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SUBSTANCE USE DISORDERS AMONG ADOLESCENTS AND TRANSITIONAL AGE YOUTH (TAY)

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SPEAKER'S DISCLOSURE

I have no financial relationship(s) with any ineligible companies to disclose.

OUTLINE

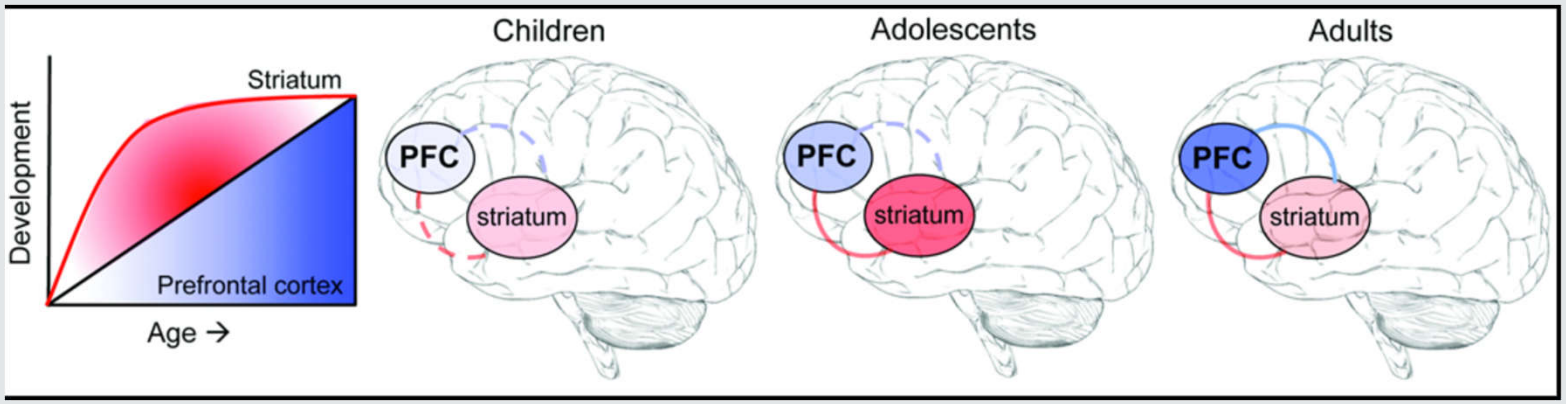
- Describe neurobiological changes that put this population at risk for substance use disorders and impact clinical interventions
- Describe national trends in substance use among adolescents
  - *Marijuana*
  - *Vaping Nicotine*
  - *Alcohol*
- Discuss impact of substance use in this population
- Describe screening and evaluation tools
- Develop an initial treatment plan for adolescents with substance use disorders including ways to engage families to be a part of treatment interventions


"Sometimes I like to circle someone perfectly
healthy just to mess with their head."

DEFINITIONS

Cognitive control: the process by which goals or plans influence behavior. Resistance from temptation or delay of immediate gratification	Risk taking: sensation seeking
Impulse control: difficulty in accomplish goal directed behavior in the face of competing actions	Motivation: process that initiates, guides, and maintains goal-oriented behaviors.

