

Cannabis Use in the Pregnant and Breastfeeding Mother: What Preventionists Should Know

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This session is recorded and all materials will be posted on pttcnetwork.org within 1 week.

Purpose of the PTTC Network

- Improve implementation and delivery of effective substance use prevention interventions
- Provide training and technical assistance services to the substance use prevention field
 - Tailored to meet the needs of recipients and the prevention field
 - Based in prevention science and use evidence-based and promising practices
 - Leverage the expertise and resources available through the alliances formed within and across the HHS regions and the PTTC Network.

PTTC Network Approach

- ▶ Develop and disseminate tools and strategies needed to improve the quality of substance abuse prevention efforts
- ▶ Provide intensive technical assistance and learning resources to prevention professionals in order to improve their understanding of
- ▶ prevention science,
- ▶ how to use epidemiological data to guide prevention planning, and
- ▶ selection and implementation of evidence-based and promising prevention practices.
- ▶ Develop tools and resources to engage the next generation of prevention professionals.

Focus Areas and Working Groups

Learn more: <https://pttcnetwork.org/centers/global-pttc/pttc-areas-focus>

1. Community coalitions and collaborators
2. Building Health Equity & Social Justice
3. Data-informed decisions
4. Implementation Science
5. Cannabis Prevention
6. Workforce Development

Cannabis Working Group Members

- ▶ Britany Wiele, Chair
- ▶ Scott Gagnon, Co-Chair
- ▶ Michelle Frye-Spray
- ▶ Ken Winters
- ▶ Susie Villalobos
- ▶ Jeanne Pulvermacher
- ▶ Deborah Nixon-Hughes
- ▶ Taylor Cook

Dr. Sheryl Ryan



Disclosures

- ▶ I have nothing to disclose

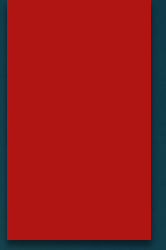
Learning Objectives

- ▶ Describe the biology of cannabis products and the endocannabinoid system.
- ▶ Explain the adverse short and long-term health effects of cannabis products especially during pregnancy and breast-feeding on fetal and neonatal development.
- ▶ Discuss prevention strategies including multi-sector approaches and recommendations for people who are pregnant, planning pregnancy, or breastfeeding.

History of cannabis

- ▶ 2900 BC – Chinese Emperor Fu His – “popular medicine”
 - ▶ In Chinese pharmacopeia
- ▶ 1800s – “mainstream” Western medicine
 - ▶ Many uses – headaches, pain, appetite stimulant, sleep aid
 - ▶ On US Pharmacopeia as patent medicine – “tinctures” for variety of disorders including as treatment for opiate addiction
- ▶ 1940’s – Cannabidiol first extracted from hemp plant
- ▶ 1964 – THC molecule first identified
- ▶ 1990 – Endocannabinoid receptor identified
 - ▶ 1992 – first endocannabinoid discovered
- ▶ 1996 – California is first state to legalize medical cannabis
- ▶ 2013 – Colorado is first state to legalize recreational cannabis
- ▶ Now – 44 states with legalized medical/recreational cannabis; 22 states and D.C have legalized recreational use
- ▶ Estimated that more than 13 million people worldwide are *dependent* on MJ

Biology of Cannabis



Cannabis Biology

- The cannabis plant: contains more than 200 biologically active substances - cannabinoids
- Numerous species and subspecies
 - Cannabis sativa and indica the two most common.
 - Cause a variety of psychotropic effects
- Both species have been hybridized repeatedly



Cannabis Biology

- ▶ Delta 9 –Tetrahydrocannabinol - **THC**
 - ▶ The primary psychoactive cannabinoid in the cannabis plant.
 - ▶ High affinity for CB receptors in the brain
- ▶ Selective breeding has resulted in higher concentrations of THC in plant products
- ▶ From 1995 to 2013 - ~4% to 17% THC
 - ▶ Now > 20%
- ▶ New ways of using (dabbing, volatilizing oils) create even higher concentrations – 39-80%
 - ▶ More potent psychotropic effects as well as increased risk of adverse effects



Cannabis Strength

(80-90% THC) Concentrates



"Green Crack"
wax



"Ear Wax"



Butane Hash Oil
(BHO)



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Hash Oil Capsules



"Budder"

"Shatter"

