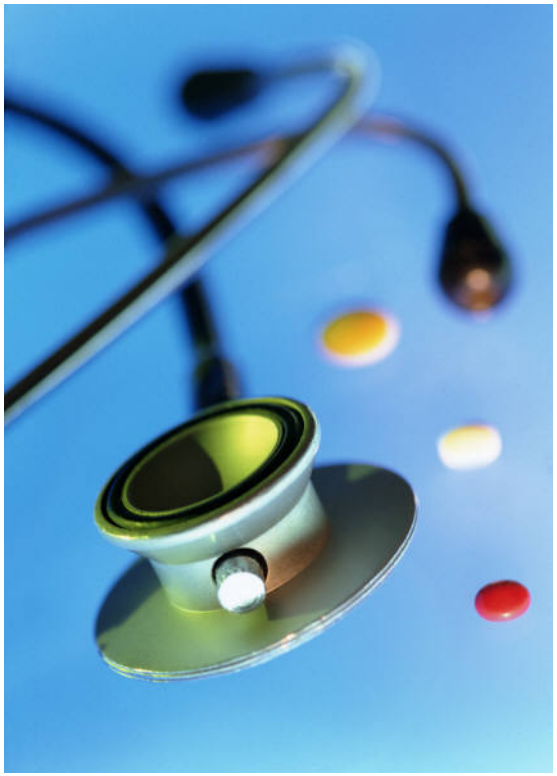

TREATMENT OF OPIOID ADDICTION

Neurobiology of Addiction

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- President, Northwest Chapter of the American Society of Addiction Medicine

- No disclosures

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INTRODUCTION

- 2.5 million Americans are addicted to opioids
- 1.68 million years potential life lost in 2016
- 48,000 deaths in 2017 from opioid overdoses
- That's 130 every day
- Cost to society of $504 billion in 2015*
  - The Council of Economic Advisers
  - *$1,575 per capita (pop 320 million)
  - *13% of federal budget (3.8 trillion)
  - *2.7% of GNP (18.75 trillion)

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OUTLINE

- ABCs of addiction
- Addiction as a brain disease, neuroadaptation
- Results of non-medication treatment
- Why opioid addiction is different from other substances
- Breaking the cycle of opioid addiction
- Details of MAT programs
- Efficacy and safety of MAT

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- "The standard treatment for opioid addiction (heroin or prescription opioids) is referral to detox, followed by counseling and AA/NA for support and to learn the skills necessary to stay off drugs."
- A commonly held belief among the lay public, medical profession, and even in the addiction treatment field.
- This is WRONG – and dangerous!

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"Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 2)."

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Recommendations and Reports / March 18, 2016 / 65(1);1–49

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"The Administration prioritizes several distinct initiatives to achieve these goals. First, a proactive response to overdoses to ensure that the patient can enter into a treatment program designed to meet his or her individual needs. Second, consistently using evidence-based approaches to treatment and making Medication-Assisted Treatment (MAT) a standard of care for opioid addiction."

National Drug Control Strategy - A Report by the Office of National Drug Control Policy. January 2019

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"Currently, three medications are approved for treating OUD: methadone, buprenorphine, and ER naltrexone. Along with psychosocial support, they comprise the current standard of care for reducing illicit opioid use, relapse risk, and overdoses, while improving social function."

The President's Commission on Combatting Drug Addiction and the Opioid Crisis. November 1, 2017. Chairman Gov. Chris Christie.

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Many people, including some policymakers, authorities in the criminal justice system, and treatment providers, have viewed maintenance treatments as "substituting one substance for another" and have adhered instead to an abstinence-only philosophy that avoids the use of medications, especially those that activate opioid receptors. Such views are not scientifically supported; the research clearly demonstrates that MAT leads to better treatment outcomes compared to behavioral treatments alone. Moreover, withholding medications greatly increases the risk of relapse to illicit opioid use and overdose death. Decades of research have shown that the benefits of MAT greatly outweigh the risks associated with diversion.

U.S. Department of Health and Human Services (HHS), Office of the Surgeon General, Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. Washington, DC: HHS, November 2016.

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"Strong scientific evidence unequivocally shows that for opioid use disorder, medication is the essential component of treatment, not merely one component.

