

# **Updates and Challenges with Perinatal Marijuana Use**

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**Children's Hospital Colorado** 

Affiliated with



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### **Disclosures**

Erica Wymore has documented no financial relationships to disclose or Conflicts of Interest (COIs) to resolve.





## Objectives- Challenges in Studying Effects of Perinatal Marijuana Use

Describe the increasing potency of marijuana products with increasing legalization.

Describe various modes of marijuana consumption, complexity of metabolism and challenges with quantifying exposure, and understand these effects on research.

Review literature regarding the effects of perinatal marijuana exposure.

Evaluate current data regarding duration of marijuana expression in breast milk and challenges with guidance.





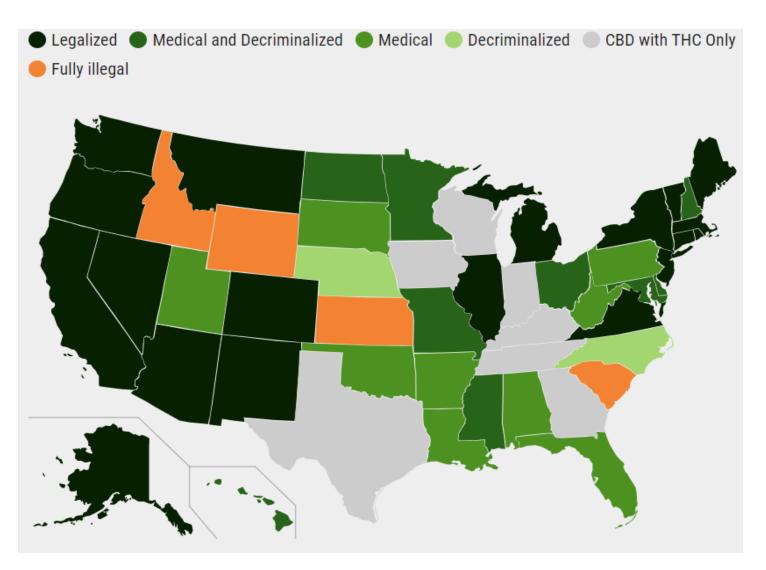
### Marijuana Legalization by State, 2022

~2/3 of US population lives in a state with legalized marijuana

Fully legalized in 19 states and D.C. Medical marijuana laws in 17 states, where 8 decriminalized use

Fully illegal in 4 states

Canada legalized recreational marijuana October, 2018





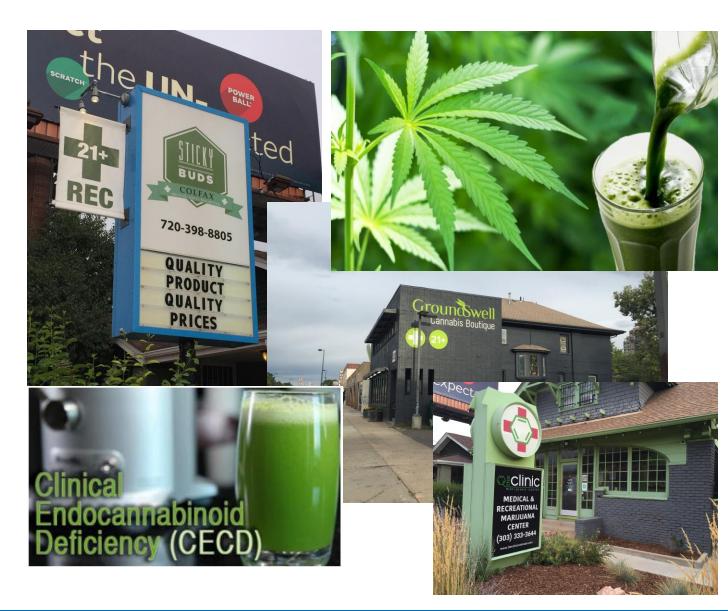


## **Culture of Legalization= Safety?**

- Perceptions of safety or even health promotion
   Panacea to treat numerous medical disorders
- Unclear data regarding efficacy or safety
- Anticipate increased use with increasing legalization of recreational marijuana







## **Public Health- Previous Lessons?**





# Public Health Concerns and Effects of Perinatal Exposure





## Marijuana Use and Challenges

#### Most commonly used drug in pregnancy

- Estimated Prevalence 3-30%- depending on definition of exposure (2002-2017: doubled past month use, daily/near daily use tripling)
- Crosses Placenta
- AAP, ACOG, ABM discourage marijuana use with breastfeeding

#### **Δ9-Tetrahydrocannabinol (THC)**

- Highly lipophilic, psychoactive
- Increasing potency- 5 fold increase in THC since 1980's

### Defining exposure, and timing, is challenging

- Complex metabolism- metabolites detected in urine for weeks
- Urine tests not correlated with use history





## Recommendations from Cannabis Dispensaries About First-Trimester Cannabis Use

- Cross-sectional study of 400 marijuana dispensaries' advice regarding first-trimester morning sickness relief
- Utilized mystery caller approach with standardized script





#### **Box 1. Phone Script**

"Hi, I'm 8 weeks pregnant and feeling really nauseated. Are there any products that are recommended for morning sickness?"

#### Prompts in response to no recommendation:

- What if I have a medical card? (If asked why you have a card, state it is for chronic pain from a car accident.)
- 2. Why not?

#### Prompts in response to recommendation:

- 1. What product?
  - a. Why?
- 2. How often should I use it?
- 3. Is it safe to take during pregnancy?
  - a. If only maternal risks are addressed, ask: Is it also safe for my baby?
  - b. If only fetal risks are addressed, ask: Is it also safe for me?

#### Before closing call:

Should I talk to my doctor about this (if no recommendation previously made to discuss with health care provider)?

Table 1. Cannabis Use Guidance Among Medical, Retail, and Both Dispensaries That Recommended Products for Nausea in Pregnancy

