ADDICTION: OVERVIEW OF DEVELOPMENT AND TREATMENT

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Every 12 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

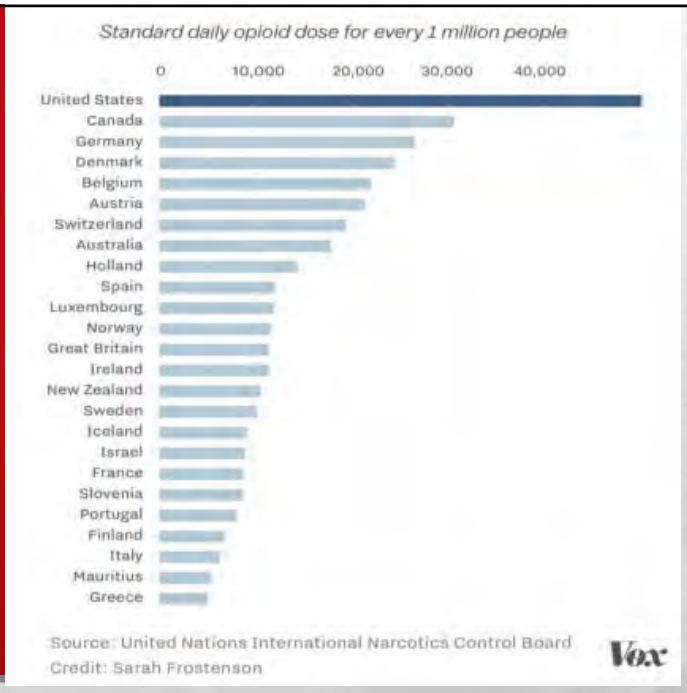
- The Issue in our Country
  - Current State and how did we get here
- Substance Use Disorder
  - The Disease
  - How does it develop
  - Adolescents and Prevention
  - Stigma
- Medication-Assisted Treatment (MAT)
  - History, evidence, indications and contraindications
  - Comprehensive Integrated Addiction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

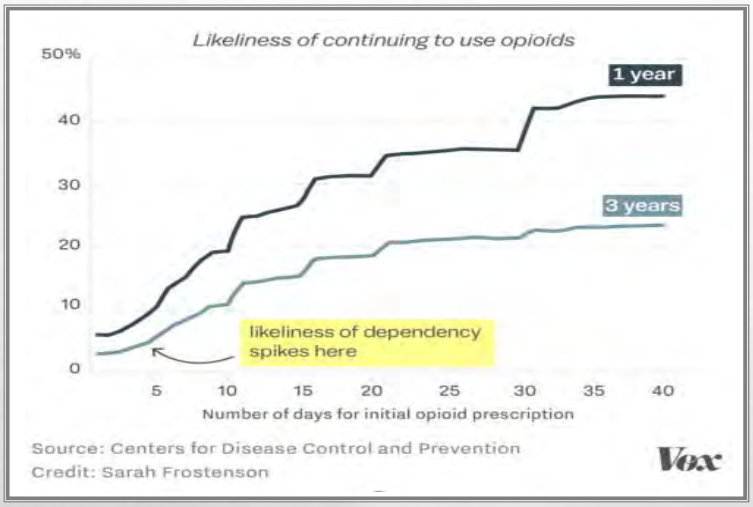
THE ISSUE

- 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 1999–2016
    - MMWR (CDC)
  - CDC estimates over 42,000 people died in 2016 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