Despite this settled knowledge, some vocal constituents within the addiction treatment community and some policy makers dangerously continue to lobby for the treatment of opioid use disorder without medication."

Andrew Saxon, Elinore McCance-Katz, Journal Addiction Med, May/June 2016

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ASAM DEFINITION

- 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. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.
- Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

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ADDICTION - THE "C"S

- Loss of Control
- Continued use in spite of adverse ~
- Consequences
- Compulsion and Cravings
- lack of Consciousness (denial)

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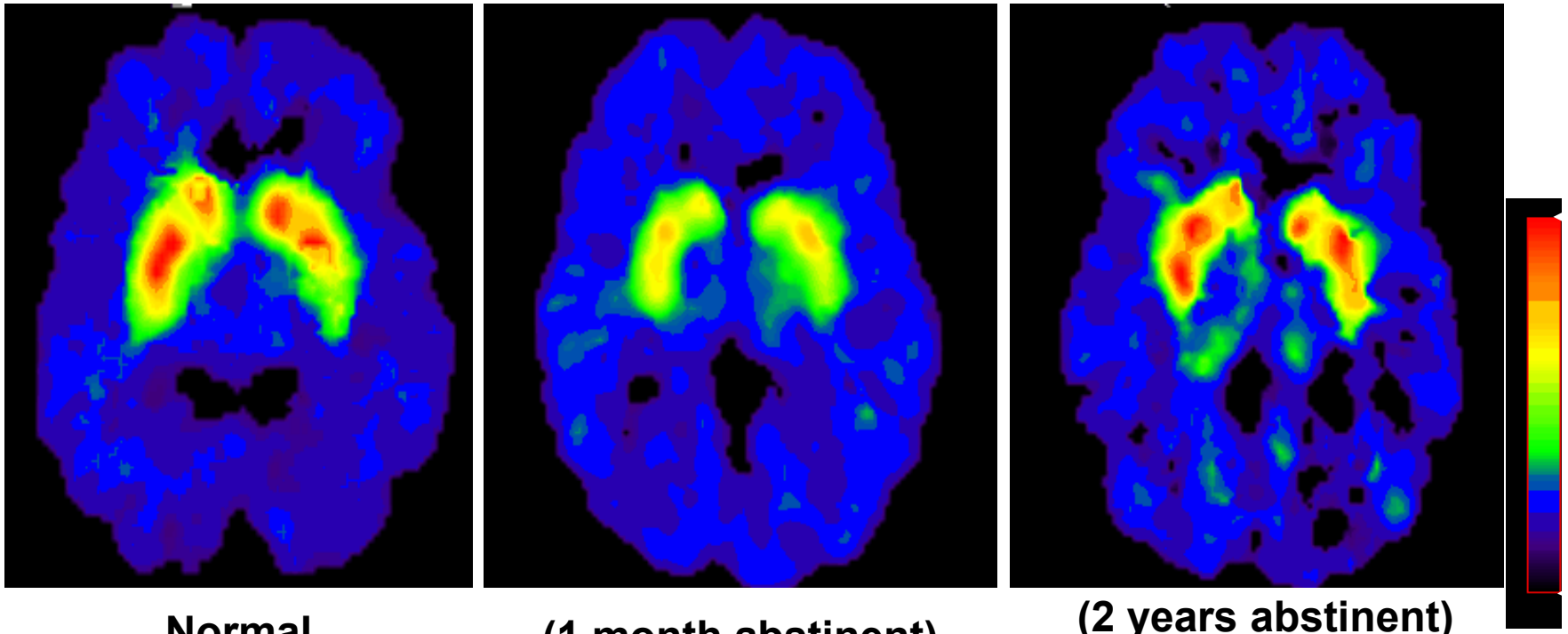
Partial Recovery of Brain Dopamine Transporters in Methamphetamine (METH) User After Protracted Abstinence



Normal **(1 month abstinent)** **(2 years abstinent)**

METH user

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NIDA, 2007..

Structurally . . .

