

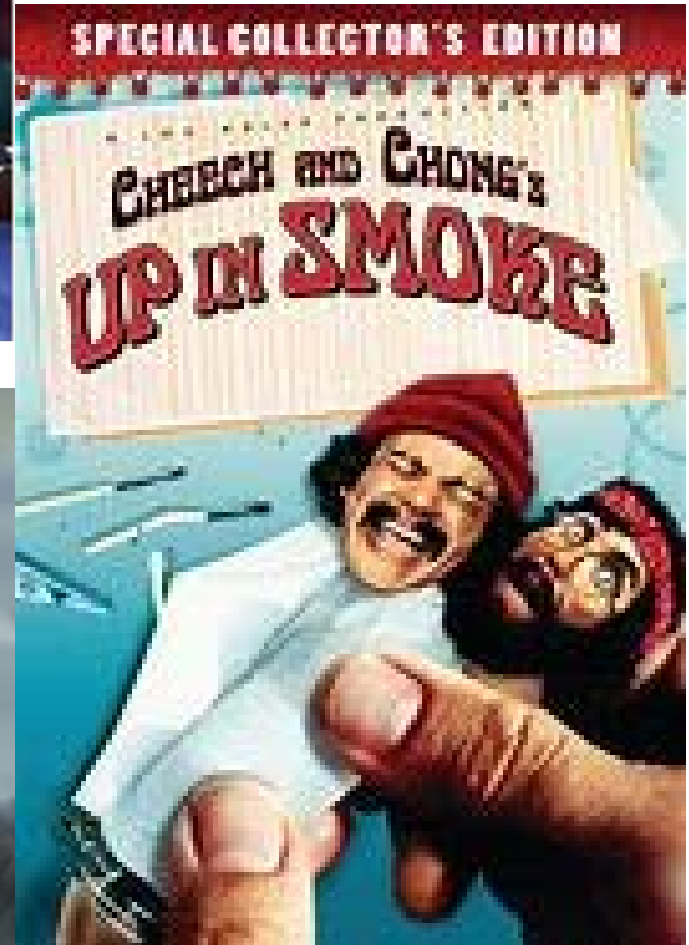


Cannabis and Pregnancy: Up in Smoke?

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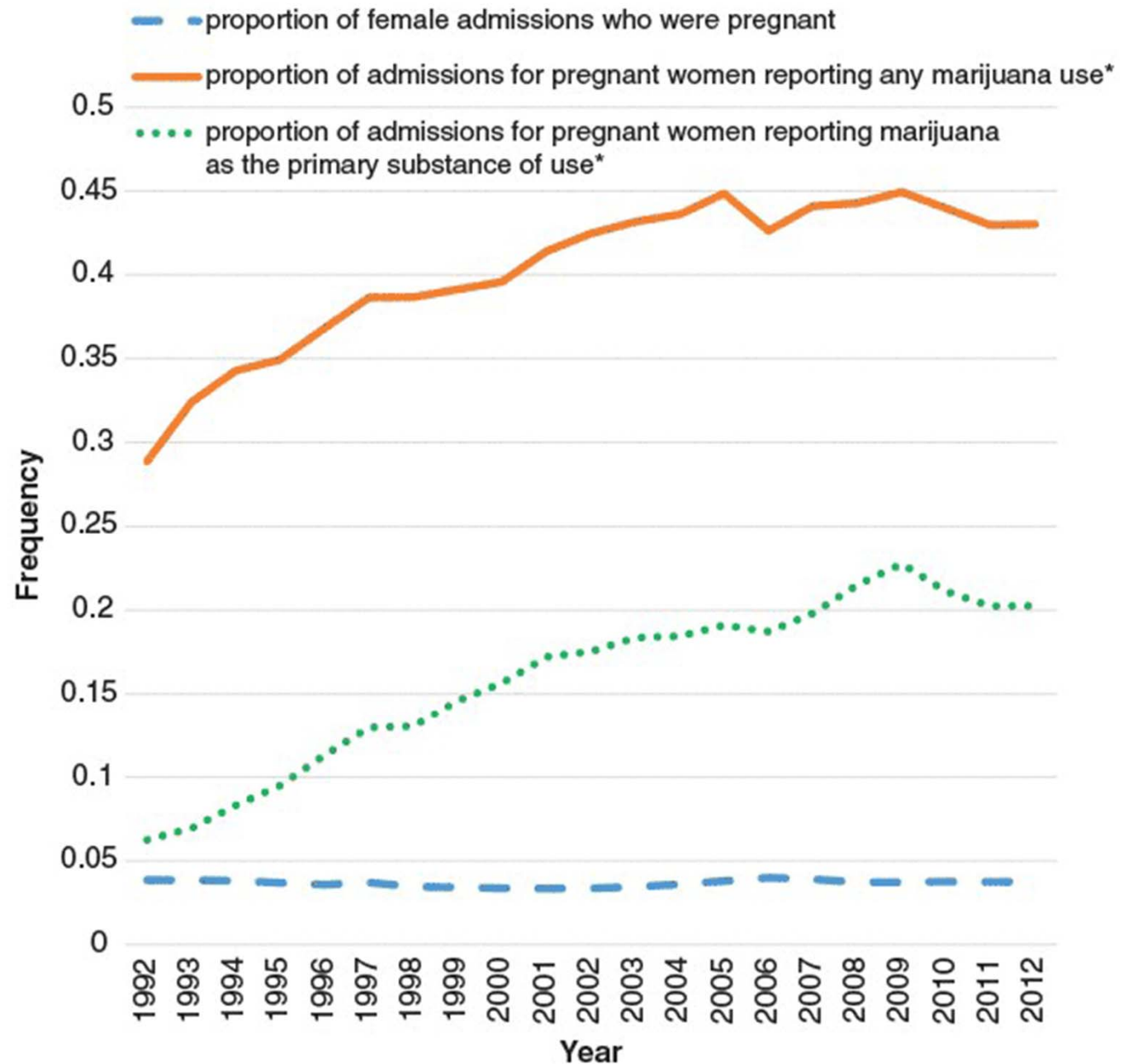
Chief Scientific Officer

