



# CANNABIS: IMPLICATIONS FOR PREGNANCY, FETAL DEVELOPMENT AND LONGER-TERM HEALTH OUTCOMES

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## SUMMARY OF THE MAIN POINTS

Cannabis is the most commonly used illicit substance among pregnant women in fact, seven out of ten women report that they believe that cannabis is not harmful in pregnancy. In the United States, more than 1 in 10 pregnant women reported using cannabis in the past 12 months. Its reputation of being a harmless drug and the imminent legalization of cannabis in Canada only serves to reinforce the belief that there is no health risk associated with using cannabis.

Research in the area of cannabis and pregnancy is limited, and for good reason. It is not possible to do research on illegal substances, many users of cannabis also use other substances, making it difficult to attribute direct causation and there will never be ethical approval for a randomized controlled trial. The evidence that we do have is persuasive but not definitive. Well-designed studies have found that maternal cannabis crosses the placenta, and does enter the fetal brain and tissues.

Cannabis use during pregnancy has been shown to affect reproductive function, pregnancy outcomes, the growth and development of the baby, as well as lead to long-term neurocognitive effects. More specifically, prenatal exposure to cannabis has been shown to impact fetal growth and development and has been associated with adverse effects on cognitive development and academic achievement. There are also effects on behaviour, including attention deficits, increased hyperactivity and impulsivity as well as increased incidence of tremors, exaggerated startles and diminished crying in the neonates. Emerging evidence suggests an increased likelihood of smoking, substance abuse and delinquency among adolescents who were prenatally exposed to cannabis. In this respect, cannabis is a neuroteratogen.

The science is not conclusive and can neither definitively tell us an *absolute safe amount* nor an *absolute harmful amount* of cannabis on pregnancy or fetal growth and development. Because of this, we observe the “precautionary principle”; we are unlikely ever to have evidence of the quality required to demonstrate causation, but for the affected child there is only one opportunity to avoid harm. The safest practice is to avoid cannabis use during pregnancy.

## CANNABIS USE AND WOMEN

After tobacco and alcohol, cannabis is the most commonly abused substance by women of childbearing age<sup>1</sup> and, in the United States, cannabis represents 64 to 79 percent of female drug use<sup>1-3</sup>. The Canadian Alcohol and Drug Use Monitoring Survey found that among women of childbearing age, 90.1% reported past year substance use; nearly 11% reported past year use of cannabis.<sup>4</sup>

As cannabis becomes more widely legalized, use by women may increase. Females appear to be more sensitive to the behavioral and physiological effects of cannabis and cannabis-like substances<sup>5</sup> and use disrupts female endocrinology and reproductive function.<sup>6</sup> Carefully controlled regulation of the Endocannabinoid System (ECS) is required for successful reproduction, and exogenous cannabinoids may disrupt the delicate balance of the ECS in the female reproductive system.<sup>6</sup>

The population of substance users is diverse in its composition. The health issue is complex and differs across populations groups. Currently, it is estimated that females account for approximately 40% of the substance using (licit and illicit) population.<sup>7</sup> However, this gender inequality is decreasing as the proportion of women using addictive substances increases.<sup>8,9</sup> Specifically, women are most at risk of substance use during their reproductive years, especially between the ages of 18 to 29 years.<sup>10</sup> Those women who use substances in pregnancy are the women most likely to have additional risk factors, and include those who use cannabis as a coping mechanism for stresses in their lives. Those stresses are an additional risk factor for fetal growth and neuro-cognitive development, and multiple stresses have an amplifying impact on the fetus. The epigenetic effects of cannabis on pregnancy and pregnancy outcome are entirely unknown.

## CANNABIS USE DURING PREGNANCY

Several trends suggest that, of all substances used during pregnancy, tobacco is the most prevalent, followed by alcohol, cannabis, cocaine, and other illicit drugs.<sup>5,11-13</sup> Substance use among pregnant women varies widely, and is reflective of differences in race, ethnicity, age, socioeconomic status, and modes of screening.<sup>5,14-17</sup> Additionally, simplifying “substances” to mean only one drug is not necessarily reflective of the reality of the situation. Polysubstance use (the use of multiple substances at any given time) is common during pregnancy and may occur in as many as half of all pregnancies by women who use substances.<sup>4,11,18</sup>

