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Marijuana Use in Pregnancy and the Effects on the Fetus/infant

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Abstract

Background/Purpose: The purpose of this paper is to critically examine the literature and evidence that is available surrounding pre-pregnancy and prenatal use of marijuana and the effects it has on the developing fetus/infant.

Theoretical Framework: The Modeling and Role-Modeling Theory created by Erickson, Tomlin, and Swain will be the theoretical framework used for this paper. The modeling aspect of this theory speaks to a person developing a picture and perception of another person's world. The person develops this picture by viewing the other person's framework, points of view, values, experiences and perspectives.

Methods: Twenty research articles were found and critically reviewed to determine if there are adverse effects associated with marijuana use during pre-pregnancy, pregnancy, and postpartum.

Results/Findings: It was found that across most findings that further research needs to be done on the use of marijuana prior to pregnancy, during pregnancy, and postpartum. It has also been found that screening and counseling needs to be done and focused on prior to pregnancy and during pregnancy and postpartum. Potential adverse effects in the fetus/infant associated with marijuana use prior to pregnancy, during pregnancy, and postpartum included growth restriction, low birth weight, small for gestational age, higher rates of spontaneous preterm birth, increased risk of neonatal morbidity, placental abruption, increased NICU admissions, stillbirth, and anencephaly.

Implications for Research and Practice: Healthcare professionals have the opportunity to establish a trusting relationship with their patients and to be able to effectively educate and counsel their patients regarding the use of marijuana prior to pregnancy, during pregnancy, and postpartum.

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Chapter I: Introduction

It is not hard to determine that marijuana use in the United States has skyrocketed in the past two decades. This is due in large part to the medical legalization of marijuana and the most recent legalization of it for recreational use in multiple states. There are currently 33 states along with the District of Colombia that have legalized marijuana in some type of form, either for medical use or recreational use (State marijuana laws, 2019).

Marijuana, sometimes referred to as cannabis, pot, hash, or Maryjane, has a history tracing back 5000 years in Romania (Bridgeman & Abazia, 2017). Marijuana contains a mind-altering substance called delta-9-tetrahydrocannabinol, often referred to as THC. Marijuana is the most commonly used illicit drug worldwide. Marijuana is typically taken one of three ways: Inhalation via smoking, inhalation via vaporization, or through consumption of an edible product containing THC. Marijuana is a Schedule 1 controlled substance that has limited medicinal use and has a high risk for potential abuse and dependence. There is also a national concern that it is a gateway drug to more dangerous substances (Bridgeman & Abazia, 2017).

Medical marijuana as a therapy has been the dominant topic of conversation in the last few years. There are legal, ethical, and societal issues associated with its use for medicinal purposes (Bridgeman & Abazia, 2017). Concerns include safe packaging, proper administration, dispensing, and the adverse consequences that come along with its use. The Food and Drug Administration (FDA) has said that it needs to investigate the claims that medicinal marijuana is beneficial; research is ongoing regarding this (Bridgeman & Abazia, 2017).

Marijuana use in pregnancy has increased dramatically since its legalization for medicinal and recreational purposes (Stickrath, 2019). Marijuana is currently the most

commonly used illicit substance in pregnancy. That stems from the increasing use across all populations due its legalization both medicinally and recreationally. It has been found that 3.9% of pregnant women have used marijuana in the past month (1 or more times) and 7% of pregnant women have used in the past year. Pregnancy is a time of extreme anatomical and physiological changes in the woman (Soma-Pillay, Nelson-Piercy, Tolppanen, & Mebazaa, 2016). The anatomical and physiological changes help to nurture and grow a developing fetus inside the mother's body. Conception to birth has a wide array of changes and they are all important to growing a healthy fetus inside the womb. This is an extremely vulnerable part of a fetus's journey; without a mother taking care of her body with adequate nutrition and lifestyle factors, there is risk to the fetus (Soma-Pillay et al., 2016).

These numbers all come from self-report, therefore the likelihood of the numbers being higher is probable. The legalization of marijuana for medicinal and recreational purposes has led to the general population's decreased perception of the risks associated with its use. Findings show that since the legalization of marijuana, THC has increased in marijuana from 4% in 1995 to 12% in 2019. There is a recommendation that all women be screened for marijuana use in pregnancy and if they are found to have a positive drug screen, they should be encouraged to discontinue use (Stickrath, 2019).

The concerns regarding marijuana use during pregnancy are related to the development of the fetus in utero and the long-term effects associated with marijuana use. It is known that THC crosses the placenta and reaches the fetus (Stickrath, 2019). The data on marijuana use has focused on growth restriction, stillbirth, congenital anomalies, and neurodevelopmental effects on the developing fetus. This data comes from self-reported use and there are usually other factors, such as tobacco use, which can make the data difficult to interpret (Stickrath, 2019).

Statement of Purpose

The purpose of this paper is to critically examine the literature that is available on marijuana use in pre-pregnancy and pregnancy and determine if there are adverse effects on the fetus/infant. It will examine the effects of marijuana use in women, on preterm birth, breastfeeding, cognitive deficits, and neurodevelopmental delays in children later in life. The Modeling and Role-Modeling theory will be examined and applied to the topic. The modeling aspect of this theory speaks to a person developing a picture and perception of another person's world. The person develops this picture by viewing the other person's framework, points of view, values, experiences, and perspectives (Nouri, Ebadi, Alhani, & Rejeh, 2014).

Evidence Demonstrating Need

Marijuana is one of the most widely used substances during pregnancy. Marijuana use is also increasing in mothers who breastfeed. There has been emerging data regarding the ability of THC to cross the placenta, affecting development of the fetus (Grant, Petroff, Isoherranen, Stella, & Burbacher, 2018). There has been widespread social media use recommending marijuana for severe nausea during pregnancy. There is little information available to the general public about the effects of marijuana use during pregnancy on the growing fetus.

In 2017 the American College of Obstetricians and Gynecologists (ACOG) recommended that all women before pregnancy and in early pregnancy be questioned about their use of tobacco, alcohol, and drugs including marijuana (ACOG, 2017). If women report use of marijuana, they should be counseled about the potential adverse health consequences during pregnancy. Women who are pregnant or who are thinking about pregnancy should be encouraged to discontinue marijuana use. Women who are using marijuana for medicinal purposes during

pregnancy should be counseled to select a different therapy that has better data available on its use. ACOG also recommends discouraging the use of marijuana during breastfeeding due to insufficient data available on the effects of the marijuana on the infant (ACOG, 2017).

"The Association of Women's Health, Obstetric, and Neonatal Nurses (AHWONN) (2018) supports the implementation of legislation, policies, and public health initiatives that help raise awareness, remove stigma, discourage use, and facilitate access to prenatal and maternity care for women who use marijuana during pregnancy." AWHONN also supports ongoing research of the short- and long-term effects for the woman, fetus, and newborn (AWHONN, 2018).

Significance to Nurse-Midwifery

Nurse-midwives practice as primary health care providers for women and newborns up to the age of 28 days. As described in the American College of Nurse-Midwives (ACNM) Hallmarks of Midwifery, nurse-midwives care for women and assist with health promotion, disease prevention, and health education (ACNM, 2012). Nurse-midwives also incorporate scientific evidence into clinical practice and provide skillful communication, guidance, and counseling to their patients. Nurse-midwives also seek to empower women as partners in health care (ACNM, 2012).

Nurse-midwifery practice encompasses a holistic overview of a woman's life. As compassionate care providers, the possibility of having lifelong relationships with women in healthcare is an advantage of having the potential to influence a woman's decisions about her healthcare in a positive way. Nurse-midwives can counsel a woman who uses marijuana either pre-pregnancy or prenatally to influence her decision on whether to quit using marijuana. This

can have lifelong implications not only for the woman using the marijuana but also for the babies she goes on to deliver.

Theoretical Framework

Erickson, Tomlin, and Swain developed the Modeling and Role-Modeling Theory in 1982 (Nouri, Ebadi, Alhani, & Rejeh, 2014). The modeling aspect of this theory speaks to a person developing a picture and perception of another person's world. The person develops this picture by viewing the other person's framework, points of view, values, experiences, and perspectives (Nouri, Ebadi, Alhani, & Rejeh, 2014). Role-modeling involves how the person who is caring for the patient cares for and nurtures the patient to attain, maintain, and promote health (Modeling and role-modeling, 2016). Role-modeling accepts the patient as they are and then works the best way possible to come up with unique interventions characteristic to that person's personality. The patient is typically the expert in his or her care and usually knows what is best for themselves (Modeling and role-modeling, 2016).

The theory of modeling and role-modeling explains how nurses provide care based on the individualized person and the way that particular person views the world (Koren & Papamiditriou, 2013). It is basically like trying to see the world through the patient's eyes. It is important to develop a trustworthy relationship with the patient in order to have any kind of influence in the patient's life (Koren & Papamiditriou, 2013).

As nurse-midwives, developing a rapport with patients is of the utmost importance. If a visit for a patient who admits to smoking marijuana starts with the nurse-midwife instructing her to stop and listing the affiliated ramifications, it may not go over well. Instead, if a rapport is built first and it is in a nonjudgmental way, there is a much higher chance of being able to persuade the woman to not smoke marijuana. Meeting the patient where she is and trying to

figure out why she is smoking marijuana is also a key factor in determining the plan of action. If the patient is smoking marijuana due to stress, then a nurse-midwife should help her figure out where the stress is coming from and consider other interventions that are healthier and safer for the mom, and if she is pregnant, her baby. By seeking to find the patient's perspectives and viewpoints, the next move is to role-model for the patient the best care for both mother and baby. This can only be done if there is a level of trust and commitment from the provider to the patient's perspective.

Attributes of a role model that can contribute to the person's perception of the role model include similarities between the two, levels of success for the role model, and the role aspirant's belief of whether or not abilities are fixed or changeable (Morgenroth, Ryan, & Peters, 2015). Healthcare practitioners must remember that their patients are watching their every move. If patients can see the healthcare provider as successful and relatable, they are much more likely to listen and take to heart when the recommendation is to not smoke marijuana.

Summary

The use of marijuana has increased in the past two decades due in large part of its legalization both medicinally and recreationally. The number of pregnant women using marijuana has also increased and women that are using marijuana while pregnant have a decreased perception of the harmful effects of marijuana because it is legalized in many states. The data on potential adverse effects on the fetus during pregnancy from the use of marijuana is limited but the recommendation is to discontinue use in pregnancy if a positive drug screen comes up in the lab work. Nurse-midwives have a unique opportunity to positively influence the women they come into contact with and help them achieve the best outcomes prenatally and for their infants postpartum.

Chapter II: Methods

This chapter will clearly explain the process used to obtain and review the literature related to marijuana use during pre-pregnancy, pregnancy, and postpartum and whether there are any effects on the fetus/infant. It will include the criteria used for inclusion, exclusion, and a summary of the studies that were selected. The studies found were analyzed for setting, study sample, results, conclusions, and relevance to the topic according to the Matrix method by Garrard (2017). The studies were also analyzed for different articles in the references section to obtain more information. The level and quality of evidence were also reviewed and ultimately 20 articles were selected.

Search Strategies

The critical review of the literature was done across multiple databases including CINAHL, PubMed, and Google Scholar. The key search terms used included "marijuana," "cannabis," "pregnancy," "women," and "effects on fetus/infant". A CINAHL search using the words "marijuana," "women," and "pregnancy" provided a search result of 36 articles. A CINAHL search using the words "cannabis," "pregnancy," and "effects on fetus" provided a search result of 15 articles. A PubMed search using the words "marijuana," "effects," and "pregnancy" provided a search result of 277 articles. A snowball technique was also used in relevant research articles to obtain additional literature to review.

Criteria for Inclusion and Exclusion

The selected articles for this review of the literature were included based on whether or not the results from marijuana use showed impact or effects on the fetus or infant. These effects

included preterm birth, congenital defects, developmental issues later in life, fetal development including brain development, small for gestational age, and stillbirth. The criteria for dating the articles included sources published from 2009 to the present.

