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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Cannabis Use During Pregnancy: Safety

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Research Questions

1. What is the clinical evidence regarding the safety of cannabis use during pregnancy?

Key Findings

Two systematic reviews with meta-analyses and nine non-randomized studies were identified regarding the safety of cannabis use (medical or recreational) during pregnancy for pregnant women and their children.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, and meta-analyses, randomized controlled trials, non-randomized studies, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and April 13, 2017. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Pregnant women and their children (up to age five)
Intervention	Cannabis use (medical or recreational) during pregnancy
Comparator	No cannabis use during pregnancy
Outcomes	Safety (maternal outcomes during pregnancy, delivery, and post-partum, fetal and neonatal health and development, early childhood development [e.g., cognition, executive function social skills, behaviour])
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Two systematic reviews with meta-analyses and nine non-randomized studies were identified regarding the safety of cannabis use (medical or recreational) during pregnancy for pregnant women and their children. No relevant health technology assessments, randomized controlled trials, or evidence-based guidelines were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Two systematic reviews with meta-analyses[1-2] and nine non-randomized studies[3-11] were identified regarding the safety of cannabis use (medical or recreational) during pregnancy for pregnant women and their children. There was a general disagreement in the results of these studies. One systematic review with meta-analysis[2] and five non-randomized studies[3,5,9-11] observed an increased risk for various adverse neonatal outcomes in women using cannabis during pregnancy. These outcomes included anaemia,[2] decreased birth weight,[2,3,9,10] increased need for intensive neonatal care,[2,9] spontaneous preterm birth,[5] and an increased risk for stillbirth.[11] These results were contradicted by another systematic review with meta-analysis[1] and three non-randomized studies,[4,6,8] where the authors concluded that cannabis use during pregnancy did not result in increased risk for adverse neonatal outcomes. Detailed study characteristics are provided in Table 2.

Table 2: Summary of Included Studies on the Safety of Cannabis Use During Pregnancy for Pregnant Women and their Children

First Author, Year	Study Characteristics	Intervention	Comparator	Outcomes	Conclusions
Systematic Reviews and Meta-Analyses					
Conner, 2016[1]	• 31 included observational studies • N = NR	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Low birth weight • Preterm delivery • Birth weight • Gestational age at delivery • Level II or greater nursery admission • Stillbirth • Spontaneous abortion • Apgar score • Placental abruption • Perinatal death	• Cannabis use did not have an effect on adverse neonatal outcomes when other confounding factors were controlled for
Gunn, 2016[2]	• 24 included case-control studies, cross-	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Anaemia • Birth weight • Neonatal length	• Cannabis use during pregnancy led to an increased number of

Table 2: Summary of Included Studies on the Safety of Cannabis Use During Pregnancy for Pregnant Women and their Children

First Author, Year	Study Characteristics	Intervention	Comparator	Outcomes	Conclusions
	sectional, and cohort studies • N = NR			• Placement in the neonatal intensive care unit • Gestational age • Head circumference • Preterm birth	adverse outcomes for women and their children (including anaemia, decreased birth weight, and increased likelihood to need placement in the neonatal intensive care unit)
Non-Randomized Studies					
Brown, 2016[3]	• N = 344	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Infant birth weight • Gestational age	• Cannabis use during pregnancy led to increased risk of low birth weight and increased likelihood of being small for their gestational age
Dotters-Katz, 2016[4]	• N = 1,867	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Death • Intraventricular hemorrhage • Periventricular leukomalacia • Bronchopulmonary dysplasia • Necrotizing enterocolitis • Cerebral palsy • Bayley II Scales <70 at age 2	• Marijuana exposure in-utero was not associated with adverse neonatal or childhood outcomes
Leemaqz, 2016[5]	• N = 5,588	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Preeclampsia • Gestational hypertension • Small-for-gestational-age • Spontaneous preterm births • Gestational diabetes	• Cannabis use led to increased risk for spontaneous preterm birth
Mark, 2016[6]	• N = 396	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Incidence of low birth weight • Preterm delivery • Neonatal intensive care unit admissions • Prenatal care utilization	• There were no differences in measured outcomes between the two groups

Table 2: Summary of Included Studies on the Safety of Cannabis Use During Pregnancy for Pregnant Women and their Children