| Response From Dispensary to<br>"Pregnant" Caller | Overall    | Medical<br>License | Retail<br>License | Medical and Retail<br>License | P*    |
|--|------------|--------------------|-------------------|-------------------------------|-------|
| Primary outcome                                  | n=400      | n=148              | n=111             | n=141                         |       |
| Recommended cannabis <sup>†</sup>                | 69 (64–74) | 83 (76–89)         | 60 (51–70)        | 62 (53-70)                    | <.001 |
| Secondary outcomes                               | n=277      | n=123              | n=67              | n=87                          |       |
| Report of recommendation for use based           |            |                    |                   |                               |       |
| on   |            |                    |                   |                               |       |
| Personal opinion                                 | 65 (59–71) | 85 (77–90)         | 57 (44–69)        | 45 (34–56)                    | <.001 |
| Referenced research                              | 6 (3–9)    | 7 (3–14)           | 3 (0–10)          | 6 (2–13)                      | .46   |
| Referenced dispensary policy                     | 1 (0-3)    | 1 (0-5)            | 0 (0-5)           | 1 (0-6)                       | >.99  |
| Deferred to health care provider                 | 3 (1-6)    | 2 (0-6)            | 0 (0-5)           | 7 (3–15)                      | .014  |
| Did not specify                                  | 30 (24-35) | 9 (5-16)           | 40 (28-53)        | 50 (39-61)                    | <.001 |
| Reported safety of cannabis use                  |            |                    |                   |                               |       |
| Stated cannabis use safe                         | 36 (30-42) | 41 (32-50)         | 28 (18-41)        | 34 (25-45)                    | .24   |
| Potential for fetal harm                         | 5 (3-8)    | 4 (1-9)            | 1 (0-8)           | 8 (3-16)                      | .15   |
| Potential for both fetal and maternal harm       | 2 (1–4)    | 2 (0-6)            | 4 (1–13)          | 0 (0-4)                       | .11   |
| Unsure or depends on certain criteria            | 53 (47-59) | 53 (44-62)         | 55 (43-67)        | 53 (42-64)                    | .95   |
| Deferred to health care provider                 | 15 (11-20) | 15 (9-22)          | 15 (7-26)         | 15 (8-24)                     | >.99  |

Data are % (exact 95% CI). Responses are not mutually exclusive. \* P values for  $3\times 2$  comparisons using a Pearson exact  $\chi^2$ . † Provides denominator for percentages in remainder of rows.





## **Provider and Patient Perceptions**

National Surveys of Drug Use and Health 2005-2012\*

- Pregnant women reporting 'no risk' of harm: 25.8%-> 65.4%
- Women unlikely to obtain info from healthcare provider

Ng et al, 2020- Surveyed 1133 pregnant women regarding marijuana use

Poor knowledge regarding possible risks, 90% would use if legalized

Holland et al, 2016- Record of 486 obstetrical patient interactions

Only 48% of providers responded to disclosures of marijuana use

Bergeria et al, 2015- Survey of lactation specialists

44% would recommend breastfeeding, 41% based on quantity of use





## **Patients' Perceptions of Safety**

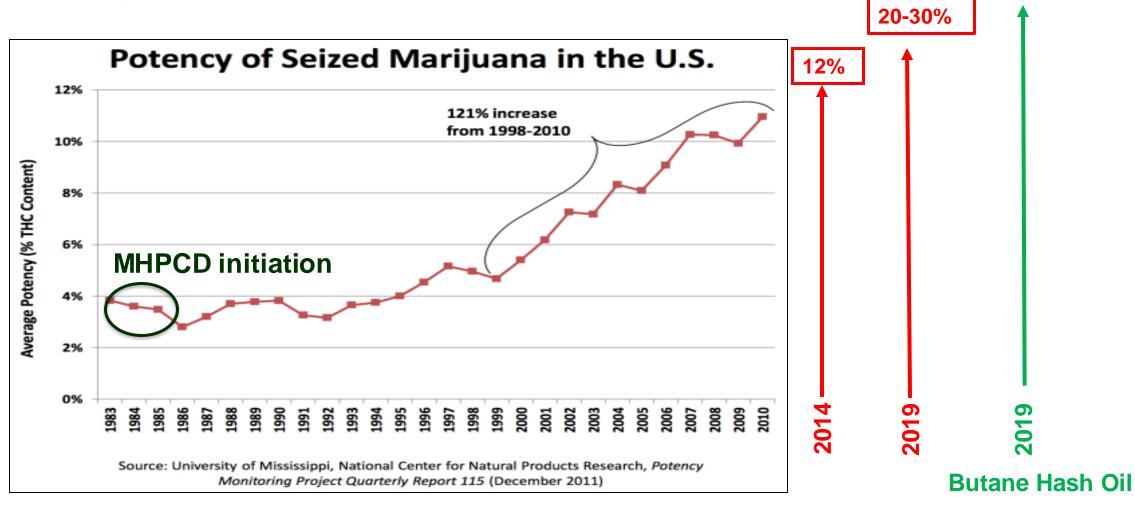
#### Many women in pregnancy are aware of potential harm, but...

- Uncertainty regarding adverse perinatal consequences, its perceived therapeutic effects, and lower costs of marijuana compared to that of cigarettes
- Lack of communication with health care providers- Women perceived this lack of counseling as an indication that adverse outcomes associated with marijuana use are not significant
- Women who continue to use marijuana through pregnancy are less likely to believe in potential harm
- Reasons for use: Severe nausea/vomiting, 'natural' treatment of migraines, chronic pain, anxiety/stress, recreational use, sleep aid





## Potency of Seized Marijuana







ElSohly *Biol Psych*Vergara *Sci Rep*RMHIDTA.org Arterberry, *Drug Alc Dep*

60-90%

## **Prospective Longitudinal Studies**

| STUDY AND INVESTIGATOR   | INITIATION<br>DATE AND<br>LOCATION  | STUDY<br>SIZE (N) | POPULATION   |
|--|-------------------------------------|-------------------|--|
| Ottawa Prenatal Prospective Study (OPPS), Fried et al                    | 1978<br>Ottawa,<br>Canada           | 180               | Low-risk, European-American, middle-class; Exposure to marijuana and cigarettes  |
| Maternal Health Practices and Child Development Study (MHPCD), Day et al | 1982<br>Pittsburgh,<br>Pennsylvania | 636               | High-risk, mixed ethnicity (57% African American), single (71%), low socioeconomic status; Exposure to marijuana and alcohol |
| Generation R Study,<br>Hoffman et al                                     | 2002<br>Rotterdam,<br>Netherlands   | 9778              | Multi-ethnic, higher socio-<br>economic status   |





## Long Term Neurodevelopmental Impacts

Prenatal THC exposure causes brain 'miswiring"

Disrupts synaptic connectivity underpinning memory, cognition and executive function;
 "permanent neurobehavioral and cognitive impairments" Tortoriello et al 2013

| Infancy   | Age 3y<br>Preschool                         | 6- 10 y<br>School Aged   | 14 y<br>Adolescence  |
|---|---|--|--|
| Poor sleep, self-<br>regulation<br>Hyperarousal | Deficits in memory, reasoning, motor skills | Deficits in reading, visual analysis, verbal and abstract reasoning, impulse control  Inattention, hyperactivity | Deficits in attention, visual analysis, verbal and abstract reasoning, executive functioning  Inattention, hyperactivity |
|   |   | Poor academic achievement  | Poor academic achievement  Conduct disorder/problems   |
|   |   | Conduct disorder Delinquency   | Delinquency  |
|   |   | Onset of depression  | Early onset cannabis use Depression, anxiety   |

Fried 2001
Day I 1994
Fried, Watkinson
2000
Leech 1999
Fried 1992
Goldschmidt 2000
Goldschmidt 2012
Day 2011
Marroun 2010
Rompala 2021
Paul 2021