Exclusion criteria included all studies conducted before 2009. Articles that were poor in quality, according to the John Hopkins method of research, were also excluded. The research database for marijuana use was limited due to minimal research on the subject; therefore, there was not a lot of exclusion criteria implemented.

Summary of Selected Studies

The relevant studies found in the search process yielded a total of 328 potential articles. Upon reviewing the possibilities, there were 20 studies included in this review of the literature. The studies included retrospective cohort studies, case-controlled studies, secondary analysis studies, experimental studies, longitudinal studies, cross-sectional studies, and non-experimental studies. Most of the research was conducted in the United States with some being done in Canada, Australia, New Zealand, Ireland, and the United Kingdom. No randomized control trials were found in this search.

Evaluation Criteria

The articles in this review were analyzed using the Johns Hopkins Research Evidence Appraisal Tool (Dang & Dearholt, 2018). Using this tool created the opportunity to grade the level of evidence on a scale of I-IV. Level I studies include experimental studies, randomized controlled trials (RCTs), explanatory mixed-method designs that include only a level I quantitative study, and systematic reviews of RCTs with or without meta-analysis. Level II studies include quasi-experimental studies, explanatory mixed-method design with only level II quantitative studies, systematic reviews of a combination of RCTs, and quasi-experimental

studies with or without meta-analysis. Level III studies include nonexperimental studies, systematic reviews of a combination of RCTs, quasi-experimental and nonexperimental studies, non-experimental studies with or without meta-analysis, exploratory, convergent, or multiphasic mixed-methods studies, explanatory mixed-method designs that include only a level III quantitative, and qualitative study meta-synthesis. Level IV studies include opinions of respected authorities, clinical practice guidelines, consensus panels, and position statements. Level V studies are based on experiential and non-research evidence (Dang & Dearholt, 2018).

After deciding on the level of evidence of the study, the article was then critiqued to determine the quality of evidence (Dang & Dearholt, 2018). The classifications include low, good, or high. The articles were classified based on the quality of the sample size, if the conclusions were definitive, if the results were consistent, and if the results were generalizable (Dang & Dearholt, 2018). Many of the studies used in this literature review were level III studies.

Summary

This literature review was completed over several months using CINAHL, PubMed, and Google Scholar. Although the research on marijuana use during pregnancy is limited, there is research available and ultimately 20 articles were chosen based on relatability and quality of evidence. The analysis of the research was conducted using the Johns Hopkins Research Evidence Appraisal Tool.

Chapter III: Literature Review and Analysis

Synthesis of the Critical Review of the Literature

The data was synthesized in Appendix 1 of this paper and common themes were found amongst the data. The level of evidence and quality of each research study was appraised using the Johns Hopkins Research Evidence Appraisal Tool (Dang & Dearholt, 2018). The matrix format included purpose, sample/setting, level of evidence, quality of evidence, design method and instruments, results, conclusion, strengths, and limitations. The findings are displayed with the level I study first, and then nineteen level III studies in alphabetical order. The purpose, design, and synthesis of the information found in these studies will be presented in Chapter III.

Further Research Needed

A common theme in a few of the research articles reviewed was that more research needs to be done because there were no concrete outcomes found. Examples of this theme are described below.

Bertrand et al. (2018) found that women who breastfed used marijuana the most frequently among illegal drugs. Fifty breastfeeding women who admitted to marijuana use supplied breastmilk samples between 2014-2017. Participants recalled marijuana exposure up to 14 days before the breastmilk sample was collected. THC was measured and in two-thirds of the breastmilk samples provided were found to be highly variable in concentration. One of the limitations of this study is that the breastmilk samples were collected under various conditions. This was the first study to calculate specific cannabinoid levels in human milk and the study was conducted with a relatively large sample of mothers who provided a detailed and varied history

of marijuana use. Bertrand et al. (2018) found that there is a need for further research related to this subject.

Conner et al. (2015) performed a retrospective cohort study, the purpose of which, was to determine whether marijuana use in pregnancy was related to risk factors and occurrence was associated poor neonatal outcomes. All term pregnancies occurring over a four-year period at Washington University, which is located in St. Louis Medical Center, that met criteria equaled 8,138 women. All women who tested positive for marijuana in a drug screen or admitted use through self-report were included. Neonatal morbidity was found in 11.6% of women who used marijuana compared with 8% of women who did not use marijuana. After adjusting for confounding variables, there was not a significant difference in neonatal morbidity for women who used marijuana and those who did not. Further research is needed to determine the amount and extent of marijuana use and the relationship to adverse neonatal outcomes (Connor et al., 2015).

Mark et al. (2015) conducted a retrospective cohort study on a University-based prenatal care clinic from July 2009 to June 2010. They were looking at primary exposure of marijuana use that was defined by either self-report or urine toxicology. Marijuana use was not found to be related to low birth weight (13.8% vs 14.0%, p=1.00), preterm delivery (17.7% vs 12.0%, p=0.325), or NICU admissions (25.5% vs. 15.8%, p=0.139). Study results also showed that prenatal care utilization was equal between the two groups of marijuana users and non-users. The authors concluded that marijuana use in early pregnancy is common, but it is also common for moms to stop smoking marijuana by the time of delivery. As marijuana use increases in pregnancy, larger prospective trials are warranted in order to determine the impact of different

levels of marijuana use on birth outcomes and long-term neurological developments in infants (Mark et al., 2015).

Roberson et al. (2014) conducted a study with secondary analysis on data from the Pregnancy Risk Assessment Monitoring System (PRAMS) from Hawaii from 2009-2011. They found that 6.0% (95% CI: 5.2-6.8) of women reported marijuana use in the month before their most recent pregnancy and 2.6% (95% CI: 2.2-3.2) reported using marijuana during their most recent pregnancy. Approximately 21.2% of women with live births in Hawaii where this study was done developed severe nausea during their most recent pregnancy. Women who reported severe nausea during pregnancy were more likely to report marijuana use during pregnancy (3.7% vs. 2.3%; PR=1.63, 95% CI: 1.08-2.44) than those women who did not have severe nausea during the course of their pregnancy. The association of marijuana use for severe nausea was statistically significant (p=0.034). The findings of this study indicate women use marijuana as an anti-emetic for severe morning sickness. Additionally, marijuana use before pregnancy has been found to be associated with an increased likelihood of severe nausea during pregnancy. A limitation of this study is that as a single site study, it may not be generalizable to other regions of the country. These preliminary findings warrant further research being done on cannabinoid hyperemesis syndrome. This is an increasingly documented phenomenon in pregnant women who use marijuana prior to pregnancy (Roberson et al., 2014).

Screening and Counseling

A common theme found in many of the articles is that screening for marijuana use needs to be done in women before pregnancy and early on in their prenatal visits. Additionally, extensive counseling needs to be done with women who admit to marijuana use or who show up positive on drug screening tests done routinely prenatally in the first trimester.

Chabarria et al. (2016) conducted a retrospective cohort case study design that included 12,069 subjects who were able to provide information regarding their marijuana use and pregnancy outcomes. In the initial cohort analysis, marijuana exposure during pregnancy was not associated with significant perinatal adverse outcomes; however, it was found that concurrent use with cigarettes increased risk over either factor alone. Preterm birth was significantly higher in women reporting cigarette use as well as both cigarette use and marijuana use. Chabarria et al. (2016) found that it is important to counsel patients about the use of cigarettes and marijuana in pregnancy due to the high number of women who use both concurrently.

Martin et al., (2015) conducted a data analysis study using information that was obtained from the Treatment Episodes Data Set from the years 1992-2012 and analyzed the data over time using Chi Square, Cochran-Armitage, and Moran's I tests. The objective was to investigate recent trends in marijuana use during pregnancy in the United States. They found that the number of pregnant women who had treatment admissions remained fairly stable at 4%. They found that marijuana use has increased from 29% to 43% ($p<0.01$) during these years. They concluded that even though more women using marijuana are seeking treatment during pregnancy, health care providers, specifically prenatal caregivers, should be targeting certain at-risk groups and improving screening and treatment referrals for marijuana use during pregnancy. The strength of this study was that it had a well-balanced cohort across multiple covariates including maternal age, socioeconomic status, and tobacco smoking (Martin et al., 2015).

Ko et al., (2015) conducted a study to obtain national prevalence, patterns, and correlates of marijuana use in the past month and also in the past 2-12 months amongst women of reproductive age by pregnancy status. It was found that 3.9% (95% CI, 3.2-4.7) of pregnant women in this study used marijuana in the past month and 7.0% (95% CI, 6.0–8.2)

of pregnant women had used in the past 2-12 months. Among those pregnant women who admitted to marijuana use in the past year, 16.2% used marijuana daily. It was found that 18.1% of pregnant women who used marijuana met the criteria for abuse and/or dependence. The authors concluded that healthcare providers should be aware of marijuana use amongst their patients and should be able to provide the proper resources necessary to their patients who are using marijuana. Medical and recreational marijuana use is being legalized in states and there needs to be further research done on the potential adverse effects of marijuana use in pregnancy (Ko et al., 2015).

De Genna et al. (2015) conducted a prospective study that examined 456 pregnant women ranging in age from 13 to 42 years. These women were asked about their cannabis use one year prior to pregnancy, in each of their trimesters of pregnancy, and at 6, 10, 14, and 16 years postpartum. A growth mixture model (GMM) was used to explore different trajectories of use over time. The GMM indicated four patterns of maternal cannabis use over time. These are best described as non/unlikely to use at any time point which accounted for 61%, late desistance (no use during pregnancy but reported use 6 and 10 years postpartum) which accounted for 15%, decreasing likelihood of use meaning used in the year prior to pregnancy and then with a steady decline in use over the postpartum period which accounted for 11%, and increasing likelihood/chronic users which accounted for 14%. The results of the study showed that younger mothers are more likely to use cannabis across 17 years. These findings have important benefits for both the prevention and treatment of cannabis use in mothers (De Genna et al., 2015). This can guide healthcare professionals to tailor their screening, counseling and education based on these findings to decrease marijuana use during pregnancy.

Day et al. (2006) conducted a study to determine the effects of prenatal marijuana exposure based on the age of onset of use and frequency of use amongst 14-year-olds whose mothers used marijuana prenatally. The sample for this study was taken from women aged 18-42 who were receiving care in a prenatal clinic that was based out of a hospital. There were 563 (mother and daughter) pairs included in this study. Most of the participants qualified as light to moderate marijuana users during pregnancy. The study showed that prenatal marijuana exposure predicted the start and frequency of marijuana use amongst 14-year-old children even when all other variables were considered. It was also found that mothers who had depression were more likely to have children who start using marijuana at an early age. Current maternal tobacco use was also significantly associated with the frequency of adolescent marijuana use. The conclusion was that prenatal exposure to marijuana, along with other factors, has a significant association with marijuana use at age 14. A strength of this study was that the women were followed throughout pregnancy and multiple times throughout childhood and there was an adequate number of women who participated in this study. One limitation of the study is that it was mostly done in women from lower socioeconomic status, making it less generalizable to the public (Day et al., 2006). The results from this study can show parents that exposure prenatally to marijuana might predict the use of marijuana in their children and this is an important message to counsel patients about.

Oh et al. (2017) conducted a study to examine correlations between prenatal marijuana use and the effects of marijuana-specific risk/protective influences on marijuana use trends. The study was done using data taken from the National Survey on Drug Use. There were 7627 female respondents aged 18-44 included in the sample. The effect of marijuana use was analyzed using logistic regression analysis while adjusting for complex sampling design effects and controlled

for sociodemographic and marijuana-specific factors. Data utilized came from the years 2005-2014. During this period unmarried pregnant women's incidence of marijuana usage increased by 85%, whereas married pregnant women's marijuana use remained steady. The authors concluded that preventative efforts should be made with unmarried pregnant women and education and counseling should be given about the potentially harmful effects of marijuana smoking on maternal and child health. Education of all pregnant women about the effects of marijuana should be done and especially for unmarried pregnant women. Findings also suggest that emphasis should be placed on providing attention to unmarried pregnant women's mental health issues along with their associated health-risk behaviors (Oh et al., 2017).