TRANSITION FROM CHILDHOOD TO ADULTHOOD

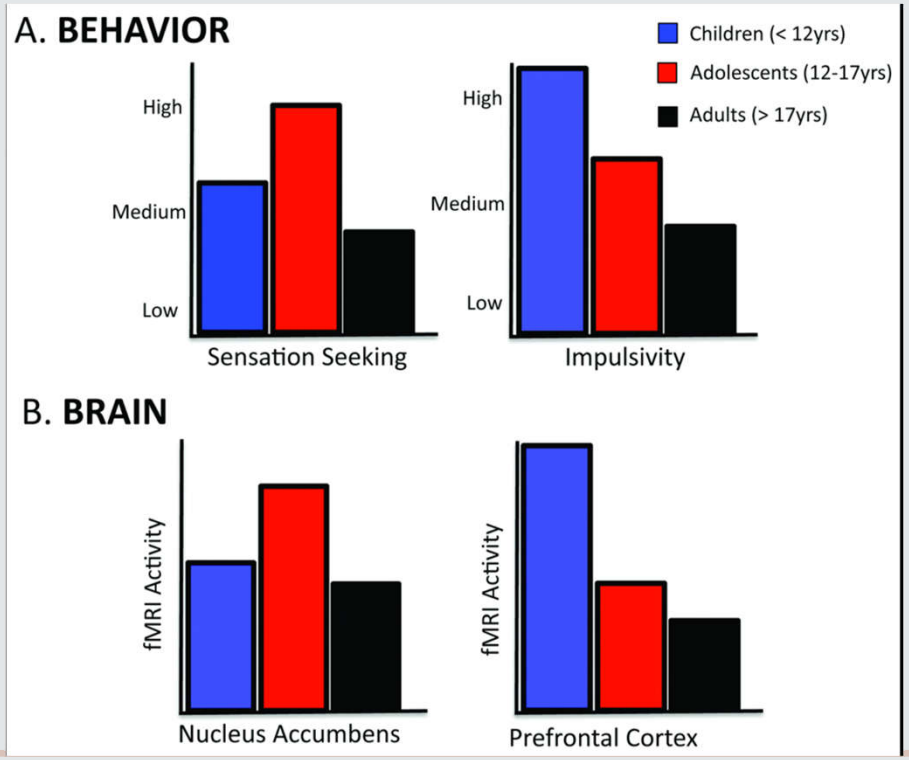


RISK TAKING VS IMPULSIVITY

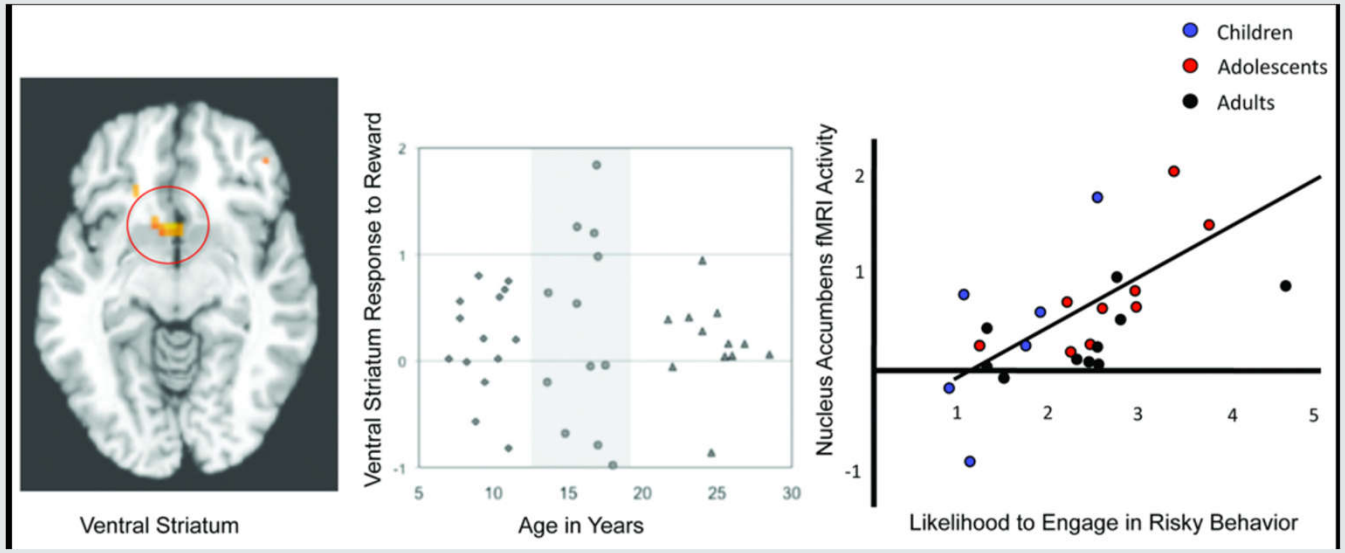
- Risk taking = high inclination to see excitement + immature capacity for self- control

- Impulse control
  - *Linear*
  - *Mediated by pre-frontal cortex*

- Risk taking
  - *Sensitivity to rewards/incentive Peaks between 13 and 17*



VENTRAL STRIATAL ACTIVITY TO REWARD AND ASSOCIATION WITH RISK- TAKING



COGNITIVE CONTROL

- Mediated by top-down processes
- Can be modulated by emotional driven contexts
- Can be modulated by motivation
  - *Rewarded for a task → work harder*
  - *Control can be hard if requires suppression of thoughts/actions towards desirable cues (drugs)*

MOTIVATION

- Motivation is a process that initiates, guides, and maintains goal-oriented behaviors.
- Adolescents and adults with substance use disorders choose smaller/immediate rewards
- Motivation and environment can be more influential in adolescence than in adulthood
- Influenced by peers more in adolescence than later adulthood
  - *Increased susceptibility of motivating properties of drugs/alcohol*

MOTIVATION

More likely to choose smaller/immediate rewards ➢ *Ventromedial PFC and ventral striatum*	Less likely to choose larger/delayed rewards ➢ *Dorsal PFC*

NEUROBIOLOGICAL CHANGES

2 critical periods	Birth to 3 years old and late adolescence (ages 13-25)
Early life stressors may impact these changes	Low SES, neglect, abuse (Increased risk in parental substance use) Atypical connectivity between subcortical structures and prefrontal cortex

NEUROBIOLOGICAL CHANGES

Prefrontal Cortex

- Cognitive control
- Linear
- Later development
- D1 and D2 receptors peak late in adolescence and in early young adulthood
- Delayed maturation on imaging studies
- Inversely correlated with impulsivity

Striatum

- Detect and learn about rewarding cues
- Curvilinear
- Early development
- D1 and D2 receptors peak in adolescence, loss of receptors by young adulthood
- Early maturation of imaging studies
- Increased sensitivity to reward and risk taking (but not impulsivity)

ADOLESCENT BRAIN: DEVELOPMENT MISMATCH

Prefrontal Cortex

- Late development
- Motivation
- Correlated with Cognitive control
- Inversely correlated with impulsivity
- D1 and D2 receptors peak late adolescence/ young adulthood