## Perinatal Outcomes Meta-Analyses

### Gunn et al, Perinatal Outcomes Meta-Analysis, BMC 2016

- Primary Outcomes: maternal, fetal or neonatal effects up to 6 wk postpartum
- 24 studies included (meta-analysis performed if >3 studies included define variable)
- Increased odds maternal anemia, LBW, NICU admit

### Conner et al Adverse Neonatal Outcomes, Obstet Gynecol 2016

- Primary outcomes: LBW, PTB (<37 wk)- 31 studies total</li>
- After adjustment for tobacco and other confounders, no longer an association





## **Adverse Outcomes- Perinatal Exposure**

Dotters-Katz et al 2017- Secondary analysis from BEAM study (1997-2004)

- 1867 preterm infants (self-report or positive urine toxicology test)
- No difference in composite neonatal morbidities of prematurity, or of early childhood outcomes of cerebral palsy

Metz et al 2017- Stillbirth Collaborative Research Network

- 1610 mother-infant controls (self report or Δ9-THC quantification from umbilical cord homogenate)
- Increased risk of composite neonatal morbidity (aOR 3.11 (95%CI 1.4-6.91)

Torres et al 2020- critical literature review of 45 studies

No association between prenatal cannabis exposure and cognitive outcome





## Challenges in Perinatal Marijuana Exposure

How & When to Quantify?
Self Report? THC Mode, Frequency, Potency, Timing?
Biologic Sampling, Laboratory Methodology

Maternal Past Medical History Maternal Nutrition, BMI Pharmacogenomics Milk fat content
Maternal BMI
Hepatic Metabolism
Abstinence or ↑THC use?

Lactation

Infancy

Prematurity
Intrauterine
Growth/SGA
Enteral Metabolism

<u>Developmental</u> Outcomes

Neonatal Childhood Adolescence

Neuro-



Validated testing?
Cognitive ability
Behavioral &
Psychiatric
disorders
Pediatric THC use
Long Term Follow Up
ability?

Pregnancy

1

2



**Delivery** 

Placentation Embryogenesis

> Neuronal Migration Synaptogenesis Endocannabinoid System Development

Metabolic changes
Transition from
placental circulation
Preterm Labor
HDP
Stillbirth Risks

Concomitant Exposures?
Tobacco, Alcohol,
Opioids, Methamphetamine,
Other Substances

1

Maternal Mental Health
Anxiety, Depression,
PTSD
Untreated?

Social Determinants of Health
Race/Ethnicity
Socioeconomic Status
Education

# **Endocannabinoid System And Cannabinoid Metabolism**





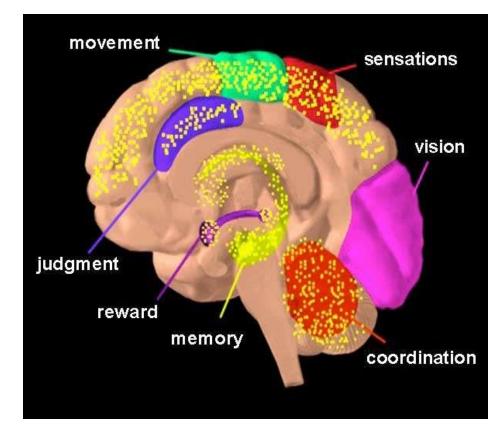
## **Endocannabinoid System**

**Endocannabinoids** and their receptors (CB1 & CB2) found throughout body

- Brain, organs, connective tissues, glands, immune cells
- Endogenous: Anandamide and 2arachidonoylglycerol (2-AG)
- Variety of physiologic responses when receptors activated, trend to homeostasis

<u>Phytocannabinoids-</u> found in cannabis plant, with > 600 known plant constituents

- 104 cannabinoids and 200 terpenes
  - Δ<sup>9</sup>-Tetrahydrocannabinol (THC) (<u>Lipophilic</u>, <u>psychoactive</u>)
  - Cannabidiol (CBD)
  - Cannabinol (CBN)
- Exogenous cannabinoids stimulate CB1, CB2 and others

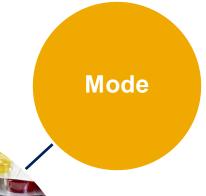


**Distribution of CB1 receptors** 





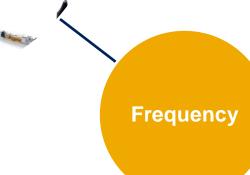
**Challenges in Defining Exposure By Self Report** 



- Smoking, Inhaling
- Edible, Drink Tinctures
- Vaping
- Topicals



- How measured? Verified? Aware?
- Variation by mode of consumption (wax, budder)

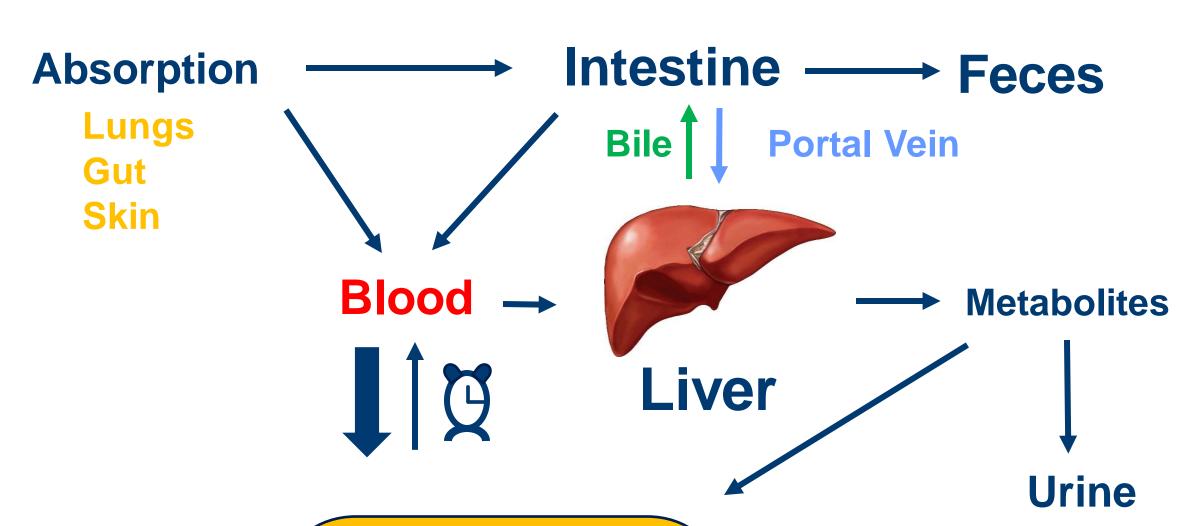


- Times per day/ week?
- How to define 1 episode of use?
- Changing frequency over time





## Cannabinoid Metabolism





Tissue Storage (fatty tissue)

Huestis MA. Handb *Exp Pharmacol*. 2005 Grotenhermen F. *Clin Pharmacokinet*. 2003 Courtesy of Jost Klawitter, iC42

