THE SCIENCE OF ADDICTION: ADOLESCENT EXPOSURE AND THE TRAJECTORY OF ADDICTION

SHAWN A. RYAN, MD, MBA

- Assistant Professor, Dept. of Emergency Medicine, University of Cincinnati
- President & CMO, Addiction Specialist, BrightView
- President, Ohio Society of Addiction Medicine
- Chair, Payer Relations ASAM

★ Every 16 minutes, a person in the United States dies from an opioid overdose.

U.S. SURGEON GENERAL, VIVEK MURTHY MD

- AN ESTIMATED 20.8 MILLION PEOPLE IN OUR COUNTRY ARE LIVING WITH A SUBSTANCE USE DISORDER. THIS IS SIMILAR TO THE NUMBER OF PEOPLE WHO HAVE DIABETES, AND 1.5 TIMES THE NUMBER OF PEOPLE WHO HAVE ALL CANCERS COMBINED. THIS NUMBER DOES NOT INCLUDE THE MILLIONS OF PEOPLE WHO ARE MISUSING SUBSTANCES BUT MAY NOT YET HAVE A FULL-FLEDGED DISORDER. WE DON'T INVEST NEARLY THE SAME AMOUNT OF ATTENTION OR RESOURCES IN ADDRESSING SUBSTANCE USE DISORDERS THAT WE DO IN ADDRESSING DIABETES OR CANCER, DESPITE THE FACT THAT A SIMILAR NUMBER OF PEOPLE ARE IMPACTED. THAT HAS TO CHANGE.

AGENDA

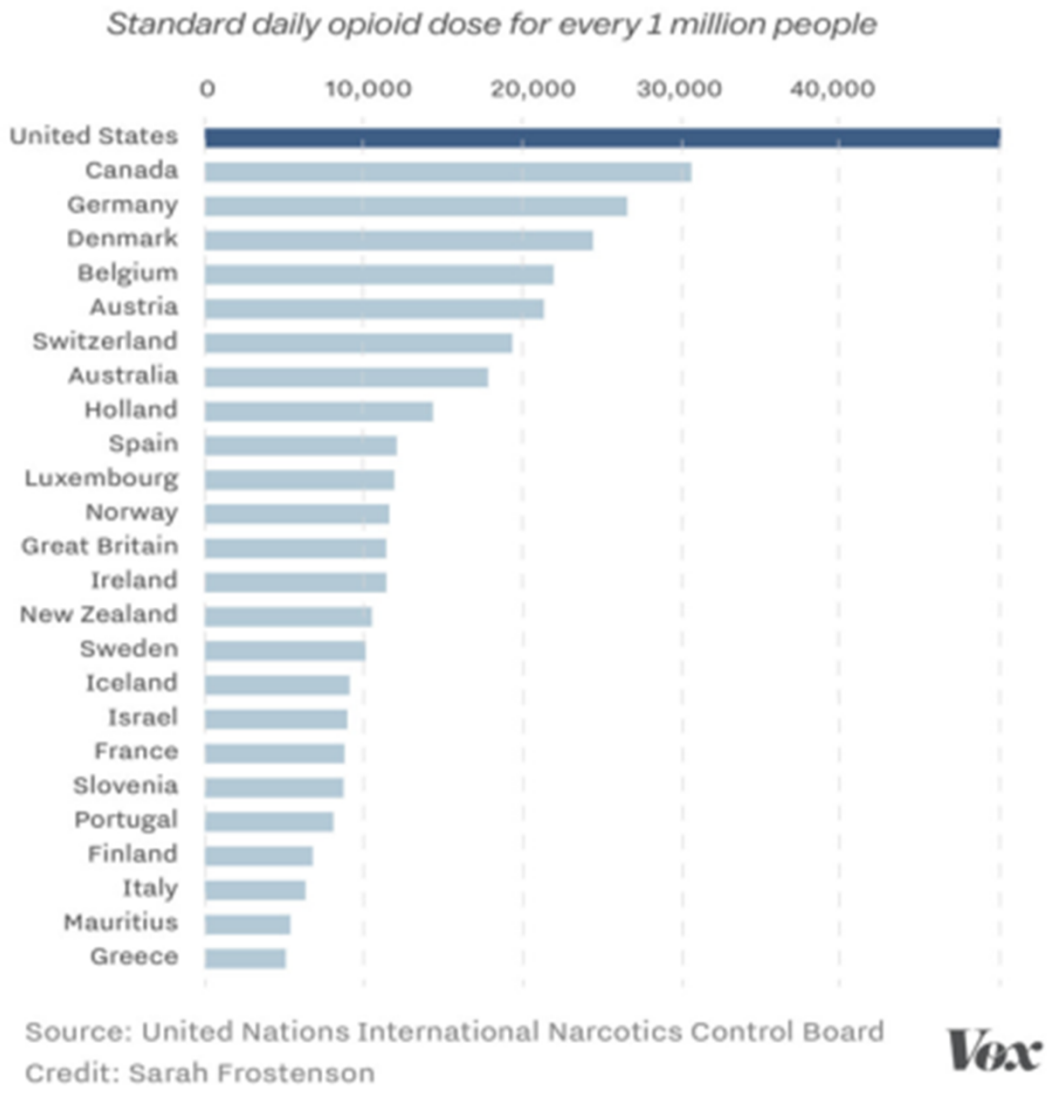
- The Issue in our Country
  - Current State and how did we get here
- Substance Use Disorder
  - The Disease
  - How does it develop
  - Adolescents and Prevention
- Medication-Assisted Treatment (MAT)
  - History, evidence, indications and contraindications
  - Comprehensive Integrated Addiction Treatment (For Opioids = COAT)

