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**Marijuana Use During Pregnancy: Outcomes for the Pregnant Person, the Fetus, and
Provider Recommendations**

Anna Sump

University of South Dakota

April 20, 2023

Acknowledgments

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Abstract

Background

Marijuana is the most commonly used federally illicit substance in the United States, with the Centers for Disease Control and Prevention (CDC, 2022) reporting it was used by an estimated 48.2 million people in 2019. The legalization of marijuana for medical and recreational use, as well as its decriminalization over the past 20 years, has created a new challenge for healthcare providers and researchers. As of December 2022, 18 states and the District of Columbia have legalized recreational use, while the remaining 32 do not offer legalized recreational use (U.S. Department of Health and Human Services, 2022). Regardless of its legal status, people use marijuana, pregnant or not. A 2019 study using National Survey on Drug Use and Health data found just under a half a million participants, 4.71% used marijuana for medical and/or non-medical purposes while pregnant (Volkow, et al.).

Objectives

The objective of this rapid review is to determine if high quality research projects have identified the effect(s) of marijuana use during pregnancy on the pregnant person, the fetus, and what provider recommendations around the use of marijuana during pregnancy entail. The target population is pregnant patients. The intervention was marijuana use during pregnancy - medical or recreational use. The comparison was no marijuana use during pregnancy. The outcome examined was effects on the pregnant person and the fetus. This review set out to find published studies that answer this question: What are the most current provider recommendations on marijuana use during pregnancy, taking into account the effects of use on the pregnant person and the fetus?

Data Sources

PubMed (December 2017 to December 2022) and CINAHL Complete (via EBSCOhost) (December 2017 to December 2022).

Study Eligibility Criteria, Participants, and Interventions

Published articles related to marijuana use during pregnancy were included in this review. In order to be included, the articles were required to be peer reviewed, published in the last 5 years (2017-2022), in the English language, and accessible to students for free through the USD Library resources as a full text. Empirical studies as well as review studies were included.

Study Appraisal and Synthesis Methods

Evidence was synthesized by being placed into one or more of the following categories: (1) marijuana use causes negative effects in the fetus, (2) marijuana use does not cause negative effects in the fetus, (3) marijuana use causes negative effects in the pregnant person, (4) marijuana use does not cause negative effects in the pregnant person, (5) marijuana use has unknown effects on the pregnant person, (6) future research is needed, (7) provider/researcher recommendation given/suggested, and (8) other. The majority of studies included in this review were placed in two or more categories as their focus and results indicated several of the above listed categories.

Results and Limitations

This review found 499 articles, which was reduced to 39 after screening and relevance checks (see Table 1, Table 2, and Diagram 1 for a detailed analysis).

Conclusion and Implications of Key Findings

Several studies found negative outcomes to the fetus when the pregnant person used marijuana, while others found no negative outcomes. Some studies noted changes to the placenta

when the participants used marijuana, while others noted no changes. Very few studies looked at the outcomes for the pregnant person. More research is needed to determine the full range of effects of marijuana use during pregnancy. In many studies, the time of use and amount were unable to be determined or directly correlated to the outcomes experienced by the fetus and the pregnant person. Looking at provider recommendations, the studies that included this topic stated providers should 1) encourage abstinence and 2) create an environment that allows for open communication between provider and patient, rather than one of fear and judgment.

Introduction

Rationale

Recreational and medical marijuana legalization has spread rapidly across the United States over the past two decades. The use of marijuana, both legally and illicitly, has created numerous questions for the medical community. A consequential one being, how should providers counsel patients on marijuana use prior to, during, and after a pregnancy?

Objectives

Examination of published literature to answer the PICOT question: What are the most current provider recommendations on marijuana use during pregnancy, taking into account the effects of use on the pregnant person and the fetus?

Definition of Terms

Marijuana - “the psychoactive dried resinous flower buds and leaves of the female hemp or cannabis plant (*Cannabis sativa* or *C. indica*) that contain high levels of THC and are smoked, vaped, or ingested (as in baked goods) especially for their intoxicating effect” (Merriam-Webster, 2023 Marijuana)

Cannabis - “the psychoactive dried flower buds, leaves, or preparations (such as hashish) or chemicals (such as THC) that are derived from the cannabis plant” (Merriam-Webster, 2023 Cannabis)

Cannabinoid - “any of various naturally-occurring, biologically active, chemical constituents (such as cannabidiol or cannabinol) of hemp or cannabis including some (such as THC) that possess psychoactive properties” (Merriam-Webster, 2023 Cannabinoid)

The terms “marijuana” and “cannabis”, defined above, will be used identically and interchangeably throughout this review.

Methods

Eligibility Criteria

The eligibility criteria for this rapid review was articles published in peer reviewed journals and written in the English language. Articles also needed to be empirical studies that utilized qualitative, quantitative, or mixed methods approaches, or review articles. Finally, all articles needed to be accessible to students for free through the USD Library resources as full text.

Information Sources

A rapid review of articles using PubMed (December 2017 to December 2022) and CINAHL Complete (via EBSCOhost) (December 2017 to December 2022).

Search

Table 1

PubMed Search

| | Subject Heading Search | Search Results | Inclusion/Exclusion Criteria | Total | Total Articles Included |
|---|--|----------------|---|-----------------------|-------------------------|
| 1 | “marijuana use” | 24,510 | published last 5 years (2017-2022), free full text (and full text), English | 4,962 | |
| 2 | “pregnancy or pregnant or prenatal or antenatal” | 1,171,612 | published last 5 years (2017-2022), free full text (and full text), English | 127,823 | |
| 3 | “medical marijuana” | 7,920 | published last 5 years (2017-2022), free full text (and full text), English | 2,361 | |
| 4 | 1 and 2 | 1,431 | published last 5 years (2017-2022), free full text (and full text), English | 261 | |
| 5 | 2 and 3 | 447 | published last 5 years (2017-2022), free full text (and full text), English | 117 | |
| 6 | 1, 2, and 3 | 439 | published last 5 years (2017-2022), free full text (and full text), English | 98 | 34 |
| | | | | Total Included | 34 |

Refer to Diagram 1 for records removed.

Table 2*CINAHL Complete (via EBSCOhost) Search*

| | Subject Heading Search | Search Results | Inclusion/Exclusion Criteria | Total | Total Articles Included |
|---|--|----------------|--|-----------------------|-------------------------|
| 1 | “marijuana use” | 6,117 | 2017-2022, full text, academic journal | 1,170 | |
| 2 | “pregnancy or pregnant or prenatal or antenatal” | 303,287 | 2017-2022, full text, academic journal | 34,581 | |
| 3 | “medical marijuana” | 3,009 | 2017-2022, full text, academic journal | 914 | |
| 4 | 1 and 2 | 383 | 2017-2022, full text, academic journal | 95 | |
| 5 | 2 and 3 | 86 | 2017-2022, full text, academic journal | 20 | |
| 6 | 1, 2, and 3 | 60 | 2017-2022, full text, academic journal | 19 | 5 |
| | | | | Total Included | 5 |

Refer to Diagram 1 for records removed.

Combined Pubmed and CINAHL Results = 39 Results

Data Collection Process

The review author assessed studies for inclusion, extracted the data, and entered the data into Table 4.

Data Items

The Johns Hopkins Nursing Evidence-Based Practice (EBP) classification of evidence level was used to determine the level of evidence and quality rating of each source (The Johns Hopkins Hospital/Johns Hopkins University School of Nursing, 2017). Level I includes experimental studies, randomized controlled trials (RCT), and systematic review of RCTs, with or without meta-analysis. Level I evidence is considered high quality. Level II includes quasi-experimental studies, as well as systematic reviews of a combination of RCTs and quasi-experimental studies, or quasi-experimental studies only, with or without meta-analysis. Level II evidence is considered good quality evidence. Level III evidence includes non-experimental studies and systematic reviews of a combination of RCTs, quasi-experimental, and nonexperimental studies, or nonexperimental studies only, with or without meta-analysis. Level IV evidence includes the “opinion[s] of respected authorities and/or nationally recognized expert committees or consensus panels based on scientific evidence” such as, clinical practice guidelines and consensus panels/position statements. Level V evidence is based on experiential and non research evidence, this includes integrated reviews, literature reviews, quality improvement, program, or financial evaluation, case reports, and opinions of nationally recognized expert(s) based on experiential evidence.

