

# Addressing the Opioid Epidemic

## Medication Assisted Treatment of Opioid Use Disorder

September 26, 2018



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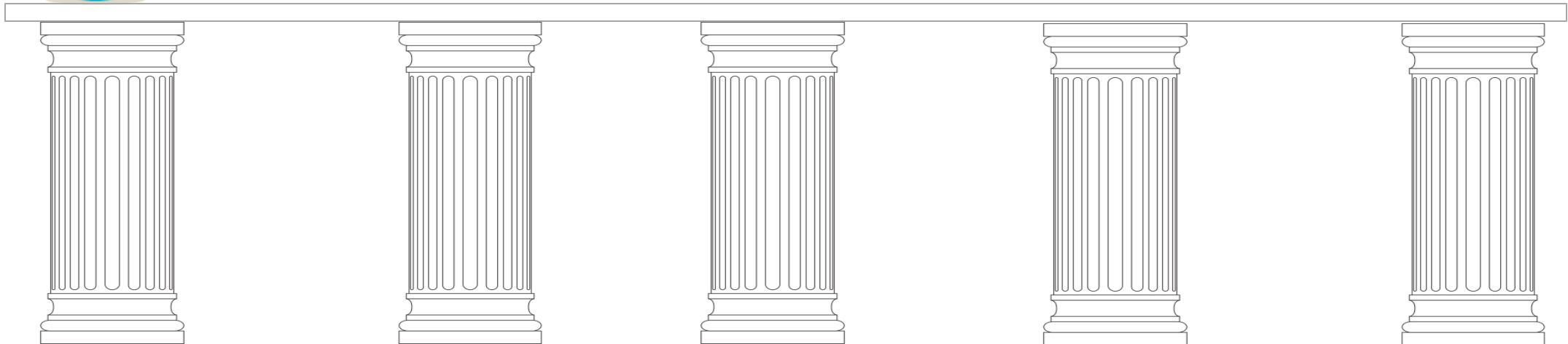
**LAW ENFORCEMENT**



**PRESCRIPTION DRUG  
MONITORING PROGRAM**



**TREATMENT**



# Today's Speaker

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Heartview Foundation

Bismarck, ND



# Medication Assisted Treatment for Opioid Use Disorder

September 26, 2018

Missy Henke, MD

Heartview Foundation Medical Director

# Learning Objectives

- Understand the impact of opioid addiction
- Define Medication Assisted Treatment (MAT)
- Identify medication used in the treatment of Opioid Use Disorder (OUD)
- Discuss benefits of MAT and how to address associated stigma

# Outline

- The disease of addiction
- The neuroscience of addiction
- Prescription pain relievers and heroin
- Opioid overdose
- Medication Assisted Treatment (MAT)
- MAT and pregnancy
- Take home points

# Addiction does not discriminate



# The disease of addiction

- Addiction is a chronic, often relapsing brain disease that causes compulsive drug seeking and use, despite harmful consequences to the addicted individual and to those around him or her
  - [Drugabuse.gov](http://Drugabuse.gov) June 30, 2016
- Chronic diseases can be controlled but not cured
- Like diabetes, cancer and heart disease, addiction is caused by a combination of behavioral, environmental and biological factors