Adverse Effects

There is a general consensus that more research is needed to determine how marijuana use during pregnancy could impact the health and development of infants. The research is needed due to changing regulations on marijuana, increased access to marijuana for pregnant women, as well as an increasing number of pregnant women who are using marijuana in the past decade. There are only a few studies that have done that have found associations between marijuana use in pregnancy and adverse effects on the infant/fetus.

The longitudinal study by Carter et al. (2016) was the first human study to show distinct patterns of pathology with multiple substance use. This study examined the effects of prenatal alcohol, methamphetamine and marijuana exposure on infant development. These mothers were recruited from birthing units that mainly served the economically disadvantaged. The final sample included 103 placentas from mothers who had multiple substance use and were examined by a senior placenta pathologist. This study showed that women who used marijuana also participated in poly-substance abuse. Other results from this study were associated with

increased placental weight which suggests different components for the damage caused by the exposure. These results are important as the placenta serves as the vital regulator of the intrauterine environment, and increased placenta growth could be a direct response of chronic hypoxia from marijuana use (Carter et al., 2016).

The goal of the study by Warshak et al. (2015) was to analyze a group of 6,648 women to determine if there are associations between marijuana use in pregnancy and adverse effects in the mom and baby. A retrospective cohort study of all deliveries of single babies that were born over 20 weeks' gestation was completed at a large university hospital. Logistic regression was then performed to evaluate their goal. There were 14 outcomes examined using a significant P-value of 0.004. This study did not find any adverse outcomes with marijuana use and preterm birth (p=0.15), pre-eclampsia (p=0.12), stillbirth (p=0.54), or unplanned cesarean section (p=0.75). Marijuana use was significantly correlated with higher rates of small for gestational age babies (p=0.001). The authors also found a trend towards marijuana users and higher rates of NICU admissions and perinatal mortality, but they were not statistically significant (p= 0.01 & p=0.14).

Much like the Warshak et al. (2015) study, the study by Corsi et al. (2019), showed there was evidence to support the correlation between cannabis use and an increased risk of preterm birth. This study was also a retrospective cohort analysis that included women 15 years of age or greater who delivered at a gestational age of 20 weeks or greater. Women who self-reported use of cannabis during pregnancy were compared with women who did not report use: this was done using standardized mean differences (SMD); SMD greater than 10% were considered suggestive of a meaningful difference across the two groups (Corsi et al., 2019). The results of this study showed an increase in preterm delivery in the cannabis-using group. The preterm risk difference

(RD) was 5.88%. There was also a relationship between cannabis use and small for gestational age infants (Corsi et al., 2019).

The study by van Gelder et al. (2009) analyzed data from a case study from the National Birth Defects Prevention Study. The goal of the study was to determine if there were positive associations between periconceptional illicit drug use and 20 different birth defects categories. This study found marijuana to be the most frequently reported illicit drug. Cannabis use was associated with an increased risk of anencephaly (OR=1.7/CI=0.9-3.4). This study did not find any other associations between periconceptional cannabis use and other congenital malformations (Gelder et al., 2009).

The Stillbirth Collaborative Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development with Varner et al. (2014) conducted a study on the effect of smoking and other illicit drug use on stillbirth. Comprehensive standardized fetal postmortem examination was done by several perinatal pathologists. The results showed that women who experienced a stillbirth were twice as likely to report addiction to an illicit drug. The most common drug detected was tetrahydrocannabinol acid which was significantly associated with stillbirth (OR 2.34, 95%, CI 1.13-4.81). Cannabis use increased the odds of stillbirth twofold per this study (Varner et al., 2014).

The secondary analysis from the Stillbirth Collaborative Research Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development by Metz et al. (2017) examined marijuana use and any adverse pregnancy or neonatal morbidity outcomes. The adverse pregnancy outcomes were small for gestational age babies, hypertension, and preterm birth. Neonatal morbidity outcomes included neonatal intensive care unit (NICU) admission and

other conditions that would cause a NICU admission. There were no associations with adverse

pregnancy outcomes (Metz et al., 2017).

In the study by Benevenuto et al. (2016) there was an investigation of the effects of

inhaled cannabis in mice. Twenty healthy female mice were divided into two groups of 10 each.

The mice in the cannabis group were exposed daily for 5 minutes to marijuana smoke. Urine was

then collected every 24 hours after exposure. Half of the dams were euthanized, their fetuses and

placentas were removed, weighed and checked for malformations. The other half of the mice

were delivered naturally and monitored. The statistical significance was set at $p<0.05$. The

results showed that fetal weight was significantly lower in the pups delivered from the cannabis

smoke group ($p=0.02$), the placental weight was greatly increased in this group as well ($p=0.04$).

These results show that smoking marijuana during pregnancy, even in low doses can be fatal to

the embryo and fetus (Benevenuto et al., 2016).

Marroun et al. (2009) performed a multiethnic population-based prospective cohort study

using information from the Generation R study. They explored the timing and frequency of

substance use with measures using self-report. A total of 7452 mothers participated in this study

to determine if cannabis use has affects fetal growth. Of the women who reported cannabis use

during pregnancy, 85% of those mothers also smoked tobacco. The results of this study indicated

that continued cannabis use during pregnancy showed growth reduction of $p=.052$ in mid-

pregnancy with a reduction of 277 g at birth ($p=.001$). Another finding of significance was a

smaller head circumference of -0.21 mm/week ($p=.001$). Decreases in fetal growth and head

circumferences are known risk factors for neurodevelopment and behavioral problems. This

study also suggested a dose-response association: Heavier cannabis use during pregnancy is

correlated with lower birth weight (Marroun et al., 2009).

Crume et al. (2018) performed a cross-sectional study using population-based data regarding cannabis use during and after pregnancy from a random sample of 3207 women who delivered a live born infant between January 1, 2014, and December 31, 2015. They sought to look at the relationship between maternal cannabis use at any time during pregnancy and adverse neonatal outcomes such as low birth weight, small for gestational age, NICU admission, and preterm birth. They found the overall rate of cannabis use at any time during pregnancy was 5.7% (95% CI). Any cannabis during any time of pregnancy was correlated with an 80% increased likelihood of an infant with low birth weight (OR, 1.8; 95% CI, 1.3-2.4; p = .0008). A strength of this study is that it used the Pregnancy Risk Assessment Monitoring System (PRAMS), which is the largest state-based surveillance program of pregnant women and live births in Colorado. A limitation of this study was self-reported maternal cannabis, which could result in inaccurate information. The study found that maternal cannabis use at any time during pregnancy was associated with a 50% increased likelihood of low birth weight, independent of other factors including tobacco use during pregnancy. This information highlights the importance of healthcare providers screening for cannabis use during pregnancy and the need for counseling about the adverse health effects of continued use during pregnancy postpartum including during lactation (Crume et al., 2018).

Data from the analysis by Leemaqz et al. (2016) was obtained from the Screening for Pregnancy Endpoints (SCOPE) study. Data from the 5,588 participants was included to examine the association of maternal marijuana use with pregnancy outcomes. Results showed that concurrent use of cigarettes and marijuana at 20 weeks' gestation was associated with small for gestation age (p=0.001), and spontaneous preterm birth (SPTB) (p=0.001). Breslow Day testing showed there was no difference in the results between marijuana and tobacco smokers versus

marijuana use only (p=0.238). The Mantel-Haenszel test showed the association between marijuana use and SPTB was independent of the smoking status, with adjusted common odds of 2.28. Based on this finding it is likely that maternal marijuana use is an independent risk factor for SPTB (Leemaqz et al., 2016).

Synthesis of the Major Findings

Several themes were identified in the 20 scholarly articles in this review among women who used marijuana pre-pregnancy and prenatally. A common theme included that more research was needed to draw definitive conclusions, and screening and counseling needed to be done among pre-pregnant and pregnant patients. There were adverse effects associated with marijuana use in pregnancy that included growth restriction in the neonate, low birth weight, small for gestational age, spontaneous preterm birth, increased risk of neonatal morbidity, placental abruption, increased NICU admissions, stillbirth, and anencephaly.

Chapter IV: Discussion, Implications, and Conclusions

The purpose of the critical review of this literature was to determine if adverse effects on the fetus/infant occur as a result of marijuana use in the mother pre-pregnancy, during pregnancy, and postpartum. For this review, twenty research articles were used; each was pertinent to the question being asked. The articles were reviewed using the John Hopkins Research Evidence Appraisal Tool. After the critical review of the literature was done the implications for nurse-midwifery were obtained and the limitations were also identified. Chapter IV will discuss the implications for nurse-midwifery along with the opportunities for further research that can be done. The chapter will conclude with the integration of Modeling and Role-Modeling Theory into nurse-midwifery practice and how to apply it to women who are using marijuana pre-pregnancy, during pregnancy, and postpartum.

Literature Synthesis

The research question posed for the critical review of the literature was to find out whether marijuana use in women pre-pregnancy, during pregnancy, or postpartum had any effect on the fetus/infant of that mother. Research regarding marijuana use is not complete as this is a new area of research, due to its legalization both medicinally and recreationally. There was one level I study found that was an animal study, and the remainder of the studies found were level III studies. The critical review of the literature revealed the following themes: Further high-level research needs to be done, screening and counseling of women using marijuana was necessary, and that several adverse effects were associated with marijuana use. There was a significant

overlap throughout the research articles that called for more research in order to obtain a stronger correlation between marijuana use and adverse effects.

Current Trends and Gaps in the Literature

Further Research Needed Nursing related research surrounding marijuana use is new and has not yet been able to reach statistically significant findings proving causality. Several authors (Bertrand et al., 2018, Connor et al., 2015, Conner et al., 2015, Mark et al., 2015) conducted research that found non-significant results. (See the Appendix 1 for findings and results). Marijuana use has increased dramatically in the last two decades due in large part to its medical and recreational legalization. This is going to be an issue that needs to be dealt with increasingly as more and more mothers are turning to marijuana for ailments in pregnancy and recreational use.

Screening and Counseling Screening for drug use needs to be done not only prenatally, but also prior to pregnancy. This gives the provider an opportunity to offer counseling before pregnancy happens in order to achieve the best and safest results possible related to pregnancy. With the increasing use of marijuana comes the increasing need for screening and counseling among women. This counseling needs to be extensive if a woman admits to marijuana use or shows up positive on routine drug screens in pregnancy. (Chabarria et al., 2016, Martin et al., 2016, Ko et al., 2015, DeGenna et al., 2015, Day et al., 2006, and Oh et al., 2017).

Adverse Effects Identified The number one thing that patients want to know when it comes to marijuana use in pregnancy is whether the research is saying definitive adverse effects have been identified. The consensus is that more research is needed to determine how marijuana use during

pregnancy can affect the health and development of fetuses/infants. There are only a few studies that show negative effects of marijuana use during pregnancy.

Carter et al. (2016) found that women who use marijuana during pregnancy were also abusing other illicit substances during pregnancy. Increased placental weight was associated with exposure to marijuana and other substances (Carter et al., 2016).

Warshak et al. (2015) found that marijuana use was significantly correlated with higher rates of small for gestational age infants born (p=0.001). It was also found that marijuana use was associated with higher rates of NICU admissions and perinatal mortality, but they were not statistically significant (p=0.01 & p=0.14). Corsi et al. (2019) found a correlation between cannabis use and an increased risk of preterm birth. They also found a relationship between cannabis use and small for gestational age infants (Corsi et al., 2019). Marijuana was the most commonly reported illicit drug and was associated with an increased risk of anencephaly (Gelder et al., 2009).

