PHARMACOTHERAPY: PERINATAL SUBSTANCE USE DISORDERS

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SUBSTANCE USE & WOMEN'S HEALTH

APPROACH TO TREATMENT OF PSUD

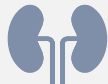
- Mother-Infant Dyad & Family Unit
- Kindness, Respect & Compassion
- Empower: Give voice and choice
- Patient-Centered Care and Shared Decision Making
- Social & Structural Determinants of Health for Women/Mothers
- Comorbid Trauma & Mental Health
- Integrated Prenatal Care and SUD Treatment
- Postpartum Contraception Plan [*Plan for all Individuals of Reproductive Age]

PHYSIOLOGICAL CHANGES IN PREGNANCY IMPACT PHARMACOKINETICS- WHAT THE BODY DOES TO THE DRUG

Absorption

Slower gastric emptying, bowel and colonic transit time

- Increase drug absorption; Increase drug levels



Distribution

Increased plasma volume each trimester (12.5%>32.5%>50%), protein binding, lower lean muscle/adipose ratio

- Increased volume of distribution; Decrease drug levels

Metabolism

Hepatic: Cytochrome P450 & UGT Increase

- Increase CYP450 and UDT; Decrease drug levels

Elimination

Renal: Increased renal blood flow increases GFR

- Increase Drug Elimination; Decrease drug levels

PERINATAL SUBSTANCE USE DISORDERS (SUDS)

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

PAST MONTH, 2017-2020 NSDUH, PREGNANT WOMEN 15-44

Percent Using

	2017	2018	2019	2020
Illicit Drugs	194K 8.5%	128K 5.4%	120K 5.8%	‡169K ‡8.3%
Tobacco Products	334K 14.7%	271K 11.6%	198K 9.6%	‡171K ‡8.4%
Alcohol	261K 11.5%	233K 9.9%	197K 9.5%	‡215K ‡10.6%
Marijuana	161K 7.1%	111K 4.7%	112K 5.4%	‡164K ‡8.0%
Opioids	32K 1.4%	22K 0.9%	8K 0.4%	‡8K ‡0.4%
Cocaine	8K 0.4%	*	3K 0.2%	‡6K ‡0.3%

* Estimate not shown due to low precision.

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

‡ 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.

PERINATAL SUDS

Pregnancy:

- Most common: tobacco, alcohol, cannabis
- 50% endorse polysubstance

Postpartum:

- High rate of return to substance use use (~80% within first few months postpartum) and mortality

Comorbidity:

High rate of substance use and mental health conditions

DELAYED PRENATAL & SUD CARE

- Typically present at approximately 20-24 weeks gestation
    - Delays in prenatal care
    - Delays in treatment
- Lack of knowledge of pregnancy
- Fears: separation from baby, DSS case, other legal consequences, judgement
- Other social determinants of care: transportation, childcare, insurance
- Lack of understanding of what treatment looks like

APPROACH TO TREATING PSUDS WITH MEDICATIONS

- Risks/Benefits of Medication Vs. Risk of Untreated Illness
- Shared Decision Making: Informed Treatment Choices
- Treatment Choices Prioritize Women's Health
- Continue Effective Treatments at Therapeutic Dose
- Starting Treatment: Use the one the worked the best in the past
- Minimize Polypharmacy
- Optimize therapy, supports and resources
- Postpartum Contraception Plan [*Plan for all Individuals of Reproductive Age]

COMMONLY USED SUBSTANCES IN PREGNANCY
TOBACCO

TREATMENT OF
TOBACCO USE DISORDER IN PREGNANCY

Behavioral Interventions

- Motivational Interviewing (Pregnancy & Postpartum)
- Contingency Management (Pregnancy)
  - Financial Incentives

Medications

- Nicotine Replacement Therapy
- Varenicline
- Bupropion

Vs.