First Author, Year	Study Characteristics	Intervention	Comparator	Outcomes	Conclusions
McLemore, 2016[7]	• N = NR	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Fetal gestational age • Neonatal responses • Cognitive and behavioral skills • Birth length and weight • Neonatal body length • Infant-child sleep, cognition, and behavioral parameters • Growth • Infant-child attention and aggression	• No results or author's conclusions were available in the abstract
Conner, 2015[8]	• N= 8,138	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Birth weight • Neonatal intensive care unit admission • 5-minute Apgar score • Umbilical artery pH	• The use of marijuana during pregnancy did not significantly increase poor neonatal outcomes after adjusting for other risk factors
Warshak, 2015[9]	• N = 6,468	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Preterm delivery • Pre-eclampsia • Gestational diabetes • Cesarean delivery • Fetal growth restriction • Stillbirth • Neonatal intensive care unit admission • Perinatal mortality	• Marijuana use during pregnancy increased the risk for small for gestational age and neonatal intensive care unit admissions
Janisse, 2014[10]	• N = 3,164	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Gestational duration • Fetal growth and birth weight	• Marijuana use decreased birth weight
Varner, 2014[11]	• N= 2,595	• Cannabis use during pregnancy	• No cannabis use during pregnancy	• Rate of stillbirth	• Cannabis use was associated with an increased risk of stillbirth

Abbreviations: NR = not reported.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-Analyses

1. Conner SN, Bedell V, Lipsey K, Macones GA, Cahill AG, Tuuli MG. Maternal marijuana use and adverse neonatal outcomes: a systematic review and meta-analysis. Obstet Gynecol. 2016 Oct;128(4):713-23.
PubMed: PM27607879

2. Gunn JK, Rosales CB, Center KE, Nunez A, Gibson SJ, Christ C, et al. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. BMJ Open. 2016 Apr 5;6(4):e009986. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4823436

PubMed: PM27048634

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

3. Brown SJ, Mensah FK, Ah KJ, Stuart-Butler D, Glover K, Leane C, et al. Use of cannabis during pregnancy and birth outcomes in an Aboriginal birth cohort: a cross-sectional, population-based study. BMJ Open. 2016 Feb 23;6(2):e010286. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4769386

PubMed: PM26908527

4. Dotters-Katz SK, Smid MC, Manuck TA, Metz TD. Risk of neonatal and childhood morbidity among preterm infants exposed to marijuana. J Matern Fetal Neonatal Med. 2016 Dec 6;1-19.
PubMed: PM27921445

5. Leemaqz SY, Dekker GA, McCowan LM, Kenny LC, Myers JE, Simpson NA, et al. Maternal marijuana use has independent effects on risk for spontaneous preterm birth but not other common late pregnancy complications. Reprod Toxicol. 2016 Jul;62:77-86.
PubMed: PM27142189

6. Mark K, Desai A, Terplan M. Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes. Arch Womens Ment Health. 2016 Feb;19(1):105-11.
PubMed: PM25895138

7. McLemore GL, Richardson KA. Data from three prospective longitudinal human cohorts of prenatal marijuana exposure and offspring outcomes from the fetal period through young adulthood. Data Brief. 2016 Dec;9:753-7. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5096595

PubMed: PM27833935

8. Conner SN, Carter EB, Tuuli MG, Macones GA, Cahill AG. Maternal marijuana use and neonatal morbidity. Am J Obstet Gynecol. 2015 Sep;213(3):422-4.
PubMed: PM26026918

9. Warshak CR, Regan J, Moore B, Magner K, Kritzer S, Van Hook J. Association between marijuana use and adverse obstetrical and neonatal outcomes. J Perinatol. 2015 Dec;35(12):991-5.
PubMed: PM26401751

10. Janisse JJ, Bailey BA, Ager J, Sokol RJ. Alcohol, tobacco, cocaine, and marijuana use: relative contributions to preterm delivery and fetal growth restriction. Subst Abus. 2014;35(1):60-7.
PubMed: PM24588295

11. Varner MW, Silver RM, Rowland Hogue CJ, Willinger M, Parker CB, Thorsten VR, et al. Association between stillbirth and illicit drug use and smoking during pregnancy. Obstet Gynecol. 2014 Jan;123(1):113-25. Available from:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3931517
PubMed: PM24463671

Guidelines and Recommendations

No literature identified.