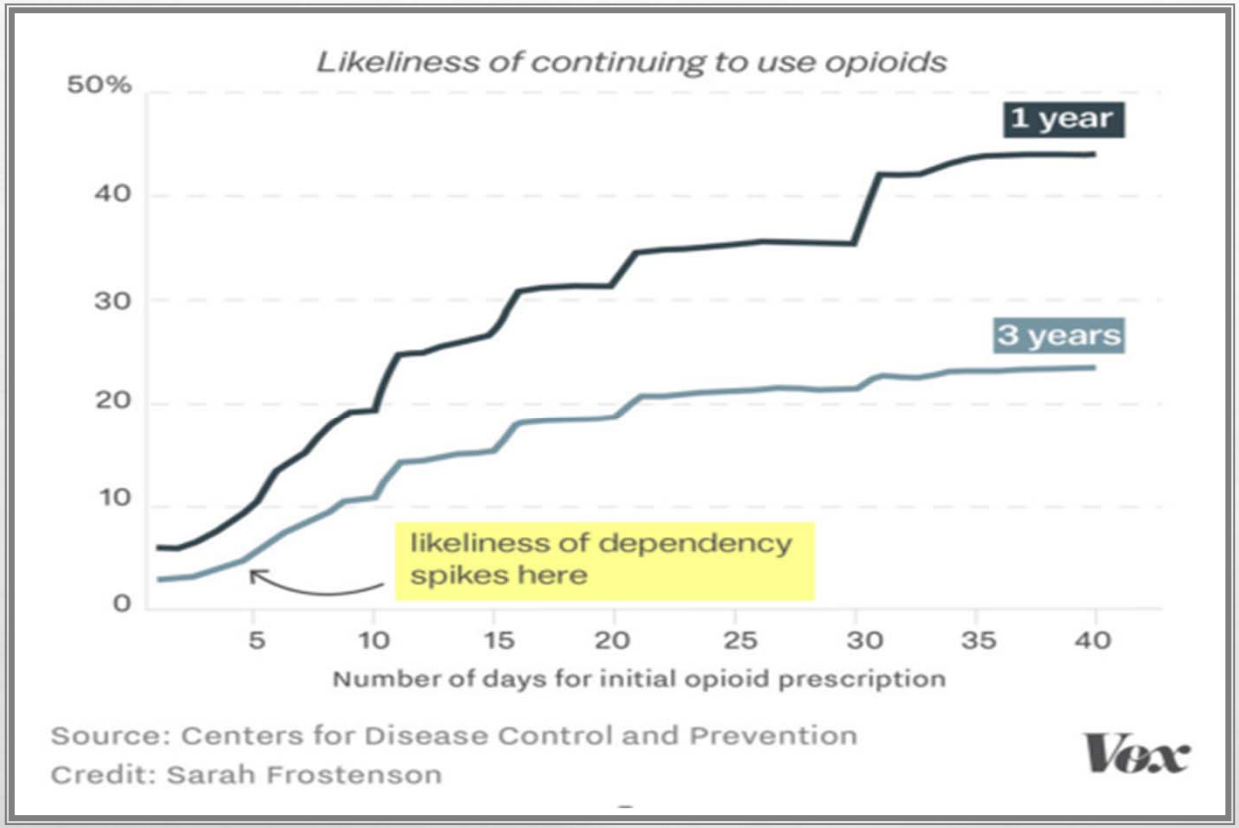
THE ISSUE

- Substance Use Disorder (SUD) is a chronic, relapsing disease, which has significant economic, personal, and public health consequences.
  - Abuse of and addiction to alcohol, nicotine, and illicit and prescription drugs cost Americans more than $700 billion a year in increased health care costs, crime, and lost productivity
  - Nationally, death rates from Rx Opioid overdoses QUADRUPLED during 1999–2013
    - MMWR (CDC)
  - CDC estimates over 33,000 people died in 2015 from overdoses involving opioid pain relievers.

THE ISSUE

- AMERICANS CONSUME MORE OPIOIDS THAN ANY OTHER COUNTRY IN THE WORLD





THE ISSUE

- RISK OF CONTINUED OPIOID USE INCREASES AT 4-5 DAYS

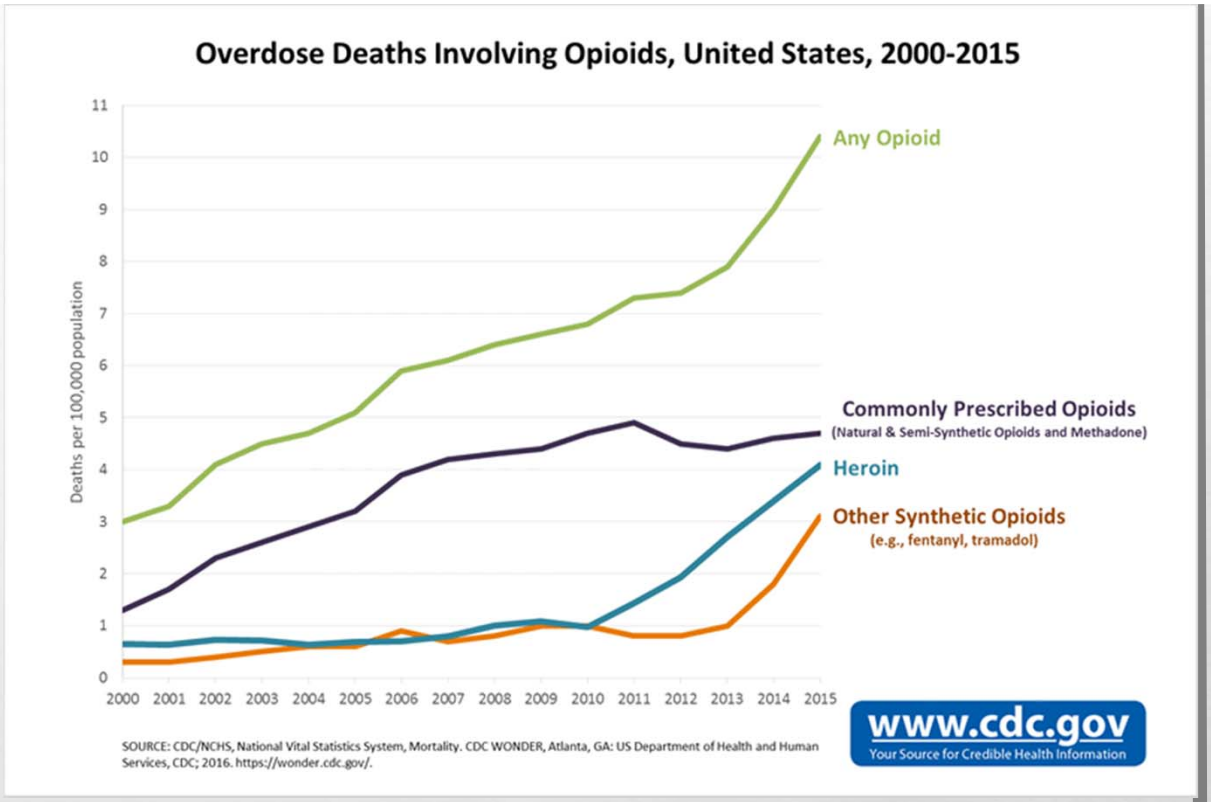
THE RESULT

On an average day in the U.S.:

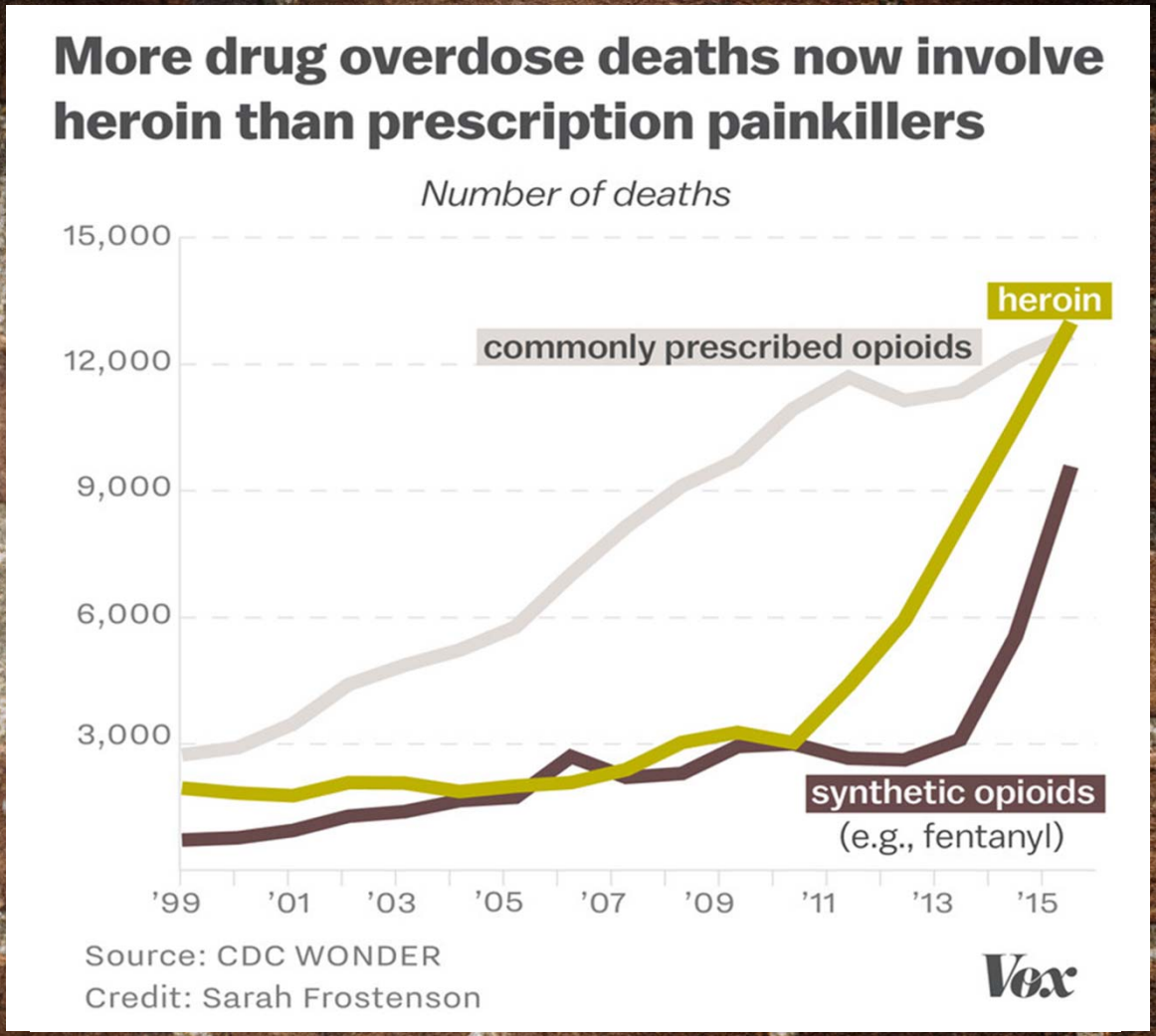
- More than **650,000 opioid prescriptions** dispensed[1]
- **3,900 people** initiate nonmedical use of prescription opioids[2]
- **580 people** initiate heroin use[2]
- **7[illegible] people** die from an opioid-related overdose*[3]

*Opioid-related overdoses include those involving prescription opioids and illicit opioids such as heroin

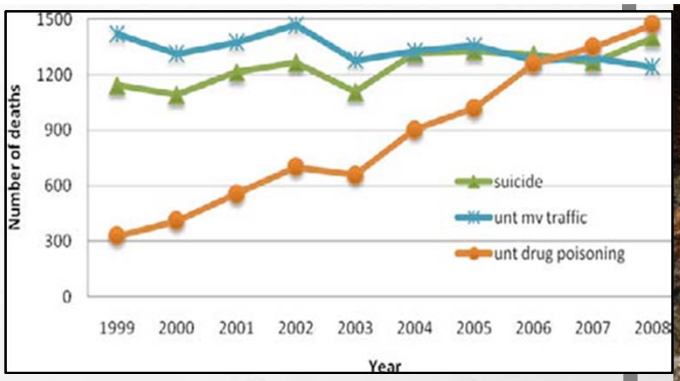
Source: IMS Health National Prescription Audit[1] / SAMHSA National Survey on Drug Use and Health[2] / CDC National Vital Statistics System[3]



SHIFT TO HEROIN & FENTANYL

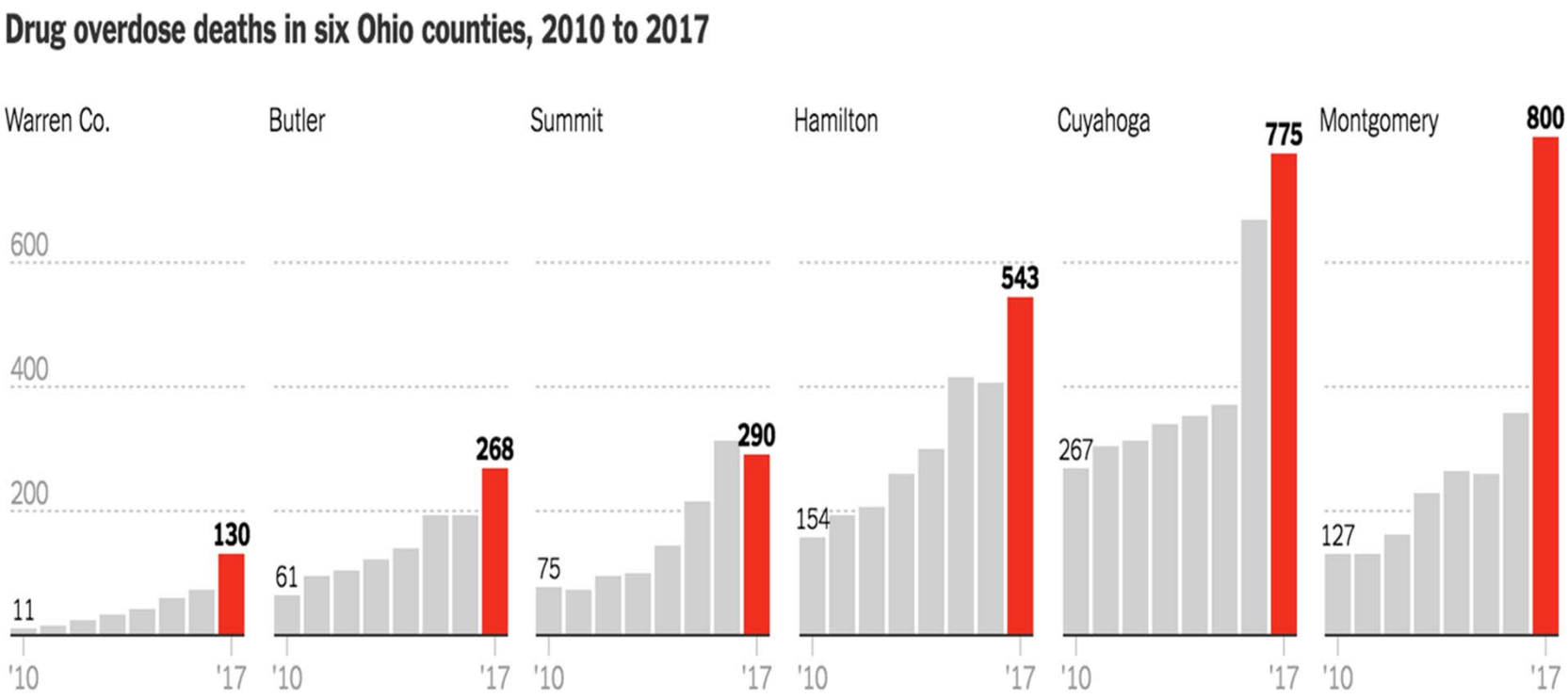


THE ISSUE – OUR REGION



- This disease is devastating our communities
  - 2007 - Unintentional drug poisoning became the leading cause of injury death in Ohio, surpassing motor vehicle crashes for the first time on record.
  - From 1999-2012, Ohio's death rate due to unintentional drug poisonings increased 440 percent, and the increase in deaths has been driven largely by prescription drug overdoses.
  - Ohio's death rate has grown faster than the national rate, with southern Ohio being affected more than the rest of the state. On average, nearly 6 people die each day in Ohio due to drug-related poisoning.
  - Kentucky reported a 279% increase in heroin deaths from 2010 to 2012

