Marijuana in Pregnancy and While Breastfeeding

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HEALTH
UNIVERSITY OF UTAH

Disclosure Statements

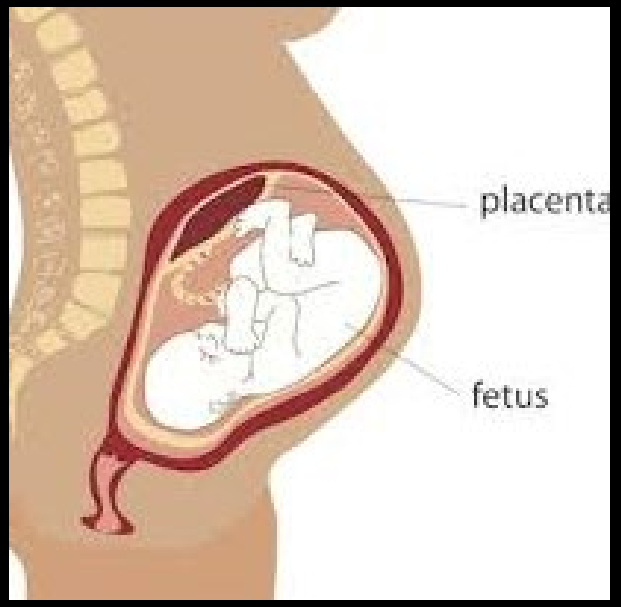
- I have no relevant financial relationships to disclose or conflicts of interest to resolve.

Learning Objectives

- Define prevalence of marijuana use in pregnancy and reported reasons for use.
- Counsel women regarding the risks of marijuana use during pregnancy and lactation based on current evidence.
- Recommend and utilize available on-line resources when counseling women regarding marijuana use in pregnancy and lactation.

Background

- Marijuana is the most common illicit drug used in pregnancy
- Crosses the placenta
- Anticipate increased use with increasing legalization of recreational marijuana

