Opioid Replacement Therapy for adolescents with opioid use disorder

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Disclosures

None to report

Objectives

- At the end of this presentation, participants will be able to:
- Identify the difference between abstinent based treatment and opioid replacement therapy for adolescents with opioid use disorder
- Understand the Federal Requirements of opioid replacement therapy for buprenorphine /naloxone and methadone.
- Name two concerns regarding withholding buprenorphine/naloxone and methadone from adolescents with opioid use disorder.

Overall, most youth are NOT using

30-Day Use of Alcohol, Cigarettes, Marijuana, and Prescription Drugs

PERCENT: 0, 10, 20, 30, 40

YEAR: 2000, 2002, 2004, 2006, 2008, 2010, 2012, 2014, 2016

- Alcohol
- Cig/Tob
- Marijuana
- Prescription

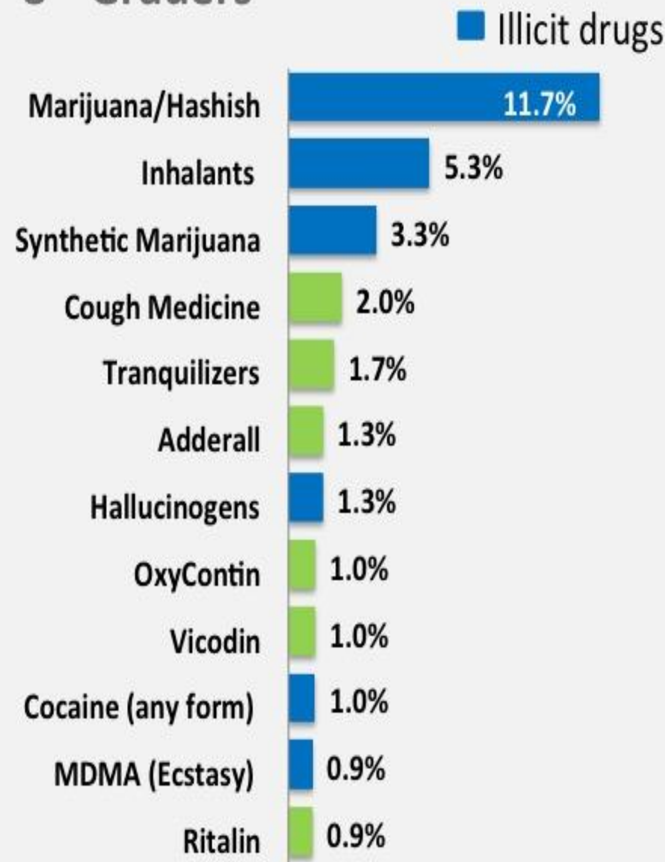
Vocabulary (aka new math)

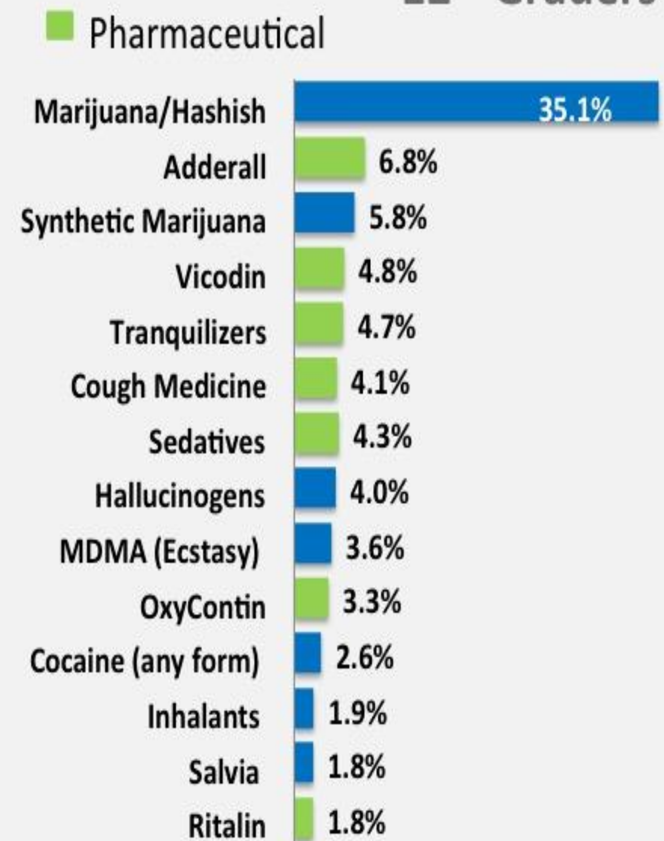
- Opioids/opiates:
  - natural, synthetic or semisynthetic but act on the same mu receptor in the brain.
    - Morphine
    - Hydrocodone, (Vicodan), oxycodone
    - Heroin
- Opioid Use Disorder   (previously known as opioid dependence in DSM IV)
- Medication Assisted Therapy (previously opioid replacement therapy)
    - Methadone
    - Buprenorphine/naloxone
    - Naltrexone
- Abstinent Based Treatment
  - that you will be discharged from treatment without an opioid replacement therapy

