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Rapid Review: Evidence Regarding Use of Cannabis during Pregnancy and Lactation

Method

The Mendeley search function was used to identify key recent articles concerning the prevalence and effects of cannabis use by pregnant and/or lactating women. In the case of some review articles or commentaries, the original source publication(s) was/were retrieved. Because of the rapidly-evolving nature of this field of research, the review focused on articles published since 2018. The search was supplemented with a search for guidelines that may be utilized by Canadian healthcare practitioners.

Results

A total of 45 publications published since 2018 in medical journals were reviewed. Table 1 shows the breakdown by research or publication type.

Table 1: Recent Publications Included in Rapid Review

Type of Publication	Number
Longitudinal cohort studies	8
Narrative reviews	7
Letters to the editor and editorials regarding a reviewed publication	7
Systematic reviews	5
Clinical studies	5
Secondary analysis of health administrative data	5
Cross-sectional, nationally-representatives surveys	5
Canadian clinical guidelines/health professional recommendations	3
Qualitative research	1

Findings have been organized into the following broad categories:

1. Current practices
2. Potential benefits
3. Potential harms
4. Healthcare messaging to patients or clients

Following an examination of the information on these topics, a section will describe potential conclusions.

1. Current Practices

In looking at current practices, it is important to consider

a) Prevalence of cannabis use during pregnancy and/or lactation
b) Attitudes of women, healthcare providers and dispensaries that may influence practices

c) Mode of administration

Addressing these questions should give insights useful for patient or public health services.

a) Prevalence of cannabis use during pregnancy and/or lactation

Table 2: Summary of Cannabis Use During Pregnancy

Data type	Identifier of Cannabis Use	Age Group	Cannabis Use During Pregnancy
U.S. cross-sectional survey[1]	Self-report	12-44 yrs.	Between 2002/03 and 2016/17, overall past-month cannabis use increased from 3.4% to 8.0% For the 1st trimester, use rose from 5.7% to 12.1%
U.S. cross-sectional survey[2]	Self-report	12-44 yrs.	11% in month 1 3% in 2nd trimester 2% in 3rd trimester
Data from Ontario Better Outcomes Registry & Network Study[3]	Self-report	-	1.2% in 2012, increasing to 1.8% in 2017
Data from 3,207 respondents from 2014/15 Colorado Pregnancy Risk Assessment Monitoring System[4]	Self-report	-	5.7% reported cannabis use at any time during pregnancy; 4.8% during 1st trimester and 2.4% in the 3rd trimester 5% of women who reported ever breastfeeding also reported postnatal cannabis use
Data from U.S. Pregnancy Risk Assessment Monitoring System [5]	Self-report		4.2% reported cannabis use during pregnancy and 6.8% after
U.S. Retrospective cohort study [6]	Toxicology testing or self-report	13-22 yrs.	8.5% by self-report; 17.5% by urine toxicology
U.S. Cohort study [7]	Self-report	-	12% before pregnancy and 3% during
U.S., Administrative database[8]	Women admitted to publicly-funded specialty substance use treatment facilities	12-49 yrs.	Rate of admission for substance use treatment increased by 4.69/100,000 women in states with legal medical marijuana, relative to other states
Observational study of pregnant women recruited from 2 urban university obstetric clinics [9]	Self-report	-	12.1% reported cannabis only use, 9.0% cannabis and tobacco

Systematic review [10]	Self-report or toxicology testing	Varied by study	Cannabis use ranged between 4% and 7% in most studies In lower SES/ethnic minority samples, up to 11% by self-report and 28% by toxicology testing
Systematic review[11]	Varied by study	Varied by study	Overall prevalence of cannabis use ranged from 0.24% and 22.6%, with the greatest use in the 1st trimester
Narrative review [12]	Varied by study	Varied by study	U.S. data suggest 3.9% of pregnant women used cannabis in past month and 7% in past year

