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EVIDENCE BRIEF

Health Effects of Cannabis Exposure in Pregnancy and Breastfeeding

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Key Messages

- There is very limited evidence on the impact of cannabis use in preconception, pregnancy and breastfeeding on neonatal, behavioural and neurocognitive outcomes in early life.
- There is inconsistent evidence on the effects of cannabis exposure on health outcomes such as low birth weight and preterm delivery, depending on the ability to control for tobacco use.
- Main limitations of the current evidence include: relatively few studies on humans, poor control for concurrent exposures including alcohol and tobacco, as well as other potential confounders and lack of consistent and accurate measures of cannabis exposure.
- Guidelines recommend routine screening, providing comprehensive care, counselling on the risks of substance use and encouraging breastfeeding unless risks outweigh benefits.

Background

Cannabis is the term used to refer to the cannabis plant, *Cannabis sativa*, and its products.[1] It contains the compound delta-9-tetrahydrocannabinol (THC), the main psychoactive component which produces a number of effects, such as euphoria and changes in perception following inhalation or ingestion.[2,3] Cannabis is the most frequently used substance worldwide, aside from alcohol and tobacco.[4] In the United States, 24 states and Washington DC have passed legislation permitting medical use of cannabis; eight of those states have also legalized cannabis for non-medical use.[5] Medical use of cannabis has been legal in Canada since 2001,[6] non-medical use of cannabis became legal in fall 2018.

Cannabis Legalization

In June 2018, the Government of Canada passed legislation to legalize recreational cannabis as of October 17, 2018. In its *Final Report* (submitted November, 2016), the Government's Task Force on Cannabis Legalization and Regulation proposed a regulatory framework that aims to limit access and minimize cannabis-related harms.[7] First among its stated objectives is the protection of children and youth, who may be particularly susceptible to the neurodevelopmental effects of cannabis.

Prevalence of Cannabis Use in Preconception, Pregnancy and Breastfeeding

According to the 2015 Canadian Tobacco, Alcohol and Drugs Survey (CTADS), 13% of Ontario adolescents and adults reported using cannabis in the past year and 45% reported using it at least once in their lifetime.[8] Young adults (age 20-24 years old) were most likely to report using cannabis, with 30% reporting that they had used it in the past year. The 2015 prevalence of cannabis use increased among all females from 7% in 2013 to 10% in 2015.[8] As almost half of pregnancies are unplanned[9,10] and many women do not realize they are pregnant until the fifth week of gestation,[11] some women who wish to avoid cannabis use during pregnancy may not be able to do so. The 2009 Canadian Maternity Experiences Survey showed approximately 7% of women reported non-medical street drug use in the three months before pregnancy.[12]

Cannabis is the most frequently used substance in pregnancy, aside from tobacco and alcohol.[13,14] The 2009 Canadian Maternity Experiences Survey showed 1% of women reported using cannabis during pregnancy;[12] however, further Canadian data on the use of cannabis in pregnancy is limited. In the United States, the 2016 National Survey on Drug Use and Health (NSDUH) estimated past month cannabis use in all pregnant women 15-44 years is approximately 4.9%.[15] One study using NSDUH data showed a 62% increase in cannabis use in pregnant women 18-44 years, from 2.4% in 2002 to 3.9% in 2014.[16] Estimates of cannabis use at any time during pregnancy depend upon the population studied. For example, prevalence can range between 1.0% in the general population to 28% in women who reported using drugs at least once during the pregnancy.[17] Higher rates of cannabis use have been reported in women who are 18 to 25 years, unmarried or have a lower income.[18] Although past-month cannabis use has been reported to be highest among those in their first trimester (7.4%) and lowest

among those in their third trimester (1.8%),[18] one study reported substance use rebounds in the three months postpartum.[19]

There are minimal data on the prevalence of cannabis use during the lactation period. One recent study from Colorado, a state with legalized cannabis for medical and non-medical use, estimated 5% of mothers who reported ever breastfeeding, also reported using cannabis in the postpartum period.[20] This estimate was similar to the reported use any time during pregnancy of 5.7%. Cannabis use in pregnancy has not been shown to affect likeliness to breastfeed; however, prenatal and postnatal uses of cannabis were both associated with shorter breastfeeding duration.[20]