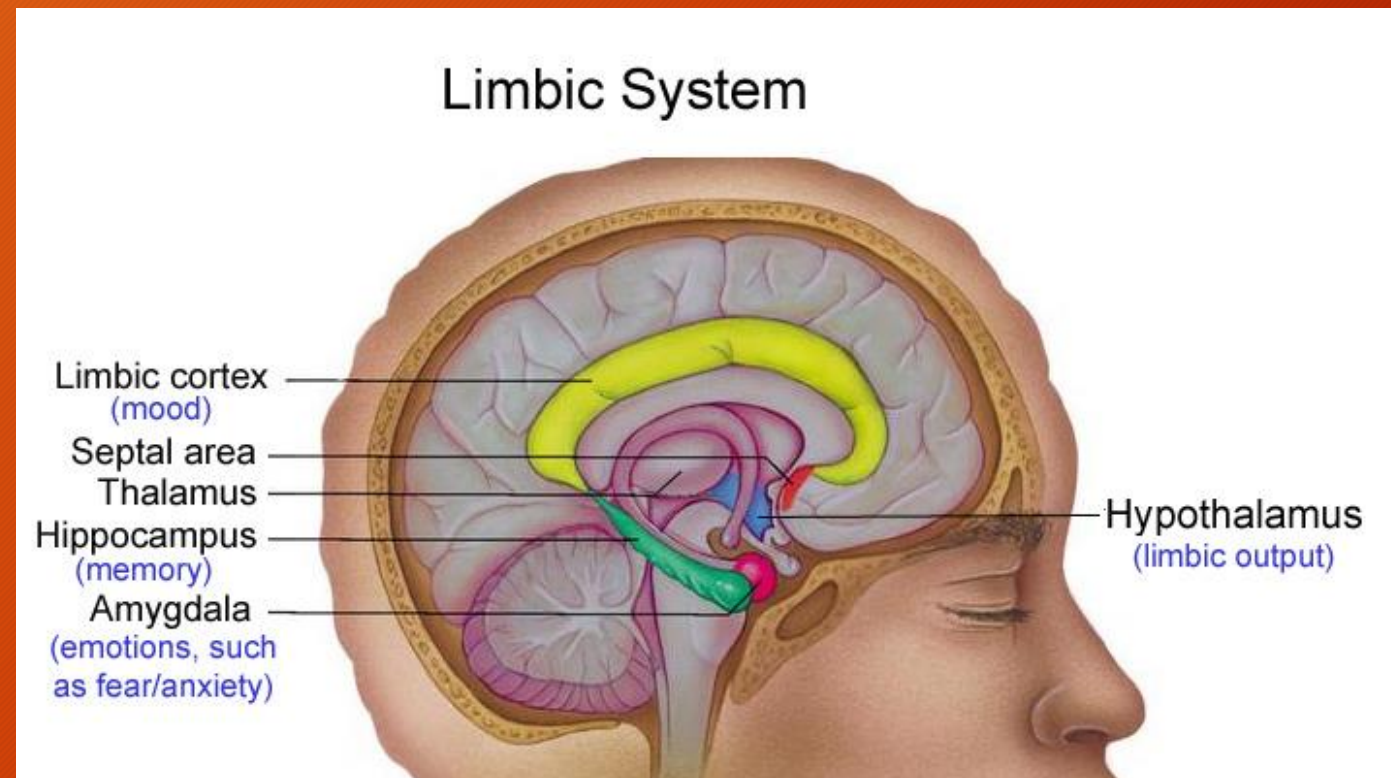


# Genetics of Addiction

- Genetic risk factors account for about half of the likelihood that an individual will develop addiction
  - National Center on Addiction and Substance Abuse 2017
- Children of addicts are 8 times more likely to develop an addiction
  - Prescott, C.A., & Kendler K.S., Genetic and environmental contributions to alcohol abuse and dependence in a population-based sample of male twins. *Am J Psychiatry*, 1999. 156(1): p. 34-40

# Neurochemistry of Addiction

- Limbic system contains the brain's reward circuitry



# Limbic System

- Controls and regulates our ability to feel pleasure which motivates us to repeat behaviors that we need to survive
- Activated by healthy, life-sustaining activities but also drugs of abuse
- Dopamine is the key neurotransmitter in the limbic system

# Limbic System

- Responsible for our perception of other emotions, both positive and negative



# Dopamine

- Dopamine regulates movement, emotion, motivation and feelings of pleasure
- Drugs mimic the brain's own chemicals and lead to abnormal messages being transmitted through the network
- Drugs of abuse target the brain's reward system by flooding the circuit with dopamine producing euphoria
- When the reward circuit is activated, the brain triggers a memory and teaches us to repeat that behavior

# Dopamine

- Average brain - 50 ng/dL daily of dopamine
- Tobacco - 450 ng/dL
- Marijuana - 650 ng/dL
- Heroin- 975 ng/dL
- Methamphetamine - 1100 ng/dL

# Dopamine

- With continued exposure to high levels of dopamine, the brain downregulates the number of receptors and natural dopamine release
- Less receptors means that the person's ability to experience any pleasure is reduced
- This leads to ongoing drug abuse in order to try and increase the levels of dopamine

# Overprescribing

- Extensive prescribing of opioids began in the mid-1990s
  - The VA health system adopted the idea of pain as the 5<sup>th</sup> vital sign in 1990s and it became a Joint Commission standard in 2001 that pain be assessed in all patients
  - The U.S. is 5% of the world's population though we consume 80% of the world's prescription opioids
  - Prescribing rates for prescription opioids among adolescents and young adults nearly doubled from 1994 to 2007



# Opioid Overdose

- October 2017 President Trump declared the Opioid Epidemic a National Public Health Emergency
- Opioid Overdoses May be Seriously Undercounted
  - Side Effects Public Health, March 21, 2018
- Emergency department visits for opioid overdoses rose 30% in all parts of the US from July 2016 through September 2017
  - Increases included both sexes and all age groups

# Overprescribing

- 2012 - 259 million prescriptions for opioids which is enough for every American adult to have their own bottle
- 2013, 2014 and 2015 saw a decline in prescriptions for the first time since the mid 90s
- In 2015 the amount of opioids prescribed was enough for every American to be medicated **around the clock for 3 weeks**