WE CAN NOT FORGET ABOUT THE ISSUES OF ALCOHOL AND OTHER DRUGS



THE ISSUE – OHIO

THE DISEASE

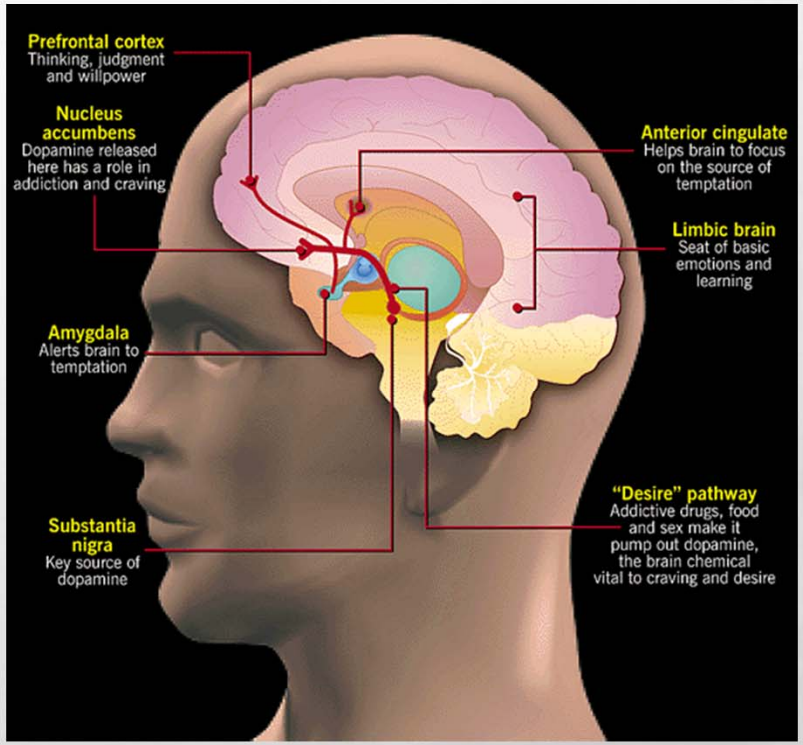
- Definition of disease: Any deviation from or interruption of the normal structure or function of any body part, organ, or system that is manifested by a characteristic set of symptoms and signs and whose etiology, pathology, and prognosis may be known or unknown.

- ASAM definition of the disease of addiction: addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations.

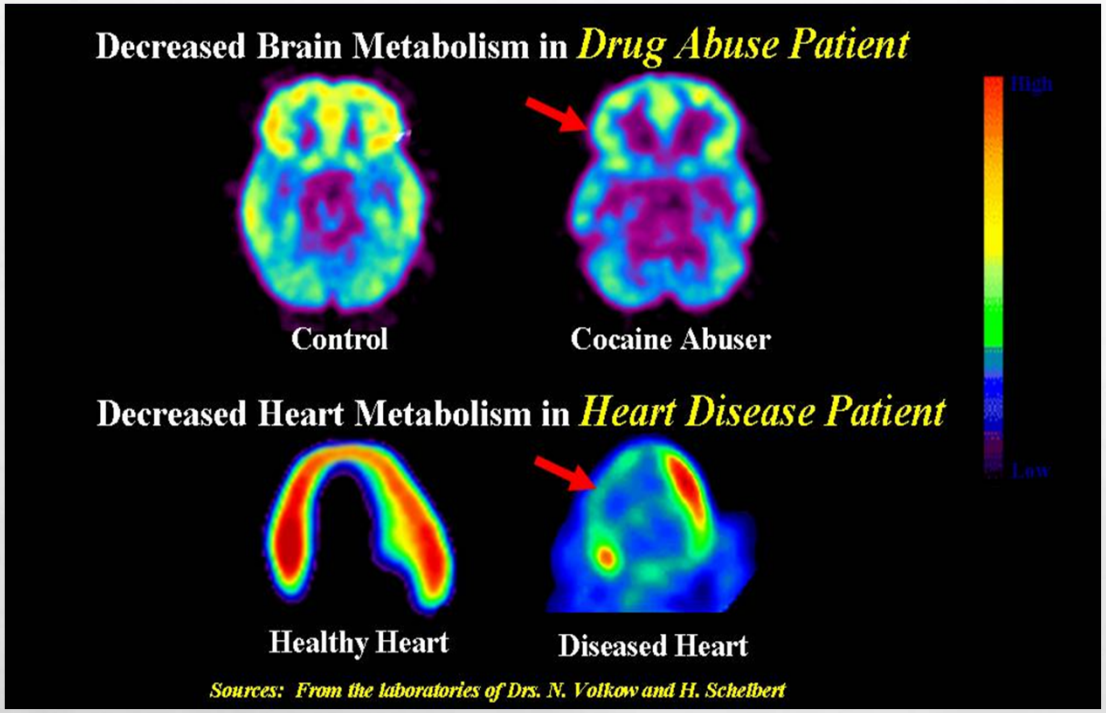
- IT FITS THE DEFINITION; AND IT CAN BE FATAL WITHOUT TREATMENT.