Risks of Untreated Tobacco Use Disorder

- Maternal & Obstetric Health
- Newborn Health
- Child Development

RISKS OF TOBACCO USE IN PREGNANCY & POSTPARTUM

Pregnancy

- 54% of women discontinue use

Postpartum

- 50-60% return to use within 1 year

Maternal and Obstetric Risks	Newborn & Child Health
• Orofacial clefts • Fetal growth restriction • Placenta Previa • Placental abruption • PPROM • Low birth weight • Increased perinatal mortality • Ectopic pregnancy • Decreased thyroid function	• Respiratory infections • Asthma • Colic • SIDS • Bone fractures • Childhood obesity • Dev/Behavioral Disorders *Breastfeeding • Transfers at 2x rate of placental transfer

TREATMENT OF TOBACCO USE DISORDER IN PREGNANCY

NICOTINE REPLACEMENT THERAPY (NRT)

Efficacy in Pregnancy	No Increased Risk	Unknown Risk of Treatment
8 trials: n=2,199 RCTs: Not effective compared to placebo	• Prematurity • Miscarriage/Sp. Abortion • Birth weight • Neonatal Death • Caesarean section, • Congenital abnormalities • NICU admission	• Asthma* • Obesity* • ADHD* + • Addiction*

Nicotine Replacement Therapy (NRT) (e.g., gum, lozenges, spray, patch):

- Risks of nicotine remain; need cessation plan (6-12 weeks)

*Animal studies demonstrate risk
+ Animal and 1 human study demonstrates risk

(Coleman, 2015; De Long, 2014)

NICOTINE REPLACEMENT THERAPY (NRT)

Efficacy in Pregnancy vs. Individual?	Risks of Treatment	Risks of Continued Smoking
RCTs: Not effective Individual: Effective?	No Increased Risks • Prematurity • Miscarriage/Sp. Abortion • Birth weight • Neonatal Death • Caesarean section • Congenital abnormalities • NICU admission Unknown • Asthma* • Obesity* • ADHD* + • Addiction*	• Orofacial clefts • Fetal growth restriction • Placenta Previa • Placental abruption • Prematurity • PPROM • Low birth weight • Increased perinatal mortality • Ectopic pregnancy • Decreased thyroid function • SIDS • Asthma • Dev/Behavioral • Overweigh/Obese

*Animal studies demonstrate risk

+ Animal studies and 1 human study demonstrate risk

NICOTINE REPLACEMENT THERAPY (NRT)

- **Ideal Patient for NRT in Pregnancy**
  - Great response to NRT in past
  - Needs only a short course of NRT
    - Need cessation plan 6-12 weeks
  - Understands risks of NRT and risks of smoking in pregnancy and feels risks of NRT are less than smoking
  - Will stop NRT if resumes smoking
  - Removes patch at night

TREATMENT OF
TOBACCO USE DISORDER IN PREGNANCY

VARENICLINE

Efficacy in Pregnancy	Risks	Recommendation
No RCTs No retrospective No prospective controlled studies No data in lactation	Unknown	Do not use during pregnancy Do not use in lactation

BUPROPION

Efficacy in Pregnancy vs. Individual?	Risks of Treatment	Risks of Continued Smoking
RCTs: None Cohort Study Individual: Effective?	No Increased Risks • Fetal Anomalies • Still birth • Low birth weight • PTB • Neonatal death Unknown long-term effects	• Miscarriage • Placenta previa • Placental abruption • Preterm birth • Stillbirth • Low birth weight • IUGR • SIDS • Asthma • ADHD • Developmental delays • Cognitive problems (IQ) • Behavioral problems • School achievement • Overweight/obese • Smoking

TREATMENT OF
ALCOHOL USE DISORDER IN PREGNANCY

Behavioral Interventions

- Motivational Interviewing (Pregnancy & Postpartum)
- Contingency Management (Pregnancy)
  - Financial incentives

Management of Withdrawal

- Benzodiazepines

Medications

- Acamprosate
- Naltrexone
- Disulfiram

Vs.