Summary Measures

Data were summarized based on an analysis of results that pertained to outcomes of the pregnant person using marijuana on themselves and the fetus, as well as provider recommendations about marijuana use by pregnant individuals. Articles were then categorized in the aforementioned scheme (see Study Appraisal and Synthesis Methods).

Synthesis of Results

Evidence was synthesized by being placed into one or more of eight categories (see Study Appraisal and Synthesis Methods). Results are summarized in Table 3.

Table 3

Synthesis of Results

| Synthesis Category | Number of Articles (Total: 39) |
|--|-----------------------------------|
| (1) marijuana use causes negative effects in the fetus | 27 |
| (2) marijuana use does not cause negative effects in the fetus | 4 |
| (3) marijuana use causes negative effects in the pregnant person | 4 |
| (4) marijuana use does not cause negative effects in the pregnant person | 2 |
| (5) marijuana use has unknown effects in the pregnant person | 1 |
| (6) further research is needed | 19 |
| (7) provider/research recommendation given/suggested | 10 |
| (8) other | 7 |

Risk of Bias Across Studies

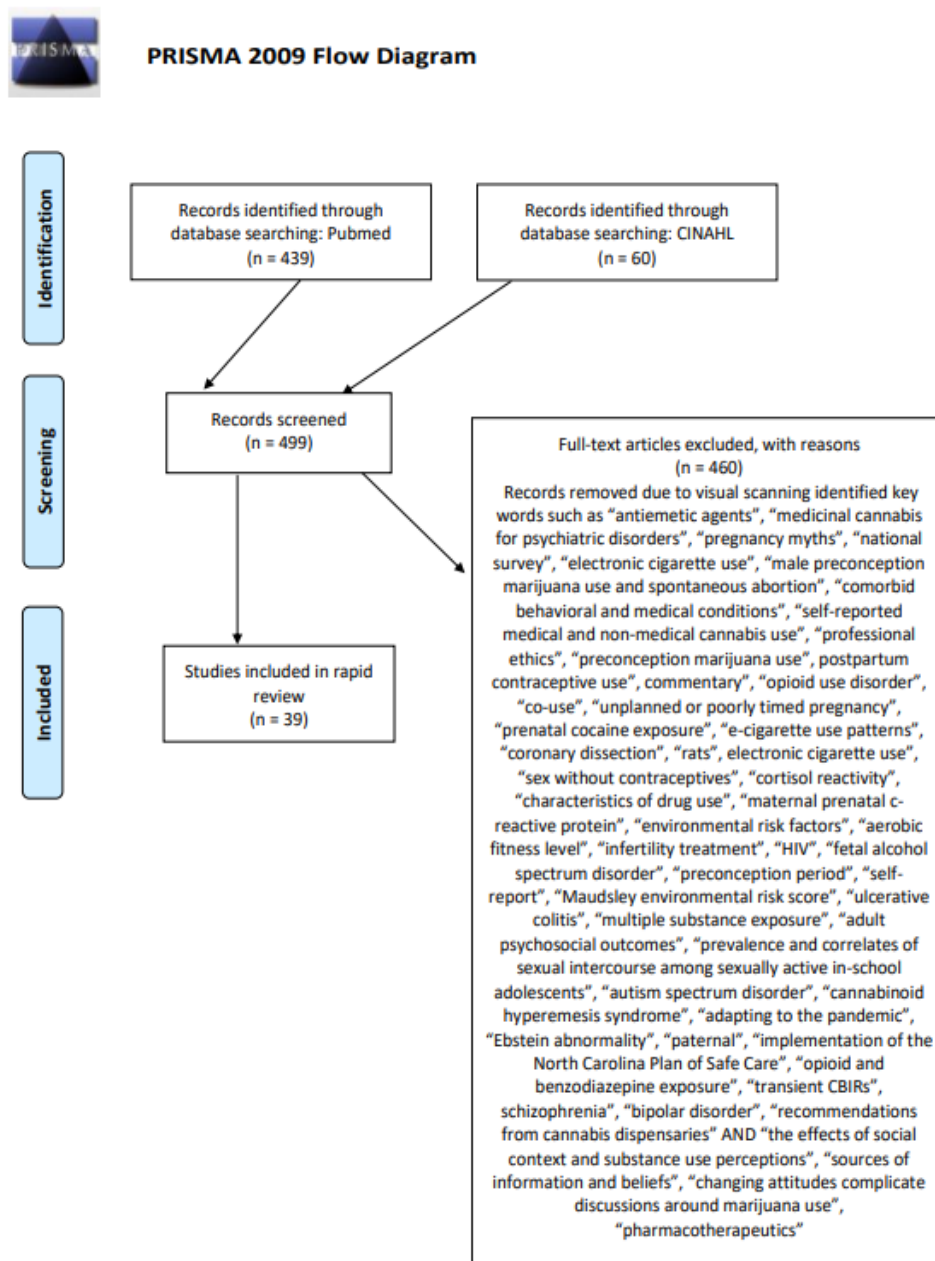
1. Publication bias - Only studies with significant findings are often published.
2. Level I evidence - Studies reviewed constitute a variety of levels of evidence; however, Level I studies are lacking.
3. Quality of studies - See Table 4 for levels of evidence.
4. Populations included/surveyed - Many included studies included pregnant participants primarily or solely from one socioeconomic group or one racial group.

Results

Study Selection

Diagram 1

Study Selection Flow Diagram



Summary of Reviewed Literature

Table 4

Summary of Reviewed Literature

| Reference | Evidence Level / Study Design | Study Aims | Setup and Outcomes Assessed | Results | Authors' Conclusions |
|--|---|--|--|---|--|
| (Agolli, Agolli, et al., 2022) Pubmed | Level V / literature review | “summarize the effects of cannabis use on fetal development during the COVID-19 pandemic” | | “Covid-19 pandemic has served as an additional stimulus that has increased cannabis use among pregnant women. Prenatal cannabis use is associated with health risks, in mother and child. Children born by cannabis using mothers are associated with low infant birth weight and potential effects on offspring neurodevelopment.” | “It is essential that clinicians educate pregnant women about the harms of prenatal cannabis use, elaborate support for women at risk, implement intervention strategies to help them stop using cannabis and offer psychosocial support.” |
| (Allen, Jung, et al., 2020) Pubmed | Level III / cross-sectional, population-based surveillance system | “to determine the association between stressful life events (SLEs) in the year prior to childbirth with (1) pre-pregnancy cannabis use, (2) cessation of cannabis use during pregnancy and (3) postpartum relapse to | <u>Design:</u> data from Pregnancy Risk Assessment Monitoring System (PRAMS) 2016 (a cross-sectional, population-based surveillance system) <u>Setting:</u> survey via mail and telephone in Alaska, Maine, | Pre-pregnancy, 16.4% of respondents used cannabis, with 36.4% continuing to use during pregnancy. Among the 63.6% who did not report use during pregnancy, 23.2% restarted use postpartum. Nine of the 14 | “Stressful life events during the year prior to childbirth appear to be linked to greater odds of women's cannabis use during the perinatal period, especially during pre-pregnancy.” |

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| | | cannabis use” | <p>Michigan, Washington, and Colorado (USA)</p> <p><u>Participants:</u> 6,061 women who delivered a live infant within the last 6 months and had data on cannabis use.</p> <p><u>Measurements:</u> Self-reported data included SLEs and cannabis use. The associations between SLEs and cannabis use were studied via logistic regression models. Models were adjusted for maternal demographics, geography, and cigarette smoking.</p> | <p>SLEs tested were associated with increased odds of pre-pregnancy cannabis use, but only four were associated with increased chance of continued cannabis use during pregnancy. The odds of postpartum relapse to cannabis use were significantly associated with two SLEs (husband or partner said they did not want the pregnancy, and husband or partner or mother went to jail).</p> | |
| (Ayisire, Okobi, et al., 2022) Pubmed | Level V / literature review | “Review existing literature and possible effects of marijuana on PPD documented in published experimental-controlled trials from 1985 to 2022.” | “The literature search strategy was based on the use of online databases such as Google Scholar, PubMed, and Medline by using the keywords such as “cannabis,” “marijuana,” “postpartum depression,” “peripartum depression,” and “depression” and “anxiety,” and “effects of | “the association between cannabis and its use in managing PPD has not been fully explored. In some self-reported studies, marijuana use was linked to positive effects on mood, anxiety relief, sleep regulation, nausea and vomiting reduction, and appetite stimulation-symptoms similar | “as the call for expanding the legalization of marijuana increases, we call for caution. Further research is therefore needed to douse the anecdotal claims of the use of cannabis in managing PPD.” |

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| | | | <p>cannabis.” These keywords and Boolean operators of AND, OR, and NOT were also used to narrow down the search results. The search results were then reviewed and analyzed. However, distinct inclusion and exclusion criteria were developed for the literature so that only relevant studies could be used for this literature review.”</p> | <p>to PPD symptoms. Others strongly discouraged the use of marijuana during the postpartum period. However, we could not find any randomized clinical study involving humans that examined the use of cannabis for the treatment of PPD. Generally, cannabis is considered a recreational drug, which many clinicians discourage during pregnancy and postpartum.”</p> | |
| <p>(Bailey, Wood, et al., 2020) CINAHL</p> | <p>Level II / population-based cohort</p> | <p>“To examine associations between in utero marijuana exposure and birth outcomes.”</p> | <p>“In two separate cohorts (Appalachian, Rocky Mountain), data were collected from medical records. Marijuana exposure was positive based on urine drug screening at delivery, with nonexposed controls matched on multiple factors including other substance exposure.”</p> | <p>“Marijuana-exposed newborns (n = 531) had significantly worse birth outcomes than controls (n = 531), weighing 218 g less, 82%, 79%, and 43% more likely to be low birth weight, preterm, or admitted to the NICU, respectively, and significantly lower Apgar scores.”</p> | <p>“Marijuana exposure in utero predicted newborn factors linked to longer-term health and development issues... Findings add to growing evidence linking marijuana exposure to adverse birth and longer-term outcomes. Women should be encouraged to avoid marijuana use during pregnancy.”</p> |
| <p>(Chang, Tarr, et al., 2019)</p> | <p>Level III / observational study</p> | <p>“to qualitatively describe the marijuana use</p> | <p>“semi-structured interviews with pregnant women</p> | <p>“Main themes that emerged from the interviews were</p> | <p>“Pregnant women who used marijuana in</p> |

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| Pubmed | | experiences, beliefs, and attitudes of women who used marijuana during pregnancy.” | [25] who had either reported current marijuana use or had urine testing positive for marijuana. Interviews were transcribed verbatim and analyzed for patterns and themes.” | that women: 1) reported higher amounts of marijuana use prior to pregnancy and attempted to reduce their use once they realized they were pregnant; 2) used marijuana to help with nausea and appetite changes during pregnancy or to improve mood; 3) described marijuana as “natural” and “safe” compared to other substances such as alcohol, tobacco, other recreational drugs, and prescribed medications; 4) had conflicting opinions regarding whether marijuana was addictive; and 5) were uncertain but had some concerns regarding potential risks of prenatal marijuana use.” | pregnancy held contradictory beliefs about continued use... These findings have implications for how practitioners address prenatal marijuana use and highlight the need for further research on developmental outcomes.” |
| (Coleman-Cowger, Oga, et al., 2018) Pubmed | Level III / cohort | “to document the prevalence and correlates of co-use of cannabis and tobacco cigarettes among adult pregnant women utilizing secondary data from a larger study that compared and | Pregnant women from two urban university hospitals were recruited from January to December 2017. Demographics as well as cannabis and tobacco cigarette use characteristics | 9.0% of participants reported co-use of cannabis and tobacco, 12.1% reported only cannabis use, 7.8% reported only tobacco cigarette use, and 71.1% reported no cannabis or tobacco cigarette use in the | “Screening and interventions to address concurrent cannabis and tobacco use during pregnancy are needed, particularly among subpopulations with higher co-use rates. It is imperative to |

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| | | validated screeners for illicit and prescription drug use during pregnancy” | were obtained via self-report. Urine and hair samples were used for drug testing. Participants EMRs were reviewed within two weeks post-birth to determine birth outcomes. | past month. The co-use group had the highest odds of a small head circumference and birth defects compared with other use groups. The cannabis only group had 12 times higher odds of a stillbirth or miscarriage. | further explore and highlight the possible health implications of maternal co-use given the high prevalence rates found in this study sample.” |
| De Genna, Goldschmidt, et al., 2018) Pubmed | Level III / longitudinal cohort study | “to assess if prenatal and postnatal co-use of cannabis and tobacco predict co-use and drug use by adult offspring” | Data from a 22-year longitudinal study was used to identify long-term maternal patterns of cannabis and tobacco co-use from the first trimester of pregnancy until 16 years postpartum. | “Maternal patterns of co-use predict substance use in young adult offspring. Offspring of decreasing co-users (with prenatal exposure) more likely to co-use. Offspring of chronic co-users more likely to have drug use disorder by age 22.” | “The results of this study demonstrate that there is heterogeneity in maternal co-use of cigarettes and cannabis over time. Moreover, this heterogeneity in maternal co-use trajectories has implications for the inter-generational transmission of risk for substance use and abuse in young adult offspring.” |
| (Ezechuku, Diya, et al., 2020) Pubmed | Level V / review | To “highlight the recent advances in the field, which explore the role of endocannabinoids in early pregnancy and the effects of excessive intake of phytocannabinoid | | <i>See Authors’ Conclusions</i> | "endocannabinoids modulate pregnancy, and excessive cannabis intake in early pregnancy has the capacity to control successful pregnancy outcomes. Exposure to |

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| | | s in pregnancy outcomes” | | | cannabis and phytocannabinoids has the capacity to alter fetal development; however, more research is required in this field. Outcomes from these studies may be useful in the development of informed guidelines for the use of cannabis in pregnancy." |
| (Gesterling, & Bradford, 2022) CINAHL | Level V / State of Science Review | “examines the prevalence of cannabis use in pregnancy, its pharmacodynamics and how that is influenced by pregnancy, and associated adverse perinatal and neonatal outcomes” | Trends of cannabis use during pregnancy; pharmacodynamics of cannabis; perinatal and neonatal outcomes; implications for practice | Cannabis is the most used substance in pregnancy (2-26%), often used to treat nausea, vomiting, and poor appetite without consultation of a healthcare provider; THC crosses the placenta, metabolic changes in pregnancy can increase the metabolism and clearance of THC; neonatal outcomes are difficult to define due to numerous potential confounding variables, perinatal outcomes may include preterm prelabor rupture of membranes, placenta previa, chorioamnionitis, | “Cannabis use during pregnancy is not without potential harm. Despite the increasingly permissive legalization of cannabis across the United States, research on cannabis use has methodologic limitations and lacks conclusive findings regarding associated adverse outcomes.” |

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| | | | | and longer hospital stay postpartum; varying state laws regarding legalization, marijuana's Schedule I designation, a lack of clear guidelines from national organizations, and provider bias limit the education being given to pregnant women as well as their ability to be honest with their provider. | |
| (Gnofam, Allshouse, et al., 2020) CINAHL | Level III / retrospective cohort | “to assess whether marijuana legalization was associated with a difference in prevalence of prenatal use or an increase in incidence of adverse perinatal outcomes” | “retrospective cohort of September and October deliveries in the years 2012 through 2015 at a tertiary center in Colorado... Primary outcome of the study was use of marijuana, defined by self-report or biodetection. Secondary outcomes of the study included growth restriction, spontaneous preterm birth, stillbirth, preeclampsia, and neonatal or maternal death. Marijuana use prevalence was compared by year, | “More women used marijuana over the period of legalization (trend $p = 0.01$). Odds of marijuana use were higher after legalization versus before (adjusted odds ratio [aOR] = 1.8, 95% confidence interval [CI]: 1.2–2.6). Incidence of growth restriction was higher after legalization (2.9 vs. 5.1%, $p = 0.0084$). This difference persisted after adjustment for ethnicity and other drugs in multivariable modeling (aOR = 1.9, 95% CI: 1.2–3.0).” | “The prevalence of prenatal marijuana use increased over the time of legalization. Further investigation into the population impact of legalization on obstetrical outcomes is warranted given the observed increase in growth restriction.” |