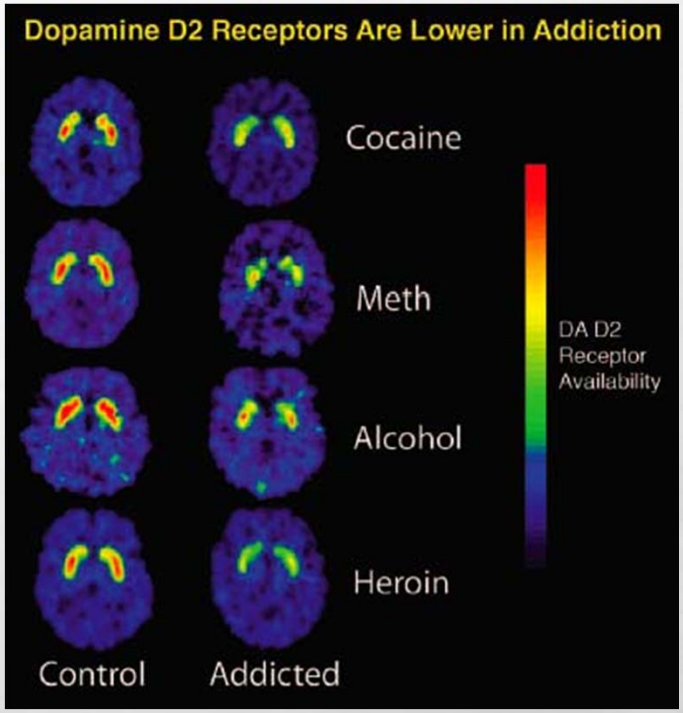
THE DISEASE OF ADDICTION

- Addiction affects neurotransmission and interactions within reward structures of the brain, such that motivational hierarchies are altered and addictive behaviors supplant healthy, self-care related behaviors.
  - However, the neurobiology of addiction encompasses more than the neurochemistry of reward.
- The connections between the frontal cortex and circuits of reward, motivation and memory are fundamental in the manifestations of altered impulse control.
  - The frontal lobes are still maturing during adolescence, and early exposure to substance use is another significant factor in the development of addiction**
- Genetic factors account for about half of the likelihood that an individual will develop addiction. Environmental factors interact with the person's biology and affect the extent to which genetic factors exert their influence.



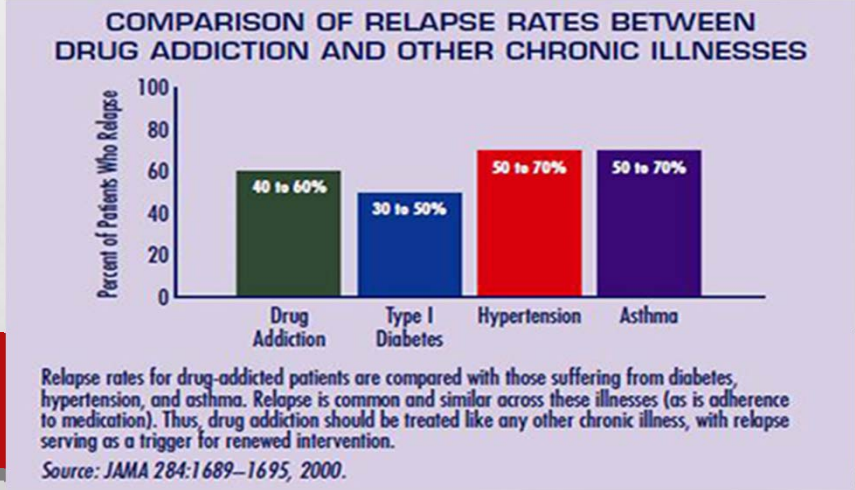
IMAGING EVIDENCE OF THE BRAIN DISEASE

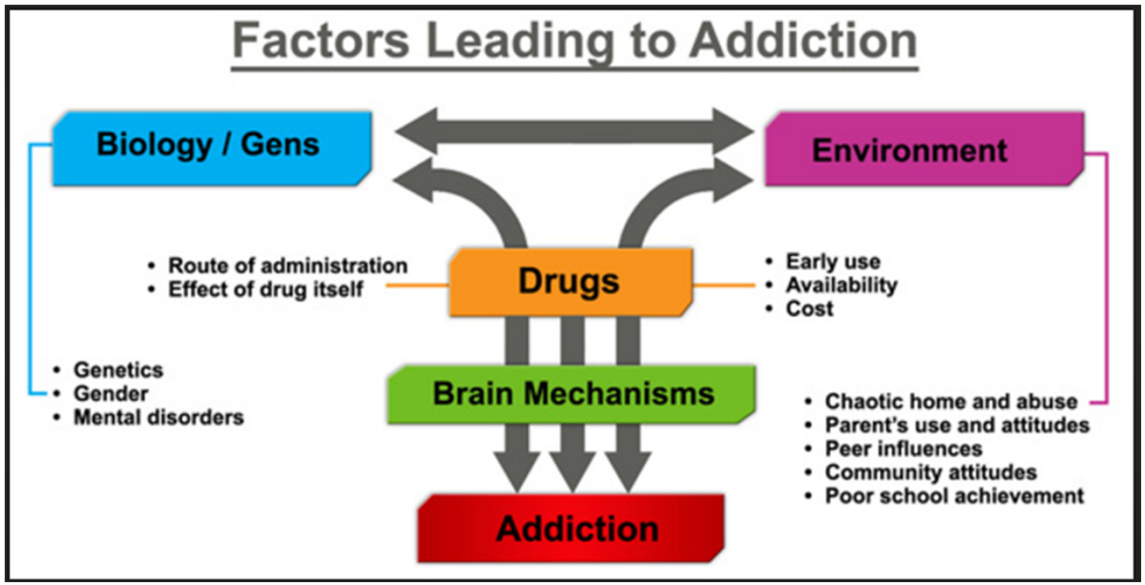




COMPARISON TO OTHER DISEASES

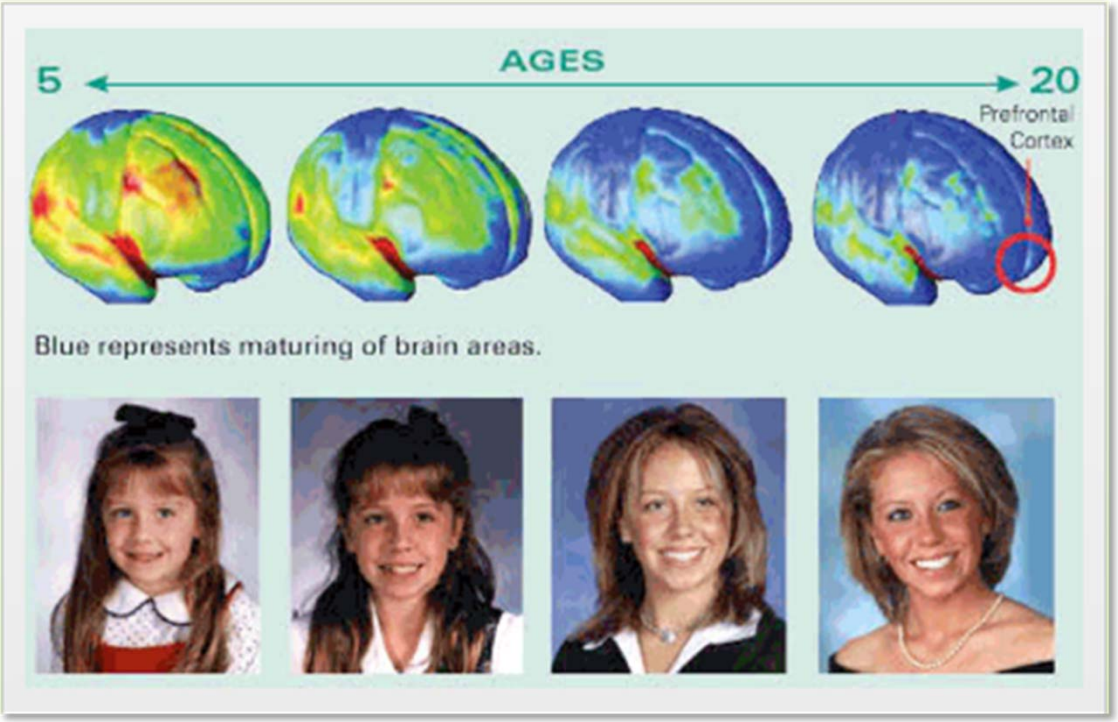
- WHO definition of diabetes type 2: Results from the body's ineffective use of insulin. This type of diabetes comprises the majority of people with diabetes around the world, and is largely the result of excess body weight and physical inactivity with some predisposing genetic factors.
- The disease of addiction is also a state of dysfunction contributed to by genetic factors (obviously not choice) as well as environmental ones such as abuse (mental or physical, again not a choice) and exposure (potentially a choice). Just like diabetes type 2, it is progressive without treatment and potentially life and limb threatening.
  - The approximate rate of relapse of both diseases is also very similar