Surveys have demonstrated increases over time in the prevalence of cannabis use among both non-pregnant and pregnant women. The prevalence of use appears to be higher in American, as opposed to Canadian, studies. A nationally-representative study of women in the U.S. reported that in 2014-2017 (as of 2017, 8 states and Washington D.C., had legalized recreational cannabis and 33 medicinal use), 7.9% (95% CI 9.8, 10.3) of non-pregnant women aged 12-44 years reported past 30-day cannabis use, compared to 8.1% (95% CI 6.4,10.2) of those in their first trimester of pregnancy, and 2.5% (95% CI 1.7, 3.8) in their third. 2 Data from an Ontario database in 2017, a year prior to recreational cannabis legalization in Canada, found the prevalence of cannabis use in pregnancy increased from 1.2% in 2012 to 1.8% in 2017. 3 Rates are probably changing in response to evolving cannabis legislation. There is evidence from the U.S. showing that states with legalized medical cannabis have higher rates of admissions by pregnant women 18 and older for cannabis treatment.8

The prevalence of cannabis use during pregnancy varies according to how use is measured and pregnancy stage. In a cohort study set in a single tertiary-care centre, use was 8.5% based on self-report but increased to 17.5% when identified by urine toxicology.6 Data from a review of six surveys estimated that two-thirds of cannabis using women reported stopping use after becoming pregnant.[10] For example, Volkow et al. report that in 2016/17, past-month self-reported daily/near daily cannabis use among pregnant American women was 5.3% in the first trimester, 2.5% during the second, and 2.5% during the third.1

Cannabis use disorder or dependence may help to explain why some women continue to smoke during pregnancy and breastfeeding. Alshaarway et al. found the prevalence of cannabis dependence was higher among pregnant cannabis-using women (19.2%, 95% CI 15.5, 23.6) than cannabis-using non-pregnant women (12.7%, 95% CI 12.3, 13.2%), with no substantial variation in cannabis dependence prevalence by trimester or month.2 Another study found 18% of pregnant women using cannabis met DSM-IV criteria for cannabis abuse or dependence. [10] Alternately, legalization of cannabis may increase the likelihood of treatment (vs. criminalization) of dependance. One study reported that in

states with legalized medical cannabis, increases in cannabis treatment admissions by pregnant women were associated with healthcare and other referrals ("other" including self, school, employment, or community referrals), as opposed to interventions by the criminal justice system. 8

Studies have reported similar demographic trends in the use of cannabis by pregnant women. Users tend to be younger (one study reported a 18% relative decrease in cannabis use with each additional year of maternal age), with less formal education, lower socioeconomic status, and report a higher frequency of mental health diagnoses. [3, 4, 5, 10, 11]

Better data are needed on multisubstance use during pregnancy. For example, in some analyses of the effects of cannabis use during pregnancy results may vary according to whether concomitant tobacco use is taken into account (e.g., Meinhofer et al. 2019 [12]). In a cohort of pregnant females in the Kaiser Permanente North California health system, a third of those who screened positive for prenatal cannabis also used other substances, such as alcohol, nicotine, opioids, and illicit drugs.[13] In a study of pregnant women recruited from two urban university obstetrics clinics in 2017, 9.0% reported concurrent use of cannabis and tobacco. 9

Little research has been conducted on the community prevalence of cannabis use during lactation. Data from an unselected pregnancy surveillance registry in the U.S. found an average of 4.2% of women reported cannabis during pregnancy, ranging from 2.8% to 6.6% depending on the US state. Of those who indicated cannabis use after pregnancy, 72.4% reported breastfeeding for 8 weeks or more, 18.0% for up to 8 weeks, and 0.6% never breastfeeding.5 In contrast, statistics from one Colorado health department suggested 18% used cannabis while breastfeeding. In this population, over a third (36%) of the women reported using cannabis at some point in their pregnancy, so these results may not be generalizable to other populations. [14, 15] A study enrolling 50 breastfeeding women who reported cannabis use (88% at least daily) found detectable levels of delta-9-tetrahydrocannabinol (Δ9-THC) in 63% of the 54 breast milk samples.[16]

b) Attitudes of women, healthcare providers and dispensaries that may influence behaviour