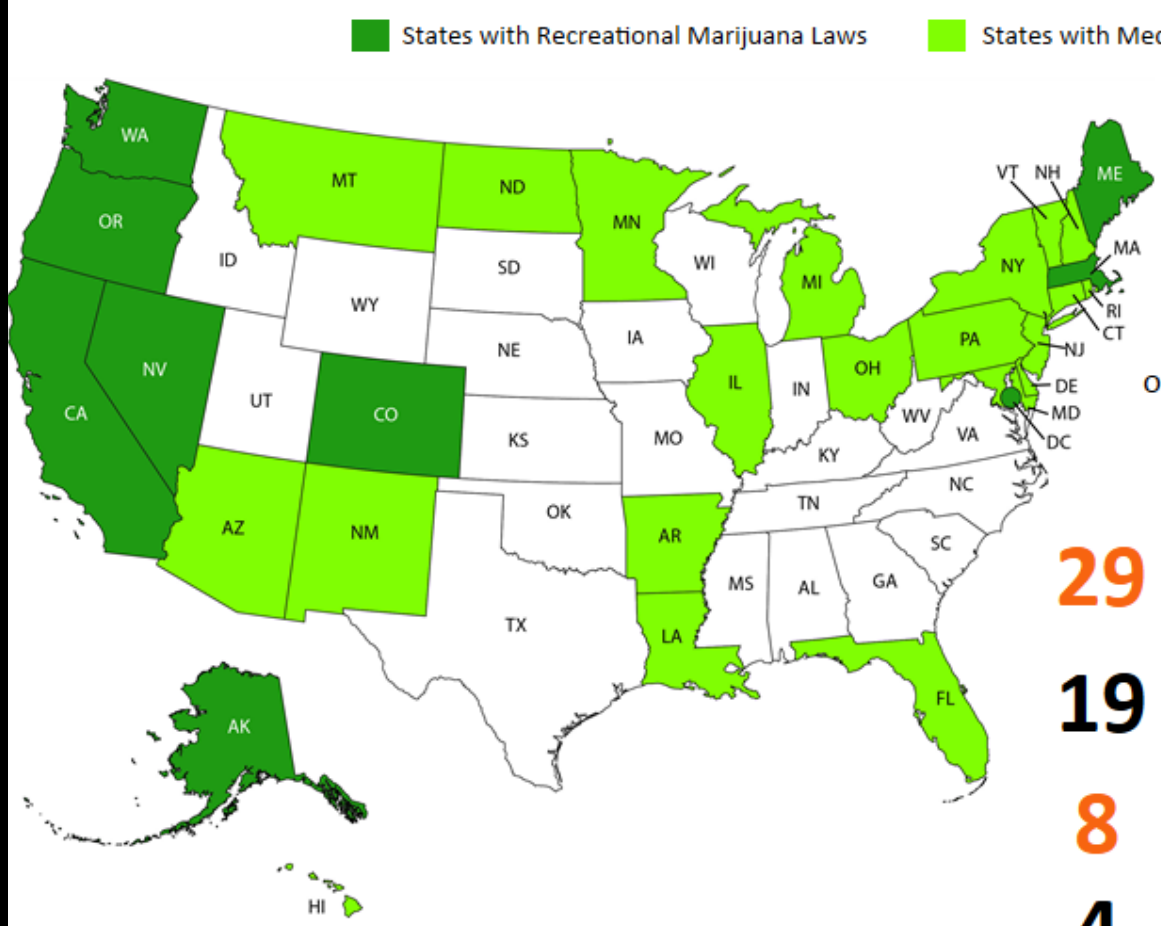


www.babymed.com

Chart of the Week

Marijuana Business Daily

Marijuana Legalization by State



Key Statistics

59.3%

of the U.S. population now lives in a state where marijuana has been legalized

29 states plus Washington DC have medical marijuana laws ...

19 plus Washington DC have operating dispensaries

8 states plus Washington DC have recreational marijuana laws ...

4 with operating retail stores

Source: Marijuana Business Daily, U.S. Census Bureau

https://mjbizdaily.com/chart-majority-of-u-s-embraces-legal-marijuana

What is marijuana?

- *Cannabis sativa* plant
- Contains over 600 chemicals
  - THC: psychoactive component
  - Cannabidiols: sedative, ? therapeutic effect
- Modes of consumption
  - Smoking
  - Vaping
  - Eating
  - Topical (lotions)

Prevalence of Marijuana Use

- Reported prevalence 3-30%
- Data from National Surveys on Drug Use and Health
  - Cross sectional, nationally representative
- Pregnant women who used marijuana in last month
  - 2.4% in 2002, 3.9% in 2014, 4.9% in 2016

Brown et al JAMA 2016, https://www.samhsa.gov/data/report/results-2016-national-survey-drug-use-and-health-detailed-tables

CCTSI Cross-Sectional Pilot Results

- N=116 paired samples (cord & survey)
- 2.6% reported to healthcare provider
- 6.0% reported use in last 30 days on anonymous survey
- 10.3% THC-A above LOQ (200 pg/g) in the umbilical cord homogenate
- 22.4% THC-A above LOD (100 pg/g)

Metz Obstet Gynecol 2018

WIC Survey of Marijuana Use

- Tricounty Health Department in CO surveyed women participating in Special Supplemental Nutrition Program for Women Infant and Children (WIC)
- Monthly caseload of 25,000 clients
- Convenience sample of approx. 1700 women

CDPHE, Monitoring Health Concerns Related to Marijuana in Colorado: 2014

Perceived Benefits WIC Survey

Reasons for Use	Ever Users (%, n)	Current Users (%, n)	Past Users (%, n)
Help with depression/anxiety/stress	35% (164)	63% (60)	28% (103)
Help with pain	29% (135)	60% (57)	21% (78)
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)

CDPHE, Monitoring Health Concerns Related to Marijuana in Colorado: 2014

Increasing Perceived Safety

- National Survey on Drug Use and Health data

	No past 30 day use, pregnant	No past 30 day use, non-pregnant	Past 30 day use, pregnant	Past 30 day use, non-pregnant
2005	3.5%	3.1%	25.8%	23.7%
2015	16.5%	14.8%	65.4%	62.6

Jarlenski et al 2017

Problems with Existing Studies

- Lack of quantification/timing of exposure
- Difficulty adjusting for tobacco, other drugs, sociodemographic factors
- Reliance on self-report
  - Shiono et al (1995) completed a prospective cohort study with structured interviews and maternal serum toxicology screens
  - 70% of women with positive THC on serum tox screen denied use in structured interview

Shiono Am J Obstet Gynecol 1995

CAMP Project

- Retrospective cohort adolescents with universal biological sampling
- Evaluated if MJ use associated with composite adverse pregnancy outcome
  - Stillbirth
  - Hypertensive disorders of pregnancy
  - Spontaneous preterm birth
  - Small for gestational age