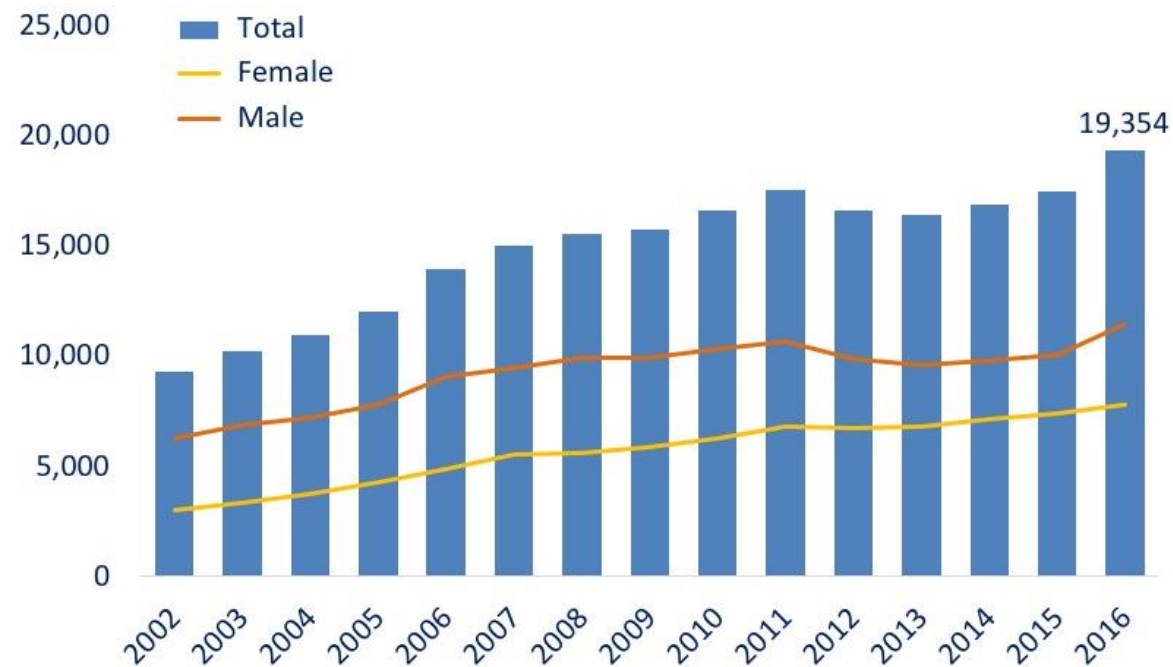
# Opioid Overdose

NIH National Institute on Drug Abuse



## National Overdose Deaths

Number of Deaths Involving  
Opioid Pain Relievers (excluding non-methadone synthetics)



