



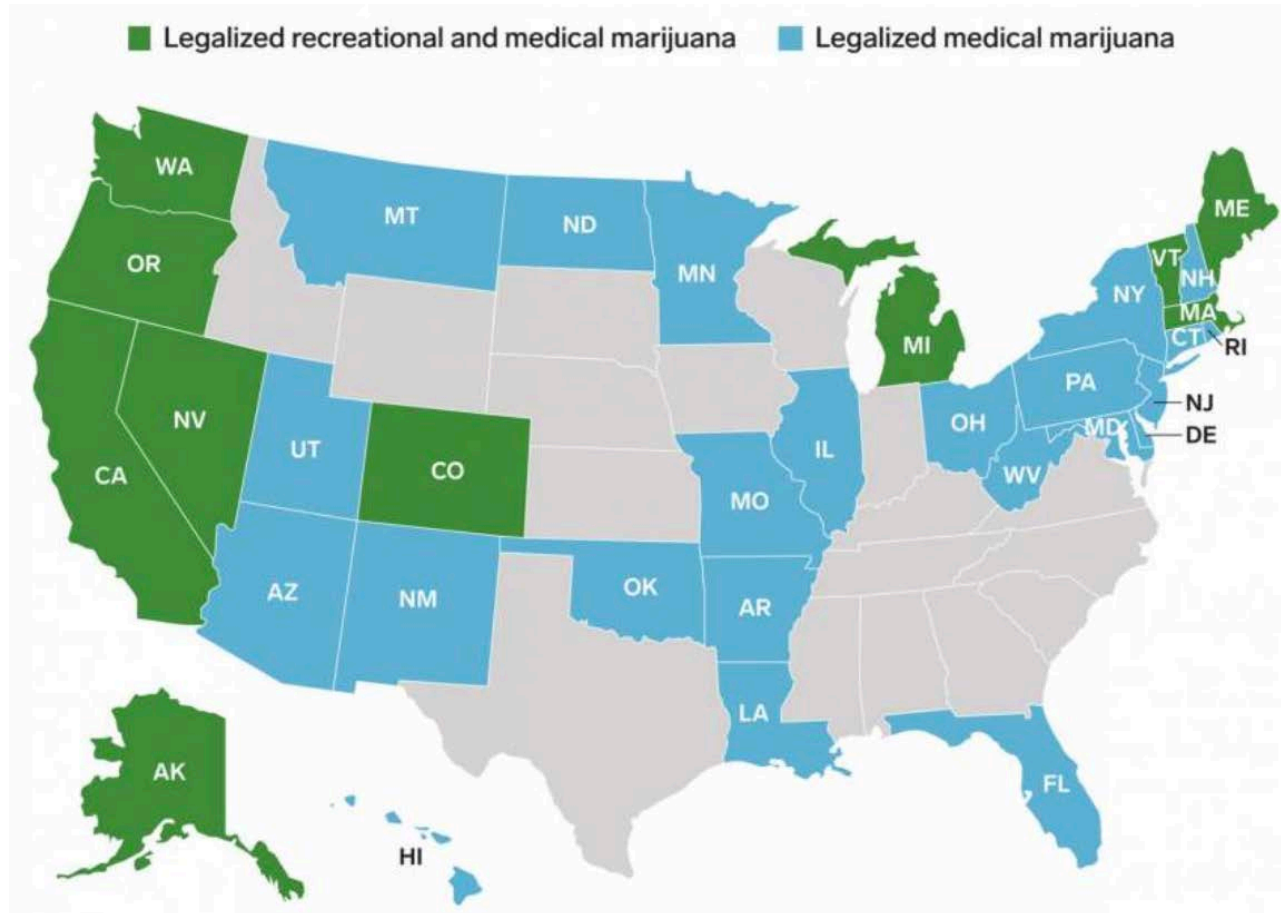
Maternal Cannabis Use in Pregnancy and Lactation

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December 18, 2020**

Disclosures

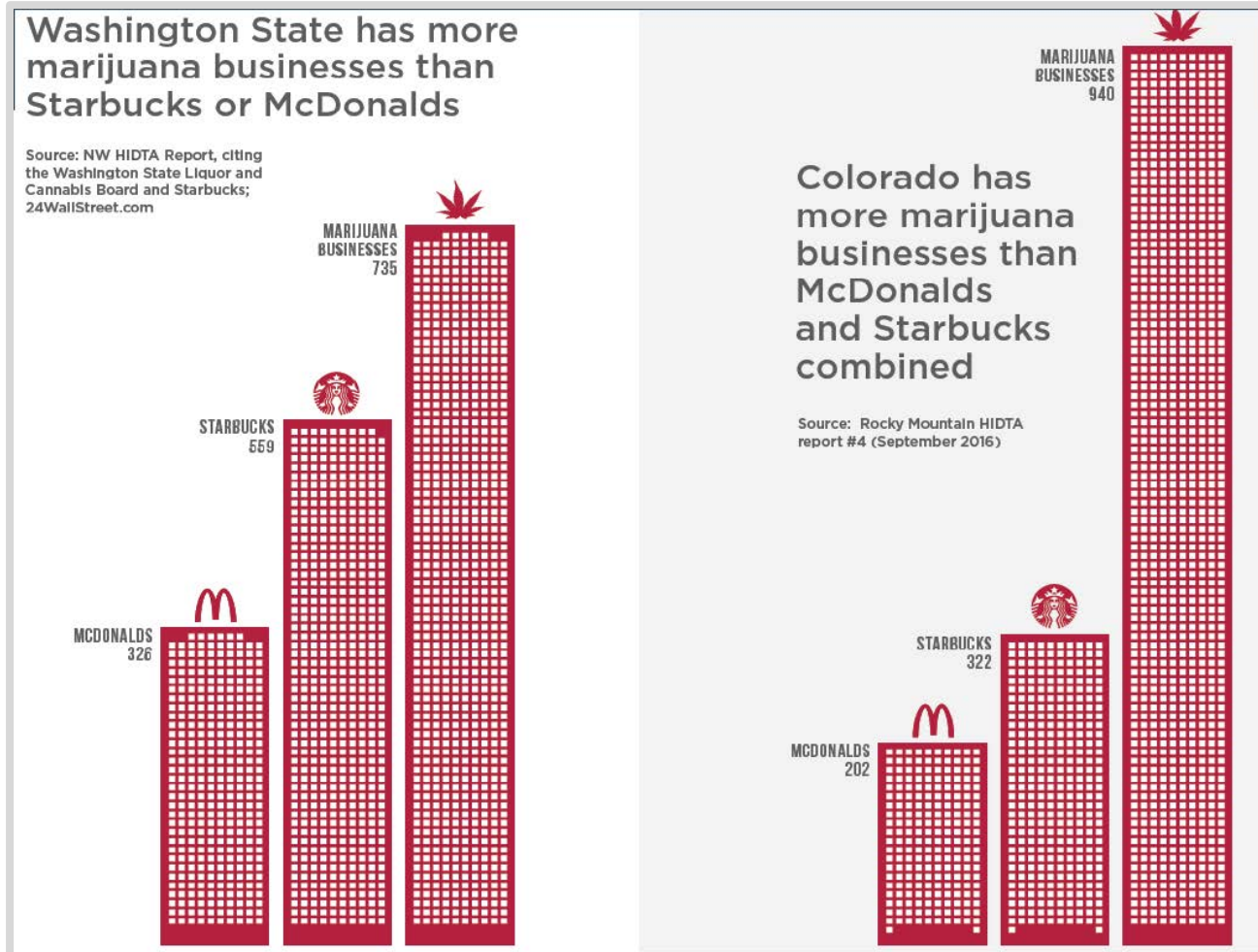
- I have no relevant financial relationships to disclose or conflicts of interest to resolve