DEVELOPMENT OF ADDICTION

- BIOLOGY (GENETICS)
- ENVIRONMENT
- EXPOSURE



DEVELOPMENT OF THE BRAIN

- One of the last parts of the brain to mature is the prefrontal cortex
  - Enables us to make rational, sound decisions. It also helps us to override impulsive urges
- Significant changes in the brain occur during adolescence, which may enhance vulnerability to drug use and the development of addiction and other mental disorders.
- Adolescents exposed to ANY mind altering substances have a significantly increased risk of developing addiction

SO WHAT ARE WE GOING TO DO BRAIN??

MULTI-FACETED SOLUTION

- Prevention: preventing youth drug use before it starts
- Treatment: creating better pathways to treatment and recovery
- Law enforcement: cracking down on drug trafficking
- Appropriate prescribing: encouraging appropriate use and availability of pain medication
- Harm reduction: saving lives by expanding access to naloxone, etc.

ADOLESCENTS & PREVENTION

- The IOM has described three categories of prevention interventions:
  - Universal, Selective, and Indicated.

- Universal interventions are aimed at all members of a given population (for instance, all children of a certain age)
- Selective interventions are aimed at a subgroup determined to be at high-risk for substance use (for instance, justice-involved youth)
- Indicated interventions are targeted to individuals who are already using substances but have not developed a substance use disorder

ADOLESCENTS & PREVENTION

- The Surgeon General's report reviewed 600 prevention programs and found 42 evidence-based strategies that were proven to successfully reduce the number of people who start using alcohol or drugs or who progress to harmful use.
  - School based programs
    - LifeSkills Training, keepin'it REAL, Project Toward No Drug Abuse
  - Family-based Programs
    - Strengthening Families Program: For Parents and Youth 10–14 (SFP), Coping Power, etc
  - Internet-based Programs
    - I Hear What You're Saying, Project Chill
- Fear based or educational only programming does not work – has been associated with higher drug use
  - D.A.R.E. - A meta-analysis in 2009 of 20 controlled studies by statisticians at the University of Cincinnati, and University of Central Florida revealed that teens enrolled in the program were just as likely to use drugs as were those who received no intervention.

JUST SAY NO DOES NOT WORK

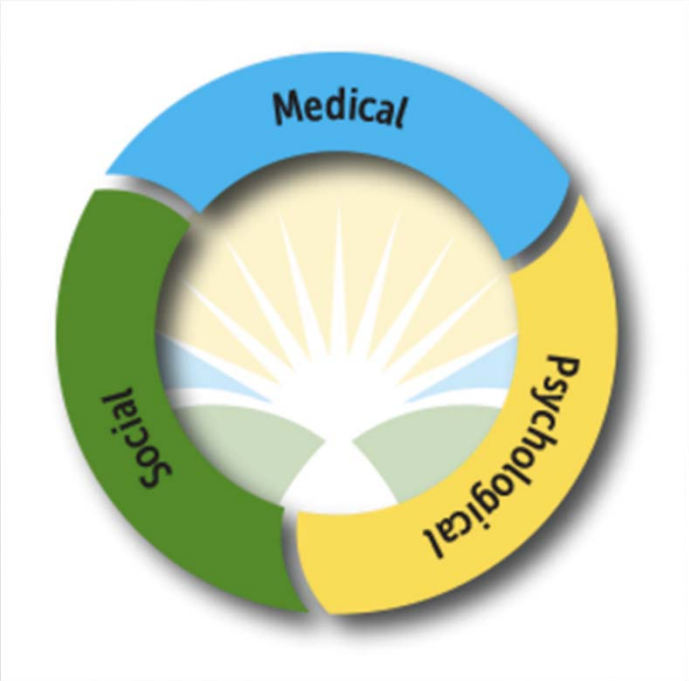
THE TRAJECTORY - ARREST THE DESCENT

- 3 general categories of patients
  - Never exposed, or minimally exposed with no dependence
    - Keep it that way
  - Exposed & dependent – Early identification/screening
    - Taper and transition to other multi-modal pain treatments
    - Buprenorphine can have a role
  - Opioid use disorder
    - Long term MAT for most with psychological and social interventions as well

ASAM DEFINITION… AGAIN

- Chronic Relapsing Biopsychosocial Disease
- The Treatment for this Disease must address all Three components
  - Biological - Medical
  - Psychological
  - Social

TREATMENT



- **Medical** (addiction treatment)
  - Comprehensive assessment & intake – SAME DAY or NEXT DAY
  - Outpatient withdrawal management (and ongoing pharmacological management)
  - Medical stabilization services (general condition treatment until seen by or referred to PCP)
  - Care coordination and monitoring (ex: referrals to other physicians and monitoring of pdmps)
- **Psychological**
  - Clinical assessment (ASAM PLACEMENT CRITERIA)
  - Therapy (individual, group, and family, etc.)
- **Social**
  - Case management
    - Can include all of the following: crisis support, family services, legal services, vocational services, transportation, housing, etc.
  - Involving social support networks – AA, NA, Peer Support, etc

MEDICATION *FOR* ADDICTION TREATMENT - HISTORY

- Serious attempts to find medications for opioid addiction are traced to the early 1920's
- Investigation of over 150 compounds including: Metopon, Heroin("mistake"), Nalorphine, etc.
- 1962 - Dr. Vincent P. Dole, a specialist in metabolism at the Rockefeller University, became chair of the narcotics committee of the health research council of New York City. He read "the drug addict as a patient" by Dr. Marie E. Nyswander (1956) - a psychiatrist with extensive experience treating patients who were addicted to opioids.
  - She also believed that many would have to be maintained on opioids for extended periods to function *because a significant number of people who attempted abstinence without medication relapsed, in spite of detoxifications, hospitalizations, and psychotherapy*
- Narcotic Addict Treatment Act of 1974, effectively limited methadone maintenance treatment to the context of the Opioid Treatment Program (OTP) (i.e., methadone clinic) setting.
- 1963 – Naltrexone first synthesized – Trials (mixed and approved in 1984 for OUD, 1995 for AUD
- 1966 – Buprenorphine synthesized from thebaine
- 1996 – Approved for treatment of OUD in France; 2002 in US (DATA 2000)