Medical counseling and public health education have traditionally focused on the health risks associated with tobacco and alcohol use during pregnancy. Messaging about cannabis use during pregnancy is less common and constrained by the limited nature of available data. A survey of 74 lactation consultants in New England found 41% said their advice would depend on the amount of cannabis used, 44% would recommend breastfeeding despite cannabis use, and only 15% would recommend a cannabis-using mother not breastfeed.[17]

In the absence of strong messaging that cannabis during pregnancy and/or pregnancy is unsafe, beliefs that cannabis is "natural" and therefore "safe" may flourish. In one study, 30% of pregnant women did not believe cannabis use during pregnancy could harm the fetus [18]; in another survey, 70% of pregnant and non-pregnant past-year cannabis users perceived slight or no risk of harm from using cannabis once or twice a week. [10]

The perceived ability of cannabis to treat nausea and vomiting of pregnancy (NVP) may also be an important consideration. Young-Wolf et al. report that between 2009 and 2016, cannabis use during pregnancy not only increased, but had a direct relationship with NVP severity; compared to pregnant women without NVP, those with mild NVP had an adjusted Odds Ratio (OR) of 2.37 (95% CI 2.17-2.59) and those with severe NVP an OR of 3.80 (95% CI 3.19-4.52) of cannabis use.[19] Cannabis dispensaries may reinforce or even promote the image of cannabis as a safe option during pregnancy and lactation. A study of 400 cannabis dispensaries in Colorado found 69% recommended cannabis for pregnant women experiencing NVP; an additional 36% told a caller that cannabis products were safe during pregnancy.[20]

There is little information on the extent to which healthcare providers screen pregnant women on cannabis use or advise on what to do during and after pregnancy. In one U.S. study, women reported communications with healthcare providers on cannabis use during pregnancy tended to focus not on health outcomes but rather the legal consequences and the potential involvement of child welfare agencies. [10]

c) Mode of administration

Little information is available on the method of administration used by pregnant or lactating women who use cannabis. In one study of women in northern California, the most common mode of administration was smoking (42.1%), followed by vaping (15.8%), edibles (15.8) and lotions (5.3%). The majority (84.6%) reported using only one mode of administration, while 15.4% used two or more. 7

2. Potential Benefits

A handful of studies have suggested there may be some benefits associated with prenatal cannabis use. They include:

- Maternal preeclampsia and gestational diabetes: Data from the Better Outcomes Registry and Network (BORN) in Ontario compared matched samples of women who used cannabis during pregnancy to those who did not and found cannabis use was associated with a reduced risk of maternal preeclampsia (4.4% vs 4.9%, RR=0.90, 95% CI 0.86-0.95) and gestational diabetes (4.3% vs. 4.7%, RR=0.91, 95% CI 0.91-0.96).[21]

- Maternal inflammation: A study of 138 pregnant women who used tobacco found that those who also used cannabis had decreased pro-inflammatory immune responsivity in one of 8 markers (TNF-α).[22]
- Conditions associated with pregnancy: A review by Thompson et al suggests that cannabis may be helpful in the treatment of postpartum depression, back pain, and NVP.[23] The authors also make the point that as THC has the ability to cross the placenta, its perinatal effects are uncharted and there is currently no recognized safe dose. The perception that cannabis may be helpful for managing NVP may help to explain increases in its use over time. Young-Wolff et al reported that between 2009 and 2014, the use of cannabis by women with NVP increased from 6.5% to 11.1%. Among pregnant women without NVP, rates of use increased but were substantially lower (for the same time period, increasing 3.4% to 5.8%). [24]

3. Potential Harms

A number of systematic and narrative reviews have been published that combine results from preclinical (i.e., animal and/or cellular) and clinical studies.