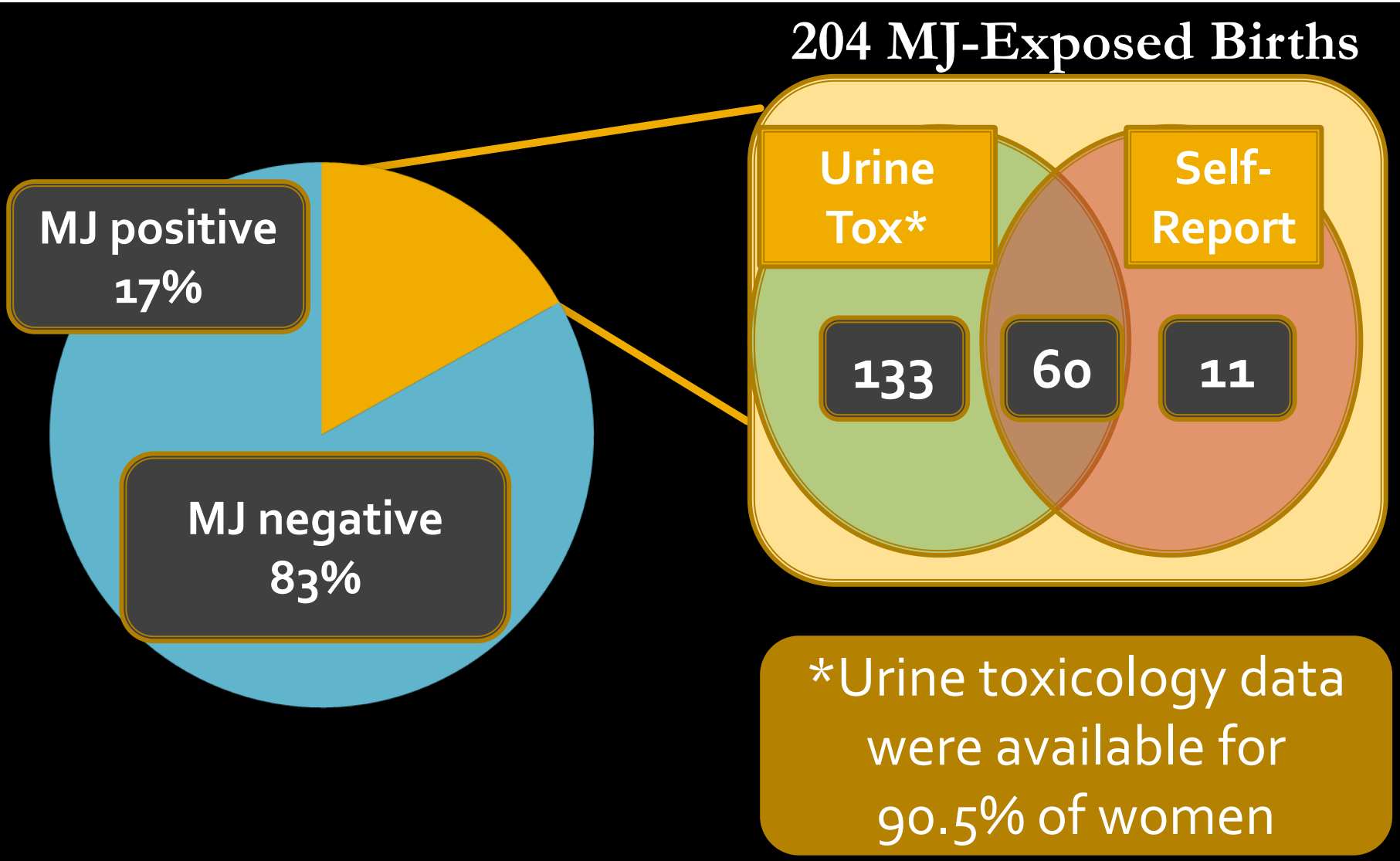
Rodriguez et al unpublished data

CAMP Project

- Marijuana exposure
  - Urine toxicology positive for MJ or
  - Self-reported use of MJ on uniformly administered questionnaire

Rodriguez et al unpublished data

MJ Exposure (N=1206)



Multivariable Modeling

- MJ use (utox or self-report) was associated with primary composite adverse outcome

aOR= 1.57 (95% CI 1.15-2.14)

- When modeled using self-report alone, MJ was not associated with primary outcome

aOR= 1.06 (95% CI 0.66-1.71)