Marijuana Legalization Trend



- **Marijuana** is the most commonly used illicit drug in pregnancy
- **33 states** and Washington DC have legalized medical marijuana
- **11 states** and Washington DC have legalized recreational marijuana
- To address the opioid crisis, **3 states** have passed laws to allow marijuana to be prescribed in place of opioids

Understanding the Impact of Legalization

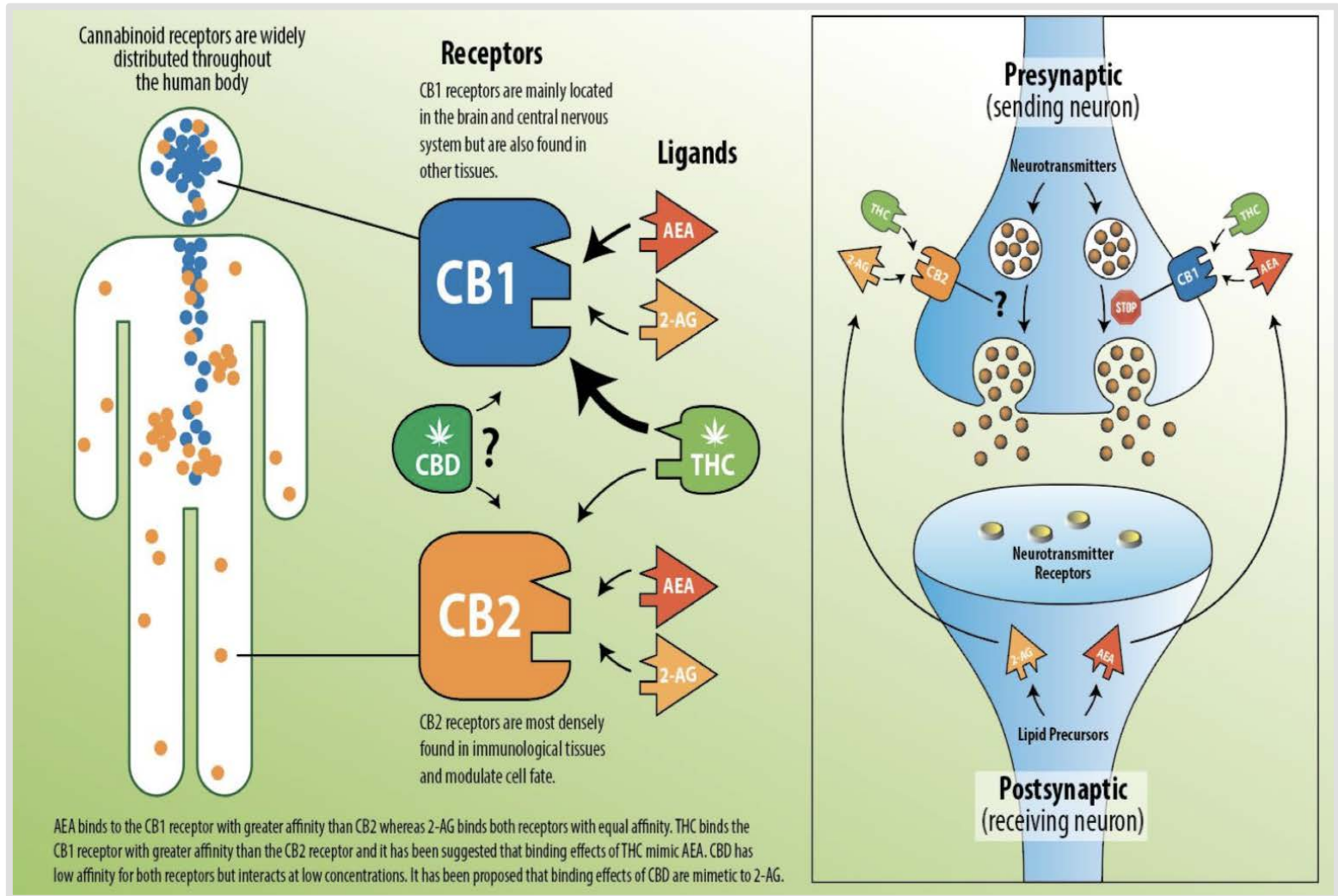


What is marijuana?