There is concern that legalization of non-medical use will lead to social normalization and low perceived risk of harms.[21] Women have reported using cannabis during pregnancy to alleviate nausea in the first trimester. One Canadian survey found 77% of medicinal cannabis use during pregnancy was related to nausea.[22] This use may reflect advice provided by sellers. A survey of cannabis retail outlets in Colorado found 69% recommended cannabis products for "morning sickness" and 36% endorsed the safety of cannabis products during pregnancy.[23]

Potential Adverse Outcomes of Cannabis Use in Pregnancy and Breastfeeding

The effects of alcohol and tobacco use during pregnancy are well established. Although less well studied, there may also be adverse effects from exposure to cannabis in-utero (through maternal use prior to or during pregnancy) or through breastfeeding.[24] As cannabis is now legal, it is important to understand the effects of exposure to cannabis in pregnancy and through breastfeeding. A study in rats indicates that THC crosses the placenta.[25] While studies in humans were not identified, similar results would be expected in other mammals. THC is a lipophilic compound that is absorbed into fat tissue and has been shown to remain in human breast milk for several weeks.[26,27] THC functions as an agonist to cannabinoid receptors, which make up the endocannabinoid system: essential for attention, cognition, memory and emotion.[28] Based on these mechanisms, in utero exposure to cannabis may result in growth restriction and poor neurodevelopmental outcomes.[29] These include growth (birth weight, length, head circumference), preterm delivery, stillbirth, neonatal behaviours (stimuli habituation, tremors and startle, nighttime arousal and sleep time) and cognitive outcomes (verbal/memory processing, attention, impulsivity, cognitive performance).[30]

Issue and Research Question

With the legalization of non-medical cannabis use in Canada, public health providers may get more questions regarding cannabis use in pregnancy and while breastfeeding. This Evidence Brief addresses two questions:

1. What are the child and youth outcomes associated with exposure to maternal cannabis use during preconception, pregnancy or breastfeeding?

2. What are the current clinical recommendations for providers caring for reproductive-age, pregnant or breastfeeding women who may use cannabis?

Methods

Public Health Ontario (PHO) Library Services conducted an extensive search from 2006 until April 2018. Database searches were conducted in Ovid MEDLINE, Embase, PsycINFO and CINAHL. Search terms related to cannabis, conception, pregnancy, breastfeeding and infancy were used. Searches were limited to review-level articles published in the English language. Titles and abstracts were independently screened by two reviewers. Full-text articles meeting inclusion criteria were retrieved and independently screened by both reviewers. Disagreements at either screening stage were resolved through consensus. A search of the grey literature was also conducted to identify reviews and clinical practice guidelines.

Articles were eligible for inclusion if they were: systematic reviews, human studies and reported on the effects of cannabis exposure on offspring through maternal use during preconception, pregnancy, infancy or childhood. All health, developmental or social outcomes were included. Guidelines were included if they used a structured approach to review scientific literature and a transparent method for generating evidence-based recommendations.

Data extraction for all included articles was conducted by a single reviewer. Quality of included articles was conducted by two reviewers using The Health Evidence (HE) Quality Assessment Tool[31] for systematic reviews and the AGREE II Guideline Appraisal Tool for clinical practice guidelines.[32] The full search strategy, data extraction tables, PRISMA flow chart and quality appraisal tables, are available from PHO on request.

Main Findings

The search results identified 4,164 articles. After title, abstract screening and full text review, six systematic reviews,[33-38] three with meta-analyses[33-35] and five guidelines[39-43] met the inclusion criteria for this brief.

Four systematic reviews were rated as 'strong,' two were rated as 'moderate' (Table 1).