- Preliminary evidence of dose response (>1 utox)

aOR= 3.75 (95% CI 1.59-8.85)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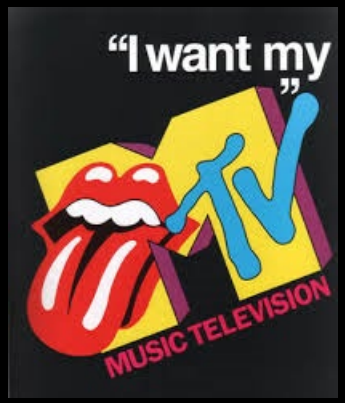
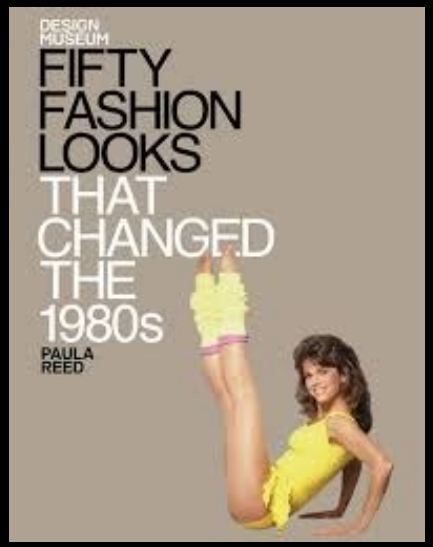

"I want my"
MTV
MUSIC TELEVISION


Top 10 Action Movies of the 1980s
PLAY


DESIGN MUSEUM
FIFTY FASHION LOOKS THAT CHANGED THE 1980s
PAULA REED

Fetal Growth Restriction

- DATA ARE MIXED
- Meta-analysis (English et al 1997) focused on association between marijuana exposure and birth weight
  - Women who consumed marijuana > 4 times per week had babies that weighed less than non-users by 131 grams on average
  - However, pooled odds ratio for low birth weight with any marijuana use was 1.09 (95% CI 0.94-1.27)

English Addiction 1997

Fetal Growth Restriction

- Generation R study assessed fetal growth by ultrasound
  - Fetuses exposed to cannabis in early pregnancy (n=214) grew 11.2 grams/week less than non-users
  - Fetuses exposed to cannabis throughout pregnancy (n=41) grew 14.4 grams/week less than non-users
- Only study using ultrasound to assess fetal growth rather than using neonatal birth weight

El Marroun J Am Acad Child Adolesc Psychiatry 2009

Preterm Birth

- DATA ARE MIXED
- Australian cohort (N=24,874) who self-reported MJ use at prenatal care intake
  - MJ use was associated with preterm birth (OR 1.5, 1.1-1.9)
- Second study ICD-10 codes for substance use
  - Increased incidence of preterm birth among MJ users (18.8% vs 5.8%)
- ALSPAC (N=12,129) preterm birth rate same among users and non-users (4.6% both groups)

Fergusson BJOG 2002, Hayatbakhsh Pediatr Res 2012, Burns Addiction 2006

Preterm Birth

- Only 31% of women with a positive serum screen self-reported marijuana use in a structured interview
- Conversely only 43% of women who self-reported use had a positive serum screen
- No association with PTB with self-report and/or serum screen positive
  - Serum positive for THC associated with PTB (OR 1.3, 95% CI 1.0-1.7)

Shiono et al Am J Obstet Gynecol 1995

Spontaneous Preterm Birth

- Saurel-Cubizolles (n=13,545)
  - 1% prevalence of use
  - Any marijuana use associated with SPTB (OR 2.15, 95% CI 1.10, 4.18)
- Dekker (n=3,184)
  - 7% marijuana-exposed by self-report in structured interviews
  - Pre-pregnancy use associated with SPTB with intact membranes (OR 2.34, 95% CI 1.22, 4.52)

Saurel-Cubizolles et al BJOG 2014, Dekker et al PLOS One 2012

Stillbirth

- DATA ARE LIMITED
- Case-control study by Stillbirth Collaborative Research Network
  - Association between stillbirth and marijuana use as demonstrated by cord homogenate positive for THC (OR 2.34, 95% CI 1.13-4.81)
  - Adjusting for cotinine in the maternal serum to account for tobacco use reduced the stillbirth OR for marijuana by approximately 10%

Varner Obstet Gynecol 2014

Congenital Anomalies

- DATA ARE LIMITED AND MIXED
- Linn et al 1983 found no association with major malformation (OR 1.36, 95% CI 0.97-1.91)
- Large retrospective cohort studies based on birth defects registries
  - Incomplete ascertainment of confounding factors
  - Potential for recall bias
- Currently not adequate evidence that marijuana exposure is associated with any specific congenital birth defect

Linn Am J Public Health 1983, Gibson Aust NZJ Obstet Gynaecol 1983

NICU Admission

- Warshak et al 2015 retrospective cohort
- N=6468 women
  - 6,107 non-users
  - 361 marijuana users (self-report or positive tox screen)
- Increased risk of NICU admission
  - 12.5% vs 17.2% (aOR 1.54, 95% CI 1.14-2.07)