MAT – EVIDENCE FOR AGONISTS

Methadone – full Mu agonist

- Fullerton CA, et al. Medication-assisted treatment with methadone: assessing the evidence. Psychiatric services in advance. November 18, 2013
  - Meta-analyses, systematic reviews, and individual studies of MMT from 1995- 2012.
  - **Nine studies** - High level of evidence for the positive impact of MMT on treatment retention and illicit opioid use

Buprenorphine – partial Mu agonist (Suboxone, Zubsolv, Bunavail – Bup/Naloxone)

- Thomas CP, et al. Medication-assisted treatment with buprenorphine: assessing the evidence. Psychiatric services in advance. November 18, 2013
  - **Sixteen studies** - High level of evidence for the positive impact of BMT on treatment retention and illicit opioid use

MAT – EVIDENCE FOR AGONISTS

- Methadone and Buprenorphine - More studies/guidelines coming out frequently
  - D'Onofrio, et al JAMA 2015 - ED initiation of Buprenorphine
    - Increased attendance of outpatient treatment at 30 days
    - 78% in the buprenorphine group vs 37% patients in the referral group
    - The buprenorphine group also reported greater reductions in the average number of days of illicit opioid use
  - Dunlap, et al JAMA 2016 - JAMA Clinical Guidelines Synopsis: Clinical Management of Opioid Use Disorder
    - MAT is superior to withdrawal alone in multiple studies
  - Sordo, et al BMJ 2017 - Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies
    - Meta-analysis - 19 eligible cohorts, following 122,885 people treated with methadone over 1.3-13.9 years and 15831 people treated with buprenorphine over 1.1-4.5 years.
    - Retention in MMT and BMT is associated with substantial reductions in the risk for all cause and overdose mortality

MAT – EVIDENCE FOR AGONISTS

- Surgeon Generals Report
  - Abundant scientific data show that long-term use of maintenance medications successfully reduces substance use, risk of relapse and overdose, associated criminal behavior, and transmission of infectious disease, as well as helps patients return to a healthy, functional life.
  - Use of medications to treat addiction - controversial at times because of a longstanding misconception that methadone and buprenorphine are merely “substitute one addiction for another.”
    - This belief has reinforced scientifically unsound “abstinence-only” philosophies in many treatment centers and has severely limited the use of these medications.

- VA Clinical Practice Guideline For the Management of Substance Use Disorders
  - Strong recommendation for patients with OUD
    - Buprenorphine/naloxone or methadone in an opioid treatment program
  - For patients with OUD for whom opioid agonist treatment is contraindicated, unacceptable, unavailable, or discontinued and who have established abstinence for a sufficient period of time:
    - Extended-release injectable naltrexone (Vivitrol)

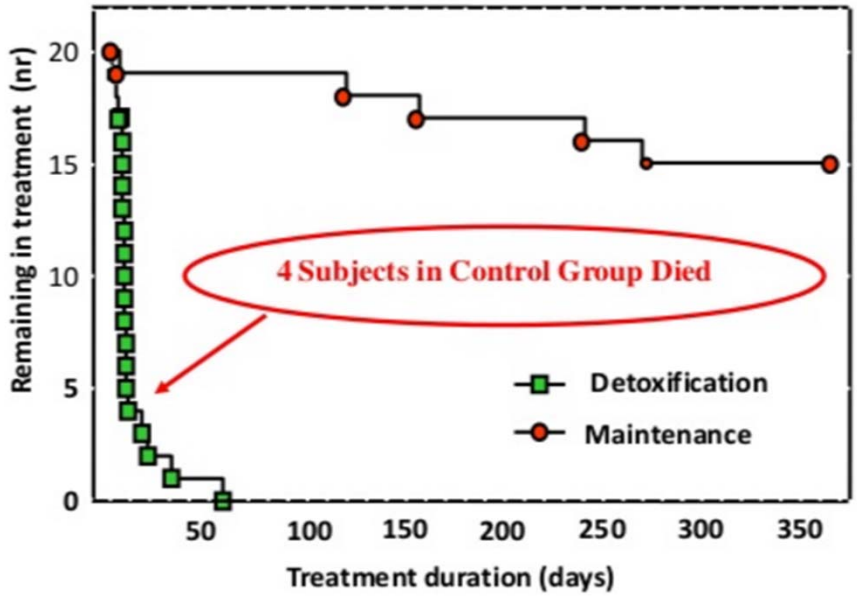
DETOX (Withdrawal management) VS MAINTENANCE

- There is NO GOOD EVIDENCE for Detoxification alone

Buprenorphine Treatment for Hospitalized, Opioid-Dependent Patients
A Randomized Clinical Trial
JAMA Internal Medicine August 2014 Volume 174, Number 8

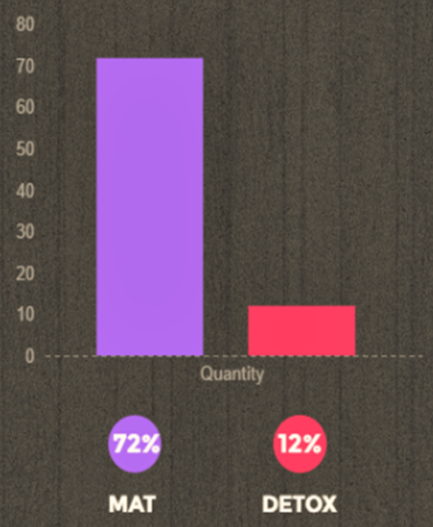
Buprenorphine vs. Placebo for Heroin Dependence

Kakko, Lancet 2003



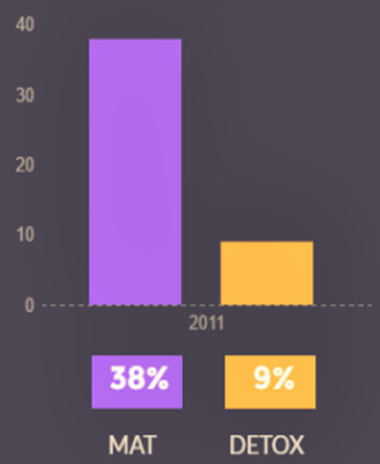
Rates of Treatment Continuation after discharge from Hospital

With detoxifiation alone and no continuation of MAT(medically assisted treatment), patients rarely ever continued their outpatient treatment plan



Cessation of Illicit Opioid Use

Rates of cessation of Illicit Opioid use at 6 month were much better with linkage to care and continuation of MAT than with detoxification alone



MAT – EVIDENCE FOR ANTAGONISTS

- Generally positive but sometimes mixed evidence
  - Generally recommended for “Highly Motivated Patients” – Revia (oral)
    - Extended-Release (Vivitrol) tends to have better compliance and abstinence rates
  - Extended-Release Naltrexone to Prevent Opioid Relapse in Criminal Justice Offenders – NEJM 2016, Lee J. et al
    - Time to relapse was significantly longer in the extended-release naltrexone group than in the usual-treatment group: 10.5 weeks versus 5.0 weeks
    - Several important secondary outcomes did not differ significantly between the groups: rates of cocaine, alcohol, and intravenous drug use and self-reported reincarceration

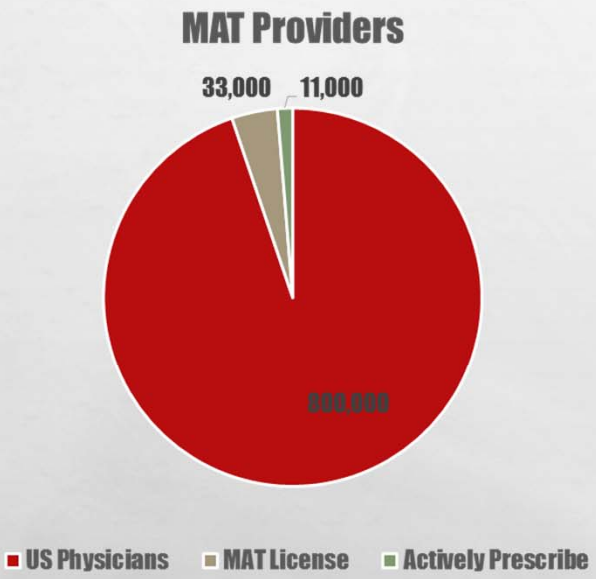
EVIDENCE FOR COAT – COMPREHENSIVE OPIOID ADDICTION TREATMENT

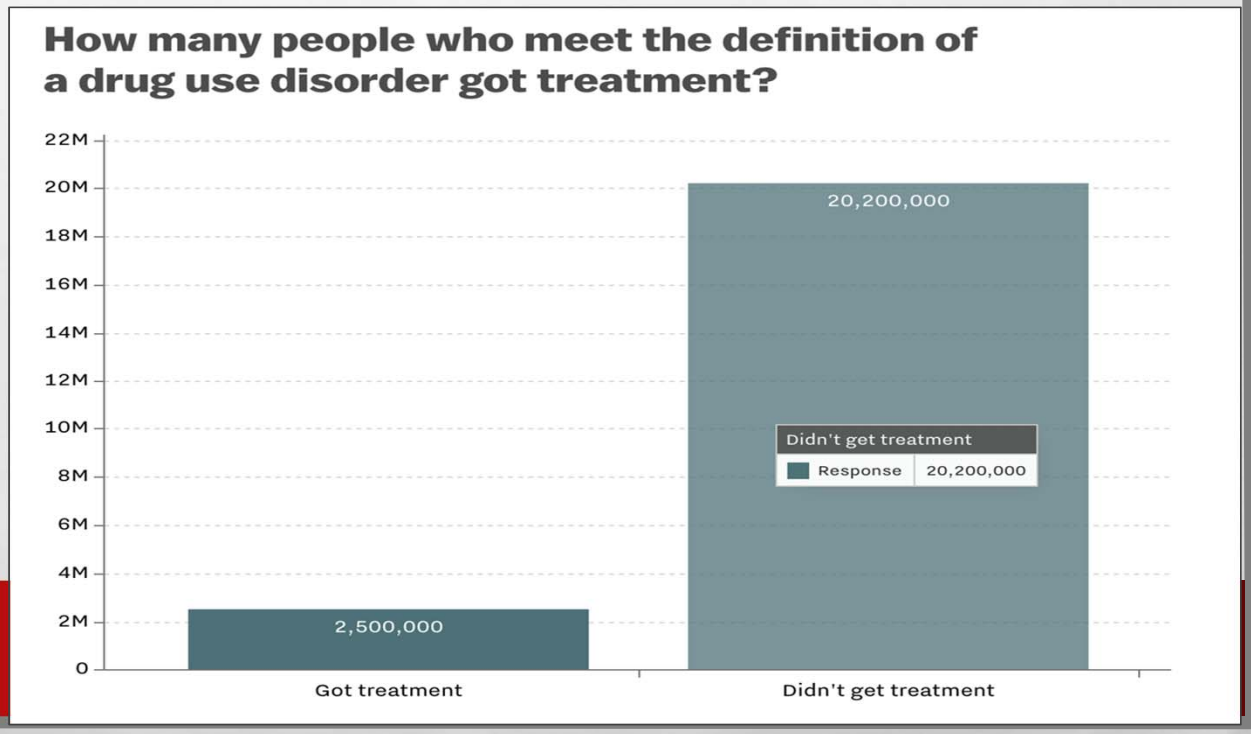
- EVERY RECOMMENDATION for MAT includes need for psychosocial interventions
  - ASAM, NIDA, SAMHSA, Surgeon General, VA Guidelines, etc
- Weiss, et al – Drug and Alcohol Dependence, 2014
  - Patients who had ever used heroin and received drug counseling in addiction to buprenorphine/naloxone were more likely to be successful (abstinent or nearly abstinent)
- Lynch et al. Addiction Science & Clinical Practice, 2014
  - Patients receiving MAT (medically assisted treatment) plus addiction counseling had significantly lower total health care costs than patients with little or no addiction treatment ($13,578 vs. $31,055 = 56% reduction)
- JAM (Journal of Addiction Medicine) 2016 – A Systematic Review on the Use of Psychosocial Interventions in Conjunction With Medications for the Treatment of Opioid Addiction. Dugosh, et al.
  - Results generally support the efficacy of providing psychosocial interventions in combination with medications to treat opioid addictions, although the incremental utility varied across studies, outcomes, medications, and interventions.
  - Unclear as to the type of therapy that is superior and in what patient population

NO QUESTION THAT OPIOID AGONIST THERAPY *ALONE* REDUCES MORTALITY – HARM REDUCTION

TREATMENT NEED

- Approx. 10-20% of patients with illicit drug use receive treatment
  - Estimated 5-10X increase in need for addiction treatment





TREATMENT IMPACT

- For every $1.00 spent on treatment:
  - The costs of crime and lost productivity are reduced by $7.46
  - The total societal and medical costs are estimated to be reduced by as much as $18.54
- Patients with substance use disorder often use a disproportionate amount of healthcare in very inefficient ways.
  - Mean annual direct health care costs for opioid abusers were more than 8 times higher than for nonabusers ($15,884 versus $1,830, respectively) – White, 2010
- Reminder - patients receiving MAT (medically assisted treatment) plus addiction counseling had significantly lower total health care costs than patients with little or no addiction treatment ($13,578 vs. $31,055 = 56% reduction); As much as 90% reduction has been seen in other studies.

SUMMARY

- This is a disease and prevention is important
  - Adolescent drug exposure can have important effects
- MAT works and it saves lives
  - Abstinence from opioids and mortality reduction
  - COAT is best practice
- We have a long way to go to turn the tide on opioid epidemic
  - Hope – new evidence coming out often
    - New medication and therapies are promising

LIST OF RESOURCES

- ASAM - AMERICAN SOCIETY OF ADDICTION MEDICINE
- COPE - COALITION ON PHYSICIAN EDUCATION IN SUBSTANCE USE DISORDERS
- SAMHSA – SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION
- NIDA – NATIONAL INSTITUTE ON DRUG ABUSE
- HAMILTON COUNTY AREA– INJECTHOPE.COM
- SURGEON GENERALS REPORT ON ALCOHOL, DRUGS, AND HEALTH
- VA CLINICAL PRACTICE GUIDELINE ON SUBSTANCE USE DISORDER TREATMENT
- MULTIPLE ARTICLES AS REFERENCED IN THE PRESENTATION