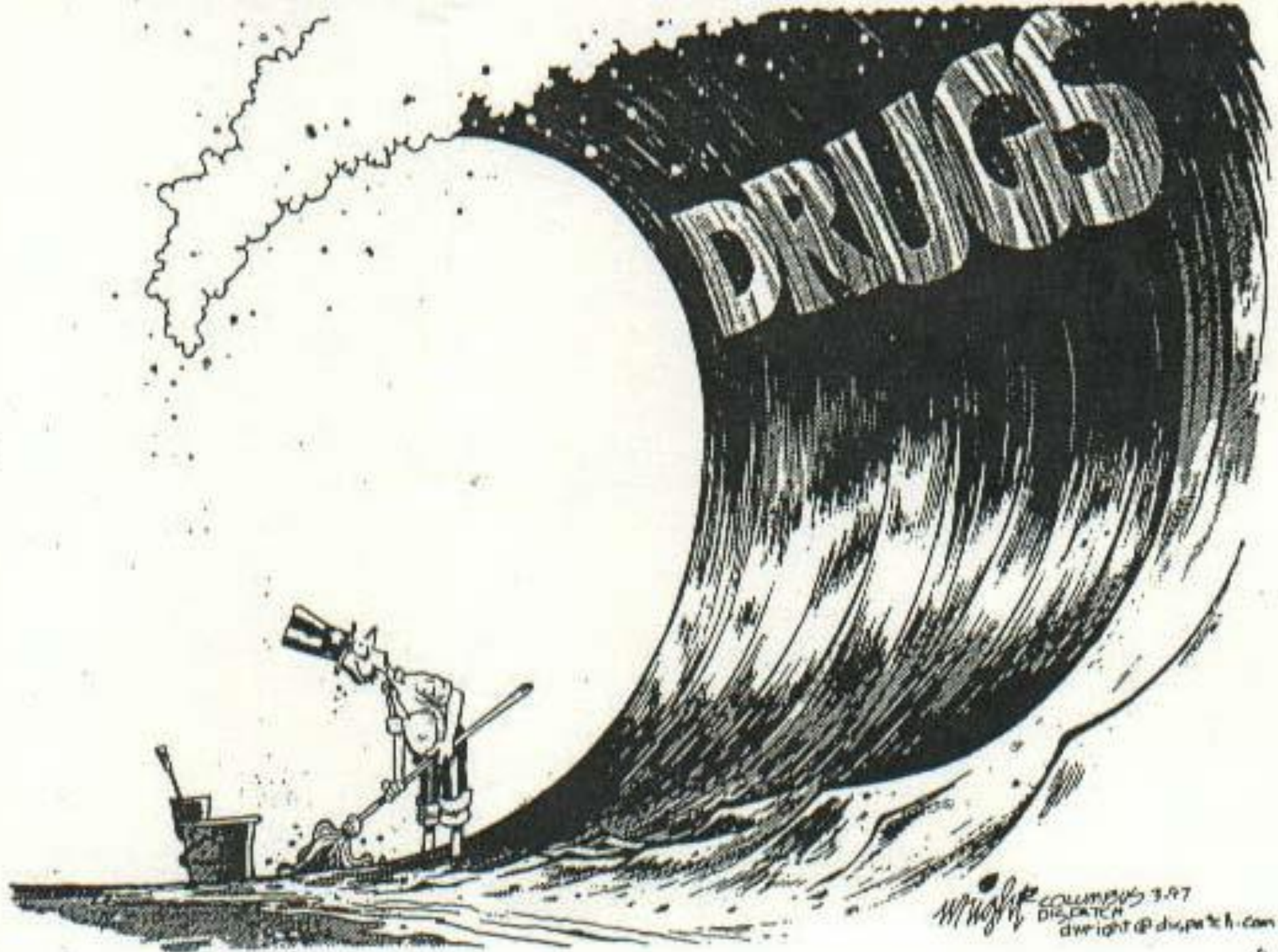
**HOW BIG IS THE PROBLEM? WHY
SHOULD PHYSICIANS DEAL WITH IT?**

Consider This

- A medical condition
 - runs a chronic course
 - causes many serious medical and surgical complications
 - is highly debilitating and potentially fatal
 - even when it does not kill, it has a profound impact on the health and lives of the patients, their families, and the society.

Now Consider This

- This condition has highly efficacious, cost-effective and safe treatments
- Treatment can lead to a full or partial remission in over 80% of cases and cut the risk of death by over 75%
- But less than a quarter of the patients can get it.
- What if we were talking about cancer, heart disease, diabetes, or virtually any other condition but an addiction?



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Continuum of Substance Use

Percent of Population Age 12+
by Level of Substance Use*



* Includes tobacco, alcohol, illicit drugs and misuse of controlled prescription drugs. Source: CASAColumbia® analysis of *The National Survey on Drug Use and Health* (NSDUH), 2010.

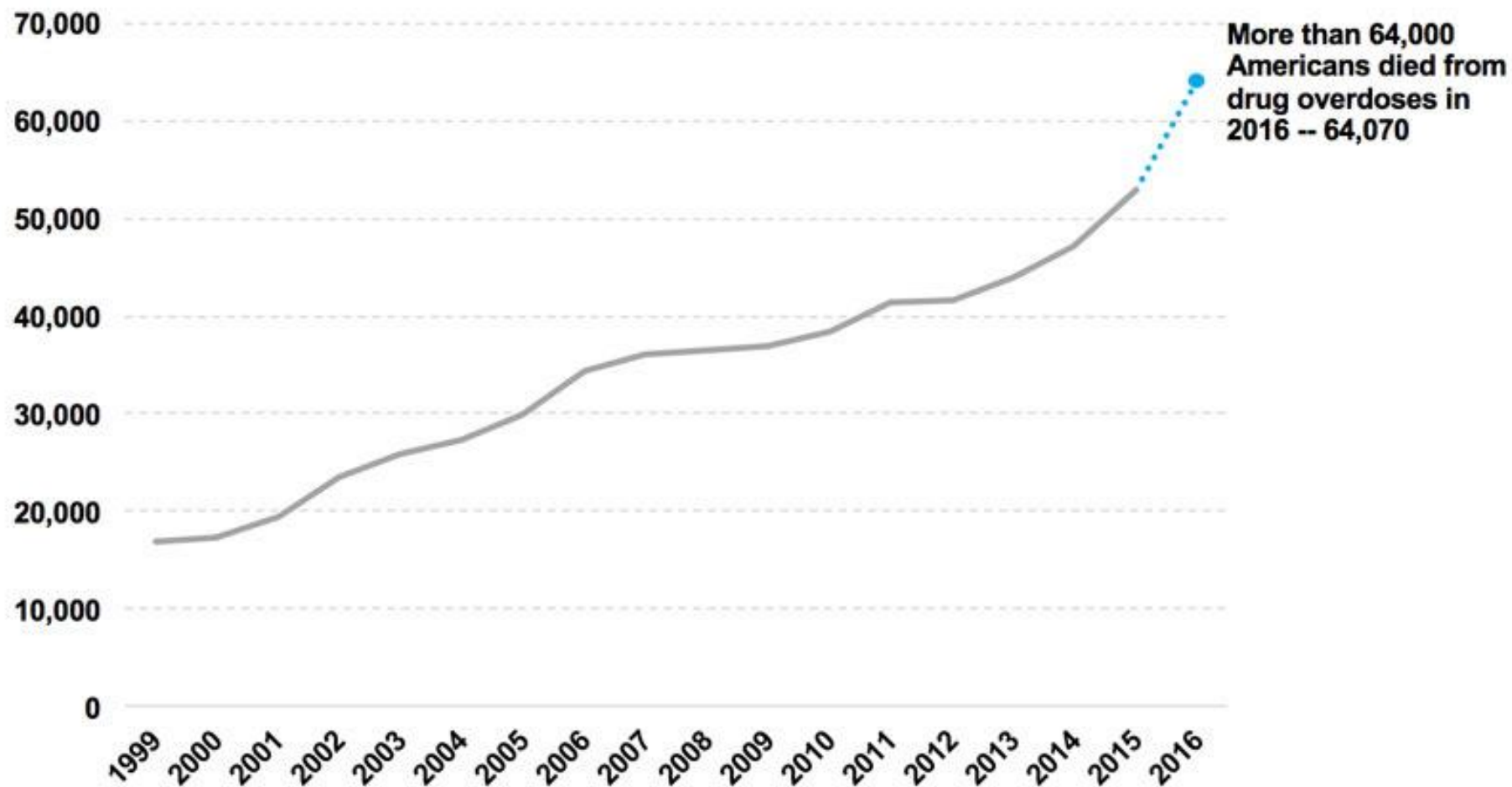
“An Urgent Health Crisis...”*

- “The opioid epidemic” is a growing problem nationally, with opioid use, misuse, addiction, overdose, death.
- Ever larger numbers of patients needing and receiving treatment for opioid use disorder.
- Still, fewer than a quarter of the patients who need treatment actually receive it.