Women who had a stillbirth were twice as likely to report addiction to an illicit drug and the most common drug detected was THC as found in marijuana. The use of cannabis in pregnancy increased the odds of stillbirth twofold per this study (Varner et al., 2014). Metz et al. (2017) also found a correlation between marijuana use and small for gestational age infants, preterm birth, and increased NICU admissions (Metz et al., 2017). Crume et al. (2018) concluded that marijuana use during pregnancy was associated with an 80% increased likelihood of low birth weight in infants born to those mothers (Crume et al., 2018).

Benevenuto et al. (2016) concluded that fetal weight was significantly lower in the mice pups delivered from the group which had inhaled marijuana. It was also found that placental

weight was significantly greater in this group as well. This study concluded that smoking marijuana during pregnancy can be embryotoxic and fetotoxic (Benevenuto et al., 2016).

Marroun et al. (2009) showed that women who used marijuana during pregnancy had babies born with growth reduction on average of 2277 grams at birth and smaller head circumferences. These are significant findings because decreases in fetal growth and head circumferences are known risk factors for neurodevelopment and behavioral problems later on in life (Marroun et al., 2009). Leemaqz et al. (2016) found that marijuana use and cigarette smoking at 20 weeks' gestation was associated with small for gestational age infants and spontaneous preterm birth. Marijuana use is likely an independent risk factor for spontaneous preterm birth (Leemaqz et al., 2016).

Implications for Practice

As marijuana becomes increasingly popular across the United States, it means that healthcare professionals need to take an active role in the screening, counseling, and education of their patients. Mainstream media is going to tell the public what they want to hear, which will typically be that there is no concrete evidence that marijuana in pregnancy causes birth defects or adverse outcomes. The *Core Competencies for Basic Midwifery Practice* outline the Hallmarks of Midwifery, which include incorporating scientific evidence into clinical practice and using skillful communication, guidance, and counseling (ACNM, 2012). It is critical for healthcare professionals who deal with the pregnant population to continue to stay up to date on the research that is coming out. More research is being done on marijuana use in pregnancy; in the next few years there will likely be more definitive answers relating to marijuana use in pregnancy and the adverse effects associated with its use.

It is well known that midwifery care boasts a different kind of care for women than the typical physician practice. Midwives are known to spend ample time with their patients and to develop long-lasting relationships with their patients. Midwives can use this to their advantage by counseling patients that they know are using marijuana prior to pregnancy to help them to live the healthiest life possible. If midwives can counsel their patients before pregnancy and help them make decisions regarding cessation of marijuana use, it will prepare them to have the healthiest pregnancy possible in the future. Having a trustworthy and respectful relationship with a patient helps the patient trust the care provider, and the patient will also typically value the opinions and education presented by the care provider. This is one of the most important cornerstones of midwifery care.

Recommendations for Further Research

Throughout the research review process several areas were found that warrant further research. These include the quantity and frequency of marijuana use and its effect on the developing fetus/infant. There also needs to be more research allowing the possibility to look at marijuana use in pregnancy without concurrent cigarette use. Some of the most important research on marijuana use during pregnancy provides a glimpse into those groups of women at higher risk for marijuana use in pregnancy. This offers the care provider a unique perspective concerning who their high-risk patients are, and who they should be spending more time with regarding the education and counseling aspect of discouraging the use of marijuana during pregnancy and postpartum. There is an opportunity for further research in terms of how education and counseling can be offered most effectively to these groups.

Due to marijuana's legalization there will be an opportunity to have more studies with women consenting to research on marijuana use during pregnancy as time goes on. Health care

providers desire research that can help them effectively educate, counsel, and advise their patients on marijuana use. In time, there will also be increasing numbers of women who have previously used marijuana during pregnancy which will allow for increasing research to be done on the long-term effects of marijuana use in pregnancy.

Integration of Modeling and Role-Modeling Theory

The Modeling and Role-Modeling Theory was developed in 1982 by Helen Erickson, Evelyn Tomlin, and Mary Anne Swain (Nouri, Ebadi, Alhani, & Rejeh, 2014). The basis of this theory speaks to a person developing a picture and perception of another person's world. The person develops this picture by viewing the other person's framework, points of view, values, experiences, and perspectives. The Modeling and Role-Modeling Theory offers a unique perspective for care providers and the care they can provide to their patients.

By developing a trustworthy relationship with a patient, the care provider is allowed a unique and intimate relationship. Building a rapport with a patient that is trustworthy, honest, and caring allows for counseling and education on a level that the patient feels comfortable accepting. A nurse-midwife who truly seeks to investigate the woman's life and to determine why she is doing something can help to tailor the education and counseling to be most effective. The nurse-midwife can incorporate concepts of the Modeling and Role-Modeling theory to her advantage to connect with patients on a level that they may not necessarily get in a busy OB/GYN setting.

Conclusion

The pertinent findings of this critical review of the literature include adverse effects related to prenatal marijuana use, the need for more research, and the need for screening and counseling. Perhaps the most important of these is the need for extensive screening and

counseling of women who are of childbearing age. The need for screening, guidance, and education in women who are thinking about getting pregnant in the future is of the utmost importance. By establishing early on that marijuana use during pregnancy and possibly prepregnancy may have detrimental effects, care providers can give their patients and their patients' potential offspring the best possible chance at a healthy life.

Nurse-midwives are at a unique advantage with their patients due to the specific nature of their role and their ability to develop lifelong relationships, fostering a true and lasting trust between the two parties. Nurse-midwives follow the Hallmarks of Midwifery that speak to the therapeutic value of human presence, skillful communication, guidance and counseling, and to the empowerment of women as partners in healthcare (ACNM, 2012). This allows nurse-midwives to truly empathize with the patient and allow her to be a part of her care and plan of care. It is important that human beings remain autonomous in their healthcare decisions while seeking care from a healthcare provider. It is also important that the nurse-midwife incorporate scientific evidence into clinical practice (ACNM, 2012). The balance and art of midwifery combine all these things into a beautiful display of compassionate care that is evidence-based. This is truly a lifelong learning journey that gets better with time. The ability to support women as nurse-midwives in a world where marijuana becomes increasingly legal and more prevalent is an opportunity to create changes that will have ripple effects for lifetimes to come.

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Appendix 1: Matrix of the Literature

Source: Benevenuto, S., Domenico, M., Martins, M., Costa, N., De Souza, A., Cista, J., Tavares, M., Dolhnikoff, M., & Veras, M. (2017). Recreational use of marijuana during pregnancy and negative gestational and fetal outcomes: an experimental study in mice. T*oxicology,376*(1), 94-101. https://doi.org/10.1016/j.tox.2016.05.020			
Purpose/Sample	**Design (Method/Instruments)**	**Results**	**Strengths/Limitations**
Purpose: To experimentally investigate the effects of maternal inhalation of *Cannabis sativa* smoke representing as nearly as possible conditions of human marijuana use in terms of dose and use to evaluate the effects on gestational and fetal outcomes. **Sample/Setting:** 20 female mice age 60 days, and 3 male mice, age 80 days with proven fertility. **Level of evidence:** I	20 pregnant mice were placed randomly into two groups, one exposed (nose-only) daily for 5 min to marijuana smoke or filtered air in the control group. Mice were weighed daily during the exposure period, and food intake was recorded. On GD 18.5, half of the mice were euthanized, the abdominal wall was immediately opened, and the uterus was examined carefully. The fetuses and placentas were removed, checked for malformations, and weighed. The other half of pregnant mice delivered naturally, and they were continuously monitored in order to verify whether the offspring born were dead or alive	Marijuana smoke inhalation negatively affected the gestational and fetal outcomes in the mice. Five minutes of daily (low dose) exposure during pregnancy resulted in reduced birth weight, and litter size was not altered; however, the number of male pups per litter was higher. Besides, placental wet weight was increased, and fetal-to-placental weight ratio was decreased in male fetuses, showing a sex-specific effect. **Conclusion:** The results indicate that smoking marijuana during pregnancy even at low doses can be	**Strengths:** This exposure model has already proven successful, once it was confirmed the presence of THC–COOH in urine. Furthermore, it also proved to be a safe and not stressful method, causing no deaths during the exposure process and no changes in feeding behavior. **Limitations:** The small volume of urine that was collected after the exposures, and the low-dose exposure that was adopted in this study, imposed many difficulties to determinate its quantities in this biological matrix.

Quality of evidence: High		embryotoxic and fetotoxic, increasing implantation failures and compromising fetal development.	

Author Recommendations:
More studies are needed to recognize and better understand the impacts of smoking marijuana during pregnancy and its impacts on future health.

Summary for current clinical practice question:
With more and more legalization of recreational use of *Cannabis,* there is an urgent need of further toxicological studies to better recognize the effects and explain the mechanism involved with Cannabis use in pregnancy.

Source:
Bertrand, K., Hanan, N., Honerkamp-Smith, G., Best, B., & Chambers, C. (2018). Marijuana use by breastfeeding mothers and cannabinoid concentrations in breast milk. *Pediatrics, 142*, (3), 1-8. DOI: 10.1542/peds.2018-1076

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: To quantify cannabinoids in human milk after maternal marijuana use. **Sample/Setting:** 50 breastfeeding women who reported marijuana use between 2014-2017. **Johns Hopkins Evidence Appraisal:** **Strength:** Level II **Quality:** Good	Volunteers residing in the United States and Canada have been recruited into the University of California, San Diego Mommy's Milk, the human milk biorepository (HMB) through a variety of sources including social media. Breastfeeding mothers completed an interview providing demographics, maternal and child health history, and details regarding exposures to medications, alcohol, tobacco, and other recreational substances. Participants recalled their exposures for the 14 days before milk sample collection.	Δ9-THC was measurable in highly variable concentrations in the breast milk of approximately two-thirds of samples from women who reported marijuana use during breastfeeding and up to 6 days since last reported dose. **Conclusion:** Marijuana is the most commonly used recreational drug among breastfeeding women; information regarding risks to breastfeeding infants is urgently needed.	**Strengths:** This is the first study used to calculate levels of specific cannabinoids detectable in human milk in a relatively large sample of mothers with detailed and varied histories of recent marijuana use. **Limitations:** Samples were collected under different conditions, not all breast milk collections were directly observed, and we relied on maternal report of marijuana exposure.

Author Recommendations:
There is a critical need for further research on neurodevelopmental outcomes in infants breastfed by mothers using marijuana.

Summary for current clinical practice question:
Because the brain rapidly develops during the time period when, ideally, a child's main source of nutrition is human milk, brain development may be altered by marijuana exposure.

Source: Carter, R., Wainwright, H., Molteno, C., Georgieff, M., Dodge, N., Warton, F., Meintjes, E., Jacobson, J., & Jacobson, S. (2016), Alcohol, methamphetamine, and marijuana exposure have distinct effects on the human placenta. Alcoholism: *Clinical Experimental Research, 40*, 753-764. doi:10.1111/acer.13022			
Purpose/Sample	**Design (Method/Instruments)**	**Results**	**Strengths/Limitations**
Purpose: To see what effects, if any, of prenatal exposure to methamphetamine, marijuana, and cigarette smoking on placental development. **Sample/Setting:** 103 placentas from pregnant women recruited at their first prenatal visit. **Johns Hopkins Evidence Appraisal:** **Strength:** Level II **Quality:** Good	Longitudinal study. The women in the sample were recruited between October 2011 and October 2014 from 3 antenatal midwife obstetric units that serve economically disadvantaged Cape Colored communities in Cape Town. Sixty-six heavy drinkers and 37 nondrinkers were interviewed about their alcohol, cigarette smoking, and drug use at 3 antenatal visits. A senior pathologist, blinded to exposure status, performed comprehensive pathology examinations on each placenta using a standardized protocol. In multivariable regression models, effects of prenatal exposure were examined on placental size, structure, and presence of infections and meconium.	Alcohol exposure was related to decreased placental weight and a smaller placenta-to-birthweight ratio. By contrast, methamphetamine was associated with larger placental weight and a larger placenta-to-birthweight ratio. Marijuana was also associated with larger placental weight. Alcohol exposure was associated with increased risk of placental hemorrhage. Prenatal alcohol, drug, and cigarette use were not associated with chorioamnionitis, villitis, deciduitis, or maternal vascular under perfusion. Alcohol and cigarette smoking were associated with a decreased risk of intrauterine passing of meconium, a sign of acute fetal stress and/or hypoxia; methamphetamine, with an increased risk.	**Strengths:** This is the first human study to show that alcohol, methamphetamine, and marijuana were associated with distinct patterns of pathology, suggesting different mechanisms mediating their effects on placental development. **Limitations:** Measurement error surrounding estimates of true alcohol exposure to the fetus may obscure some group differences. Given that urine testing was not available for all women reporting methamphetamine use, we could not separate effects of methamphetamine on the placenta from

			potential effects of methaqualone.
		Conclusion: Given the growing body of evidence linking placental abnormalities to neurodevelopmental deficits, these findings may be important in the long-term teratogenic effects of prenatal alcohol and drug exposure.	