Risks of Untreated Alcohol Use Disorder

- Maternal & Obstetric Health
- Newborn Health
- Child Development

RISKS OF ALCOHOL USE IN PREGNANCY

Leading Preventable Cause of Birth Defects and Developmental Disabilities

Maternal and Obstetric Risks	Newborn & Child Health
• Spontaneous abortion (miscarriage) • Preterm labor • Placental abruption • Bleeding in pregnancy • Intra-amniotic infection • Low birth weight • Congenital anomalies • Fetal demise	**Fetal Alcohol Spectrum Disorders (FASD)** • Fetal alcohol syndrome (FAS) • Abnormal appearance (short height, low weight, small head) • Low intelligence • Behavioral problems • Hearing/sight problems • Developmental Delay • Cognitive deficits

RISKS OF ALCOHOL USE IN PREGNANCY

- **Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE)**

<u>**Impairment in Functional Domains**</u>

1) **Self-Regulation:** attention, mood, behavior, and impulses
2) **Neuro-Cognition:** IQ, executive functioning, memory, visual-spatial reasoning skills, and their ability to learn
3) **Adaptive Functioning:** communication, daily living skills, motor skills, and social skills

RISKS OF ALCOHOL USE IN PREGNANCY

FAS or ND-PAE In Real Life

- Problems in School
  - Suspension, expulsion 2/2 disobedience, and truancy
- Legal Problems
  - Criminal justice system 2/2 anger, frustration, understanding motives of others, susceptible to persuasion/manipulation
- Substance Use Disorders
  - >33% inpatient treatment for drugs and/or alcohol use
- Unemployment
  - Difficulty holding a job and living independently
- Mental Health Problems
  - ADHD, conduct disorder, depression, psychosis

TREATMENT OF ALCOHOL USE DISORDER IN PREGNANCY

Pregnancy

- Motivational enhancement therapy
- Brief psychodynamic psychotherapy
- Interpersonal psychotherapy
- Educational interventions
- Family-focused problems
- Professional group education
- Self-help
- Cognitive behavioral therapy

TREATMENT OF ALCOHOL USE DISORDER IN PREGNANCY

Drug	Efficacy in Pregnancy	Risks Pregnancy	Recommendation*
Naltrexone	No efficacy studies	Unknown Preclinical- concern for alterations in mu-opioid receptor	Do not typically use during pregnancy- unless clear history of benefit or *.
Disulfiram	No efficacy studies	Possible Malformation, Hypertension. Disulfiram-alcohol reaction is unknown	Do not use during pregnancy*
Acamprosate	No efficacy studies	Unknown	Do not use during pregnancy*