The epidemiology of cannabis use in pregnancy in Canada is relatively unknown. According to the Canadian Tobacco, Alcohol, and Drugs Survey (CTADS), 10.6% of women in Canada reported past year cannabis use in 2015,<sup>19</sup> and likely is under-reported due to the current illicit status. In one study exploring the outcomes of prenatal cannabis and alcohol exposure on academic achievement, Goldschmidt et al.<sup>20</sup> reported on the frequency of concurrent cannabis and alcohol use during pregnancy. In their study, 14% of women reported heavy use of cannabis (i.e., one or

more joints per day) during the first trimester of pregnancy, compared to 5.3% and 5.0% respectively during the second and third trimesters of pregnancy.

Recent studies from the United States report that prevalence of past-month cannabis use by pregnant women is increasing and is between 4% and 8%. Among past-year cannabis users (n = 17,934), use almost daily was reported by 16.2% of pregnant women; and 18.1% of pregnant women met criteria for abuse and/or dependence.<sup>21</sup>

In one prospective study, data suggest that many women achieve abstinence in pregnancy. In their sample of former users, during pregnancy, 78% reported abstaining from cannabis.<sup>18</sup> Similarly, Chasnoff et al. (2005) also reported decreased cannabis use in women after pregnancy recognition, but not abstinence.<sup>22</sup> Forray et al. (2015)<sup>18</sup> found that of those who achieved abstinence during pregnancy, 41% who used cannabis experienced a relapse by 3 months postpartum. These findings suggest a need to improve the general understanding of substance use over the course of pregnancy and in the postpartum period; and the tools and strategies that would be most helpful to promote lifelong abstinence.

Knowledge about potential risks of cannabis use during pregnancy remain largely unknown. There is a prevalent belief that cannabis “natural” and an “herb” and “vegan” that can be safely used for nausea in pregnancy.<sup>23</sup> One study reports that approximately 70% of both pregnant and nonpregnant women believe there is slight or no risk of harm from using cannabis once or twice a week.<sup>21</sup> In a cross-sectional convenience sample survey of women presenting for prenatal care, investigators examined pregnant women’s cannabis use patterns in the context of their views on legalization and knowledge regarding potential harms. Of 306 women surveyed, 35% reported current use, and 34% of those planned to continue use in pregnancy. Almost all participants (96%) with ongoing use reported using marijuana for nausea. Overall, 70% of participants reported perceived risks of use in pregnancy, and 62% cited risk to the pregnancy as a reason to cut back or quit. Women with ongoing use were more likely to believe there was no harm of use during pregnancy compared with women who quit (75% vs 26%, P,.001). Ten percent reported they would be more likely to use cannabis during pregnancy if it were legalized.<sup>23</sup>

In Colorado, a recent survey of cannabis dispensaries found that 69% recommended the use of cannabis for nausea and vomiting of pregnancy. Medical dispensaries were even more likely to recommend use; 83 % of those with medical license to dispense gave this advice. The evidence base most frequently cited was personal experience. <sup>24</sup>

Few studies have specifically examined the effects of cannabis on pregnancy, delivery, and lactation. Observational studies in humans can be confounded by inaccurate self-reporting of cannabis use and of behavioral and sociodemographic variables that correlate with prenatal cannabis use and may impact pregnancy outcomes (e.g., age, socioeconomic status, prenatal care access, and use of tobacco, alcohol and other illicit drugs).

A recent meta-analysis of 31 studies by Conner et al.<sup>25</sup> showed that, an association between heavy use and adverse outcomes. Another meta analysis, however, revealed that infants exposed

to cannabis in utero had a decrease in birth weight compared with infants whose mothers did not use cannabis during pregnancy and were also more likely to need placement in the neonatal intensive care unit compared with infants whose mothers did not use cannabis during pregnancy.<sup>26</sup>

Another study showed that prenatal cannabis use was associated with a 50% increased likelihood of low birth weight, independent of maternal age, race/ethnicity, level of education, and tobacco use during pregnancy.<sup>27</sup>

Data from three (one Canadian) prospective longitudinal human cohorts confirm that there are cognitive, psychological and behavioral effects of prenatal cannabis exposure, some of which persist into young adulthood.<sup>28</sup> Longer studies have not been completed to date.