Saline Amph

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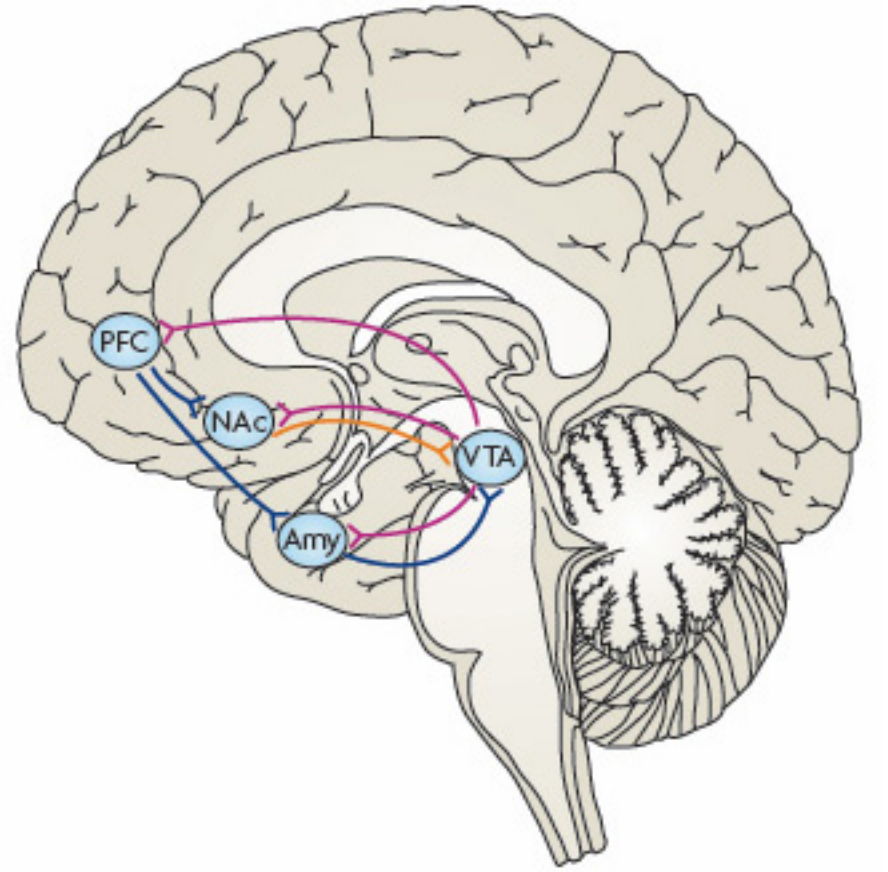
BRAIN REWARD CIRCUITRY



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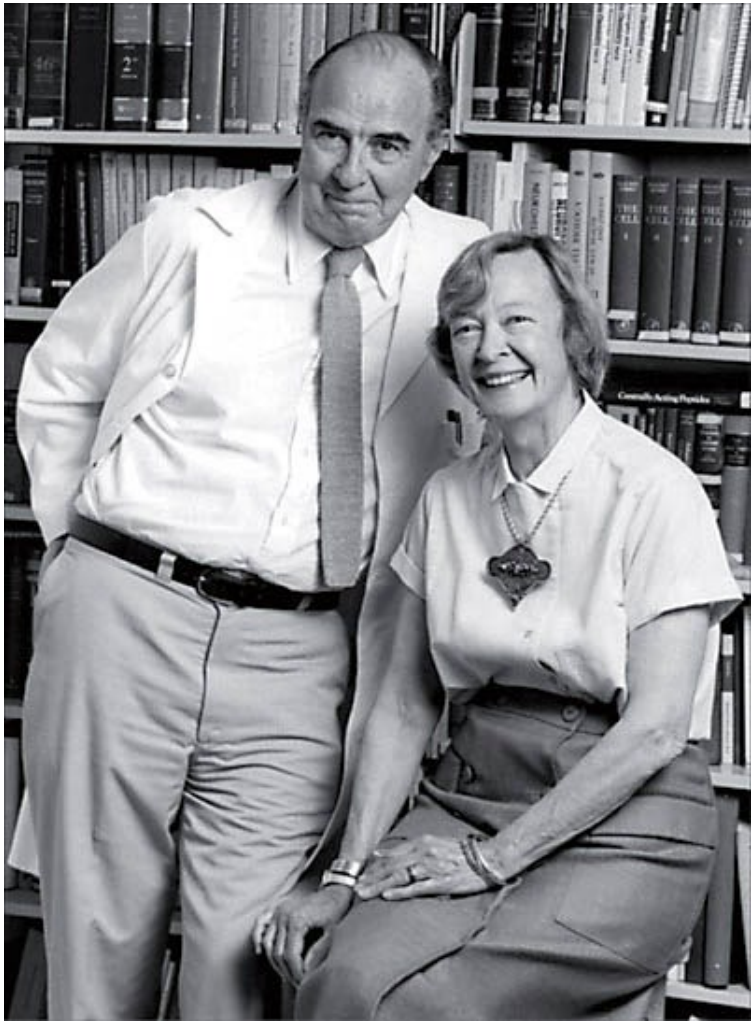
WHOSE BRIGHT IDEA?