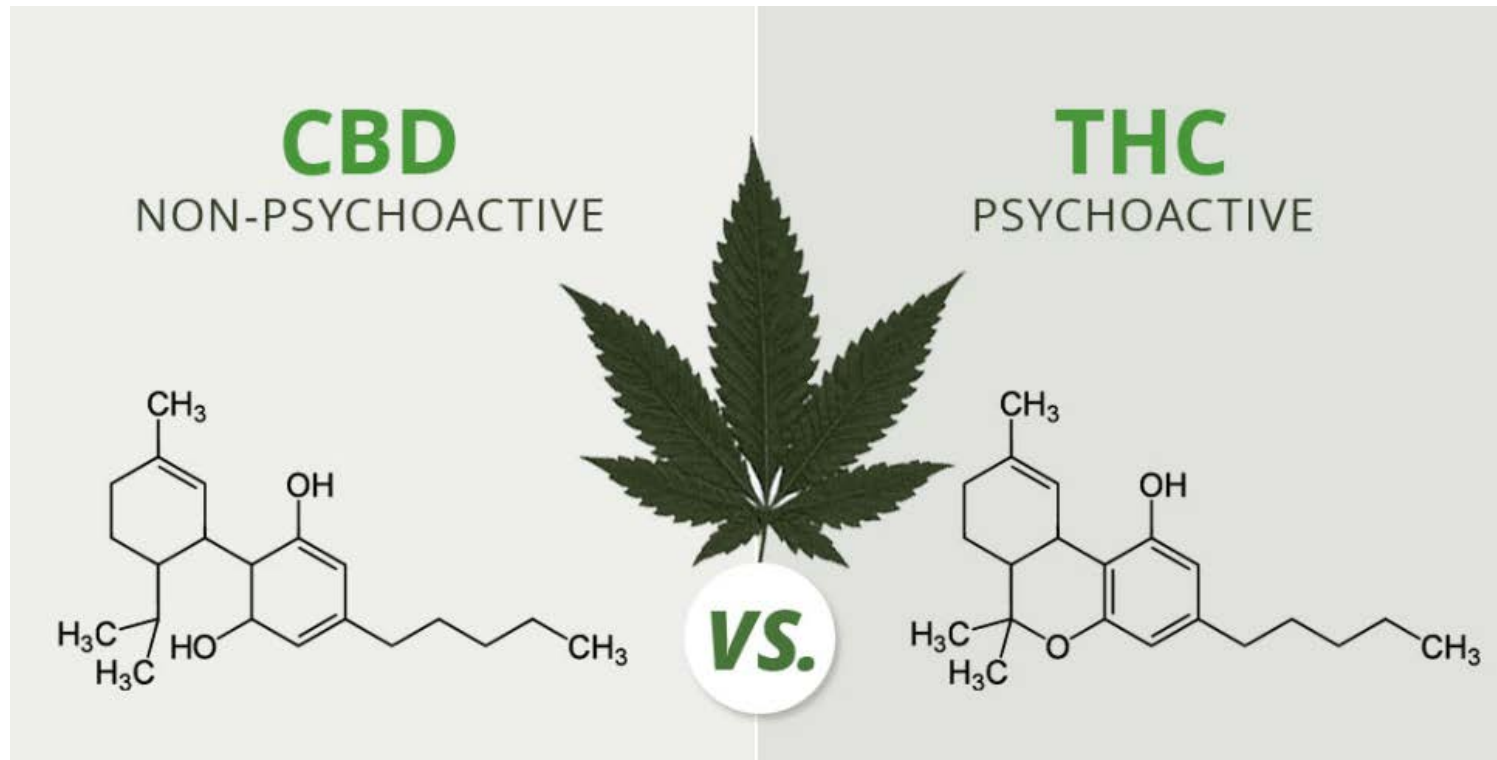
- *Cannabis sativa* plant
- Contains over 600 chemicals
 - **Delta-9-tetrahydrocannabinol (THC)**: main psychoactive component
 - Small and highly lipophilic
 - Rapidly distributed to the brain and fat
 - Metabolized by the liver
 - Half-life is 20-36hrs to 4-6 days
 - Detectable up to 30 days after using
 - **Cannabidiol (CBD)**: second most prevalent main active ingredient



Endocannabinoid System



Cannabidiol vs. Delta-9-tetrahydrocannabinol



- CB1 receptor (found on neurons and glial cells in the brain)
 - Binding of THC results in euphoric effects
 - CBD has 100 fold less affinity to CB1 receptor than THC

What is CBD?

- One of the 80 active components in the marijuana plant
 - Mainly from hemp plant
- Therapeutic effects (pre-clinical models)
 - Anti-seizure
 - Anti-oxidant
 - Neuroprotective
 - Anti-inflammatory
 - Analgesic
 - Anti-tumor
 - Anti-psychotic
 - Anti-anxiety



Therapeutic Effects of CBD

- FDA approved Epidiolex[®] in 2018
- First cannabis-derived medicine containing CBD
- Treatment of severe, childhood-onset epilepsy associated with Lennox-Gastaut syndrome or Dravet syndrome



Safety of CBD

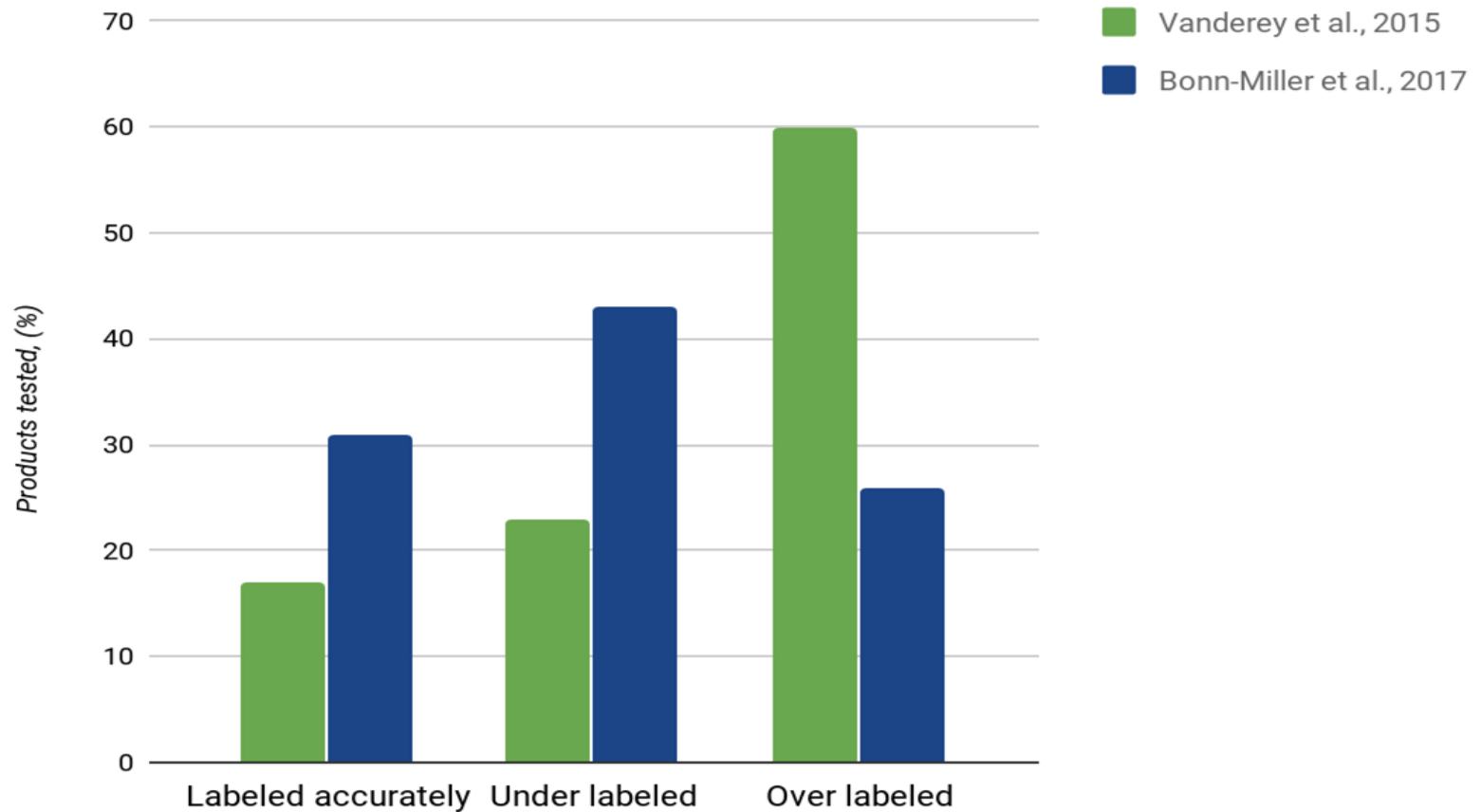
- Different safety profile than THC
- No significant side effects
- Safety and purity is not FDA regulated
 - May contain other elements such as pesticides, heavy metals, bacteria and fungus
 - Many products that claim to contain CBD do not, or have more than the legal limit of THC