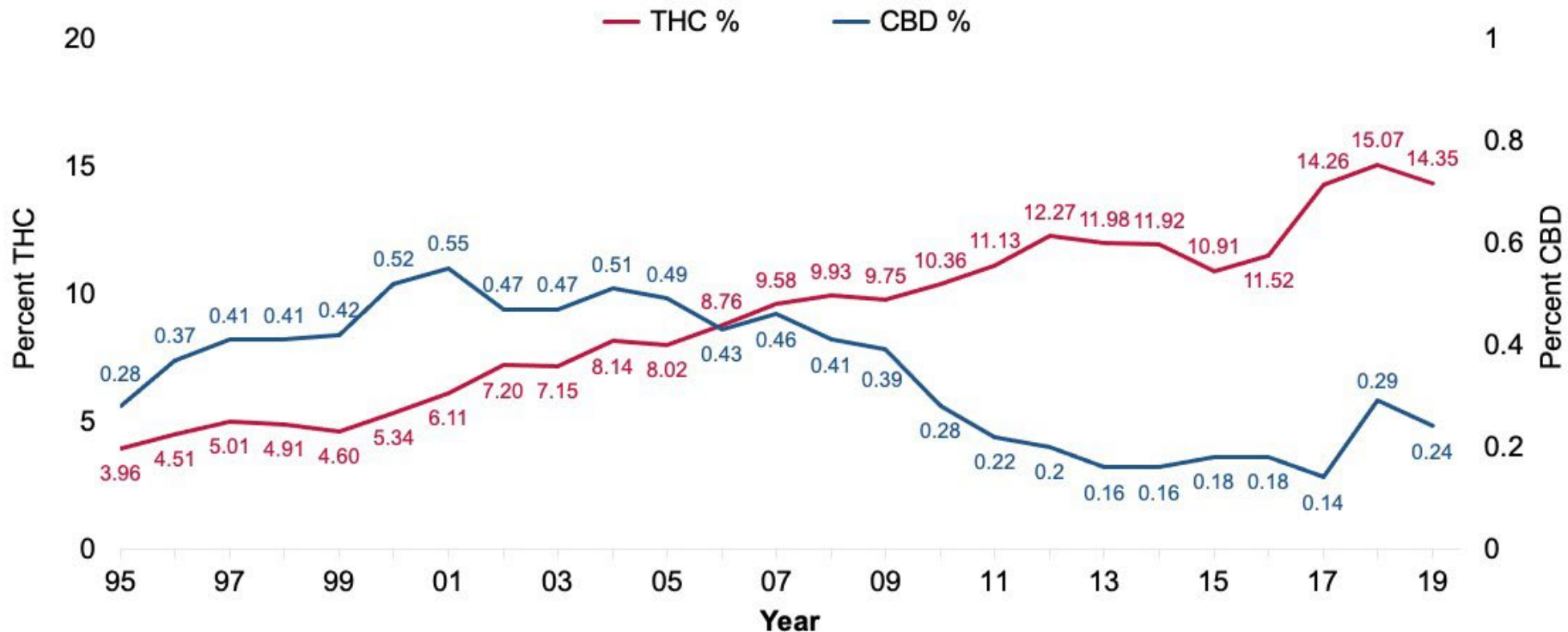


Cannabidiol (CBD)

- ▶ CBD - non-psychoactive cannabinoid.
 - ▶ Low affinity for CB receptors in the brain
 - ▶ Non-competitive antagonist of CB1 receptors; inverse antagonist of CB2 receptors (potentiates CB receptors)
 - ▶ Inhibits the reuptake and degradation of main endocannabinoid AEA (opposite effect of THC)
 - ▶ Agonist of serotonin 5HT1A receptors
 - ▶ ?Responsible for its role as potential anti-depressant, anxiolytic, and procognitive agent
 - ▶ Modulates neural substrates involved in reward behaviors
 - ▶ Potent antioxidant and anti-inflammatory
- ▶ *Focus on CBD for medicinal effects*
- ▶ Mechanisms of action are not fully understood!
- ▶ Little is known about dose-response relationships of CBD and mechanisms of action for specific conditions



Percentage of THC and CBD in cannabis samples seized by the DEA from 1995-2019



<https://www.drugabuse.gov/drug-topics/cannabis/cannabis-potency>

Thanks to Vent Vrana, Ph.D.



Endocannabinoid System: ECS

The Endocannabinoid System: ECS

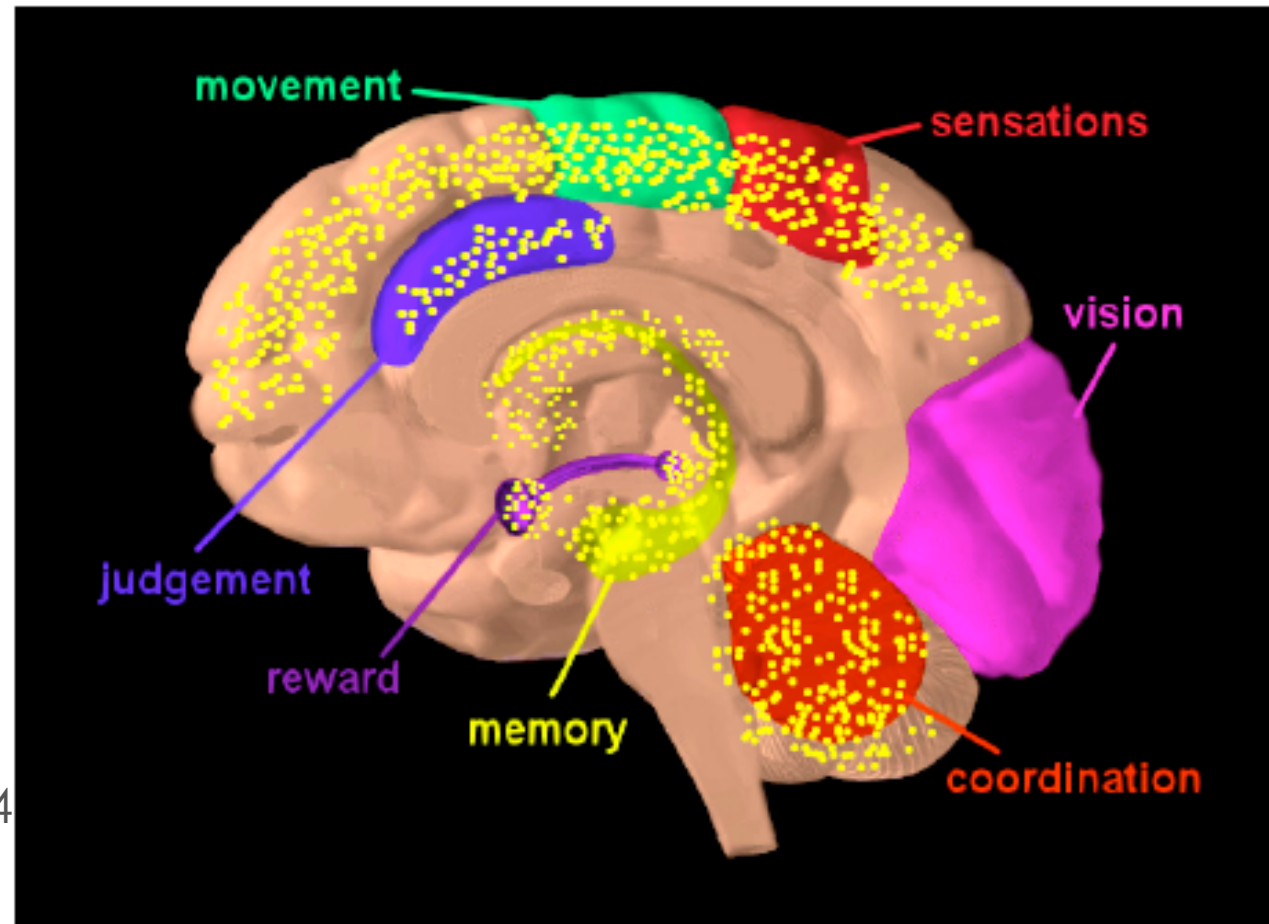
- ▶ Humans produce 2 main “endocannabinoids”
 - ▶ Anandamide and 2-AG (2-arachidonoylglycerol).
 - ▶ Biologically active molecules that serve a number of regulatory functions throughout the body
- ▶ Two endocannabinoid receptors: CB1 and CB2.
 - ▶ CB1 - in the brain and nervous system
 - ▶ CB2 - in immune system cells, wide range of somatic cells.
- ▶ **Can be detected as early as 5 weeks gestation**
 - ▶ **THC and CBD interact directly with ECS**