- Scheyer et al report a positive association between cannabis exposure in utero and disturbed emotional and psychiatric health of the offspring, although they admit a genetic driver cannot be ruled out. Consequences tend to be subtle, however, and, unlike the effects of prenatal cigarette or alcohol exposure, appear to manifest over time.[25]
- Pinkey et al conclude that there is good evidence from animal studies that prenatal cannabinoid exposure leads to widespread changes in a number of neurotransmitter systems important in shaping offspring development and behaviour. As many of these observed alterations may be time-dependent and vary by dose, cannabinoid type, timing, and duration of exposure, it may be difficult to generalize conclusions.[26]
- Based largely on animal studies, Dong et al theorize that exogenous cannabinoids may disrupt the functioning of the maternal endogenous cannabinoid and immune system. This may have implications for fertility and pregnancy, and immune functioning of offspring. [27]
- A narrative review by El Marroun et al was unable to find what the authors considered definitive research findings on the effect of prenatal cannabis exposure to fetal development and long-term offspring outcomes. Suggestions are made for future research, including prospective longitudinal studies with longer follow-up periods, studies that differentiate between causal and non-causal associations, and research examining the role of public policies on prenatal cannabis use. Such research would fill some of the gaps in our current knowledge and provide a better basis for public policies and healthcare education and counselling. [28]

One new study by Myran, Roberts, Pugliese et al (2023)[37] examined the rate of acute care related to cannabis use during pregnancy, finding an increase in the rate between pre and post legalization time points. While the absolute numbers are small, the trend of the increasing rate of a need for medical care due to non-medical cannabis use, is worthy of note, and, as the study authors conclude, points to a need for education on cannabis-related harms for pregnant people and their care providers.

Table 3 summarizes clinical studies that have been published on the effects of maternal cannabis use. These studies tend to focus on prenatal exposure versus the effects of cannabis use while breastfeeding.

Table 3: Summary of Research on Potential Harms of Cannabis Use During Pregnancy

Data Type	Cannabis Use	Outcomes Studied	Results
Cross-sectional study of mothers who delivered a live-born infant in Colorado 4	Self-report	Low birth weight and other outcomes	Maternal use of cannabis associated with a 50% increased likelihood of low birth weight, independent of maternal age, tobacco use, race/ethnicity, or education. Prenatal cannabis use independent of tobacco use was not associated with small for gestational age, preterm birth and neonatal intensive care unit admission.
Observational study of 500 urban patients 9	Self-reported (yes/no)	Stillbirth or miscarriage, smaller head circumference, birth defects,	Cannabis-only group had 12 times higher odds of stillbirth or miscarriage. Co-users of cannabis and tobacco had 5.7 greater odds of small head circumference and 3.1 times greater odds of birth defects (adjusted)
Retrospective cohort study set in a single tertiary-care centre of pregnant women 13-22 years 6	Self-report and toxicology testing	Composite outcome was spontaneous preterm birth, hypertensive disorders of pregnancy, stillbirth, or small for gestational age	Composite outcome occurred in 46% of pregnancies exposed to cannabis vs. 34% of those not exposed (p<.001), and remains significant after adjusting for race/ethnicity and tobacco exposure (adjOR=1.50, 95% CI 1.09-2.05). Of the 5 individual outcomes, only small for gestational age had a statistically significant between groups (25.7% for exposed to cannabis vs. 17.1% for not exposed, p=.005). Of 8 secondary outcomes, there were significant differences for 3: abruption (2.8% vs. 0.7%, p=.016), mean infant birthweight in grams (2966 [43.2] vs. 3108 [16.4] p=.002), and mean infant head circumference (33.2 [0.15] vs. 33.6 [0.06] p=.01).
Data from Pregnancy Risk Assessment Monitoring System5	Self-report	Gestational age and birthweight	After adjustment, no difference in gestational age or birthweight associated with prenatal cannabis use. Postpartum cannabis use was associated with depressive symptoms and shorter breastfeeding duration.