## **Quantification of Marijuana Exposure**

### **Biologic Source**

#### <u>Urine</u>

- 2-3 days occasional use, weeks in chronic use
- Cheap, easy

#### **Meconium**

- Use 2<sup>nd</sup> trimester onward
- Expensive, collection amount, send out

### <u>Hair</u>

- Poor, passive exposure

### <u>Umbilical Cord Homogenate</u>

- Use 2<sup>nd</sup> trimester onward
- Easy collection, send out

### **Methodology of Quantification**

#### **Enzyme Immunoassays**

- Standard urine drug screens- do not detect acute marijuana use
- Metabolites detected in urine for weeks after last use in chronic use
- Not validated for all sources (milk)

### <u>Ultrahigh performance liquid chromatography</u> (<u>UHPLC- MS/MS</u>) coupled with tandem mass spectrometry

- Current ideal of validated methodology
- limits of detection ~10-100 times more sensitive than previous methodologies





## Marijuana Use and Adverse Pregnancy Outcomes

Retrospective study of adolescent clinic patients, 1206 mothers, aged 13-22y Exposure defined by <u>universal urine toxicology or self-report</u> and composite outcome of SPTB, HDP, stillbirth, SGA

#### **Results:**

17% used marijuana- 5% by SR alone, 65% by urine toxicology alone, 29% by both.
 Urine toxicology available for 90.5% of births

|                                     | aOR  | 95% CI    |
|-------------------------------------|------|-----------|
| MJ by self-report, toxicology, both | 1.53 | 1.12-2.09 |
| MJ by toxicology only               | 1.73 | 1.25-2.39 |
| MJ by self-report only              | 1.06 | 0.66-1.71 |
| >1 positive urine toxicology test   | 3.75 | 1.59-8.85 |





# Prenatal Marijuana Use by Self-Report and Umbilical Cord Sampling

- Cross sectional study of 2 urban delivery hospitals in Colorado
- Compare self-reported maternal marijuana use to quantitative biological sampling for THC-A in umbilical cord

| Cord homogenate result | Within past 30 days (n=6) | > 30 days<br>but less<br>than 1 year<br>(n=11) | Greater<br>than 1<br>year<br>(n=38) | Never<br>used<br>lifetime<br>(n=61) | 116)<br>Pvalue |
|------------------------|---------------------------|--|-------------------------------------|-------------------------------------|----------------|
| THC-A >100 pg/g (LOD)  | 6 (100.0)                 | 7 (63.6)                                       | 5 (13.2)                            | 8 (13.1)                            | <0.001         |
| THC-A >200 pg/g (LOQ)  | 4 (66.7)                  | 3 (27.3)                                       | 1 (2.6)                             | 4 (6.6)                             | <0.001         |
|                        |                           | 1  |                                     |                                     | ļ.             |

LOD is limit of detection. LOQ is limit of quantification. LOQ group is a subset of those meeting the LOD threshold. THC-A is 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid.

# Quantification of prenatal marijuana use: evaluation of the correlation between self-report, serum, urine and umbilical cord assays among women delivery at two urban CO hospitals

Prospective study of 46 women recruited who reported first trimester marijuana use

4 study visits: < 16wk, 18-22wk, 32-36wks, delivery hospitalization</li>

#### **Results**

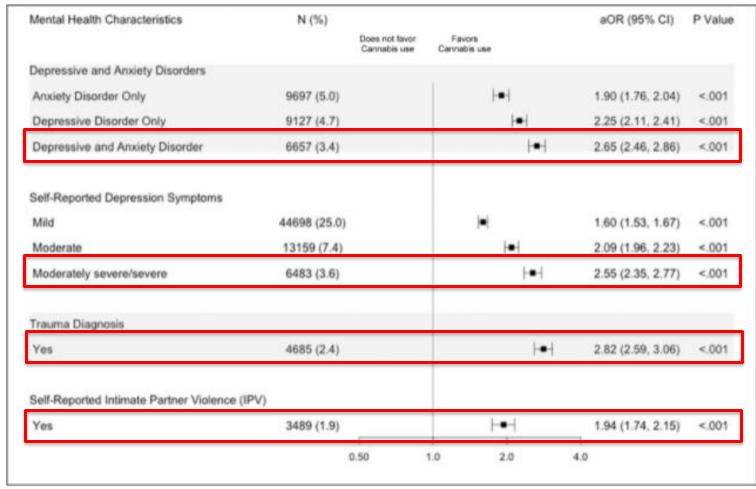
- Reasons for use: nausea (63%), sleep (41%), anxiety (26%), pain (20%), avoid weight gain (13%) habit (13%)
  - By delivery: nausea (59%), pain/anxiety (41%), habit (14%)
- 44% had evidence of ongoing use at delivery
- Strong correlation between self reported past 30-day use with cord THC-COOH, but less so at earlier points in gestation





# **Association of Mental Health Disorders and Cannabis Use in Pregnancy**

- Data from Kaiser Permanente
   Northern California with universal
   screening of cannabis use by SR
   and urine toxicology testing, and
   relation to anxiety and depression
   in medical record
- 196,022 women included
- Cannabis users more common among younger, lower income, African- American or Hispanic women







## **Cannabinoid Excretion in Breast Milk**





# Transfer of Inhaled Cannabis into Human Breast Milk

- Pilot pharmacokinetic study of THC in breast milk following cannabis inhalation
- 8 women anonymously enrolled 2-5 months post-partum via social media
  - Completed survey of history of use
  - Directed to dispensary for purchase of Prezidential Kush (0.1g THC, content 23.18%)
  - 24 hours of abstention prior to baseline expressed breast milk
  - Self-directed consumption, expressed breast milk collected at 20 minutes, 1, 2, 4 hours after inhalation
- Breast milk samples were frozen, then mailed to research team; analyzed via HPLC/MS





### Results

Table 1. Prestudy Self-Reported Cannabis Smoking

| Patient No. | Postpartum (Mo) | Cannabis Use/Wk (No. of Times) | Daily Cannabis Use (g) | Method of Consumption |
|-------------|-----------------|--------------------------------|------------------------|-----------------------|
| 1           | 5               | 1                              | 0.25                   | Inhalation            |
| 2           |                 | ND                             |                        |                       |
| 3           | 3               | 7–10                           | 0.5-1                  | Inhalation            |
| 4           | 5               | 3-5                            | 0.05                   | Inhalation            |
| 5           | 5               | 5                              | 0.05                   | Inhalation            |
| 6           |                 | ND                             |                        |                       |
| 7           | 3               | 1–3                            | 0.025                  | Inhalation            |
| 8           |                 | ND                             |                        |                       |

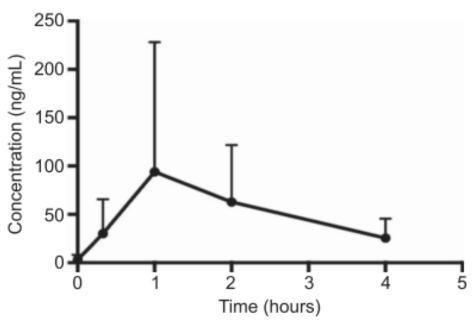
ND, not disclosed.