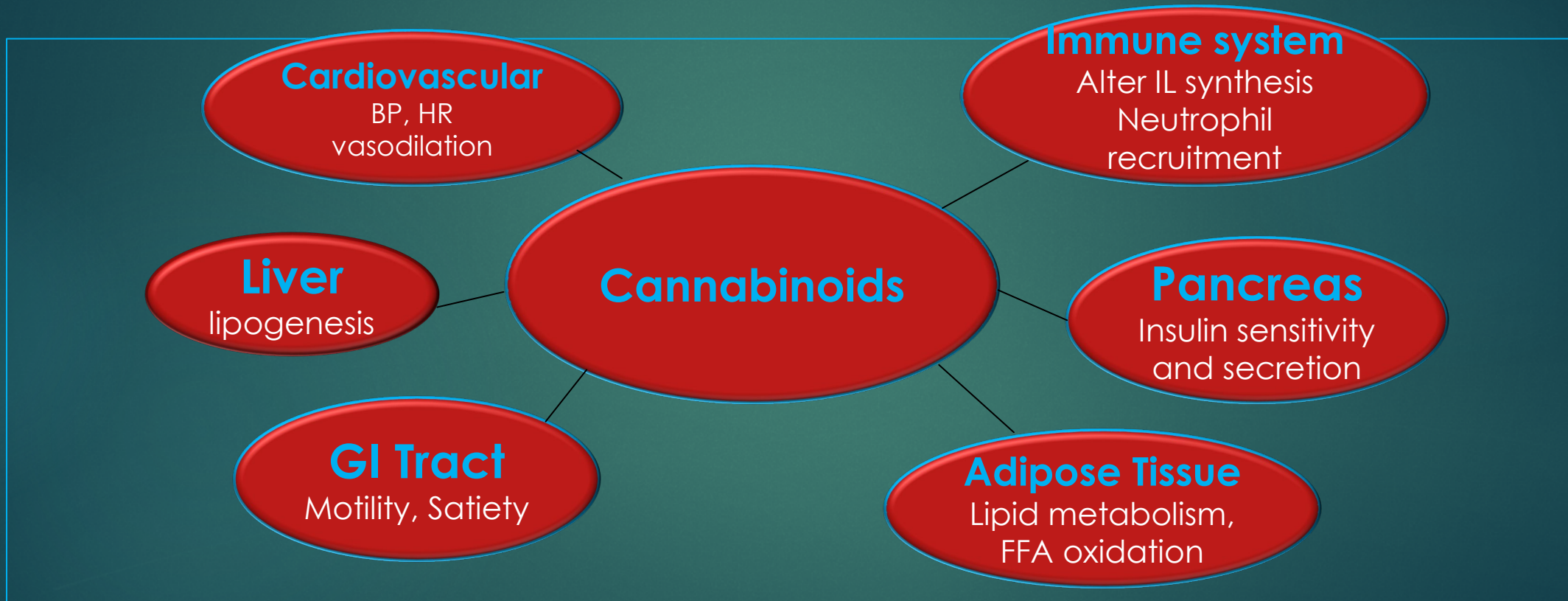
Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

- Brain Development
- Memory and Cognition
- Motivational Systems & Reward
- Appetite
- Immunological Function
- Reproduction
- Movement Coordination
- Pain Regulation & Analgesia

Volkow NIDA 2014



Mechanisms of action: Endogenous Cannabinoids





Effects of THC and Cannabidiol (CBD)

Acute Effects: THC

- ▶ Intoxication
 - ▶ Euphoria, relaxation/sedation, change in pain sensation, distortion of sensory perception, thought and time distortion
- ▶ Delayed motor coordination, slowed reaction to stimuli
- ▶ Increased heart rate; decreased blood pressure
 - ▶ 4.8 fold increase in chance of having a heart attack within 1st hour after using drug
 - ▶ Cough, blood-shot eyes
- ▶ Hallucinations, paranoia, anxiety, psychosis – toxic reaction
- ▶ Memory Impairment

EFFECTS WITH REGULAR/HEAVY USE

- Decreased cognitive functioning
 - Poorer executive function, learning and memory deficits, attention
 - Memory/Cognitive impairment can be long-lasting
 - Amotivational syndrome – poorer psychosocial development and educational attainment
- Higher rates of schizophrenia, anxiety and mood disorders
 - Especially with family history of psychosis
- Unclear association with chronic bronchitis and respiratory diseases
- Disrupted sleep architecture and increased sleep onset
- 50-90% more car accidents when also used with alcohol
- Higher rates of use of tobacco and other drugs
- Excessive vomiting - hyperemesis syndrome
- Dependence in 1 in 6 teens who use regularly
 - Craving, tolerance leads to increased usage over time
 - Withdrawal symptoms
 - DSM V Diagnosis – “cannabis use disorder”

CBD – Adverse Effects

- ▶ **Not risk-free**
- ▶ Pre-clinical studies – in-vitro experiments
 - ▶ Impairs function of perinatal rat cortical neurons and astrocytes
 - ▶ Especially during critical periods of brain development
 - ▶ Can interfere with ECS – causing reduced viability and cell death
 - ▶ Disrupt delicate homeostatic balance between neural cells → developmental malfunction
- ▶ Pre-Clinical – Animals
 - ▶ Embryo-fetal mortality
 - ▶ CNS inhibition and neurotoxicity
 - ▶ Hepatocellular injuries
 - ▶ Spermatogenesis reduction and male reproduction system effects
- ▶ Human studies
 - ▶ Drug-drug interactions – CP450 system (CYP2C19 and CYP3A4) and UGP
 - ▶ Hepatic abnormalities
 - ▶ Vomiting and Diarrhea
 - ▶ Fatigue/Somnolence

*Huestis MA et al Current Neuropharmacology. 2019. 17:974-989.