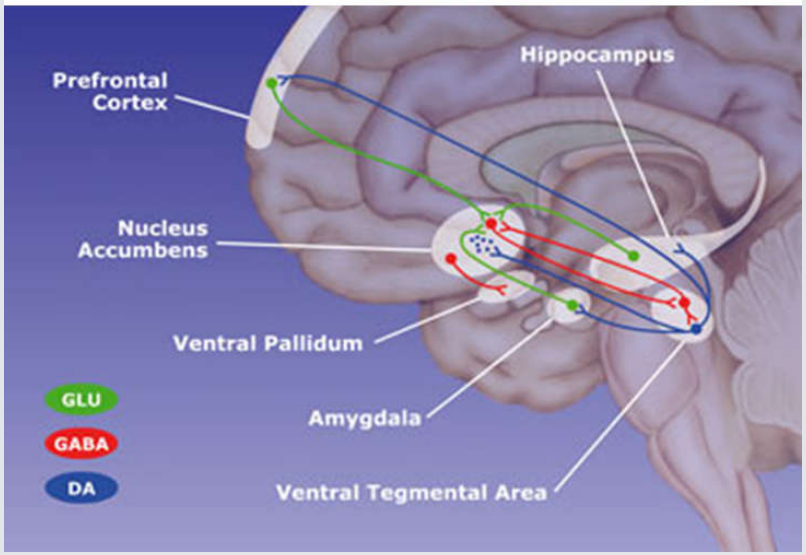
Striatum/Nucleus Accumbens

- Early development
- Motivation, risk taking
- D1 and D2 receptors peak in adolescence, loss of receptors by young adulthood
- Preference for low effort but high excitement activities

ADOLESCENT BRAIN: DEVELOPMENT MISMATCH

Amygdala

- Integrates emotions of pleasurable and aversive experiences
- Early development
- Tendency to react w/ “hot” emotions rather than controlled “cool” emotions
  - ➢ *Important how they interact not just how each region operates (frontostriatal)*



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RISK FACTORS FOR HIGH-RISK SUBSTANCE USE

- Family history of substance use
- Favorable parental attitudes towards the behavior
- Poor parental monitoring
- Parental substance use
- Family rejection of sexual orientation or gender identity

RISK FACTORS FOR HIGH-RISK SUBSTANCE USE

- Association with delinquent or substance using peers
- Lack of school connectedness
- Low academic achievement
- Childhood sexual abuse
- Mental health issues

HIGH RISK SUBSTANCE USE PREVENTION

- Parent or family engagement
- Family support
- Parental disapproval of substance use
- Parental monitoring
- School connectedness

EPIDEMIOLOGY: CANNABIS (MONITORING THE FUTURE 2022)

- Adolescent cannabis use and nicotine vaping *decreased* after the onset of pandemic in 2021 and these lowered levels of use continue into 2022
- Percentage of 12th graders who used cannabis in the past 12 months
  - *2022: 31%*
  - *2021: 31% (largest one-year decline ever recorded in the 48years of the survey)*
  - *2020: 35%*
  - *2019: 36%*
- Cannabis vaping increased significantly among 8th, 10th and 12th graders

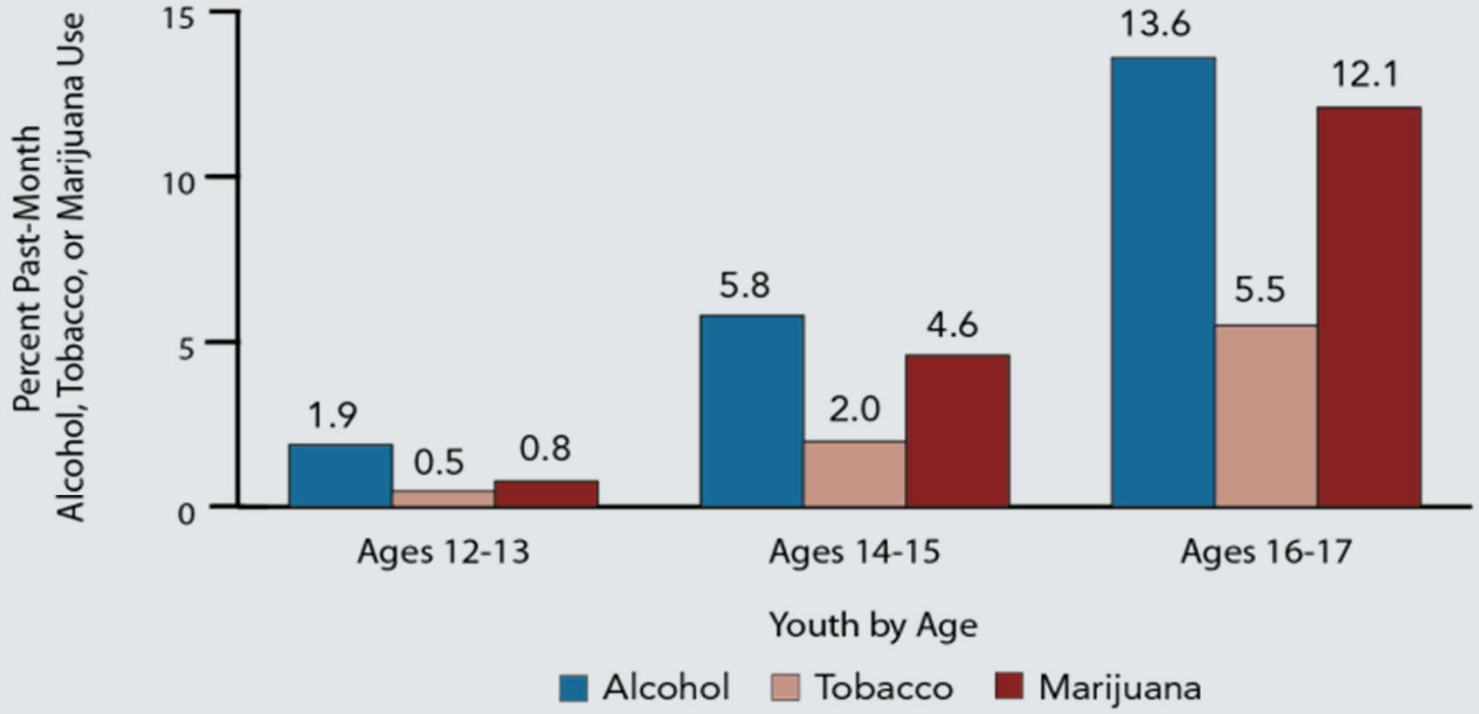
EPIDEMIOLOGY: ALCOHOL(MONITORING THE FUTURE 2022/NSDUH 2021)