Source: National Center for Health Statistics, CDC Wonder

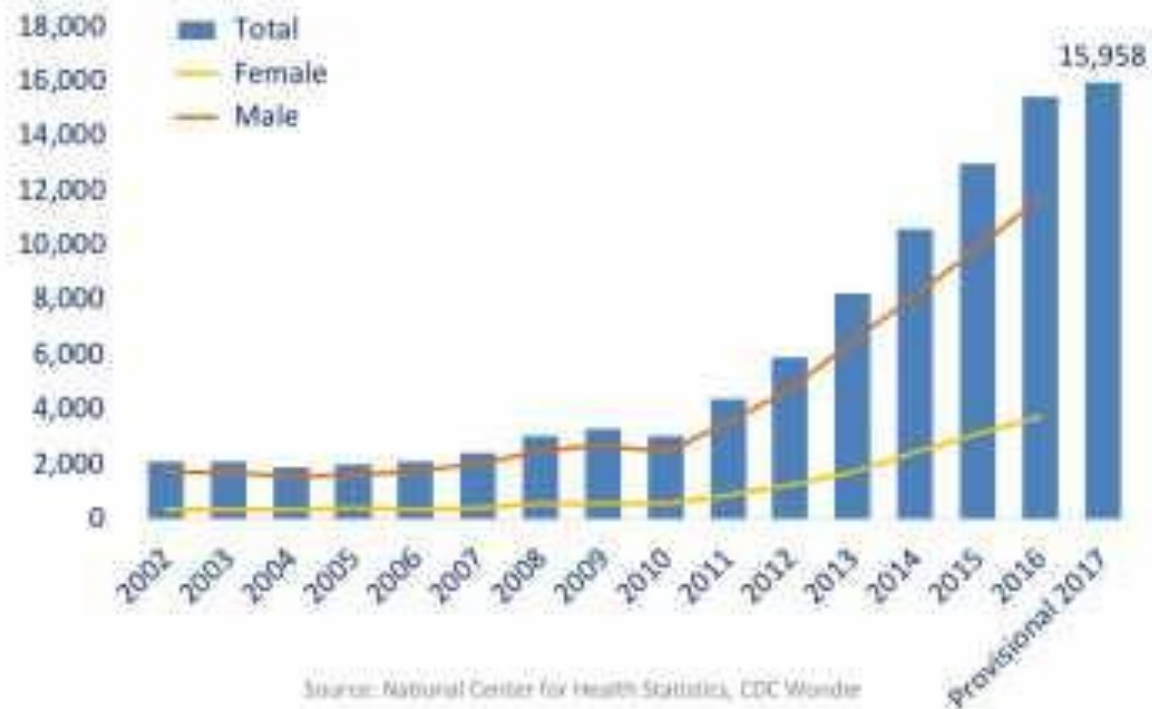
# Opioid Use Disorder - Heroin

- 4 in 5 new heroin users started out misusing prescription painkillers
- 94% of respondents in a 2014 survey said they chose to use heroin because prescription opioids were “far more expensive and harder to obtain”

# Opioid Overdose



## National Overdose Deaths Number of Deaths Involving Heroin



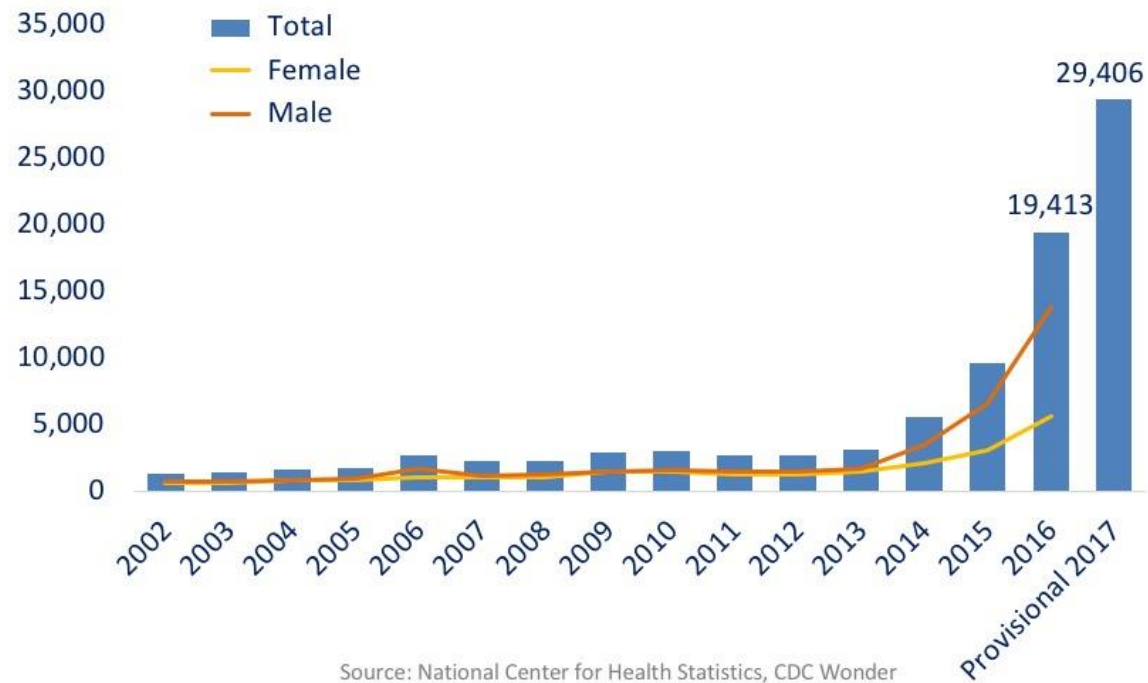
Source: National Center for Health Statistics, CDC Wonder

# Opioid Overdose



## National Overdose Deaths

Number of Deaths Involving  
Other Synthetic Opioids (Predominately Fentanyl)



Source: National Center for Health Statistics, CDC Wonder

# Opioid Overdose - Fentanyl

- 50 to 100 times more potent than morphine
- Available as a transdermal patch, lozenge or liquid
- In March 2015, DEA issued a nationwide alert identifying fentanyl as a threat to public health and safety
- In 2016 more overdose deaths were due to Fentanyl and other synthetic opioids than from any other type of opioid