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WHO'S BRIGHT IDEA?

- Dole and Nyswander, early 1960s

Detox → Treatment → Failure

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RESULTS OF OPIOID DETOX

- VA study 2006 – 112 patients – inpatient detox followed by outpatient treatment and naltrexone
- 78% successfully completed detox
- At 90 days, only 22% remained in treatment
- At 90 days, <3% had negative urine samples
- At 1 year, 40% readmitted, 4.5% had died

Outpatient treatment engagement and abstinence rates following inpatient opioid detoxification. Davison, et al. J Addict Dis, 25(4), 2006:27-35

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COUNSELING WITHOUT MEDS

- Study after study with the same conclusion:

~ Detox and counseling, without medication, does not work for the vast majority of patients with moderate or severe opioid use disorder. More than 9 out of 10 patients will relapse within a few months.

~ For patients who are on medication, stopping the medication puts them at high risk of relapse, whether they have counseling or not.

~ Patients who relapse have a high mortality rate.

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ABSTINENCE BASED TREATMENT INCREASES MORTALITY

- 276 patients admitted to IP treatment in Norway
- In 1st 4 weeks after discharge, death rate from OD was 16 times higher than baseline
- Elevated risk "is so dramatic that preventative measures should be taken."

Mortality among drug users after discharge from inpatient treatment: an 8 year prospective study. Ravndal E, Amundsen E, Drug and Alc Dependence. 108 (2010): 65-69

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MORTALITY OF OPIOID ADDICTION

- 10 year study of heroin addicts in Catalonia
- 30% died, yearly rate 3.4% and mortality ratio was 28.5

Ten-year survival analysis of a cohort of heroin addicts in Catalonia: the EMETYST project, Sanchez-Carbonell X, Seus L. Addiction 2000 Jun 95(6):941-8

- 5-8 year study of heroin addicts in Sweden
- Mortality ratio 63 times higher, 40% died over 8 years

Mortality in heroin addiction: impact of methadone treatment, Gronbladh L, Ohlund L, Gunne L. Acta Psychiatr Scand 1990: 82: 223-7

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MORTALITY OF ADDICTION

- Average decrease in life expectancy:
  - Opioids – 15-20 years
  - Alcohol – 10-15 years
  - Tobacco – 5-10 years
  - Diabetes II – 5-10 years
  - Hypertension – 5 years

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WHY THEY FAIL - PROLONGED WITHDRAWAL

- Acute withdrawal symptoms resolve usually in 5-7 days
- Patients don't feel normal for months - dysphoria
  - Low energy
  - Depression
  - Poor sleep
  - Restlessness
  - Irritability
  - Poor appetite
  - Anhedonia
  - Cravings
- Symptoms may persist for over a year

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PRIMARY MOTIVATION - OPIOIDS

- Initially – Euphoria
- Long Term ~ Dysphoria

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OPIOID WITHDRAWAL LEADS TO

- Desperation, which leads to
  - Demanding, aggressive behavior with providers
  - Criminal activity
  - Diversion/selling of drugs
  - Hazardous sexual activity, STDs
  - Risk for infectious diseases – Hep C, HIV, endocarditis
  - Neglect of other responsibilities (job, kids, spouse)