Author Recommendations:
Future studies are needed to examine the effects of growth restriction on growth and neurodevelopment and the long-term developmental consequences of the exposure-related placental abnormalities for the child.

Summary for current clinical practice question:
Increased placental growth may occur in response to chronic hypoxia caused by marijuana.

Source: Chabarria, K. C., Racusin, D. A., Antony, K. M., Kahr, M., Suter, M. A., Mastrobattista, J. M., & Aagaard, K. M. (2016). Marijuana use and its effects on pregnancy. *American Journal of Obstetrics and Gynecology, 215*(4), 1-6. https://doi.org/10.1016/j.ajog.2016.05.044

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: The primary aim of this study was to examine both maternal and neonatal outcomes associated with smoking, both marijuana and tobacco, and to evaluate for adverse outcomes alone or in combination. **Sample/Setting:** Sample: 12,069 women with singleton pregnancies who delivered at one of the tertiary referral hospitals associated with Baylor College of Medicine. **Johns Hopkins Evidence Appraisal: Strength:** Level III for quantitative **Quality:** Good quality due to a sufficient sample size, and reasonably consistent results.	**Design:** This was a retrospective cohort study design that included 12,069 subjects with available information on marijuana use and pregnancy outcomes. Since 2011, they had routinely questioned all gravidae regarding use of marijuana, tobacco, and nicotine-containing products. Perinatal outcomes in marijuana smokers vs. nonsmokers, as well as patients reporting both marijuana and cigarette smoking. Multivariate analysis enabled determination of adjusted odds ratios for maternal and fetal outcomes, adjusting for cofounders. Significance was determined with Mann-Whitney U, X2, and Fisher exact tests (as appropriate).	Marijuana use alone was not associated with a significant difference in head circumference <25th percentile or birthweight <25th percentile. However, cigarette smoking was found to be significantly associated with the rate of delivery of relatively small-for-gestational age neonates. Specifically, in multivariate-adjusted models, head circumference <25th percentile was significantly more common among smokers. Pregnancies occurring among gravidae with marijuana use were not found to be associated with an increased rate or occurrence of preterm birth. However, preterm birth was significantly increased in women reporting cigarette smoking as well as both cigarette	**Strengths:** A large, clinically relevant cohort was utilized. The results were stratified by race and ethnicity and therefore could potentially be generalizable to a number of populations. Cigarette use and marijuana use were able to be delineated which could potentially be used to provide new insight into a synergistic relationship. Data was not only curated from electronic medical records but also from personal interviews and direct patient questioning in each subject's native language. **Limitations:** In a database this large there are going to be unaccounted for cofounders and occasional missing data. Patient reported use of marijuana use within

		smoking and marijuana use. **Conclusion:** In the initial cohort analysis, after controlling for potential confounders, while marijuana exposure alone was not associated with significant perinatal adverse outcomes, co-use with cigarette smoking rendered increased risk over either alone. Due to observed prevalence of concurrent cigarette and marijuana use, it is of likely importance to counsel patients regarding use in pregnancy.	the population for this study was notably lower than reported rates of use.

Author Recommendations:
In summary, in our contemporary population-based study we analyzed the impact of maternal tobacco and marijuana, alone and in combination, on multiple perinatal outcomes. The authors hope that their study will prompt further analysis inclusive of prospective evaluations, with consideration for possible synergism of tobacco and cannabis effects on perinatal health. With these and other studies' future findings, we will be able to best counsel patients regarding potential risks as marijuana use becomes more widely accepted.

Summary for current clinical practice question:
This study shows us that marijuana use alone was not associated with significant perinatal adverse outcomes. Co-use with cigarettes rendered increased risk of significant perinatal adverse outcomes over either alone. We are seeing more co-use of cigarette and marijuana use and therefore it is of importance to counsel patients during pregnancy regarding the use of these substances together.

Source: Conner, S. N., Carter, E. B., Tuuli, M. G., Macones, G. A., & Cahill, A. G. (2015). Maternal marijuana use and neonatal morbidity. *American Journal of Obstetrics & Gynecology*, *213*(3), 422.e1-422.e4. https://doi-https://doi.org/10.1016/j.ajog.2015.05.050			
Purpose/Sample	**Design (Method/Instruments)**	**Results**	**Strengths/Limitations**
Purpose: To determine the occurrence and risk factors for marijuana use in pregnancy and to evaluate whether marijuana use is autonomously associated with poor neonatal outcomes. **Sample/Setting:** All term deliveries occurring over a 4-year period from 2004 to 2008 at Washington University in St Louis Medical Center. 8138 women met all inclusion criteria. **Level of evidence:** Level 1	Retrospective cohort study of all successive term deliveries occurring over a 4- year period. Women with marijuana use during pregnancy, either by self-report or positive urine drug screen, were compared with women who did not use marijuana. Inclusion criteria consisted of all women with term, live, singleton pregnancies who delivered at Washington University in St. Louis Medical Center during the study period. Exclusion criteria were met for women with preterm deliveries, known fetal congenital anomalies, or multiple gestations. For all women in the study, detailed demographic information was removed from the medical record by trained obstetric research nurses. Data gained included patient medical and surgical history, obstetric and gynecological history, prenatal history, antepartum records, delivery records, and postpartum records.	A total of 674 patients (8.3%) had the composite outcome. The composite of neonatal morbidity was found in 11.6% of women who used marijuana compared with 8.0% of women who did not. After adjusting for smoking tobacco, other drug use, and African American race the composite neonatal morbidity was not significantly different between women who used marijuana during pregnancy and those who did not **Conclusion:** This study found marijuana use is common in pregnancy, with 8.4% of this studies population found to use marijuana. This study found that after adjusting for confounding factors, term infants	**Strengths:** This study provides, new, valuable information regarding neonatal outcomes not previously reported. This study allowed evaluation of more subtle markers of neonatal morbidity. Finally, by focusing on live births and term deliveries, we can exclude many potential confounding factors. **Limitations:** Unable to control for marijuana smoked. Defining marijuana use through self-report may have led to a misclassification bias. Study was done in a tertiary hospital with a high African American population.

| Quality of evidence:

Good; ample sample size, but no controls. | The primary outcome measures were composite neonatal morbidity and its distinct components. Measures of neonatal morbidity included birthweight less than 2500 g, neonatal intensive care (NICU) admission, 5-minute Apgar score less than 7, and umbilical artery pH less than 7.10. Infants with 1 or more morbidities were considered positive for neonatal composite morbidity. Infants with more than 1 criterion for neonatal morbidity were counted only once. | of women who use marijuana during pregnancy are not at an increased risk for neonatal morbidity. | |

Author Recommendations:
Further study is needed for controlling for the amount and extent of marijuana use and trimester of use as well as applying objective analyses to determine use to more definitively determine the relationship between marijuana and adverse neonatal outcomes.

Summary for current clinical practice question:
The practice of marijuana use is increasing making it likely that use in the obstetric population will increase as well. It is important that practitioners be able to adequately counsel patients who use marijuana regarding the potential effects on their pregnancy.

Source: Corsi, D., Walsh, L., Weiss, D., Hsu, H., El-Chaar, D., Hawken, Fell, D., & Walker, M. (2019). Association between self-reported prenatal cannabis use and maternal, perinatal, and neonatal Outcomes. *JAMA*, *322*(2), 145–152. doi:10.1001/jama.2019.8734			
Purpose/Sample	**Design (Method/Instruments)**	**Results**	**Strengths/Limitations**
Purpose: To assess whether there are associations between self-reported prenatal cannabis use and adverse maternal and perinatal outcomes. **Sample/Setting:** Women aged 15 years and older in Ontario, Canada, between April 2012 and December 2017. This study included 661,617 pregnancies and 9427 reported cannabis users **Level of evidence:** III **Quality of evidence:** Good	Population-based retrospective cohort study covering live births and stillbirths. The primary outcome was preterm birth before 37 weeks' gestation. Ten secondary outcomes were examined including small for gestational age, placental abruption, transfer to neonatal intensive care, and 5-minute Apgar score. Coarsened exact matching techniques and Poisson regression models were used to estimate the risk difference (RD) and relative risk (RR) of outcomes associated with cannabis exposure and control for confounding.	The rate of preterm birth among reported cannabis users was 12% vs 6% in nonusers, a statistically significant difference. **Conclusion:** Among pregnant women in Ontario, Canada, reported cannabis use was significantly associated with an increased risk of preterm birth. Findings may be limited by residual confounding.	**Strengths:** The matched cohort was balanced across covariates, including maternal age, socioeconomic status, tobacco smoking, and other correlates of cannabis exposure. A large, population-based pregnancy cohort, a significant association was observed between reported prenatal cannabis use and preterm birth. **Limitations:** Findings may be limited by residual confounding. In BORN and other administrative data, there is likely misclassification of cannabis exposure in pregnancy. The sources may be influenced by social stigma, desirability bias, and fear of intervention by child

			protection or social services.
Author Recommendations: Recent evidence suggests that cannabis use during pregnancy is increasing, although population-based data about perinatal outcomes following in utero exposure remain limited.			
Summary for current clinical practice question: Need for further research to determine if preterm birth is increased with marijuana use.			

Source:
Crume, T. L., Juhl, A. L., Brooks-Russell, A., Hall, K. E., Wymore, E., & Borgelt, L. M. (2018). Cannabis use during the perinatal period in a state with legalized recreational and medical marijuana: The association between maternal characteristics, breastfeeding Patterns, and neonatal outcomes. *The Journal of Pediatrics, 197*. 90-96. https://doi.org10.1016/j.jpeds.2018.02.005

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: To evaluate prevalence estimates of prenatal and early postnatal marijuana use in a state that has legalized medicinal and recreational marijuana and the association with adverse neonatal outcomes. **Sample/Setting:** 3207 respondents from the 2014-2015 Colorado Pregnancy Risk Assessment Monitoring System with state-developed questions on cannabis use. **Johns Hopkins Evidence Appraisal: Strength:** Level III due to it being a cross-sectional study, which is an observational type of study and is nonexperimental.	A cross-sectional study was conducted using population-based data regarding cannabis use during and after pregnancy from a stratified random sample of women who delivered a live-born infant between January 1, 2014 and December 31, 2015. Neonatal outcomes of interest abstracted from the Colorado birth certificate included: LBW (birth weight of <2500g), preterm birth (birth at <37 weeks), small for gestational age (birth weight of less than or equal to 10% for gestational age based standardized national sex-specific infant growth charts), and NICU admission. The relationship between maternal cannabis use at any time during pregnancy and adverse neonatal outcomes (LBW, small for gestational age, NICU admission, and preterm birth) was evaluated in separate	The overall prevalence of cannabis use at any time during pregnancy was 5.7% (95% CI, 4.8%-6.8%). The analytic sample was 3178 for LBW, 3146 for NICU admission, 3178 for preterm birth, and 2983 for small for gestational age. Cannabis use at any time during pregnancy was associated with 80% increased likelihood of LBW (OR, 1.8; 95% CI, 1.3-2.4; P = .0008), independent of maternal age, race/ethnicity, and level of maternal education. **Conclusion:** The findings from this study highlight the importance of screening for cannabis use during pregnancy and the need for counseling about the adverse health consequences of continued use	**Strengths:** The PRAMS is the largest state-based surveillance program of pregnant women and live births in Colorado. The neonatal outcomes variables were chosen based on previous literature suggesting high validity. **Limitations:** Maternal cannabis use was self-reported which could result in misinformation being given.

	multiple logistic regression models.	during pregnancy and lactation. It was found that maternal cannabis use at any time during pregnancy was associated with a 50% increased likelihood of LBW, independent of tobacco use during pregnancy and other confounders.	
Quality: High quality due to the consistent, generalizable results, and sufficient sample size. This study also provides consistent recommendations.			