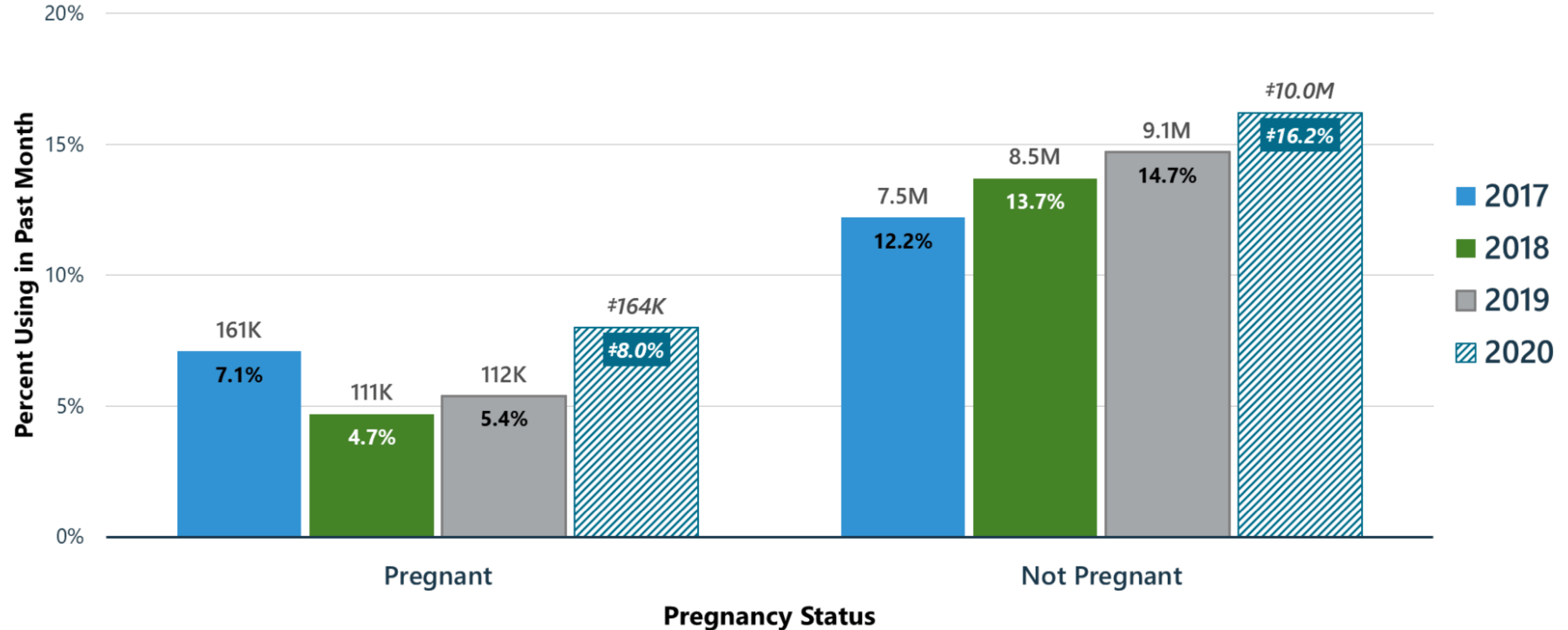
*Must be weighted against the risk of relapse to alcohol use

TREATMENT OF ALCOHOL USE DISORDER IN PREGNANCY

Drug	Efficacy in Pregnancy	Risks Pregnancy	Recommendation*
Naltrexone	No efficacy studies for AUD, but cohort studies for OUD	Studies are limited but, compared to methadone or buprenorphine, Naltrexone: Similar low rates of malformations (*urogenital defects) Similar low rates of obstetric risks (*ectopic pregnancy) Lower rates of NAS/NOWS	Do not use during pregnancy- Unless clear history of benefit or risk of alcohol use is greater than risk of naltrexone & unknown.

Crosses the placenta w/ similar concentrations of naltrexone in maternal and umbilical cord blood.
If naltrexone stopped >60 hrs prior to delivery, drug not detected in maternal or umbilical cord blood.