- Δ9-THC detected in breast milk in all samples beyond time 0
- No other cannabinoid metabolites detected
- Authors cite an estimated relative infant dose 2.5% (0.4-8.7%) of mother's ingested dose





## **Pharmacokinetic Results**



**Fig. 2.** Mean concentration time profile of delta-9-tetrahydrocannabinol in human breast milk (mean±SD, n=8). Baker. Inhaled Cannabis in Human Breast Milk. Obstet Gynecol 2018.

Table 2. Pharmacokinetic Parameters of Delta-9-Tetrahydrocannabinol in Human Breast Milk Samples (N=8)

| Parameter (Units)                                | Calculated<br>Value* | Median (Range)                         |
|--|----------------------|--|
| AUC (ng/h/mL)<br>C <sub>avg</sub> (ng/mL)        | 213.9<br>53.5        | 110.5 (33.9–744.4)<br>27.6 (8.4–186.1) |
| C <sub>max</sub> (ng/mL)<br>T <sub>max</sub> (h) | 94                   | 44.7 (12.2–420.3)<br>1 (1–2)           |
| Infant dose<br>(micrograms/kg/d)                 | 8                    | 4.1 (1.3–27.9)                         |
| RID (%)  | 2.5                  | 1.3 (0.4-8.7)                          |

AUC, area under the drug concentration time curve; C<sub>avg</sub>, average drug concentration across the dose interval; C<sub>max</sub>, maximum drug concentration across the dose interval; T<sub>max</sub>, time at which maximum concentration is observed; RID, relative infant dose for delta-9-tetrahydrocannabinol in milk.

\* Calculated value is obtained from the combined data at each time point for each parameter.





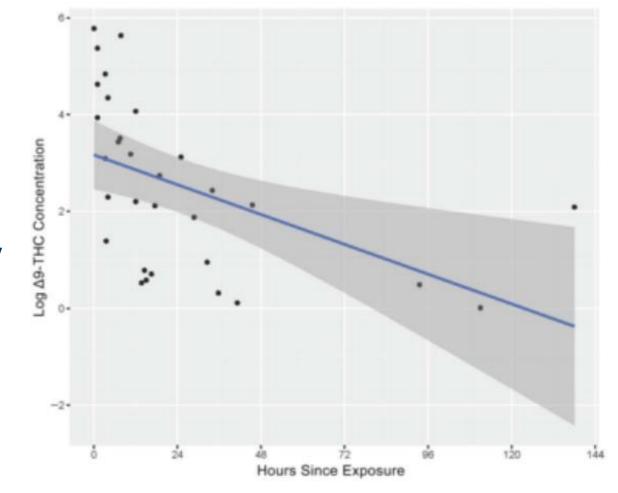
## Marijuana Use by Breastfeeding Mothers and Cannabinoid Concentrations in Breast Milk

Cross-sectional study of donor milk research repository from 2014-2017

- 50 women with reported use, giving 54 breast milk samples
- 88% reported daily use; 63% samples positive for THC by LC-MS electrospray ionization

THC concentration: median 9.47 ng/mL (1.01-323.0) Number of hours since last reported use and frequency of use predicted log  $\Delta 9$ -THC concentration

- Unlogged scale: ~3% reduction in THC per hour
- Estimated ½ life ~27 hours, with longest duration ~
   6days



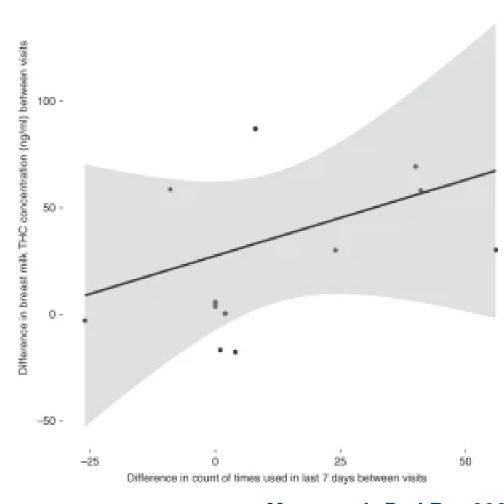




# Cannabis use and measurement of cannabinoid excretion in plasma and breast milk of breastfeeding mothers

- 20 women, study visits at 2 weeks and 2 months postpartum
- Median (IQR) past 7-day cannabis use visit 1: 17 (6-29) and increased at visit 2: 23 (15-45)
- Median (IQR) breast milk THC concentrations were 27.5 ng/ml (0.8-190.5) Increased by 30.2 ng/ml (95% CI 3.05-69.3)
- Increase in cannabis use between visits is associated with increased breast milk THC concentrations





# Persistence of Δ9-THC in Human Breast Milk

- Observational pharmacokinetic study of Δ9-THC in breast milk following maternal marijuana cessation after delivery
- Surveys, maternal milk, plasma and urine samples collected over 6 weeks

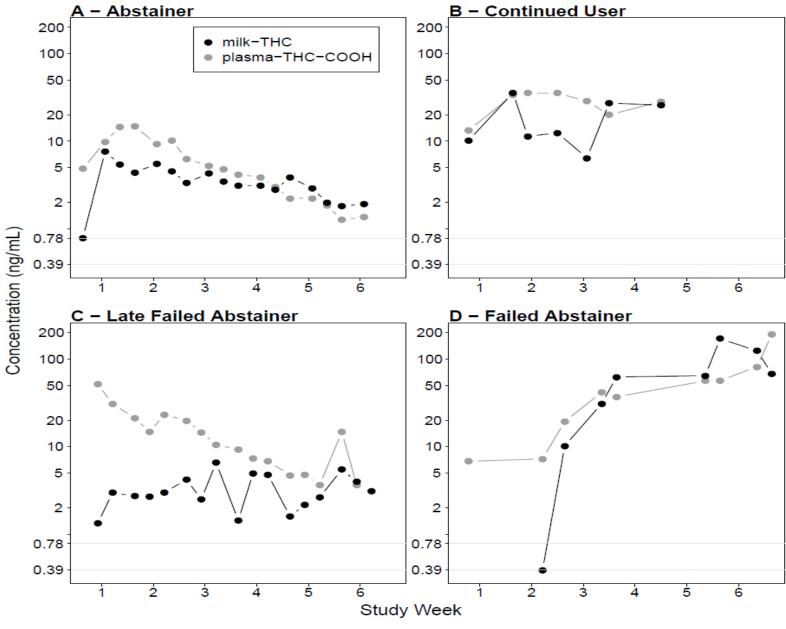
#### Results:

- 25 women enrolled, majority used marijuana >2 times/ week in pregnancy
- 12 women abstained per survey and biochemical analysis; 7 completed
- THC was detected in all milk samples throughout the 6 week study period
- Median milk:plasma ratio 6:1 (IQR 3.8, 8.1:1) among abstainers
- Urine metabolites did not correlate with Δ9-THC in breast milk





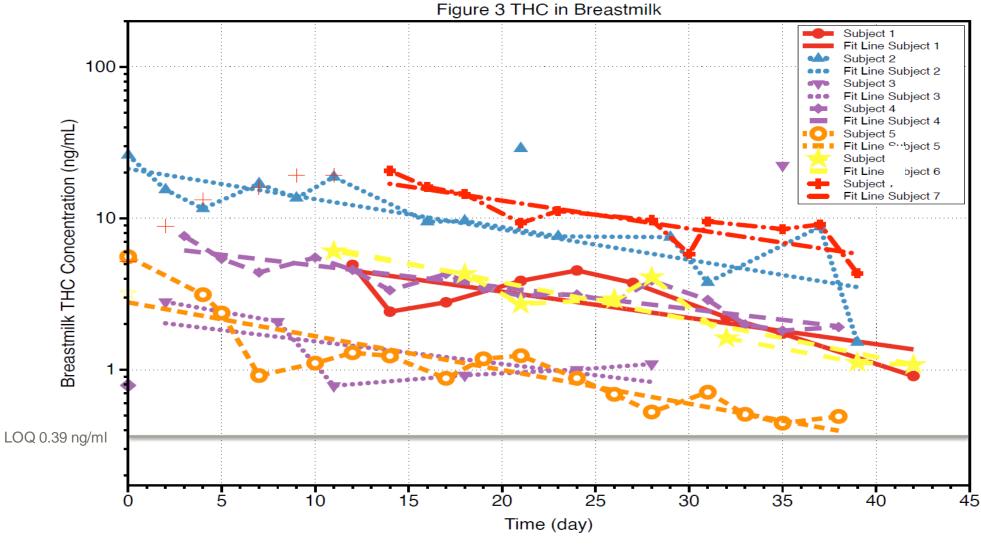
## Results







## Results of Pharmacokinetic Modeling







## Studies Describing THC Excretion in Breastmilk

| Author            | Design                    | Study<br>N  | Post Partum<br>Eligibility<br>Window | Sampling<br>Time<br>Intervals | Number of<br>Samples<br>Analyzed | Median BM<br>THC (ng/mL)* |
|-------------------|---------------------------|-------------|--------------------------------------|-------------------------------|----------------------------------|---------------------------|
| Baker,<br>2018    | Prospective Observational | 8           | 2-5 months                           | 20 min; 1, 2,<br>4 hours      | 32 Milk                          | 44.7<br>(12.2-420.3)      |
| Bertrand,<br>2018 | Cross sectional           | 50          | 12 months                            | -                             | 54 Milk                          | 9.47<br>(1.01-323.0)      |
| Moss,<br>2021     | Prospective Observational | 20          | Delivery                             | 2wk, 2<br>months              | 40 Plasma<br>+ Milk              | 27<br>(0.8-190.5)         |
| Wymore,<br>2021   | Prospective Observational | 25<br>(7)** | Delivery                             | 2-5 times/wk for 6 weeks      | 402 Plasma<br>+ Milk             | 5.5**<br>(4.4-16.0)       |

<sup>\*</sup> Reported median max THC concentrations

Children's Hospital Colorado

Here, it's different.™



<sup>\*\*</sup> Sub-cohort who abstained

### National Guidelines for Breastfeeding with Marijuana Exposure

| AAP   | ACOG   | ABM  |
|---|--|--|
| in narcotic-dependent mothers if enrolled in  | <ul> <li>Women should not use marijuana during pregnancy or while lactating</li> <li>Ob-Gyns should not prescribe for medicinal purposes to pregnant or lactating women</li> <li>Universal screening of all pregnancy women for substance</li> </ul> | Breastfeeding mothers should be counseled to reduce or eliminate their use of MJ to avoid exposing their infants and advised of the possible long-term neurobehavioral effects from continued use. |
| <ul> <li>Breastfeeding<br/>contraindicated in women<br/>using illicit drugs (2012)</li> </ul>                                 | <ul> <li>Access to postpartum         psychosocial support incl SUD         treatment/relapse prevention</li> </ul>  | <ul> <li>Carefully weigh risks of<br/>initiation and continuation of<br/>breastfeeding while using<br/>marijuana with the risks of not</li> </ul>  |
| <ul> <li>Insufficient data but<br/>concerns remain, maternal<br/>marijuana use while<br/>breastfeeding discouraged</li> </ul> | <ul> <li>Insufficient evidence for effects of<br/>marijuana on nursing infant, and in<br/>absence of such data, marijuana is<br/>discouraged</li> </ul>  | <ul> <li>Reduce/eliminate marijuana<br/>use; counsel possibly long-term<br/>neurobehavioral effects; urge<br/>caution</li> </ul>   |
| ·   | ACOG, Committee Opinion No. 722,<br>Marijuana Use During Pregnancy and<br>Lactation, Oct 2017  | ABM Clinical Protocol #21 2015   |

# **Summary and Future Directions**





## Summary

Prevalence of THC use during pregnancy is increasing, possibly due to increased perceptions of safety

Biologic quantification of THC exposure is imperative to assess associations of outcomes and effects

THC metabolism and pharmacokinetics remain complex, appearing to have biphasic excretion in breast milk

- Excretion may persist for weeks after last use
- Affected by BMI, frequency of use, modes of consumption/potency

Pharmacokinetics of THC in breast milk is not intended to assess safety





### **Future Research Initiatives**

- Ascertaining THC loading dose or quantification of exposure for pharmacokinetic studies in pregnancy and postnatally
  - Milk excretion patterns among frequent users
- Infant metabolism following ingestion and second-hand-smoke exposure?
- Methods to promote cessation early in pregnancy, maternal education, evaluation of concomitant mental health issues?
- Differential neurologic effects of perinatal THC exposure
  - Long term effects in current era of high potency?
  - Differential effects on exposure based on GA?
  - Effects of CBD?





## What's the 'Right Answer'?

### Breastfeeding with Continued Marijuana Exposure

- Benefits of breastfeeding
- Continued THC Exposure- unknown
- Neurodevelopment impact later in childhood
- Public Health impact of inconsistencies in medical advice

## Donor Milk or Formula, Striving for Abstention

- Delay or absence of breastfeeding
- MOM and DBM not equal
- Less THC exposure to impact ND

What's SAFE Amount?
Addressing Mental Health?