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| | | | and secondary outcomes between two periods, before and after the opening of the first recreational dispensary.” | | |
| (Grant, Conover, & Chambers, 2020) Pubmed | Level V / literature review | To provide an overview of the literature on the developmental consequences of marijuana use during pregnancy and lactation | | <p>“There is a strong increase in prevalence trends for cannabis use during pregnancy and lactation as more states legalize use of this drug. Information on the teratogenic risk of cannabis is limited but some important themes can be gleaned. Studies have not found a unique phenotypic signature of prenatal exposure but an increased risk of congenital anomalies, particularly gastroschisis, has been reported. Changes in fetal growth have been described in some epidemiological studies but long-term patterns of physical growth appear unaffected. Prenatal exposure to cannabis is not generally associated with reductions in global IQ but specific cognitive</p> | <p>“there is a strong need for prospective birth-cohort studies that collect biological samples to quantify exposure. Data from such studies will be critical to overcoming the weaknesses of past cannabis research and are essential to establishing reliable information on the risks of maternal use. Until that time, health care providers should be encouraged to talk about the risks and benefits associated with cannabis use during pregnancy and lactation with their patients, emphasizing that fetal and neonatal risks cannot be excluded at this time.”</p> |

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| | | | | <p>skills, especially attention and memory, can be negatively impacted. Long-term impacts on psychological health include increased rates of depressive symptoms and anxiety as well as delinquency. Relatively little is known about the risk of maternal cannabis use during lactation but data suggest that infant exposure is relatively low compared to maternal exposure.”</p> | |
| <p>(Greiner, Lo, et al., 2022) Pubmed</p> | <p>Level III / retrospective cohort</p> | <p>“To determine the adverse prenatal effects of marijuana use in women with hypertension in pregnancy.”</p> | <p>“individuals with hypertension in pregnancy that delivered ≥ 23 weeks’ gestation at Oregon Health & Science University [1,217 individuals] (October 2013-September 2018). The primary exposure assessed was marijuana use, identified by chart review of documented patient self-report or positive urine toxicology screen. Individuals were stratified into two groups by</p> | <p>“Women using marijuana in pregnancy were more likely to be younger, non-Hispanic White, publicly insured and using other substances compared to women who did not use marijuana. There were no differences in the overall distribution of hypertensive disorders, including preeclampsia with severe features, in women who used marijuana versus those who did not</p> | <p>“Marijuana use in pregnancy was not associated with maternal or neonatal outcomes or worsened hypertensive disease among women with hypertension in pregnancy after adjusting for maternal characteristics, including use of other substances. Our data highlight the need to consider use of other substances when evaluating the association</p> |

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| | | | <p>marijuana use: use during pregnancy versus never used. Primary outcomes included composite adverse maternal and neonatal outcomes. Secondary outcomes included individual maternal outcomes, rarer neonatal outcomes and severe features of preeclampsia. Differences were analyzed by Fisher's exact, t-test, and logistic regression."</p> | <p>(p = .80). In multivariable analyses, after adjusting for maternal factors and other substance use, marijuana use was not associated with adverse maternal (aOR 1.23, 95% CI 0.43–3.50, p = .69) or neonatal (aOR 0.90, 95% CI 0.28–2.89, p = .86) outcomes."</p> | <p>between marijuana use in pregnancy and adverse pregnancy outcomes"</p> |
| <p>(Gross, Le Neveu, 2022) Pubmed</p> | <p>Level III and V / retrospective cross-sectional qualitative study and literature review</p> | <p>To "advance an empirically informed ethical analysis of this issue [medicinal marijuana use in pregnancy and bias]"</p> | <p>"First, we performed a retrospective cross-sectional qualitative study of prenatal and postpartum records from a random sample of 150 women delivered in an academic hospital system in 2017 to provide evidence and context regarding breastfeeding management in relation to marijuana use. We then perform a scoping literature review on infant</p> | <p>(1) Medical records show punitive language pertaining to the medicinal use of marijuana in pregnancy and misinterpretation of national guidelines. (2) There are likely neurodevelopmental harms from breastmilk exposure to THC. Evidence of effects to the infant from breastmilk exposure to marijuana is limited and largely confounded by additional pregnancy exposure and/or undisclosed exposures.</p> | <p>"Policy interpretations which discourage rather than encourage breastfeeding among women who use of marijuana may cause net harm, compromise autonomy, and disproportionately threaten health and wellbeing of underserved women and infants."</p> |

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| | | | <p>risks from breastmilk marijuana exposure and risks associated with not breastfeeding for infants and women. Finally, we analyze this issue vis-a-vis ethical principles of beneficence, autonomy, and justice.”</p> | <p>“(3) Discouraging breastfeeding for women with marijuana use in pregnancy contradicts beneficence, as it neglects women's health considerations and incorrectly assumes that risks exceed benefits for infants. Restrictive hospital practices (e.g., withholding lactation support) compromise maternal autonomy and exploit power asymmetry between birthing persons and institutions, particularly when compulsory toxicology screening prompts child welfare investigations. Finally, recommending against breastfeeding during prenatal care and imposing restrictions during postpartum hospitalization may exacerbate racial disparities in breastfeeding and related health outcomes.”</p> | |
| (Hasin, 2018) | Level V / literature | "provides an overview of the | | “Potential problems [of cannabis use] | "the need for further research on |

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|---|----------------------------------|---|--|---|--|
| Pubmed | review | changing US epidemiology of cannabis use and associated problems" | | include harms from prenatal exposure [anemia, low birth weight, restricted fetal growth, high NICU admission rates] and unintentional childhood exposure; decline in educational or occupational functioning after early adolescent use, and in adulthood, impaired driving and vehicle crashes; cannabis use disorders (CUD), cannabis withdrawal, and psychiatric comorbidity." | cannabis use and pregnancy outcomes is clear" |
| (Hurd, Manzoni, et al., 2019) Pubmed | Level V / literature review | To "provide insight about specific molecular, epigenetic, neurophysiological, and neural circuits affected by exposure to cannabis and THC during different developmental stages: <i>in utero</i> , nursing, and adolescence" | | <i>See Authors' Conclusions</i> | "In conclusion, common themes have emerged from diverse seminal papers and a growing number of new research studies providing significant evidence that prenatal, perinatal, and adolescent cannabis exposure can induce a wide array of brain and behavioral alterations in adulthood." |
| (Jones, Lotfi, et al., 2022) | Level III / retrospective cohort | "The objective of this study was to examine the | "Meconium drug screens obtained on infants born in | "1,540 meconium drug screens were included in the | "Prenatal marijuana exposure was |

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| Pubmed | study | relationship of prenatal marijuana exposure on neonatal outcomes in infants with marijuana exposure confirmed with meconium drug testing.” | <p>a hospital system in the Pacific Northwest in the USA over a 2.5-year period. 1,804 meconium drug screens were initially obtained, with 1,540 drug screens included in the analysis.”</p> <p>“The following neonatal outcomes were examined: gestational age, preterm birth (<37 weeks), birth weight, low birth weight (defined as birth weight <2.5 kg), length, head circumference, Apgar scores and admission to the neonatal intensive care unit (NICU). Using multivariable logistical and linear regression, we controlled for confounding variables.”</p> | <p>analysis, with 483 positive for delta-9-THC only. Neonates exposed to delta-9-THC had significantly lower birth weight, head circumference and length ($p<0.001$). Neonates with THC exposure had 1.9 times the odds (95% CI 1.3 to 2.7, $p=0.001$) of being defined as low birth weight. Birth weight was on average 0.16 kg lower (95% CI 0.10 to 0.22, $p<0.001$) in those exposed to THC.”</p> | significantly associated with decreases in birth weight, length and head circumference, and an increased risk of being defined as low birth weight.” |
| (Kim, Minnes, et al., 2022) CINAHL | Level III / longitudinal investigation | To investigate “co-occurrence of psychopathology problems in adolescents with biologic and/or environmental susceptibility, including prenatal drug exposure.” | “358 adolescents (54% girls) recruited at birth from an inner-city hospital for a longitudinal investigation of the developmental effects of prenatal polydrug exposure”; | “Latent class modeling indicated four patterns: Normative (57%), substance-use (SU; 24%), mental-health-problems-without-substance-use (MH; 11%), and substance-use-and-other-mental- | The study revealed that prenatal polydrug exposure results in numerous negative effects to the offspring psychopathologically, including increased likelihood of |