– (*Vivek Murthy, MD, Former US Surgeon General)

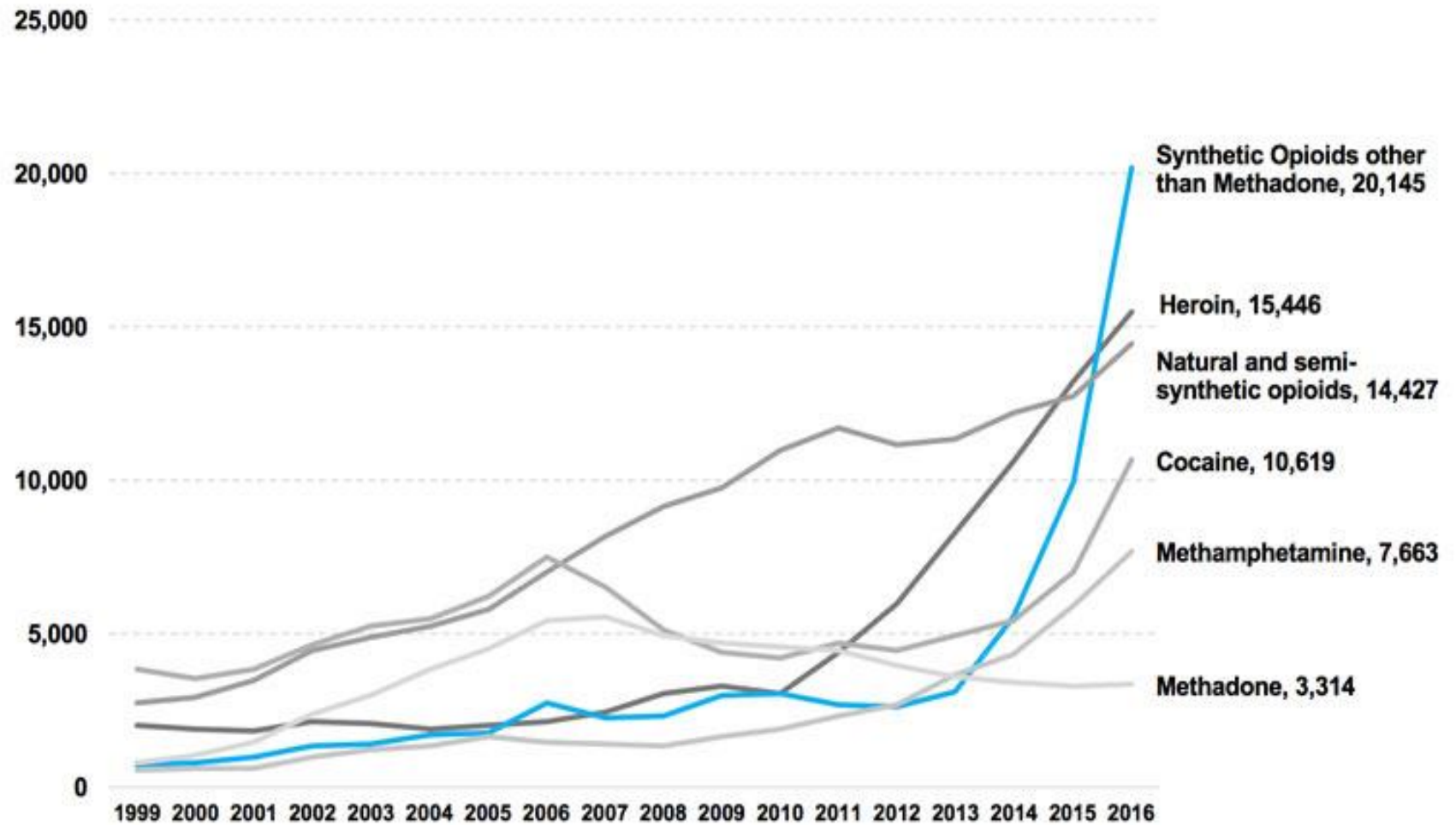
U.S. Drug Deaths

Chart Area



Source: CDC WONDER

Drugs Involved in U.S. Overdose Deaths, 2000 to 2016



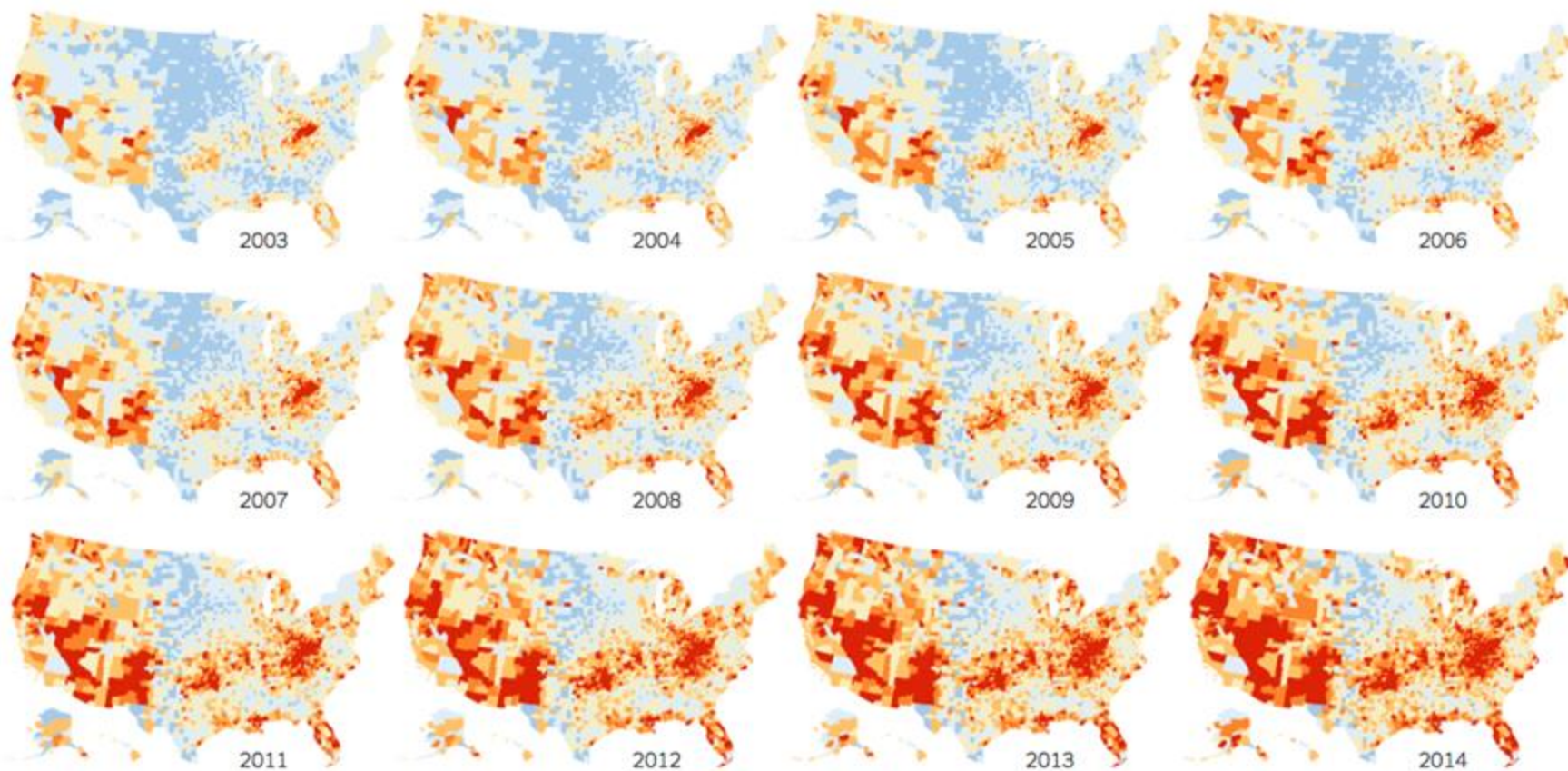
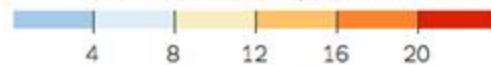
Source: NIDA

Current Epidemic of Opioid Addiction

- US consumes
 - >99% of the world's hydrocodone,
 - >80% of oxycodone,
 - >65% of hydromorphone
 - >80% of all opioids prescribed in the world.
- US has <5% of the world's population
- Primary Care providers account for about half of the opioid prescriptions

*Source: Medscape

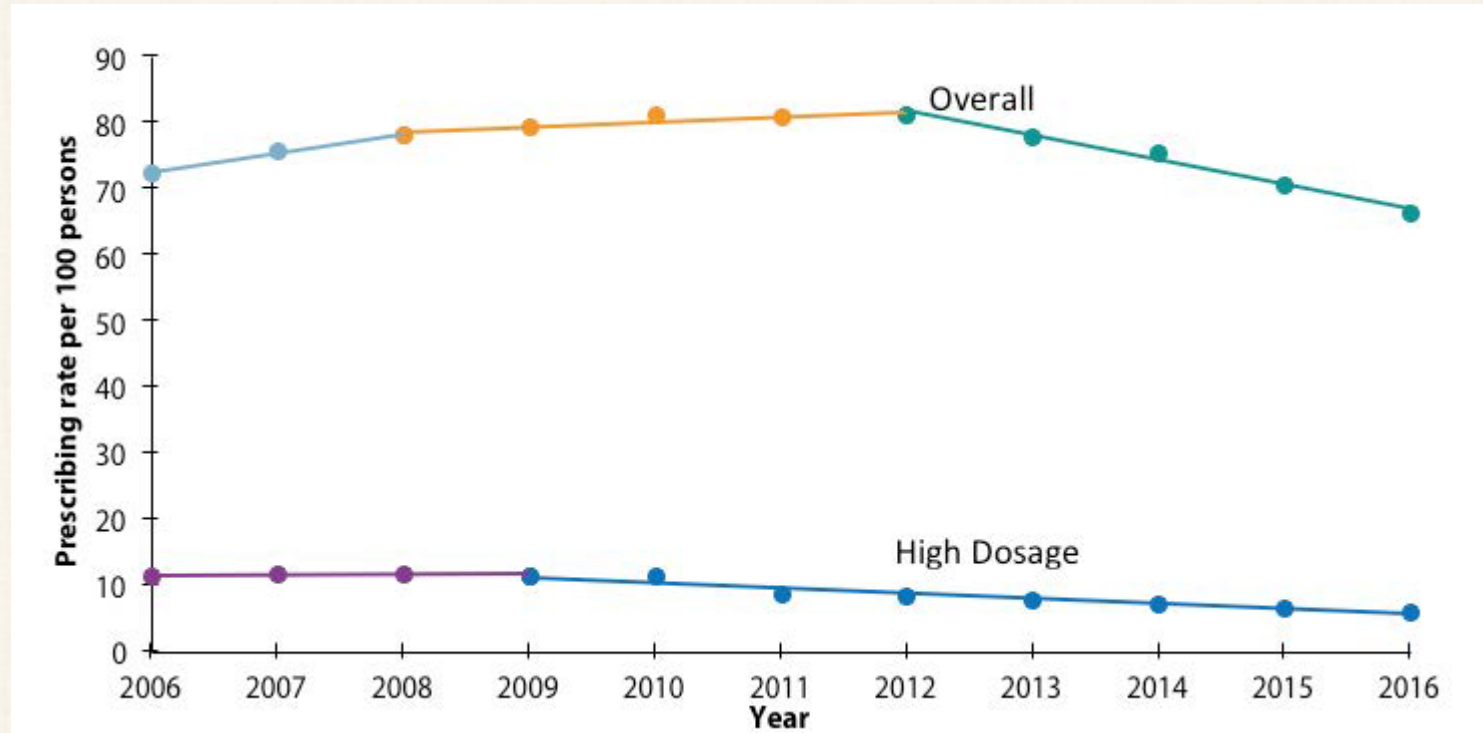
Overdose deaths per 100,000



"We know of no other medication routinely used for a nonfatal condition that kills patients so frequently."