- Levels of alcohol use *increased* significantly between 2021 and 2022, returning to pre-pandemic levels (MTF 2022)
- In 2022, the proportion of 8th, 10th, and 12th graders who reported drinking an alcoholic beverage in the 30-day period prior to the survey were 6%, 14% and 28% respectively (MTF 2022)
- People ages 12 to 20 in 2021, 15.1% (59 million) were past month alcohol users (NSDUH 2021)
- Binge alcohol use and heavy alcohol use in the past month among underage people were 8.3% (3.2 million) and 1.6% (613,000) respectively (NSDUH 2021)

EPIDEMIOLOGY: ALCOHOL(NSDUH 2021)

- 29.5 million people 12 or older meet criteria for an alcohol use disorder
  - 26 or older: 23.6 million
  - 18-25 age group: 5 million
  - *12-17 age group: 894,000 (~600,000 girls and ~300,000 boys)*
- Historically, adolescent boys were more likely to drink and binge drink than girls. Now, that relationship has reversed
- Alcohol use in recent years has declined more among adolescent boys than among girls, with more adolescent girls reporting alcohol use and binge drinking than boys
- 4,300 deaths annually are caused by underage drinking

More adolescents use alcohol than tobacco or marijuana



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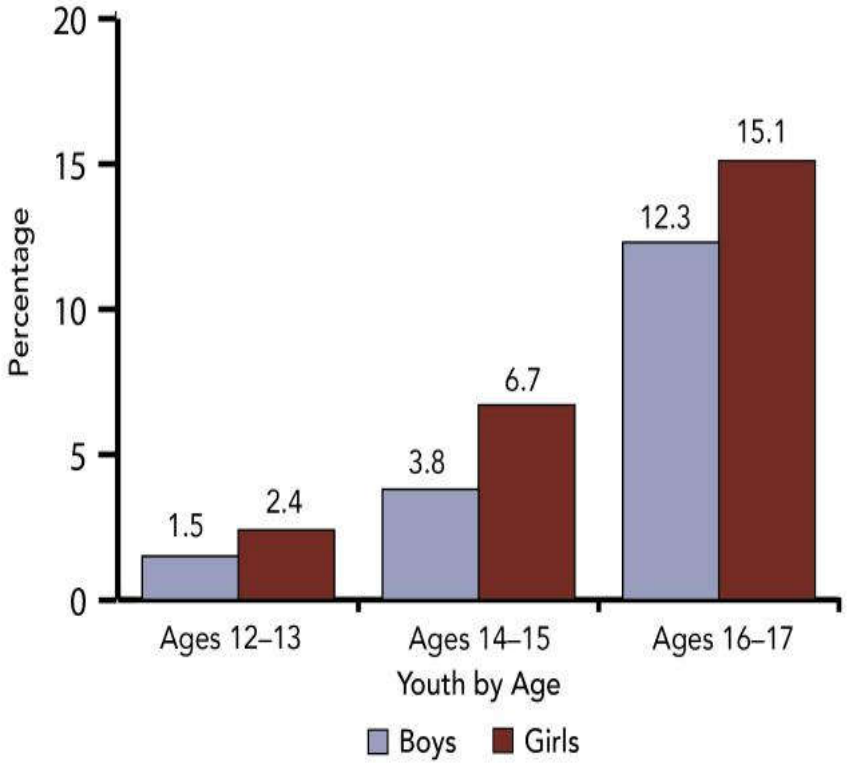
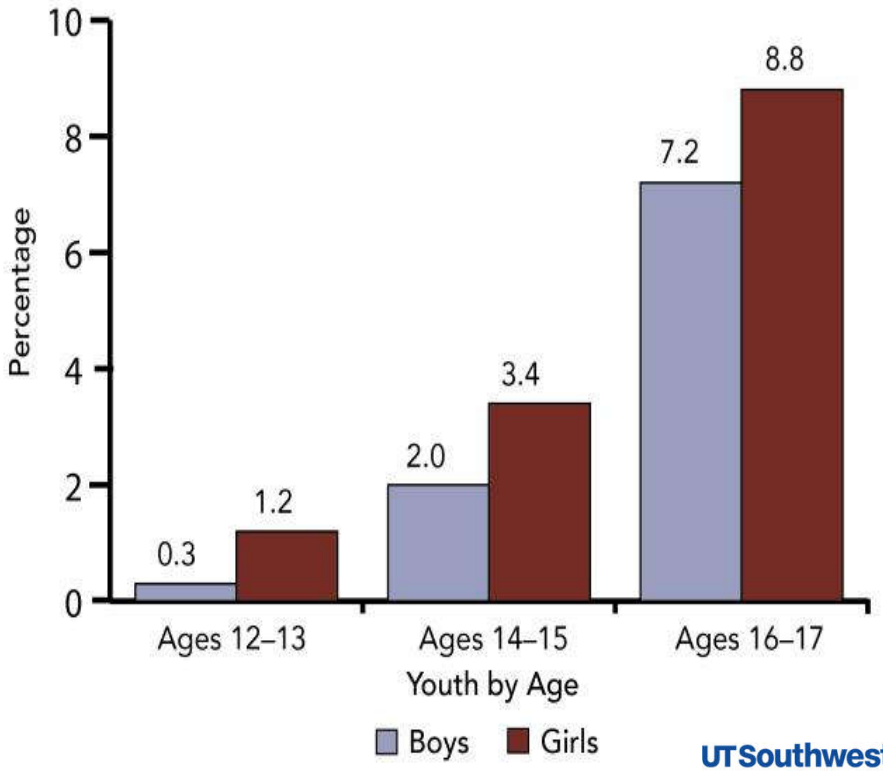
A Comparison of U.S. Boys and Girls: Past-month alcohol use