Marijuana Use in Past Month: Among Women Aged 15-44; By Pregnancy Status



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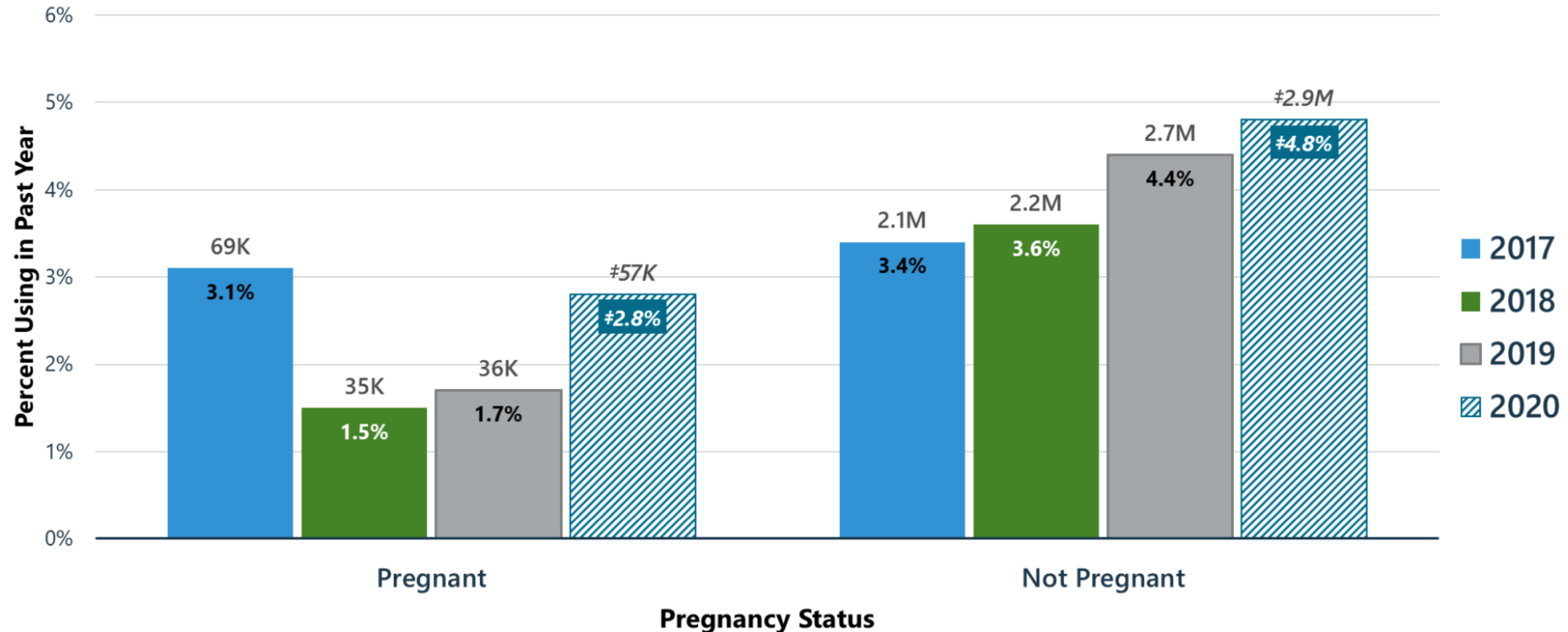
SAMHSA
Substance Abuse and Mental Health Services Administration

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



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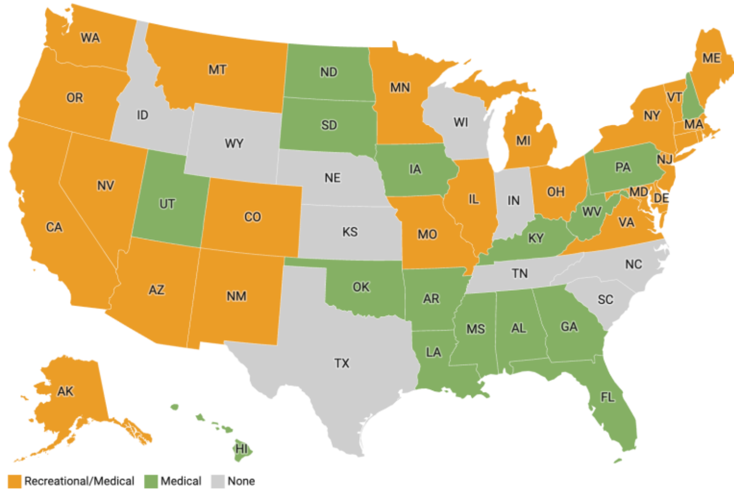

MARIJUANA STATE LAWS NON-PREGNANT VS PREGNANT INDIVIDUALS

- States Laws on "Substance Affected Infants" & Reporting

https://www.guttmacher.org/state-policy/explore/substance-use-during-pregnancy

- Reason For Use
  - Anxiety
  - Sleep
  - Pain
  - Stress
  - Nausea/Vomiting

CANNABIS PREGNANCY AND BREASTFEEDING PHARMACOKINETICS- WHAT THE BODY DOES TO THE DRUG

Pregnancy

- Readily crosses placenta
- Highly lipophilic (distributes in fetal brain and fat)
  - Cannabinoid receptors found as early as 14 weeks gestation and expression fluctuates throughout gestation, particularly in the limbic regions
- Infant plasma levels ~10% of maternal levels

Breastfeeding

- Cannabinoids can accumulate in breast milk due to lipophilic nature
  - Within 4 hours of a single inhalation, breastfed infants ingest about 2.5% of the maternal THC dose
  - Cannabis can remain in breastmilk for days to weeks and infant can test positive via urine or feces
  - Do not recommend breastfeeding or cut down cannabis use as much as possible.