*-Tom Frieden, MD
Former Director, CDC*

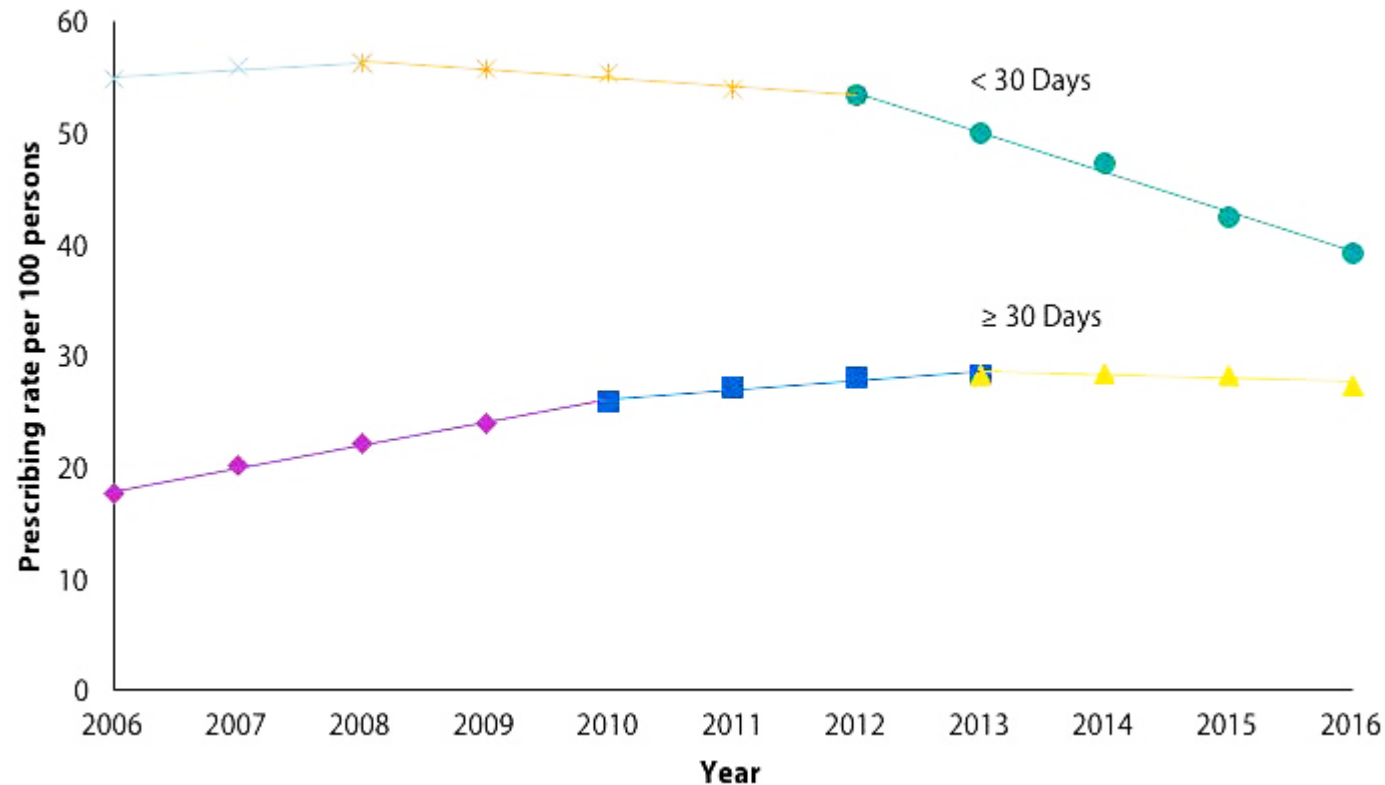
Opioid Prescription Trends



High Dose = ≥ 90 MME/day

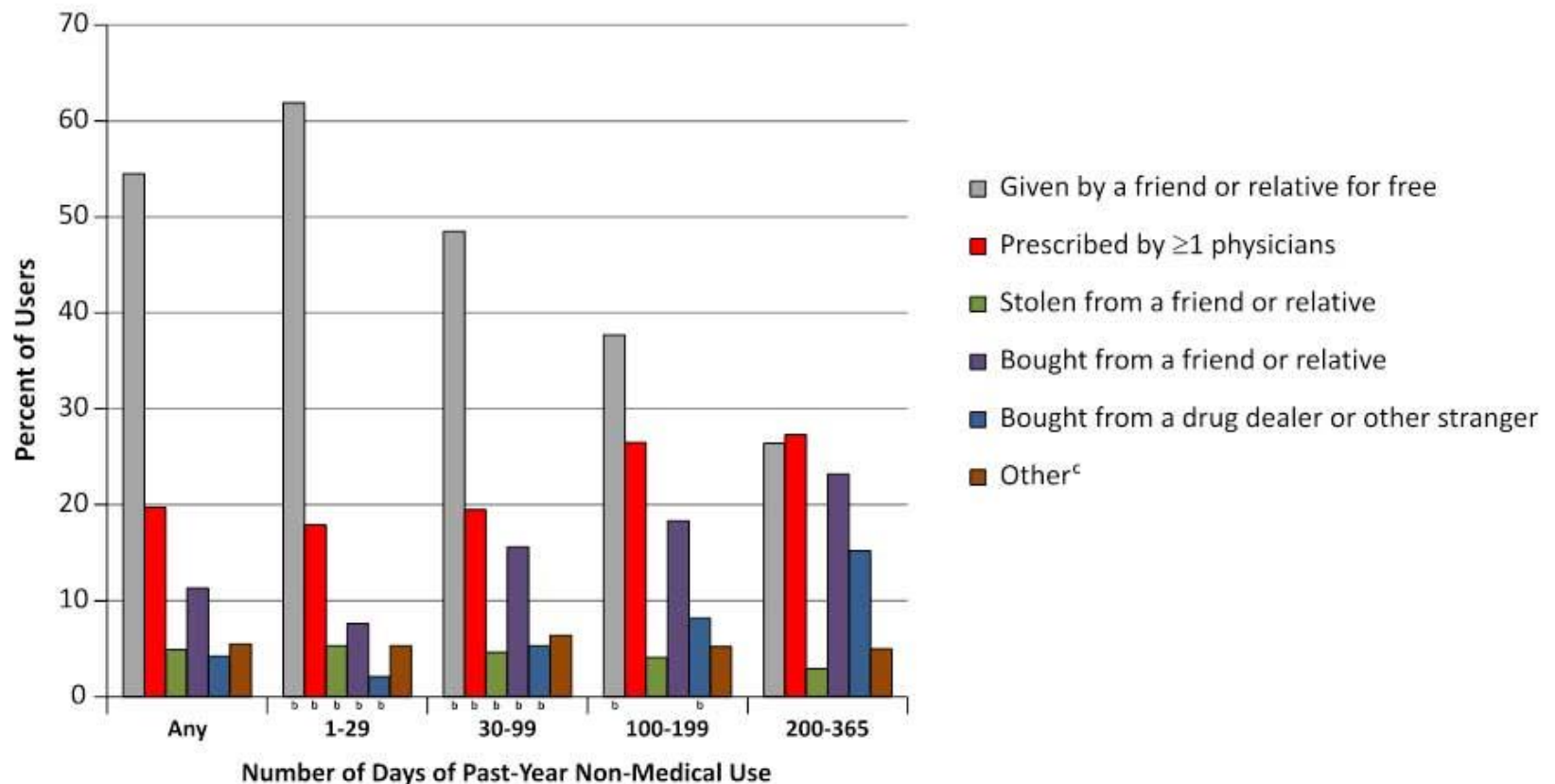
CDC. Annual Surveillance Report of Drug-Related Risks and Outcomes — United States, 2017. Surveillance Special Report 1. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. Published August 31, 2017. Accessed 10/13/17 from <https://www.cdc.gov/drugoverdose/pdf/pubs/2017cdc-drug-surveillance-report.pdf>

Opioid Prescription Trends



CDC. Annual Surveillance Report of Drug-Related Risks and Outcomes — United States, 2017. Surveillance Special Report 1. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. Published August 31, 2017. Accessed 10/13/17 from <https://www.cdc.gov/drugoverdose/pdf/pubs/2017cdc-drug-surveillance-report.pdf>

Sources of Prescription Opioids Among Past-Year Non-Medical Users^a



^a Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.⁵

^b Estimate is statistically significantly different from that for highest-frequency users (200-365 days) ($P < .05$).

^c Includes written fake prescriptions and those opioids stolen from a physician's office, clinic, hospital, or pharmacy; purchases on the Internet; and obtained some other way.

SOURCE: Jones C, Paulozzi L, Mack K. Sources of prescription opioid pain relievers by frequency of past-year nonmedical use: United States, 2008–2011. JAMA Int Med 2014; 174(5):802-803.

Mea culpa

"What I was trying to do was create a narrative so that the primary care audience would ... feel more comfortable about opioids in a way they hadn't before. ... and because the primary goal was to destigmatize, we often left evidence behind.....Clearly if I had an inkling of what I know now then, I wouldn't have spoken in the way that I spoke. It was clearly the wrong thing to do."

Russell Portenoy, MD

(Quoted on CNN.com: "Opioid history: From 'wonder drug' to abuse epidemic" by Sonia Moghe, 10/14/2016)

The “Evidence”

Editor's Note: For reasons of public health, readers should be aware that this letter has been “heavily and uncritically cited” as evidence that addiction is rare with opioid therapy. [Leung et al.](#) describe its history.