Effects of Prenatal Exposure to Cannabis

SHORT AND LONG TERM EFFECTS SEEN IN
CHILDREN AND ADOLESCENTS

Rates of use of Cannabis During Pregnancy and Breastfeeding

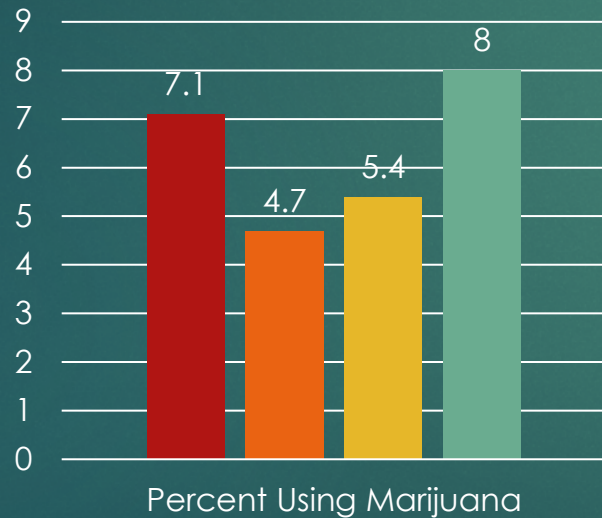


- ▶ Most widely used *illicit* substance in pregnancy
 - ▶ Anecdotally recommended for morning sickness and widely accepted as a harmless drug
 - ▶ Tobacco and alcohol still most widely used substances
- ▶ Increasing rates of use in both pregnancy and breastfeeding*
 - ▶ 34-60% of users “used throughout” pregnancy
 - ▶ Reasons – recreation -39%; N/V – 48%; pain 60%
- ▶ Users – more likely to be young, lower SES, smoke cigarettes, report significant emotional distress**

*Wang, J, Med Toxic 2017;13:99-105; ** Young-Wolff JAMA 2017;318:2490-2491.

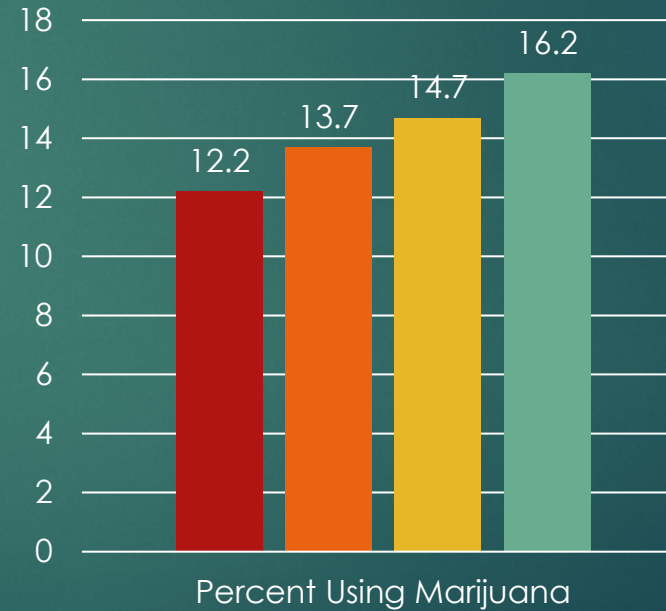
Past Month Use of cannabis: Pregnant vs. Non-Pregnant Women, 2020 NSDUH