# Fentanyl analogues

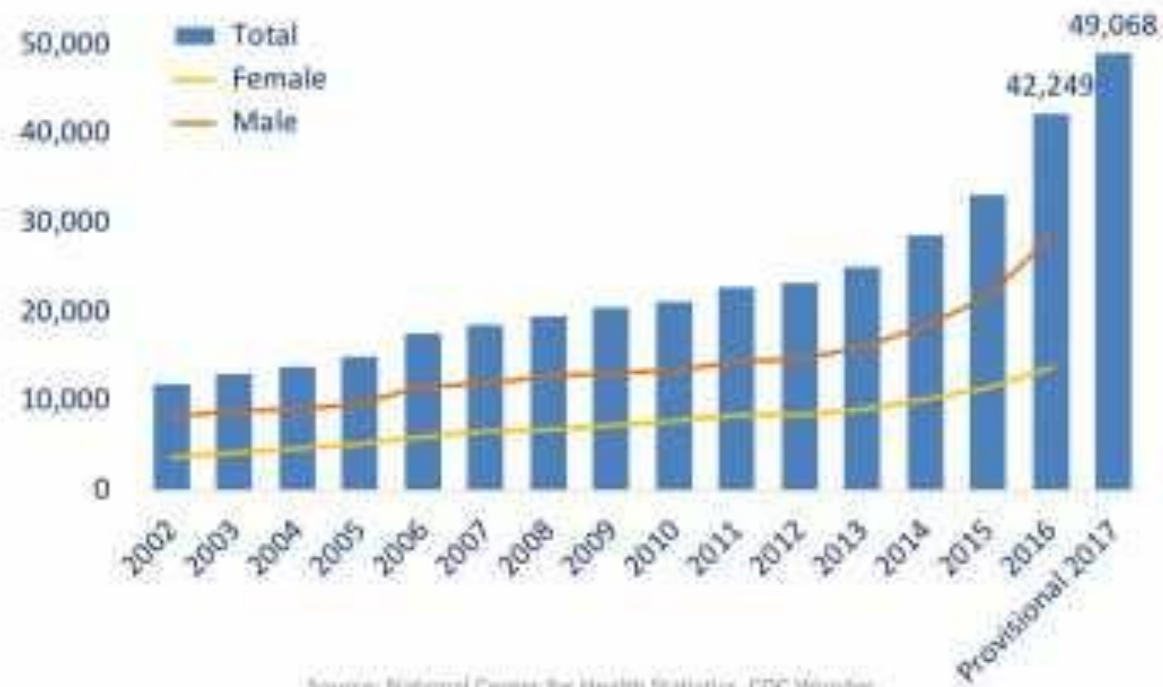
- Synthetic opioid overdose death rates (other than methadone) increased across all demographics, regions and numerous states in 2016
- Acetylfentanyl, furanylfentanyl and carfentanil
- Carfentanil is estimated to be 10,000 times more potent than morphine