Author Recommendations:
Our findings of a relationship between prenatal cannabis use and LBW underscore the 2015 recommendations by the American College of Obstetricians and Gynecologists for clinical management of cannabis use during pregnancy and lactation. Pregnant women should be asked about cannabis use and advised to discontinue cannabis use during pregnancy and lactation. Obstetrics providers should refrain from prescribing or recommending cannabis for medical purposes during preconception, pregnancy, and lactation. Given the higher levels of use among women of younger age and lower socioeconomic status, guidance and messaging should be incorporated into prenatal care, WIC, and Medicaid services. Screening of pregnant women at risk for cannabis dependency should be linked to treatment options and, based on this study, should include the assessment of other maternal risk factors such as tobacco use, stress, food insecurity, and prenatal vitamin use.

Summary for current clinical practice question:
Marijuana use should be advised against during any point in the pregnancy due to the strong correlation to lower birth weight infants being born to mothers who used marijuana in their pregnancies. Small for gestational age, preterm birth, and neonatal intensive care unit admission were not associated with prenatal cannabis use, independent of prenatal tobacco use.

Source: Day, N. L., Goldschmidt, L., & Thomas, C. A. (2006). Prenatal marijuana exposure contributes to the prediction of marijuana use at age 14. *Addiction, 101,* 1313-1322. https://doi.org/10.1111/j.1360-0443.2006.01523.x

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: To determine the effects of prenatal marijuana exposure on the age of onset and frequency use amongst 14-year-olds.	Study began in 1982 when the mothers were in their fourth prenatal month. 2 study cohorts were formed. - women who used marijuana at least twice per month - women who used less than twice a month or none at all.	Prenatal marijuana exposure predicted age of onset and frequency of marijuana use amongst 14-year-old offspring even when all variables in the data were considered. Current maternal tobacco use was significantly associated with the frequency of adolescent marijuana use.	**Strengths:** The results agree with other reports that have found a preponderance of child factors as predictors of early onset substance use. There was an adequate number of women who participated in the study who used marijuana prenatally
Sample/Setting: Sample was from recruitment out of a hospital-based prenatal clinic. Women aged 18-42. Half were African American, and half were Caucasian. Most from lower socioeconomic status. Most were light to moderate substance users during pregnancy and subsequently. 563 pairs (mother and daughter) were included in this study. **Johns Hopkins Evidence Appraisal:**	Women were also interviewed in their 7th prenatal month, at delivery, at 8 and 18 months postpartum, and 3,6,10 & 14 years postpartum. Two outcome variables were used for the analyses. - age of marijuana onset - frequency of marijuana use	Maternal depression was significantly associated with an earlier age of initiation in the offspring. Child's gender, race, and IQ did not predict age of onset or frequency of marijuana use at age 14. **Conclusion:** Prenatal exposure to marijuana, in addition to other factors, is a significant predictor of marijuana use at age 14.	Women were followed throughout pregnancy and multiple times throughout childhood. **Limitations:** The cohort was weighted toward substance-using women making it less generalizable. The women in the study were mostly from lower socioeconomic status, which makes the study less generalizable to the general public.

Strength: Level III Quality: Good			

Author Recommendations:
There are 3 mechanisms by which prenatal marijuana exposure could predict marijuana use in offspring. This could result from:

1. Genetic or familial factors
2. Characteristics of the current environment
3. Gestational exposures

More studies in these areas will go on to provide more information.

Summary for current clinical practice question:
Even though we don't have strong evidence showing an association between prenatal marijuana exposure and birth defects, the data from this study can show parents that marijuana exposure prenatally can possibly predict the use in their offspring, and this is an important thing to counsel our patients on.

Source: De Genna, N., Cornelius, M., Goldschmidt, L., & Day, N. (2015). Maternal age and trajectories of cannabis use. *Drug and Alcohol Dependence, 156*, 199-206. https://doi.org/10.1016/j.drugalcdep.2015.09.014			
Purpose/Sample	**Design (Method/Instruments)**	**Results**	**Strengths/Limitations**
Purpose: The goal of this study was to identify trajectories of maternal cannabis use, and to determine if maternal age was associated with different trajectories of use. **Sample/Setting:** Data for this study are from three birth cohorts that are part of a consortium of studies on the effects of substance use on offspring physical and neurobehavioral development. These data were collected as part of three NIH-funded studies: the teen mother cohort and two adult mother cohorts. The two adult mother cohorts were combined. Teen	This prospective study examined 456 pregnant women recruited at a prenatal clinic, ranging in age from 13 to 42 years. The women were interviewed about their cannabis use 1 year prior to pregnancy and during each trimester of pregnancy, and at 6, 10, 14, and 16 years post-partum.	A growth mixture model of cannabis use reported at each time point clearly delineated four groups: non/unlikely to use, decreasing likelihood of use, late desistance, and increasing likelihood/chronic use (Lo–Mendell–Rubin adjusted LRT test statistic $= 35.7$, $p < .001$). The youngest mothers were least likely to be in the "non/unlikely to use" group. Younger maternal age also differentiated between late desistance and increasing likelihood/chronic use, versus decreasing likelihood of use post-partum. **Conclusion:** This is the first study to demonstrate that younger mothers are more likely to use cannabis across 17	**Strengths:** This study provided the first empirical evidence that age does matter for trajectories of maternal cannabis use. **Limitations:** These results may not generalize to mothers from other regions of the country, to mothers of other racial and ethnic backgrounds, or to mothers from more advantaged backgrounds who do not give birth in an urban, university teaching hospital. This study provides no data on cannabis use in mothers of Hispanic or Asian-American descent. Another limitation of the current study is the reliance on self-report for cannabis use.

| Cohort mothers were 13–18 years old and Adult Cohort mothers were 18–42 years old at the beginning of the studies

Level of evidence:

III

Quality of evidence:

Good | | years, including later desistance post-partum and increasing/chronic use.
Other substance use and chronic depressive symptoms were also associated with more frequent use. | |

Author Recommendations:
These findings have implications for both prevention and treatment of cannabis use in mothers.

Summary for current clinical practice question:
These results have important implications for the physical and mental health of our youngest mothers, given the effects of cannabis use on the still-developing adolescent brain.

Source:
El Marroun, H., Tiemeier, H., Steegers, E., Jaddoe, V., Hofman, A., Verhulst, F., Brink, W., Huizink, A. (2009). Intrauterine cannabis exposure affects fetal growth trajectories: the generation r study. *Journal of the American Academy of Child & Adolescent Psychiatry, 48*(12), 1173-1181.   https://doi.org/10.1016/s1090-798x(10)79394-2

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: This study examined the relation between maternal cannabis use and fetal growth until birth in a population-based sample. **Sample/Setting:** **Level of evidence:** III **Quality of evidence:** Good	Approximately 7,452 mothers enrolled during pregnancy and provided information on substance use and fetal growth. Fetal growth was determined using ultrasound measures in early, mid-, and late pregnancy. Additionally, birth weight was assessed.	Maternal cannabis use during pregnancy was associated with growth restriction in mid- and late pregnancy and with lower birth weight. This growth reduction was most pronounced for fetuses exposed to continued maternal cannabis use during pregnancy. Fetal weight in cannabis-exposed fetuses showed a growth reduction of j14.44 g/week (95% confidence interval j22.94 to j5.94, p = .001) and head circumference (j0.21 mm/week, 95% confidence interval j0.42 to 0.02, p = .07), compared with nonexposed fetuses. Maternal cannabis uses during pregnancy resulted in more pronounced growth restriction than maternal tobacco use. Paternal cannabis use was not	**Strengths:** Strengths of this investigation include the large population-based prospective cohort we used to examine these associations, the use of ultrasound measurements in combination with information collected at birth that enabled us to determine growth trajectories throughout gestation until birth, and the possibility to control for important confounding factors, including lifestyle factors, socioeconomic factors, and known determinants of fetal growth. **Limitations:** Used self-reported data on substance use. Both potential misclassification and selection bias may have led to an underestimation of the prevalence of cannabis

		associated with fetal growth restriction.	use and an underestimation of the effects of cannabis exposure on fetal growth and brain size parameters. The effects of maternal cannabis use on fetal characteristics may have been underestimated because the early pregnancy measurements were used for pregnancy dating, if the variation in growth before the first measurement is zero.
		Conclusion: Maternal cannabis use, even for a short period, may be associated with several adverse fetal growth trajectories.	

Author Recommendations:
Our findings suggest the importance of educating future mothers about the consequences of prenatal maternal cannabis use. Our findings may imply that different messages could be transmitted to tobacco and cannabis users.

Summary for current clinical practice question:
To prevent the potential harmful effects of intrauterine cannabis exposure, women should quit using cannabis before conception.

Source: Ko, J., Farr, S., Tong, V., Creanga, A., & Callaghan, W. (2015). Prevalence and patterns of marijuana use among pregnant and nonpregnant women of reproductive age. *American Journal of Obstetrics & Gynecology, 213*(2), 201-211. https://doi.org/10.1016/j.ajog.2015.03.021

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: The objective of the study was to provide national prevalence, patterns, and correlates of marijuana use in the past month and past 2/12 months among women of reproductive age by pregnancy status. **Sample/Setting:** Pregnant and nonpregnant women 18-44 years of age. Women self-reported marijuana use in the past month and past 2-12 months (use in the past year but not in the past month). **Level of evidence:** III **Quality of evidence:**	The study combined public use data from the 2007/2012 National Surveys on Drug Use and Health (NSDUH). The NSDUH is a cross-sectional survey designed to estimate prevalence and correlates of substance use in US household populations aged 12 years or older.	More than 1 in 10 pregnant and nonpregnant women reported using marijuana in the past 12 months. A considerable percentage of women who used marijuana in the past year were daily users, met abuse and/or dependence criteria, and were polysubstance users. **Conclusion:** Comprehensive screening, treatment for use of multiple substances, and additional research and patient education on the possible harms of marijuana use are needed for all women of reproductive age	**Strengths:** Findings from this study have clinical and public health implications. **Limitations:** Pregnancy status was self-reported at the time of the interview; nonpregnant women who did not yet know that they were pregnant may have been misclassified. Furthermore, marijuana use in the past 2-12 months may not have occurred during pregnancy. Second, marijuana and other substance use were self-reported and not validated with biological samples.

Strong			
Author Recommendations: Clinicians should be aware of the prevalence of marijuana use among their patients who are pregnant or at risk of becoming pregnant and have the training, tools, and resources to provide appropriate screening, patient education and care to women using or abusing marijuana, including comprehensive treatment for women also using other substances.			
Summary for current clinical practice question: As states legalize the medical and/or recreational use of marijuana, it will be important to continuously monitor national and state trends in their use and examine potential adverse effects on pregnancy.			