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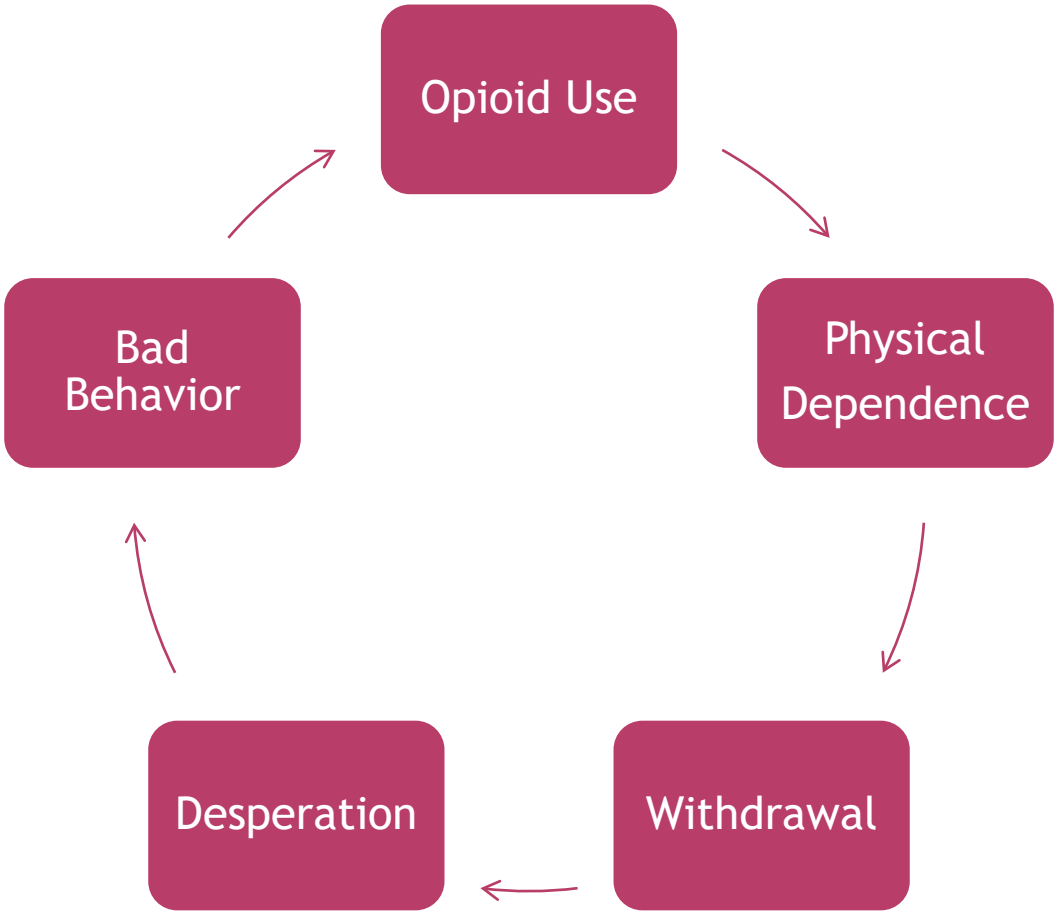
BREAKING THE CYCLE