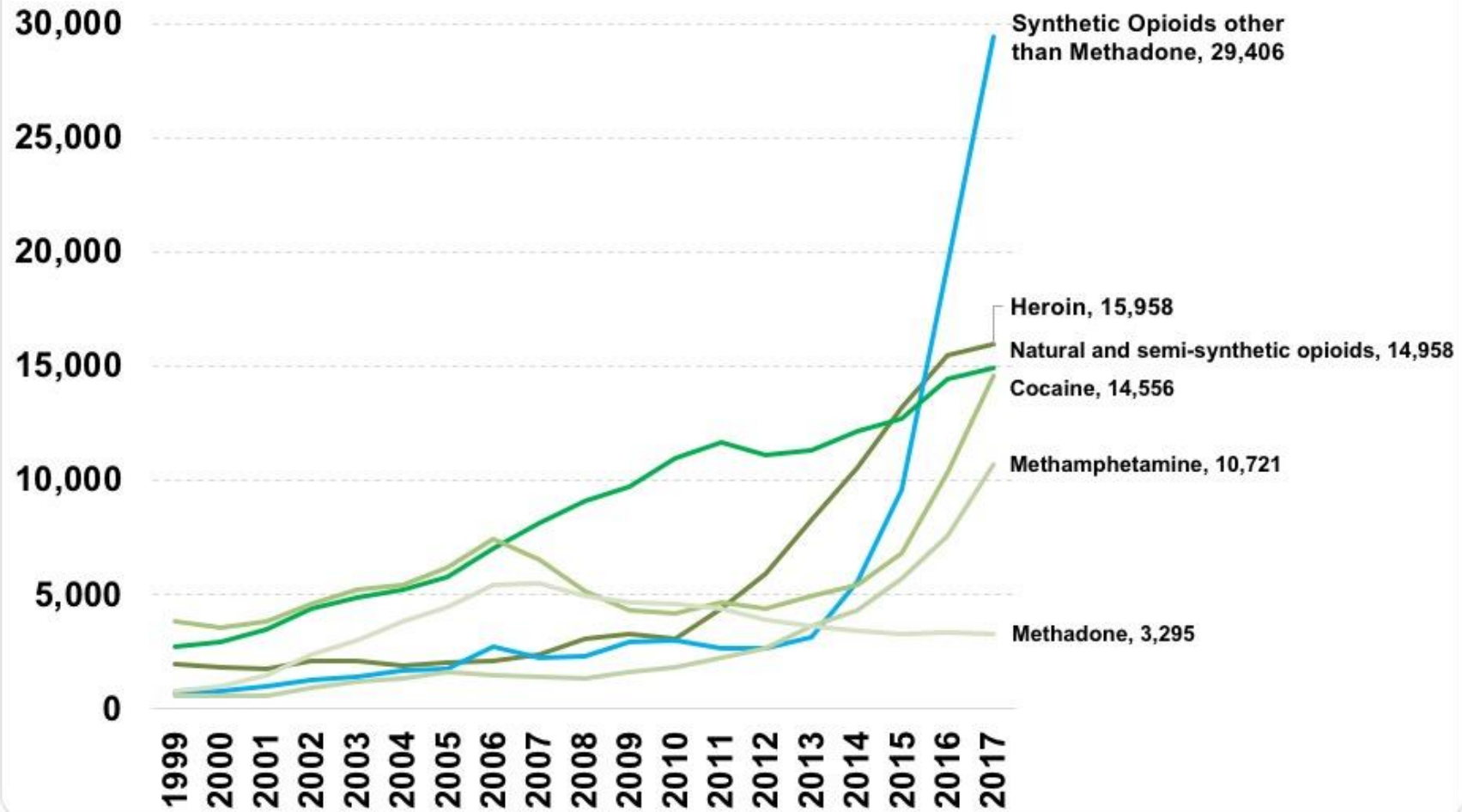
# Opioid Overdose



## National Overdose Deaths Number of Deaths Involving Opioids



## Drugs Involved in U.S. Overdose Deaths, 1999 to 2017



# Opioid Overdose

- 134 Americans die every day from an opioid overdose (197 die daily of all drug overdoses combined)
- Between 2001 and 2016, the number of opioid-related deaths in the US increased by 345%
- In 2017 more people died from opioid overdoses than car accidents or guns

# Opioid overdose

- Accidental drug overdose remains the leading cause of accidental death in the U.S.
- The U.S. claims 27% of the world's drug overdose deaths
  - United Nations Office on Drugs and Crime
- 15-24 year olds - 1 in 10 deaths were related to opioids in 2016
- 25-34 year olds - 1 in 5 deaths were related to opioids in 2016

# Opioid Overdose

- National Institute of Health calculated that more than 72,000 people died of drug overdoses in 2017 (>49,000 were attributed to opioids)
  - 58,200 US troops died in Vietnam War between 1955 and 1975
  - 43,000 people died due to HIV/AIDS during that epidemic's peak in 1995
  - 2,996 people died in 9/11

# Medication Assisted Treatment

- Evidence-based practice that combines pharmacological interventions with substance abuse counseling and social support
- It is NOT
  - Replacing one addiction with another
  - Replacing one drug for another
  - Keeping someone sick in their addiction
  - Keeping someone from finding recovery

# Medication Assisted Treatment

- Has been shown to
  - Improve survival
  - Increase retention in treatment
  - Decrease illicit opioid use
    - Relapse rates without MAT exceed 80%
  - Decrease hepatitis and HIV seroconversion
  - Decrease criminal activities
  - Increase employment
  - Improve birth outcomes for patients and babies

# Medications Used in MAT

- Methadone
- Buprenorphine (Subutex, Sublocade, Probuphine)
- Buprenorphine/Naloxone (Suboxone, Zubsolv, Bunavail)
- Naltrexone (Revia, Vivitrol)
- Naloxone (Narcan)



# Methadone

- Methadone - Gold standard for MAT for opiates
  - Only available through Opioid Treatment Program (OTP)
    - Federally regulated
      - Drug Enforcement Agency (DEA)
      - Substance Abuse and Mental Health Services Administration (SAMHSA)
    - State regulated
      - Administrative Rules
      - State Opioid Treatment Authority (SOTA)
  - OTPs in 49 states (not Wyoming)

# Methadone

- Methadone
  - Full mu agonist
  - Dosed once daily at the OTP
  - Multiple drug-drug interactions
  - Risk for Qtc prolongation

# Methadone

- Higher doses are more effective at reducing heroin use - Usually 80-120 mg daily
- Good outcomes are contingent on length of treatment
  - Patients who stay in MAT with methadone for less than three months usually show little or no continued improvement
  - 80% of people who leave methadone treatment and pursue no additional treatment will relapse

# MAT during pregnancy

- Methadone has been the standard of care for 40 years (Methadone Maintenance Therapy or MMT)
- May produce serious adverse effects
  - Methadone enters fetal circulation via the placenta
  - Fetus experiences withdrawal - Neonatal Abstinence Syndrome (NAS)- hypersensitivity, hyperirritability, tremors, vomiting, respiratory difficulties, poor sleep, low grade fevers
  - NAS requires hospitalization and treatment including morphine taper