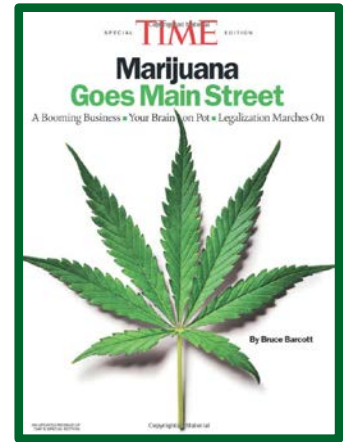
Accuracy of labeling

- THC present in 21.4% of products labeled CBD only



Scope of the Issue

- Marijuana is commonly used for pregnancy ailments
- THC readily crosses the placenta
- THC concentration has increased at least 3-fold in the past decade
 - Marijuana in dispensaries ~17.7-23.2% THC up to 75.9% THC
- Prenatal marijuana exposure has been associated with:
 - Miscarriage and stillbirth
 - Intrauterine growth restriction and low birth weight
 - 5-fold increase in dysmorphic features associated with FASD
 - Impaired fetal neurodevelopment
 - Childhood attention and learning disorders

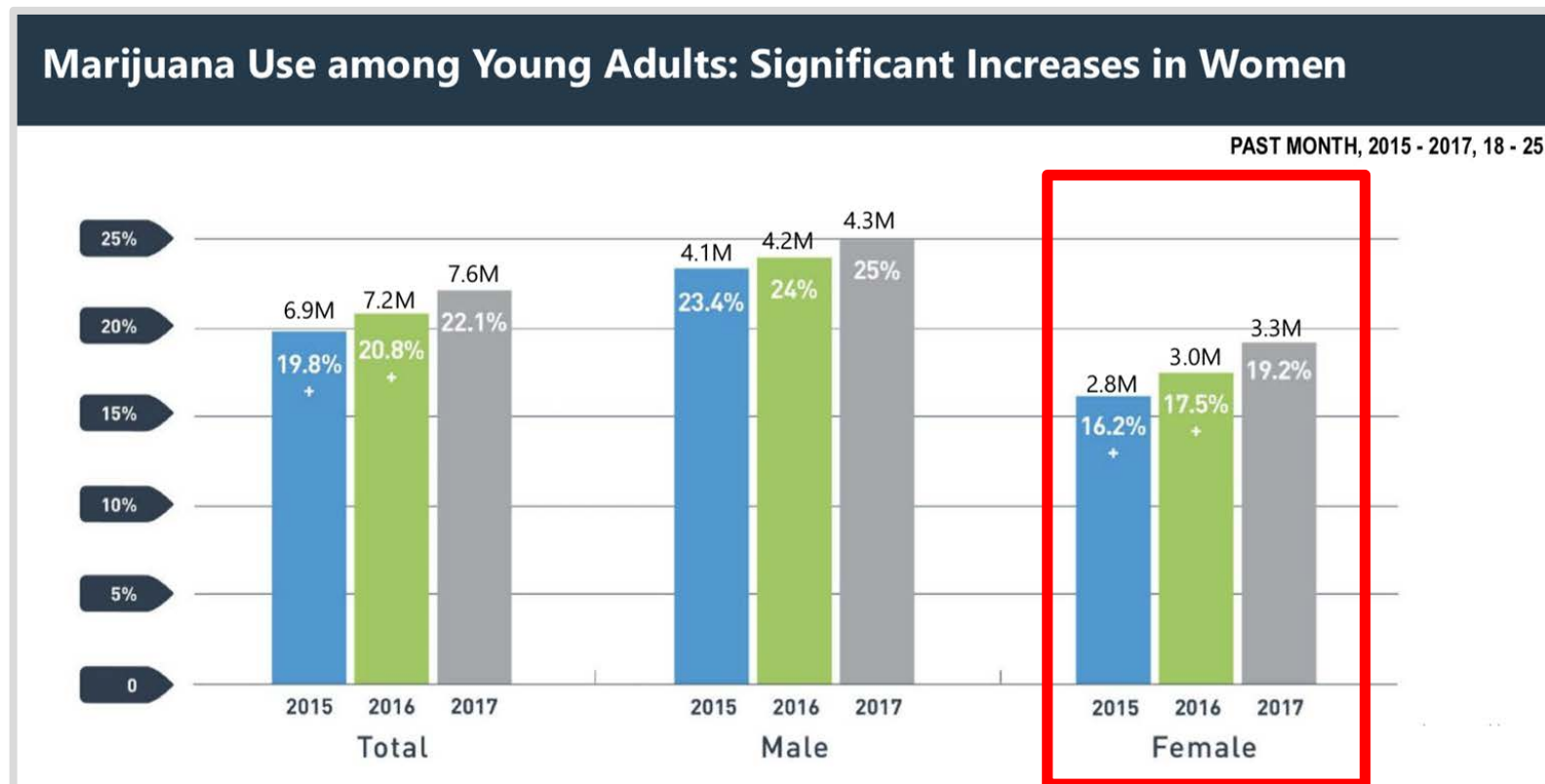


Incidence of Use

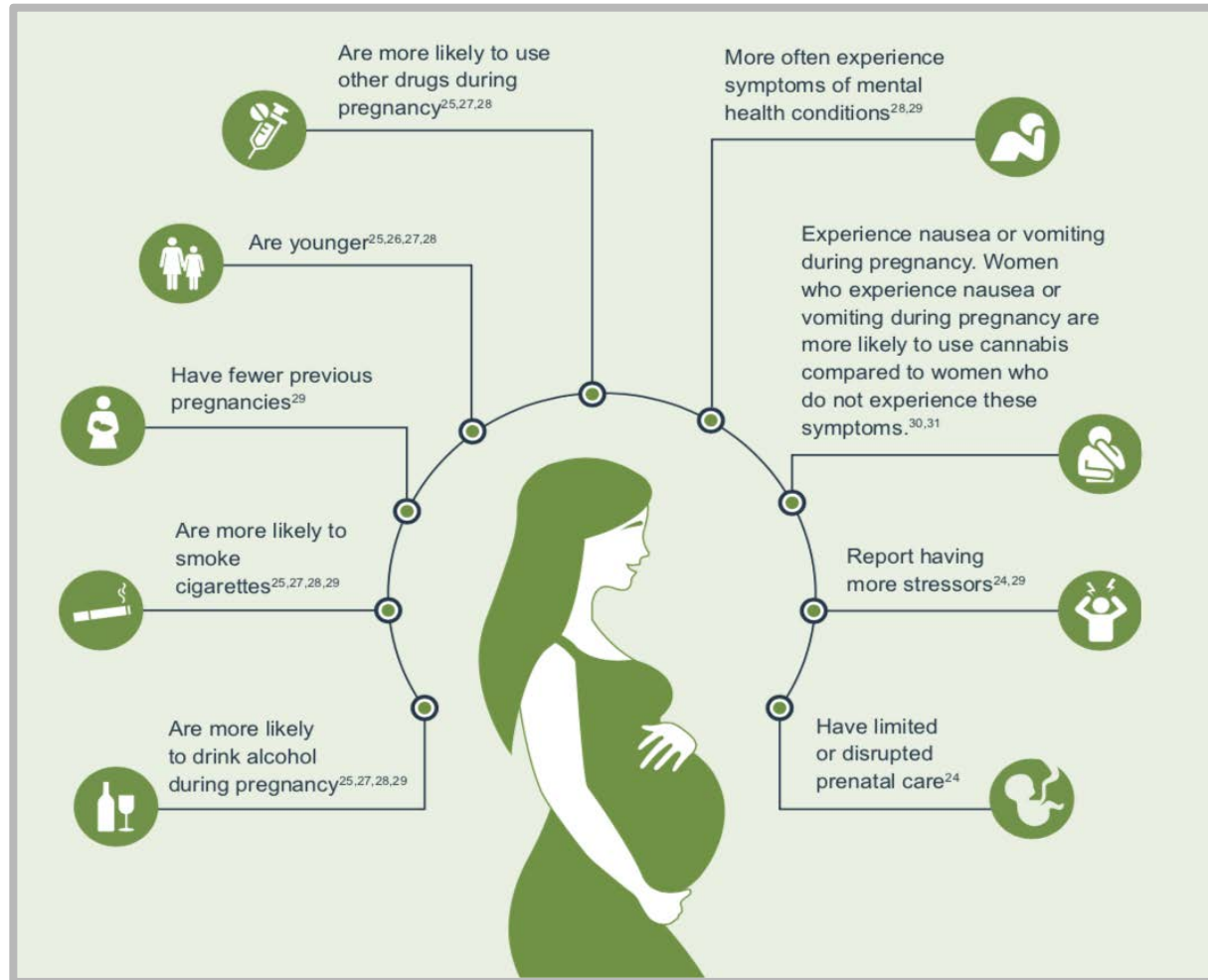


- Self-reported prevalence of use in pregnancy ranges from 2-5% to 30%
- **U.S. National Survey on Drug Use and Health (2017)**
 - 3.9% of pregnant women used in the last month in 2014 (2.4% in 2002)
- **Young-Wolff et al. Cross-sectional Northern California study**
 - (2017) 22% of young females ages 12-17 years and 19% of women ages 18-24 used marijuana by self report or urine testing
 - (2019) Frequency of use in the year before and during pregnancy has increased from 2009 to 2017, daily use increasing most rapidly
- **Rodriguez et al. (2019) Retrospective cohort study (n=1,206)**