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| | | | <p>adolescents and caregivers were assessed by separate examiners at birth as well as 11, 12, 15, 17, and 21 years.</p> | <p>health-problems (SUMH; 7%). Higher irritability increased the odds of developing the MH pattern, whereas higher social disinhibition increased the odds of developing the SU pattern. The odds of manifesting the SUMH pattern were higher for children with higher irritability. For children with higher social disinhibition, the odds of manifesting the SUMH pattern were higher at a trend level. Adolescent comorbidity patterns were differentially associated with problematic tobacco and marijuana use and clinically relevant mental health problems in emerging adulthood, and completion of high school education. Peri-pubertal identification of individual differences in irritability and social disinhibition may mitigate the emergence of</p> | <p>problematic drug use themselves.</p> |
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| | | | | adolescent psychopathology, which could influence emerging adulthood adjustment in this at-risk population.” | |
| (Klebanoff, Fried, 2020) Pubmed | Level III / ambidirectional cohort (historical cohort with continuous follow-up) | To assess the association of in utero marijuana exposure with executive function and aggression at ages 3 ½ to 7 years. | Sample included “women enrolled in the Perinatal Research Repository during prenatal care at Ohio State University Wexner Medical Center and their children, recontacted 3½-7 years post-birth. Children complete 1-2 study visits including cognitive testing, behavioural observation, and maternal and teacher report of behaviour. Family and social environmental factors are assessed.” | “362 eligible children; 32% had mothers who used marijuana during pregnancy, 10% of mothers completed college, and 23% did not complete high school. Mean maternal age at study registration in pregnancy was 26.4 years, and 63% of mothers were African American.” | "The LEAF Study will document the association of prenatal marijuana exposure with development and behaviour in the current era when marijuana is more potent than when previous cohorts were studied. The results may inform policy and interventions to counsel reproductive-aged women about the risks of use during pregnancy and guide prevention and treatment of adverse effects among children. |
| (Ko, Coy, et al., 2020) Pubmed | Level IV / morbidity and mortality weekly report (MMWR) | “To provide population-based estimates of use surrounding pregnancy, identify reasons for and mode of use, and understand characteristics of women who continue versus | Analysis of “data from eight states participating in the 2017 Pregnancy Risk Assessment Monitoring System (PRAMS) marijuana supplement” | “Overall, 9.8% of women reported marijuana use before pregnancy, 4.2% during pregnancy, and 5.5% after pregnancy. The most frequently reported reasons for marijuana use during pregnancy | “Continuous surveillance of marijuana use in the perinatal period can inform clinical guidance, provider and patient education, and public health programs to support evidence-based approaches |

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| | | cease marijuana use during pregnancy” | | were to relieve stress or anxiety, nausea or vomiting, and pain.” | to addressing substance use.” |
| (Marchand, Masoud, et al., 2022) Pubmed | Level V / systematic review and meta-analysis | “To assess available data on neonatal outcomes in marijuana-exposed pregnancies” | “PubMed, Medline, ClinicalTrials.gov, Cochrane, Scopus, and Web of Science were searched from each database's inception until August 16, 2021... All interventional and observational studies that included pregnant women who were exposed to marijuana compared with pregnant women who were not exposed to marijuana and that reported neonatal outcomes were included... All outcomes were formulated prior to data collection” | 16 studies including 59,138 patients found significant increases in 7 adverse neonatal outcomes among women who were exposed to marijuana during pregnancy vs those who were not exposed during pregnancy. These included increased risk of birth weight less than 2,500 g, small for gestational age, preterm delivery, and NICU admission, along with decreased mean birth weight, Apgar score at 1 minute, and infant head circumference. | “women exposed to marijuana in pregnancy were at a significantly increased risk of some adverse neonatal outcomes. These findings suggest that increasing awareness about these risks may be associated with improved outcomes” |
| (Martínez-Peña, Perono, et al., 2021) Pubmed | Level V / literature review | “to discuss the role of the endocannabinoid system during pregnancy and the effects associated with prenatal exposure to cannabinoids in animal and human studies” | | “While several studies have linked prenatal cannabis use with negative birth outcomes, as well as long-lasting neurobehavioral alterations, the impact on other physiological aspects such as metabolic and | “more insight is needed regarding the mechanisms through which gestational exposure to cannabis constituents may result in persistent long-term alterations on the offspring” |

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| | | | | <p>reproductive health have received less attention. In addition, most studies have focused on Δ9-THC and synthetic cannabinoid receptor agonists, with very little research addressing the effects of CBD or endogenous ECS ligands. However, other cannabis components may also disrupt the fetal ECS and have long-term effects, highlighting the need for more whole cannabis exposure models, as well as experiments that consider other popular cannabis components such as CBD.”</p> | |
| <p>(Massey, Mroczek, et al., 2018) Pubmed</p> | <p>Level III / retrospective cohort study</p> | <p>To examine differential associations by infant sex and multiplicative effects associated with the co-use of marijuana and tobacco during pregnancy.</p> | <p>Participants were mother-infant dyads with complete data on all study variables derived from Growing Up Healthy, Behavior and Mood in Babies and Mothers, and the Early Growth and Development Study. Linear regression analysis was used to estimate the direct</p> | <p>Mean birth weight and length of gestation were 3,277 grams and 37.8 weeks, respectively. Rates of prenatal use were as follows: any use, 62.8%; marijuana use, 22.9%; tobacco use, 51.0%; co-use of marijuana and tobacco, 19.3%; alcohol use, 39.0%; other drug use, 9.7%. For all</p> | <p>“Examination of dose-dependence in relationships found in this study, using continuous measures of exposure, is an important next step. Finally, we underscore the need to consider (a) the potential moderating influence of fetal sex on exposure-related neurodevelopment</p> |

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| | | | effects on birth weight and length of gestation associated with marijuana use, tobacco use, and co-use. This was done for the full sample, as well as male and female infants separately. | infants, birth weight was affected by marijuana use and tobacco use separately, but no greater effects were seen from co-use. In analyses stratified by sex, lower birth weight following marijuana use was seen in male infants but not female infants. | al risks; and (b) the importance of quantifying expressions of risk through subtle alterations, rather than dichotomous outcomes.” |
| (Meinhofer, Witman, et al., 2021) Pubmed | Level II / multi-period difference-in-difference (DID) estimator | To determine the effects of medical marijuana law and recreational marijuana law implementation on perinatal outcomes. | “multiperiod difference-in-differences estimator that exploited variation in effective dates of medical marijuana laws (MML) and recreational marijuana laws (RML)” | “the proportion of maternal hospitalizations with marijuana use disorder increased by 23% (0.3 percentage points) in the first three years after RML implementation, with larger effects in states authorizing commercial sales of marijuana. This growth was accompanied by a 7% (0.4 percentage points) decline in tobacco use disorder hospitalizations, yielding a net zero effect over all substance use disorder hospitalizations. RMLs were not associated with changes in newborn health. MMLs had | “In absolute numbers, our findings implied modest or no adverse effects of marijuana liberalization policies on the array of perinatal outcomes considered” |

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| | | | | no significant effect on maternal substance use disorder hospitalizations nor on newborn health and fairly small effects could be ruled out” | |
| (Metz & Borgelt, 2018) Pubmed | Level V / literature review | “Two recent systematic reviews and meta-analyses provide a comprehensive review of the human literature related to marijuana and pregnancy outcomes... to provide evidence-based information regarding the biologic plausibility of existing findings and expand on outcomes not addressed in the meta-analyses in order to provide a practical review of the available literature” | | | “The heterogeneity of findings in the scientific literature leads to uncertainty in counseling women regarding marijuana use in pregnancy. While more evidence is needed for informed decision-making, it seems reasonable to follow ACOG guidelines recommending that women be discouraged from using marijuana during pregnancy and lactation. The rationale to follow these recommendations stems from a growing body of studies showing potential harm to fetuses with evidence of decreased growth (in particular with heavy use), and concern from longitudinal |

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| | | | | | studies for long-term neurologic effects. Marijuana use may be associated with spontaneous preterm birth, stillbirth, and neonatal intensive care unit admission. The health effects on the mother remain largely unknown.” |
| (Metz, Allshouse, et al., 2022) CINAHL | Level III / secondary analysis of a multicenter and case-control study | “to evaluate the association between maternal marijuana use and the feto-placental weight ratio (FPR). Secondarily, we aimed to compare placental histology of women who used marijuana to those who did not” | “Prior marijuana use was detected by [EMR] abstraction or cord homogenate positive for 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid... The primary outcome was FPR. Association of marijuana use with FPR was estimated with multivariable linear modeling adjusted for fetal sex, preterm birth, and tobacco use. Comparisons between groups for placental histology were made using Chi-square and stratified by live birth and stillbirth, term and preterm deliveries, and fetal sex.” | “Of 1,027 participants, 224 were stillbirths and 803 were live births. Overall, 41 (4%) women used marijuana during the pregnancy. The FPR ratio was lower among exposed offspring but reached statistical significance only for term stillbirths (mean 6.84 with marijuana use vs. mean 7.8 without use, $p < 0.001$). In multivariable modeling, marijuana use was not significantly associated with FPR ($p = 0.09$). There were no differences in histologic placental features among those with and without marijuana | Exposure to marijuana does not appear to be associated with FPR, nor were there any placental histologic features associated with marijuana exposure. Further studies are needed to understand the association between prenatal marijuana use and poor fetal growth. |