A Comparison of U.S. Boys and Girls: Past-month binge drinking



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EPIDEMIOLOGY: NICOTINE VAPING(NSDUH 2021)

- Percentage of people who vaped nicotine in the past month was highest among young adults 18 to 25years: 14.1 (4.7 million)
- The next largest group is adolescents aged 12 to 20: 5.2% or 1.4 million

EPIDEMIOLOGY: OTHER SUBSTANCE USE (MTF 2022)

- Significant past 30-day increase in the use among 12th graders for the following:
  - *Cocaine*
  - *Hallucinogens*
  - *Heroin*
  - *Prescription opioids*
  - *MDMA*
  - *Crack*
  - *Tranquilizers*
  - *Anabolic steroids (creatine, androstenedione)*

ADOLESCENT BINGE DRINKING(BD)

Girls

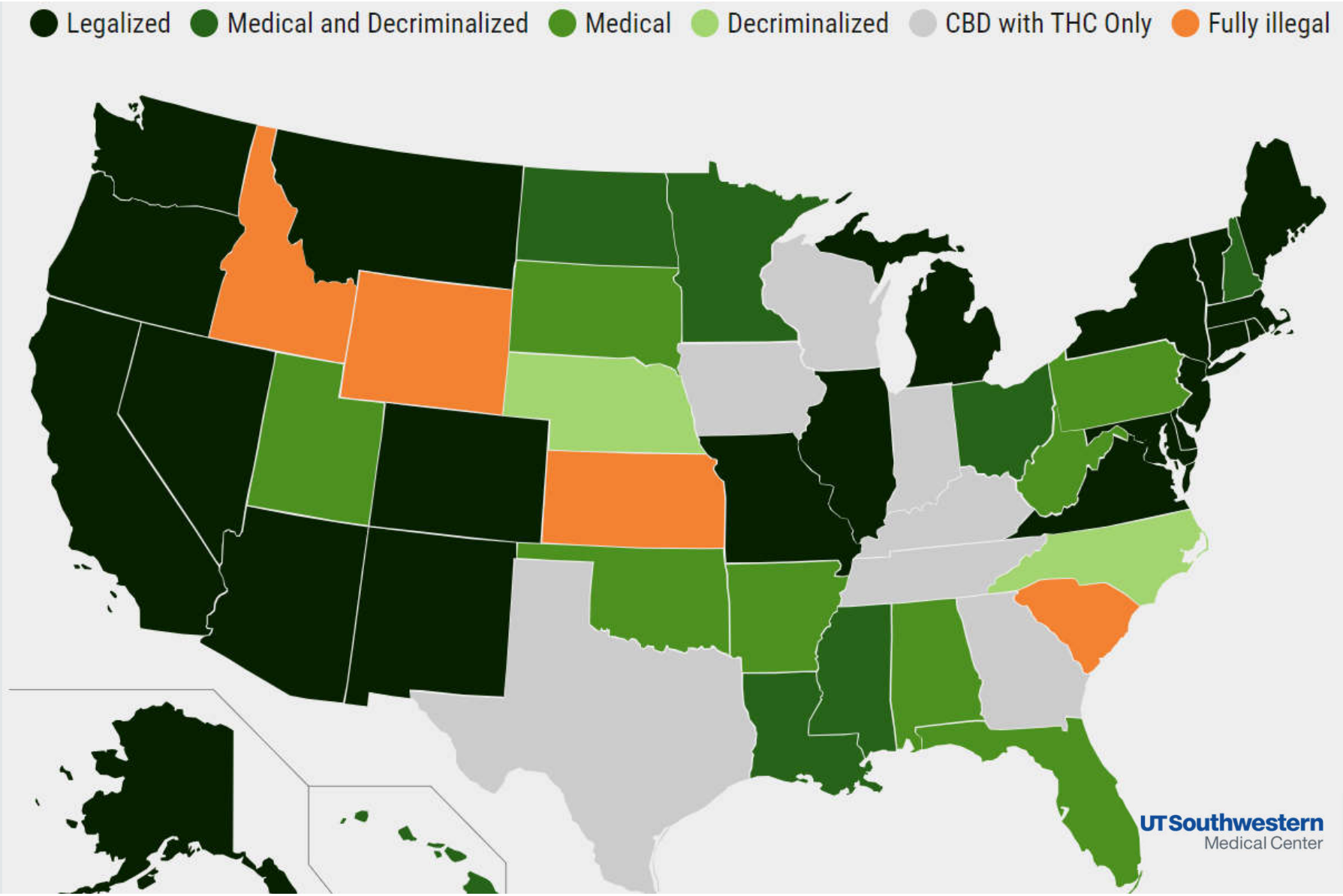
- Internalizing symptoms, including depression and anxiety, have been linked to BD
- More sensitive to the negative effects and experience them at lower doses
- “Telescoping”
- Trauma

Boys

- Externalizing symptoms including impulsivity and sensation seeking, linked to BD among boys
- More sensitive to the rewarding effects
- Data on social influences is mixed

ADOLESCENT CANNABIS EXPOSURE

- Associated with negative life outcomes
- Impairments in cognition: partial cognitive recovery with cessation (attention/full scale IQ)
- Increased prevalence and worse outcomes of psychotic, mood and other substance use disorders
- These associations are stronger in adolescents with *earlier age of onset, frequent & heavy use and high potency cannabis use*


Legalized
Medical and Decriminalized
Medical
Decriminalized
CBD with THC Only
Fully illegal
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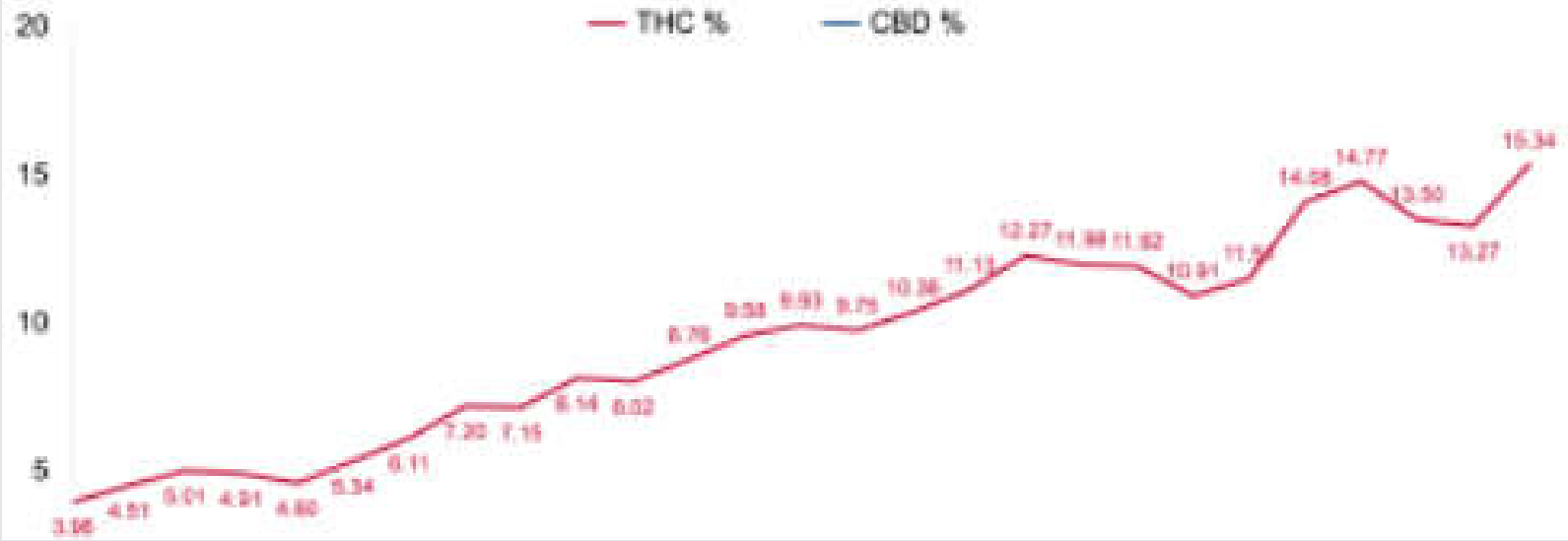
Percentage of THC and CBD in Cannabis Samples Seized by the DEA, 1995-2021



IMPACT OF MARIJUANA LEGALIZATION

- Legalization has not led to an increase in recreational use by adolescents
  - *However, states that have legalized marijuana had relatively higher rates of adolescent cannabis use before legalization occurred*
- Risk perception is at an all time low
- Young people who use medical marijuana are more likely to have used cannabis regularly between ages 13-19years
- Increased potency and reduced cost
- Expanded preparation and routes of administration (i.e., edibles, waxes, extracts, and vaping)

IMPACT OF MARIJUANA LEGALIZATION

- Increased motor vehicle accidents and fatalities secondary to cannabis use
- Accidental overdoses by young children and pets
- Increased emergency department visits and hospitalizations resulting of chronic daily use of high potency cannabis

ADOLESCENT OVERDOSE

- Adolescents and young adults have experienced a greater increase in overdose mortality
- In a 12-year period, fentanyl-related fatalities increased by 23.5-fold among youth, with
  - *~77% Fentanyl*
  - *~6% Prescription opioids*
  - *~2% Heroin*
- Five times higher mortality rates among African American teens

IMPACT OF ALCOHOL AND SUBSTANCE USE

- Sexual risk behavior
- Experience of violence
- Mental health and suicide risks
- Poorer physical health
- Academic decline
- Greater involvement with the legal system
- Progression to developing a substance use disorder (SUD)

HIGH RISK SEXUAL BEHAVIOR

- 19% drank alcohol or used drugs before last sexual intercourse
- 20% of all new HIV diagnoses were among young people (aged 13–24) in 2020
- More than half of the nearly 20 million new STDs reported in 2020 were among young people (aged 15–24)
- More than 145,000 infants were born to adolescent females in 2021

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"*WHEN I READ ABOUT THE EVILS OF DRINKING, I GAVE UP READING*" HENNY YOUNGMAN

SCREENING TOOLS: RATIONALE AND BENEFITS

- Normalize discussions with adolescents about substance use
- Reinforce and promote healthy behaviors and choices
- Identify adolescents who are potentially at risk for SUD
- Guide brief interventions and referrals for treatment