The Society of Obstetricians and Gynaecologists of Canada



Pregnancy and Marijuana Use Among Substance Use Treatment Admissions (USA 1992-2012)

- *Substance use treatment* for pregnant women remained stable (4%)
- Pregnant women reporting *marijuana use* increased (29-43%)
- Pregnant women reporting marijuana as *primary substance of use* increased (6% - 20%)





Approximately 70% of both pregnant and nonpregnant women believe there is slight or no risk of harm from using marijuana once or twice a week

- *It's natural!*
- *It's organic!*
- *It's vegan!*
- *It helps with nausea!*





AUTOFLOWERING SEEDS

FEMINIZED SEEDS

CBD SEEDS

MORE RQS

ly for your body because you are
Type to search
Item(s) - € 0.00
use of alcohol,
tobacco and even coffee is frowned upon.

CATEGORIES

- Cannabis Blog
- Cannabis Strains
- Growing Cannabis
- Medical Marijuana
- More

♡ 22 💬 1 2 May 2014

Medical marijuana is an entirely different factor that researchers have tried to study for many years. Marijuana is simply a plant cultivated for hundreds of years. Even with hybrid varieties grown everyday, medical marijuana is not laced with any drugs or chemicals, unlike harmful cigarettes or alcohol. Should you use cannabis during pregnancy? Negative stigma and skewed results in unrelated experiments often scare people away from the benefits of medical marijuana during pregnancy

The Uniqueness of the Prenatal Period

- Prenatal period plays a fundamental role of the future prospective of a child, by shaping development from pre-conception, through pregnancy and onwards
- Identification of Fetal Alcohol Syndrome (FAS) was an important milestone in bringing the behavioral teratological approach to human studies.
 - Exposure to agents that are relatively harmless to the mother may have adverse effects on the developing fetus
 - The CNS is vulnerable to injury from fetal life and all aspects of CNS development may be affected.
 - Do not always result in CNS malformations, but there may be functional abnormalities that may not be evident at birth

Fetal Programming

- The field is heavily steered by Barker's work that explored associations between prenatal environmental events, birth outcome and postnatal development - *fetal programming*
 - DOHaD researchers have broadened their interest towards mental health
- Increasing use of cannabinoids during the last decades has raised questions about their effects on the mother and developing fetus

Cannabis, Pregnancy and the Fetus

- The potential deleterious effects of cannabis consumption for fertility and pregnancy outcome has been recognized for years....
- The main psychoactive molecule of cannabis, $\Delta(9)$ -tetrahydrocannabinol (THC) is able to cross the placenta and accumulate in fetal tissue and maternal milk



So what's the deal with effects of cannabis use during pregnancy?



