# Cannabinoids and Pregnancy: ASAM Physicians, Patients and the Public - A Vital Discourse/Debate

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### **Disclosure Information**

Cannabis Use and Pregnancy: What is a provider to do?

April 25, 2025, 3-4:15 PM

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\* No commercial interests or disclosures



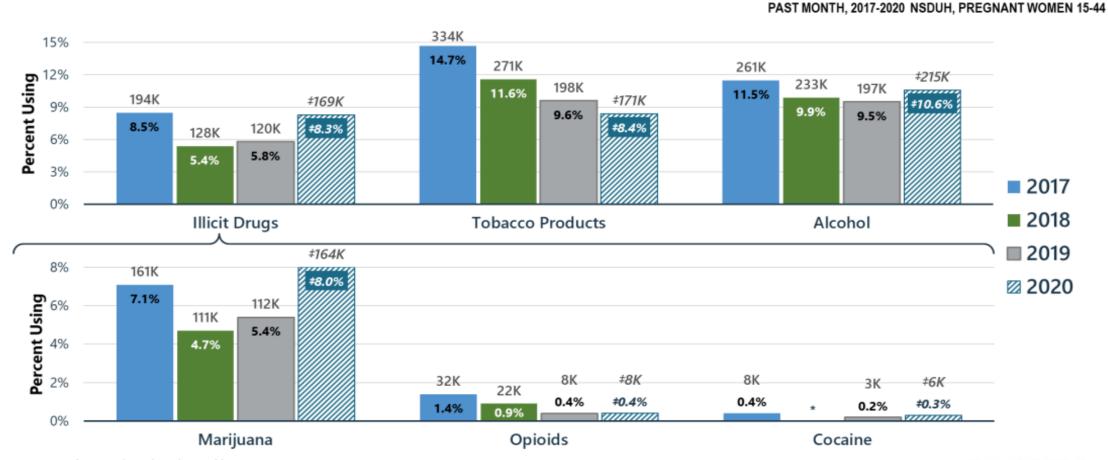


## **Learning Objectives**

- \*To discuss the trends of cannabis use in pregnant persons
- \*To understand the role of the ECS (endocannabinoid system) in placental and fetal brain development
- \*To define the consequences of cannabis use in pregnant persons and their infants



# Substance Use in Past Month: Among Pregnant Women Aged 15-44



<sup>\*</sup> Estimate not shown due to low precision.

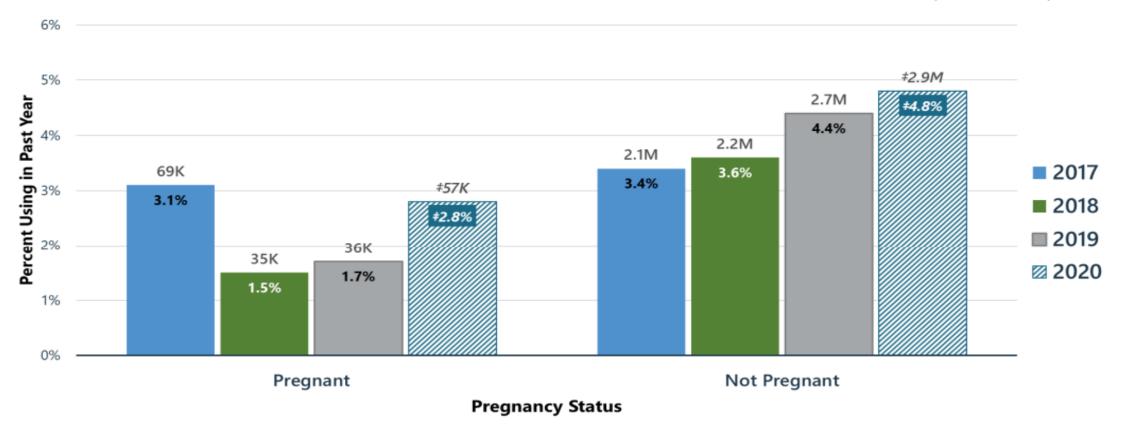


Tobacco products are defined as cigarettes, smokeless tobacco, cigars, and pipe tobacco.

<sup>\*</sup> Estimates on the 2020 bars are italicized to indicate caution should be used when comparing estimates between 2020 and prior years because of methodological changes for 2020. Due to these changes, significance testing between 2020 and prior years was not performed. See the 2020 National Survey on Drug Use and Health: Methodological Summary and Definitions for details.

# Daily or Almost Daily Marijuana Use in Past Year: Among Women Aged 15-44; By Pregnancy Status

PAST YEAR, 2017-2020 NSDUH, WOMEN 15-44

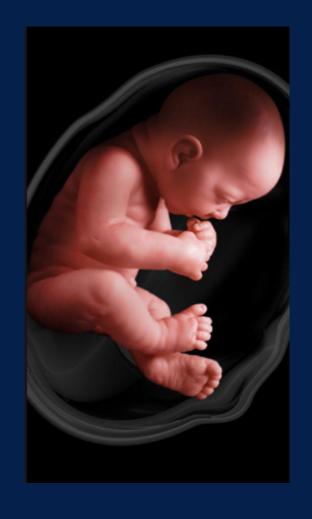


<sup>‡</sup> Estimates on the 2020 bars are italicized to indicate caution should be used when comparing estimates between 2020 and prior years because of methodological changes for 2020. Due to these changes, significance testing between 2020 and prior years was not performed. See the 2020 National Survey on Drug Use and Health: Methodological Summary and Definitions for details.