Source: Leemaqz, S. Y., Dekker, G. A., McCowan, L. M., Kenny, L. C., Myers, J. E., Simpson, N., Poston, L., & Roberts, C. T. (2016). Maternal marijuana use has independent effects on risk for spontaneous preterm birth but not other common late pregnancy complications. *Reproductive Toxicology, 62,* 77-86. https://doi.org/10.1016/j.reprotox.2016.04.021

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: This study aimed to examine the association of maternal marijuana use (from pre-pregnancy and up to 20 weeks' gestation) in a multi-center cohort with major pregnancy complications, amongst both cigarette smokers and non-smokers, controlling for well-known risk factors, as well as its effects on length of gestation. **Sample/Setting:** A total of 5588 participants were included in the analysis, with 1155 participants recruited from Australia, 2014 from New Zealand, 1765 from Ireland, and 654 from the United Kingdom.	Details of maternal age, BMI and socioeconomic index (SEI), medical and family history, along with dietary and lifestyle questionnaires with self-reported marijuana and cigarette smoking were recorded at 15 weeks' and 20 weeks' gestation and entered into an internet-accessed database. Breslow-Day test was used to assess the homogeneity of the odds of marijuana use between cigarette smokers and non-smokers, along with an adjusted common odd estimated from Mantel-Haenszel test. Marijuana and cigarette smoking status were then analyzed with mixed effects logistic regression to determine the association with pregnancy outcomes, adjusting for maternal age, BMI and SEI, and with recruiting center differences accounted for as a random effect. A linear mixed model	Marijuana use and cigarette smoking at 20 weeks of gestation were both associated with small gestation age (SGA) and spontaneous preterm birth (SPTB). The odds of SPTB for any marijuana use three months prior to or during pregnancy was more than doubled for both cigarette smokers and non-smokers. Similarly, as expected, continuing to smoke cigarettes at 20 weeks' gestation was associated with SGA. The predicted length of gestation was lower for women who continued to use marijuana at 20 weeks of gestation for both cigarette smokers and non-smokers, with an estimated gestation of less than 37 weeks when more than 100 episodes of marijuana use within the previous three months	**Strengths:** A strength of this study was its large international multicenter prospective cohort with excellent follow-up and complete data available for this analysis. Interaction tests were performed on this data. Hence, with complete quality data available from this study, interactions between marijuana use and cigarette smoking status may be examined while also adjusting for potential confounders. **Limitations:** The use of self-reported marijuana use, and cigarette smoking status is a limitation as this can be subject to participant recall bias. This study was also only carried out on nulliparous women, which means the findings may only apply to nulliparous women.

Johns Hopkins Evidence Appraisal: **Strength:** Level III due to it being a nonexperimental study. **Quality:** Good quality due to sufficient sample size and reasonably consistent recommendations.	was also fitted for length of gestation, with quadratic terms for the number of times marijuana was used over the preceding 3 months at 15 and 20 weeks of gestation, age, and BMI, to investigate the dose effect of marijuana and cigarette smoking status on the length of gestation adjusted for other factors in the model.	before 20 weeks' gestation. **Conclusion:** Based on the current findings and some earlier reports, it is likely that maternal marijuana use is an independent risk factor for SPTB. If there was no maternal marijuana exposure the incidence of SPTB would be expected to decrease by 3 cases per 1000 pregnant women.	

Author Recommendations:
The data indicates that increasing use of marijuana among young women of reproductive age is a major public health concern. The increasing exposure to marijuana in women of reproductive age and its contribution to the risk for preterm birth make it a modifiable target for intervention.

Summary for current clinical practice question:
In this large prospective cohort, maternal marijuana use had a major contribution to SPTB and this association was consistent for both cigarette smokers and non-smokers, with doubled odds in women who used marijuana three months prior to or during pregnancy. For women who use marijuana during pregnancy, it should be emphasized that stopping early in pregnancy should be encouraged since continued use of marijuana at 20 weeks of gestation was associated with a five-fold increased risk of SPTB in this study following adjustment for other confounders, including maternal age, BMI, SEI, and cigarette smoking. In this cohort of nulliparous women, we estimate there would be an estimated 6.2% reduction in the incidence of SPTB if women were not exposed to marijuana during pregnancy.

Source: Mark, K., Desai, A.N., & Terplan, M. (2015). Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes. *Archives of Women's Mental Health, 19*, 105-111. https://doi.org/10.1`007/s00737-015-0529-9

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: This study examines the prevalence, behaviors, and birth outcomes associated with marijuana use in pregnancy. **Sample/Setting:** This was a retrospective cohort from a university-based prenatal care clinic from July 1, 2009 to June 30, 2010. The primary exposure was marijuana use, defined by self-report or urine toxicology. **Level of evidence:** III **Quality of evidence:** good	A chart review of all patients presenting for prenatal care at a single, urban, university-affiliated clinic from July 1, 2009 to June 30, 2010 was performed. Intake data were retrieved from the prenatal chart which included a complete social work evaluation. Prenatal care visits, labor and delivery triage visits, and postpartum visits were obtained from billing records. Birth outcome data were retrieved from hospital records, delivery summaries, and postpartum follow-up.	Marijuana use was not related to incidence of low birth weight (13.8 % vs 14.0 %, p= 1.00), preterm delivery (17.7 % vs 12.0 %, p=0.325), or NICU admissions (25.5 % vs 15.8 %, p=0.139). Prenatal care utilization was equal between marijuana users and non-users. **Conclusion:** Data demonstrates that marijuana use in early pregnancy is common, as is cessation of use by delivery. Marijuana use is associated with use of other substances, most notably tobacco. The impact of marijuana on birth outcomes was limited.	**Strengths:** There were several differences in demographics, behaviors, and psychosocial characteristics in the cohort who used marijuana as compared with those who did not. Most significant was the correlation between tobacco use and marijuana use. **Limitations:** This is a retrospective cohort that relies partially on provider documentation of screening. There may have also been selection bias as not all patients were consistently screened with urine toxicology. Additionally, the frequency of marijuana use was not elicited, nor was detailed information about a quit date obtained. These facts limit our ability to determine

			any type of dose-dependent relationship with birth outcomes.
Author Recommendations: As the rates of marijuana use in pregnancy are increasing, larger prospective trials on the impact of varying levels of marijuana use on birth outcomes and long-term development are warranted.			
Summary for current clinical practice question: More large studies need to be investigated.			

Source: Martin, C., Longinaker, N., Mark, K., Chisolm, M., Terplan, M. (2015). Recent trends in treatment admissions for marijuana use during pregnancy. *Journal of Addiction Medicine, 9*(2), 99-104. https://doi.org/10.1097/adm.0000000000000095

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: The objective of this study was to investigate recent trends in marijuana use during pregnancy in the United States.	Data was obtained from the Treatment Episodes Data Set from 1992-2012 and analyzed for trends over time using X, Cochran-Armitage, and Moran's I tests.	The proportion of treatment admissions for women who were pregnant remained stable at 4%; however, admissions of pregnant women reporting any marijuana use increased substantially from 29% to 43% (P < 0.01). The West North Central census division (20%) experienced the greatest increase followed by the Middle Atlantic (18%) and Pacific (14%) divisions. The demographic characteristics of regnant marijuana admissions changed over time, with white non-Hispanic women, criminal justice referrals, and those with a psychiatric comorbidity becoming more common whereas polysubstance users decreased (P < 0.01).	**Strengths:** The matched cohort was balanced across covariates, including maternal age, socioeconomic status, tobacco smoking, and other correlates of cannabis exposure. A large, population-based pregnancy cohort, a significant association was observed between reported prenatal cannabis use and preterm birth.
Sample/Setting: The data set is estimated to include 83 % of all eligible drug or alcohol treatment admissions in the United States			
Level of evidence: III **Quality of evidence:** Good		**Conclusion:** Even though more women using marijuana are seeking and receiving substance abuse treatment during pregnancy, targeting certain risk groups while improving screening and treatment referral systems by health care providers, such as prenatal caregivers, should be emphasized.	**Limitations:** Findings may be limited by residual confounding. In BORN and other administrative data, there is likely misclassification of cannabis exposure in pregnancy. The sources may be

			influenced by social stigma, desirability bias, and fear of intervention by CPS

Author Recommendations:
Prenatal care and substance use programs need to better tailor their interventions to the changing demographics to better meet the needs of substance using mothers.

Summary for current clinical practice question:
Interventions should focus on screening and treatment referral by health care providers as we are in the preferred position to provide the access and address barriers to care.

Source:
Metz, T., Allshouse, A., Hogue, C., Goldenberg, R., Dudley, D., Varner, M., Conway, D., Saade, G., Silver, R. (2017). Maternal marijuana use, adverse pregnancy outcomes, and neonatal morbidity. *American Journal of Obstetrics & Gynecology*, *217*(4), 478.e1-478.e8. https://doi.org/10.1016/j.ajog.2017.05.050

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: To examine if maternal marijuana use is associated with increased odds of adverse pregnancy outcomes and neonatal morbidity among live-born controls. **Sample/Setting:** 663 still births and 1932 live births. The SCRN study encompassed a Data Coordinating and Analysis Center (DCAC), Research Triangle Park (RTI), International, North Carolina, and five clinical sites: Brown University, Rhode Island; Emory University, Georgia; University of Texas Medical Branch at	Case controlled study. In the SB group, there were 707 fetuses. Of these cases, 654 (98.6%) had placental examination. Of these LB controls, 1804 (93.4%) had placental examination. The SCRN study encompassed a Data Coordinating and Analysis Center (DCAC), Research Triangle Park (RTI) International, North Carolina, and five clinical sites: Brown University, Rhode Island; Emory University, Georgia; University of Texas Medical Branch at Galveston, Texas; University of Texas Health Sciences Center at San Sciences Center, Utah. Maternal marijuana uses as measured by self-report and/or the presence of 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid (THC-COOH) in umbilical cord homogenate. abstraction by the research team.	Maternal marijuana use was not associated with a composite adverse pregnancy outcome of SGA, SPTB, and HTN independent of tobacco use, but was associated with neonatal morbidity. **Conclusion:** Maternal marijuana use was 2.7 %, tobacco use was 12.9%. Adverse pregnancy outcomes were greater in this group, though not significantly reportable.	**Strengths:** The use of biological sampling from umbilical cord homogenate to objectively assess maternal marijuana use. There was vigorous data collection by trained people, population-based sampling resulting in a racially, ethnically, and geographically diverse population; large sample size. **Limitations:** Infrequency of marijuana use in this cohort, and the lack of available data regarding individual use patterns. There was poor agreement between self-reported marijuana use and objective documentation, limiting the value of self-reported data. There is no long-term follow-up data on

Galveston, Texas; University of Texas Health Sciences Center, Utah. **Level of evidence:** III **Quality of evidence:** High; Multivariable logistic regression models. Large sample study and dependable results.			the neonates to assess for childhood outcomes.

Author Recommendations:
Further studies are needed to determine whether the use of marijuana in pregnancy causes adverse perinatal outcomes.

Summary for current clinical practice question:
Providers need to be able to educate women about the anticipated effects of maternal marijuana use in pregnancy.

Source:
Oh, S., Salas-Wright, C., Vaughn, M., & DiNitto, D. (2017). Marijuana use during pregnancy: a comparison of trends and correlates among married and unmarried pregnant women. *Drug and Alcohol Dependence, 181*, 229-233. https://doi.org/10.1016/j.drugalcdep.2017.09.036

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: To examine trends and links of prenatal marijuana use and the effects of marijuana-specific risk/protective influences on marijuana use trends.	Data resulting from the National survey on Drug Use and Health from 2005-2014. The significance of marijuana use was tested using logistic regression analysis while adjusting for complex sampling design effects and controlling for sociodemographic and marijuana-specific factors.	During the data time 2005-2014, unmarried pregnant women's incidence of marijuana increased by 85%, whereas married pregnant women's marijuana use remained steady.	**Strengths:** Large sample size from a well-established national survey. Consistent results with other known studies.
Sample/Setting: Data was from the National Survey on drug use. Include were 3640 married women and 3987 unmarried pregnant women in the United States.	7627 female respondents aged 18-44 were included in the final analytical sample.	**Conclusion:** Increase the understanding of marijuana use in pregnant women. Preventative efforts should be made with unmarried pregnant women with education of potential harmful effects of marijuana smoking to maternal and child health.	**Limitations:** Unable to draw casual conclusions regarding the links between marijuana use and protective factors or mental health links. Second, data was self-reported therefore it could be over or under reported. Small number of married women who reported marijuana use may limit the ability to find significant relationships.
Level of evidence: III **Quality of evidence:**			

High Quality			
Author Recommendations: Increased attention should be paid to reducing prenatal marijuana use among unmarried women. Findings also suggest the need to attend to unmarried pregnant women's mental health problems as well as their physical health-risk behaviors.			
Summary for current clinical practice question: Education of all pregnant women, but especially unmarried pregnant women on the potential of adverse effects of marijuana use on maternal and child health.			