Pregnant Women 15-44 yrs



■ 2017 ■ 2018 ■ 2019 ■ 2020

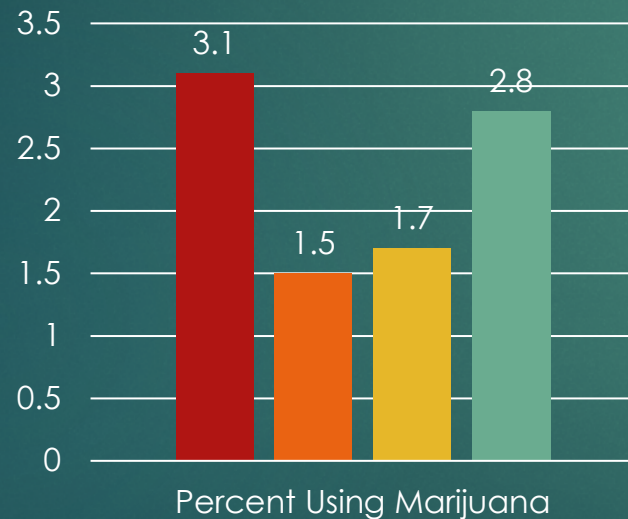
Non-pregnant 15-44 yrs



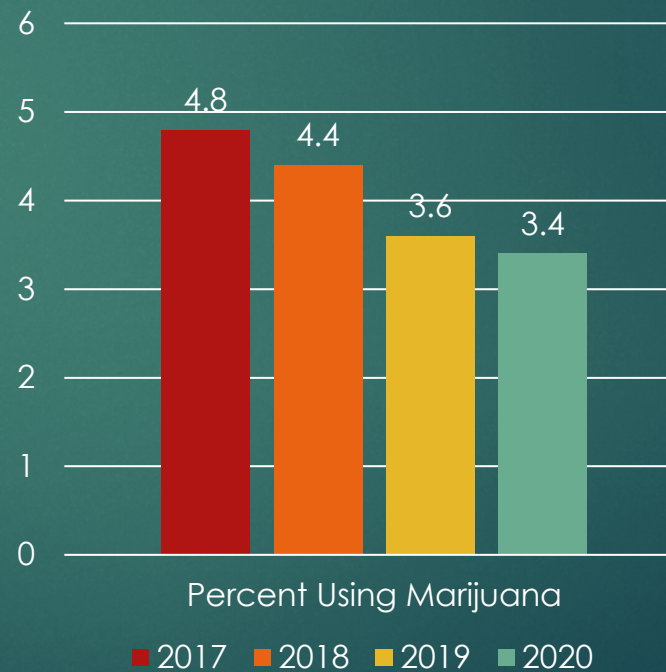
■ 2017 ■ 2018 ■ 2019 ■ 2020

Daily Use of cannabis: Pregnant vs. Non-Pregnant Women, 2020 NSDUH

Pregnant Women 15-44 yrs



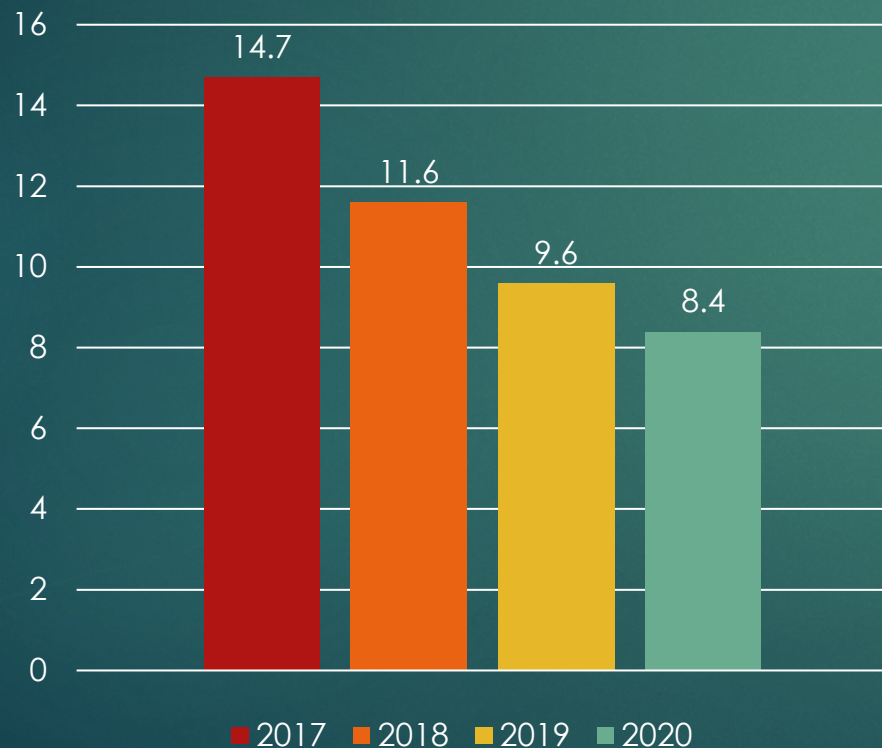
Non-pregnant 15-44 yrs



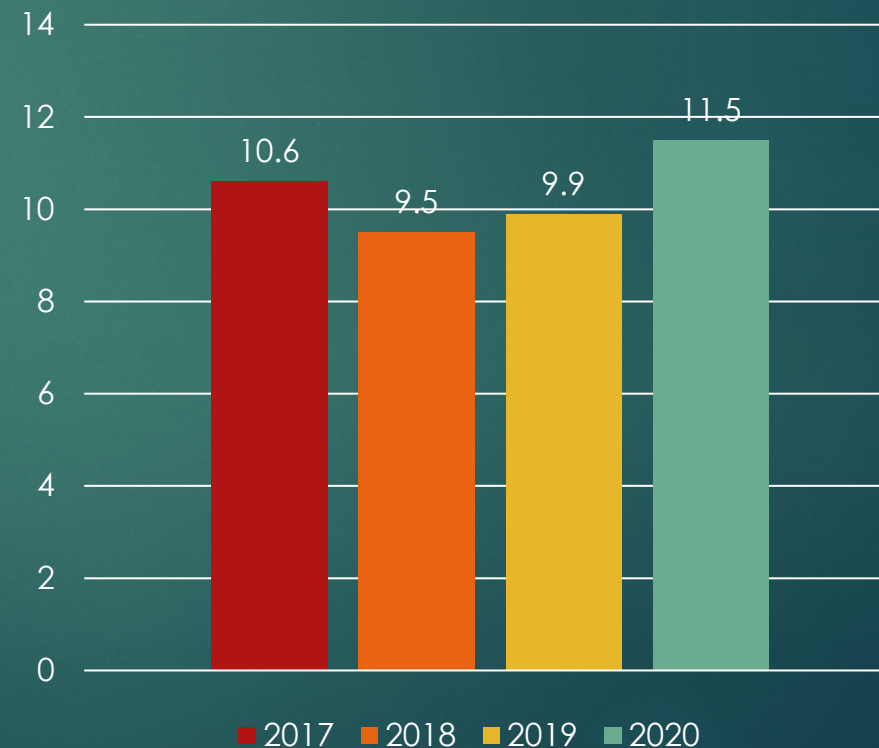
■ 2017 ■ 2018 ■ 2019 ■ 2020

Use of Tobacco and Alcohol: Pregnant Women 15-44 yrs, 2020 NSDUH

Past month use of Tobacco



Past month use of Alcohol



Why do we need to be concerned about cannabis use during pregnancy and breastfeeding?

Because of the Endocannabinoid system!(ECS)

And because THC and CBD cross placenta!



The ECS During Fetal Period

- ▶ ECS very important in early *placental* development and growth and implantation of embryo.
- ▶ ECS also detected as early as 5 weeks of gestation in *fetal brain*
- ▶ CB1 receptors are expressed in different areas of brain compared with adult brain
 - ▶ Locations change throughout pregnancy
 - ▶ Concentrated in mesocorticolimbic system
 - ▶ Key roles in motivation, emotional regulation, reward, and cognition
- ▶ Anandamide and 2-AG are synthesized on demand, bind to CB1 Receptors in presynaptic terminals
 - ▶ Play critical role in regulating neurotransmitter release
 - ▶ GABA, Glutamate, and Dopamine

Role of ECS Prenatally

- ▶ Critical for early fetal neurodevelopment
 - ▶ Mechanisms still being elucidated
 - ▶ Neuronal proliferation and migration, synaptogenesis
 - ▶ Role in microtubule function → axonal growth
 - ▶ Involved in *orderly* fetal development of key neural systems
 - ▶ Mesocorticolimbic system and projections to prefrontal cortex
 - ▶ Decision-making, higher order thinking
 - ▶ Later in life, CB receptors more widely distributed throughout the brain
- ▶ ECS is also critically important on maternal side for placenta development and implantation

How does THC effect the fetal ECS?

- ▶ **THC from cannabis crosses placental readily – 10% maternal level**
 - ▶ Binds to CB1 receptors in fetal brain – *Direct Effect*
 - ▶ Can “highjack” or disrupt this highly sequenced pattern of normal neuronal development
 - ▶ Concern for development in areas of brain where CB receptors mainly located
 - ▶ May explain underlying mechanism for neurodevelopmental deficits seen after prenatal exposure
 - ▶ *Indirect effects* through epigenetic changes in how genes are expressed
 - ▶ Enhanced responsiveness of systems regulated by dopamine
 - ▶ May explain increased vulnerability to substance use disorders later in life



Effects of THC on Maternal Outcomes and Early Brain Development

CONSEQUENCES OF POSTNATAL PERIOD, CHILDHOOD, AND
ADOLESCENCE

Maternal Effects of THC

- ▶ Physiological effects on placenta
 - ▶ Increase CO when smoked (5 times more than tobacco)
 - ▶ Vasoconstriction of placental vein
 - ▶ Increased resistance of uterine artery
 - ▶ Affects placental circulation, development and implantation
 - ▶ THC crosses placenta- causes vasoconstriction –
 - ▶ Subcellular stress (pre-clinical and clinical data)
- ▶ Maternal effects: meta-analysis*
 - ▶ No evidence to support adverse maternal effects:
 - ▶ No increased risk of placental abruption, pre-eclampsia, maternal death, stillbirth