Prescription Drug Abuse

90% of addictions start in the teenage years
1 in 6 teens have used medicine to get high
27% of teens AND 16% of parents
believe that using prescription drugs to get high is safer than using street drugs to get high

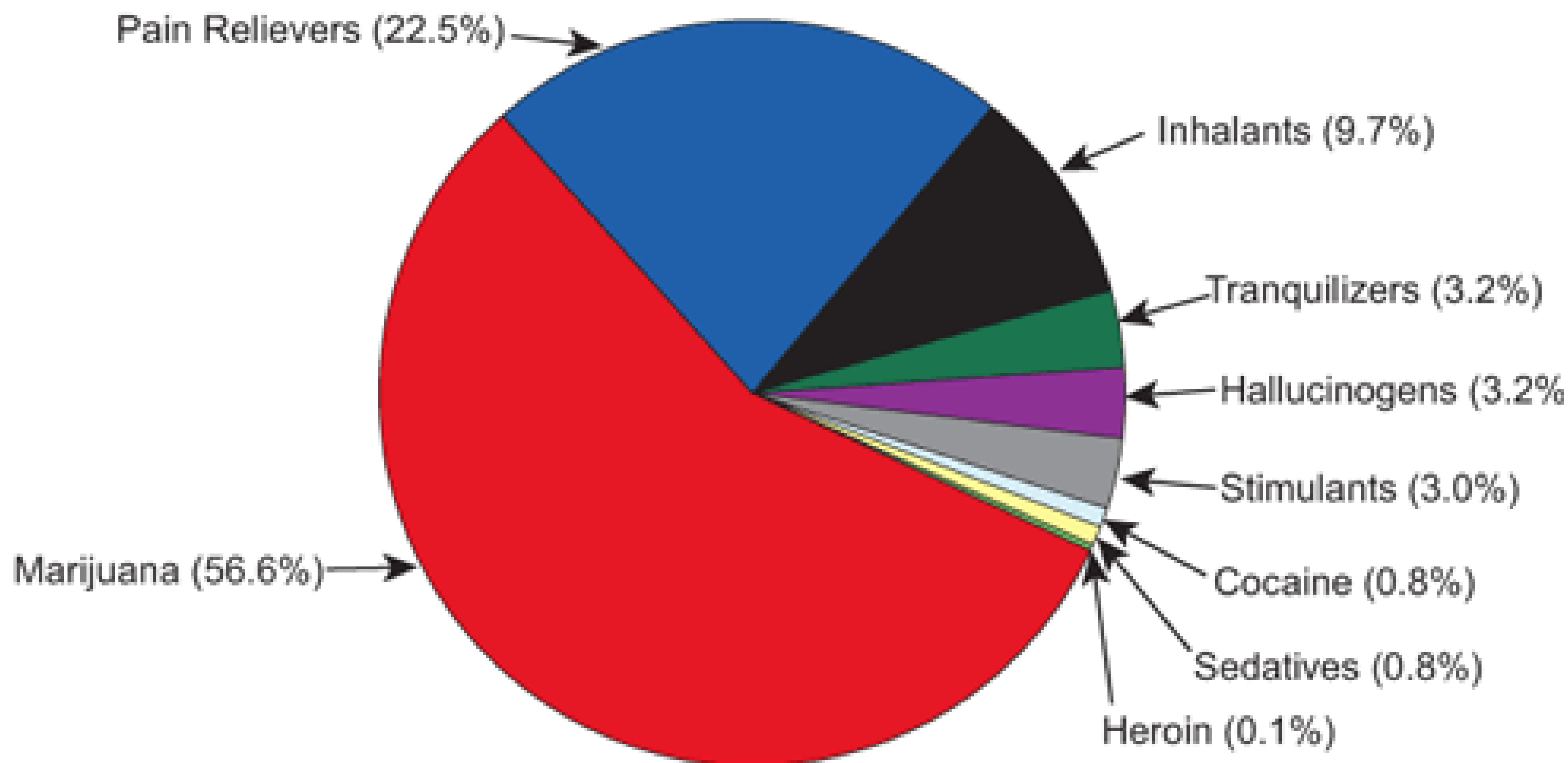
Top Drugs among 8th and 12th Graders, Past Year Use