Data Type	Cannabis Use	Outcomes Studied	Results
Prospective study of 247 mother/infant dyads [29]	Self-report verified using maternal saliva and infant meconium	Child behaviour	No direct association between tobacco exposure with or without cannabis and child externalizing behaviour at either 24 or 36 months. Tobacco and cannabis co-exposure was associated in indirect pathways to fewer regulation deficits
Mother-infant dyads from 4 cohort studies [30]	Self-report of amount of use verified by toxicology testing	Birth weight and length of gestation	In the pooled sample, 22.9% reported any cannabis use and 19.3% co-use of tobacco and cannabis. Co-exposure to cannabis and tobacco was associated with an estimated 18% reduction in birth weight not attributable to earlier delivery, exposure to alcohol or other drugs, or maternal socioeconomic status. Tobacco use was associated with lower birth weight in both sexes but cannabis use only in male infants
Cohort of mother-infant dyads; mothers reported cannabis and tobacco use but not heavy drinking or other illicit drug use [31]	Self-report and biological assays	Child and maternal behaviour	Indirect association was found between prenatal tobacco or co-exposure with cannabis in toddler emotional regulation. Mothers who co-used displayed lower sensitivity during play interactions with their infants.
Cohort of mother-infant pairs from a low-income, diverse sample [32]	Self-report with biochemical confirmation	Child behaviour	Compared to newborns with no exposure, those exposed to both cannabis and tobacco showed decreased ability to self-soothe and attend to stimuli, needed more external soothing and were more lethargic. The effects were worse for female than male infants.
421 females and 200 males in a reproductive health study conducted at a fertility clinic[33]	Self-report	Infertility treatment outcomes	No statistically significant differences in adjusted probabilities of implantation, clinical pregnancy, or live birth between never and ever cannabis users. The 12 women who were cannabis users at enrollment had more than double the adjusted proportion of pregnancy loss than the 409 women who were past or never users (54% vs., 26%, p=.003).
Follow-up of cohort study of cannabis and tobacco co-use during pregnancy [34]	Self-report of co-use of cannabis and tobacco	Drug use disorders in adult offspring	Maternal patterns of co-use of cannabis and tobacco predicted co-use in adult offspring. Offspring whose mothers were chronic co-users (7% of mothers) were more than twice as likely to have a drug use disorder
Longitudinal cohort study in the Netherlands [35]	Self-report and urine testing	Child development	Maternal cannabis use during pregnancy was associated with teacher- and child self-report of externalizing problems (aggression, rule-breaking) but not with internalizing problems

Data Type	Cannabis Use	Outcomes Studied	Results
			(e.g., anxiety, depression, withdrawal, etc.).
Systematic review of 21 reports from 7 longitudinal studies [36]	Varied	Behavioural outcomes in offspring	Possible negative associations were found between prenatal cannabis exposure and neuropsychological function in children (e.g., attention, memory, impulse control) but effect sizes were small and many not statistically significant after adjusting for other factors. Possible positive association with language development, reading and composite IQ scores.
Canadian cross-sectional survey[37]	Hospital admission record	10-55 yrs.	An increase of 11.0 per 100,000 pregnancies to 20.0 per 100,000 pregnancies

Of the 13 studies summarized in Table 3, the main findings are:

- Stillbirth or miscarriage was looked at in two studies: one found an association with prenatal cannabis exposure 9 and the other did not 6
- Low birth weight was looked at in two studies: one found a significant effect for cannabis users even after adjusting for concurrent tobacco use 4 and one an effect for male infants but not females [30]
- Birth weight was compared in two studies: one reported (even after adjustment for tobacco) that infants of cannabis users had a significantly smaller mean birth weight 6 while the other showed no effect after adjustment 5
- Small for gestational age was observed in two studies: one reported a significant association with cannabis use during pregnancy 6 but another found no association once the analysis was adjusted to include concurrent tobacco use4
- Head circumference was looked at in two studies: 1 found the mean head circumference was smaller for infants of co-users of cannabis and tobacco9 and another reported a difference even after adjusting for concurrent tobacco use6
- Outcomes of infertility treatment were the subject of one study that found no statistically significant differences in the adjusted probabilities of implantation, clinical pregnancy, or live birth between never and ever cannabis users, although there was some evidence that cannabis users may have a higher rate of pregnancy loss [33]
- Behavioural issues among cannabis user offspring were looked at in six studies: 3 reported indirect associations between cannabis exposure and externalizing behaviour, [29, 31, 35] one poorer neuropsychological functioning (although effect sizes were small and many not significant after adjusting for other factors), [36] one reported (when combined with tobacco exposure) decreased abilities to self-soothe and attend to stimuli, [32] and one found a higher rate of drug use disorder in