Source: Roberson, E., Patrick, W., & Hurwitz, E. (2014). Marijuana use and maternal experiences of severe nausea during pregnancy in Hawai'i. *Hawai'i Journal of Medicine & Public Health: A Journal of Asia Pacific Medicine & Public Health, 73*(9), 283-7.

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: To determine the prevalence of marijuana use, during and immediately before pregnancy in Hawaii and describe differences in marijuana use during and immediately before pregnancy in Hawaii.

Sample/Setting: Data from 4,735 respondents were used to estimate prevalence of self-reported marijuana use during and in the month before pregnancy, as well as severe nausea during pregnancy | Secondary analysis. Hawaii Pregnancy Risk Assessment Monitoring System (PRAMS) data from 2009 to 2011 was conducted. Follow a standardized data collection protocol centering on self-administered mailed questionnaires with telephone follow-up for non-responders.

Women are selected for participation in the Hawaii PRAMS survey as part of a stratified sample drawn from the certificates of live births in Hawaii Participants complete the survey 3-8 months postpartum, with the majority responding 3-4 months postpartum. Maternal age, race/ethnicity, nativity, education, and parity were determined based on linked birth certificate variables included in the Hawaii PRAMS dataset. Federal Poverty Level (FPL) was based on maternal report of household annual income and number of dependents | 6.0% (95% CI: 5.2-6.8) of women reported using marijuana in the month before their most recent pregnancy, and 2.6% (95% CI: 2.2-3.2) reported using marijuana during their most recent pregnancy. Approximately 21.2% (95% CI:19.8-22.8) of women with live births in Hawaii reported severe nausea during their most recent pregnancy. Compared to those who did not report severe nausea during pregnancy, women who reported severe nausea during pregnancy were more likely to report marijuana use during pregnancy (3.7% vs 2.3%; PR=1.63, 95% CI:1.08-2.44) (Table 1). This association was statistically significant (P=.034). | **Strengths:** This data source has advantages over smaller studies in that it provides population-based estimates representing all pregnancies resulting in live births in Hawaii in a given time period.

Limitations: The data source for this study relates to the uniqueness of Hawaii itself, therefore the generalizability of research findings from studies conducted outside the state is unclear. Questions related to marijuana use did not have information on amount or frequency of use, pregnancy trimester of usage, or if the marijuana was recreational or prescribed by a physician. The survey question related to severe morning |

Level of evidence: Level VI **Quality of evidence:** High. Large population size, population-based estimates. Only studied Hawaiian pregnancies.	in the year before delivery and was calculated according to Hawaii specific threshold guidelines. Prevalence estimates, confidence intervals, and P-values were generated using SAS 9.2 (SAS Institute Inc., Cary, NC) and SAS-callable SUDAAN 10.0 (RTI International, Research Triangle Park, NC) to account for complex sampling. Chi-square tests were calculated to determine statistical significance. Maternal age, race/ethnicity, nativity, education, and parity.	**Conclusion:** The findings could indicate use of marijuana as an anti-emetic among those experiencing severe morning sickness. Marijuana use before pregnancy was also associated with an increased likelihood of severe nausea during pregnancy, although the difference was not statistically significant.	sickness during. There may also be some effects due to mode bias (mail versus telephone).

Author Recommendations:
These preliminary findings warrant further research into the subject, with special attention paid to the relatively rare, but increasingly documented cannabinoid hyperemesis syndrome (CHS).

Summary for current clinical practice question:
More research is needed to investigate the exact nature of the relationship between marijuana use and severe nausea during pregnancy.

Source: Van Gelder, M., Reefhuis, J., Caton, A., Werler, M., Druschel, C., Roeleveld, N., & The National Birth Defects Prevention Study. (2009). Maternal Periconceptional Illicit Drug Use and the Risk of Congential Malformations. *Epidemiology, 20*(1), 60-66. Retrieved from www.jstor.org/stable/25662671			
Purpose/Sample	**Design (Method/Instruments)**	**Results**	**Strengths/Limitations**
Purpose: To determine if there are true associations between illicit drug use and congenital malformations.

Sample/Setting: Data was analyzed from the National Birth Defects Prevention Study, a case-control study of major birth defects, and assessed all birth defects categories in which there were at least 250 interviewed case mothers.

Level of evidence:

III

Quality of evidence: Good | This study used multivariable logistic regression to estimate the associations between cannabis, cocaine, and stimulant use in the month before pregnancy or during the first trimester (periconceptional period) and the occurrence of selected birth defects. | In the periconceptional period, 5% of the 15,208 mothers reported any use of illicit drugs. We did not find associations between illicit drug use and most of the 20 eligible categories of congenital malformations. Periconceptional cannabis use seemed to be associated with an increased risk of anencephaly (adjusted odds ratio 1.7; 95% confidence interval 0.9 –3.4), whereas cocaine use in the periconceptional period was associated with the risk of cleft palate (2.5; 1.1–5.4).

Conclusion: There were very few suggestions of positive associations between periconceptional illicit drug use and | **Strengths:** Many of the defects included have not been studied before in relation to periconceptional illicit substance use. Also, we implemented an extensive standardized interview that included detailed questions on illicit drug use and important covariates.

Limitations:

It is likely that the use of illicit drugs was underestimated in our study and other studies based on self-report. Respondents often falsely deny use because of the social stigma associated with use and fear of judgment or prosecution. Unintentional denial in the form of incomplete recall might also have been an issue in this study. |

		the 20 birth defects categories.	

Author Recommendations:
Cannabis use may be associated with an increased risk of anencephaly in offspring, and the risk of cleft palate appears to be increased for infants exposed to cocaine in the periconceptional period.

Summary for current clinical practice question:
The present findings showed very few positive associations between periconceptional illicit drug use and selected birth defects. Although the number of infants exposed to cocaine and stimulants was low, the statistical power of the data was enough to rule out 2- to 4-fold or greater increases in the risk of the selected birth defects.

Source:		
Varner, M., Silver, R., Rowland Hogue, C., Willinger, M., Parker, C., Thorsten, V., Goldenberg, R., Saade, G., Dudley, D., Coustan, D., Stoll, B., Bukowski, R., Koch, M., Conway, D., Pinar, H., & Reddy, W. for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Stillbirth Collaborative Research Network (2014). Association between stillbirth and illicit drug use and smoking during pregnancy. *Obstetrics and Gynecology*, *123*(1), 113–125. doi:10.1097/AOG.0000000000000052			

Purpose/Sample	Design (Method/Instruments)	Results	Strengths/Limitations
Purpose: To compare illicit drug and smoking use in pregnancies with and without stillbirth.

Sample/Setting: March 2006 to September 2008, covering more than 90% of deliveries to residents of five priori–defined geographically diverse regions. 663 stillbirths and 1,932 live births were included in the study

Level of evidence:

III | The Stillbirth Collaborative Research Network conducted a case–control study. Umbilical cord samples from cases and controls were collected and frozen for subsequent batch analysis. Maternal serum was collected at delivery and batch analyzed for cotinine.

For 663 stillbirth deliveries, 418 had cord homogenate and 579 had maternal cotinine assays performed. For 1,932 live birth deliveries, 1,050 had cord homogenate toxicology and 1,545 had maternal cotinine assays performed. | In this population-based study of stillbirth, there was a twofold increase in stillbirth in women with positive umbilical cord homogenate screening. The most common drug detected was tetrahydrocannabinol acid, which was significantly associated with stillbirth (OR 2.34, 95% CI 1.13–4.81).

Conclusion: Positive toxicology screen for illicit drugs was associated with a two- to threefold increase in stillbirth risk. Documentation of tetrahydrocannabinol acid indicating cannabis use | **Strengths:** The study was population-based and racially and ethnically diverse. Participants were evaluated with a thorough standardized protocol that minimized variability in data and sample collection. The study also included a maternal interview and medical record abstraction to allow for in-depth questions about smoking and drug use. Finally, in addition to self-reported substance abuse, exposure to tobacco and illicit drugs was confirmed by analyses that were blinded to the clinical outcome.

Limitations: Participants who did not have cotinine and toxicology testing differed in race or ethnicity and gestational age from |

Quality of evidence: High		increased the odds of stillbirth twofold.	those whom samples were available for testing, which may bias our findings. Second, drug use during pregnancy declines at term, which may have been another source of bias. The study also lacked a sample size to make definitive conclusions regarding the relationship between some individual drugs and stillbirth and among cannabis use, smoking, and stillbirth.

Author Recommendations:
Cannabis users often smoke as well, and more research is needed to investigate the interaction of tetrahydrocannabinol acid and cigarette smoking.

Summary for current clinical practice question:
Cannabis use may be increasing with increased legalization; clinicians should be alert to these risks and should educate women regarding dangers associated with marijuana use and active and passive smoke exposure during pregnancy.

Source: Warshak, CR., Regan, J., Moore, B., Magner, K., Kritzer, S., & Van Hook, J. (2015). Association between marijuana use and adverse obstetrical and neonatal outcomes. *Journal of Perinatology, 35*, 991-995. https://doi.org/10.1038/jp.2015.120			
Purpose/Sample	**Design (Method/Instruments)**	**Results**	**Strengths/Limitations**
Purpose: To examine the associations between marijuana use and certain adverse obstetrical and neonatal outcomes, excluding women with polysubstance use and stratifying for coexisting tobacco use

Sample/Setting: Included in this study were 6468 women, 6107 nonusers and 361 marijuana users at the University of Cincinnati Medical Center between January 2008 and January 2011. | A retrospective cohort study of all singleton deliveries born over 20 weeks. Evaluating various obstetrical and neonatal outcomes including preterm delivery, pre-eclampsia, gestational diabetes, cesarean delivery, fetal growth restriction, a composite which included stillbirth or neonatal intensive care unit admission, and perinatal mortality. Stratified study groups according to the maternal tobacco use and performed a logistic regression analysis. | The results included 6468 women, 6107 nonusers and 361 marijuana users. After adjustment for maternal age, race, parity, body mass index and no prenatal care, we found higher rates of small for gestational age and neonatal intensive care unit admission in women who were not tobacco users. Other obstetrical outcomes including preterm delivery and fetal anomalies were not increased with maternal marijuana use

Conclusion: Maternal marijuana use does not increase the risk of adverse obstetrical outcomes or fetal anomalies but does | **Strengths:** Large number of women included in the analysis and the ability to control the confounding medical and social factors, such as race, obesity and lack of adequate prenatal care. In addition, maternal exposure data were taken directly from the medical record and based upon a combination of self-report and toxicology screen results and may be more accurate as opposed to reliance on self-reporting in birth certificate records.

Limitations: Not designed to determine dose-related effects. The setting is a high-risk academic center with a large referral base, and as such the rates of exposures and outcomes may vary from other regions. Does not have enough power to draw conclusions for all the outcome variables |

Johns Hopkins Evidence Appraisal: Strength III Quality: High, large population		increase the risk for small for gestational age and neonatal intensive care unit admission.	studied, including perinatal mortality.

Author Recommendations:
Further study of the complications of marijuana exposure in pregnancy, especially as political and social changes evolve that could increase the rate of this exposure in pregnant women.

Summary for current clinical practice question:
A good understanding of the risks to marijuana use in pregnancy is needed so providers can educate women who are planning to become pregnant or who are pregnant.