* Only 12th graders surveyed about sedatives use

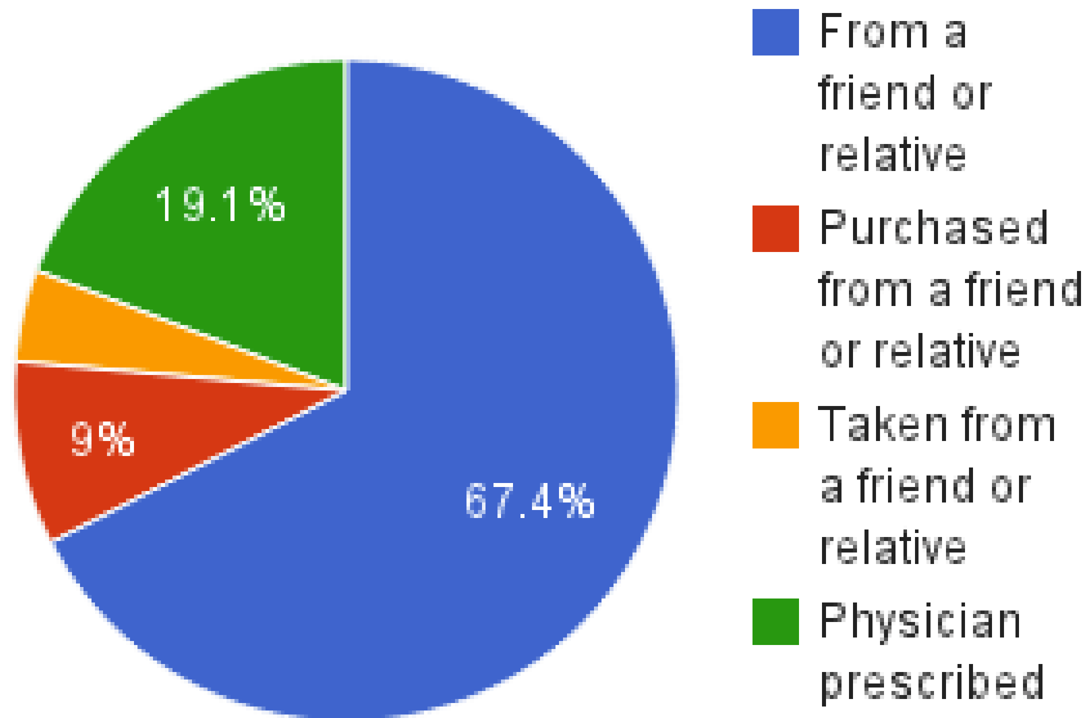
Source: University of Michigan, 2014 Monitoring the Future Study