### Why are women using cannabis during pregnancy?

- Anecdotally recommended for morning sickness and widely accepted as a harmless drug
  - Increasing rates of use in both pregnancy and breastfeeding
  - \* 34-60% of users "used throughout" pregnancy
- \* Reasons
  - "negative symptoms of pregnancy"\*- anxiety, nausea and vomiting\*\* (48%), sleep disturbances and pain (60%)\*\*
  - Also recreation -39%
  - Users more likely to be 18-25 yo, lower SES, smoke cigarettes, report significant emotional distress\*\*\*





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

Because of the ECS and because THC crosses the placenta!





### **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 beyond placenta?
    - 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, stillbirths.





# The Endocannabinoid System: ECS

- # Humans produce 2 endogenous "endocannabinoids"
  - \* Anandamide and 2-AG (2-arachidonoylglycerol).
  - Biologically active molecules that serve many regulatory functions throughout the body
  - Two endocannabinoid receptors:
    - \* 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





# Role of ECS Prenatally

- Critical for early fetal neurodevelopment
  - Neuronal proliferation and migration, synaptogenesis
  - ➤ Role in microtubule function → axonal growth
  - > Involved in *orderly* fetal development of key neural systems
  - > Receptors throughout entire brain during fetal development
    - Focused in areas such as mesocorticolimbic system and projections to prefrontal cortex
      - > Areas involved in decision-making, higher order thinking
      - Also involved in serotonergic pathways



### **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 are most dense when exposed to THC.
    - May explain underlying mechanism for neurodevelopmental deficits seen after prenatal exposure



# **Early Neonatal Effects**

- Early Neonatal Outcomes
  - Newer data now supporting:
    - Lower birth weight SGA status
      - Secondary to effects on placental circulation?
    - Preterm births,
    - NICU admissions,
    - Inconsistent re: early neonatal behaviors,
      - Increased tremors, high-pitched cry, reactivity,
      - No clear withdrawal syndrome
  - No evidence for physical anomalies, increased perinatal deaths.





# Longitudinal Studies: Long-term Effects on Children

- Several studies provide most data
- > Earlier studies:
  - OPPS Ottawa Prenatal Prospective Study: low-risk, white, middle-class, N=180\*
    - > Followed sample from 1978 (prenatal) through to age 22 years
    - ➤ MHPCD Maternal Health Practices and Child Development Study\*\*
      - ➤ High-risk, low SES, more diverse; N=324
      - > Followed from prenatal (1982) through age 16 years
- ➤ Newer study- ABCD Adolescent Brain and Cognitive Development Study
  - Data showing effects of prenatal exposure on early learning/behavioral deficits and psychiatric disorders in early teens.\*\*\*
- > Remember! Studies done when THC % low 4% now >20+%



#### **Neurocognitive and Behavioural Effects**



18 months

Increased aggressive behaviour<sup>o</sup>

Attention deficits (females)º



3-6 years

#### Deficits in:

- Verbal and perceptual skills<sup>ab</sup>
- Verbal reasoning
- Visual reasoning<sup>ab</sup>
- Verbal and quantitative reasoning<sup>b</sup>
- Short-term memoryab

Hyperactivity<sup>ab</sup> Attention deficits<sup>ab</sup> Impulsivity<sup>ab</sup> Impaired vigilanceb



9-10 years

#### Deficits in:

- Abstract and visual reasoning
- Executive functioning<sup>ab</sup>
- Reading
- Spelling

Hyperactivity<sup>ab</sup>

Attention deficits<sup>b</sup>

Impulsivity<sup>b</sup>

Depressive and anxious symptoms<sup>b</sup>

#### Deficits in:

Visual-cognitive functioning<sup>a</sup>

14-16 years

- Academic achievement<sup>b</sup>
- Information processing speed<sup>b</sup>
- Visual motor coordination<sup>b</sup>

Delinquency<sup>b</sup>



17-22 years

#### Deficits in:

- Executive functioning<sup>a</sup>
- Response inhibition<sup>a</sup>
- Visuospatial working memory<sup>a</sup>

Smoking<sup>ab</sup>

Substance use<sup>ab</sup>

Early initiation of substance use<sup>ab</sup>

Generation R

From: Canadian Centre on Substance Abuse: Clearing the Smoke on Cannabis



# **ABCD Study**

#### Research Letter



September 12, 2022

### Association of Mental Health Burden With Prenatal Cannabis Exposure From Childhood to Early Adolescence

Longitudinal Findings From the Adolescent Brain Cognitive Development (ABCD) Study

