Cannabis use in pregnancy: Clinical and policy implications

NATIONAL MATERNAL AND INFANT NUTRITION INTENSIVE COURSE

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Conflict of Interest Disclosure

*I have no relationships, financial or otherwise, with any manufacturer or provider of any commercial product or service that relates to the topic of this presentation.*
1. What is cannabis?
2. What is the epidemiology of cannabis use in pregnant and reproductive-aged women?
3. What are hypothesized risks of cannabis use in pregnancy?
4. Does cannabis use cause adverse perinatal or child outcomes?
5. What are the policy implications of cannabis use in pregnancy?
6. How can we deliver high-quality prenatal and postpartum care to women who use cannabis amid scientific uncertainty?
1. What is cannabis?
**Cannabis**

**Cannabis sativa** plant contains cannabinoids, some of which have psychoactive properties.

**Marijuana**: American term for dried flowers and leaves of the plant.

**Hashish**: Resin product made by extracting cannabinoid-rich structures from the plant.
Psychoactive properties of cannabis - THC

- Delta-9-tetrahydrocannabinol (THC) is the primary psychoactive component (and best-understood cannabinoid)
- THC interacts with receptors CB1 and CB2
- Receptors are activated with exogenous cannabinoids (THC) and endogenous cannabinoids (anandamide)
- Experience of intoxication may include increased focus on sensory experience, reduced short-term memory, increased appetite
Other properties of cannabis - CBD

- Cannabidiol (CBD) is a second compound in cannabis
- CBD is not an intoxicant but may interact with THC
- CBD is hypothesized to have anti-psychotic effects
- Recent trial published in *NEJM* showed CBD to reduce convulsive seizures in children with Dravet syndrome, relative to placebo
2. What is the epidemiology of cannabis use in pregnant and reproductive-aged women?
Prevalence of marijuana use among women of reproductive age


Astirisk indicates past 2—12 month use defined as use in the past year but not in the past month.

Year-to-Year Prevalence of Past-Month Marijuana Use Among Pregnant and Nonpregnant Women, Overall and by Age, 2002-2014

From: Trends in Marijuana Use Among Pregnant and Nonpregnant Reproductive-Aged Women, 2002-2014
Marijuana use across trimesters of pregnancy

Cannabis use is much higher in certain subgroups

• Maryland: 29% of 369 pregnant patients self-disclosed or tested positive for marijuana use (Mark et al, 2016)
• Pittsburgh: 27% of 422 pregnant patients self-disclosed or tested positive for marijuana use (Chang et al, 2017)
• Among women with opioid use disorders, 32.4% of reproductive-aged women and 35.1% of pregnant women report past-month marijuana use (Jarlenski et al, 2017)
Time trends in perception of risk of cannabis use among reproductive-aged women

From the NSDUH, women ages 18-44y.

“How much do people risk harming themselves physically and in other ways when they smoke marijuana once or twice a week?”

“No Risk” ↑ 400%
“Slight Risk” ↑ 67%
“Great Risk” ↓ 37%
Times trends in perception of “no risk” of using marijuana once or twice a week, among women 18-44 y. Adjusted for age, race/ethnicity, and educational attainment. From the NSDUH.
Mode of cannabis consumption

• Possible mode of consumption:
  • Smoking (combustible inhalation)
  • Vaping (non-combustible inhalation)
  • Edible products
  • Transdermal products

• No published research to date on mode of consumption in pregnant women
Why do pregnant women use cannabis?

A Balm When You’re Expecting: Sometimes Pot Does the Trick

The New York Times

The New York Times reported this month that expectant mothers are taking marijuana in increasing numbers. We asked women who used marijuana during pregnancy to share their stories.
3. What are hypothesized risks of cannabis use in pregnancy?
THC rapidly crosses the placenta

- Animal models show:
  - THC rapidly crosses the placenta after dosing
  - Fetal clearance of THC is slow → Prolonged fetal exposure
  - This THC exposure may affect fetal development

Wu et al, *Future Neurol*, 2011
Cannabis use in pregnancy

Cannabinoids Endanger Fetal Development by Multiple Mechanisms

Inhibition or ingestion of Cannabis product

leads to

Prolonged elevation of serum cannabinoid concentration

resulting in

Embryological or fetal exposure to cannabinoids

Which alters:

- VEGF
- Folic Acid
- PCNA
- MAPK (ERK1/2/3)
- Cellular migration
- CHOP activation
- BDNF Pathway

Disrupting

Angiogenesis
- Neurogenesis
- Replication
- Cellular development
- Tissue differentiation
- Cellular processes
- Cognitive development

END RESULT

Miscarriage
- Low birth weight
- Developmental delay
- Birth defects
- Other unknown complications

Friedrich et al, BMC Pharmacol Toxicol, 2016
THC concentration in marijuana is increasing
4. Does cannabis use cause adverse perinatal or child outcomes?
### Cannabis use and links with adverse health outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Quality of data in humans</th>
<th>Strength of evidence for association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana dependence</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Fetal growth effects</td>
<td>Medium, but variable by study</td>
<td>Medium</td>
</tr>
<tr>
<td>Spontaneous preterm birth</td>
<td>Low</td>
<td>?</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>Low</td>
<td>?</td>
</tr>
<tr>
<td>Child cognitive function</td>
<td>Medium, but variable by study</td>
<td>Medium</td>
</tr>
</tbody>
</table>
Marijuana dependence

- An estimated 25%-30% of U.S. women who use marijuana meet criteria for abuse or dependence (similar estimates in men)
- Dependence estimates among users appear stable over time (Hasin et al, *JAMA Psychiatry*, 2015)
- 18.1% of U.S. pregnant women who use marijuana meet criteria for abuse or dependence (Ko et al, *AJOG*, 2015)
Women may progress more rapidly to cannabis dependence, relative to men.

Marijuana use is increasing in substance use treatment admissions among pregnant women.

FIGURE 1. Pregnancy and marijuana use among substance use treatment admissions, 1992-2012. Although the proportion of substance use treatment admissions for pregnant women remained stable from 1992 to 2012, admissions for pregnant women reporting marijuana use (any use or as the primary substance) increased over time.*Cochran-Armitage test for trend significant at \( P < 0.01 \).

Cannabis exposure and fetal growth

Fig. 1 Estimated growth curve and difference in fetal weight because of maternal cannabis use in pregnancy compared with fetuses of mothers who did not use cannabis or tobacco. Estimates of differences were obtained from fitting the fractional polynomial model, adjusted for maternal age, body mass index, height, educational level, national origin, first trimester alcohol use, parity, gravidity, fetal sex, and maternal psychopathology.

Cannabis exposure and neurobehavioral and cognitive effects

2 longitudinal studies in humans:

- Ottawa Prenatal Prospective Study (1978)
Cannabis exposure and neonatal and post-neonatal neurobehavior

• Neonates may have: sleep disturbances, altered responses to stimuli, tremors (Fried and Smith, Neurotoxicol Teratol, 2001)

• Children exposed to marijuana in the third trimester had decreased cognitive scores at 9 months of age, but no significant differences at 19 months of age (Richardson et al, Neurotoxicol Teratol, 1995)
Prenatal cannabis exposure independently predicts academic achievement at age 10

<table>
<thead>
<tr>
<th>First-trimester use</th>
<th>Group 1: none (n = 353)</th>
<th>Group 2: light/moderate (n = 166)</th>
<th>Group 3: heavy (n = 87)</th>
<th>P</th>
<th>Significant group differences at P = 0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reading recognition (WRAT)</td>
<td>95.5</td>
<td>94.9</td>
<td>89.9</td>
<td>0.009</td>
<td>1 and 3; 2 and 3</td>
</tr>
<tr>
<td>Spelling (WRAT)</td>
<td>94.4</td>
<td>94.9</td>
<td>90.1</td>
<td>0.03</td>
<td>1 and 3; 2 and 3</td>
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<tr>
<td>Mathematics (WRAT)</td>
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<td>90.7</td>
<td>85.7</td>
<td>0.01</td>
<td>1 and 3; 2 and 3</td>
</tr>
<tr>
<td>Reading comprehension (PIAT)</td>
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<td>93.6</td>
<td>89.0</td>
<td>0.001</td>
<td>1 and 3; 2 and 3</td>
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<tr>
<td>Teacher’s rating</td>
<td>3.1</td>
<td>3.1</td>
<td>2.6</td>
<td>0.008</td>
<td>1 and 3; 2 and 3</td>
</tr>
<tr>
<td>% Underachieving</td>
<td>9.9</td>
<td>10.2</td>
<td>12.6</td>
<td>0.7</td>
<td>1 and 3; 2 and 3</td>
</tr>
</tbody>
</table>