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| (Mouhamed, Vishnyakov, et al., 2018) Pubmed | Level V / literature review | “to supplement the Health Canada document by providing physicians with a critical yet concise update on the recent advancements for the prescribed use of MM [medical marijuana]”... and “to offer physicians an educational tool that provides a necessary, evidence-based analysis of the therapeutic potential of MM and to ensure physicians are making decisions on the therapeutic use of MM in good faith” | “literature search identified articles using PubMed, EMBASE Ovid, and the Cochrane Library to determine high-quality, multicenter randomized controlled trials, systematic reviews, meta-analyses, and practice guidelines from February 2013 to August 2017” | <i>See Authors’ Conclusions</i> | “Numerous gaps in knowledge about the effects of cannabis remain. Additional research is needed in numerous areas including modes of administration, controlling for cannabis users and cannabis naïve individuals, as well as for other contraindications. For patients younger than 25 years of age, those who are pregnant or those with a history of mental health and substance use, providers should err on the side of caution and avoid suggesting medical marijuana.” |
| (Mumford, Flannagan, et al., 2021) Pubmed | Level III / prospective cohort study | To determine if cannabis use during the preconception period is associated with fecundability, live birth and pregnancy loss. | Women aged 18-40 years with a history of pregnancy loss were recruited from four clinical centers. Women self-reported preconception cannabis use at baseline and urinary tetrahydrocannabinol metabolites | Preconception cannabis use was 5% and 1.3% used cannabis during the first 8 weeks of gestation. Women with preconception cannabis use had reduced fecundability. There were also suggestive, though imprecise, associations with | “These findings highlight potential risks on fecundability among women attempting pregnancy with a history of pregnancy loss and the need for expanded evidence regarding the reproductive health effects of cannabis |

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| | | | were measured throughout preconception and early pregnancy. Time to hCG-detected pregnancy, and incidence of live birth and pregnancy loss were assessed prospectively. | anovulation and live birth in cannabis users versus 55% in nonusers. No associations were observed between preconception cannabis use and pregnancy loss. Similar results were observed after additional adjustment for parity, income, employment status and stress. | use in the current climate of increasing legalization.” |
| (Murnan, Keim, & Klebanoff, 2022) Pubmed | Level III / cohort with logistic regression model analysis | “to examine relationships between maternal perceptions of Fetal Health Locus of Control (FHLC) and perceived risk/benefit related to prenatal marijuana use with maternal marijuana use behaviors during pregnancy.” | “The sample included women seeking prenatal care at The Ohio State University Wexner Medical Center (OSUWMC, Columbus OH) between 2010 and 2015, who participated in a follow-up study (2019–2020). Logistic regression models were run to estimate associations between maternal perceptions and prenatal marijuana use behaviors.” | “Higher perceived benefit to mother (AOR = 1.53, 95% CI: 1.08–2.17) and lower perceived risk to children (AOR = 0.59, 95% CI: 0.45–0.78) were related to increased prenatal marijuana use, adjusted for confounders. In contrast, FHLC perceptions were not associated with maternal marijuana use; however, FHLC predicted women’s perceptions of risk and benefit which in turn was associated with marijuana use during pregnancy.” | “Understanding how maternal perceptions influence health-related risk behaviors during pregnancy is important because perceptions are feasible intervention targets.” |
| (Murnan, Keim, et | Level III / prospectiv | To determine developmental | “PME was determined from | “Compared to non-exposed children, | “behavioral problems |

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| <p>al., 2021) Pubmed</p> | <p>e cohort</p> | <p>and behavioral impacts of prenatal marijuana exposure (PME) on young children given modern day “highly potent marijuana”.</p> | <p>maternal self-report, medical chart abstraction, and urine toxicology from prenatal visits and delivery. At age 3.5 years, 63 offspring children completed tasks assessing executive function (EF), visual spatial ability, emotion regulation, and aggressive behavior... Logistic regressions and analyses of covariance controlling for key variables were used to examine associations between PME and child outcomes”</p> | <p>children with PME had more sleep-related problems, withdrawal symptoms, and externalizing problems, including aggressive behaviors and oppositional defiant behaviors. Children with and without PME did not differ in terms of executive functioning”</p> | <p>associated with PME may manifest by age 3.5” [years]</p> |
| <p>(Nashed, Hardy, & Laviolette, 2021) Pubmed</p> | <p>Level V / literature review</p> | <p>“to summarize recent findings of clinical and preclinical data on neonatal outcomes, as well as long-term physiological and neurodevelopmental outcomes of prenatal cannabis exposure”</p> | | <p>“prenatal cannabis exposure has been linked to low birth weight, and emerging evidence suggests that prenatal exposure to $\Delta 9$-THC, which crosses the placenta and impacts placental development, may have wide-ranging physiological and neurodevelopmental consequences... early reports suggest $\Delta 9$-THC</p> | <p>“In light of the current trends in the perception and use of cannabis during pregnancy, we emphasize the social and medical imperative for more rigorous investigation of the long-term effects of prenatal cannabis exposure.”</p> |

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| | | | | increases the risk of cognitive impairment and neuropsychiatric disease, including psychosis, depression, anxiety, and sleep disorders.” | |
| (Nawa, Garrison-Desany, et al., 2020) Pubmed | Level III / cohort | “to investigate whether maternal marijuana use was independently associated with gestational age, preterm birth, and two preterm birth subtypes (spontaneous vs clinician-initiated).” | “Participants included 8,261 mother-newborn pairs from the Boston Birth Cohort. Information on gestational age was collected from electronic medical records. Marijuana use and tobacco smoking during pregnancy were assessed through a standard questionnaire after birth. Linear and log-linear regression models were used to assess associations between marijuana use with and without tobacco smoking during pregnancy and the outcomes of interest.” | “Of the 8,261 mothers, 27.5% had preterm births. About 3.5% of mothers with term deliveries and 5.2% of mothers with preterm births used marijuana during pregnancy. Marijuana use and cigarette smoking were independently associated with a decrease in gestational age by 0.50 weeks (95% confidence interval [CI] -0.87, -0.13) and 0.52 weeks (95% CI -0.76, -0.28), respectively. Marijuana use during early or late pregnancy was associated with a similar decrease in gestational age by 0.50 weeks. When we examined the effects on the preterm birth subtypes, simultaneous marijuana use and tobacco smoking | “maternal marijuana use and cigarette smoking during pregnancy were independently associated with shorter gestational age. When we examined the effects on preterm birth subtypes, the elevated risk was only observed with spontaneous preterm birth.” |

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| | | | | were associated with higher risk of spontaneous preterm birth (RR 1.64, 95% CI 1.23, 2.18). The elevated risk was not observed with clinician-initiated preterm birth.” | |
| (Peterson, Rosen, et al., 2020) Pubmed | Level II / multi-center cohort study | “To identify the associations of prenatal exposure to illicit drugs with organization of the newborn brain” | Volunteer sample of illicit drug-using and nonusing mothers and their newborns from prenatal clinics and drug abuse treatment programs in New York, New York. Study began in September 2004 and continued through 2018. Of 118 mothers, 42 (35%) were in the control group, 29 (25%) were in the cocaine group, 29 (25%) were in the marijuana group, and 18 (15%) were in the methadone and/or heroin group (participants and newborns were predominantly from minority groups and economically disadvantaged). Unsedated MRI of newborn brains was performed | “Anatomic abnormalities were detected in similar locations across all 3 drug exposures and included smaller volumes in the dorsal, medial, and ventral surfaces of the frontal lobe and dose-related increases in volumes in the lateral temporal lobe, dorsal parietal lobe, and superior frontal gyrus. Dose-related increases in diffusion tensor measures of tissue organization, decreases in T2 relaxometry times, and increases in spectroscopy metabolite concentrations were similar across exposures. These associations of exposures with brain measures were similar to the associations of newborn age with | “prenatal drug exposure is associated with measures of newborn brain tissue in patterns that may indicate that exposures accelerated normal fetal brain maturation, which in turn mediated the associations with poorer 12-month infant outcomes.” |