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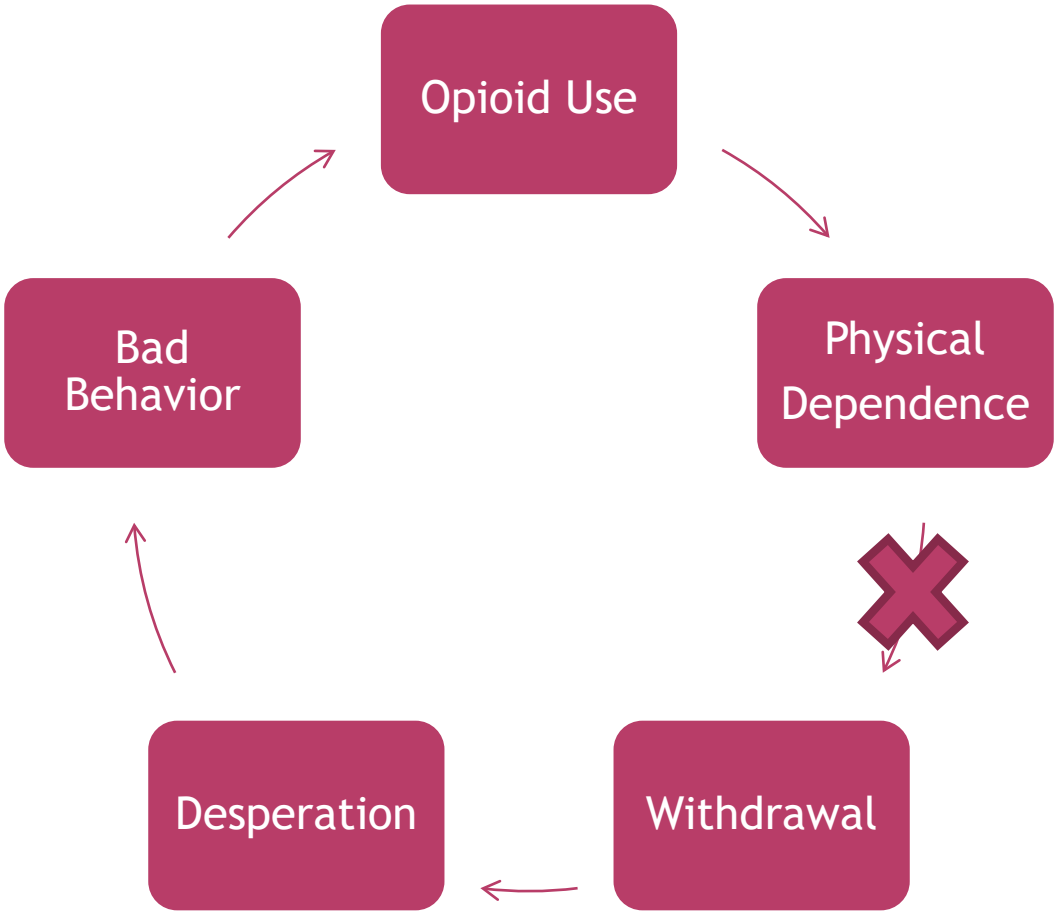
BREAKING THE CYCLE



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OPIOID AGONIST TREATMENT

- Use a drug with a long half life
  - Gets patients off of the "roller coaster"
  - Relieves withdrawal and cravings
  - Does not produce euphoria in tolerant patients
- Block the euphoric effects of other opioids
  - Buprenorphine – high affinity for receptor
  - Methadone – induces significant opioid tolerance and competitive blocking at the opioid receptor
- Use in a controlled setting
  - Decrease risks of diversion, IV use
  - Combine with counseling, other services

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GOALS FOR MEDICATION

- No withdrawals
- No other opioid use
- Blockage of the euphoric effects of opioids
  - Minimal side effects
  - Improved function