 - Deliveries from 2011-2017, noted 17.5% (n=211) used marijuana

2017 National Survey on Drug Use and Health



Who is Using Cannabis in Pregnancy?



Perceived Benefits



- Most commonly used for nausea and vomiting, postpartum depression, and pain
- **Roberson et al. (2014)** found that women who used marijuana in pregnancy were more likely to report severe nausea (3.7 vs 2.3%, PR 1.63, 95% CI 1.08-2.44)
- **Westfall et al (2006)** reported on 79 women who used medicinal marijuana in pregnancy
 - 40 (51%) used marijuana to treat nausea and vomiting of pregnancy and 92% of them felt it was effective

Reasons for Using Cannabis in Pregnancy

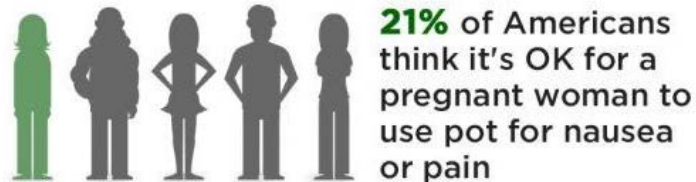
Survey respondents – WIC mothers	Ever users % (#)	Current users % (#)	Past users % (#)
To help with depression/anxiety/stress	35% (164)	63% (60)	28% (103)
To help with pain	29% (135)	60% (57)	21% (78)
To help with nausea/vomiting	23% (108)	48% (46)	17% (62)
For fun/recreation	59% (277)	39% (37)	65% (240)
Other reason	16% (75)	14% (13)	16% (58)

Perceived Safety

- U.S. National Survey on Drug Use and Health (2017)

Use	Pregnant and no past 30 day use	Non-pregnant and no past 30 day use	Pregnant with past 30 day use	Non-pregnant with past 30 day use
2005	3.5%	3.1%	25.8%	23.7%
2015	16.5%	14.8%	65.4%	62.6%

- Yahoo Survey (2017)