SCREENING TOOLS: BSTAD AND S2BI

- **Brief:** BSTAD and S2BI can be administered **in less than two minutes**
- **Scientifically validated:** BSTAD and S2BI were validated in adolescent samples, demonstrating accuracy in identifying adolescents with and without substance use disorders who were seen in pediatric primary care settings

SCREENING TOOLS: BSTAD AND S2BI

- Easy administration: BSTAD and S2BI can be self-administered, or provider administered using a tablet or computer. Providers are encouraged to consider patient self-administration to save time
- Follow-up: In addition to the risk score, clinicians receive information about the score's implications, suggested actions and additional resources that were compiled through subject matter expert consensus

BSTAD: BRIEF SCREEN FOR TOBACCO, ALCOHOL AND OTHER DRUGS

- In the PAST YEAR, on how many days did you smoke cigarettes or use other tobacco products?
- In the PAST YEAR, on how many days did you have more than a few sips of beer, wine, or any drink containing alcohol?
- In the PAST YEAR, on how many days did you use marijuana (weed; blunts)?

S2BI: SCREENING TO BRIEF INTERVENTION

- In the PAST YEAR, how many times have you used tobacco?
- In the PAST YEAR, how many times have you used alcohol?
- In the PAST YEAR, how many times have you used marijuana?
  - *Never/Once or twice/Monthly/Weekly or more*

RED FLAGS OF EARLY ONSET SUBSTANCE USE

- New onset of depression and affective instability
- New onset of anxiety
- Changes in sleep pattern
- Tendency to isolate
- Socially withdrawn from family and friends
- Academic decline
- Change in friend group

TEXAS LAWS REGARDING TREATMENT AND CONFIDENTIALITY

- Texas has laws allowing minors to receive counseling related to drug or chemical addiction or dependency without prior parental consent and counseling related to suicide prevention, and sexual, physical, or emotional abuse
- The Texas laws that require mental health and substance use communications and records to be confidential also provide for disclosure based on consent of the patient, consent of the parent of a minor, or if the patient presents a threat of imminent danger to self or others

TREATMENT INTERVENTIONS:

- Psychosocial Interventions
  - *Evidence based behavioral treatments*
  - *Group therapy including 12 step recovery models*
  - *Partial hospital programs (PHPs)*
  - *Intensive outpatient programs (IOPs)*
  - *Residential treatment programs*
- Pharmacological interventions

EVIDENCE BASED BEHAVIORAL TREATMENTS

- Cognitive-behavioral therapy (CBT)
  - *CBT is a well-studied approach focusing on the thoughts, behaviors, and triggers that reinforce substance use*
  - *This approach encourages patients to utilize coping skills and problem-solving skills and to find healthy alternative behaviors to replace substance use*
  - *It should be considered as a first-line treatment for highly motivated patients or patients who have already started treatment, but it may have limited utility in more ambivalent patients*

EVIDENCE BASED BEHAVIORAL TREATMENTS

- Contingency management (CM)
  - *CM uses incentives like vouchers or prizes to reinforce milestones in treatment, such as adherence to treatment or negative drug screens*
- Motivational enhancement therapy (MET)
  - *MET is an empathetic approach, focusing on individualized goals and psychoeducation. MET is often less time and resource intensive than CBT*
  - *MET may be ideal for patients who are ambivalent or who are just starting treatment*

PHARMACOLOGICAL INTERVENTIONS: ALCOHOL

FDA approved

- Disulfiram
- Naltrexone
- Acamprosate

Non-approved

- Baclofen
- Gabapentin
- Topiramate

NALTREXONE

- Full antagonist at the mu opioid receptor (MOR) and to a lesser extent the kappa opioid receptor (KOR) and delta opioid receptor (DOR)
- Approved in 1994 for alcohol dependence (Revia)
- Reduces drinking via several mechanisms:
  - *Reduces positively reinforcing effects of alcohol by reducing the mesolimbic opioidergic activity*
  - *Enhances the sedative effects of alcohol*
  - *Decreases cravings for alcohol*
- Start with 25mg at bedtime for 7 days and then increase to 50mg daily

NALTREXONE

- Has an active metabolite 6β-naltrexol
- Half life Naltrexone: 4hours; 6β-naltrexol: 13hours
- Time to peak plasma levels: 60 minutes
- Obtain liver function tests (LFTs) at baseline and then every 6 months
- Cannot start Naltrexone if baseline LFTs are > 3Xs the upper limit of normal and/or Total bilirubin >3mg/dl

NALTREXONE

- Side effect profile is benign, common side effects are nausea, sedation, headaches, dizziness
- Helps patients abstain as well as decrease alcohol use
- RCT trial by Miranda et.al. comparing naltrexone (50mg/day) to placebo in 22 adolescent problem drinkers aged 15-19years showed
  - *Reduced likelihood of drinking and heavy drinking*
  - *Blunted cravings*
  - *Altered subjective responses to alcohol*

EXTENDED-RELEASE NALTREXONE(DEPOT NALTREXONE)

- Medisorb drug delivery technology
- Naltrexone is embedded within biodegradable polymer microspheres released over at least 30 days
- Recommended dose is 380mg every 4 weeks intramuscular in the gluteal region
- It has two peaks at 2 hours and 3 days
- After day 14, levels tend to decline

EXTENDED-RELEASE NALTREXONE(DEPOT NALTREXONE)

- Improves compliance with treatment
- Hepatically safer since it bypasses the first pass metabolism
- Helps patients abstain as well as decrease alcohol use