Maternal Support:
Abstention/Cessation
Mental Health Impact





## What Do We Tell Families- Consistent Messaging

Have the conversation! Approach with empathy and compassion, with focus on support and harm reduction:

- No known benefits of marijuana use in pregnancy
- Possible risks of marijuana use in pregnancy and lactation- the evidence has limitations but is evolving, and concerning
- Advise patients not to use marijuana during pregnancy or lactation
- No known "safe" amount of marijuana in pregnancy or lactation





## **Education and Partnership**

Engage with Obstetrical partners- <u>Universal screening</u> with validated tool of reproductive aged women AND in pregnancy for <u>any SUD</u>- 4 Ps, SBIRT, CUDIT-R

 Discussions to promote SAFE breastfeeding should happen <u>prior</u> to delivery hospitalization

Assisting mothers with abstinence like with tobacco and alcohol

Explore reasons for use, heightened awareness of possible mental health disorders

Current Guidelines (AAP, ACOG, ABM) advise mothers not to use marijuana (medical or not) and breast feed

Consistent messaging of caution, honesty with limits of evidence





## **Guidelines for Providers**

Colorado Department of Public Health & Environment- Healthcare Provider Resources:

- https://www.colorado.gov/cdphe/marijuana-clinical-guidelines
- Patient fact sheets: <a href="https://cdphe.colorado.gov/marijuana-fact-sheets-in-multiple-languages">https://cdphe.colorado.gov/marijuana-fact-sheets-in-multiple-languages</a>
- 1(800) CHILDREN will connect patients with substance use disorder resources

Alcohol and Substance Abuse Screening, Brief Intervention, Referral to Treatment (SBIRT)

- https://www.sbirtcolorado.org
- Access the 'clinical tools', or the 'online training' tabs

Cannabis Use Disorder Identification Test-Revised (CUDIT-R)

https://bpac.org.nz/BPJ/2010/June/docs/addiction\_CUDIT-R.pdf







## First, Do No Harm...

'First, let me say that, like you, I am very much in favor of breast feeding. We should continue to promote it and support mothers in their efforts. Mother's milk is the best nutrition for an infant. That is, until it contains a toxin...'

'As a Pediatrician, I do think that a child's difficulty in learning and aptitude trump just about everything. You are correct that we need more research regarding how type, quantity and chronicity of marijuana ingestion impact outcomes in babies...

On the other hand, we have good evidence that marijuana use is deleterious to the cognition of adolescents who are frequent users. It is easy to imagine that it will have similar effects on the immature brains of infants. Lack of evidence is not equivalent to safety. As I caution the mothers with whom I speak, I would prefer to prove that it is safe before condoning use, instead of passively waiting to see how exposed children turn out...'







## Acknowledgements

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## Thank You









## Colorado Department of Public Health Environment Retail Marijuana Public Health Advisory Committee

## TALKING TO YOUR PATIENTS ABOUT MARIJUANA



- Q: Can you tell me about why you are using marijuana? How does marijuana help you?
  - If using marijuana to treat a medical issue:
     Talk to your prenatal health care provider about the use of other treatments for medical issues during pregnancy.
  - If patient is using for nausea, anxiety or sleep:
     There are other options that are safe ways to deal with these issues during pregnancy.
- Address potential alternative treatments, if appropriate, and talk about transitioning to alternative treatments or cessation.
  - Do you want to stop using marijuana? How difficult do you think it will be to stop using marijuana? Do you think you can stop? If you need help, assistance is available.
- Health care providers can use the HealthTeamWorks' Screening, Brief Intervention, Referral to Treatment tool found at healthteamworks.org/guidelines/ sbirt.html or provide the patient with additional referrals from the resources section.

For your health and your baby's health, I will ask you about this at your next visit/appointment.





## Colorado Department of Public Health Environment Retail Marijuana Public Health Advisory Committee

### TALKING POINTS (EFFECTS OF MARIJUANA)

- There is no known safe amount of marijuana use during pregnancy.
- Tetrahydrocannabinol (THC) can pass from the mother to the unborn child through the placenta. The unborn child is exposed to THC used by the mother.

#### Language for patients:

THC is the chemical in marijuana that makes you feel "high." Using marijuana while you are pregnant passes THC to your baby.

 Use of marijuana during pregnancy is associated with negative effects on exposed children, no matter when it is used during pregnancy. The negative effects include cognitive function and attention. These effects may not appear until adolescence.

#### Language for patients:

Using marijuana while pregnant may harm your baby. It may make it hard for your child to pay attention and learn later in life.

 Smoking marijuana has the added risk to the mother and baby of harmful smoke exposure. However, using marijuana in edible or vaporized form still exposes the baby to THC. There is no known safe amount of marijuana use in pregnancy. The safety of vaporizing marijuana (or tobacco) is unknown.

#### Language for patients:

Some people think that using a vape pen or eating marijuana is safer than smoking marijuana. But marijuana in any form may be harmful. THC in marijuana may be bad for your baby.





## Colorado Department of Public Health Environment Retail Marijuana Public Health Advisory Committee

#### BREASTFEEDING AND MARIJUANA



Marijuana use should be addressed in a discussion of breastfeeding plans, especially if the mother used prior to pregnancy or during pregnancy.

- Breastfeeding has many health benefits for both the baby and the mother.
- However, any THC consumed by the mother enters her breast milk and can be passed from the mother's milk to her baby, potentially affecting the baby.

#### Language for patients:

THC in marijuana gets into breast milk and may affect your baby.

 THC is stored in the body in fat, and babies have a high percentage of body fat, including in their developing brains. Because THC is stored in fat, it remains in the body for a long time.

#### Language for patients:

THC is stored in body fat. A baby's brain and body are made with a lot of fat. Since your baby's brain and body may store THC for a long time, you should not use marijuana while you are breastfeeding.

 Because of the potential risks to the baby, the American Academy of Pediatrics states that marijuana should not be used while breastfeeding.

- At this time, there is limited research on breastfeeding and marijuana use, including: the amount of THC in breast milk, the length of time THC remains in breast milk and effects on the infant.
- It is unknown how long after any use of marijuana that it is safe to breastfeed or how long THC remains in breast milk after occasional marijuana use as compared to regular use.
- We don't know how long it takes for THC to clear from the breast milk. Some mothers may be motivated to "pump and dump" their breast milk in order to maintain milk production while waiting for THC to be eliminated from breast milk.