What has the Preclinical and Clinical Research Shown?

- Alterations in fetal growth
- Low birth weight/IUGR
- Preterm labor
- Altered growth trajectories
- Neurodevelopmental impacts (structural and functional)
- Short and long-term neurobehavioural impacts
- Congenital malformations
- Compromised placental efficiency
- Pre-disposure to diseases later in life (DOHaD)
- Sex differences

Cannabis Prevalence During Pregnancy

- Cannabis is the most commonly used illicit drug in pregnant women, with prevalence rates ranging between 3 and 25% in Western countries
- Often used with tobacco

How might Cannabis Affect Pregnancy?

- CB1 receptor mRNA has been found in the uterus, and the crucial role of this receptor in the normal onset of labor has been also suggested
 - THC-mediated cell migration ability was decreased in preterm labor derived cells
- Cannabinoid receptors found in the human placenta
 - Cannabinoid exposure may be able to affect placental functioning
- Mouse models found that there was significantly less maternal weight gain, smaller babies, shortened gestation

Cannabis Effects on Pregnancy

The Placenta!

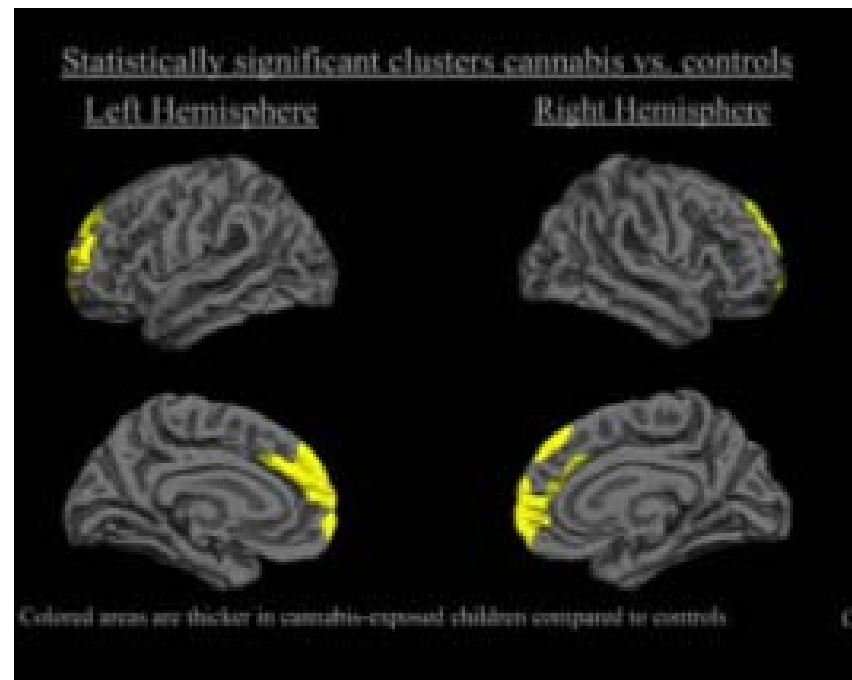
- THC inhibited the migration of human amniotic epithelial cell through the regulation of MMP2 and MMP9, which in turn altered the development of the amnion during the gestation and partially resulted in preterm labor and other adverse pregnancy outcomes.

How might Cannabis Affect the Developing Fetus?

- Expression of cannabinoid CB1 and CB2 receptors' messenger RNA (mRNA) has been detected as early as the preimplantation period in the embryonal mouse and human term placenta
- Prenatal cannabis exposure associated with an increased fetal pulsatility index and resistance index of the uterine artery, suggesting increased placental resistance during pregnancy
- Smaller inner diameter of the aorta in cannabis-exposed fetuses
- In the fetal brain, cannabinoid CB1 and CB2 receptors are present from early developmental stages
 - There is evidence that the endocannabinoid system has a central signaling role in brain development
 - Could account for some of the executive functioning effects in humans
- Exposure to exogenous cannabinoids during a precisely timed fetal brain developmental trajectory may, in theory, impact the normal developmental course, and lead to adverse outcomes
- Data on whether prenatal cannabis exposure alters the structural or molecular human fetal brain are scarce, though some preclinical evidence can be found