CORRESPONDENCE

ARCHIVE

Addiction Rare in Patients Treated with Narcotics

N Engl J Med 1980; 302:123 | [January 10, 1980](#) | DOI: 10.1056/NEJM198001103020221

Article

Citing Articles (265)

To the Editor:

Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients¹ who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,² Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

Jane Porter

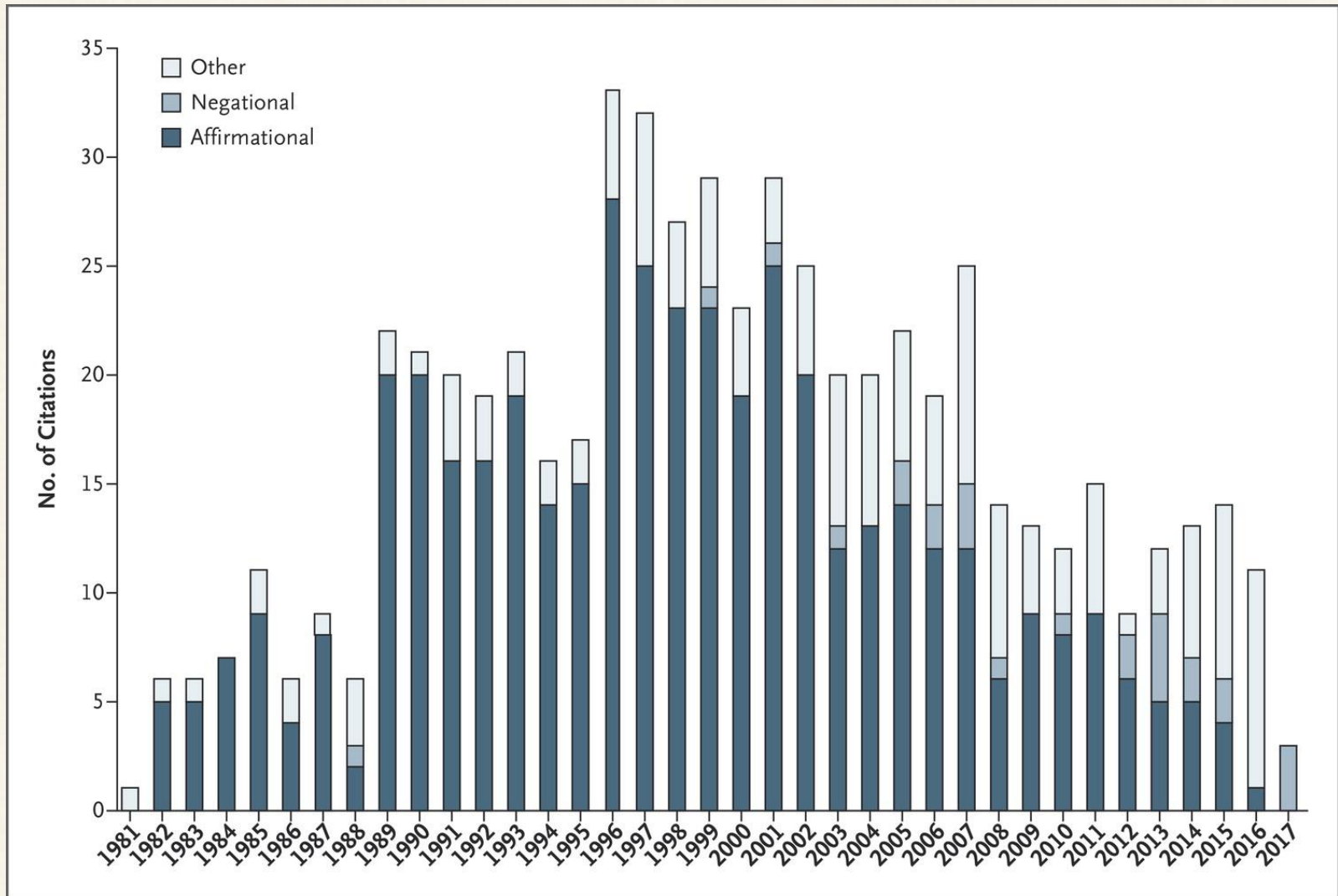
Hershel Jick, M.D.

Boston Collaborative Drug Surveillance Program Boston University Medical Center, Waltham, MA 02154

2 References

- 1 Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. . Comprehensive drug surveillance . JAMA . 1970; 213:1455–60.
[CrossRef](#) | [Web of Science](#) | [Medline](#)
- 2 Miller RR, Jick H. . Clinical effects of meperidine in hospitalized medical patients . J Clin Pharmacol . 1978; 18:180–8.
[CrossRef](#) | [Web of Science](#) | [Medline](#)

Citations of the 1980 Letter



Leung et al., NEJM 2017

ADDICTION AS A DISEASE

Addiction, a Disease

- Known risk factors:
 - family history
 - male sex
 - genes play a central role
- Typical course and outcomes:
 - chronic
 - punctuated by periods of abstinence followed by relapse
 - sometimes fatal
- Current conceptualization focuses on compulsive use rather than dependence or withdrawal
 - addiction diminishes, but does not completely eliminate voluntary behavioral control

Drugs and the Reward System

- In humans, the capacity for cognitive control over reward-seeking is a relatively stable trait that predicts life success.
- Deficits in cognitive control, such as in ADHD, are also known to increase vulnerability to substance use.
- Drugs “hijack” the reward system by direct pharmacological action, so that drug-seeking acquires salience over all other goals.
- Rational goals such as self-care, work, parenting, etc, are devalued.

Success Rates in Drug Treatment

Disorder	Success* rate (%)
Alcohol dependence	50 (40-70)
Opioid dependence	60 (50-80)
Cocaine dependence	55 (50-60)
Nicotine dependence	30 (20-40)

* Defined as >50% reduction in drug use at 6 months

Compliance and Relapse in Medical Disorders

	Compliance and relapse
DM (insulin dependent)	
Medication regimen	<50%
Diet and foot care	<30%
Relapse*	30-50%
Hypertension	
Medication regimen	<30%
Diet	<30%
Relapse*	50-60%

*Retreatment within 12 months by physician, emergency room or hospital.

**MANAGING PATIENTS IN PRIMARY
CARE**

SCREENING AND ASSESSMENT

Case Identification

- Self report
- Collateral information.
- Red flags- “lost” prescriptions; early refill requests.
- Health complications related to drug use
- PDMP database.
- A positive drug test.
- Maintain a non-judgmental, supportive, approach.

Screening Tool: CAGE-AID

- The CAGE-AID (“Adapted to Include Drugs”)* should be preceded by these two questions:

1. Do you drink alcohol?

2. Have you ever experimented with drugs?

(Brown RL, et al. *Preventive Medicine*. 1998;27:101-110)

CAGE-AID

In the last three months: (Yes/No responses)

1. Have you felt you should **Cut down** or stop drinking or using drugs? (You may ask more specifically about beer, wine, liquor, marijuana, non-prescribed medications, etc, based on clinical suspicion)

2. Has anyone **Annoyed** you or gotten on your nerves by telling you to cut down or stop drinking or using drugs?

3. Have you felt **Guilty** or bad about how much you drink or use drugs?

4. Have you been waking up wanting to have an alcoholic drink or use drugs (**Eye-opener**)?

A “Yes” response to one or more questions should lead to further exploration.

Single-question Screens

- “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”
- “How many times in the past year have you had X or more drinks in a day?” (X = 5 for men, X = 4 for women).

McNeely J, et al. Validation of Self-Administered Single-Item Screening Questions (SISQs) for Unhealthy Alcohol and Drug Use in Primary Care Patients. J Gen Intern Med. 2015 Dec;30(12):1757-64.

Assessment

- If non-medical substance use is identified on screening follow up with questions about:
 - Which substance/s?
 - How much?
 - How often?
 - Route of administration?
 - When last used?
 - Past experience of withdrawal?
 - Use of any other drugs/alcohol?
 - Interest in seeking treatment?

Stage of Change

- Pay attention to patient's Stage of Readiness to Change:
 - Precontemplation: "I don't have a problem"
 - Contemplation: "Maybe, I do have a problem"
 - Preparation: "How can I get treatment?"
 - Action: "I am already in treatment"
 - Maintenance: "I am in treatment and haven't used since _____"
 - Relapse: "I was doing well, but fell off the wagon"

MAKING SENSE OF DRUG TESTS



"You're fired, Jack. The lab results just came back, and you tested positive for Coke."

Common Problems

- Very often, too much is read into single drug test results
- Complexity of drug testing is not often evident to people who use it
- Serious consequences may follow from misinterpretation of drug tests, e.g., termination from treatment, loss of a job, separation of a child from its parent, imprisonment, inappropriate medical treatment.

“Positive” and “Negative”

- The terms “Clean” and “Dirty” have pejorative connotations and should be avoided.
- What is meant by a “Positive” test?
- What is meant by a “Negative” test?

Definitions

- **Positive Test:** A positive test for a substance implies that the specimen *contained the particular substance at a concentration exceeding a predetermined cut-off level*.
- **Negative Test:** A negative test for a substance implies that the specimen did not contain the substance that was tested for, or *contained the particular substance at a concentration below a predetermined cut-off level*. Substances not tested for may be present.

Opioids

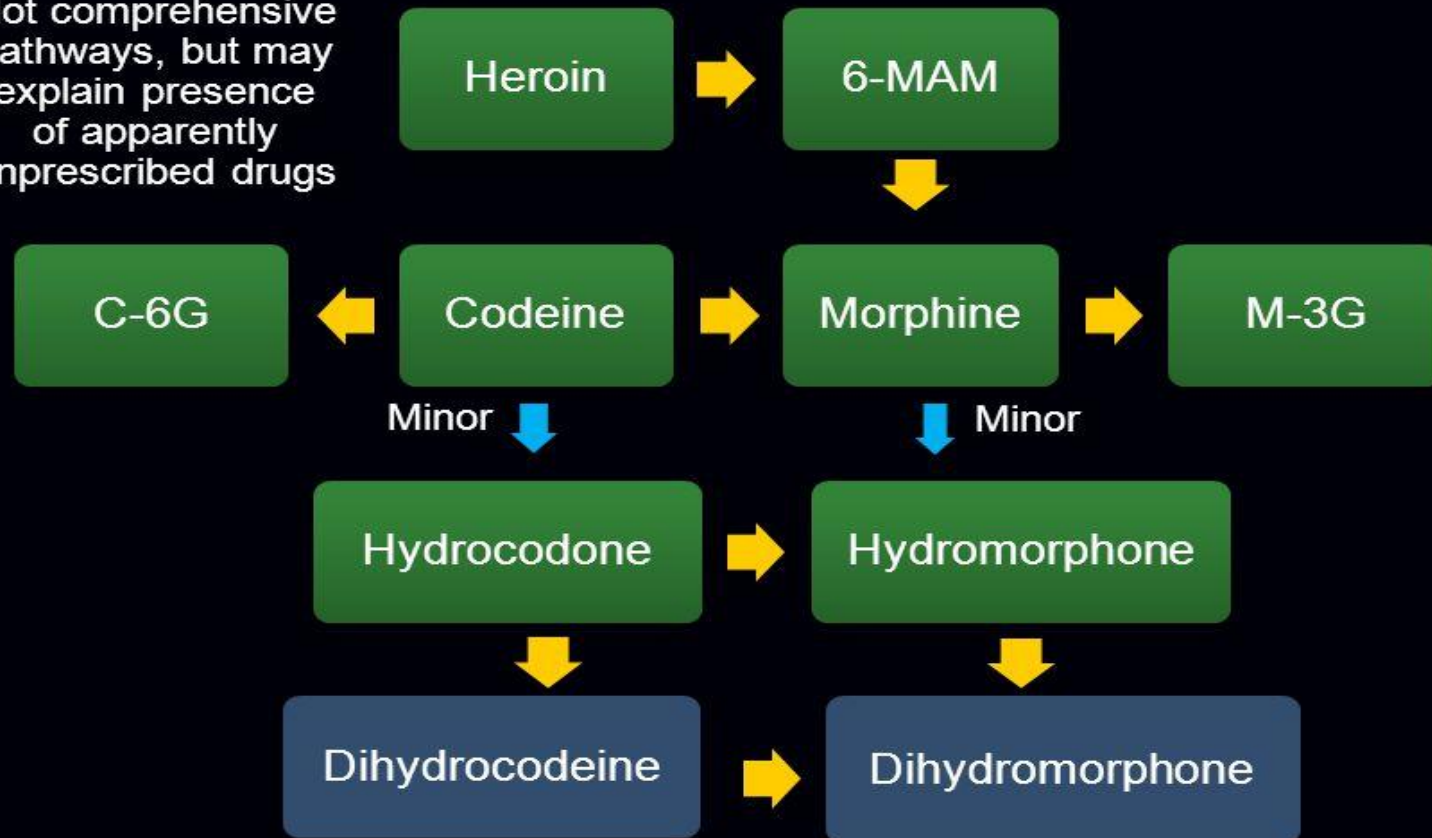
- Three classes of opioids
 - Natural (“Opiates”-alkaloids from *Papaver somniferum*) alkaloids in opium: morphine, codeine, thebaine
 - Semisynthetic: heroin, oxycodone, oxymorphone, hydrocodone, hydromorphone, buprenorphine
 - Synthetic: methadone, fentanyl, propoxyphene, meperidine