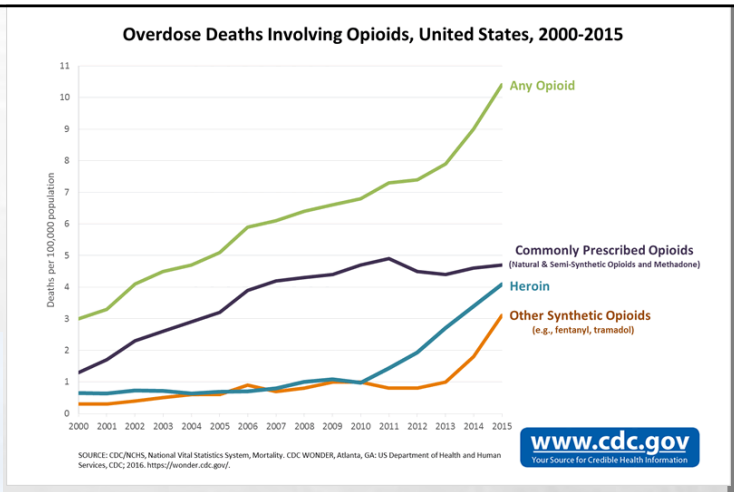
116 AMERICANS die every day from an **opioid overdose** (that includes prescription opioids and heroin).

On an average day in the U.S.:

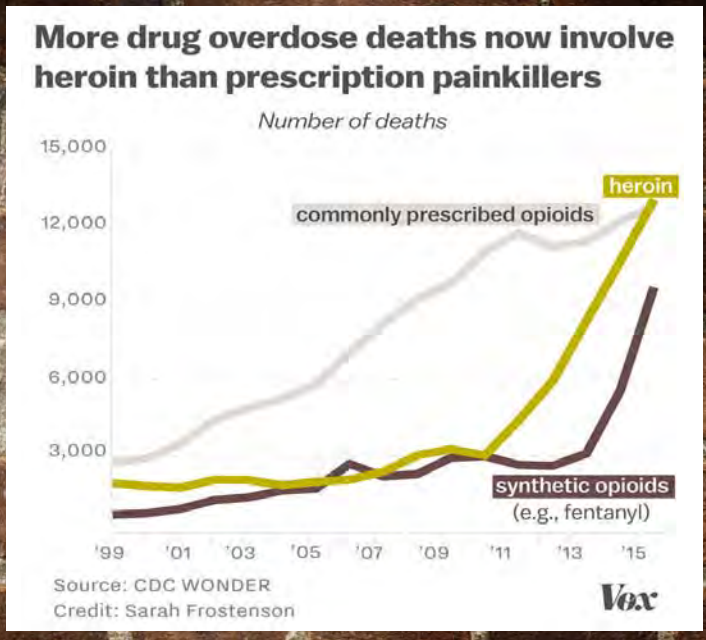
- More than **650,000 opioid prescriptions** dispensed[1]
- **3,900 people** initiate nonmedical use of prescription opioids[2]
- **580 people** initiate heroin use[2]
- **78 people** die from an opioid-related overdose*[3]