Warshak et al J Perinatol 2015

Perinatal Outcomes Meta-Analysis

- Gunn et al conducted a systematic review and meta-analysis
  - Primary Outcomes: maternal, fetal or neonatal up to 6 weeks postpartum after cannabis exposure
  - Conducted meta-analyses when 3 or more studies available with same outcome (anemia, LBW, BW, neonatal length, NICU admission, GA at del, head circumference, PTB)
- Increased odds anemia, LBW, NICU admit
- More studies needed

Gunn et al BMC Open, 2016

Neonatal Outcomes: Meta-Analysis

- Conner et al performed systematic review and meta-analysis
- Aim: estimate if marijuana use increases risk of adverse neonatal outcomes
  - Primary outcomes: LBW (<2500gm), PTB (<37 wk)

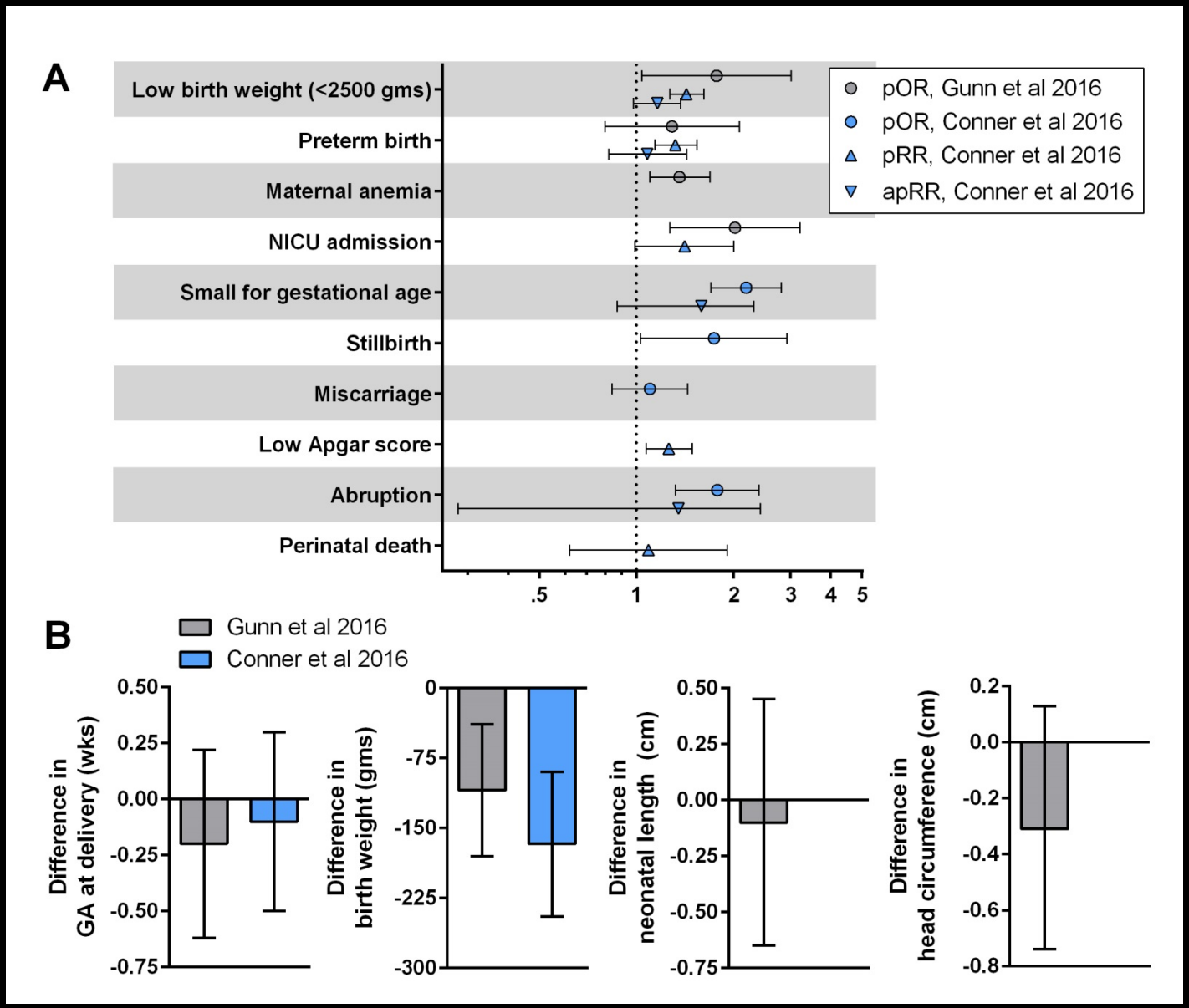
Conner et al Obstet Gynecol 2016

Neonatal Outcomes: Meta-Analysis

- 31 studies total (12 LBW, 14 PTB)
- Pooled unadjusted data demonstrated an association between THC and LBW/PTB
  - LBW (15.4% vs 10.4%, RR 1.43, 95% CI 1.27-1.62)
  - PTB (15.3% vs 9.6%, RR 1.32, 95% CI 1.14-1.54)
- After adjustment for tobacco and other confounders no longer an association
  - LBW (pooled RR 1.16, 95% CI 0.98-1.37)
  - PTB (pooled RR 1.08, 95% CI 0.82-1.43)

Conner et al Obstet Gynecol 2016

Summary Meta-Analyses



Metz and Borgelt Obstet Gynecol 2018

NASEM Report

- National Academies of Sciences, Engineering and Medicine
  - Health Effects of Cannabis and Cannabinoids
- Cannabis associated with lower BW
- Insufficient evidence to determine if there is an association between cannabis and other perinatal outcomes

https://www.nap.edu/initiative/committee-on-the-health-effects-of-marijuana-an-evidence-review-and-research-agenda

MAY 25, 2015

TIME

The Highly Divisive, Curiously Underfunded and Strangely Promising **World of Pot Science**

BY BRUCE BARCOTT & MICHAEL SCHERER

time.com

Neurodevelopment

- Alterations in neurotransmitters in rat models
  - Especially dopaminergic pathways
- Postmortem human fetal brains (elective terminations 17-22 weeks)
  - Dopamine receptors reduced in marijuana-exposed fetuses
  - Most prominent effect in males
  - Directly correlated with amount of marijuana used during pregnancy

Hurd YL et al Neurotoxicol Teratol 2005; Jutras Aswad et al Eur Arch Psychiatry Clin NeuroSci 2009