Relationship of prenatal marijuana exposure and maladjustment to adult roles may be mediated by early onset of marijuana use.
Cannabis use and spontaneous preterm birth

• Most prospective research has not found any association between cannabis exposure and spontaneous preterm birth

• However, most studies relied on self-report of marijuana use
  (Metz, Am J Obstet Gynecol, 2015)
Cannabis use while breastfeeding

- THC can be passed via breastmilk to infants
- Scarce data on effects of THC in breastmilk on child health
Limitations to drawing causal inference

- Not able to randomize women to cannabis exposure (selection bias)
- Imperfect measurement of THC exposure (misclassification)
- Cannabis is not a standardized product (imprecision)
5. What are the policy implications of cannabis use during pregnancy?
57% of births are in states permitting medical or recreational marijuana use. Proportion of births calculated from 2014 vital statistics data. State law data from the National Conference on State Legislatures.
Mandatory reporting and legal consequences

- Federal law requires states to have “mandatory reporting” policies and procedures to:
  - Require health care providers to report to child protective services infants “born with and identified as being affected by substance abuse or withdrawal symptoms resulting from prenatal drug exposure, or a Fetal Alcohol Spectrum Disorder”
  - Develop a “plan of safe care” for such infants, including health and substance use disorder treatment needs of the infant and “affected family or caregiver”

42 USC 5106a
Example: Minnesota law

Minn. Stat. § 626.5562 (2015)

626.5562 TOXICOLOGY TESTS REQUIRED

Subdivision 1. Test; report. -- A physician shall administer a toxicology test to a pregnant woman under the physician's care or to a woman under the physician's care within eight hours after delivery to determine whether there is evidence that she has ingested a controlled substance, if the woman has obstetrical complications that are a medical indication of possible use of a controlled substance for a nonmedical purpose. If the test results are positive, the physician shall report the results under section 626.5561. A negative test result does not eliminate the obligation to report under section 626.5561, if other evidence gives the physician reason to believe the patient has used a controlled substance for a nonmedical purpose.

Subd. 2. Newborns. -- A physician shall administer to each newborn infant born under the physician's care a toxicology test to determine whether there is evidence of prenatal exposure to a controlled substance, if the physician has reason to believe based on a medical assessment of the mother or the infant that the mother used a controlled substance for a nonmedical purpose during the pregnancy. If the test results are positive, the physician shall report the results as neglect under section 626.556. A negative test result does not eliminate the obligation to report under section 626.556 if other medical evidence of prenatal exposure to a controlled substance is present.

Subd. 3. Report to Department of Health. -- Physicians shall report to the Department of Health the results of tests performed under subdivisions 1 and 2. A report shall be made on the certificate of live birth medical supplement or the report of fetal death medical supplement filed on or after February 1, 1991. The reports are medical data under section 13.384.
Criminal prosecution for prenatal cannabis use varies

Metro woman arrested after caught smoking marijuana in vehicle with three-week-old baby

DEL CITY, Okla. - A metro woman is behind bars after getting caught smoking marijuana with her infant in the car.

What caught the officer’s attention first was Ashley Robertson’s speeding through a school zone.

Alcohol is not suspected to be involved, however, with the woman in custody.

The 25-year-old was driving a 2007 Hyundai Elantra when police said they requested a catalytic converter to look into.

Robertson’s three-week-old baby was in the car, authorities said.

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“The use of the legal system to address perinatal alcohol and substance abuse is inappropriate. [Providers] should be aware of the reporting requirements... within their states. They are encouraged to work with state legislators to retract legislation that punishes women for substance abuse during pregnancy.”

ACOG Committee Opinion #473, 2011
6. How can we deliver high-quality prenatal and postpartum care to women who use cannabis?
What happens in prenatal care for women who use cannabis?