*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

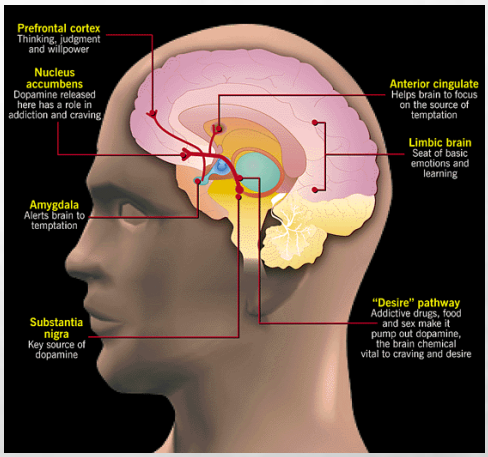


THE DISEASE

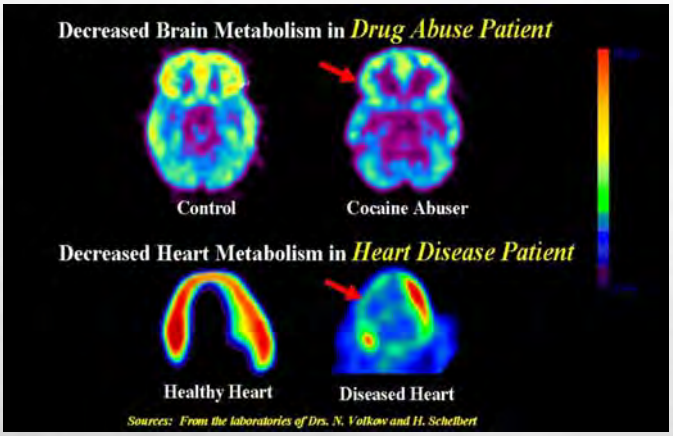
- Definition of disease: Any deviation from or interruption of the normal structure or function of any body part, organ, or system that is manifested by a characteristic set of symptoms and signs and whose etiology, pathology, and prognosis may be known or unknown.
- ASAM definition of the disease of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

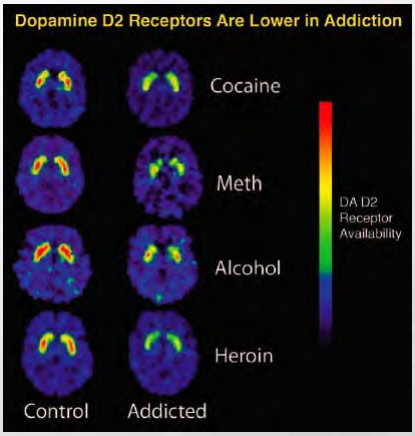
THE DISEASE OF ADDICTION

- 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.



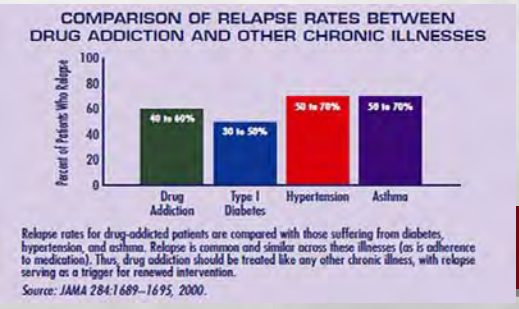
IMAGING EVIDENCE OF THE BRAIN DISEASE

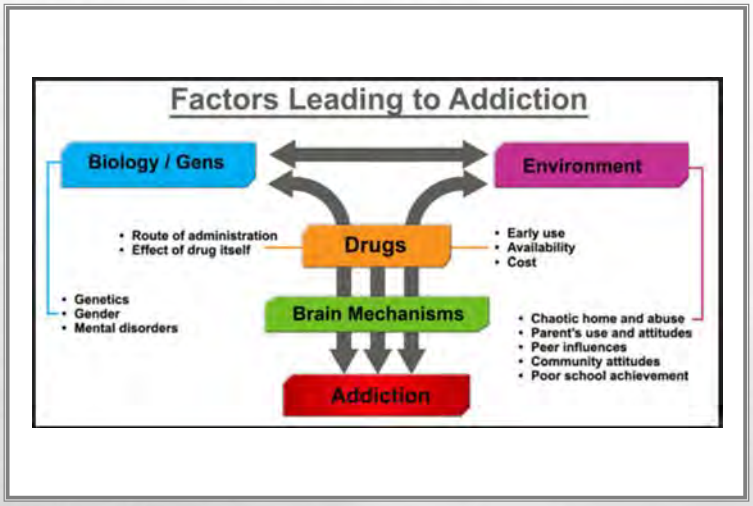




COMPARISON TO OTHER DISEASES

- 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

STIGMA IS WRONG

- Stigma is wrong and allowing it to be a part of how anyone treats patients in any setting is counterproductive
- Providers and patients both benefit from an understanding of the complex chronic disease
- Language matters and it can significantly affect patients either positively or negatively

* Shatterproof

Words to avoid	Words to use
Addict	Person with substance use disorder
Alcoholic	Person with alcohol use disorder
Drug problem, drug habit	Substance use disorder
Drug abuse	Drug misuse, harmful use
Drug abuser	Person with substance use disorder
Clean	Abstinent, not actively using
Dirty	Actively using
A clean drug screen	Testing negative for substance use
A dirty drug screen	Testing positive for substance use
Former/reformed addict/alcoholic	Person in recovery, person in long-term recovery
Opioid replacement, methadone maintenance	Medication assisted treatment

By using person-first language like this, we can make great progress toward reducing the deadly stigma associated with addiction.