Testing for Opioids

- Two main testing techniques
 - Immunoassay for screening
 - Gas Chromatography-Mass Spectrometry for confirmation
- The common “Opiates” test on screening panels tests for morphine using immunoassay
- There is some cross-reactivity between certain semisynthetics and the opiates test, especially at high dose levels (e.g., 5% cross-reactivity for oxycodone)
- Others, including methadone and buprenorphine, have to be tested for individually

Opioid Metabolism

Not comprehensive pathways, but may explain presence of apparently unprescribed drugs



Gourlay D, et al. http://www.familydocs.org/assets/171_UDT%202006.pdf. Accessed March 2010;
Cone EJ, et al. *J Anal Toxicol*. 2006;30:1-5; Heit HA, Gourlay D. Personal Communication. 2008.

Testing for Opioids

- Heroin (di-acetylmorphine) is rapidly converted after ingestion to mono-acetylmorphine (within minutes)
- Mono-acetylmorphine also has a short half-life (about 8 hours) and is converted to morphine
- Detection time for heroin is extended indirectly by identifying “cutting agents” such as quinine
- A part of ingested codeine is converted to morphine
- A small proportion of oxycodone is converted to morphine

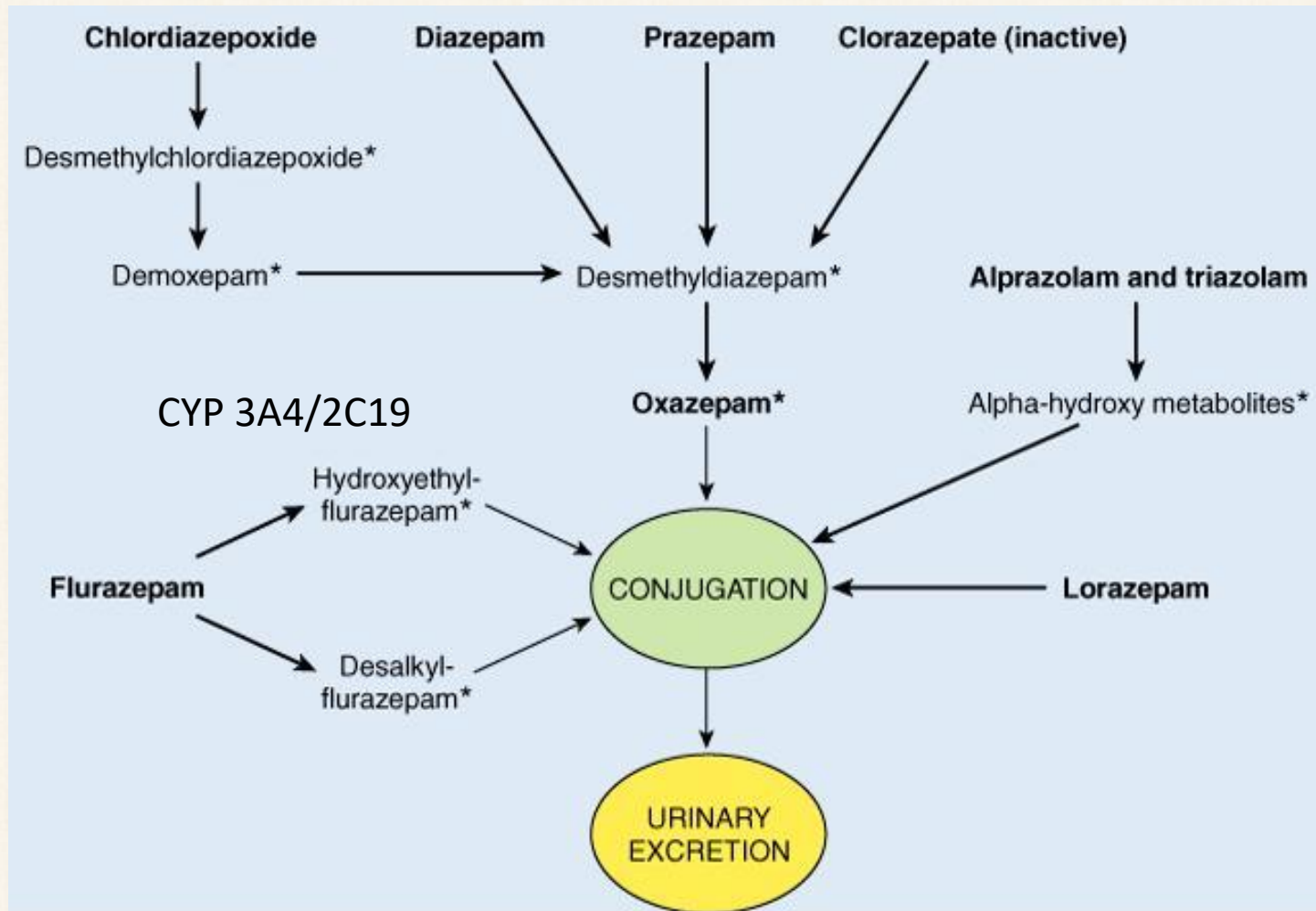
Alcohol Testing

- Can be tested for in blood, urine or breath, but short window of detection
- May be detected for a longer period by testing urine for ethyl glucuronide (EtG)
- Several other biomarkers may be helpful in detecting recent heavy drinking: AST, ALT, GGT, CDT, MCV, etc.
- May get a positive urine test for ethanol in some diabetic patients due to fermentation of sugar in urine
- False positives possible from non-beverage alcohols, e.g., isopropyl alcohol

Benzodiazepines

- Tests generally detect oxazepam/nordiazepam which are common metabolites of many benzodiazepines.
- Hard to identify which benzodiazepine was used based on the test
- Test may remain positive for weeks after ingestion of long-acting benzodiazepines with active metabolites (e.g., diazepam (Valium®) or chlordiazepoxide (Librium®))
- False positives reported with sertraline (Zoloft®) and oxaprozin.

Benzodiazepine Metabolism



Important to Remember

- A drug test does **NOT** diagnose
 - Substance use disorder
 - Physical dependence
 - Impairment
 - Diversion
- An unexpected result should lead to a differential diagnosis and a conversation rather than a jump to a definitive conclusion

MANAGEMENT

Opioid “Detoxification”

- Term “detox” commonly used but a misnomer.
- Alternative term “medically supervised withdrawal” favored by some
- Does not produce any lasting benefit
- >90% relapse quickly after a short detox
- High risk of death from overdose after a detox due to loss of tolerance

Recommend Maintenance

- All patients should be offered long-term maintenance treatment
- If the patient accepts, initiate a referral or start buprenorphine (or methadone, if inpatient) as soon as possible to ensure a seamless transition to treatment
- Continue buprenorphine until transfer and provide a hand-off to the program/prescriber

MEDICATION “ASSISTED” TREATMENT

Medication Assisted Therapy (MAT) for Opioids

- Opioid Full Agonist- Methadone
- Opioid Partial Agonist- Buprenorphine
- Opioid Antagonist-
 - Naltrexone
 - Extended Release Naltrexone Injection

Methadone

- Narcotics Addiction Treatment Act of 1974 limited treatment of opioid dependence with methadone primarily to regulated opiate agonist treatment programs
- Nationally this system can accommodate approximately 250,000 individuals with opioid use disorder
- Currently over 2 million individuals are estimated to be addicted to heroin and prescription opioids

Buprenorphine

- Schedule III medication, FDA approved for use with a waiver under Drug Addiction Treatment Act of 2000
- Can be used in an office based practice by qualified physicians with a DEA waiver (“X number”)
- Prescribing recently extended to qualified NPs and PAs with additional training
- Most commonly prescribed as buprenorphine+ naloxone combination formulation (Suboxone film/Zubsolv tab/generic tabs) in a 4:1 ratio available in 2/4/8/12mg (or equivalent Zubsolv) strengths

Effectiveness

- Methadone has been in wide use since 1972 and buprenorphine since 2002
- Methadone and buprenorphine are among the most researched and effective medications in all of medicine
- Strong evidence that both are about equally effective in promoting abstinence from opioids and retaining people in treatment
- Both
 - Reduce opioid cravings
 - Reduce opioid use
 - Reduce criminal activity
 - Reduce complications of opioid use
 - Reduce mortality