2.9 Million Initiates of Illicit Drugs

Why it is so easy?
Why is the use of prescription drugs increasing?

receive pills



- Trends and Pattern of Drug Abuse Deaths in Maryland Teenagers

- Maryland recorded a total of 149 drug abuse deaths of teenagers aged 13–19 years. 1991 and 2006.
  - 96 (64.4%) were caused by the use of narcotic drugs only,
  - 29 (19.5%) by both narcotics and cocaine,
  - four (2.7%) by both narcotics and MDMA
  - six (4.0%) by cocaine only
  - 14 (9.4%) by volatile substances (e.g., butane, Freon, nitrous oxide, and propane).

Treatment

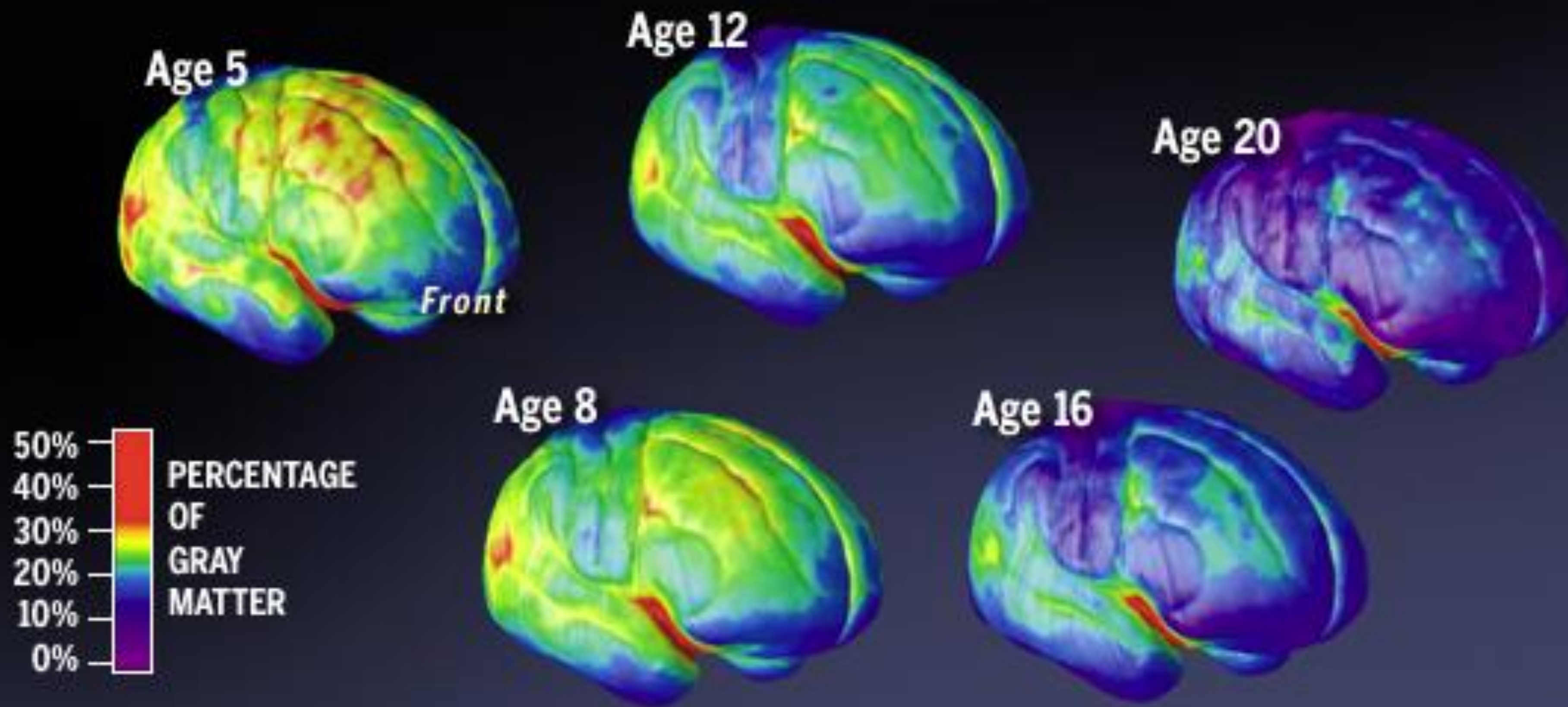
- Evidenced based
- Individualized
- Find a treatment program that encourages retention in treatment
- Outpatient vs Inpatient