Table 1: Quality appraisal of articles

Study design	Reference	Rating
Systematic review and meta-analysis	[Gunn 2016]	10/10
Systematic review and meta-analysis	[Connors 2016]	9/10
Systematic review and meta-analysis	[Ruisch 2018]	9/10
Systematic review	[Ordean 2013]	9/10

Study design	Reference	Rating
Systematic review	[Seabrook 2017]	6/10
Systematic review	[Brown 2018]	5/10

The findings below summarize current evidence from systematic reviews of cannabis exposure during pregnancy and lactation, followed by a description of current clinical practice guidelines. There was no review-level evidence identified that examined cannabis exposure explicitly during the preconception period.

Exposure to Cannabis during Pregnancy

Three strong systematic reviews with meta-analyses examined child and youth health outcomes associated with cannabis use during pregnancy.[33-35]

The first systematic review by Conner et al. (2016) identified 31 primary studies examining cannabis use during pregnancy on multiple neonatal outcomes including low birth weight, preterm delivery, birth weight, gestational age at delivery, level II or greater nursery admission, stillbirth, spontaneous abortion, Apgar score, placental abruption and perinatal death. The majority of studies used maternal self-report to measure cannabis exposure. The pooled unadjusted estimates showed infants born to women who used cannabis were at increased risk for low birth weight (RR: 1.43, 95% CI 1.27-1.62) and preterm delivery (RR: 1.32, 95% CI 1.14-1.54).[33] In this study, multiple meta-analyses were conducted to assess the independent risk of cannabis separately from tobacco use and other substances, as well as socioeconomic and demographic factors. Despite unadjusted estimates showing increased risk for multiple outcomes, the pooled adjusted estimates were not statistically significant. The meta-analysis was limited by small sample sizes of the included studies and was likely underpowered to detect significant differences. Authors concluded that when confounding factors were controlled for, cannabis use did not have an effect on adverse neonatal outcomes.[33]

The second systematic review and meta-analysis by Gunn et al. (2016) identified 24 primary studies. The main outcomes that were examined included maternal anaemia, birth weight, neonatal length, placement in the neonatal intensive care unit (NICU), gestational age, head circumference and preterm birth. The review conceded the main limitation of the primary studies identified was the inability to separate cannabis use from poly-substance use because in most of the studies these data were unavailable. As such, the meta-analysis was unable to control for these important factors. Results showed, based on pooled data, pregnant women who used cannabis during pregnancy had a 1.36 (95% CI 1.10-1.69) higher odds of anaemia compared to those who did not use cannabis. There was a significant reduction in birth weight of 109.42 g (95% CI 38.72-180.12) and higher odds of low birth weight (<2500 g) (pooled OR (pOR): 1.77, 95% CI 1.07-3.01).[34] NICU admission was also significantly increased for infants with cannabis exposure in pregnancy compared to those not exposed (pOR: 2.02, 95% CI 1.27-3.21). The authors concluded that cannabis use during pregnancy was associated with poor

outcomes for both women and their children; however, they could not control for the use of other substances such as alcohol and tobacco.[34]

Finally, Ruisch et al. (2018) examined substance use (caffeine, alcohol, tobacco and cannabis) during pregnancy and the association with conduct problems in children. In this review, only three studies were identified that examined cannabis use.[35] The age of assessment for conduct problems was between 5 and 18 years. Results from the pooled data did not indicate a significant association between cannabis use in pregnancy and conduct problems in children or youth (pOR: 1.29, 95% CI 0.93-1.81); however, the quality assessment of the three included studies was 'low to very low' and the authors determined there were insufficient studies to draw conclusions for this association.[35]

Exposure to Cannabis during Lactation

Three systematic reviews were identified that examined the association between cannabis use during breastfeeding and infant outcomes.[36-38] One review identified three studies in humans and three in animals.[37] The other review included the same three human studies and identified an additional prospective cohort study.[36] The third review included the two previous systematic reviews and one additional primary study.[38] The primary studies included in all three reviews were limited in number, dated and had overlap between reviews.