Prospective Longitudinal Studies

STUDY AND INVESTIGATOR	INITIATION DATE AND LOCATION	STUDY SIZE (N)	POPULATION
Ottawa Prenatal Prospective Study (OPPS), Fried et al	1978 Ottawa, 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 Pittsburgh, Pennsylvania	636	High-risk, mixed ethnicity (57% African American), single (71%), low socioeconomic status; Exposure to marijuana and alcohol
Generation R Study, Hoffman et al	2002 Rotterdam, Netherlands	9778	Multi-ethnic, higher socio-economic status

Drug Alcohol Depend 1980;5:415-24. Neurotoxicol Teratol 1998;20:293-306. Clin Perinatol 1991;18:77-91. Neurotoxicol 13:329-34. Paediatr Perinat Epidemiol 2004;18:61-72. Prog Neuropsychopharmacol Biol Psychiatry. 2014;52:45-52.

Neurodevelopment

- DATA ARE LIMITED BY CONFOUNDING
- OPPS
  - No differences between groups below age 4 years
  - At age 4 years, increased behavioral problems, worse language comprehension, decreased sustained attention and memory difficulties
- MHPCD
  - Decreased verbal reasoning at age 6 years
  - Worse academic performance at age 10 years
  - Increased substance use at age 14 years

Fried Life Sci 1995, Day Neurotoxicol Teratol 1994

Summary of Findings CDPHE

Moderate evidence	Limited evidence	Insufficient evidence	Mixed evidence
Decreased growth	Stillbirth	Psychosis symptoms	Preterm delivery
Decreased IQ scores in young children	SIDS (evidence of no association)	Initiation of future marijuana use	Decreased birth weight
Decreased cognitive function	Increased depression symptoms		Newborn behavior issues
Decreased academic ability	Delinquent behavior		Breastfeeding and infant motor development
Attention problems	Isolated simple ventricular septal defects		Birth defects, including NTD, gastroschisis
			Frequency of use during adolescence

Breastfeeding

- THC passes to the neonate in breastmilk
- Letter to the editor NEJM of two patients
  - Estimated exposure 0.8% of maternal exposure to one joint
  - Chronic heavy users up to 8x plasma

Perez-Reyes NEJM 1982

Breastfeeding

- Observational study of 8 women
  - Purchased product with known concentration of THC
  - Abstained from use for 24 hrs prior
  - Inhaled cannabis then collected breast milk at 20 minutes, 1, 2 and 4 hours
  - Exclusively breastfed infant ingests mean of 2.5% of maternal dose