What do we know besides that this is an urgent matter

- Substance Use effects
  - social and developmental trajectories
  - “can interfere with normal brain maturation”
- Adult-Sized Opioid Addiction Treatment is not fitting.
  - Example: have you been to an NA meeting.
- Teenagers rarely enter or stay in rehab voluntarily.
- A large percent of kids 12 to 17 do not receive treatment

Time-Lapse Brain

■ Gray matter wanes as the brain matures. Here 15 years of brain development are compressed into five images, showing a shift from red (least mature) to blue.



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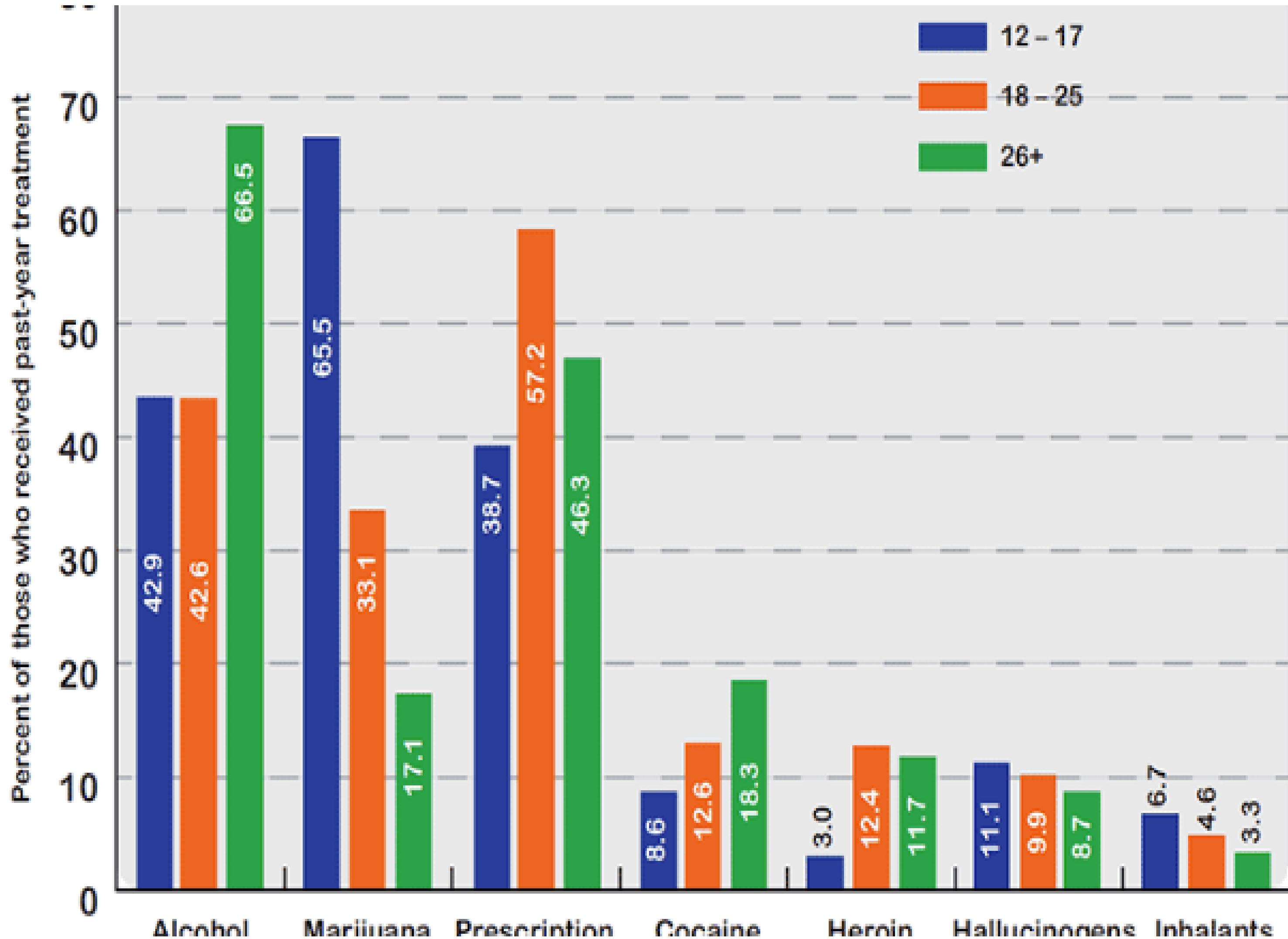
Percent of those who received TX