Across systematic reviews, cannabis use during breastfeeding was not found to be associated with any health outcomes in humans or animals. Infant health outcomes examined included mental and motor development at one year of age, physical growth and sudden infant death syndrome (SIDS). Overall, there were very few studies and the quality was rated as 'moderate' to 'very low.'[36] A main limitation of the studies included in the systematic reviews is the failure to adjust for maternal cannabis use in the first trimester of pregnancy.[44] The conclusions from one review emphasizes informed decision making where pregnant women need to be counselled on the potential risks of cannabis use and benefits of breastfeeding, before deciding on infant feeding practices.[36] While the authors of the other two reviews interpreted the evidence with a precautionary perspective and concluded women who are breastfeeding should be advised to reduce or abstain from cannabis use.[37,38]

Clinical Guidelines

Each guideline identified was quality appraised by two reviewers. Two guidelines were rigorously developed, had multiple stakeholder involvement and clear recommendations.[39,41] Three guidelines were limited by incomplete search strategies, lack of criteria for selecting evidence and less stakeholder involvement.[40,42,43] One guideline was excluded due to poor quality; specifically the lack of a systematic strategy for identifying evidence.[45]

Guidelines from the Society for Obstetrics and Gynecologists of Canada (SOGC) and the World Health Organization (WHO) were identified that provided recommendations to screen, treat and manage substance use in women who are pregnant and breastfeeding. The American College of Obstetrics and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP) released guidelines that focused specifically on the use of cannabis and cannabinoid-containing products in pregnancy and breastfeeding.

One additional guideline was included that focused on cannabis use in breastfeeding from the Academy of Breastfeeding Medicine (ABM). Recommendations for health care providers on cannabis use during pregnancy and breastfeeding are presented in Table 2.

There are consistent recommendations for health care providers to counsel women to abstain or reduce cannabis use while pregnant. In addition, the AAP recommends counseling young women in the preconception period about the lack of evidence and potential risks of cannabis exposure on infant and child development.[42] For breastfeeding, there is consensus among professional societies for health care providers to counsel breastfeeding mothers on the potential risks of cannabis use during lactation and support efforts to abstain from use. For mothers with substance use disorders, the WHO recommends that breastfeeding should be encouraged "unless the risks clearly outweigh the benefits."[41] The strength of this recommendation was reported "conditional" because of the likely dose response of substance use; individuals with heavy or chronic use may accumulate higher concentrations of THC in the breast milk and therefore pose higher risks to exposed infants.[41] These recommendations were based on low quality evidence.

Table 2: Recommendations and guidelines from other organizations

Organization	Recommendation
During pregnancy	
Society of Obstetricians and Gynaecologists of Canada (SOGC)	"Health care providers should advise pregnant women to **abstain** from or **reduce** cannabis use during pregnancy to prevent negative long-term cognitive and behavioural outcomes for exposed children (II-1A)"[39] p.932
World Health Organization (WHO)	"Health-care providers should, at the earliest opportunity, advise pregnant women dependent on alcohol or drugs to **cease** their alcohol or drug use and offer, or refer to, detoxification services under medical supervision where necessary and applicable."[41]
American College of Obstetricians and Gynaecologists (ACOG)	"Women who are pregnant or contemplating pregnancy should be encouraged to **discontinue** marijuana use"[43] p.3
American Academy of Pediatrics (AAP)	"Women who are considering becoming pregnant or who are of reproductive age need to be informed about the **lack of definitive research** and counseled about the current concerns regarding potential adverse effects of THC use on the woman and on fetal, infant, and child development. Marijuana can be included as part of a discussion about the use of tobacco, alcohol, and other drugs and medications during pregnancy."[42] p.10-11 "As part of routine anticipatory guidance and in addition to contraception counseling, it is important to advise all adolescents and young women that if they become pregnant, marijuana **should not be used** during pregnancy."[42] p.11