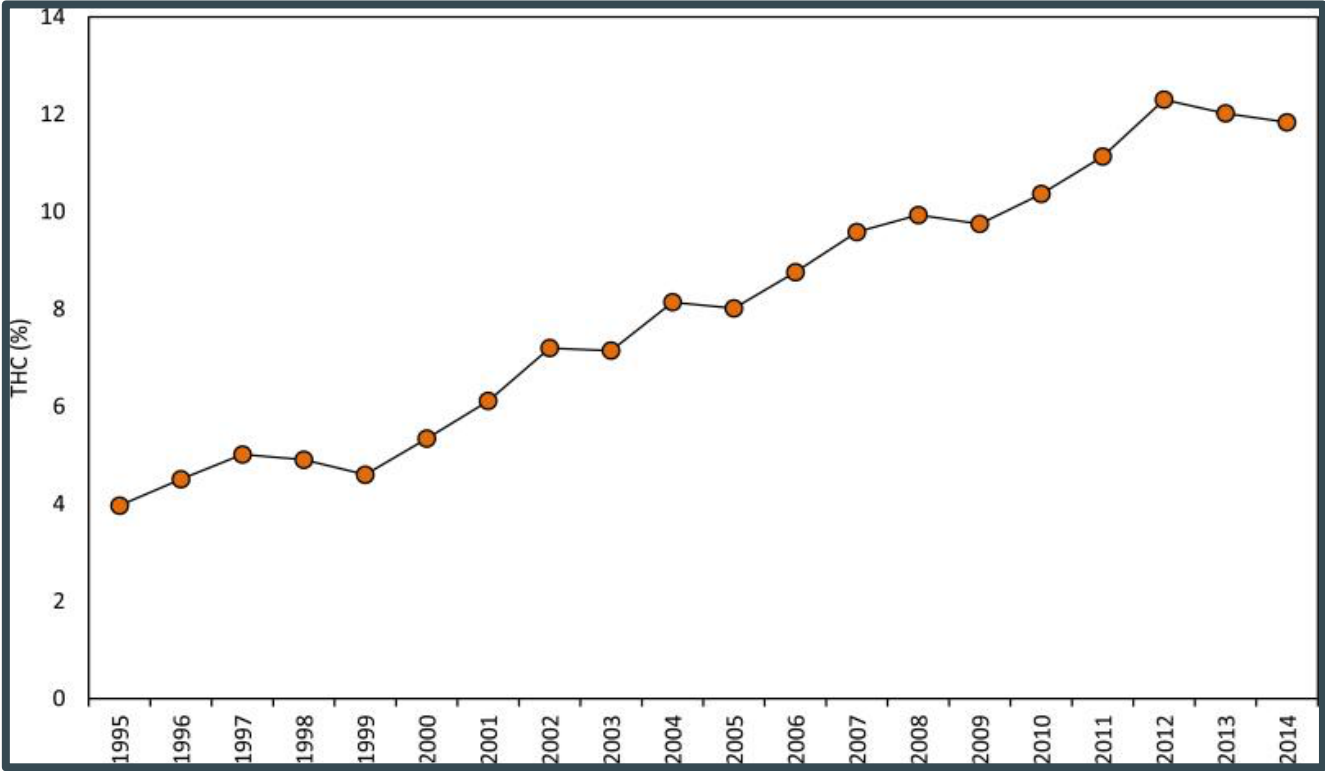


Among Americans who use marijuana regularly, **40%** think it's OK for a pregnant woman to use pot for nausea or pain





Increase in THC concentration (1995-2014)



2020

Reference: ElSohly et al, 2016

Common forms and methods of THC use

- **Inhaled**
 - Smoking, vaporizing, dabbing
 - Quickest method, less chance of overconsumption
- **Oral or gastrointestinal (GI) absorption**
 - Oral: Drops, tinctures, sprays, lollipops, strips
 - GI: Edibles, candies, drinks, snacks, capsules
 - Delay in onset of symptoms
 - Higher likelihood of overconsumption
- **Skin absorption**
 - Topicals: Balms, lotions, salves, bath soaks
 - Transdermals: Patches and gels
- **Suppositories**
 - Oils and waxes that can be used rectally or vaginally
 - Vaginal suppositories have similar onset times to oral absorption
 - Rectal suppositories not as readily absorbed, less psychoactive

Method	Onset (min)	Duration (hrs)
Inhaled	1-3	1-3
Oral	10-25	1-3
Ingested	30-90	6-8
Topical	15-30	3-6
Transdermal	15-30	6-8
Vaginal sup.	20	3-6

Routes of administration before and during pregnancy

- Young-wolff et al. (2019), Northern California 2018-2019 (n=585)
 - Self reported use in the year before and during pregnancy
 - 12% (n=71) used before vs. 3% (n=19) used during pregnancy
 - Among users, 43% used >1 mode before vs. 15% during pregnancy

Mode of Delivery	Before Pregnancy (%)	During Pregnancy (%)
Smoking	58	42
Edibles	27	16
Vaping	23	16
Lotions	11	5
Other	10	0

Methods for testing in pregnancy

- **Maternal**
 - **Serum**
 - 2-3 days
 - **Urine**
 - 2-3 days for occasional and weeks in chronic user
 - **Hair**
 - Up to 90 days
- **Neonatal**
 - **Umbilical Cord Homogenate**
 - Send out lab
 - Utilizes otherwise discarded specimen
 - Easier to collect than meconium
 - **Meconium**
 - Identifies maternal marijuana use >24w



Limitations of the urine drug screen

- Are often immunoassays that detect the major urinary metabolite of THC (11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid)
- Prone to false positives
 - NSAIDs and PPIs have been reported to cause false positives on drug screens
 - If a false positive or negative is suspected, confirmatory testing is with gas chromatography-mass spectrometry or liquid chromatography-tandem mass spectrometry
- Synthetic or designer cannabinoids are not detected by urine drug screens



Surgeon General's Advisory

The New York Times

Surgeon General Warns Pregnant Women and Teenagers Not to Smoke or Vape Marijuana

Dr. Jerome Adams, the surgeon general, said they may be unaware that modern crops pose greater health risks because of their potency.



The U.S. surgeon general stressed that modern marijuana is far more potent than products from 20 years ago, with much higher levels of T.H.C., marijuana's active ingredient. Richard Vogel/Associated Press

***“No amount
of marijuana
use during
pregnancy or
adolescence
is safe.”***

ACOG and AAP



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

American Academy
of Pediatrics



- **ACOG's Committee opinion states:**
 - Before pregnancy and in early pregnancy, all women should be asked about tobacco, alcohol and other drugs used for nonmedical reasons
 - Women reporting marijuana use should be counseled regarding potential adverse health effects of continued use during pregnancy
 - Women who are pregnant, contemplating pregnancy, or lactating should be encouraged to discontinue marijuana use, even if for medicinal purposes
 - Ob-gyns should not prescribe for medicinal purposes to pregnant or lactating women
 - Insufficient evidence for effects on nursing infant
- **American Academy of Pediatrics (AAP) policy statement on “Breastfeeding and the Use of Human Milk”:**
 - Breastfeeding contraindicated in women using illicit drugs including marijuana

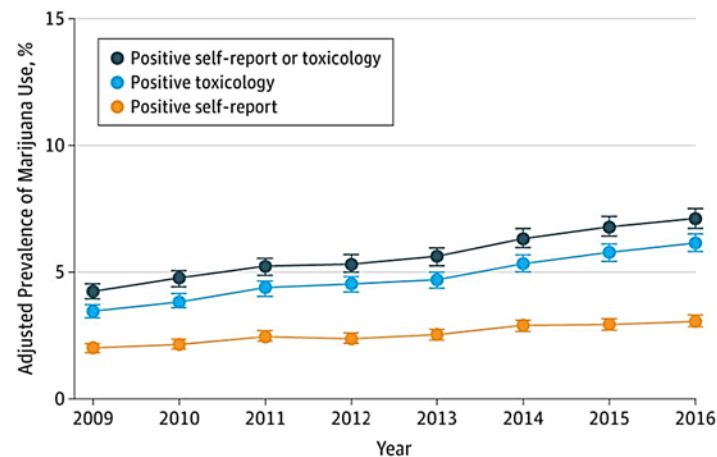
Problems with existing studies

- Retrospective or observational design
- Small sample size
- Lack of quantification/timing of exposure
- Most studies reflect marijuana exposure through smoking
- Confounded by tobacco, polysubstance use, alcohol, nutrition, and sociodemographic factors
- Most of the literature is from the 1980s when marijuana products were less potent



Existing studies rely on self report

- **Shiono et al (1995), n=7,470**
 - Prospective multi-center cohort study, interviews and serum screening
 - 60-70% with positive THC on serum screen denied use in interview
- **Rodriguez et al. (2019), n=1,206 women, 17.5% (n=211) used marijuana**
 - Retrospective cohort study, nearly universal urine toxicology screen
 - 8.5% (n=18) self-report, 63% (n=133) urine screen, and 28.4% (n=60) both
- **Young-wolff et al (2019), n=279,457, Northern California from 2009-2016**
 - Screening through self-report and biochemical testing



Prenatal outcomes

Marijuana AND Pregnancy

If you use marijuana during pregnancy, you may be putting your health and your fetus's health at risk.