Case 1

- MG is a 14 y/o with opioid use disorder, heroin. He is brought to the clinic by his mother but referred by his case manager.
  - First use was 12 y/o's old and now uses 1 gram of IV heroin a day.
  - He does not say how he obtains his heroin. There is strong suspicion and concern that he and/or other family members are using him for sexual favors.
- Medical
  - He is malnourished, with old and new track marks
  - Positives for hepatitis C, and chlamydia, and negative for HIV and gonorrhea
- Social History

-He lives with his single mother. She recently started a new job at a local food factory.

-His two younger siblings are in CYFD custody and his mother does not have visitation. It is not clear why. There is not an open CYFD custody on him.

-He does not attend school last grade completed was 6th.

Obvious Barriers for treatment.

- Limited access because of insurance or # of treatment beds
- Teenage perspective on addiction
  - You can't make me do that (and in some cases that is true)
  - I don't use heroin anymore (last use was a week ago)
  - I don't want to take a medication that is going to make me addicted or sick
- Psychosocial
  - I kicked it so can he
  - I have to work and he needs to grow up
  - Let his probation officer deal with it

Less Obvious

- Legal
- Stigma
- Poor understanding of substance use and recovery
  - He has been to treatment too many times to count
  - He is not even trying because he is making the same mistake over and over again.

Legal

Laws

- Title 42 of the Code of Federal Regulations Part 8 (42 CFR § 8) are to be satisfied by opioid treatment programs (OTPs).
- SAMHSA certification, and Drug Enforcement Administration (DEA) registration
- 2006 New Mexico Statues- Section 32-A6-14 Treatment and habilitation of children; liability.

Federal Guidelines for methadone

- 16 years > < 18 years
- meet the criteria for opiate use disorder.
- have a history of at least 2 previous failed abstinence based treatment attempts.
- have at least a 1 year history of opiate use disorder.
- the written consent of the legal guardians

State Laws

- Is Parental Consent Require
- New Mexico
  - Any child shall have the right, with or without parental consent, to consent to and receive individual psychotherapy, group psychotherapy, guidance, or counseling at age 14
  - But no psychotropic medications or interventions without parental consent

Stigma and poor understanding about substance use and recovery
Random quotes from the Internet

- “Addiction is NOT a brain disease it is a choice”
- Comment made about Phillip Seymour Hoffman’s accidental overdose was “thoughtless and irresponsible, leaving behind three children and a partner”.
- “Take the blame if it’s your fault as being stupid is not a disease”
- “I really believe that most hard drug users are just useless pieces of ….. that parasite on society and deserve nothing more than to die in horrible pains”

Stigma that patients, friends, 12 step programs can bring to the table have regarding MAT

- Methadone (and now buprenorphine/naloxone) --- Harmful
  You are not in Recovery
  You should not get pregnant
  Belief they are substituting One Drug or One Addiction for another.
- Doctors (health care providers)
  look at you differently. They treat you like an "Addict."