Organization	Recommendation
During breastfeeding	
Society of Obstetricians and Gynaecologists of Canada (SOGC)	"Women with active substance use should be encouraged to **discontinue** alcohol or other drug use while breastfeeding, and the risks and benefits of breastfeeding versus breast milk exposure to substances should be discussed (II-2B)"[39] p.933-4
World Health Organization (WHO)	"A. Mothers with substance use disorders should be **encouraged to breastfeed** unless the risks clearly outweigh the benefits. B. Breastfeeding women using alcohol or drugs should be advised and supported to cease alcohol or drug use; however, substance use is not necessarily a contraindication to breastfeeding. SOR: Conditional; Quality of Evidence: Low"[41] p.15
American College of Obstetricians and Gynaecologists (ACOG)	"Breastfeeding women should be informed that the potential risks of exposure to marijuana metabolites are unknown and should be **encouraged to discontinue** marijuana use."[43] p.3
American Academy of Pediatrics (AAP)	"Present data are insufficient to assess the effects of exposure of infants to maternal marijuana use during breastfeeding. As a result, maternal marijuana use while breastfeeding is discouraged. Because the potential risks of infant exposure to marijuana metabolites are unknown, women should be informed of the potential risk of exposure during lactation and **encouraged to abstain** from using any marijuana products while breastfeeding."[42] p.11
The Academy of Breastfeeding Medicine (ABM)	"A recommendation of **abstaining** from any marijuana use is warranted. At this time, although the data are not strong enough to recommend not breastfeeding with any marijuana use, we urge **caution**."[40] p.139

*Bold emphasis added

Discussion

There are three main limitations of the current evidence on the effects of cannabis use in pregnancy and breastfeeding: 1) relatively few studies on humans, 2) poor control for concurrent exposures including alcohol and tobacco, as well as other potential confounders and 3) lack of consistent and accurate measures of cannabis exposure.

Lack of Human Epidemiologic Studies

The primary studies that were included in the three systematic reviews were predominantly from three longitudinal cohort studies: the Ottawa Prenatal Prospective Study (OPPS) in Ottawa, Maternal Health Practices and Child Development Project (MHPCD) in Pittsburgh and the Generation R study in Rotterdam, the Netherlands. The OPPS and MHPCD were initiated in the 1980s and have followed children into adulthood. However, potency of cannabis consumed has changed substantially; average THC concentration increased from 4% in 1995 to 12% in 2014.[46] As such, results from studies based on

past use may not be applicable to current use. These cohorts also had relatively small sample sizes, specific populations and looked at different outcomes, which increases the heterogeneity of studies included in meta-analyses. Therefore to understand the current effects of cannabis use, new high quality observational studies are required.

Poor Control of Concurrent Exposures and Other Confounders

Poly-substance use with cannabis is common. In one study, 5.5% of all women reported simultaneous alcohol and cannabis use.[47] Children exposed to alcohol, tobacco and other illicit drugs have known negative health outcomes. Therefore, if studies are unable to control for poly-substance use it will limit our understanding of the independent effects of cannabis. Similarly, exposure to other chemicals in the community and work environment, which have been associated with outcomes of interest, was not well addressed in most studies. Conner et al., (2016) and Gunn et al., (2016) included 31 and 24 studies, respectively; however, only eight studies were reported in both systematic reviews and only one study was used in both meta-analyses of low birth weight.[33,34] The conclusions of these two reviews were conflicting; Conner reported no independent risk of cannabis on any neonatal outcomes while Gunn reported overall adverse effects of cannabis use during pregnancy. The difference between these two meta-analyses was the ability to control for poly-substance use, especially tobacco. Conner et al., included only four studies that had reported tobacco use and could be adjusted for. Gunn et al., acknowledged the inability to control for tobacco use as a limitation of their study and had a total of 12 studies included in the meta-analyses.