David A. A. Baranger, PhD<sup>1</sup>; Sarah E. Paul, MA<sup>1</sup>; Sarah M. C. Colbert, BA<sup>2</sup>; et al

> Author Affiliations | Article Information

JAMA Pediatr. 2022;176(12):1261-1265. doi:10.1001/jamapediatrics.2022.3191



### **Potential Bias in Studies**

- Measured effect of prenatal use of all substances used on birth outcomes and later cognitive, developmental, social, and substance use behaviors
  - Had to control statistically the independent effects of cannabis on outcomes
- Difficult to disentangle effects of cannabis from other substances also used during pregnancy
  - Concern that sociodemographic and environmental factors are confounding maternal and child outcomes seen in those using cannabis vs. controls
  - Higher rates of cannabis use among racial/ethnic minorities and lower SES
    - This may account for outcomes seen, not cannabis use
  - May have effect of limiting screening only to "at-risk" populations rather than using universal screening
- Results support reason for concern about prenatal exposure
  - Consistency of results across studies
  - Mandates more carefully done research studies!
  - Even more concern now with higher % of THC in available products!

### **Current Recommendations: ACOG**

- In 2017, the American College of Obstetricians and Gynecologists (ACOG) Committee Opinion on Opioid Use and Opioid Use Disorder in Pregnancy included the following recommendations and conclusions:
  - Early universal screening, brief intervention, and referral for treatment (SBIRT) of pregnant women with opioid use or opioid use disorder improve maternal and infant outcomes.
  - Screening for substance use should be part of comprehensive obstetric care and should be done at the first prenatal visit in partnership with the pregnant woman.
  - Routine screening should rely on validated screening tools.
  - \* Abstinence recommended for all substances.

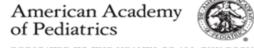
ACOG Committee; Ob and GYN. 2017; 130(4):e205 – 209



### **Current Recommendations: AAP**

- Screen women considering pregnancy, or pregnant, and counsel that safety of marijuana using pregnancy not known – we have reason to be concerned.
- Encourage to stop using MJ during breast-feeding 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

 ${\color{blue} \textbf{CLINICAL REPORT}} \quad \textbf{Guidance for the Clinician in Rendering Pediatric Care}$ 



DEDICATED TO THE HEALTH OF ALL CHILDREN

Marijuana Use During Pregnancy and Breastfeeding: Implications for Neonatal and Childhood Outcomes

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# Final Takeaways/Summary

- Increasing number of women are using marijuana and cannabis products in pregnancy and during lactation, because of view that it is safe.
- Data does *not* support that marijuana use increases risks of adverse maternal outcomes
- Data does support "reason for concern" regarding long-term neurodevelopmental effects of prenatal exposure to offspring
- Ethical issues need to be considered when screening women for prenatal substance use
- Education of patients on part of heath care provider is paramount.



### References

- 1. Baranger DA, Paul SE, Colbert SM, Karcher NK, et.al. Association of mental health burden with prenatal cannabis exposure from childhood to early adolescence: Longitudinal findings from the Adolescent Brain and Child Development (ABCD) Study. JAMA Pediatr. 2022; 176(12):1261-1265.
- 2. Chang JC, Tarr JA, Holland CL, DeGenna NM, Richardson GA, Rodriguez KL, et. al. Beliefs and attitudes regarding prenatal marijuana use: Perspectives of pregnant women who report use. *Drug Alcohol Depend*. 2019; 196:14-20.
- 3. ElMarroun H, Tiemeier H, Steegers EA, et.al. Intrauterine cannabis exposure affects fetal growth trajectories: the Generation R Study. J Am Child Adolesc Psychiatry. 2008; 48(12):117301181.
- 4. Gunn JK. Rosales CB, Center KE, et.al. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. BMJ Open. 2016;6(4): e009986
- 5. Hayer S, Mendelbaum AD, Watch L, Ryan KS, Hedges MA, et.al. Cannabis and Pregnancy: A review. *Obstet Gynecol Surv*. 2023; 78(7):411-428.



### References – Cont.

- 1. Tortoriello G, Morris CV, Alpar A, et.al. Miswiring the brain: delta-9-tetrahydrocannabinol disrupts cortical development by inducing an SCG10/stathmin-2 degradation pathway. *EMBO J.* 2014; 33(7): 668-685.
- 2. Wu TC, Tashkin DP, Djahed B, Rose JE. Pulmonary hazards of smoking marijuana as compared with tobacco. N Eng J Med. 1988; 318(6): 347-351.
- 3. Westfall RE, Janssen PA, Lucas P, Capler R. Survey of medicinal cannabis use among childbearing women: patterns of its use in pregnancy and retroactive self-assessment of its efficacy against "morning sickness". *Complement Ther Clin Pract*. 2006; 12(1) 27-33.
- 4. Young-Wolff KC, Sarovar V, Tucker LY, Avalos LA, Alexeeff S, Conway A, et.al. Trends in marijuana use among pregnant women with and without nausea and vomiting in pregnancy, 2009-2016. *Drug Alcohol Depend*. 2019; 196:66-70.