PHARMACOLOGICAL INTERVENTIONS: MARIJUANA

- No FDA approved treatments
- N-acetylcysteine (NAC)
- Naltrexone
- Gabapentin
- Cannabidiol (CBD)

N-ACETYLCYSTEINE

- Serves as a prodrug to L-cysteine which is a precursor to anti-oxidant glutathione
- Used in paracetamol overdose, as a mucolytic and in contrast-induced nephropathy
- Metabolized extensively by the liver
- Half-life 6hours
- Nausea, vomiting, rash and fever are common side effects
- There is an abundance of literature implicating glutamatergic abnormalities in SUDs
- Data are emerging suggesting a role of oxidative stress in the pathophysiology of SUDs

N-ACETYLCYSTEINE

- Research has explored the modulation of glutamatergic pathways by NAC in preclinical models
- N-acetylcysteine has been shown to reverse the decline in cystine–glutamate exchange through the cystine–glutamate antiporter and thereby assist in the restoration of glutamatergic pathways in SUDs
- Study by Gray et. al. investigated the use of NAC (2400 mg/d) in an open-label study of 24 dependent marijuana users who reported an interest in reducing their use

N-ACETYLCYSTEINE

- Following treatment, users reported reductions in days/week of use and “number of hits”
- Reductions in reported compulsivity, emotionality and purposefulness regarding marijuana use were reported
- Start treatment with NAC 600mg twice daily for 7days and then increase to 1200mg twice a daily
- Stronger evidence for NAC’s efficacy in the 15-21 age group

NALTREXONE FOR CANNABIS USE DISORDERS(CUD)

- Single doses of naltrexone(12-100 mg) have been found to enhance misuse-related effects of cannabis
- Daily administration of naltrexone (50 mg) for 3 weeks reduced cannabis self-administration and use in people not seeking treatment for CUD

OTHER STUDIES FOR CUD: GABAPENTIN AND CBD

- In a placebo-controlled trial (N=50), gabapentin administered at 1200 mg/day showed significant reductions in objective and subjective markers of cannabis use, withdrawal, and craving
- In a recent RCT with individuals seeking treatment for CUD (N=48), oral CBD (400-800 mg/day) was associated with reduced cannabis use, favorable retention, and no significant adverse events

OTHER STUDIES FOR CUD: GABAPENTIN AND CBD

- Of note, commercially available OTC CBD products should not be used for medical treatment because they usually contain lower doses of CBD (e.g., 5-100 mg) than those administered in these studies

PHARMACOLOGICAL INTERVENTIONS: OPIOIDS

- Methadone
- Buprenorphine
- Naltrexone

METHADONE: PHARMACOLOGY

- Full mu agonist
- NMDA antagonist and is an SNRI
- Oral bioavailability 80%
- T1/2 24 hours ,metabolized by CYP450 3A4, also 1A2 & 2D6
- Induction does not require patient to be in withdrawal

METHADONE: PHARMACOLOGY

- Approved for opioid addiction (liquid/wafer) and analgesia (tablets)
- Dose range 60-120mg
- Schedule II
- Dispensed for addiction treatment, prescribed for pain
- Approved in pregnancy

METHADONE: PHARMACOLOGY

- May prolong QTc
- Limited to people in large metropolitan areas
- Person under 18 years of age is required to have had two documented unsuccessful attempts at short-term withdrawal management or drug-free treatment within a 12-month period to be eligible for maintenance treatment

METHADONE: PHARMACOLOGY

- No person under 18 years of age may be admitted to maintenance treatment unless a parent, legal guardian, or responsible adult designated by the relevant State authority consents in writing to such treatment
- No randomized controlled trials have been done with methadone
- *Highly stigmatized treatment*

BUPRENORPHINE: PHARMACOLOGY

- Partial mu agonist
- Partial agonist at the nociceptin opioid receptor
- Weak kappa antagonist
- Antagonist at the delta opioid receptor
- S/L bioavailability 29%
- T1/2 37hrs,metabolized by CYP450 3A4

BUPRENORPHINE: PHARMACOLOGY

- Induction requires patients to be in withdrawal
- Tablets/Film/SQ injection approved for opioid use disorder, patch approved for pain (Butrans)
- Monthly and weekly injectable preparations
- Dose range 8-24mg
- Schedule III
- Prescribed to treat opioid use disorder

BUPRENORPHINE: PHARMACOLOGY

- Studied in pregnancy (MOTHER Study)
- MOTHER study: decreased severity of Neonatal Opioid Withdrawal Syndrome (NOWS)
- No cardiotoxicity
- Has increased access to care
- Buprenorphine is FDA approved for individuals 16years and older
- *Less Stigma associated*

BUPRENORPHINE: CLINICAL PRACTICE

- Adolescents with OUD have limited access to opioid agonist medications and standard models of opioid agonist-based care for OUD youth are lacking
- Most adolescents with OUD do not receive treatment and those who do, primarily receive abstinence-based residential treatment or outpatient psychosocial therapy – strategies that produce high rates of dropout and relapse
- Among adolescents who receive treatment for OUD, less than three percent receive opioid agonist treatment .Those who do receive opioid agonist treatment, primarily receive short-term withdrawal treatment instead of longer-term treatment

EXTENDED-RELEASE NALTREXONE(DEPOT NALTREXONE)

- In 2010 FDA approved the extended-release Naltrexone (XR-NTX) 380mg monthly IM primarily based on Russian data
- Two recent studies showed that both XR-NTX and BUP-NX were equally safe and effective (XBOT Clinical Trials Network and Tanum et.al.)
- No randomized controlled trials have been done with XR-NTX