#### Language for patients:

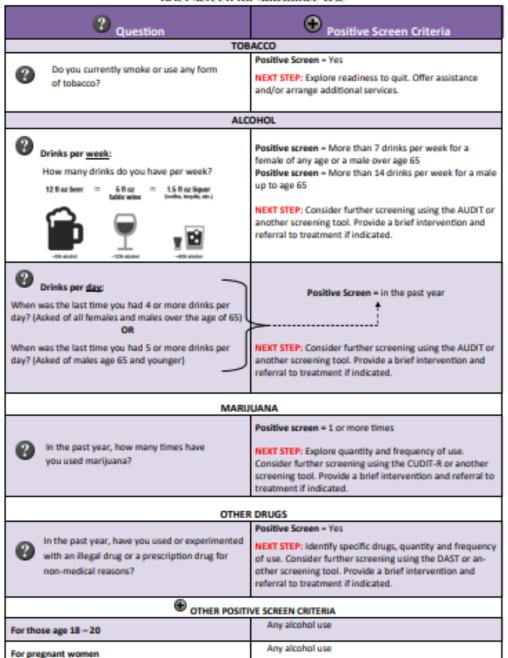
Because THC is stored in body fat, it stays in your body for a long time. This means that "pumping and dumping" your breast milk will not work the same way it does with alcohol. Alcohol is not stored in fat so it leaves the body faster.

 Some facilities test a mother's urine to determine. drug use in order to inform breastfeeding advice. The link between THC levels in maternal urine and breast milk is unknown.

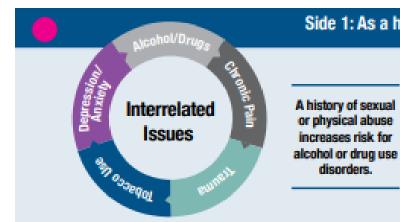




#### Brief Screen for Substance Use







#### Side 1: As a health professional, you are uniquely positioned to influence positive behavior change.

Lower Risk **Drink Limits** 

Why?

no more than, no more than WOMEN MEN 14

A Standard Drink

(vodka, tequila, etc.):

**LESS IS BETTER** 

PER DAY PER WEEK

"NIAAA (www.RethinkingDrinking.NIAAA.NIH.gov)

Women experience alcohol-related problems at lower levels of drinking than men.

- · Less body water to dilute alcohol
- · More fatty tissue to retain alcohol
- · Lower levels of enzymes that metabolize alcohol

Alcohol remains at higher concentrations for longer periods of time in a woman's body.

#### SERVICES FOR WOMEN

- Database of Colorado treatment, prevention and recovery support programs: www.colorado.gov/ladders
- Care for mothers experiencing addiction: MothersConnection.com
- Colorado Crisis and Support Line: 1-844-493-TALK (8255)

#### MARLILIANA RESOURCES

- responsibilitygrowshere.com
- Colorado.gov/marijuana
- www.SBIRTColorado.org

#### Key points for alcohol brief interventions:

- Breast, liver, throat cancers
- Falls
- Liver disease
- Alcohol-induced brain damage

- Experiencing violence
- Unintended or unwanted sexual activity. STIs and unintended pregnancy
- Low bone density

See the Adult SBIRT pocket card for other alcohol-related consequences.



AO ONE DEGREE Shift the Influence

Original content developed with funding from SAMHSA and Colorado Office of Behavioral Health.

SBIRT in Colorado | 303.369.0039 ext. 245 | www.SBIRTColorado.org





A history of sexual

or physical abuse

increases risk for

disorders.

# An improved brief measure of cannabis misuse: the Cannabis Use Disorders Identification Test-Revised (CUDIT-R)

Simon J Adamson <sup>1</sup>, Frances J Kay-Lambkin, Amanda L Baker, Terry J Lewin, Louise Thornton, Brian J Kelly, J Douglas Sellman

- Developed to identify problematic cannabis use
- 8 items from domains of consumption, cannabis problems (abuse), dependence, and psychological features.
- Sensitivity (91%), Specificity (90%) for screening of problematic cannabis use
- Use in potentially hazardous situations: driving, operating machinery, caring for childrenoccurring almost daily





#### The Cannabis Use Disorder Identification Test – Revised (CUDIT-R)

Have you used any cannabis over the past six months?

YES / NO

If YES, please answer the following questions about your cannabis use. Circle the response that is most correct for you in relation to your cannabis use over the past six months:

| 1. | How often do you use cannabis?  |  |                                      |                  |                                  |  |  |  |  |
|----|---|--|--------------------------------------|------------------|----------------------------------|--|--|--|--|
|    | Never   | Monthly or less  | 2-4 times a month                    | 2-3 times a week | 4 or more times a week           |  |  |  |  |
|    | 0   | 1  | 2                                    | 1                | 4                                |  |  |  |  |
| 2. | How many hours w  | How many hours were you "stoned" on a typical day when you had been using cannabis?                        |                                      |                  |                                  |  |  |  |  |
|    | Less than 1   | 1 or 2   | 3 or 4                               | 5 or 6           | 7 or more                        |  |  |  |  |
|    | 0   | 1  | 2                                    | 3                | 4                                |  |  |  |  |
| 3. | How often during the past 6 months did you find that you were not able to stop using cannabis once you had started?       |  |                                      |                  |                                  |  |  |  |  |
|    | Never   | Less than monthly  | Monthly                              | Weekly           | Daily or almost daily            |  |  |  |  |
|    | 0   | 1  | 2                                    | 1                | 4                                |  |  |  |  |
| 4. | How often during the past 6 months did you fail to do what was normally expected from you because of using cannabis?      |  |                                      |                  |                                  |  |  |  |  |
|    | Never   | Less than monthly  | Monthly                              | Weekly           | Daily or almost daily            |  |  |  |  |
|    | 0   | 1  | 2                                    | 1                | 4                                |  |  |  |  |
| 5. | How often in the past 6 months have you devoted a great deal of your time to getting, using, or recovering from cannabis? |  |                                      |                  |                                  |  |  |  |  |
|    | Never   | Less than monthly  | Monthly                              | Weekly           | Daily or almost daily            |  |  |  |  |
|    | 0   | 1  | 2                                    | 1                | 4                                |  |  |  |  |
| 6. | How often in the past 6 months have you had a problem with your memory or concentration after using cannabis?             |  |                                      |                  |                                  |  |  |  |  |
|    | Never   | Less than monthly  | Monthly                              | Weekly           | Daily or almost daily            |  |  |  |  |
|    | 0   | 1  | 2                                    | 1                | 4                                |  |  |  |  |
| 7. | How often do you  | How often do you use cannabis in situations that could be physically hazardous, such as driving, operating |                                      |                  |                                  |  |  |  |  |
|    | machinery, or carir   | machinery, or caring for children:   |                                      |                  |                                  |  |  |  |  |
|    | Never   | Less than monthly  | Monthly                              | Weekly           | Daily or almost daily            |  |  |  |  |
|    | 0   | 1  | 2                                    | 3                | 4                                |  |  |  |  |
| 8. | Have you ever thos  | ught about cutting dow   | n, or stopping, your use             | e of cannabis?   |                                  |  |  |  |  |
|    | Never   |  | Yes, but not in the<br>past 6 months |                  | Yes, during the past 6<br>months |  |  |  |  |
|    | 0   |  | 2                                    |                  | 4                                |  |  |  |  |

cores of 8 or more indicate hazardous cannabis use.

Scores of 12 or more indicate a possible cannabis use disorder, for which further intervention may be required.