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| | | | <p>shortly after birth. Infant neurodevelopmental outcomes were assessed at 12 months of age. Infant neurodevelopmental outcomes included Bayley Scales of Infant development-III and Vineland Adaptive Behavior Scales. Statistical analyses were performed with results represented on the brain images.</p> | <p>brain measures. The anatomic and diffusion tensor imaging measures suppressively mediated the associations of prenatal exposure with poorer 12-month infant outcomes.”</p> | |
| <p>(Salzwedel, Chen, et al., 2020) Pubmed</p> | <p>Level II / cohort (linear mixed-effect model)</p> | <p>To determine the effects of prenatal drug exposure (PDE) on the fetal brain development in human neonates.</p> | <p>A “sample of 133 human neonates and leveraging a novel linear mixed-effect model designed for intersubject variability analyses, we studied the effects of six prenatally exposed drugs (i.e., nicotine, alcohol, selective serotonin reuptake inhibitor, marijuana, cocaine, and opioids) on neonatal whole-brain functional organization and compared them with five other critical nondrug</p> | <p>“Magnitude-wise, through summing across individual drug effects, our results highlighted ~5% of whole-brain functional connections (FCs) affected by PDE, which was highly comparable with the combined effects of the five nondrug variables. Spatially, the detected PDE effects featured drug-specific patterns with a common bias in higher-order brain regions/networks. Regarding brain-behavioral relationships, the</p> | <p>“Further mediation analyses supported a mediation role of the detected brain FCs between PDE status and cognitive/language outcomes. Our findings of widespread, and spatially biased PDE effect patterns coupled with significant behavioral implications may hopefully stimulate more human-based studies into effects of PDE on long-term developmental outcomes.”</p> |

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| | | | variables (i.e., gestational age at birth/scan, sex, birth weight, and maternal depression). The behavioral implications were also examined.” | detected connections showing significant drug effects also demonstrated significant correlations with 3-month behavioral outcomes.” | |
| (Stroud, Papandonatos, et al., 2018) Pubmed | Level III / prospective study | To investigate the influence of co-exposure to tobacco and marijuana on infant neurobehavioral development in the first postnatal month | Participants were 111 mother-infant pairs from a low-income, diverse sample. Tobacco and marijuana use were assessed by participant interviews with biochemical confirmation. Three groups were identified: (a) prenatal marijuana and tobacco use (b) prenatal tobacco use only, and (c) controls. Newborn neurobehavior was assessed at seven time points over the first postnatal month using the NICU Network Neurobehavioral Scale. | “MJ + TOB-exposed infants showed decreased ability to self-soothe (Self-regulation) and attend to stimuli (Attention), and increased need for examiner soothing (Handling) and low motor activity (Lethargy) versus unexposed infants. Despite low levels of MJ use in MJ + TOB co-users, co-exposure was associated with nearly double the impact on infant self-soothing and need for examiner soothing versus TOB-exposure alone. Effects of MJ + TOB co-exposure appeared more pronounced for daughters than for sons.” | Findings “highlight additional risk from dual exposure to MJ + TOB vs. TOB exposure alone, particularly for daughters. Results also highlight the critical importance of investigating prenatal exposures in concert and the need for intervention efforts to address MJ co-use in pregnant TOB users.” |
| (Stroud, Papandonatos, et al., 2020) | Level III / short-term prospective study | “to investigate the impact of prenatal MJ [marijuana] +TOB [tobacco] | “Mothers completed up to four interview sessions between | “Exposure to prenatal MJ+TOB (versus prenatal TOB-exposure | “Complementing some human and preclinical studies, associations |

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| Pubmed | | vs. TOB-only versus no substance exposure on newborn baseline cortisol and cortisol reactivity to handling stress over the first postnatal month” | 26 and 42 weeks gestation... Meconium was collected following delivery for biochemical verification of prenatal nicotine, THC, and other substance exposure. Newborn stress response sessions were conducted up to 7 times over the first postnatal month; each session included four saliva samples measured before and following infant handling (NICU Network Neurobehavioral Scale) that were assayed for cortisol.” | alone) was associated with 36% attenuated baseline cortisol levels over the first postnatal month in male offspring. Prenatal MJ+TOB exposure was also associated with a 22% decreased in cortisol reactivity over the first postnatal month, similar to effects of prenatal TOB-exposure alone.” | between prenatal MJ+TOB exposure and newborn HPA regulation were sex-specific--with most pronounced associations evident in male offspring for baseline cortisol. Future large-scale studies are needed to elucidate molecular mechanisms underlying sex differences in prenatal programming and to characterize sex-specific trajectories leading to sexually dimorphic neurodevelopmental symptoms and disorders.” |
| (Taylor, Bell, et al., 2021) Pubmed | Level III / retrospective cross-sectional study with logistical regression analysis | “contribute to the minimal literature on factors associated with cannabis use during the preconception, prenatal, and postpartum periods including state legalization status, concurrent use of tobacco and e-cigarettes and adequacy of prenatal care” | “a cross-sectional analysis using combined survey data from the 2016-2018 Pregnancy Risk Assessment Monitoring System (PRAMS) collected from 36,391 women. Logistic regression was used to estimate the impact of state-legalization, adequacy of | In the preconception period, residence in a recreationally or medically legal state compared to a non-legal state was associated with higher odds of cannabis use. In the prenatal period, residence in a recreationally legal state was associated with higher odds of cannabis use; however, there was | “Recreational cannabis legalization is associated with the use of cannabis prior to, during, and after pregnancy. Renewed clinical and policy efforts may be warranted to update prenatal substance use prevention programs, educational campaigns, and |

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| | | | prenatal care, and other substance use on cannabis use during the preconception, prenatal, and postpartum periods.” | no association with residence in a medically legal state. Tobacco use (including e-cigarettes) and moderate prenatal alcohol use were also significantly associated with cannabis use. | provider education as cannabis legalization evolves.” |
| (Willford, Goldschmidt, et al., 2021) Pubmed | Level III / longitudinal cohort study (prospectively collected data) | “to investigate the complex associations among multiple factors that may directly or indirectly be associated with marijuana use in adolescence and young adulthood and memory function in young adults” | Recruitment of pregnant women (4-5 months gestation) was completed between 1982 and 1985, yielding a cohort of 763 singleton infants. The women and their children were assessed at birth, 8 and 18 months, 3, 6, 10, 14, 16, and 22 years. The current sample has 524 individuals. | “there were indirect effects of prenatal marijuana exposure on adult memory through intelligence at age 6, memory at 10 years, and early-onset of marijuana use” | “These findings highlight the risk of prenatal marijuana exposure and early initiation of marijuana for long-term memory function in adulthood.” |
| (Young-Wolff, Adams, et al., 2020) Pubmed | Level III / self-administered questionnaire | To study “self-reported modes of cannabis administration among women in the year before and during pregnancy, and their association with self-reported cannabis use frequency” using data from a prior study. | <u>Design</u> Data from 585 women who received an expanded version of the self-administered questionnaire systematically piloted to all pregnant women at two medical centers. The pilot study was conducted to evaluate the | “The prevalence of cannabis use was 12% before pregnancy and 3% during pregnancy. Among the 71 women who reported cannabis use before pregnancy and the 19 women who reported cannabis use during pregnancy, smoking was the most common | “These novel results indicate that while smoking is the most common mode of cannabis administration during the perinatal period, there is variation in use and co-use of alternative modes. Future studies are needed to understand the relative health effects associated |