Brain Morphology

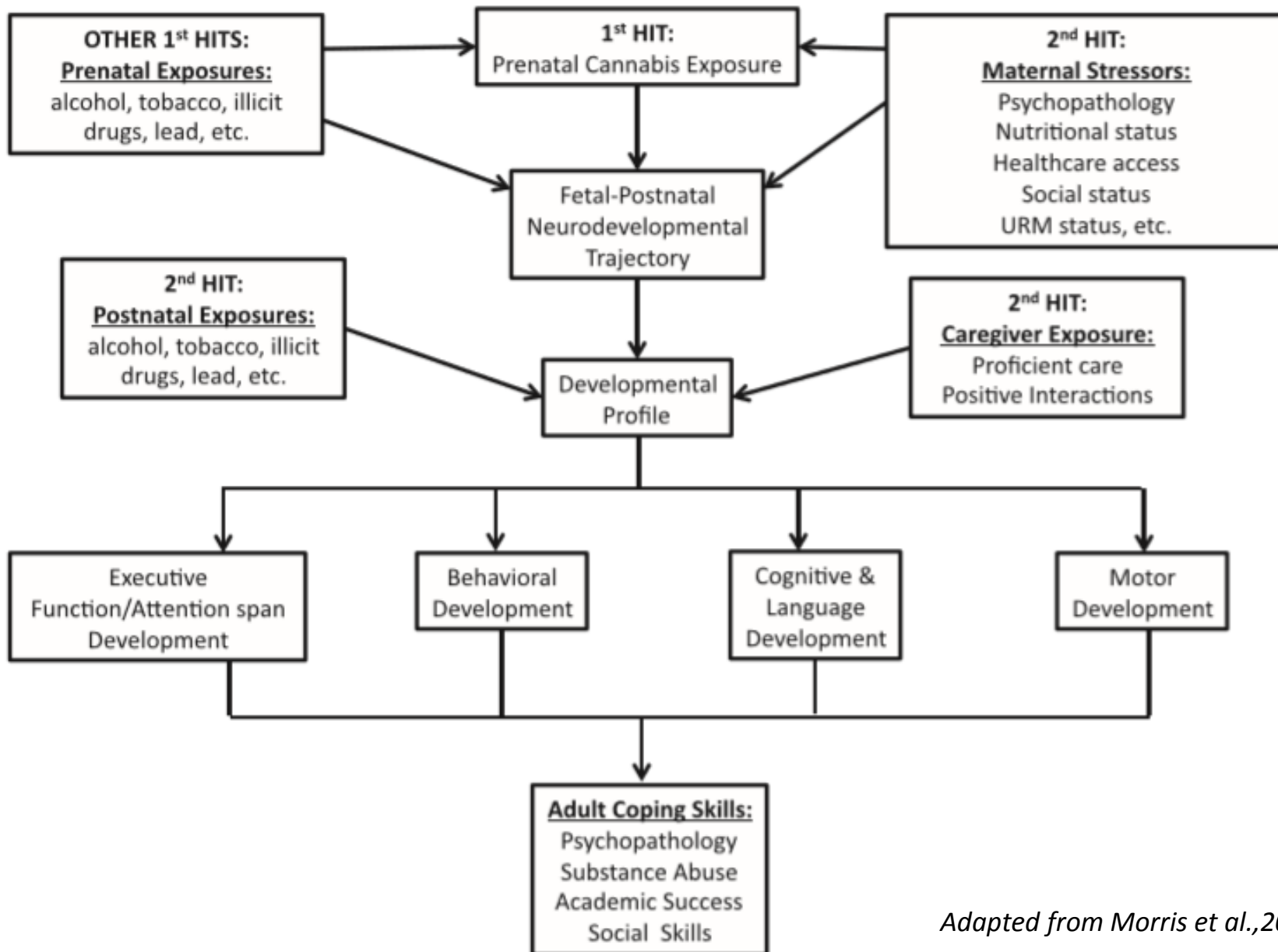
- Association between prenatal cannabis exposure and cortical thickness (nicotine makes it worse!)