Baker Obstet Gynecol 2018

Breastfeeding

- 54 samples from milk donors
- Delta-9-THC detectable 63% samples up to 6 days after last reported use
- Median concentration 9.47 ng/mL
- Number of daily uses and time from sample collection to analysis were predictors of THC concentration in breastmilk

Bertrand et al Pediatrics

Breastfeeding AAP Statement

- American Academy of Pediatrics (AAP) policy statement on "Breastfeeding and the Use of Human Milk"
  - Breastfeeding contraindicated in women using illicit drugs including marijuana

AAP. Breastfeeding and the Use of Human Milk. 2012; www.pediatrics.org/cgi/doi/10.1542/peds.2011-3552. Accessed April 30, 2015.

ACOG Committee Opinion

- Women should not use marijuana during pregnancy or while lactating
  - Ob-gyns should not prescribe for medicinal purposes to pregnant or lactating women
  - Insufficient evidence for effects on nursing infant

ACOG, Committee Opinion No. 637, Marijuana Use During Pregnancy and Lactation, Obstet Gynecol 2015

Guidelines for Providers

- colorado.gov/cdphe/marijuana-clinical-guidelines

CDPHE:
Talking about Marijuana with Patients

Marijuana Pregnancy and Breastfeeding Clinical Guidance

MARIJUANA PREGNANCY AND BREASTFEEDING GUIDANCE

FOR COLORADO HEALTH CARE PROVIDERS

March 2, 2015

SCREENING QUESTIONS

In addition to asking about alcohol, tobacco, and other drug use (including prescription drugs), now that marijuana is legal in Colorado, we recommend asking all teens and women who could become pregnant about marijuana use.

1. *Have you used marijuana in the last year?*

If no: Go to question 2

If yes: *When was the last time you used marijuana? How do you use marijuana? What form of marijuana do you use? How often do you use and how much?*

If pregnant: *How has your use of marijuana changed since finding out you are pregnant?*

If concerned about substance abuse: Use the Cannabis Use Disorder Identification Test (CUDIT) and referral recommendations found in the resources section.

2. *Does anyone use marijuana in your home?*

If yes or not: *It is important to ensure that your home is safe for your child. Make sure that any potentially harmful substances are out of reach of your child, including marijuana, alcohol, prescription drugs or household substances.*

If yes: Provide additional education on avoidance of secondhand smoke and safe storage, more information below.

TIPS FOR USING THIS GUIDANCE: All information in italics is scripted talking points to share with your patients, written at about a middle school reading level.

COLORADO

Department of Public Health & Environment

PRENATAL VISITS

It is important to reassess substance use at each visit, because many women continue using substances throughout the pregnancy or may begin or resume using substances during pregnancy.

Discuss importance of cessation of marijuana and other potentially harmful substances during pregnancy and breastfeeding and offer support if needed, found in the resource section.

Discuss patient's plan for marijuana use after pregnancy. *Tell me about whether you intend to use marijuana after delivering your baby.*

Discuss breastfeeding and marijuana: *Are you planning to breastfeed your child?* If yes, see breastfeeding section for more information.

Please inform your patient: *Marijuana is now legal for adults over 21. But this doesn't mean it is safe for pregnant moms or babies. Some hospitals test babies after birth for drugs. If your baby tests positive for THC at birth, Colorado law says child protective services must be notified.*

As a prenatal care provider, if you are concerned about a patient's substance use, you can recommend testing of mother during prenatal care and/or at delivery or testing of the newborn at birth.

Newborn testing information:

- Meconium testing generally identifies maternal marijuana use after 24 weeks gestation.
- Urine testing generally identifies maternal marijuana use after 32 weeks gestation.
- Umbilical cord testing generally identifies maternal marijuana use after 24 weeks gestation.

WELL WOMAN VISITS:

Discuss contraception options if patient wants to continue recreational or medical marijuana, alcohol or other substance use and/or does not desire pregnancy.

If patient desires a pregnancy, discuss importance of cessation of marijuana and other potentially harmful substances. Consider use of contraception while the patient is working towards cessation of substances.