*Gunn JK. 2016. BMJ Open. 2016;6(4): e009986



Early Neonatal Effects

▶ Early Neonatal Outcomes

- ▶ Lower birth weight – small amount ~200 gms.
 - ▶ Secondary to effects on placental circulation
- ▶ Inconsistent data around:
 - ▶ preterm births,
 - ▶ NICU admissions,
 - ▶ early neonatal behaviors,
 - ▶ Increased tremors, high-pitched cry, reactivity,
 - ▶ No clear withdrawal syndrome
 - ▶ SGA
 - ▶ Anomalies.
- ▶ Norwegian study – 2021 – decreased weight and birth length

*Gunn JK. 2016. BMJ Open. 2016;6(4): e009986



Longitudinal Studies: Long-term Effects on Children

- ▶ Several studies provide most data
 - ▶ OPPS – Ottawa Prenatal Prospective Study: low-risk, white, middle-class, N=180*
 - ▶ Followed sample from 1978 (prenatal) through to age 22 years (Fried, et al)
 - ▶ MHPCD – Maternal Health Practices and Child Development Study**
 - ▶ High-risk, low SES, more diverse; N=324
 - ▶ Followed from prenatal (1982) through age 16 years
 - ▶ Generation R – Netherlands – focused on early growth
 - ▶ Still following into older childhood

*Fried PA, Smith AM. Neurotoxicology Teratology. 2001b; 23:1-11.**Day NL, Goldschmidt L, Day R, Larkby C, Richardson GA. Psychol Med. 2015;45(8):1779-87.

Longitudinal cohort studies: Prenatal exposure

- ▶ Measured effect of prenatal use of alcohol, tobacco, other drugs (including cannabis) on birth outcomes and later cognitive, developmental, social, and substance use behaviors
- ▶ Problematic studies!
 - ▶ Were not able to measure use other than by self-report
 - ▶ Quantity and potency of cannabis not known
 - ▶ Controlled for use of tobacco and alcohol, other drugs statistically
 - ▶ Not able to control for environmental effects on child development
- ▶ Results support reason for concern about prenatal exposure
 - ▶ Consistency of results across studies

Neurocognitive and Behavioural Effects



18 months	3–6 years	9–10 years	14–16 years	17–22 years
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Increased aggressive behaviour^c

Attention deficits (females)^c

Deficits in:

- Verbal and perceptual skills^{ab}
- Verbal reasoning^{ab}
- Visual reasoning^{ab}
- Verbal and quantitative reasoning^b
- Short-term memory^{ab}

Hyperactivity^{ab}

Attention deficits^{ab}

Impulsivity^{ab}

Impaired vigilance^b

Deficits in:

- Abstract and visual reasoning^{ab}
- Executive functioning^{ab}
- Reading^{ab}
- Spelling^{ab}

Hyperactivity^{ab}

Attention deficits^b

Impulsivity^b

Depressive and anxious symptoms^b

Deficits in:

- Visual-cognitive functioning^a
- Academic achievement^b
- Information processing speed^b
- Visual motor coordination^b

Delinquency^b

Deficits in:

- Executive functioning^a
- Response inhibition^a
- Visuospatial working memory^a

Smoking^{ab}

Substance use^{ab}

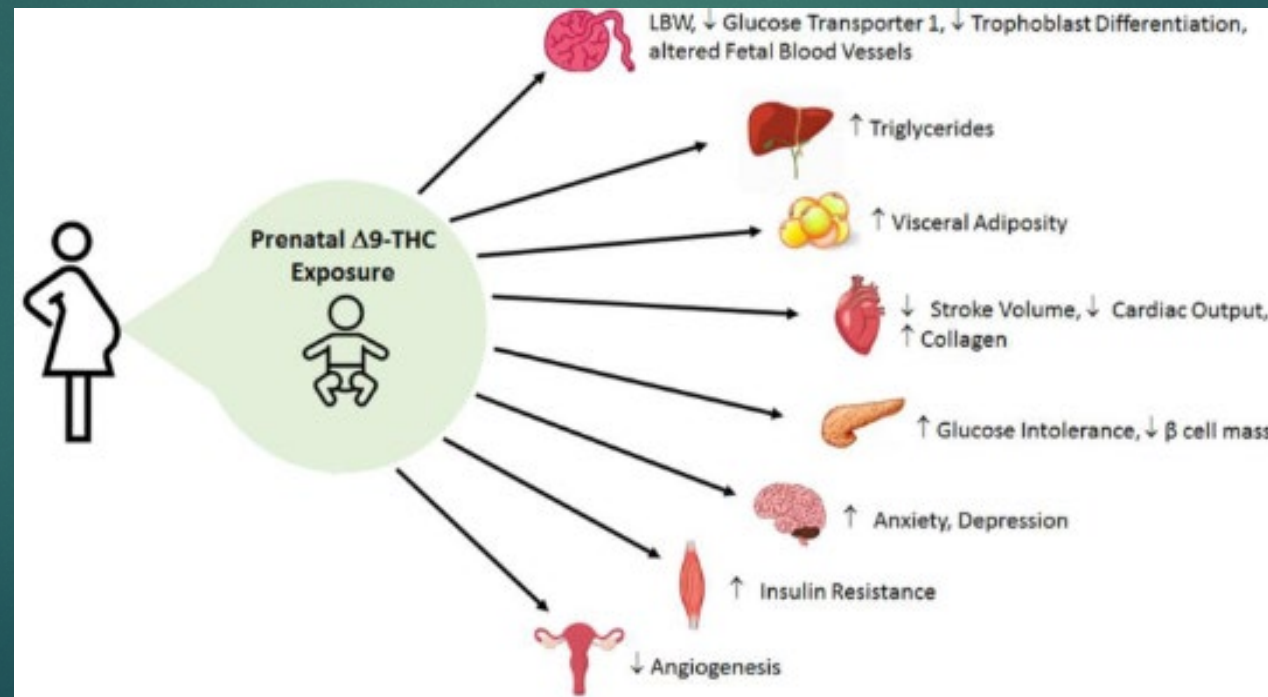
Early initiation of substance use^{ab}

^aOPPS ^bMHPCD ^cGeneration R



Postnatal Metabolic Outcomes of Gestational Exposure to THC

- ▶ Directly related to late effect of lower birth weight and “catch up” growth
- ▶ Dysmetabolism



How does CBD Affect Maternal/Fetal Physiology?