- Altered Neurodevelopmental maturation

The “Double Hit” Potential

- First “hit” prenatally to endogenous endocannabinoid signalling system
 - DOHaD
 - CV implications
- Second “hit” post-natally
 - Increased susceptibility to environmental stressors, nutrition, social determinants etc
 - Epigenetics



Adapted from Morris et al., 2011

Cannabis and Prenatal Exposure

- Longitudinal studies suggest that prenatal cannabis exposure has both short and long-term consequences
 - Aberrant behavior in newborns
 - Cognitive deficits
 - Impairments in inhibitory control
 - Delinquency
 - Increased risk of drug abuse later in life
 - Interference with endocannabinoid system and synaptic pruning

What's the Problem with the Research?

- Very difficult to control for concurrent maternal tobacco smoking
- Impact of social determinants of health hard to quantify
- THC levels in cannabis not standard
- Self-report data difficult
 - Quantification, timing of exposure, dose response
- RCTs impossible
- What's our baseline?



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The \$1,000,000 Questions...

What effects—if any—does marijuana use during pregnancy have on the fetus or child?

- Marijuana use during pregnancy is associated with clinically unimportant lower birth weights (growth differences of approximately 100 g), but no differences in preterm births or congenital anomalies
 - (strength of recommendation [SOR]: B, prospective and retrospective cohort studies with methodologic flaws).

What effects—if any—does marijuana use during pregnancy have on the fetus or child?

- Prenatal marijuana exposure isn't associated with differences in neurodevelopmental outcomes (behavior problems, intellect, visual perception, language, or sustained attention and memory tasks) at birth, in the neonatal period, or in childhood through age 3 years.
- May be associated with minimally lower verbal/quantitative IQ scores (1%) at age 6 years and increased impulsivity and hyperactivity (1%) at 10 years.
- Prenatal use isn't linked to increased substance use at age 14 years
 - (SOR: B, conflicting long-term prospective and retrospective cohort studies with methodologic flaws).



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The effects are unclear. But
there is potential....

Anything is possible....good science will bring the
evidence.

So What?

- Prenatal cannabis exposure may have selective deleterious consequences on executive functions/higher cognitive abilities
- Like EtOH may not be evident until later in life
- Like EtOH, may be life-long
- Like EtOH, this may be an “invisible disability”
- Like EtOH, there may be structural and functional impacts



THE SOCIETY OF
OBSTETRICIANS AND
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— OF CANADA —

May 9th, 2017

SOGC Position Statement: Marijuana Use during Pregnancy

Cannabis (*marijuana*) is the most commonly used illicit drug among pregnant women. Legalization of cannabis in Canada may reinforce the reputation of cannabis being a harmless drug and result in an increase of use among pregnant women.

Evidence-based data has shown that cannabis use during pregnancy can adversely affect the growth and development of the baby, and lead to long-term learning and behavioural consequences. There have been sufficient studies with comparable results, showing that cannabis use during pregnancy raises concerns of impaired neurodevelopment of the fetus, in addition to the adverse health consequences related to maternal and fetal exposure to the effects of smoking. Pregnancy is a critical time for the brain development of the baby and the adverse effects caused by cannabis exposure can be life-long.

The SOGC recommends that women who are pregnant or contemplating pregnancy should abstain from cannabis use during pregnancy.

The SOGC also Recommends That...

- Health professionals discuss the potential adverse health effects of cannabis use during pregnancy with patients who are pregnant or contemplating pregnancy.
- Women who are pregnant or contemplating pregnancy be encouraged to discontinue cannabis use.
- Use of cannabis for medicinal purposes be strongly discouraged during pregnancy, in favor of alternative therapies that have proven to be safe during pregnancy.
- Women be encouraged to abstain from cannabis use during lactation and breastfeeding.
- Further research be undertaken on the effects of cannabis on pregnancy and lactation.
- Public education be funded and made widely available to ensure that those who are pregnant or contemplating pregnancy are aware of the risks posed by cannabis.

What about Breastfeeding?

- Human and animal data have reported decreased prolactin levels as well as potential maternal psychological changes.
- Animal and human studies have reported transfer into milk; levels were detected in animal offspring, and metabolites were excreted by both human and animal offspring.

ACOG's Recommendation

- There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged

We have a lot of work to do!

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Thank you!