Measurement of Cannabis Exposure

One main limitation of studies on cannabis exposure in the pregnancy and breastfeeding period is the measurement of exposure. Self-reporting cannabis use is the most common method of ascertaining exposure; however, similar to alcohol, there are strong social desirability and reporting biases that would likely underestimate use and therefore underestimate effects.[16] Further, the previous illicit drug status of cannabis may impede mothers or any caregivers from accurately reporting use due to concerns of involvement with child protective services. There are methods of measuring cannabis exposure using biological samples including maternal serum, urine or hair, which can detect cannabis from two to three days to several weeks post exposure depending on frequency of use. To measure exposure in the infant, researchers have used meconium, the first stool of a newborn, which can detect past exposure to marijuana in the second or third trimester or neonatal hair, which can detect exposure in the third trimester. Unfortunately, these biological sampling procedures are expensive, often impractical in many sites and produce high false positive rates.[48] More research is required to develop reliable and accurate metrics for cannabis exposure.

Limitations

This evidence brief is not without limitations. Our review did not include search terms for the effect of cannabis use on parenting, parent-child attachment or any related outcomes, which may have an effect on later child health outcomes. Although there is evidence on second-hand smoke from tobacco research, the independent association of second-hand smoke from parental cannabis use and early

childhood outcomes is unknown. Future research should investigate this association. We focused on literature published since 2006, emphasized the use of systematic reviews rather than primary studies and did not include primary studies or systematic reviews only reported in the grey literature. Large well-conducted cohort studies would be most useful for studying the extent of cannabis-related harms. Ideally, such studies would examine cannabis exposures at various dosages, routes (i.e., in utero, lactation) and points in the early life course and control for important confounders.

Conclusion

There is limited and inconsistent evidence on the effects of cannabis exposure during pregnancy and breastfeeding on infant, child and youth health outcomes. Although evidence is limited, clinical guidelines for cannabis use during pregnancy provide consistent recommendations for pregnant women to abstain, although one guideline recommended women to abstain or reduce use. Similarly, in light of the established benefits of breastfeeding, guidelines recommend women should be encouraged to discontinue cannabis use while breastfeeding. In addition, many guidelines recommend informing women who are breastfeeding and using cannabis of potential risks of exposure including considerations of the frequency and amount of cannabis use. In this way, recommendations about breastfeeding for women using cannabis can be individualized during discussion with a health care provider. For additional information, the Canadian Centre for Substance Abuse (CCSA) also released an updated overview of current evidence on cannabis use during pregnancy.[1] Although the review does not provide recommendations, the author's conclusions align with those of this review.

Implications for Practice

Ontario's local public health agencies have a mandate to support healthy child growth and development and are responsible for providing relevant health advice to the public, health care providers and policy-makers.[49] For example, in collaboration with the Ministry of Children, Community and Social Services, local public health nurses deliver the *Healthy Babies Healthy Children*[50] program and provide evidence-based guidance on child health to new and expectant parents. Given the recent legalization of non-medical cannabis use in Canada, it will be increasingly important for public health staff to be equipped to address this topic with their clients.

The evidence included in this brief does not confirm or convincingly rule out that early cannabis exposure adversely impacts early childhood outcomes, but suggests possible risks.[29] Given the potential for health, social and developmental harms, a precautionary approach may be warranted. Therefore, abstinence during pregnancy and lactation is the safest approach and reduces risk of potential harms.

Public health staff may caution against maternal cannabis use during preconception, pregnancy and lactation periods and provide support for the health and social needs that may contribute to cannabis use; however, evidence on the effectiveness of this approach or on other specific interventions is lacking.

Additional surveillance of cannabis use and cannabis-related harms would also support evidence-informed decision making. The federal Task Force has recommended that the federal and provincial governments collect and share data regarding health, social and other outcomes following cannabis legalization.[7] Such data could be used to improve the quality of health advice provided by public health officials.

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Specifications and Limitations of Evidence Brief

The purpose of this Evidence Brief is to investigate a research question in a timely manner to help inform decision making. The Evidence Brief presents key findings, based on a systematic search of the best available evidence near the time of publication, as well as systematic screening and extraction of the data from that evidence. It does not report the same level of detail as a full systematic review. Every attempt has been made to incorporate the highest level of evidence on the topic. There may be relevant individual studies that are not included; however, it is important to consider at the time of use of this brief whether individual studies would alter the conclusions drawn from the document.

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