Possible Effects on Your Fetus	Possible Effects on You
<ul style="list-style-type: none"> Disruption of brain development before birth 	<ul style="list-style-type: none"> Permanent lung injury from smoking marijuana
<ul style="list-style-type: none"> Smaller size at birth Higher risk of stillbirth 	<ul style="list-style-type: none"> Dizziness, putting you at risk of falls
<ul style="list-style-type: none"> Higher chance of being born too early, especially when a woman uses both marijuana and cigarettes during pregnancy 	<ul style="list-style-type: none"> Impaired judgment, putting you at risk of injury
<ul style="list-style-type: none"> Harm from secondhand marijuana smoke Behavioral problems in childhood and trouble paying attention in school 	<ul style="list-style-type: none"> Lower levels of oxygen in the body, which can lead to breathing problems

- **Maternal**

- Increased risk of anemia
- Increased cyclic vomiting and/or hyperemesis syndrome

- **Fetal/Neonatal**

- Fetal growth restriction and lower birth weight
- Preterm birth
- Stillbirth and miscarriage
- Increased NICU admissions
- Altered neurodevelopment

Cannabinoid hyperemesis syndrome (CHS) in pregnancy

- Refractory cyclic nausea/vomiting with abdominal pain in regular users
- Retrospective study (n=1,571), 6% of patients presenting to ER with recurrent emesis had CHS
- Unclear etiology:
 - **Hypothesis 1:** Stimulation of enteric CB1 receptors inhibits gastric/intestinal motility
 - **Hypothesis 2:** Stimulation of vascular CB1 receptors induces splanchnic vasodilation
 - **Hypothesis 3:** Genetic variants cause excessive pro-emetic cannabis metabolites
- Compulsively take hot showers/baths for relief
- Long term therapy is cannabis cessation
 - Complete and permanent resolution ≤ 2 weeks weaning

Symptom	Incidence
Severe cyclic nausea and vomiting over months	100%
Abdominal pain	85.1%
\geq weekly cannabis use	97.4%
Regular cannabis use >1 yr	74.8%
Compulsive hot showers or baths for relief	92.3%
Age <50yo at time of evaluation	100%



Fetal Growth Restriction

- **English et al. (1997)**, Meta-analysis, prenatal exposure and birth weight
 - Babies of women who used >4 times/wk weighed <131 grams less
 - Low birth weight with any use was OR 1.09 (95% CI 0.94-1.27)
- **El Marroun et al. (2009)**, Large prospective trial
 - Fetuses exposed in early pregnancy (n=214) grew 11.2 grams/week less
 - Fetuses exposed throughout pregnancy (n=41) grew 14.4 grams/week less
- **Gunn et al. (2016)**, Systematic review
 - Prenatally exposed infants had decreased birth weight (OR 1.77, CI 1.04-3.01)
- **National Academies (2017)**, Systematic review
 - Significant association between maternal cannabis smoking and lower birth weight of the offspring
- **Kharbanda et al. (2019)**, Retrospective cohort study (n=3,435), ICD-10 codes
 - Prenatal use was associated low birth weight (aRR 1.69, 95% CI: 1.22-2.34)

Preterm birth (PTB)



- **Fergusson et al. (2002)**, ALSPAC Study (n=12,129)
 - PTB rate (4.6%) same among users and non-users
- **Burns et al. (2006)**, ICD-10 codes for substance use from births (n=416,834)
 - Increased incidence of preterm birth among MJ users (18.8% vs 5.8%)
- **Hayathakhsh et al. (2012)**, women (n=24,874) who self-reported MJ use
 - MJ use associated with PTB (OR 1.5, 1.1-1.9) and NICU admit (OR 2; 1.7-2.4)
- **Dekker et al. (2012)**, Identifying PTB risk factors in pregnancies (n=3,184)
 - 7% marijuana-exposed by self-report in structured interviews
 - Pre-pregnancy use associated with PTB (OR 2.34; 1.22-4.52)
- **Saurel-Cubizolles et al. (2014)**, Studied women (n=13,545) in France
 - Any use was associated with spontaneous PTB (OR 2.15, 95% CI 1.10, 4.18)
- **Corsi et al. (2019)** Canadian women (n=661,617); 9,427 (1.4%) reported MJ use
 - PTB (12% vs. 6.1%) and NICU admit (19.3% vs. 13.8%) in users vs. non-users



Stillbirth

- **National Academies (2017)** did not identify an association between cannabis exposure and stillbirth or spontaneous abortion
- **Warshak et al. (2015)**
 - Marijuana exposure and adverse obstetrical/neonatal outcomes
 - No association in cannabis users (1.1%) vs. non-users (1.5%)
- **Varner et al. (2014) Stillbirth Collaborative Research Network**
 - Population-based case-control study of illicit prenatal drug use and its association with stillbirth
 - Association between stillbirth and marijuana use as demonstrated by cord homogenate positive for THC (OR 2.34, 95% CI 1.13-4.81)
 - Partial confounding by exposure to cigarette smoking, after adjusting for tobacco use, the stillbirth OR was reduced by ~10%

Other Obstetric Complications

- No associations were found between in-utero exposure to cannabis and the following health outcomes:
 - Fetal distress
 - Maternal diabetes
 - Rupture of membranes
 - Use of prenatal care
 - Placental abruption
 - Elevated blood pressure
 - Maternal weight gain
 - Maternal postnatal issues
 - Duration of maternal hospital stay
 - Antepartum or postpartum hemorrhage
 - Hormone concentrations



Neonatal and Childhood Outcomes

Infancy

Decreased ability
to self-soothe
Sleep disturbances



Adolescence

Continued
hyperactivity,
impulsivity, inattention
Reduced school
performance
More likely to try & use
cannabis earlier

Childhood

Poorer memory, verbal reasoning skills
Less attentive, more impulsive and hyperactive
Symptoms of depression, anxiety