CANNABIS PREGNANCY AND BREASTFEEDING PHARMACOKINETICS- WHAT THE BODY DOES TO THE DRUG

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TREATMENT OF CANNABIS USE/DISORDER IN PREGNANCY

Behavioral Interventions	• Motivational Interviewing • Cognitive Behavioral Therapy • Contingency Management
Management of Symptoms	• Nausea/ Vomiting, Sleep, Anxiety, Mood, Pain
Medications	• None

Vs.

Risks of Untreated Cannabis Use/Disorder	• Maternal & Obstetric Health • Newborn Health • Child Development

RISKS OF CANNABIS USE IN PREGNANCY

Maternal and Obstetric Risks	Newborn & Child Health
• Reduced Fetal Growth • Low Birth Weight – possible dose response • Small for Gestational Age • Placental abruption • Increased NICU admissions	• Increased cognitive deficits-Executive functioning • Increased behavioral problems-Hyperactivity and Impulsivity • Increased mental health problems – Depression, Substance use and Psychosis

RISKS OF CANNABIS USE IN PREGNANCY

Maternal and Obstetric complications

- Reduced Fetal Growth
- Low Birth Weight (dose response?)
- Small for Gestational Age
- Placental abruption
- NICU admissions

CANNABIS:
LONG TERM EFFECTS OF PRENATAL EXPOSURE

Cannabinoid receptors found as early as 14 weeks gestation and expression fluctuates throughout gestation, particularly in the limbic regions

OPPS (Ottowa Prenatal Prospective Study)	MHPCD (Maternal Health Practices & Child Development Study)
4yo: ↓ Verbal reasoning, memory tasks	**9mo:** Impaired mental development
6yo: ↓ language comprehension, memory, visual fxn, perceptual fxn, reading tasks, sustained attn **6yo:** ↑ impulsivity and hyperactivity (dose responsive) **6-9yo:** ↑ behavioral problems	**3,4,6yo:** ↓ executive fxn, ↓ memory and verbal measures **6yo:** ↓ sustained attn and verbal reasoning, ↑ impulsivity and hyperactivity 10yo: ↑depression,, externalizing behaviors
9-12yo: ↓ executive functioning, impulse control, visual problem solving	**9-12yo:** ↑ hyperactivity, impulsivity, inattn **10yo:** lower reading and spelling scores (*****unlike OPPS**)
13-16yo: attn, problem-solving, visual integration, analytic skills requiring sustained attn	**14yo:** ↓ reading, spelling, and math scores
16-21yo: ↑ depression, ↑ substance use **18-22yo:** fMRI changes in neuronal activity	**14-21yo:** ↑ THC and tobacco use Young adults: ↑ psychosis
*** **Deficits in executive functioning, not intelligence**	

Patient & Provider Resources

CDC Treating for Two
https://www.cdc.gov/medicine-and-pregnancy/about/index.html

Mother-to-Baby
https://mothertobaby.org/

Mother-to-Baby Fact Sheets
https://mothertobaby.org/fact-sheets/

Lac Med
https://mothertobaby.org/lactrx/

ReproTox (Provider Only, Cost. Free for Trainees)
https://reprotox.org/

Patient or Provider Resources

Chestfeeding and Breastfeeding

Do not recommend chest/breastfeeding if:

- Using substances
- HIV or Hep C positive

Reference Lac Med
https://mothertobaby.org/lactrx/

Relative Infant Dose [RID]
$\leq$10% maternal Dose