Impact of Methadone Maintenance on Mortality

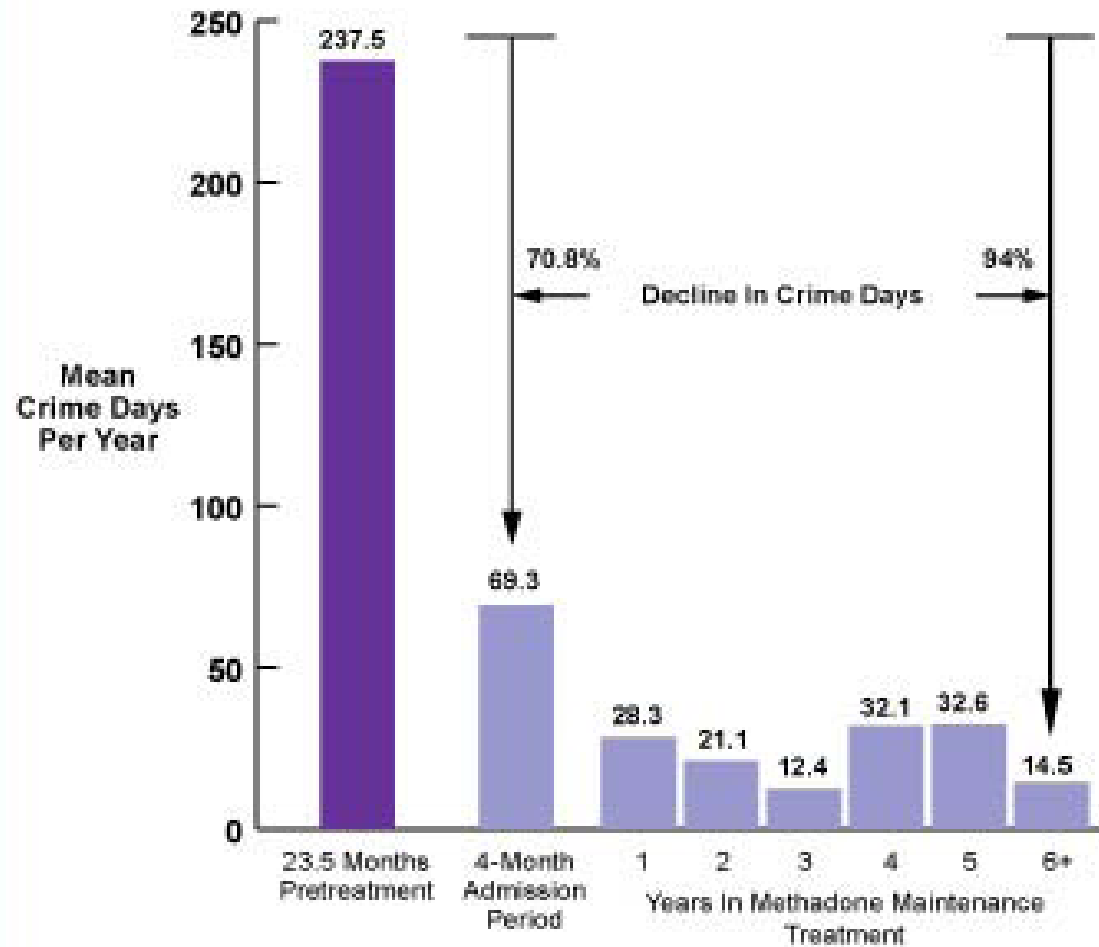
- Swedish 5-8 year follow-up study of Methadone Maintenance Treatment (MMT):
- 115 “street” heroin users not on MMT vs 166 on MMT
 - Mortality in non-MMT group **63x** expected rate for age and gender in the general population
 - Mortality in MMT group- **8x**
 - Mortality in 53 MMT pts involuntarily expelled from MMT- **55x**
 - Mortality in 34 “rehabilitated” patients therapeutically withdrawn from methadone- **4x**

(Gronbladh et al, Acta Psychiat Scand, 1990)

Methadone: Effectiveness

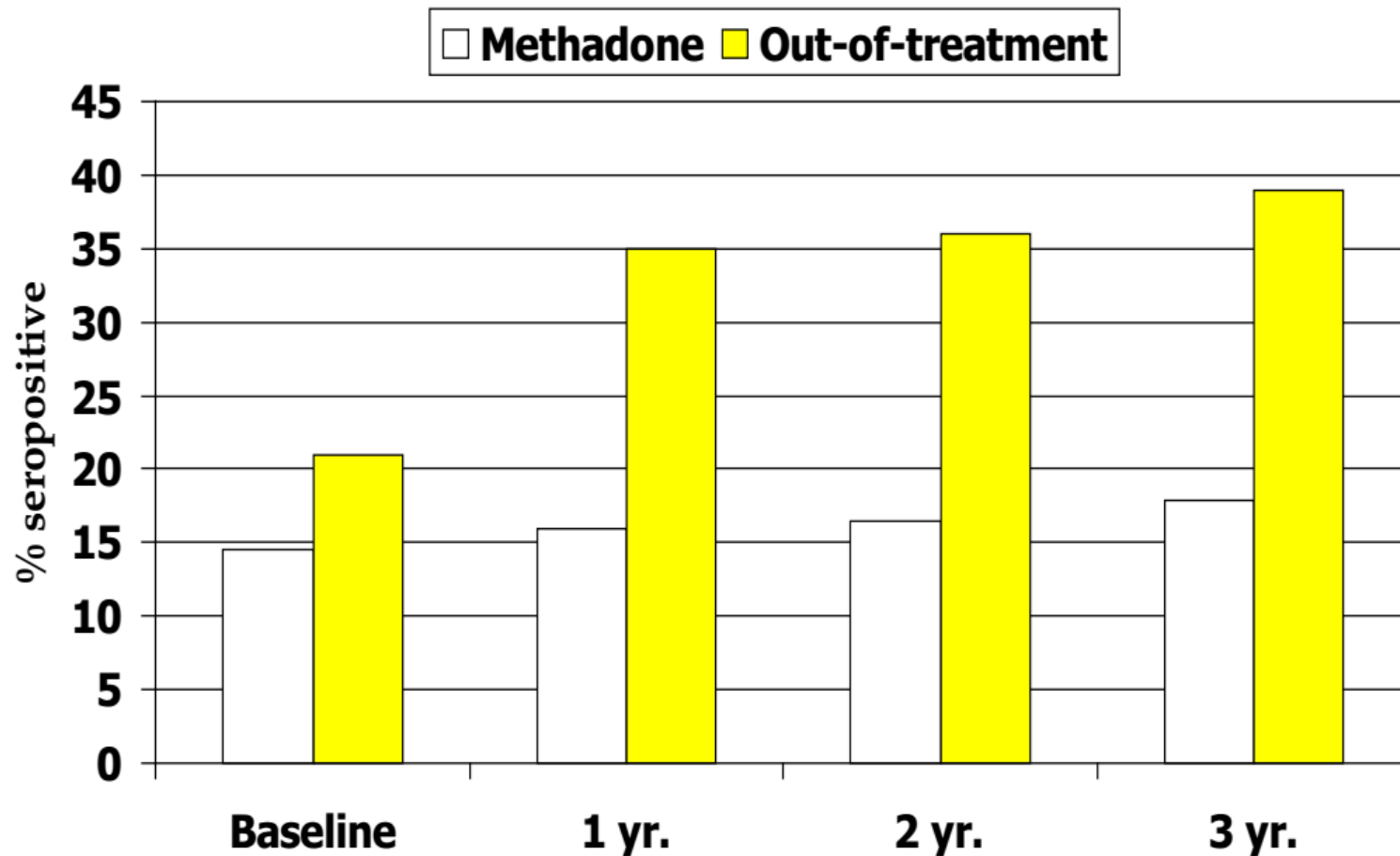
- Among the most effective medications in medicine:
 - Increases treatment retention- $\geq 70\%$ at 90 days.
 - Patients maintained on $>80\text{mg/day}$ have a much higher retention rate than those on $<60\text{mg/day}$ (up to 5x in one study)
 - $>70\%$ reduction in injection drug use
 - Reduces HIV risk behavior/ seroconversion (7x reduction over 18 months in seroconversion vs not-in-treatment controls)
 - Reduces crime and recidivism
 - Reduces mortality (0.8% vs 8.3% in one study; 4x reduction across 5 studies)

Effect of Methadone Treatment on Crime Days



(Ball and Ross, 1991)

Methadone Effect on HIV Seroconversion



Safety

- Low risk of morbidity and mortality when used under proper supervision
- Caution needed during induction period
- Few side effects- but may prolong QTc
- Elevated risk when methadone and buprenorphine are used with CNS depressants- especially benzodiazepines and alcohol

Cost and Ease of Delivery

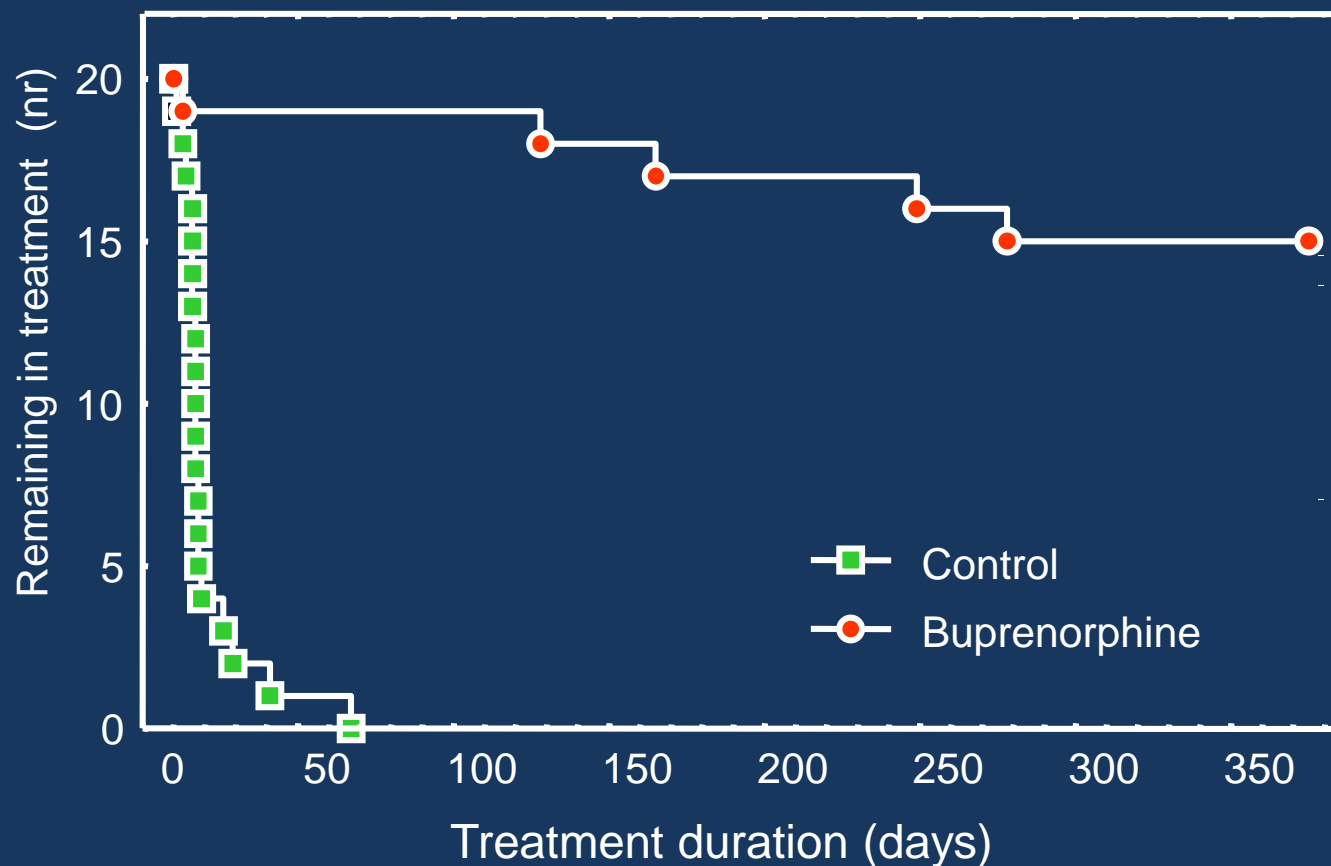
– Cost-effective:

- Annual cost of methadone maintenance is approximately \$5000 per patient
- Buprenorphine maintenance (approx \$6-8000) and injectable naltrexone (approx \$15000) cost more
- But all cost far less than incarceration (approx \$30000)

– Scalable:

- Can be delivered relatively easily to large numbers of patients
- Recent increase in buprenorphine cap helps

Buprenorphine Maintenance vs Withdrawal RCT: Retention



(Kakko et al., Lancet, 2003)

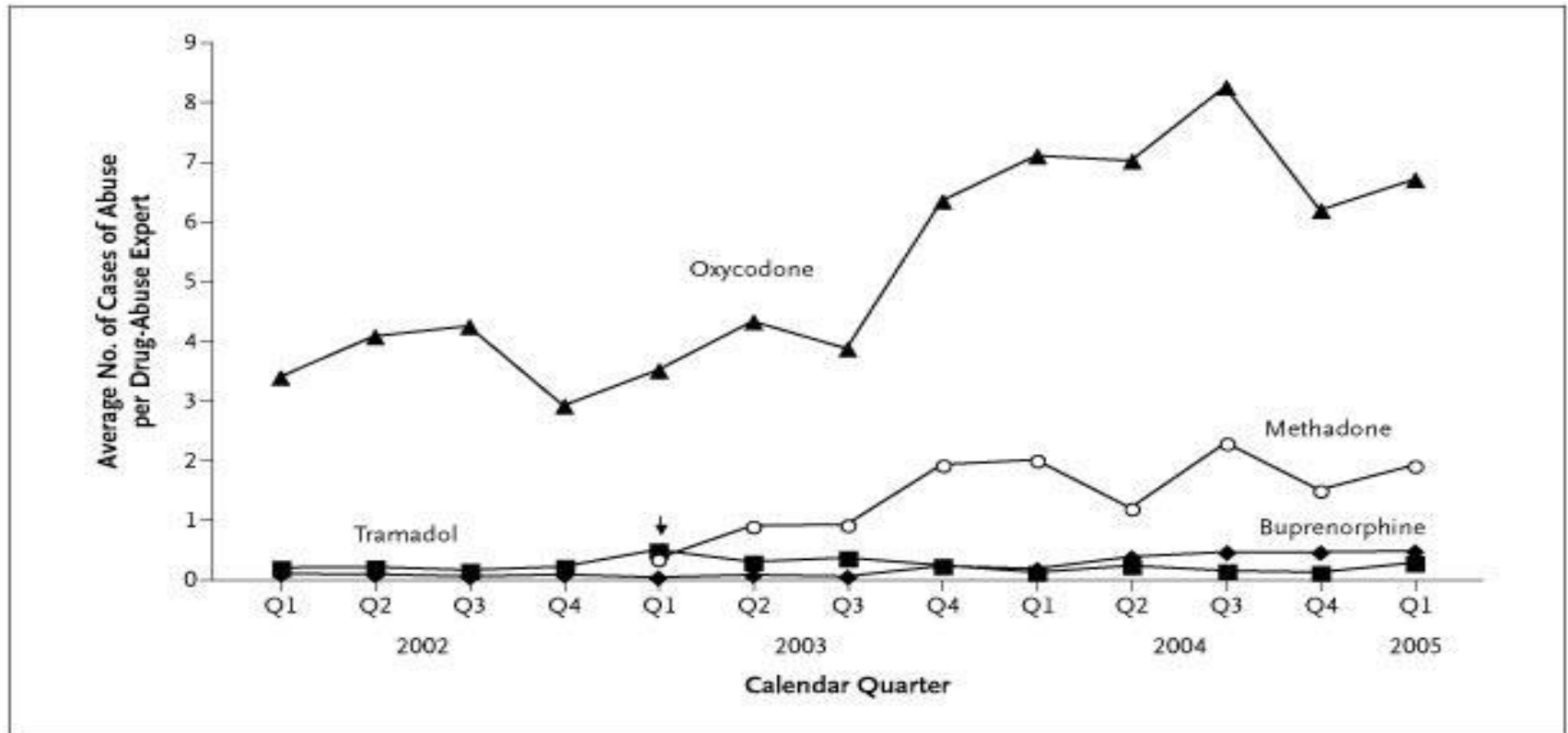
Buprenorphine in Primary Care: Barriers

- Waiver: Easy to get
- Induction: Can be done at home
- Counseling: Recommended but not required
 - “have capacity to refer”
- Drug testing: Can be done on site or via lab
- Concern about diversion: Not widespread
- Concern about patient population: Much easier to manage than an actively using patient

Role of Counseling

- Multicenter randomized clinical trial- n=653
 - Patients randomized to standard medical management (SMM) or SMM plus counseling
 - At 3 & 12 weeks of buprenorphine separate counseling did not change outcomes
-
- Weiss, RD, et al. Arch Gen Psych, 2011

Abuse/Diversion Risk



Bottom-line

- Given their predictable effectiveness in reducing opioid use and preventing associated complications, MAT with methadone or buprenorphine should be considered first-line treatment and accessible to ALL patients with opioid use disorders

Antagonist Maintenance

- Oral naltrexone was approved for opioid dependence in 1984
- Injectable extended-release naltrexone was approved for opioid dependence in 2010
- Advantages include
 - No physical dependence
 - No risk of diversion
 - Not a controlled medication
- But
 - Less strong evidence of effectiveness
 - Lower patient acceptability and adherence
 - Need for abstinence from opioids before induction
 - Possible greater risk of overdose after drop-out
 - High cost of injectable extended release naltrexone

Special Situations: Acute Pain Management

- Acute pain should be managed per normal practice while maintaining methadone at usual doses
- Buprenorphine should be discontinued while acute pain management proceeds and then reinstated after stopping the pain medication, allowing sufficient time for it to clear the patient's system
- Naltrexone (oral) should be discontinued as with buprenorphine.
- Patients on injectable naltrexone may be more difficult to manage and a pain medicine consultation should be obtained

Special Situations: Acute Pain Management

- Patients with opioid use disorders may need higher than normal doses of opioid pain medications due to tolerance
- Pain medication prescriptions should be for short duration and closely monitored
- Avoid benzodiazepines
- Naloxone should be co-prescribed and patient and family trained in its use in an overdose situation for all patients on opioid pain medications

Special Situations: Pregnancy

- Recommend methadone or buprenorphine maintenance as soon as pregnancy is confirmed. No evidence yet to support naltrexone for use in pregnant patients.
- Start MAT, if patient agrees and refer to a maintenance program
- MAT doses may need upward adjustment as pregnancy progresses and reduction after delivery

Overdose Education and Naloxone Distribution

- OEND programs now operate in many states
- Important element of any effort to reduce overdose deaths
- Educates people with opioid addiction, their family members, pain patients on opioids and general public about overdose and provides naloxone for use in an overdose emergency
- Shown to reduce overdose deaths
- Recommend co-prescribing naloxone to anyone receiving a prescription for opioids