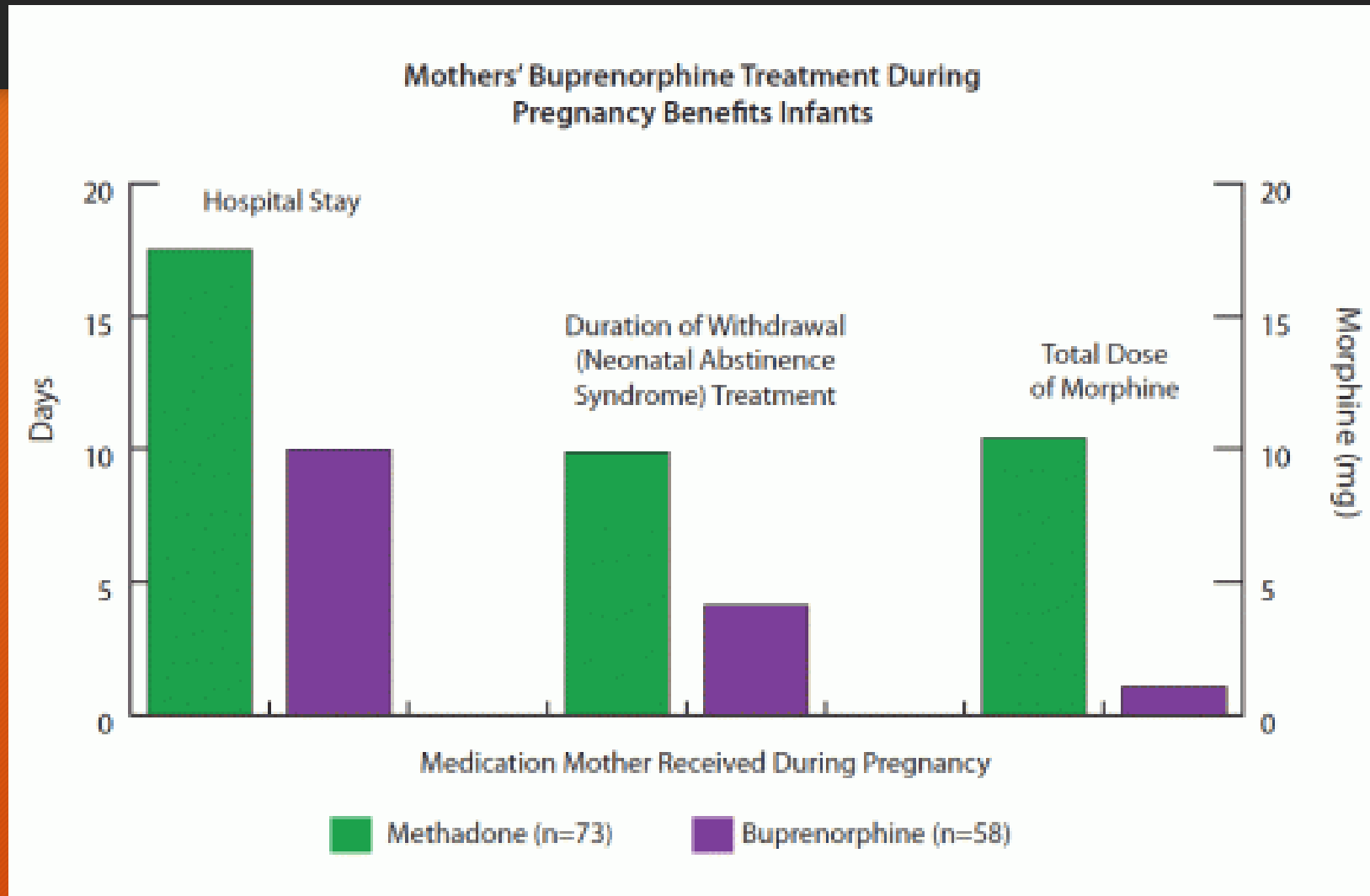
# MAT during pregnancy

- Enhances chances for a trouble-free pregnancy and a healthy baby compared to ongoing opiate use
  - Lowers risk of developing infectious diseases including HIV and HCV
  - Lowers risk of pregnancy complications including spontaneous abortion and miscarriages
  - Lowers risk of having a child with low birth weight and neurobehavioral problems

# MAT during pregnancy

- MOTHER (Maternal Opioid Treatment: Human Experimental Research) found Buprenorphine to be a safe and effective alternative and has some advantages over Methadone
  - Recruited women seeking treatment for opioid dependence at 6 treatment centers in US and 1 in Austria - 6 to 30 weeks pregnant
  - Initiated treatment with morphine until dose stabilized and then transitioned to buprenorphine for remainder of pregnancy with dose adjustments as necessary
  - 175 women started the study and 131 stayed until giving birth
  - Babies born to moms on Buprenorphine experienced milder NAS than those exposed to Methadone (infants required 11% as much morphine, finished the taper in half the time and remained in the hospital roughly half as long as infants exposed to methadone)