SO WHAT ARE WE GOING TO DO BRAIN??

MULTI-FACETED SOLUTION

- Harm reduction: saving lives by expanding access to naloxone, etc.
- 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

IMPORTANT PUBLIC HEALTH INTERVENTIONS

- RAPID NALOXONE DISTRIBUTION PROGRAMS
  - – PROVEN TO SAVE LIVES AND REDUCE MORTALITY
  - PROJECT DAWN
  - NARCAN DISTRIBUTION COLLABORATIVE
- SYRINGE EXCHANGE PROGRAMS
  - SUBSTANTIAL REDUCTION IN INFECTIOUS DISEASE TRANSMISSION
  - IMPORTANT LINKAGE TO TREATMENT

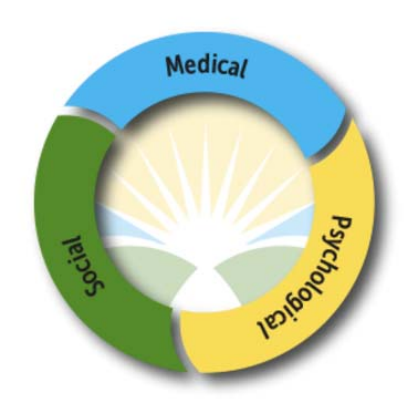
*HTTPS://WWW.CDC.GOV/HIV/RISK/SSPS.HTML

HARM REDUCTION

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

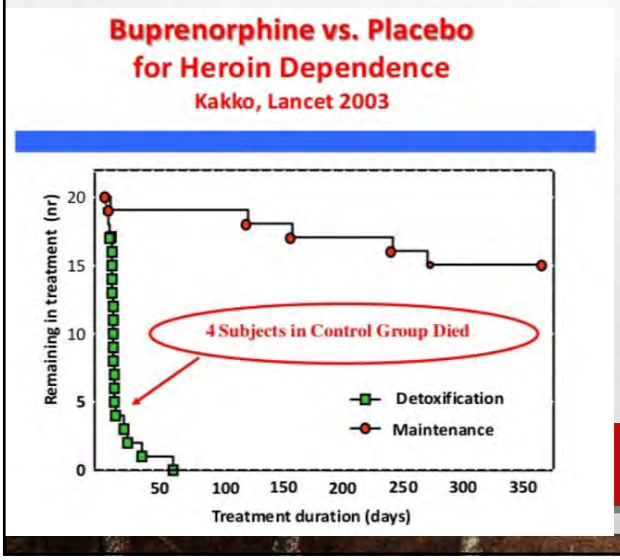
MAT – EVIDENCE FOR AGONISTS

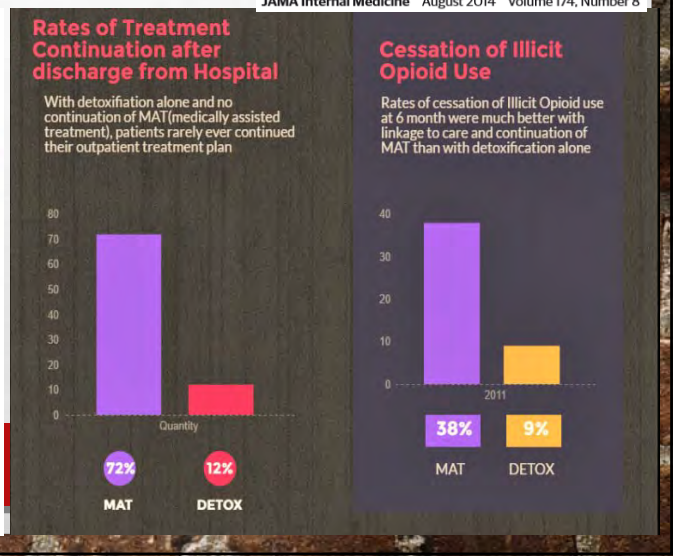
- Surgeon Generals Report
  - Abundant scientific data show that long-term use of maintenance medications successfully reduces substance use, risk of relapse and overdose, associated criminal behavior, and transmission of infectious disease, as well as helps patients return to a healthy, functional life.
  - 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





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 efficacy
  - 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 treatment group
      - 10.5 weeks versus 5.0 weeks
    - Several important secondary outcomes did not differ significantly between the groups
  - Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multi-centre, open-label, RCT. Joshua D Lee, et al 2017
    - In this population it is more difficult to initiate patients to XR-NTX than BUP-NX, and this negatively affected overall relapse. However, once initiated, both medications were equally safe and effective. Future work should focus on facilitating induction to XR-NTX and on improving treatment retention for both medications.

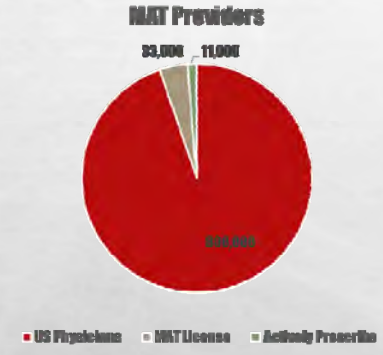
EVIDENCE FOR COAT – COMPREHENSIVE OPIOID ADDICTION TREATMENT

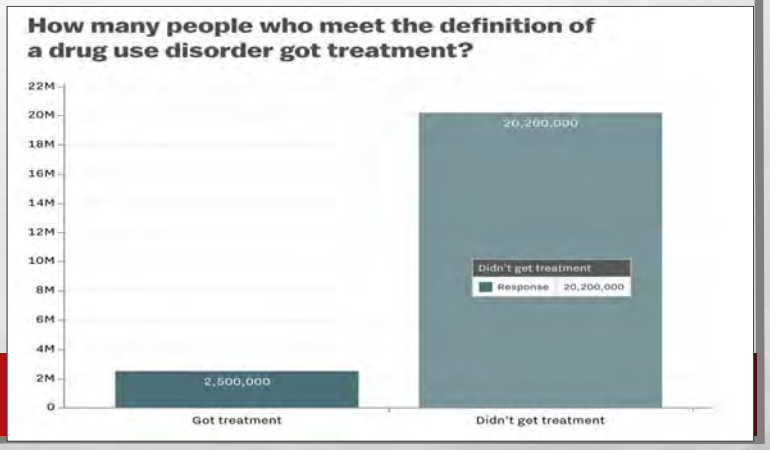
- EVERY RECOMMENDATION for MAT includes need for psychosocial interventions
  - ASAM, NIDA, SAMHSA, Surgeon General, VA Guidelines, etc
- Weiss, et al – Drug and Alcohol Dependence, 2014
  - Patients who had ever used heroin and received drug counseling in addiction to buprenorphine/naloxone were more 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.

RURAL HEALTH & INNOVATIONS

- Hub & spoke as well as ECHO
  - Models that utilize limited expertise most efficiently
- Telehealth
  - Technology more than sufficient
  - New DEA rules just released in may 18 – to allow for specific prescribing of buprenorphine
  - Reimbursement challenges being reviewed
- Digital therapies now showing promise
  - Pear therapeutics (FDA cleared), etc

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
  - Stigma is wrong and counterproductive; we must change the paradigm

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