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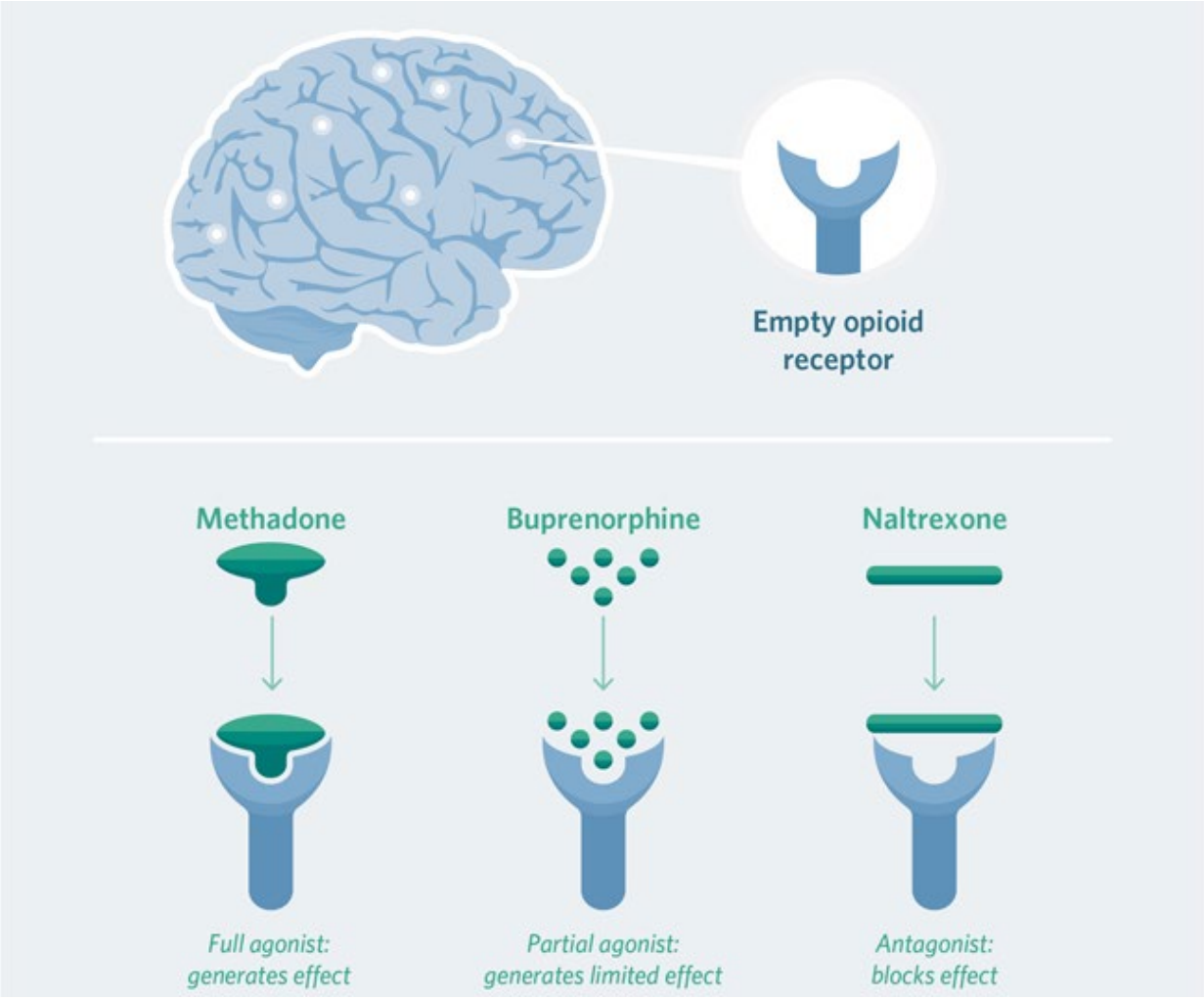
HOW MAT MEDICATIONS WORK IN THE BRAIN



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METHADONE VS. BUPRENORPHINE

Methadone

- Only in OTPs
- More effective
- More structure
- More hassle to pt
- No pt limit
- More risky in OD

Buprenorphine

- In office (with waiver)
- Equiv to ~60 mg MMT
- No daily dosing reqs
- 30, 100 or 275 pt limit
- Ceiling on respiratory effects
- More expensive

ER-Naltrexone – non-opioid monthly injection

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OPIOID TREATMENT PROGRAMS (OTPS)

- Federally licensed by SAMHSA and the DEA
- May use methadone or buprenorphine for treating OUD
- Must be able to do daily observed dosing
- Must have counselors on site
- Required to perform urine drug testing
- Inspected by JCAHO, CARF, or similar
- Able to treat higher level of care than office based treatment

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MMT DETAILS

- Patients come to clinic initially 6 days per week for observed dosing
- Maximum initial dose 30 mg, titrate over first few weeks
- Average daily dose 100-120 mg (variable)
- Strict rules for take home doses
- Regular urine drug screening
- Each patient has a counselor with regular visits and a treatment plan
- Referrals are made as needed to medical, psychiatric, counseling, social services

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GENETIC POLYMORPHISM

"Genetic polymorphism is the cause of high interindividual variability of methadone blood concentrations for a given dose; for example, in order to obtain methadone plasma concentrations of 250 ng/mL, doses of racemic methadone as low as 55 mg/day or as high as 921 mg/day can be required in a 70-kg patient."

Mol Diagn Ther. 2008;12(2):109-24.

Interindividual variability of methadone response: impact of genetic polymorphism.

Li Y1, Kantelip JP, Gerritsen-van Schieveen P, Davani S.

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DOES MAT WORK?