Childhood outcomes - Neurodevelopment

- **Guterrez Alvarez et al. (2018)**
 - Case-control study, (cases n=109, controls n=217)
 - Cases were patients with intrauterine exposure to marijuana confirmed by positive maternal urine testing for THC during any trimester of pregnancy

Months	Odds Ratio	95% CI
6	2.07	0.76-5.67
9	1.00	0.41-2.40
12	0.76	0.36-1.59
15	2.68	1.06-6.77
18	2.45	1.06-5.69
24	1.61	0.96-2.72

Behavior	Odds Ratio	95% CI
Fine Motor	2.32	0.99-5.44
Gross Motor	1.78	0.96-3.30
Language	1.06	0.64-1.76
Social	6.88	3.08-15.35

Childhood outcomes - Neurodevelopment

- **Corsi et al. (2020)**
 - Retrospective study, (cases n=109, controls n=217)
 - Ontario, Canada from April, 2007 to March, 2012
 - Increased incidence of autism spectrum disorder (ASD), intellectual disability and learning disorders in children prenatally exposed to cannabis

Outcome	Crude HR (95% CI)	Adjusted HR (95% CI)	Additionally Adjusted HR (95% CI)
Primary Outcome			
ASD	1.63 (1.29-2.06)	1.53 (1.18-1.98)	1.51 (1.17-1.96)
Secondary Outcome			
Intellectual disability and learning disorders	2.04 (1.68-2.49)	1.23 (0.97-1.55)	1.22 (0.97-1.54)
ADHD	2.60 (2.35-2.86)	1.11 (0.99-1.25)	1.11 (0.98-1.25)



Vulnerability to Drug Addiction

- The endocannabinoid system regulates dynamic changes in the mesolimbic dopamine pathway and reward-associated behaviors
- Cannabis exposure in the prenatal and postnatal period can potentially disrupt normal development and increase vulnerability to drug addiction
- Hurd et al: Post-mortem human second trimester fetal brains prenatally exposed to marijuana had decreased dopamine receptors, especially males, and was dose-dependent.
- Adult rat offspring prenatally exposed to THC:
 - Enhances heroin-seeking profiles
 - Alters expression of CB1, dopamine, and glutamate receptor genes in the brain striatum

Breastfeeding



- THC is passed in breastmilk and stored in fat
- **Bertrand et al. (2018)** Quantified THC in breastmilk after marijuana use
 - 54 samples from donors (n=50) with self-reported substance/supplement use
 - 64% inhaled marijuana, 88% used at least daily, and THC detected in 63%
 - Number of daily uses and time from sample collection to analysis were predictors of THC concentration in breastmilk
- **Baker et al. (2018)**, Observational study (n=8)
 - Breastmilk collected at 20min, 1, 2 and 4 hrs after smoking cannabis
 - Exclusively breastfed infant ingests mean of 2.5% of maternal dose
- **Astley et al. (1990)** Infant (n=136) neurodevelopment exposed via breastmilk
 - Exposed infants scored poorly on Psychomotor Developmental Index
 - 84% of women who used while pregnant continued while breastfeeding

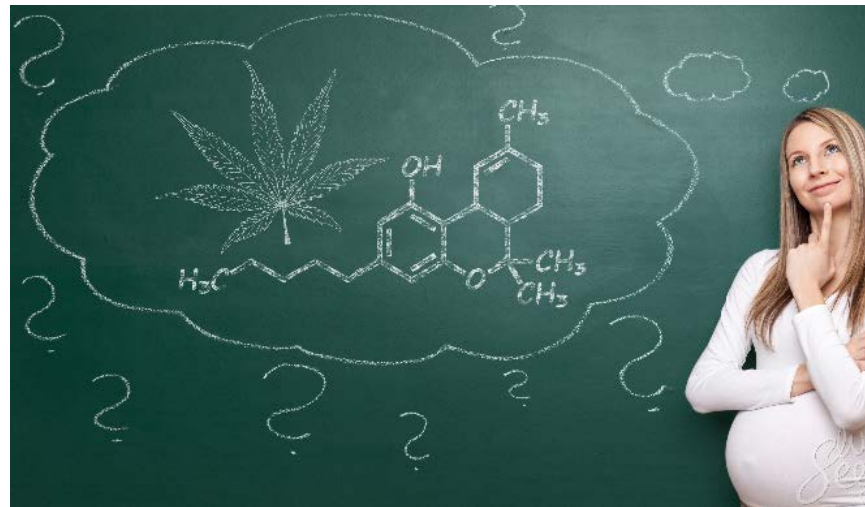


How are we doing now?

- **Holland et al (2016)**
 - Audio-recorded patient health encounters (n=468)
 - Evaluated obstetric provider (n=47) response to disclosure of marijuana use during the first prenatal visit
 - 90/460 (19%) patients reported marijuana use at OB intake
 - Half the time provider did not respond to marijuana disclosure
 - When discussed, response was:
 - Non-specific
 - Focused on legal and procedural consequences (i.e. toxicology screens and social services)
 - Did not focus largely on health or medical implications

How are we doing now?

“You have the issue now with marijuana specifically. When you just have it, illegal, it makes the time of delivery, they will do a urine drug test to see if that is your base form history of yes it gets in the effects of it. And we don't want to do that with the baby” you, like force you to talk to child protective services because it is a risk factor.”



Dispensary Project

- Statewide cross-sectional study of dispensaries in Colorado (n=400)
- Mystery shopper study, caller was 8 weeks pregnant with nausea

Phone Script Cited Here...

“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:

- 1. 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)?

- Nearly 70% had product recommendations, predominantly edibles
 - 65% based recommendation on personal opinion
 - 32% recommended discussing with OB provider without prompting



Talking with patients – what to tell them?

- No known benefits of marijuana use in pregnancy
- THC crosses the placenta and is found in breastmilk and there are possible risks of marijuana use in pregnancy and with breastfeeding
- No known “safe” amount of marijuana in pregnancy
- There are treatments to common ailments in pregnancy (i.e. nausea, anxiety) that have better safety data
- Marijuana is addictive
- There are known adverse effects associated with marijuana use in pregnancy and/or lactation
- Helpful websites:
 - <https://responsibilitygrowshere.com/>
 - <https://www.cdc.gov/marijuana/pdf/marijuana-pregnancy-508.pdf>
 - https://www.colorado.gov/pacific/sites/default/files/MJ_RMEP_Pregnancy-Breastfeeding-Clinical-Guidelines.pdf

Thank you

Wallowa Mountains, Oregon

A scenic landscape of the Wallowa Mountains in Oregon. The foreground shows a calm lake reflecting the surrounding forested hills and distant mountain peaks. The sky is a clear, bright blue. The text "Thank you" is overlaid in the upper center, and "Wallowa Mountains, Oregon" is in the bottom left corner.