48% of prenatal visits with patient disclosure had no counseling

<table>
<thead>
<tr>
<th>Domain</th>
<th>Definition and Example</th>
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</table>
| No counseling   | No health care provider response to patient’s marijuana use or disclosure; health care provider may assess last use if patient quit since confirming pregnancy but offers no information or counseling regarding marijuana use.  
Example: OB: Any smoking, drinking, or drugs? PT: I smoked marijuana a month ago to 2 months ago. OB: And how much did you used to smoke? PT: Marijuana? OB: No, cigarettes. PT: Ah a pack would last me for 2 weeks. OB: Alright Ms. X. So again it is your first time seeing us, um, so we are going to do a number of tests that we do for everybody on their first pregnancy visit. |
| Punitive        | Counseling focused on the legal ramifications of patient’s marijuana use; patient warned child protective services will be contacted or informing patient that urine drug screening will be performed (at visit; at delivery).  
Example: OB: Um, the issue with marijuana specifically is just that it is illegal. So at the time of delivery, they will do a urine drug test because you have a history of using it. If it is positive, at the time of delivery, they will often have you, like force you to talk to the child protective services because it is a risk factor. |
| Medical         | Counseling focused on medical risks of marijuana use such as comparing the negative outcomes of smoking tobacco (small gestational age, preterm birth, asthma); includes discussions regarding nausea and suggestions of using or prescribing medications for nausea in place of marijuana.  
Example: OB: We do know it can affect size of the babies and things like that. And we want your baby to develop as healthy as possible. And you know how it alters your mind when you have it, how it makes you feel, so think about what it is doing to the baby that is not even formed quite yet. It gets the effects as well. And we don’t want to do that to the baby. |
| Helpful and supportive | Counseling included offering resources such as social work or counseling referrals, providing encouragement and support to quit; health care provider notes intention to follow-up with patient on quit efforts.  
Example: OB: If you find yourself in a position where you feel like you can’t stop using...there are lots of avenues that we can help you explore...keep you clean and sober...So let us know if there is anything we can do to help. |
| Unclear         | Counseling is not specific, health care provider expressed uncertainty of effects of marijuana use during pregnancy, patients advised to quit without providing information on risks or other educational information.  
Example: OB: Ok, so our goal is to keep you off of everything during pregnancy. |

Perspectives from physicians, nurse midwives, and nurse practitioners

“We always talk about methadone and problems with [opiate] use in pregnancy ....I mean, outcomes [for marijuana use during pregnancy] are not as important. There are no syndromes caused by marijuana that we know of. It doesn’t affect the pregnancy, health outcomes the same way [as other drugs].”

“I don’t think we really know what marijuana does in pregnancy. So I think that’s a harder one to counsel people about.”

“[Using marijuana during pregnancy] is particularly bad for you socially because now that we know [about your use], you definitely have to get a urine drug test when you deliver your baby. If you test positive, then social services has to get involved and talk to you about the safety of your baby at home. So it is really important that you know that this is going to happen....”

Holland et al. *Pat Educ Counsel*, 2016
Clinical Guidelines: ACOG

• “Before pregnancy and in early pregnancy, all women should be asked about their use of tobacco, alcohol, and other drugs, including marijuana and other medications used for nonmedical reasons.

• Women reporting marijuana use should be counseled about concerns regarding potential adverse health consequences of continued use during pregnancy.

• Women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use.

• Pregnant women or women contemplating pregnancy should be encouraged to discontinue use of marijuana for medicinal purposes in favor of an alternative therapy for which there are better pregnancy-specific safety data.”
Disagreement about universal screening

Screening women for marijuana use does more harm than good

TO THE EDITORS: We read with great interest the report by Ko et al., exploring the prevalence of marijuana use among pregnant and nonpregnant women. Clearly this is a timely issue in light of the recent changes to marijuana laws in several states. Based on the data collected from several years of the National Surveys on Drug Use and Health, the manuscript suggests that women who are pregnant or are at risk of becoming pregnant should be screened for marijuana use. Given the far-reaching implications of this suggestion and the limited data reported in the current article, we believed that at least 3 issues warranted further discussion.

Universal screening of women of reproductive age for marijuana use seems unnecessarily invasive and sexist. We recognize that marijuana use, or other drug use, during pregnancy should be discouraged, but the current database does not reveal marijuana-associated fetal teratogenicity, highlighting the unjustified nature of the above proposal. Moreover, only women are proposed to be screened for marijuana use, which will uniquely expose them to legal consequences in regions in which the drug is banned.