- Retention rates ~50-75% at one year
- Improved outcomes:
  - Better treatment retention (RR = 4.44*)
  - Illicit drug use decreases (RR = .69*)
  - Criminal activity decreases (RR = .39**)
  - Mortality decreases (RR = .48**)
- Estimated to save $4-15 for every $1 spent on treatment
  - (* P< 0.05)
  - (**P>0.05)
  - 2009 Cochrane Review

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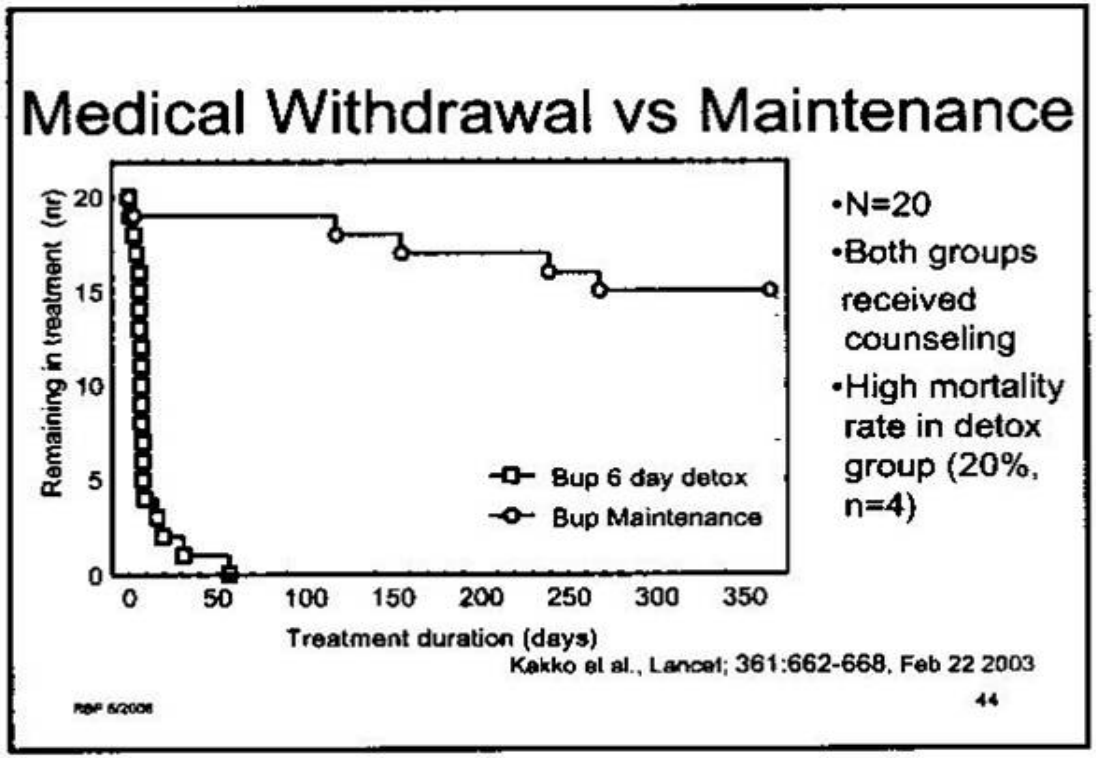
MAT VS. DETOX ONLY



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MORTALITY DECREASES

- Methadone decreases mortality by approximately 70% over untreated controls
- Buprenorphine decreases mortality by 50% over untreated controls
- Untreated 10 year mortality 30-40%
- MAT saves lives

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ADVERSE EFFECTS

- Methadone and buprenorphine have NO significant long term organ toxicity
  - NO increase in LFTs
  - NO cardiovascular issues (except methadone QTc)
  - NO drowsiness or decrease in mental function
- Minor side effects: Weight gain, constipation, decreased libido, sweating, sleep abnormalities, androgen deficiency (men)

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FALSE IMPRESSIONS OF MAT

- MAT is just "substituting one addiction for another"
- MAT providers "get people addicted to methadone"
- People on MAT "just want to get high"
- People on MAT should get off as soon as possible
- People on MAT are not really "in recovery"
- MAT just enables people to keep using drugs

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DISCONTINUING MAT

- Less than 1 year not effective
- >3 years more effective than <3 years
- Slow taper more effective than rapid
- Relapse is common during or after taper
- Buprenorphine and methadone have no long term toxicity
- Some patients have been on MAT for over 40 years
- Length of treatment needs to be determined on an individual basis

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SUMMARY

- MAT is the standard of care and should be available for all patients with OUD
- Abstinence-based treatment for OUD without medications has a low success rate and increases the risk of OD
- Untreated OUD has a high mortality rate
- Stigma, negative attitudes, and misinformation still a problem among the lay community, the medical system, and some treatment providers.

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