MEDICATIONS FOR ALCOHOL USE DISORDER

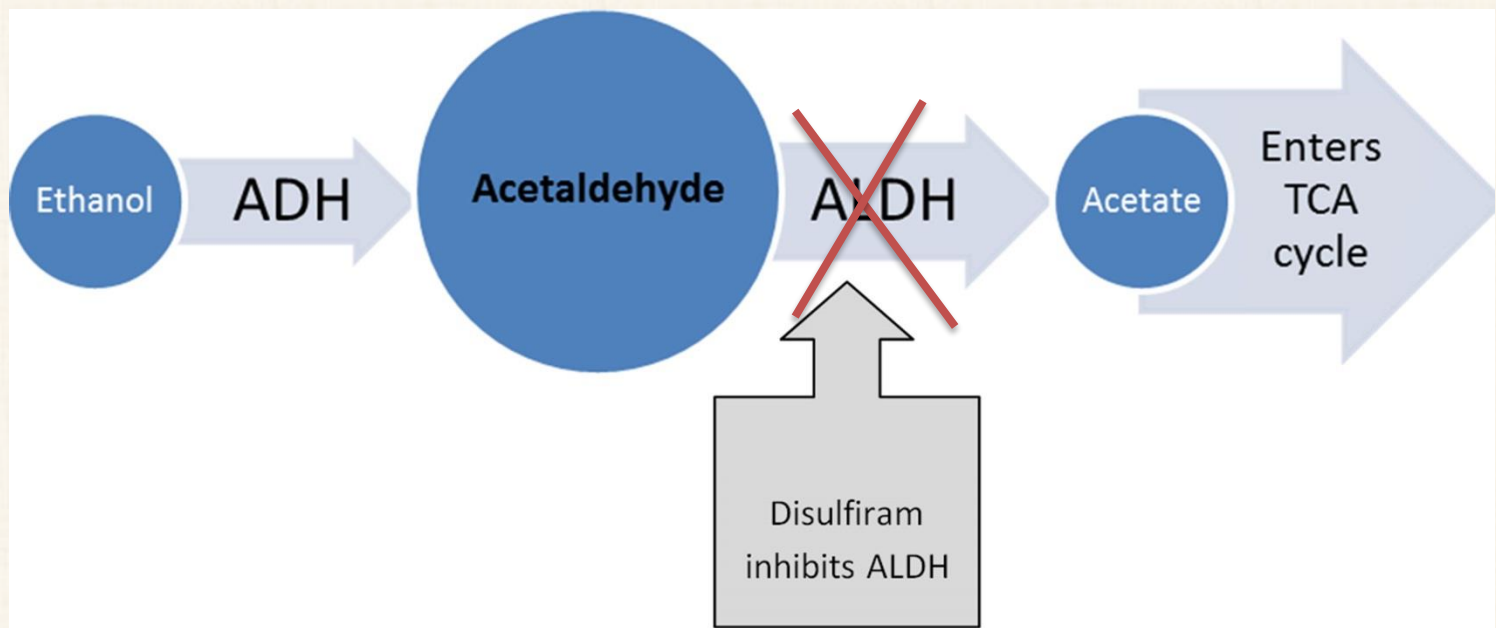
What to Expect

- Medication for AUD can be a useful adjunct to psychosocial treatment
- The effect sizes for all available treatments for AUD are much smaller compared to opioid agonist treatments for opioid use disorder
- Incorporation of medication is increasingly considered the standard of care
- Patient acceptance tends to be relatively low, but growing

FDA Approved Medications: Disulfiram

- Antabuse®: The first one approved
- Sometimes called “aversive therapy”
- Causes an unpleasant reaction (“Disulfiram-Ethanol Reaction”) with alcohol
- Observed treatment works better as compliance is a common problem
- Works well in carefully selected patients: motivated, not impulsive/risk-taker, good support system
- Can cause liver dysfunction and some unpleasant side effects

How Does It Work?



Disulfiram-Ethanol Reaction

- Occurs due to the build-up of acetaldehyde
- Signs/symptoms include: Flushing, nausea, vomiting, sweating, drop in blood pressure (sometimes severe), irregular heart rhythm (potentially dangerous; rarely, fatal)
- Severity of reaction varies- some people may have it even with small amounts of alcohol (e.g., in food/medication/mouthwash)
- Reaction may occur up to 7-14 days after stopping disulfiram

FDA Approved Medications: Naltrexone

- Revia®: Mu opioid receptor antagonist
- Reduces cravings and makes alcohol less reinforcing
- Generally well-tolerated, once daily pill
- May also cause liver dysfunction
- Compliance can be a problem
- Long-acting injectable formulation- Vivitrol®- can improve adherence
- There may be a genetic basis to response to naltrexone

FDA Approved Medications: Acamprosate

- Campral®: Glutamate receptor modulator, may work by dampening the glutamate surge that follows cessation of drinking
- Also reduces cravings and makes alcohol less reinforcing
- Generally well-tolerated, no effect on the liver, but needs to be taken three times daily, so compliance can be a problem
- Some studies show it to be no better than placebo-
??also based in genetics

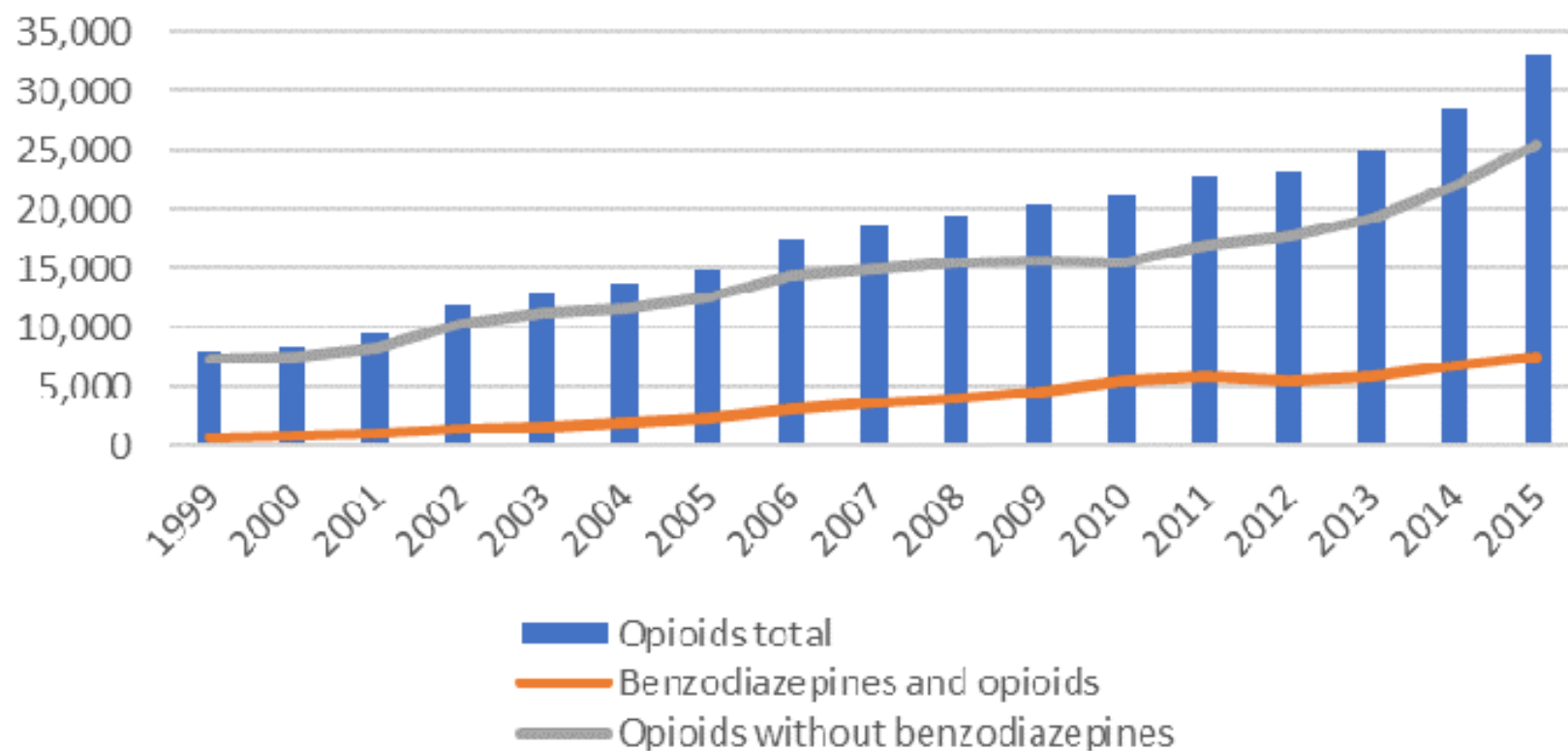
Changing Treatment Paradigm

- While disulfiram requires total abstinence, the primary objective of treatment with other medications is to reduce drinking and, therefore, reduce harm
- Some medications are also being promoted as targeted therapy, e.g., nalmefene (available in Europe), for use prior to exposure to drinking situations

BENZODIAZEPINES

AND THE “Z” DRUGS

Opioid Overdose Deaths Involving Benzodiazepines



Black Box Warning

- “Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients for signs and symptoms of respiratory depression and sedation.”

Most Prescribed Psychiatric Medications in 2013

Compound	2005	2009	2011	2013
Alprazolam	1	1	1	1
Lorazepam	5	3	4	5
Diazepam	9	10	9	11

Problems with Long Term Use

- Risk of CNS depression, esp with other CNS depressants
- Risk of falls and fractures
- Worsening of depression
- Cognitive and psychomotor impairment
- Diminishing effectiveness
- Physiologic dependence/addiction

Abrupt Cessation

- Rebound anxiety and panic
- Symptoms similar to alcohol withdrawal
- Delirium (similar to DTs)
- Seizures
- Self-harm, violence, psychosis, catatonia
- Can be life-threatening

Strategies to Manage Withdrawal

- Gradual dose reduction (GDR)
- Switch to a long-acting BZD with GDR
- Switch to a barbiturate and taper
- Switch to an anticonvulsant and taper
- Use of adjuncts

Benzodiazepine Withdrawal

- Managing BZD withdrawal can be an arduous and protracted process
- Can challenge the patient and the clinician
- Can be among the most difficult clinical problems one may have to deal with
- Prevention is much better than cure- handle BZDs with great caution

Monitoring

- Frequent, short visits
- Limited duration(weeks, max)
- Tight control over prescriptions
- Drug tests
- Communication with other providers and family
- Treatment agreement

Alternatives to BZD

- Antidepressants: SSRIs; SNRIs; Tricyclics; MAOIs
- Buspirone
- Beta blockers
- Alpha 1 antagonist- prazosin
- Antipsychotics
- Anticonvulsants

Prevention

- Primary care has an important role in preventing addiction.
 - Becoming more familiar with opioid pharmacology
 - Using prescribing best practices
 - Using PDMP
 - Using CDC Guidelines for opioid use in chronic pain
 - Using FDA's REMS
 - Identifying and assisting patients with a substance use disorder by treating or referring them to treatment

Final Word...

“The history of medicine is, in part, the history of physicians stretching the scope of their practice to answer the pressing needs of their times. In the face of OUD, a treatable illness with a striking capacity to rapidly and definitively alter the lives of our patients, their families, and the communities we serve, we have been late and ineffective in our response.....rates of active physician engagement in addiction treatment remain embarrassingly low.”

Rapoport, AB & Rowley, CF. N Engl J Med 2017; 377:705-707

Resources

- PCSS-MAT: <https://pcssmat.org/>
 - (Free buprenorphine waiver training, webinars, online modules, clinical tools, mentoring program, etc.)
- American Society of Addiction Medicine: <https://www.asam.org/>
- SAMHSA-Center for Substance Abuse Treatment:
<https://www.samhsa.gov/about-us/who-we-are/offices-centers/csat>
 - (Free publications, downloads, Treatment Locator, buprenorphine directory, waiver application, statistics, etc.)
- National Institute on Drug Abuse: <https://www.drugabuse.gov/>
- National Institute on Alcohol Abuse and Alcoholism:
<https://www.niaaa.nih.gov/>

QUESTIONS?