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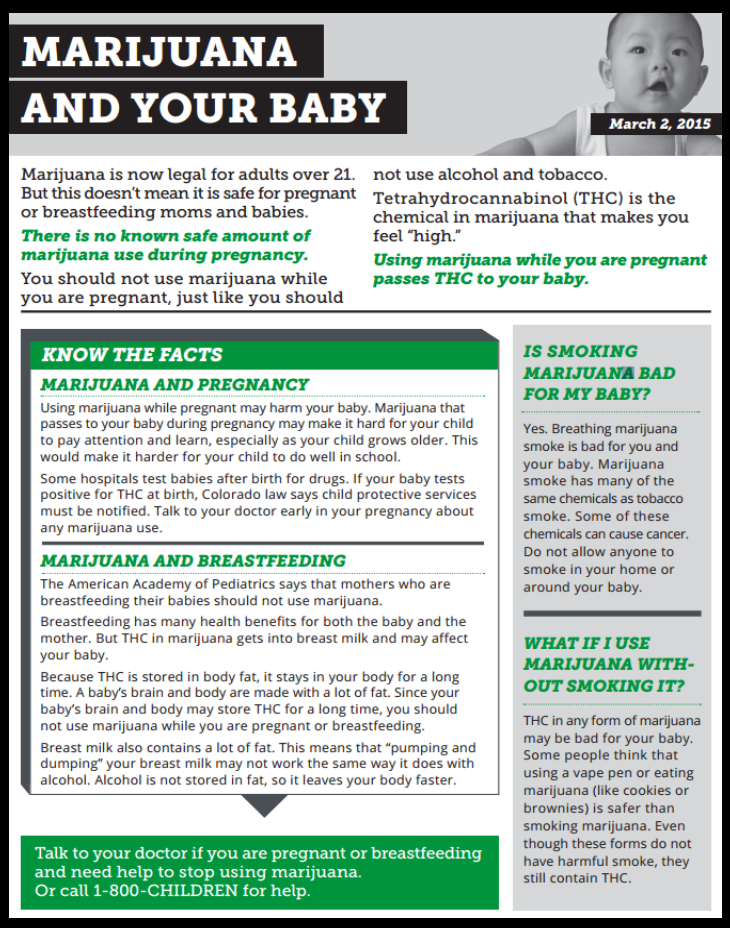
Marijuana and Your Baby Factsheet



MARIJUANA AND YOUR BABY

March 2, 2015

Marijuana is now legal for adults over 21. But this doesn't mean it is safe for pregnant or breastfeeding moms and babies.

There is no known safe amount of marijuana use during pregnancy.

You should not use marijuana while you are pregnant, just like you should not use alcohol and tobacco.

Tetrahydrocannabinol (THC) is the chemical in marijuana that makes you feel "high."

Using marijuana while you are pregnant passes THC to your baby.

KNOW THE FACTS

MARIJUANA AND PREGNANCY

Using marijuana while pregnant may harm your baby. Marijuana that passes to your baby during pregnancy may make it hard for your child to pay attention and learn, especially as your child grows older. This would make it harder for your child to do well in school.

Some hospitals test babies after birth for drugs. If your baby tests positive for THC at birth, Colorado law says child protective services must be notified. Talk to your doctor early in your pregnancy about any marijuana use.

MARIJUANA AND BREASTFEEDING

The American Academy of Pediatrics says that mothers who are breastfeeding their babies should not use marijuana.

Breastfeeding has many health benefits for both the baby and the mother. But THC in marijuana gets into breast milk and may affect your baby.

Because THC is stored in body fat, it stays in your body for a long time. 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 pregnant or breastfeeding.

Breast milk also contains a lot of fat. This means that "pumping and dumping" your breast milk may not work the same way it does with alcohol. Alcohol is not stored in fat, so it leaves your body faster.

Talk to your doctor if you are pregnant or breastfeeding and need help to stop using marijuana.
Or call 1-800-CHILDREN for help.

IS SMOKING MARIJUANA BAD FOR MY BABY?

Yes. Breathing marijuana smoke is bad for you and your baby. Marijuana smoke has many of the same chemicals as tobacco smoke. Some of these chemicals can cause cancer. Do not allow anyone to smoke in your home or around your baby.

WHAT IF I USE MARIJUANA WITHOUT SMOKING IT?

THC in any form of marijuana may be bad for your baby. Some people think that using a vape pen or eating marijuana (like cookies or brownies) is safer than smoking marijuana. Even though these forms do not have harmful smoke, they still contain THC.

What do we tell patients?

- No known benefits of marijuana use in pregnancy
- Possible risks of marijuana use in pregnancy
- Advise patients not to use marijuana during pregnancy
- No known “safe” amount of marijuana in pregnancy

Where do we go from here?

- More research needed
  - Biologic sampling critical
  - Timing and quantification of exposure
  - Additional areas of investigation
    - Congenital malformations
    - Maternal morbidity
    - Neonatal morbidity (NICU admission)

Grant Support

- CCTSI Child-Maternal Health Junior Pilot Program

- Women's Reproductive Health Research Scholar 5K12HD001271-18

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Thank you!