  You are on methadone; no need for post-op pain meds

Definitions

- Detoxification
  - Using medication to treat withdrawal with subsequent discharge without any medication assisted treatment (MAT)
- Maintenance can be psychosocial or medication assistant treatment after discharge but generally referred to MAT.
- Abstinent Based Treatment
  - Psychosocial treatments when they are age-appropriate and address age-specific issues.
    - evidence-based treatment, types of therapy that have shown scientifically validated results.
      - SBIRT
      - Functional Family Therapy
      - Motivational Enhancement Therapy
- Medication Assisted Treatment (opioid replacement therapy)
  - Suboxone
  - Methadone
    - Both prevents withdrawal symptoms and reduces craving
  - Naltrexone

Methadone

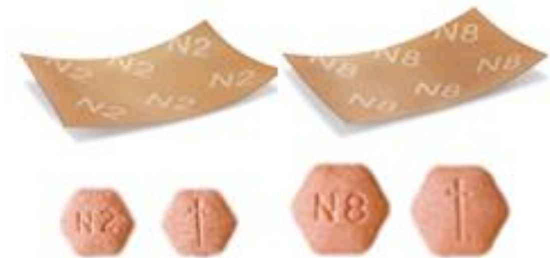
- Schedule II medication
- FDA approved for detoxification and maintenance in age 18+
- Full opioid agonist (covers the mu receptor)
- Half life 8-59 hours depending on individual (large variance depending on 2B6, 2D6, 3A4)
- Can be used in primary care for tx of chronic pain but not opioid use disorder.
- Methadone clinics can not prescribe it for chronic pain
- Gold standard for opioid addiction treatment since 1970's
- Respiratory depression and QT prolongation

Methadone

- Methadone patients must present on a daily basis to receive their dose
- Patients must follow strict federal guidelines but can work toward having take homes. For example after 90 days they can have a Sunday take home.
- After about two years of good adherence, patients qualify for take home 28 days supply of methadone

Buprenorphine/naloxone
Suboxone

- Schedule III medication
- FDA approved for individuals 16 years and older
- Partial opioid agonist (ceiling effect)
- Much higher affinity for opioid mu receptors with a half life is 20-44 hours
- Buprenorphine with naloxone (prevents IV injection use) at 4:1 ratio
- First pass effect through liver diminishes most of naloxone
- (buprenorphine alone = subutex)



Suboxone

- Ideally prescribed in an outpatient practice
- At 32 mg/day around 90% receptor saturation
- Most patients will require 8-32mg in divided doses per day (1-4 times daily depending on patient and indications for treatment)
- Absorbed best sublingually (51%), transbuccal (27.8%), GI (15%), although IV is 85% -> potential for abuse when not combined with naloxone
- Much higher cost of medication
- Only detectable on specific drug screen
- Less sedation, less likely to OD (ceiling effect)

- Burpenorphine can be used in 2 primary ways:
  - As a short course of treatment to reduce the difficulties of opiate withdrawal.
  - As a longer course of substitution maintenance treatment (many months to open-ended).
- According to a SAMHSA expert consensus panel, for adolescent opiate dependent users:[1]
  - A short course of Suboxone for detoxification followed by continuing treatment with naltrexone is the preferred treatment to start with.
  - If, after detox with Suboxone and continuing treatment with naltrexone, relapse occurs, then Suboxone maintenance treatment becomes more appropriate.

Naltrexone

- Not a Schedule Drug
- FDA approval for ages 18 and over for the prevention of relapse in adult patients following complete detoxification from opioids.
- Opioid competitive antagonist, blocks mu opioid receptor preventing opioid drugs from acting on them and thus blocking the high the user
- Monthly injection depot available (Vivitrol)
- Can cause abrupt opiate withdrawal
- Also used for alcohol use disorder
- Not useful if patient requires opiates for pain control as well