# MOTHER Results



# Buprenorphine

- Buprenorphine
  - Approved by FDA for treatment of opioid dependence in October 2002
  - Opioid partial agonist at mu receptor - Able to suppress withdrawal symptoms and less likely to cause euphoric high or lead to death by overdose
  - Blocks the effects of full agonists
  - No evidence of organ damage



# Buprenorphine

- Lower risk of abuse, addiction and side effects
- Ceiling effect for respiratory depression enhances safety profile
- Administered sublingually, buccally, subcutaneously, subdermally
- Combined with Naloxone (Suboxone, Zubsolv, Bunavail) as a deterrent to IV use

# Buprenorphine

- Office-based practice (does not require an OTP)
- Physicians require 8 hours of training to obtain XDEA
- Advanced Practice Providers require 24 hours of training to obtain XDEA
- Limitations on number of total patients a prescriber can have at any given time
  - 30 in first year
  - 100 after that
  - Up to 275 if boarded in addiction or work at licensed treatment center

# Buprenorphine Implant

- Probuphine - Marketed by Braeburn Pharmaceuticals
  - Subdermal placement of four 2 mg rods
  - 6-month duration of treatment with ability to replace once for total duration of 12 months
  - No naloxone
  - Requires special certification to implant and remove

# Buprenorphine Injectable

- Sublocade (Indivior Pharmaceuticals)
  - Monthly injectable - 300 mg first two months then 100 mg monthly thereafter
  - No naloxone
  - Only available through specialty pharmacies
  - Physician must participate in Sublocade REMS
  - Must be stabilized on transmucosal buprenorphine for 7 days
- CAM2038 (Braeburn Pharmaceuticals)
  - Awaiting FDA approval
  - Weekly doses (8 and 32 mg)
  - Monthly doses (64 and 160 mg)

# Medication Assisted Treatment

- Buprenorphine and Methadone both raise dopamine to normal levels of 40-60 ng/dL in the brain
- Patients with low dopamine levels have extremely low retention rates for treatment (less than 10%)

# Buprenorphine

- Harvard study published in 2015 demonstrated that 3 ½ years after treatment, only 10% of patients treated with buprenorphine met diagnostic criteria for opioid dependency

# Naltrexone

- Oral Naltrexone (Revia)
  - Opioid antagonist
  - Poor bioavailability when taken orally
  - Daily dose of 50-100 mg - Hepatotoxicity was seen in obese patients taking 300 mg daily
  - If opioids are in the patient's system, Naltrexone will produce opioid withdrawal
  - Compliance is an issue

# Naltrexone

- IM Naltrexone (Vivitrol)
  - Intramuscular shot given every 28 days
  - 380 mg
  - Available through specialty pharmacies
  - Well tolerated
  - Expensive - \$1300-1500/shot
    - Covered by most major insurances



# Medication Assisted Treatment

- Mortality rate for patients who pursue abstinence-based recovery is 10 times higher than individuals who receive MAT
- MAT combined with psychosocial treatment is superior to drug or psychosocial treatment alone

# Naloxone

- Naloxone (Narcan)
  - Available in community-based programs since 1996
  - Between 1996 and 2014 there were more than 26,000 opioid overdose reversals with bystander-administered naloxone
  - Safe, minimal side effects, inexpensive
  - Can be given IV, SQ, IM, IN, IO

# Naloxone

- Physicians in any state can prescribe naloxone
- Available as intranasal spray (4 mg spray), intramuscular syringe (0.4 mg/1 ml) or intramuscular auto-injector (Evzio 2 mg)
- 47 states have expanded access to Naloxone
- Surgeon General released a public health advisory April 2018
  - Be Prepared. Get Naloxone. Save a Life.

# Medication Assisted Treatment

- MAT is grossly underutilized
  - Less than 10% of patients seeking treatment for OUD receive MAT
  - Only 23% of publicly funded treatment programs reported offering any FDA-approved medications
  - There is a significant need for more prescribers of MAT in this region

# Take Home Points

- Addiction is a chronic disease of the brain
- Opioid overdoses are a national and local public health crisis
- Prescription opioids and heroin go hand in hand
- Medication Assisted Treatment is evidence-based and underutilized
- Opioid Treatment Programs are federally and state regulated

# Take Home Points

- Methadone is not reported on the PDMP
- Buprenorphine has a complex mechanism of action
- Buprenorphine is category C in pregnancy
- Be Prepared. Get Naloxone. Save a life.

# Questions

" I have  
not failed.  
I have  
just found  
**10,000 things**  
that do  
**not work."**

- Thomas Edison.

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