- ▶ Very limited safety data for use in food and as dietary supplement
- ▶ Preclinical Studies – mainly rats - Study by Henderson et.al.*
 - ▶ Maternal toxicity – at high doses, (300 mg-kg-bw/day) increased mortality, lower food consumption
 - ▶ Increased pup mortality and lower mean weight of offspring (especially females)
 - ▶ Delays in achieving developmental milestones, lower locomotor activity not seen in other studies
 - ▶ Hypertrophy/hyperplasia of liver and thyroid gland
 - ▶ No male reproductive toxicity was seen
 - ▶ Effect on placenta – impairs the protective role of placental barrier to toxins
- ▶ Depends upon dose and length of time being given.

*Henderson RG et al. Food and Chemical Toxicology.176 (2023)1113786.

Breastfeeding and Cannabis Use

Benefits of Breastfeeding

- ▶ Known benefits of breastfeeding
 - ▶ Decreased mortality in first 6 months of life
 - ▶ Reduced rates over childhood of:
 - ▶ Type 1 and 2 Diabetes, obesity, GI illnesses, childhood cancer, otitis media and respiratory illness
 - ▶ Benefits for breastfeeding mom:
 - ▶ Lower risk of breast cancer, ovarian cancer, hypertension, Type 2 DM
 - ▶ WHO recommends exclusive breastfeeding for first 6 months of life
 - ▶ AAP recommends
- ▶ It has been expected that mothers who used cannabis during pregnancy are likely to use while breastfeeding.
 - ▶ Those who used prior to pregnancy, but stopped, are more likely to begin use after birth

Cannabis and Breast Milk

- ▶ Data is limited, unlike what we know about alcohol and breast milk
 - ▶ Alcohol levels in breastmilk parallel blood alcohol concentrations in mom
 - ▶ Common practice of not breastfeeding for several hours after ingesting ETOH
 - ▶ Data supports impact on child development outcomes, lower weight, verbal IQ
- ▶ Paucity of data on effects of cannabis
 - ▶ We do know that THC and CBD cross into breast milk
 - ▶ We know less about levels in mother's plasma vs breast milk/infant plasma
 - ▶ We know even less about outcomes of cannabis use during breast feeding and infant development
 - ▶ Reliance on case reports!
 - ▶ **But – Cannabis can prolong the potential period of direct transfer of cannabinoids consumed by mom to developing infant when brain development continues**

What we do know.....

- ▶ Early studies....
- ▶ Cannabis (both THC and CBD) clearly crosses into breast milk – highly lipophilic
 - ▶ Case report* (1982): Paired samples of milk and maternal plasma
 - ▶ Milk sample 8 times higher than maternal plasma level
 - ▶ Fecal samples from the infant in this study had higher concentrations of metabolites of THC (11-OH-THC) than mother's breast milk
 - ▶ Case report** (2011): detectable levels of delta – 9- THC, 11-OH-THC in sample of human breast milk of mom using cannabis
- ▶ Conclusion that THC can accumulate in breast milk and infant can absorb and metabolize the THC after ingestion

*Peres-Reyes M, 1982; ** Marchei E et.al 2011

Cannabinoid Concentrations on Breast Milk: Bertrand et al (2018)

- ▶ Analyzed 54 samples of breast milk from cannabis using moms
 - ▶ Between 2014 and 2017 – research repository – Mommy's Milk
 - ▶ Analyzed concentrations of THC, cannabidiol, and cannabinal, as well as metabolite 11-OH-THC – LC/MS
 - ▶ 88% reported at least daily use
- ▶ Delta – 9 THC detectable in 63% of samples – up to 6 days after use
 - ▶ Also detected 11-OH-THC (9%); CBD – (9%); no cannabinal
 - ▶ Half life of THC on average 27 hours – longest up to 6 days
 - ▶ Increased uses each day and use by inhalation were associated with higher concentrations
 - ▶ *Estimated* that infant ingested dose 1000 times lower than adult plasma level
- ▶ Concern that nursing infant will accumulate cannabinoids because of slow elimination from body fat stores and daily exposure

Study Comparing Cannabinoids in Maternal Plasma vs. Breast Milk

- ▶ Assessed whether THC and CBD accumulate in breast milk*
- ▶ Twenty breast-feeding moms who used cannabis frequently and increased their use in post-partum period
 - ▶ Measured levels of THC and CBD in maternal plasma and breast milk simultaneously
 - ▶ Median levels of THC in plasma vs, breast milk – 3.7ng/ml vs. 27.5 ng/ml
 - ▶ Calculated ratio 7.0
 - ▶ Median levels of CBD in plasma vs. breast milk – 0.6 mg/ml vs.1.2 ng/ml
 - ▶ Calculated ratio 2.6
 - ▶ **Conclusion – Both THC and CBD accumulate in breast milk at levels higher than what is seen in plasma**
 - ▶ Also – the mothers reported increasing their cannabis use post-partum

* Moss, MJ et.al. 2021

Outcomes in Breastfed Infants Exposed to THC

- ▶ Paucity of data on outcomes of cannabis use, breast feeding and infant outcomes – Reliance on case reports!
 - ▶ Study by Astley and Little (1990)
 - ▶ Studied 55 12 month olds
 - ▶ Reported decreases in motor development in those exposed to breastmilk of cannabis-using mom vs. 81 infants without exposure
 - ▶ Only with daily or near daily consumption
 - ▶ Study by Tennes, however –
 - ▶ No difference mental or physical development in 27 one-year olds compared with 35 non-exposed infants
 - ▶ Intermittent use reported by cannabis-using moms.
 - ▶ Co-use with other substances complicates our understanding of its effect



Role of the Prevention Specialist

MEETING THE CHALLENGES WITH EFFECTIVE PREVENTION AND EARLY INTERVENTIONS

Why are we seeing increasing acceptance of cannabis use?

- ▶ If its legal it must be safe.....
- ▶ For teens –
 - ▶ Assumption that if it is OK for adults, it is OK for children and teens
 - ▶ There are no good public health messages that make cannabis “not cool” to use
- ▶ OB/GYN providers
 - ▶ Admitted not being familiar with risks of cannabis use during pregnancy
 - ▶ Perceived cannabis as less dangerous than other illicit drugs
 - ▶ Focused on risks of child protective services if testing positive at delivery
- ▶ **>65% of American public supports legalization of cannabis**
 - ▶ Population sees only financial benefit from taxation

Current Recommendations: ACOG

- ▶ Verbal screening of all women throughout entire pregnancy, and recommend abstinence from all substances
- ▶ Strong recommendation to abstain from cannabis use during breastfeeding – but not a contraindication

*ACOG Committee; Ob and GYN. 2017; 130(4):e205 – 209

Current Recommendations:

AAP*

- ▶ Screen women – considering pregnancy, or are pregnant, and counsel that safety of cannabis using pregnancy not known – *we have reason to be concerned.*
- ▶ Encourage to stop using MJ during breastfeeding but **not** a contraindication
- ▶ Be careful about screening – know the laws in your state so that you can counsel the woman about consequences on reporting

*Pediatrics. 2018;142(3):.e20181889.

Effect of cannabis Use on Early Parenting?

- ▶ Beyond modeling MT use by parents....
- ▶ Consider acute effects -→ Intoxication
- ▶ Consider reports linking early infant deaths from SIDS, co-sleeping, poor back-to-sleep practices with use of substances by parents and detectable levels of THC in mothers
- ▶ Needs much closer study before we draw any conclusions



Where can preventionists have the greatest effect?

- ▶ Multitude of areas where prevention and early intervention are lacking
 - ▶ Role of public health and health care professionals – education!
 - ▶ Focus on potential physical and psychological side effects
 - ▶ Ability to become addicted to cannabis – especially with young people starting use early in adolescence
 - ▶ Safety issues
 - ▶ At policy level – focus on lack of data showing effectiveness for many of the indications for which medicinal cannabis is recommended
 - ▶ Health care providers –
 - ▶ Importance of *screening* and expressing concerns about safety during pregnancy and breast-feeding
 - ▶ Lack of information by providers; Misinformation about safety through social media
 - ▶ Concerns for use by parents – beyond “modeling of use”
 - ▶ Early deaths, SIDS, lack of supervision with intoxicated parents
- ▶ Advocacy around the need for effective public health messages that provide balanced information about positive and negative effects
 - ▶ Biggest challenge is how to counteract effect of “big marijuana” companies with huge financial interests

Summary

- ▶ Increasing number of women are using cannabis and cannabis products in pregnancy and during lactation , because of view that it is safe.
- ▶ Data does not support that cannabis use has increased risks of adverse maternal outcomes
- ▶ Data do suggest that there is *reason for concern* regarding long-term neurodevelopmental and metabolic effects of prenatal exposure to offspring
- ▶ Much work that needs to be done by public health, medical field and preventionists to provide education, early intervention and much needed advocacy

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Thank you!

Questions?

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Thanks to Dr. Fernando Stein

Medicinal Effects of THC and CBD

THC

- ▶ Chronic pain
- ▶ Spasticity
- ▶ Chronic pain
- ▶ Appetite stimulant

▶ CBD

- ▶ Epilepsy – Epidiolex
- ▶ Lennox-Gastaut, Dravet's
- ▶ Anxiety
- ▶ Psychosis
- ▶ Parkinson's disease
- ▶ ?Alzheimer's (animal studies)
- ▶ Sleep aid – increase quality of sleep and onset to sleep
- ▶ ?role in cancer
- ▶ Cannabis dependence
- ▶ Neuroprotection in ischemic encephalopathy

WHAT TO WE KNOW ABOUT EFFECTIVENESS IN ADULTS?

- Strong Evidence
 - Chemo-induced nausea and vomiting – THC and CBD
 - Spasticity from MS - Oral cannabinoids and nabiximols; THC and THC/CBD combined
 - Chronic neuropathic pain – THC/CBD, inhaled MJ
- Moderate Evidence
 - Tourettes – THC; OSA, fibromyalgia, chronic pain – THC, THC/CBD
- Insufficient evidence
 - PTSD – nabilone in one study; no effect with cannabis
 - Parkinson's, schizophrenia, anxiety, cancer, addiction, IBS, glaucoma



*Source: National Academy of Sciences; 2017 – “The health effects of cannabis and cannabinoids”

HOW ABOUT CHILDREN AND TEENS?

- Evidence strongest for:
 - Chemotherapy-induced nausea and vomiting
 - Dronabinol, Nabilone and THC
 - Side effects of drowsiness and dizziness common
 - Seizure disorders: Dravet and Lennox-Gastaut syndromes
 - CBD formulations - Epidiolex
- Limited evidence:
 - spasticity from neurological conditions – Dronabinol
 - Neuropathic pain with major depression, (dronabinol) PTSD and sleep disorder (CBD), Tourette (THC)
- Insufficient/No evidence for:
 - Spasticity, neuropathic pain, PTSD, Tourette syndrome, Autism



SIDE EFFECTS OF THC AND CBD

- ▶ Need to balance potential benefits with known and unknown risks
- ▶ THC –
 - Drowsiness and dizziness, irritability, coordination, memory/learning
 - Side effects of recreational cannabis can inform potential effects of medicinal cannabis
- ▶ CBD
 - Somnolence, diarrhea, decreased appetite – 75%
 - ▶ Adults – dizziness, somnolence, dry mouth, muscle spasm, pain
 - Modulates hepatic cytochrome 450 enzymes → drug interactions
 - Long-term risks of CBD unknown
- ▶ Dronabinol – restlessness, drowsiness and dizziness
- ▶ Limited information overall.



CBD – Preclinical Studies

- ▶ CBD can attenuate the anti-cognitive effects of THC, and has direct precognitive effects
 - ▶ Supported by studies with high CBD MJ not showing memory impairments
 - ▶ Murine models show agonist activity at 5-HT receptors/glutamate result in changes suggestive of antidepressant activity
- ▶ Cytotoxic Effects
 - ▶ Can injure perinatal brain cells in concentrations measured in patients with epilepsy taking CBD as therapy.
 - ▶ Mechanisms as anti-epileptic still not fully elucidated.

Co-Exposure to Cannabis and Tobacco

- ▶ Effect on Newborn Neurobehavior over first post-natal month
- ▶ Compared non-exposed infants to those exposed to Tobacco and TB+MJ
- ▶ N = 111 mom-infant pairs; controlled for demographic confounders
- ▶ NICU Network Neurobehavioral Scale
 - ▶ Decreased ability to self-soothe (Self-regulation)
 - ▶ Decreased ability to attend to stimuli (Attention)
 - ▶ Increased need to examiner soothing (Handling)
 - ▶ Low Motor activity (Lethargy)
- ▶ Co-exposure was double the impact of tobacco exposure alone, even with low use of MJ
 - ▶ Greater for daughters than sons

*Stroud, LR. Neurotox and Terat. 2018; 70:28-39.