Side Effects

- most common are constipation, increased sweating, and pruritus.
- All opioids may decrease testosterone levels. Opioids,
- Do not result in
  - organ damage, as compared to alcohol, tobacco, and cocaine.
- Methadone does prolong the QTc interval at clinically relevant doses. Buprenorphine can also cause QTc prolongation in adolescents
- Opioids do decrease salivary flow and may have some effect on osteoclast/osteoblast function
- MYTH that methadone
  - “rots teeth and bones,”

Summary
What we know about…

- Opioid use in adolescents
- Medication assisted treatment in adults with opioid use disorder
- Medication assisted treatment in adolescents (under 18)
- About the growing evidence to support medication assisted treatment in adolescents

What we know about opioid use disorder in adolescents

- Opioids
  - Second to only marijuana in illicit drug use.
  - Prevalence of opioid use disorder has been increasing.
  - Emergency room visits and annual admissions for tx of opioids is increasing
- Are at increased risk
  - overdose death
  - HIV infection
  - Suicide
  - Social and legal negative consequences
  - Polysubstance use
  - Hepatitis C

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What we know about medication assisted treatment in adults with opioid use disorder

- High rates of recidivism and relapse rates after detoxification without subsequent Medication assisted treatment in well designed, federally funded abstinent based treatment programs
- Since 1970's is is known methadone will prolong abstinence from opioids and lead to longer-term recovery
- Methadone maintenance therapy has been and remains the gold standard for opioid use disorder
- Buprenorphine can be as efficacious as methadone but methadone continues to have better retention rates.

What we know about Medication Assistant Treatment in adolescents (under 18)

- Preliminary evidence (but research is growing)
  - Of both effectiveness and safety
  - No evidence on the neurobiological impact of these medications on the developing brain
  - Maintenance of buprenorphine-naloxone vs detoxification increases both retention and UDS negative for opiates
  - The combination of pharmacological and psychosocial interventions have better outcomes
  - Patient retention was the largest barrier to success,
- Strong evidence for
  - Decrease rate of hepatitis C infections
  - Decrease rates of accidental overdose
  - Although buprenorphine/naloxone is being increasing use off label
    - According to SAMSHA in 12 to 19 year olds with heroin dependence in 2000 only 16.1% and14.3% in 2011

Why the appropriate caution about ORT in adolescents

- serious medication, especially since most teens have relatively short abuse histories?
- There is no evidence of feels opiate withdrawal symptoms.
  - Don’t forget cravings

As the same time when it may not make sense.

- In adolescents who
  - Haven’t yet tried other forms of non-opioid treatments.
  - Have a very short history of opiate use (a few months only).
  - Have uncontrolled symptomatic mental illness that compromises the ability to comply with treatment
  - Aren’t willing or able to follow dosing directions and safety instructions.
  - Are allergic to buprenorphine or naloxone or have other health issues, such as liver dysfunction, paralytic ileus or respiratory problems that would complicate treatment.

In Summary
medication-assisted treatment (MAT) for adolescent opioid addiction is underutilized

- Even considering the concept that opioid use disorder is a chronic, relapsing brain disease
  - they often receive non-pharmacologic treatments following medication taper (detoxification).
  - Even though the evidence supports that relatively short courses of MAT do not always increase retention nor decrease the risk of relapse
  - Attitudes about MAT in adolescents persists that
    - “these medications prolong a state of opioid physical dependence”
    - Add may limit an adolescent’s chance of sustained recovery

But if you are going to MAT remember that

- After discharge from abstinent based treatment program there is a reduction in tolerance which means a patient has 7x risk of accidental overdose for the first two weeks after their release from residential treatment
- Methadone/buprenorphine/naloxone maintenance reduces risk of death up 75%
- Lower incidence of hepatitis C and HIV infection
- Lower the risk of accidental overdose
- Increase retention in treatment for a patient population that frequently does not see treatment as necessary.
- People under 18 are at heightened risk for some of the most serious dangers associated with opiate abuse – overdose death, HIV infection, suicide and other infectious diseases.[1]

- **Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction.** Treatment Improvement Protocol (TIP) Series, No. 40. Center for Substance Abuse Treatment. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2004.
- https://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/acknowledgements