adulthood for children whose mothers co-used cannabis and tobacco during pregnancy [34]

4. Healthcare Messaging to Patients or Clients

The general consensus regarding cannabis use during pregnancy is that healthcare providers and mothers need to be aware of the potential for harm. [38] [39] Schreiber and Pick go even further, suggesting that the neurological effects of cannabis exposure in utero are sufficiently recognized that they should be formalized into a "fetal cannabis spectrum disorder."[40] However, the issue of harm is complicated by the fact that an unknown proportion of women who use cannabis during pregnancy may also use other substances, such as tobacco. [41]

Clinical guidelines for healthcare providers and patients tend to be highly conservative. [42] [43] [44] [45] The logic commonly used is as follows:

1. The evidence base is limited and, in many cases, inconsistent. This is due to:
   - the small number of clinical (human) studies
   - poor control for concurrent exposures, such as alcohol and tobacco
   - lack of consistent and accurate measures of cannabis exposure
2. Despite these limitations, there is evidence suggesting detrimental effects for cannabis use alone or in combination with tobacco in respect to some pregnancy outcomes, such as birthweight,
3. Just as there is no clear evidence of harm, there is no evidence for the safety of cannabis, such as the amount that is safe to consume during pregnancy and lactation or of benefits for either the mother or offspring
4. Given the uncertain nature of the evidence, in order to reduce the risk of harm healthcare providers should counsel women to avoid or reduce using cannabis during pregnancy and lactation.

This approach is not without its critics. In their brief report on cannabis use for NVP management, Young-Wolff et al. concluded by making the familiar recommendations that healthcare providers ask about cannabis use and advise abstinence during pregnancy and lactation.[19] In response, Takakuwa and Schears write: "The implicit idea that naïve, pregnant, cannabis-using women require education is pejorative and paternalistic."[46] They note that some of the conventional medications prescribed by physicians for NVP have been approved by the US Food and Drug Administration only for nonpregnant patients and refers to thalidomide as an example of what can potentially go wrong with pharmaceutical approaches.

Conclusions

This rapid review has shown a number of gaps in the current literature on the effects of cannabis use during pregnancy and lactation. Given the rising prevalence of cannabis use by women before, during and after pregnancy, rigorous research is needed to guide women, healthcare providers, and policy-makers.

The review suggests the following are important gaps in our current understanding:

- Accurate, timely Canadian data on the prevalence of cannabis use during pregnancy, as well as during lactation. This research should take into account:
    - Social determinants of health and access to health care
    - Multi-substance use and co-use
    - Dose, timing, duration and type of cannabinoid, as well as mode of administration
    - Method of assessing cannabis use (e.g., self-report vs. toxicological testing)
- An understanding of the risk beliefs or calculations of women (i.e., perceived benefits and risks) that may help to explain changes in cannabis use during pregnancy and/or lactation.
- Longitudinal research to inform the effects of maternal cannabis use during pregnancy and/or lactation on birth outcomes and offspring neurological and developmental markers
- Studies of the intended and unintended impact of cannabis policies on maternal use and offspring outcomes
- Studies of best practices in maternal cannabis education or counselling
- Studies to establish effective protocols in cannabis use disorder treatment for pregnant or lactating women

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