Appendix — Further Information

Systematic Reviews and Meta-Analyses

Cannabis Exposure Unspecified

12. Irner TB. Substance exposure in utero and developmental consequences in adolescence: a systematic review. Child Neuropsychol. 2012;18(6):521-49. PubMed: PM22114955

Non-Randomized Studies

Alternate Outcomes

13. Carter RC, Wainwright H, Molteno CD, Georgieff MK, Dodge NC, Warton F, et al. Alcohol, methamphetamine, and marijuana exposure have distinct effects on the human placenta. Alcohol Clin Exp Res. 2016 Apr;40(4):753-64. PubMed: PM27038593

14. El Marroun H, Tiemeier H, Franken IH, Jaddoe VW, van der Luqt A, Verhulst FC, et al. Prenatal cannabis and tobacco exposure in relation to brain morphology: a prospective neuroimaging study in young children. Biol Psychiatry. 2016 Jun 15;79(12):971-9. PubMed: PM26422004

Alternate Population

15. Sonon K, Richardson GA, Cornelius J, Kim KH, Day NL. Developmental pathways from prenatal marijuana exposure to Cannabis Use Disorder in young adulthood. Neurotoxicol Teratol. 2016 Nov;58:46-52. PubMed: PM27208888

16. Day NL, Goldschmidt L, Day R, Larkby C, Richardson GA. Prenatal marijuana exposure, age of marijuana initiation, and the development of psychotic symptoms in young adults. Psychol Med. 2015 Jun;45(8):1779-87. PubMed: PM25534593

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Qualitative Studies

19. Chabarria KC, Racusin DA, Antony KM, Kahr M, Suter MA, Mastrobattista JM, et al. Marijuana use and its effects in pregnancy. Am J Obstet Gynecol. 2016 Oct;215(4):506-7. PubMed: PM27263998

Clinical Practice Guidelines - Unspecified Methodology

20. Committee on Obstetrics, American College of Obstetricians and Gynecologists [Internet]. Marijuana use during pregnancy and lactation [committee opinion no. 637]. Washington (DC): American College of Obstetricians and Gynecologists; 2015 Jul [cited 2017 Apr 20]. Available from: http://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Marijuana-Use-During-Pregnancy-and-Lactation

21. Reece-Stremtan S, Marinelli KA, and The Academy of Breastfeeding Medicine. Guidelines for breastfeeding and substance use or substance use disorder [Internet]. Breast Med. 2015 [cited 2017 Apr 20];10(3):135-141. Available from: http://www.bfmed.org/Media/Files/Protocols/Guidelines%20for%20Breastfeeding%20and%20Substance%20Use%20or%20Use%20Disorder.pdf

Review Articles

22. Forray A. Substance use during pregnancy. F1000Res. 2016 May 13;5. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4870985
PubMed: PM27239283

23. Porath-Waller AJ. Clearing the smoke on cannabis: maternal cannabis use during pregnancy – an update [Internet]. Ottawa (ON): Canadian Centre on Substance Abuse; 2015. Available from: http://www.ccsa.ca/Resource%20Library/CCSA-Cannabis-Maternal-Use-Pregnancy-Report-2015-en.pdf

24. Jaques SC, Kingsbury A, Henshcke P, Chomchai C, Clews S, Falconer J, et al. Cannabis, the pregnant woman and her child: weeding out the myths. J Perinatol. 2014 Jun;34(6):417-24.
PubMed: PM24457255

25. Behnke M, Smith VC, Committee on Substance Abuse, Committee on Fetus and Newborn [Internet]. Prenatal substance abuse: short- and long-term effects on the exposed fetus. Pediatrics. 2013 [cited 2017 Apr 20] 131(3). Available from: http://pediatrics.aappublications.org/content/131/3/e1009

26. United Nations Office on Drugs and Crime (UNODC) [Internet]. Cannabis: a short review [discussion paper]. Vienna (Austria): UNODC; 2012. Available from: https://www.unodc.org/documents/drug-prevention-and-treatment/cannabis_review.pdf
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