Together, these data suggest that cannabis use during pregnancy give ample reason for concern regarding the impact of cannabis on fetal growth. Women may believe that a smaller baby will mean an easier birth, and not understand that appropriate fetal growth is a cardinal sign of fetal wellbeing, and correlates to markers of neurocognitive function in childhood, such as school performance.

## CANNABIS EXPOSURE, FETAL BRAIN DEVELOPMENT AND LONG-TERM OUTCOMES

The neurodevelopmental data in humans and animals suggest that prenatal exposure to cannabis may lead to subtle, persistent changes in targeted aspects of higher-level cognition and psychological well-being and human and experimental studies show that long-term and heavy cannabis use during pregnancy can impair brain maturation and predispose the offspring to neurodevelopmental disorders.<sup>29</sup>

*In utero* cannabis exposure has been associated with impaired brain development and long-lasting adverse effects on cognitive function,<sup>29</sup> and data suggest suggested that maternal cannabis use during pregnancy impacts children's neurocognitive functioning, with deficits in memory, verbal, and perceptual skills; impaired performance in oral and quantitative reasoning and short-term memory, impaired executive functioning, and deficits in reading, spelling, and academic achievement.<sup>30</sup> These effects tend to be subtle and are limited by certain age groups.<sup>30</sup> In addition, children exposed to cannabis prenatally have been suggested to be more hyperactive, inattentive, and impulsive,<sup>31,32</sup> although, by adolescence, some impairments appear to be mitigated.<sup>33</sup>

There is some evidence indicating that prenatal cannabis exposure may contribute to an earlier initiation and frequency of subsequent substance use<sup>33-35</sup> as well as aggressive behaviour.<sup>36</sup>

While there is some comfort to be found that cannabis does not appear to be a powerful teratogen, there is reason to be very concerned that the neurotoxic and neuroteratogenic effects

found, while subtle, are associated with persistent changes in targeted aspects of higher-level cognition and psychological well-being.<sup>37</sup>

## CONCLUSION

Although research related to the effects of cannabis during pregnancy has its limitations, potential risks for adverse effects on pregnancy, on fetal growth and development, and for long-lasting neurobehavioural effects have been demonstrated.

Until more is known about both the short- and long-term effects of cannabis use across the lifespan (e.g., effects on babies, children, adolescents, and adults), it is safest to avoid cannabis in any of its forms—ingested, smoked or topically applied, while pregnant, while breastfeeding, and around children. Special attention will need to be paid to women who have dependency, or for those who are using it for treatment of other symptoms.

There is an urgent need for public awareness and education related to cannabis and pregnancy. A recent social media educational video released by the Society of Obstetricians and Gynaecologists of Canada, ([https://www.youtube.com/watch?v=sZ\\_1vISa\\_a8](https://www.youtube.com/watch?v=sZ_1vISa_a8)); (<https://www.youtube.com/watch?v=hxU5fBsmpKo>) with support from Health Canada, has reached over 9.7 million impressions in 4 short weeks. This one small measure is not sufficient to impact behaviour or shift entrenched beliefs.

There is also an urgent need for further research addressing the neurodevelopmental teratogenicity of cannabis and the potential long-term outcomes associated with prenatal cannabis exposure and the Canadian Institutes for Health Research has prioritized this topic area for research programs. Finally, there remains a critical need to create evidence-based practice resources for health care professionals to enable them to provide the best advice to their patients about the potential impacts of cannabis use.

The overwhelming advice of researchers in this field is that the safest course of action is to avoid cannabis exposure *in utero*, and to the developing infant, yet women and cannabis dispensers are likely to believe it is safe. There is a very real risk that *legalization may be equated to safe* in the minds of the public. The government, in legalizing cannabis, which comes from a plant containing hundreds of active chemicals, needs to:

1. Take immediate steps to ensure that the message regarding safety in pregnancy is clear and unambiguous.
2. Recognize that it we are in the unique position to address the enormous gap in research in the neurodevelopmental safety of these substances, and should commit to supporting this research
3. Provide mechanisms to support clinical/population health research including long term follow up
4. Provide guidance on regulation to ensure that false health claims are not made regarding cannabis in pregnancy

5. Support the development of clinical practice guidelines and evidence-based educational initiatives for cannabis dispensaries, health providers and pharmacists as well as knowledge dissemination.

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