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| | | | <p>feasibility of asking pregnant women questions about mode of cannabis administration.</p> <p><u>Measures:</u> Women were asked to indicate whether they used cannabis, alcohol, tobacco, and e-cigarettes/vaped in the year before and during pregnancy. For cannabis, patients were asked to indicate their mode of administration (smoked, vaped, edible/oral, lotion/ointment, and other). Women could select more than one mode of administration for cannabis, but they could not specify frequency of use for each mode.</p> <p><u>Socio-Demographic Factors:</u> Age, race/ethnicity, median neighborhood household income and trimester of screening were taken from participant's EHR.</p> | <p>mode of administration (58% and 42%), followed by edibles (27% and 16%), vaping (23% and 16%), lotions (11% and 5%), and other (10% and 0%). In the year before pregnancy and during pregnancy, monthly or less use was most common (56% and 58%), followed by weekly use (24% and 26%) and daily use (20% and 16%). Among cannabis users, 43% used more than one mode before pregnancy compared to 15% during pregnancy. Daily cannabis use was most common among women who reported smoking only or smoking in combination with other modes.”</p> | <p>with individual and combined modes of cannabis administration during pregnancy.”</p> |
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| | | | Data on pregnancy intentions (whether to remain pregnant) were based on questionnaire answers. | | |
| (Young-Wolff, Gali, et al., 2020) Pubmed | Level III / cohort | To characterize public interest in the effects of cannabis use before, during, and after a pregnancy, and to characterize provider response to questions about the topic. | “Data were medical questions on perinatal cannabis use posted online from March 2011 to January 2017 on an anonymous digital health platform. Posters were able to “thank” health care providers for their responses and providers could “agree” with other provider responses. We characterized 364 user questions and 596 responses from 277 unique providers and examined endorsement of responses through provider “agrees” and user “thanks.”” | “The most frequent questions concerned prenatal cannabis use detection (24.7%), effects on fertility (22.6%), harms of prenatal use to the fetus (21.3%), and risks of baby exposure to cannabis through breast milk (14.4%). Provider sentiment in responses regarding the safety of perinatal cannabis use were coded as 55.6% harmful, 8.8% safe, 8.8% mixed/unsure, and 26.8% safety unaddressed. Half of providers (49.6%) discouraged perinatal cannabis use, 0.5% encouraged use, and 49.9% neither encouraged nor discouraged use. Provider responses received 1,004 provider “agrees” and 583 user “thanks.” Provider | “The data indicate public interest in cannabis use effects before, during, and after pregnancy. While most health care providers indicated cannabis use during pregnancy and breastfeeding is not safe, many did not address safety or discourage use, suggesting a missed educational opportunity.” |

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| | | | | <p>responses indicating that perinatal cannabis use is unsafe received more provider “agrees” than responses indicating that use is safe (B = 0.42, 95% CI 0.02–0.82, p = 0.04). User “thanks” did not differ by provider responses regarding safety or dis/encouragement”</p> | |
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Study Characteristics

See Table 2.

Results of Individual Studies

See Table 2.

Additional Analysis

No additional analysis completed.

Discussion

Summary of Evidence

There were several themes identified in this rapid review, of the 39 studies reviewed, 27 found negative outcomes for the fetus related to marijuana use during pregnancy, while four found no significant negative outcomes. For the purpose of this review, the term “negative” will be defined as outcomes or conditions that constitute the need for medical intervention, minor or complex. Negative outcomes frequently found include decreased growth in utero, neurologic

effects in childhood and adulthood, sleep-related problems, and problems with anxiety and depression in both childhood and adulthood.

Turning to the results related to the pregnant person, four studies reviewed found negative effects to the pregnant person related to marijuana use, while two studies found no significant negative effects. These numbers are likely skewed low due to the number of studies that focused solely on the effects on the fetus, rather than the pregnant person. In studies that did look at the effects on the pregnant person, contradictory results were found. One study found no histological changes to the placenta (Metz et al., 2022), while another found that $\Delta 9$ -THC not only crosses the placenta but also impacts the development of the placenta (Nashed et al., 2021). A separate study found that perinatal outcomes may include “preterm prelabor rupture of membranes, placenta previa, chorioamnionitis, and longer hospital stay postpartum” (Gesterling et al., 2022). Looking to positive outcomes, one study noted that pregnant patients used marijuana to treat common ailments of pregnancy such as nausea and vomiting, pain, stress, and anxiety (Ko et al., 2020).

Additionally, seven studies found results related to other facets of marijuana use during pregnancy. The association between stressful life events (SLEs) and marijuana use during the preconception, prenatal, and postpartum periods were assessed in Allen et al., (2020). Results found that nine of the 14 SLEs tested were associated with increased chance of cannabis use in the pre-pregnancy period. Similarly, a study conducted by Taylor et al. (2021) looked more broadly at factors associated with use during the two of the three aforementioned periods of time. This study found that during the preconception period residence in a medically or recreationally legal state was associated with higher likelihood of marijuana use, while during the prenatal period only residence in a recreationally legal state was associated with higher likelihood of use.

It was also noted that tobacco use and moderate prenatal alcohol use were significantly associated with prenatal marijuana use. The maternal perception of the risk versus benefits of marijuana use during pregnancy and the fetal health locus of control scale (FHLCs) studied and found that higher perceived benefit to the mother and lower perceived risk to the child were related to increased prenatal marijuana use. FHLCs were not associated with prenatal marijuana use by the pregnant person (Murnan et al., 2022). Another study looked at the modes of marijuana use by pregnant people; the most common mode of consumption was smoking, followed by edibles, vaping, lotions, and lastly, other methods (Young-Wolff, Adams et al., 2020).

Suggested provider recommendations to patients or researcher's recommendations to providers more broadly were mentioned in ten studies. These recommendations consistently suggested total abstinence, in line with the current American College of Obstetricians and Gynecologists (ACOG) recommendations (Committee on Obstetric Practice, 2017). ACOG's guidelines are based on the lack of conclusive evidence suggesting safety or danger in use. Nearly half of the studies included in this rapid review (19 of 39) emphasized the importance of further research in this area.

The great need for patient education was also shown through this research. It was noted in multiple studies that patients see marijuana as "safe" or "natural" compared to illicit drug or prescription medications (Chang et al., 2019). Interestingly, pregnant study participants reported they used marijuana for stress relief, anxiety management, nausea and vomiting, and pain related to pregnancy (Ko et al., 2020). These two findings together could suggest that pregnant people using marijuana are doing so in the best interest of themselves and the fetus. This hypothesis is supported by Allen et al., 2020 which found that stressful life events in the year prior to

pregnancy are linked to marijuana use prior to, during, and after pregnancy. This is an area for patient education that should be explored, both with future research and conversations amongst providers and their patients.

Limitations

Limitations in this research are numerous. As this question deals not only with human beings but with human reproduction there are many ethical considerations that must be taken into account. A randomized control trial, the gold standard of research, is not a possible study design when attempting to answer this question as it would not be considered ethical. Therefore, researchers must rely on participant drug tests as well as self-reported characteristics of usage. It is known that patients, including study participants, underestimate their alcohol and drug usage, further complicating studies (Bone et al., 2016).

Several studies included in this review only included participants in low-income communities, which constitutes a limited sample. Patients experiencing poverty may be more likely to use alternative methods, such as marijuana, to deal with issues that arise from a pregnancy, particularly if they are unable to pay for medical visits. Food and housing insecurity may also be impacting patients in low-income communities. This lack of stability and increase in stressors may contribute to the initiation or increase of marijuana use.

Furthermore, there is no reliable way to determine if the negative birth outcomes in current or future studies are solely the result of marijuana use or if other substances play a role. Nine studies looked at marijuana use in conjunction with tobacco use directly or indirectly. Others looked at the use of additional illicit substances (cocaine, heroin, ect). It was unreported in many studies whether or not participants were taking legal medications, such as antidepressants, anti-anxiety medications, diabetes mellitus medications, ect.

Stigma surrounding marijuana use, its Schedule I designation, and difficulty getting funding are also limitations. A study by Gesterling (2022) found that marijuana's Schedule I designation is a factor that limits provider education on the topic. Per the United States Drug Enforcement Administration (DEA, n.d.), the agency in charge of drug scheduling, "Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse" (para. 3). This classification means there are many steps researchers have to go through to obtain approval for research and funding. According to National Academies of Sciences, Engineering, and Medicine (2017), in one instance, "[t]he substantial layers of bureaucracy that emerge from cannabis's Schedule I categorization is reported to have discouraged a number of cannabis researchers from applying for grant funding or pursuing additional research efforts" (p. 381). The difficulty of doing this type of research constitutes a substantial limitation.

Recommendations for Further Research

Identified limitations of current research leave much room for future research. Numerous additional topics should be addressed. The effects of the mode of consumption (smoking, oral consumption, oils, etc.) on the pregnant person and the fetus should be studied. The effects of the numerous marijuana derivatives (Δ 8-THC, Δ 9-THC, hashish, cannabinoids) available legally and illicitly should be assessed. The dose-affect ratio should also be studied; however, isolating the effects of marijuana as opposed to other factors (prescription medications, lifestyle, personal and familial medical history, ect) will be difficult.

Conclusions

The evidence presented clearly shows a great need for research about all facets of marijuana use during pregnancy - fetal implication and maternal implications. This review

reveals a great need for provider education on the topic that is peer reviewed and current.

Providers owe it to their patients to give not just opinion, but fact when decisions about one's health, and the health of their future child, are being discussed. Numerous topics for additional research were suggested to increase the pool of knowledge on this important topic.

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