This concern becomes even more pressing when one considers the impact of racial discrimination in the enforcement of drug laws. Black people are about 4 times more likely to be arrested for marijuana possession than their white counterparts, despite the fact that both races used the drug at similar rates. In other words, black women can expect to bear the brunt of the consequences that may follow.

Another concern is that the percentage of pregnant women who reported marijuana use is artificially inflated. Women were asked whether they were pregnant at the time of the survey; they were also asked whether they had used marijuana in the past 2–12 months. If they answered yes to both questions, then they were grouped as using marijuana during pregnancy. Because pregnancy duration is shorter than 12 months and because marijuana use could have occurred prior to becoming pregnant, it is inaccurate to refer to such women as reporting marijuana during pregnancy.

In the end, in our view the proposal to screen women for marijuana use does more harm than the drug itself, and we hope that in the future greater consideration will be given to the potential negative unintended consequences of drug policy recommendations.

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Obstet Gynecol, 2015
Treatment for marijuana dependence

• Treatment of co-occurring psychiatric disorder
• Cognitive behavioral therapy
• Motivational enhancement therapy
• Contingency management
• *No medications currently approved for use to treat marijuana dependence*

Breastfeeding Guidelines

• American Academy of Pediatrics: “…[C]annabis can be detected in human milk, and …use by breastfeeding mothers is of concern, particularly with regard to the infant’s long-term neurobehavioral development and thus [is] contraindicated.”

• Academy of Breastfeeding Medicine: “At this time, although the data are not strong enough to recommend not breastfeeding with any marijuana use, we urge caution… A recommendation of abstaining from any marijuana use is warranted.”
Considerations for screening in prenatal care

• Universal screening for marijuana and/or other substances?
• If yes, urine toxicology or questionnaire?
• Informed consent process for urine toxicology?
• What treatment resources are available for women with dependence?
• What are state legal requirements or hospital protocols?
Few public health departments publish information about cannabis use in pregnancy

Figure 1. Frequency of specific content items in public health agency websites pertaining to perinatal marijuana use. Data based on Internet searches conducted in February 2016 of public health agencies for 50 states and the District of Columbia, and 5 federal public health agencies.

Communications from Colorado and CDC

What You Need to Know About Marijuana Use and Pregnancy

Fast Facts
- Using marijuana during pregnancy may increase your baby's risk of developmental problems.1-7
- About one in 25 women in the U.S. reports using marijuana while pregnant.8
- The chemicals in any form of marijuana may be bad for your baby – this includes edible marijuana products (such as cookies, brownies, or candies).9
- If you’re using marijuana and are pregnant or are planning to become pregnant, talk to your doctor.

Marijuana use during pregnancy can be harmful to your baby’s health. The chemicals in marijuana (in particular, tetrahydrocannabinol or THC) pass through your system to your baby and can negatively affect your baby’s development.2-7

Can using marijuana during my pregnancy negatively impact my baby after birth?
- Research shows marijuana use during pregnancy may make it hard for your child to pay attention or to learn, these issues may only become noticeable as your child grows older.1-7

Does using marijuana affect breastfeeding?
- Chemicals from marijuana can be passed to your baby through breast milk. THC is stored in fat and is slowly released over time, meaning an infant could be exposed for a longer period of time.
- However, data on the effects of marijuana exposure to the infant through breastfeeding are limited and conflicting.
- To limit potential risk to the infant, breastfeeding mothers should reduce or avoid marijuana use.5,14-16

For more information, visit:
Cannabis use in pregnancy

Summary

• Cannabis use is not rare and is increasing among reproductive-aged and pregnant U.S. women
• One-third of women who use cannabis have dependence
• Cannabis exposure is associated with restricted fetal growth
• Cannabis exposure is associated with neurobehavioral effects in children
• Little is known about effects of cannabis use while breastfeeding
• Screening for cannabis use and dependence should be informed by treatment options and knowledge of legal consequences
Thank you!

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References to accompany: “Cannabis use in pregnancy: Clinical and policy implications.”
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Recommended Summary Readings:


Selected Clinical Guidelines:


Recent Literature Reviews and Systematic Reviews:

Other peer-reviewed studies:


