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Breastfeeding and Marijuana Use

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By

Jennifer McKinnon, MSN, APRN, IBCLC

The Ohio State University

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DNP Project Team:

Dr. Cindy M. Anderson, PhD, APRN-CNP, ANEF, FAHA, FNAP, FAAN

Dr. Jacqueline Loversidge, PhD, RNC-AWHC

Dr. Jacalyn Buck, PhD, RN, NE-BC

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Dedication

This paper is dedicated to all healthcare providers who strive to excel in their specialty, always reading, searching and staying abreast of the latest evidence-based research and innovations; demanding the best of themselves and striving to deliver superior healthcare for their patients whom entrust their most precious commodity, their health, unto us. May we go forth with a questioning mind, an empathetic heart and a caring soul.

Abstract

Marijuana is the most commonly used illicit drug in the United States (National Institute on drug Abuse [NIDA], 2018). Nationwide, 6% of pregnant women report marijuana use (Crume et al., 2018) with 5% of mothers continuing their marijuana use while breastfeeding (Crume et al., 2018). Professional guidelines established by the Academy of Breastfeeding Medicine (ABM)(Reese-Stremtan & Marinelli, 2015), the American Academy of Pediatrics (AAP)(American Academy of Pediatrics [AAP], 2012 and 2018), and the American College of Obstetricians and Gynecologists (ACOG)(ACOG, 2017) all agree that breastfeeding mothers should be screened for marijuana use and counseled based on existing evidence.

In the absence of knowing the status of the breastfeeding mother's marijuana use, the opportunity to provide evidence-based counseling regarding substance use and its impact on both the mother and nursing infant's health and milk supply is missed.

The purpose of this quality improvement project was to identify the degree to which breastfeeding mothers were using marijuana and to document evidence-based counseling on effects during breastfeeding. The project was accomplished by (1) training pediatric healthcare providers in evidence-based recommendations to breastfeeding mothers regarding marijuana use and (2) establishing an electronic system to facilitate provider counseling of evidence-based recommendations.

Primary findings were that breastfeeding mothers were not routinely screened at the two week well infant visit about maternal marijuana use and evidence-based counseling was not standardized. After provider training was delivered and electronic –associated reminder and evidence-based counseling was embedded into the health record, the percentage of breastfeeding mothers being screened about marijuana use increased by approximately 50%. Additionally,

women who acknowledged marijuana use while nursing were given standard, evidence-based counseling regarding the effects of marijuana use while breastfeeding. It was concluded that provider education and ease of standardized documentation of provider counseling increased both maternal inquiry into marijuana use and provider counseling and documentation of evidence-based counseling.

Section One: Nature of the Problem

Introduction to the Problem

Marijuana is the most commonly used illicit drug in the United Sates (National Institute on Drug Abuse [NIDA], 2018). It is made from dried parts of the *cannabis sativa* or *cannabis indica* plant. Marijuana (cannabis), classified as a schedule I illegal substance, has become legalized in several states. A schedule I drug is defined as a "drug, substance or chemical with no currently accepted medical use and a high potential for abuse" (United States Drug Enforcement Administration [DEA], 2018) There are two types of marijuana use designations: medical and recreational. Medical marijuana is defined as "using the whole unprocessed marijuana plant or its basic extracts to treat a disease or symptom" (National Institute on Drug Abuse [NIDA], 2018). The primary use of cannabis in the United States is recreational (89.5 percent of adult users) (Schauer, King, Bunnell, Promoff, & McAfee, 2016). Thirty states and the District of Columbia have laws legalizing some form of marijuana use ("State marijuana laws in 2018," 2018). Ten states (Alaska, California, Colorado, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont and Washington) and the District of Columbia have legalized recreational adult-use ("State marijuana laws in 2018," 2018).

Nationwide, 6% of pregnant women report marijuana use (Crume et al., 2018) with 5% of mothers continuing their marijuana use while breastfeeding (Crume et al., 2018). In 2014, according to the Centers for Disease Control (CDC), 79.2% of U.S. mothers initiated breastfeeding. Alaska exceeded the national initiation rate at 87.3% (Center for Disease Control, 2014). Alaskan statistics mirror the national average with 6% of pregnant women reporting

marijuana use during pregnancy but an increased 8% of nursing mothers reporting marijuana use during breastfeeding (Alaska Department of Health and Human Services, 2015) .

The literature is limited and contradictory regarding recreational marijuana use during breastfeeding, making it challenging to advise breastfeeding mothers about the impact of their marijuana use on themselves and their infant. It is unlikely that new research will be generated in this field due to ethical considerations and marijuana's schedule classification, thus limiting the body of evidence needed to inform decision making in this population.

The U.S Drug Enforcement Administration (DEA) controls substances with a high rate of abuse such as marijuana. Such drugs and their potential negative effects on communities are primary reasons why the DEA controls these drugs. On the other hand, if studies are not able to be conducted on schedule I drugs, researchers will be unable to discover the potential benefits that substances like marijuana may possess. This leads to limited studies lacking necessary rigor to review related to the topic.

When counseling breastfeeding mothers about infant effects of marijuana use during breastfeeding, a key question is whether the active substance or its metabolites will transfer through maternal breastmilk and affect the nursing infant. Regarding marijuana and its active metabolite, Δ-9-tetrahydrocannabinol (THC), the length and route of exposure, quantity and type of user (occasional or chronic) all impact how much THC is present in maternal breastmilk.

Professional guidelines based on existing animal and human research have been established by the Academy of Breastfeeding Medicine (ABM)(Reece-Stremtan & Marinelli, 2015) , the American Academy of Pediatrics(AAP), (American Academy of Pediatrics [AAP] , 2012) and the American College of Obstetricians and Gynecologists (ACOG), (ACOG, 2017) as

well as the Alaska Department of Health and Human Services (DHHS) (Butler, 2017). Though their recommendations vary, all agree that breastfeeding mothers should be screened for marijuana use and counseled based on existing evidence. The gap identified between the professional recommendations and current provider practice is evident when documentation is reviewed. The recommended surveillance of breastfeeding mothers regarding their potential marijuana use and subsequent documentation of evidence-based counseling is the basis of this DNP project.

Purpose/Objective of the Quality Improvement Project

A quality improvement project seeks to improve the processes or outcomes of the care being delivered (Mazurek Melnyk & Fineout-Overholt, 2015) The purpose of this quality improvement project is to identify the degree to which breastfeeding mothers are using marijuana and to document evidence-based counseling on effects during breastfeeding. We will accomplish this by (1) training pediatric health care providers in evidence-based recommendations to breastfeeding mothers regarding marijuana use and (2) establish an electronic system to facilitate provider counseling of evidence-based recommendations regarding marijuana use to breastfeeding mothers. We anticipate the outcome to be increased identification of breastfeeding mothers who use marijuana and improved documentation of evidence-based counseling regarding the effects of marijuana on the breastfeeding dyad.

Section Two: Review of Literature

Clinical Practice Problem Statement

Among pediatric healthcare providers who counsel breastfeeding mothers (P), how does standardized evidence-based provider training regarding counseling mothers about marijuana use during breastfeeding (I) compared to no standardized training (C) affect documentation of maternal education about marijuana use during breastfeeding (O) over a six-month period (T)?

Evaluation of Literature

Few high quality recent quantitative studies on marijuana use during breastfeeding were available for review due to marijuana's schedule 1 classification. The database search was extended to all human and animal studies dating back to the 1970's in order to provide a comprehensive review of the literature. It was determined that research publication date would not be restricted due to the limited number of studies available on the subject. Search engines included PubMed, CINAHL and Cochrane Review. Terms utilized in the search included marijuana, cannabis, THC, breastfeeding, perinatal, and lactation. A total of 272 articles were reviewed. Articles were excluded for lack of significant focus on the subject, information that overlapped with primary studies and duplicate articles. A total of 41were included in the critical analysis evaluation synthesis. These included, 5 randomized control studies, 3 experimental studies, 3 systematic reviews, 9 quasi-experimental studies, 3 non-experimental studies, 1 protocol statement, 3 policy statements, 1 expert opinion, 2 cross sectional studies, 1 qualitative study and 10 literature reviews. Articles were categorized into four main areas of focus. These were THC pharmacokinetics, marijuana effects on infants, maternal marijuana effects and professional guidelines/opinions. All articles were critically reviewed using critical appraisal

principles as described by Melnyk & Fineout-Overholt (2017, p. 87-135). Comprehensive evaluation and synthesis tables of all literature reviewed are found in Tables 1 and 2.

Overview of Literature

Tetrahydrocannabinol Pharmacokinetics

Existing research on marijuana focuses on THC, the principle psychoactive component. THC accumulation is dependent on the user's frequency of exposure (U S National Library of Medicine, 2018). THC is metabolized in the liver and has a half-life of 20-36 hours but may be as long as four days in chronic users because of its ability to be stored in body fat (Bennett, 1996). THC accumulates in fat at a rate ten times greater than any other tissue and can persist for up to two weeks (Kreuz & Axelrod, 1973), contributing to the THC long half- life. Half -life is defined as the amount of time it takes one half of a drug's dose to be excreted from the body. A recent study by Bertrand et al. (2018) found that delta-9-THC was measurable in breastmilk an average of 6 days after maternal marijuana use. The urinary half-life of THC's metabolite (THCCOOH) was calculated at 4 to 12 days for infrequent users and 17 to 27 days for frequent users (Smith-Kielland, Skuterud, & Morland, 1999). The route of THC exposure also affects when THC peaks in one's blood. Smoking marijuana causes a peak serum concentration of THC in one to two hours whereas oral consumption yields peak levels in two to four hours (Hollister et al., 1981).

Focusing on THC secretion into breastmilk, frequency of use remains a factor. Animal secretion rates into breastmilk were slower in chronic users than with occasional users (Chao et al., 1976). Human studies by Perez-Reyes & Wall (1982) found that there was an 8-fold increase in THC accumulation in breastmilk with increased frequency of use (Perez-Reyes & Wall, 1982). They calculated that 0.8% of the weight-adjusted maternal intake of one marijuana

cigarette would be transferred to the infant in one nursing (0.8% of its mother's dose/kg). This ratio was also found to be valid in another human study by Liston (1998).

THC transfer into mammal milk has been consistently documented in several human studies and is generally tested by liquid chromatography tandem mass spectrometry (Marchei et al., 2011). D'apolito (2013) outlined the factors that affected drug transfer into breastmilk. Three key areas are molecular weight, acid/base balance or pKa and lipid solubility. The lower the molecular weight of a drug, the more readily it transfers into breastmilk. Drugs that are more basic become highly ionized and will become trapped in breast milk and are found in higher concentrations in breastmilk than maternal plasma. When a drug is lipid soluble, if plasma concentrations of the drug are low, the drug becomes trapped in the fat molecule (Hale & Rowe, 2017, p. el164-172). Marijuana has a relatively low molecular weight of 314.46 g/mol, is more basic with a pKa (acid-base dissociation constant) of 10.6 and is lipid soluble (D'apolito, 2013). One additional breastmilk factor that affects drug transfer is the composition of foremilk and hindmilk. Foremilk (milk produced in the first 3 minutes of feeding or pumping) has less fat than hindmilk (the remainder of milk produced during a feeding or pumping session). Understanding that marijuana is fat soluble, increased amounts can be found in hindmilk (Gardiner, 2001). This is significant when looking at the feeding pattern of the infant and how long they are at the breast (D'apolito, 2013).

Effects of Marijuana Exposure on Infants

When one looks at specific effects of cannabis on offspring, several issues may confound findings. In human studies, it is often difficult to separate prenatal and postnatal exposures as well as environmental factors on infant outcomes from maternal marijuana use. Incorporating animal studies allows for better prenatal control but does not consider environmental factors

(Campolongo, Trezza, Ratano, Palmery, & Cuomo, 2011). Additionally, different animal species may metabolize marijuana differently possibly rendering animal studies nontransferable to human subjects. With these two key points in mind, the literature was reviewed for infant effects of maternal marijuana use focusing on marijuana exposure during lactation though several studies also reported prenatal exposure.

The endocannabinoid system is critical in neurotransmission and is the primary target of THC (Jutras-Aswad, DiNieri, Harkany, & Hurd, 2009). This system and its cannabinoid receptors are functional around nineteen weeks gestation in humans (Campolongo et al., 2011). This illustrates why prenatal cannabis exposure may be a factor when looking at infant effects but is difficult to control in human studies.

Perinatal (pre and post-natal) exposure to cannabis was associated with long term behavioral and neuroendocrine changes in adult rats (Moreno, Escuredo, Munoz, Rodriguez de Fonseca, & Navarro, 2005; Trezza et al., 2008). Newsom and Kelly (2008) also found that perinatal THC exposure in male rats makes them more susceptible to anxious behavior and altered social functioning (Newsom & Kelly, 2008).

Human studies on perinatal cannabis exposure during lactation are contradictory. Tennes et al. (1985) focused on the perinatal spectrum and concluded that there were no significant differences in growth and development of infants at one year of age and that marijuana use did not interfere with lactation (Tennes et al., 1985). A landmark study by Astley & Little (1990) concluded that infants who were exposed to THC in their first and third month of life experienced motor development delays at one year of age but could not postulate any long-term infant effects due to the short study duration (Astley & Little, 1990). The authors also reported no detectable mental developmental delays at one year of age.

THC exposure via maternal breastmilk may cause sedation, poor growth, reduced muscle tone and poor suckling in infants (Liston, 1998). Infants have also shown lethargy, less frequent feeding and shorter feeding times after THC exposure (Institute of Medicine, 1991). To summarize, prenatal use of THC targets the endocannabinoid system which is present at 19 weeks gestation. It may cause behavioral and endocrine changes exhibited by offspring such as anxiety and altered social functioning. It may cause motor delays at 1 and 3 months of life but these changes do not seem to be sustained at one year of age. THC exposure may also cause infant sedation and lethargy, poor growth, reduced muscular tone, and overall decreased feeding initiation and duration.

Maternal Effects of Marijuana

The secretion of milk by the mammary glands (lactogenesis) is triggered by the abrupt drop in the hormones progesterone and estrogen after birth. This causes the anterior pituitary gland to release large amounts of prolactin (D'apolito, 2013), prompting milk production. Oxytocin is also produced by the posterior pituitary in response to infant suckling (Tyrey & Murphy, 1988), contributing to milk ejection. Both prolactin and oxytocin secretion are affected by THC. Four animal studies have demonstrated that rats exposed to THC in maternal milk decreased both oxytocin and prolactin release in the mother (Tyrey & Murphy, 1988; (Vilela & Giusti-Paiva, 2014; Bromley, Rabii, Gordon, & Zimmerman, 1978; Asch, Smith, Siler-Khodr, & Pauerstein, 1979). Three studies on humans have also demonstrated that THC suppresses prolactin levels in nursing mothers (Murphy, Munoz, Adrian, & Villanua, 1998; Mendelson, Ellingboe, & Mello, 1984; Ranganathan et al., 2009).

THC has also been shown to affect mothers' care of their infants. Three rodent studies demonstrated that THC exposed mothers decreased their licking, retrieval and carrying of their

pups (Vilela & Giusti-Paiva, 2014) along with an overall decrease in maternal care of pups (Bromley et al., 1978) and decreased maternal nonsocial activities (Frischknecht, Sieber, & Waser, 1980). One additional study involving rhesus monkeys also demonstrated maternal depression and lethargy during nursing after THC exposure (Asch & Smith, 1986). Additionally, cannabis use with humans was shown to decrease breastfeeding initiation (Crume et al, 2018) as well as shorten breastfeeding duration (Ko, Farr, Tong, Creanga, & Callaghan, 2015).

Recommendations for Marijuana Use While Breastfeeding

The recent increase in marijuana use and legalization in the US has prompted several literature reviews on the subject. Seven reviews were analyzed with publication dates from 2009 through 2018. Authors encouraged providers to counsel mothers to avoid marijuana use while breastfeeding but failed to provide guidance regarding its use (Merritt, Wilkinson, & Chervenak, 2016). Two reviews stated that breastfeeding is contraindicated with marijuana use (Garry et al., 2009;Metz & Stickrath, 2015). Findings from the 4 remaining literature reviews reflect a cautious stance but recommended counseling breastfeeding mothers who use marijuana (Hill & Reed, 2013; Jaques et al., 2014; Mourh & Rowe, 2017; Brown, Dakkak, & Seabrook, 2018). Authors from all reviews identify the lack of rigorous human studies and confounding evidence as reasons for their lack of ability to make well-informed recommendations regarding marijuana use in lactation. Mourh & Rowe (2017 p. 594) state that the “final decision is ultimately up the individual woman”.

The AAP (2012) issued a policy statement on breastfeeding and the use of human milk. It extols the benefits of breastfeeding to reduce respiratory tract infections as well as decreasing the incidence of otitis media, gastrointestinal infections, necrotizing enterocolitis, sudden infant death syndrome and allergies. It also credits breastfeeding with reducing the incidence of celiac

disease, inflammatory bowel disease, obesity, diabetes, childhood leukemia and lymphoma and improving intelligence scores. The AAP also supports feeding preterm infants breastmilk and lists the health benefits for the mother (decreased postpartum blood loss, increased child spacing, decreased postpartum depression and weight loss). Economic benefits of breastfeeding were highlighted and exclusive breastfeeding for the first six months of the infant's life with continued breastfeeding for at least one year was recommended. The AAP states that there are a limited number of conditions where breastfeeding is contraindicated. These are infant glactosemia, mothers who are positive for human T-cell lymphtropic virus type I or II, untreated brucellosis, untreated tuberculosis or active herpes simplex lesions on the breast (though expressed breastmilk in this instance is recommended). Regarding HIV-positive mothers, if they are in the industrialized world, breastfeeding is not recommended but in developing countries, infant mortality is decreased if breastfeeding continues. Regarding "street drugs such as PCP, cocaine and cannabis", the AAP (2012) states concern regarding the infant's long-term neurobehavioral development and the stance that breastfeeding is contraindicated. The AAP cites the review article by Garry et al. (2009) specifically as the sole source for this recommendation. In an updated publication published in September of 2018, the AAP softened its stance, citing that present data is insufficient to assess the effects of marijuana exposure on breastfeeding infants and recommended that providers encourage mothers to breastfeed while "strongly encouraging that she abstain completely from using marijuana" while breastfeeding (AAP, 2018). Finally, the AAP strongly discourages the use of alcohol and maternal smoking while breastfeeding (AAP, 2012) and specifically addressed passive marijuana smoke exposure in its 2018 update (AAP, 2018).

In contrast, the ABM stated in its clinical protocol regarding breastfeeding and substance use that “breastfeeding mothers should be counseled to reduce or eliminate their use of marijuana” and “advised of the possible long-term neurobehavioral effects” (Reece-Stremtan & Marinelli, 2015 p. 138) . The ABM advised caution basing recommendations solely on the legality of marijuana due to changing laws regarding marijuana use. They also cite 7 animal and human studies, all of which have been reviewed for this project, prior to issuing their cautionary use of marijuana while breastfeeding. The ABM specifically states that current studies are insufficient to recommend complete abstention from breastfeeding but urge caution while breastfeeding while using marijuana (Reece-Stremtan & Marinelli, 2015).

The ACOG (2017) published a committee opinion that stated “insufficient evidence to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged” (ACOG, 2017 p. e205). Specifically, the committee’s opinion on marijuana use during lactation cites the ABM article by Reece-Stremtan and Marinelli (2015).

In Alaska, the Department of Health and Human Services (DHHS) published a memorandum addressed to all healthcare providers citing the AAP, ABM and ACOG published guidelines and recommended to “continue to breastfeed while making every effort to reduce the amount of marijuana consumed, whether smoked, vaped or eaten” (Butler, 2017). The memorandum further recommended stopping marijuana use during pregnancy, protecting children from second-hand marijuana smoke as well as safely storing marijuana and edibles away from children. It also advised against driving a car with child passengers while under the influence of marijuana and to have a sober, unimpaired child care provider take care of children when a parent is impaired by any substance, including marijuana (Butler, 2017). Therefore, the

consensus is to continue breastfeeding while mothers make a concerted effort to reduce their marijuana intake while nursing.

Critical Appraisal of the Evidence

The most popular illicit drug in the United States is marijuana. Given its popularity and increasing legalization rates in the US, it is not unusual that healthcare providers are experiencing an increased prevalence of use among their patients. One unique population of healthcare consumer is the breastfeeding dyad. Healthcare providers caring for breastfeeding dyads have two patients to consider when counseling mothers, both mother and nursing infant. The research regarding marijuana use and its effects on the dyad is limited. In order to cast the widest net for review, animal studies were included when generating evidence-based recommendations. Limitations with the inclusion of animal studies stem from the difference in species and translation to human effects.

To summarize, THC, the active metabolite in marijuana, transfers from maternal blood into breastmilk of mammals and can be measured in the breastfeeding infant (Asch &Smith, 1986; Chao, Green, Forrest et al, 1976; Metz & Stickrath, 2015; Perez-Reyes & Wall, 1982). Amount of THC consumed, method of ingestion and chronicity of use all are contributing factors when evaluating how much THC the infant is ingesting. Here is where the consensus ends. Infant and maternal effects of THC are frequently contradictory. Infant effects from THC exposure can include decreased neuromotor development (Astley & Little, 1990; Metz & Stickrath, 2015; Moreno et al, 2005; Trezza et al, 2008) behavioral changes (Moreno et al, 2005; Newsom & Kelly, 2008) decreased growth and muscle tone and impaired social functioning. Maternally, THC has been shown to decrease secretion of oxytocin and prolactin (Asch &Smith, 1979; Mendelson, Ellingboe & Mello, 1984; Ranganatham et al, 2009; Tyrey & Murphy, 1988);

decrease breastfeeding initiation and duration (Crume, Julh, Brooks-Russell, Hall, Wymore & Borgelt, 2018), cause maternal depression (Ko, Tong, Bombard, Hayes, Davy & Perham-Hester, 2018) and negatively affect maternal care of infants (Bromley, Rabii, Gordan & Zimmerman, 1978; Frischknecht, Sieber, & Waser, 1980; Vilela & Giusti-Paiva, 2014). All of these facts, proven in one human or animal study, have also been challenged by other researchers (Tennes et al, 1985). Even the three reviewed professional organizations, the AAP, ABM, and ACOG, differ in their published recommendations regarding counseling of breastfeeding mothers who use marijuana. The one fact that these organizations agree upon is that these mothers should be counseled regarding marijuana use while breastfeeding (AAP, 2012 & 2018; ACOG, 2017; Reece-Stremtan & Marinelli, 2015).

Gaps in Evidence

Marijuana's schedule I drug classification severely curtails the amount of studies being conducted on its use and effects, thus creating a paucity of high quality primary human research to critically appraise. With the inclusion of animal studies regarding marijuana's effect on lactating animals and their offspring, the evidence is still limited. This gap in the evidence must be acknowledged but is not likely to be bridged until the US changes marijuana's schedule I status. Even with a schedule change, there are other ethical considerations to consider. True experimental design calls for exposure of some participants to the independent variable, in this case, marijuana. It would be unethical to expose breastfeeding infants to a potentially harmful substance. These types of ethical dilemmas are the very things an institutional review board seeks to prevent. According to the FDA, an institutional review board [IRB] is tasked with monitoring research involving human subjects and seeks to protect the rights and welfare of the

subjects (U.S. Food and Drug Administration, 2018), limiting the generation of evidence needed for recommendations.

Professional consensus states that the breastfeeding mother should be counseled regarding the effects of her marijuana use while breastfeeding. This consensus provides the basis of this DNP project. The quality of care of breastfeeding mothers is impacted when this critical discussion does not occur or when critically appraised research is not included in provider recommendations. In order to address this quality gap, a critical review of the literature was completed as the basis for evidence-based healthcare provider training and implementation of counseling of breastfeeding mothers. The measure for this QI project will be the documentation that breastfeeding mothers are receiving this evidence-based counseling regarding marijuana use during breastfeeding.

Conceptual Framework

The conceptual framework for this DNP project will be Carver & Scheier's (Carver & Scheier, 1982) control theory. The key tenets of control theory postulate that a discrepancy between current practice and a standard motivates one to change their behavior to achieve the standard (Mazurek Melnyk & Fineout-Overholt, 2015, p 290). The current recommendations for nursing mothers who use marijuana is to counsel them regarding the potential effects of THC on their infant and discourage marijuana use while breastfeeding or discontinue breastfeeding. Communicating how current practice deviates from the standard should motivate providers to change practice regarding their counseling and documentation of breastfeeding mothers who use marijuana. Currently, not providing evidence-based counseling is not the standard for the selected private practice clinic in Alaska.

When applying control theory to EBP, Mazurek Melnyk and Fineout-Overholt contend that there are several barriers to successful implementation (Mazurek Melnyk & Fineout-Overholt, 2017 p. 290). Lack of knowledge and skills regarding EBP and its ability to change practice, lack of an EBP mentor, perceived inability to change practice and a lack of administrative support and possibly outright management resistance to EBP may hinder the successfull implementation of the project. Upper management buy-in will be crucial to the successful implementation of the project. Knowledge of these potential barriers will be key when undertaking this project to avoid any pitfalls to implementation and be cognizant of individuals or organizational roadblocks that would derail the project.

Utility/Feasibility

This QI project is beneficial to outpatient pediatric practices for several reasons. It is cost efficient, requiring adaptation of but no additional EHR purchases for those with existing systems. Project implemented in a state where recreational marijuana has recently become legal underscores the need for counseling based on prevalence of marijuana use during breastfeeding. As with any new practice change, ease of implementation and accepting the importance of the practice change is imperative to successful implementation and sustainability.

Key stakeholders for this type of project in an ambulatory care setting include the office manager, IT staff, administrators/decision makers in the practice and all care providers. Engagement of these key individuals is essential in planning, implementation and evaluation of the QI project. Potential barriers include lack of provider buy in and perceived lack of time during patient interactions. These barriers should be mitigated in order for the project to be successfully implemented. Engagement of stakeholders will begin during the initial planning

phase and individuals will be periodically updated throughout the project to assure continued involvement and support.

Recommendations Summary

After critical appraisal of the evidence and professional guidelines, there is consensus that all nursing mothers who use marijuana should be counseled on the potential effects of marijuana on their infant (Reece-Stremtan & Marinelli, 2015; AAP, 2012; ACOG, 2017; Butler, 2017). There remains a lack of robust evidence to guide recommendations for counseling regarding marijuana use in breastfeeding mothers, limiting provider confidence and ability to make evidence-based recommendations. Professional guidelines have not led to a definitive consensus but recommended that while the benefits of breastfeeding are significant, marijuana use should be limited or discontinued during breastfeeding based on the potential risks to the infant as a result of exposure to marijuana transferred to breastmilk and ingested by the infant.

Section Three: Methods

Assess the Need for Change in Practice

The purpose of this quality improvement project is to identify the degree to which breastfeeding mothers are using marijuana and to document evidence-based counseling on effects during breastfeeding. We will accomplish this by (1) training pediatric health care providers in evidence-based recommendations to breastfeeding mothers regarding marijuana use and (2) establish an electronic system to facilitate provider counseling of evidence-based recommendations regarding marijuana use to breastfeeding mothers. We anticipate the outcome to be increased identification of breastfeeding mothers who use marijuana and improved

documentation of evidence-based counseling regarding the effects of marijuana on the breastfeeding dyad. The project was designed to develop an evidence-based provider training on marijuana use while breastfeeding, to promote provider inquiry regarding maternal marijuana use during breastfeeding and to improve provider documentation of evidence-based maternal counseling regarding marijuana use during lactation.. The protocol for the project was approved for expedited review by The Ohio State University Biomedical Sciences Institutional Review Board.

The *Model for Evidence-Based Practice Change* was utilized as the framework for the DNP project (Rosswurm & Larrabee, 1999). The model begins with assessment of the organizational culture and need for change. This assessment should include the stakeholders and governing body of the organization. To initiate and sustain a clinical practice change, the entire organization must be ready for transformation. Assessment of the practice's readiness for change was accomplished by presenting the project plan to the provider partner/owners of the practice. All six owners are pediatricians who currently practice in the clinic. The outpatient private practice site selected for the DNP quality improvement project was located in a large city in Alaska, one of the 30 states that has legalized recreational use of marijuana. The selected practice is a leader in EHR documentation and currently is an innovative research site for the fourth largest EHR system in the country. The practice desires to be a leader at the state and national level regarding EHR documentation and strives to customize their current system and provide streamlined yet thorough documentation of patient visits, motivating their participation in this project. The clinic has developed its own customized EHR templates and actively works to update the templates based on provider feedback. The IT team was engaged and prepared to support the requirements of this project. The practice mission statement states that providers

strive to be informative while offering patient choice, consistent with evidence-based practice tenets. The project aligned with the practices' vision and mission statements and should benefit all participants.

Interventions and Outcomes

The problem of inconsistent provision of evidence-based counseling regarding marijuana use in breastfeeding mothers was based upon a paucity of current, rigorous evidence to guide recommendations, limiting implementation of recommended counseling in practice. Linking this problem to suitable interventions and outcomes is the second step of the model. The intervention selected to address the lack of evidence-based counseling was to conduct provider training to share current evidence and align approaches to counseling practices. This integrated with the third step which was locating the evidence and searching for clinical guidelines to steer the project. After review of the literature and professional guidelines, there was consensus that all breastfeeding mothers should be counseled regarding marijuana use while breastfeeding (Reece-Stremtan & Marinelli, 2015; AAP, 2012 & 2018; ACOG, 2017; Butler, 2017).

Challenges in the provision of provider counseling of breastfeeding women who use marijuana included the need to document inquiry into marijuana use and awareness of evidence-based counseling for consistent and current recommendations for maternal and infant effects. Review of the literature generated the evidence for consistent and current approaches to maternal counseling. The evidence lacked consistency in findings regarding maternal and infant effects of maternal marijuana use. Maternal effects include suppression of prolactin and oxytocin (Asch et al., 1979; Bromley et al., 1978; Mendelson et al., 1984; Murphy et al., 1998; Ranganathan et al., 2009; Tyrey, 1988; Vilela & Giusti-Paiva, 2014), and decreased breastfeeding initiation (Crume et al, 2018) and shorter breastfeeding duration (Ko et al. Farr, 2015). Additionally, animal

studies show decrease maternal care (Asch & Smith, 1986; Bromley et al, 1978; Frischknecht et al.; Sieber &Waser, 1980 and Vilela & Giusti-Paiva, 2014). The potential effects on infants, based on study findings, are variable based upon frequency, source and route and amount of maternal marijuana use. Sedation, poor growth, reduced muscle tone and poor suckling (Liston, 1998), lethargy, less frequent and shorter feeding (IOM, 1991), behavioral and neuroendocrine changes (Moreno et al, 2005; and Trezza et al, 2008) as well as anxious behavior and altered social functioning (Newsom & Kelly, 2008) were observed. Contradictory findings regarding mental and motor delays in infants at one year of age were also noted (Astley & Little, 1990 and Tennes et al, 1985).

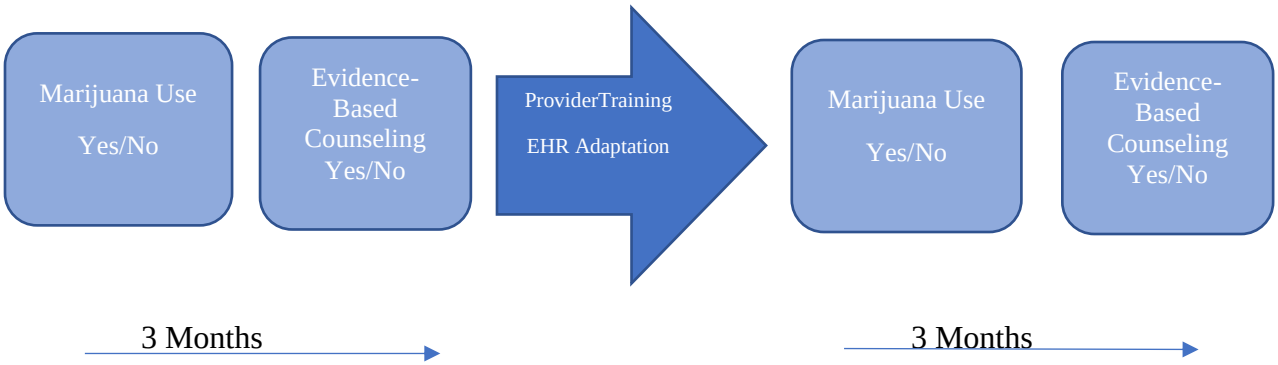
In order to share findings for evidence-based counseling of breastfeeding women who use marijuana, it was determined by consultation with practice stakeholders that the most effective way to disseminate findings and implement an office wide practice change was to conduct a provider training for all provider staff. The training was designed to promote provider inquiry regarding maternal marijuana use during breastfeeding and to improve provider documentation of evidence-based maternal counseling regarding marijuana use during lactation. To facilitate consistent documentation of inquiry into marijuana use among breastfeeding women, a modification to the EHR system was implemented to prompt providers to ask breastfeeding mothers about their marijuana use. When marijuana use during breastfeeding was confirmed, standardized patient education handouts with evidence-based recommendations were generated. Together, this intervention served to ease provider documentation while assuring the provision of evidence-based patient handouts. After provider training, the outcome of the QI project was analyzed by pre- and post-training chart evaluation of (1) frequency of documentation of inquiry

regarding marijuana use during breastfeeding and (2) provision of evidence-based education for a period of 3 months each, respectively.

Design Practice Change

Design of the practice change is the fourth step in the model. The goal of the practice change was to promote documentation of counseling of marijuana use in breastfeeding women. The timeline was as follows:

Figure 1. Project Timeline Graphic



A provider training session (Appendix A) was developed and delivered by the DNP student based upon review of the evidence. The primary focus of the training was to concisely review current research and recommendations and formulate an evidence-based response to guide providers when discussing marijuana use with breastfeeding mothers . The presentation began with an overview of the prevalence of marijuana use nationwide, highlighting high risk women and use among pregnant and postpartum mothers (ACOG, 2015; Crume et al., 2018; Gilchrist et al., 1996; NIDA, 2018; USDEA, 2018; Schauer et al., 2016 and “State marijuana laws in 2018”, 2018). The pharmacology of marijuana was reviewed and included half- life, routes of administration and THC concentration (Campolongo et al., 2001; Djulus et al., 2005; ElSohly et al., 2010; Fride, 2001; Hollister et al., 1981; Justas et al., 2009; Murphy et al., 1998;

Owens et al., 1981, and Smith et al., 1999). Time was spent reviewing the properties of marijuana that make it pass readily into breastmilk (Hale & Rowe, 2017 and Kruez & Axelrod, 1973) and reviewed concentrations of THC in fore and hindmilk (Gardiner, 2001). There was a summary of the literature presenting the studied effects of marijuana exposure on infants and mothers. Recommendations from professional organizations (ACOG, AAP, ABM and DHSS) were outlined as well as areas of consensus and deviation (ACOG, 2017; AAP 2012 & 2018; Butler, 2017; and Reece-Stremtan & Marinelli, 2015). A brief summary of maternal marijuana use during lactation was distributed to the providers for future reference.

Focus was then turned to EHR documentation of standardized counseling provided to mothers who acknowledged marijuana use while breastfeeding. Maternal choice/preference was also incorporated as a tenet of counseling. Ultimately, it would be the mother who decided her course of action based on the evidence and guidelines provided. Incorporating the patient's wishes reflected patient centered care, a standard in today's healthcare world. Linking patient centeredness and evidence-based healthcare required the patient to be informed about potential outcomes while allowing the provider to fully appreciate patient preferences (Sambare, Uhler, & Bozic, 2017).

The in-person provider training was conducted for all physician and nurse practitioner providers by the DNP student to provide current evidence-based counseling approaches and patient-centered education. The DNP student also worked closely with the office manager/IT manager to initiate an electronic mechanism for documentation of evidence-based counseling in breastfeeding women (Appendix B).

The effectiveness of the practice change was determined by a comparison of documentation before and after provider training. Data collection was based on documentation at

the 2 week well child visits as this is a critical opportunity for breastfeeding dyad counseling. Data collection occurred over a six-month period, including 3 months prior to and after provider training. Outcomes included provider documentation for frequency of documentation of maternal marijuana use before and after provider training and the provision of evidence-based recommendations for marijuana use during breastfeeding if there was confirmation of maternal marijuana use.

Implement and Evaluate Change

After IRB approval was received, the project was implemented. Provider training (Appendix A) introduced evidence and educational materials for use in the counseling of breastfeeding mothers who use marijuana. The training summarized existing data regarding marijuana use while breastfeeding. Training was focused on EHR documentation and review of the parental handout topics. The EHR icon was created in the current electronic software utilized by the office. The icon added the ICD-10 code of "newborn affected by maternal marijuana use" (P04.9) to the infant's chart. Providers were instructed on the process for insertion of the new tracking codes into the two week well visit EHR note. Under the heading of lactation marijuana use screening, the provider had the option to choose the following ICD 10 (P code) and/or procedure code (5-digit code):

No maternal marijuana use (67825)
Newborn affected by maternal marijuana use (P04.9)
Newborn affected by maternal marijuana use (67810)
Maternal Marijuana use while breastfeeding education

A patient education handout was automatically generated when the provider chose the P04.9 code and the parent(s) were given the preprinted educational material when they checked

out. The educational handout, generated from the evaluation of the current literature, was written at a 4th grade reading level. Guidance for the writing of the patient educational material (Appendix B) was obtained from the CDC handout, "Simply Put" (CDC, 2009) as well as input by the DNP student's advisory committee. It included the following:

> You should limit or stop using marijuana (weed, pot) while breastfeeding.
> There is no safe time to nurse your baby after using marijuana.
> Marijuana may:
>
> - Decrease your breastmilk supply
> - Affect your baby's brain
> - Affect your baby's behavior

The project was implemented over a six-month period. Provider documentation of maternal marijuana use and related education prior to training was completed as free text, requiring the provider to include a narrative documenting marijuana use and counseling. After training, the documentation was facilitated by the new icon in the EHR. Data was collected devoid of any identifying data and stored on The Ohio State University protected research drive (R drive).

Integrate and Maintain Practice Change

The final step of the process was the integration and maintenance of the QI practice change. This step included dissemination of QI project findings to all stakeholders and participants. Sharing of the QI project findings also took place at a scheduled provider/manager meeting and ongoing reports regarding EHR icon usage will continue to be generated to assess

ongoing compliance and quality improvement. The project intent is to continue such counseling and documentation indefinitely with adaption of counseling via provider update as needed.

Section Four: Findings

Results

Data were identified in EHR by running a report based on the ICD 10 code for a 2 week well visit from (Z00.111). Mothers who were formula feeding at the two week well visit were excluded from the report. During the 3-month pre-training period, a total of 151 participants met this criterion and were reviewed for any type of provider documentation regarding maternal marijuana use and evidence of any provider counseling to breastfeeding mothers who admitted to marijuana use. Documentation was reviewed for any evidence of the provider asking about maternal marijuana use. Among mothers who were asked about marijuana use, the documentation was reviewed for either a yes or no response to maternal use. If the mother answered affirmatively (yes), documentation of the type of provider education regarding marijuana use while breastfeeding was recorded.

Provider training was conducted on October 2, 2018. Total providers included in the project were 11 pediatricians, 6 nurse practitioners and 1 medical resident (n=18). Following the provider training, a monthly chart review was conducted for a 3-month period to assess the documentation of counseling of marijuana use in breastfeeding women. Reports were again run based on an ICD 10 code search for the 2 week well child visit. Formula feeding mothers were excluded from data collection. A total of 203 charts were reviewed during this period. The QI project concluded on January 17, 2019.

Maternal Marijuana Use and Documentation

Figure 1 illustrates findings of the degree to which breastfeeding mothers were asked about using marijuana over the 6-month project window. An EHR query was performed searching for the ICD 10 code for a 2 week well child visit (Z00.111). A total of 151 charts met criteria (n=151). Identical EHR queries generated data for three consecutive months following provider training with a total of 203 charts reviewed.

Figure 1

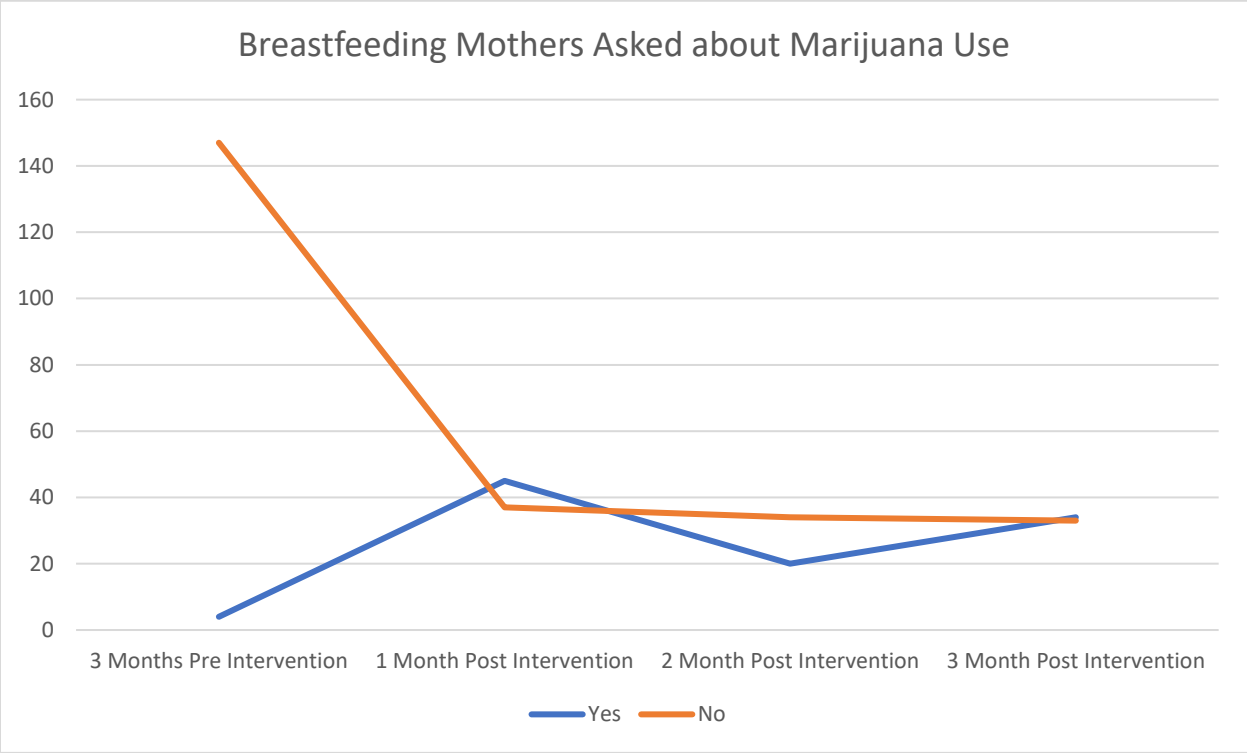


Figure 1: The X axis illustrates data points for the 3 months prior to project intervention and for each of the three months post intervention.

Prior to intervention, only 4 charts had any provider documentation for inquiry of maternal marijuana use (2.6%). The percentage of breastfeeding mothers being asked about marijuana use at the 2-week well child visit increased post intervention. For the first month post intervention (n=82), 45 mothers were asked about marijuana use (54.8%). Month 2 showed a decrease in overall charts (n=54) with 20 mothers being asked about their marijuana use. (37.0%). During month 3 of the project, a total of 67 participants met inclusion criteria (n=67) with 34 mothers being asked (50.7%).

Figure 2 illustrates documentation of evidenced based counseling for mothers who use marijuana while breastfeeding. The same queries and inclusion criteria pertained to this portion of the project analysis, yielding a total of 151 participants prior to project implementation and 203 project participants in the post training period. These charts were reviewed for any documentation regarding counseling of maternal or infant effects of marijuana use while breastfeeding

Figure 2

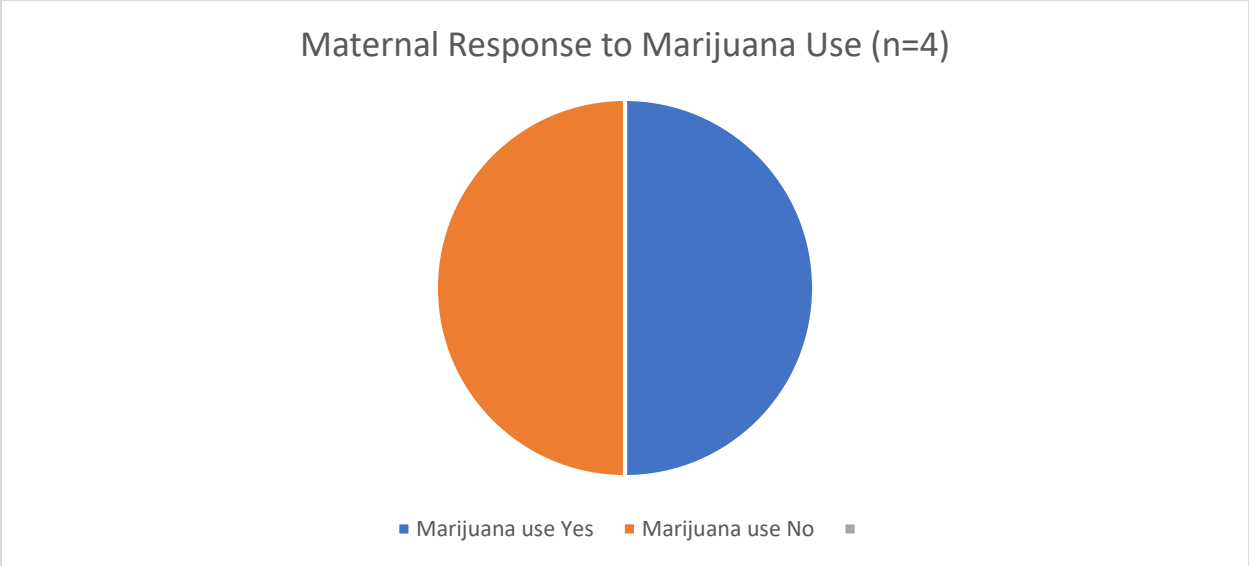


Figure 2 graphically represents maternal response to marijuana use prior to provider training (n=4). Out of the 4 mothers who were asked, 2 responded affirmatively, 2 denied use. Of the two who admitted using marijuana while breastfeeding, one was advised to decrease use and one did not receive any type of provider counseling (50%). Documentation did not address maternal or infant effects of marijuana use while breastfeeding.

Figure 3

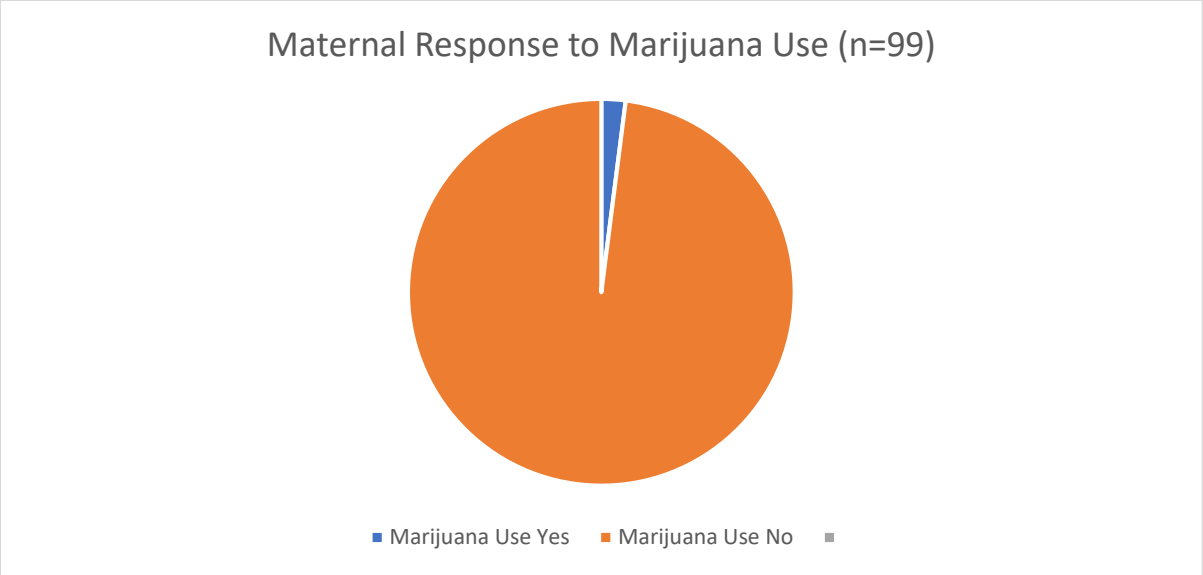


Figure 3 is a representation of mothers who were asked about marijuana use for the 3 months post provider training. Two mothers answered affirmatively and were given the standardized counseling as outlined in the provider training (100%).

Discussion

Returning to the purpose of the project, to identify the degree to which breastfeeding mothers are using marijuana and the documentation of evidenced-based counseling by the provider, both primary goals were addressed. The project trained pediatric health care providers in evidence-based recommendations to breastfeeding mothers regarding marijuana use and established an electronic system to facilitate provider counseling regarding marijuana use to breastfeeding mothers.

Marijuana Usage Among Breastfeeding Mothers

Data collected from pre and post provider training shed light on provider practices regarding mothers who breastfeed and choose to use marijuana. Prior to the training, only 2.6% of all breastfeeding mothers were asked about marijuana use. Month 1 post provider training

showed an increase in documentation of maternal marijuana use to 54.8%. This was an increase of 52.16%. The documentation percentage fell to 37% during month 2 of the project but increased to 50.7% again by month 3. Clearly, providers were better at documenting this intervention when they had received evidence-based training and had access to an EHR icon that standardized documentation.

The increase in documentation may also have been from their increased confidence in discussing marijuana use while breastfeeding due to their education during the provider training. Comments by providers during and after the training revealed a hesitancy to ask mothers about their marijuana use because they did not know what to tell parents about the effects of marijuana use on their infants. This lack of knowledge was mitigated by the provider training. This alone may have increased providers asking about maternal marijuana use.

Initially, the decrease may have been attributed to forgetting to document maternal marijuana use since it had been a month since initial training. However, during month 3, the percentage of documentation had increased again to 50.7%.

The time period for month 2 spanned from November 18th to December 17th. This period included the Thanksgiving holiday and also a 7.0 magnitude earthquake in the region. This earthquake was the largest of that magnitude in the area for several years. Since two other major holidays occurred during month 3 but did not generate a fall in documentation, it is possible that the earthquake alone may have influenced providers' documentation. It is postulated that providers, like many other residents of Alaska close to the epicenter that day, were disturbed by the earthquake which affected day to day activities. As with any natural disaster, individuals tend to become preoccupied with their own safety and security and that of their families as well.

Provider Counseling of Mothers

Findings regarding type of counseling breastfeeding mothers who disclosed marijuana use indicated only 1 of 2 women (50%) were given any counseling prior to provider training. This counseling only included decreasing marijuana use. For mothers who attested to marijuana use while breastfeeding post training, both mothers (100%) received counseling pertaining to all areas of marijuana use while breastfeeding. These included maternal lactation and infant effects of marijuana exposure while nursing.

It also must be noted that the project occurred in a state that has fully legalized all forms of marijuana use and there is no legal penalty for a parent who discloses marijuana use. This may have been a benefit to implementing this particular project, but one must also concede that marijuana use, though legal in Alaska, still has a stigma associated with it and parents may not have wanted to disclose their use to the provider, regardless of lack of repercussions.

Limitations

The project's major limitation is based on the fact that marijuana may have a stigma associated with its use which may make parents hesitant to disclose their use. There are also legal ramifications based on state laws whereas this project may not be feasibly implemented in states where full legalization of marijuana has not been achieved. The real possibility of prosecution for use of an illegal substance or loss of custody of their infant would surely deter parents from disclosing marijuana use.

Another limitation to the project is the comfort level of the provider to ask about maternal marijuana use. Personal bias regarding marijuana use may deter some providers from engaging in the discussion. This may stem from their belief that marijuana is dangerous or harmful to the infant and/or mother or that it has not been studied sufficiently to provide a definitive

recommendation to the mother. The provider may also be hesitant to ask about maternal marijuana use because they do not know how to respond to potential questions or how to broach the subject with their patients. It was hoped that the provider discussion would alleviate provider apprehension regarding recommendations, but the training did not specifically address how to ask the question initially. This was addressed during the question and answer session however by the DNP student by suggesting the provider combine the use of alcohol by breastfeeding mothers with marijuana use.

One final limitation of this project was the low number of affirmative responses to maternal marijuana use. Prior to project implementation, it was discovered that 8% of Alaska nursing mothers reported marijuana use (Alaska Department of Health and Human Services, 2015).

Only 4 mothers (1%) disclosed their marijuana use to their provider. It was expected that the opportunity for maternal teaching would have been higher during this project.

Section Five: Recommendations and Implications for Practice

Project Summary

Marijuana use among breastfeeding mothers is an emerging topic among pediatric providers and lactation consultants worldwide. Legalization of marijuana in many states is also currently being debated and will likely be on state ballots throughout the United States in the coming years. There is also a current need for increased research on marijuana for a variety of uses as well as the increased study of current strains of marijuana and its increased THC content. Practice implications of this project continue to evolve and expand as this topic is dynamic and far reaching in both the United States and throughout the world.

Implications for Nursing Practice and to the DNP Essentials

This project was grounded in the DNP essentials as outlined by the American Association of Colleges of Nursing (2009). Reflection on each of the essentials as it applies to this project should be addressed.

Essential I: Scientific Underpinning

The entire QI project was based on current research on marijuana use while breastfeeding. Due to the lack of rigorous quality studies, partially due to marijuana's level I DEA classification, older articles were included in the literature review. The provider training summarized the extensive literature review and the patient handout was created directly from literature-based evidence.

Essential II: Organizational and Systems Leadership for Quality Improvement and Systems Thinking

A need for maternal screening for marijuana use and development of an evidence-based provider training was identified by the DNP student to provider better patient care and documentation. A system wide change was developed and implemented and planned for wider dissemination in the upcoming year.

Essential III: Clinical Scholarship and Analytical Methods for Evidence-Based Practice

The project was developed using critical appraisal skills for analyzing vast numbers of research articles. The entire provider training materials and patient information was created using results gleaned from the extensive literature query as well as ongoing literature searches of new studies on the topic. The DNP student was guided by an expert advisor and committee throughout the creation, implementation and dissemination of the project findings.

Essential IV: Information Systems/Technology and Patient Care Technology for the Improvement and Transformation of Health Care

Use of information technology was essential in the development of this QI practice change. It afforded a platform to both gain insight into current practice and provided a vehicle to accurately document patient data, generate educational material and continuously screen provider compliance with the practice change. It is hoped that this EHR change will be adapted to other clients of the system throughout the country.

Essential V Health Care Policy for Advocacy in Health Care

The project was born out of the need for health care policy change generated by a statewide and national trend toward marijuana legalization. There was clearly a practice gap in the state created by recent marijuana legalization and current recommendations by governing bodies to both screen breastfeeding mothers and counsel them based on current research on the topic.

Essential VI Interprofessional Collaboration for Improving Patient and Population Health Outcomes

The student collaborated with private practice and state authorities to accomplish this practice change. A variety of disciplines were involved to create a meaningful and informative training as well as providing consistent documentation and patient education. Without interprofessional collaboration, this project could not have been as successful nor poised for wider distribution to affect healthcare change to a wide population. Stakeholder engagement was also essential to the project. Both the practice providers/owners and IT department collaboration were essential to the success of the project.

Essential VII: Clinical Prevention and Population Health for Improving the Nation's Health

The increasing incidence of marijuana legalization nationwide brings with it a change in the nation's health. It is hard to tell the long-term repercussions of this widening legalization, but it is imperative that healthcare providers screen breastfeeding mothers about their use and educate them regarding the potential effects on their nursing infants. If there are long term effects on the nursing infant, this could cause a need for specialized care of these infants as they mature. Also, if marijuana exposure through breastmilk is found to be harmful, it is the provider's duty to inform the mother and protect the child.

Essential VIII: Advanced Nursing Practice

The training should enlighten and enhance the provider's knowledge of marijuana use while breastfeeding as well as encourage them to have such discussions with their patients. Additionally, for this particular practice, iy provided exposure to the evolving role of the nurse practitioner and to the Doctor of Nursing practice degree. It may also inspire future practitioners to pursue a doctoral degree.

Methods for Dissemination

Dissemination of this project is planned for local, state and international groups over the next year. Findings of this project will begin at the office where the QI project was implemented. It is planned that the entire project will be presented at the next provider meeting as well as a full written report to be distributed to the practice partner/owners as well as the IT manager. It will be recommended that this project be continued indefinitely with the DNP student continuing to monitor documentation as well as updating provider training as needed with any new published

data. This will be accomplished by periodic literature searches as well as provider training for any new provider employees.

Statewide dissemination of this project is being planned at the Alaska State Breastfeeding Coalition annual meeting scheduled in April of 2020. This is an annual conference for anyone who provides breastfeeding support to mothers. It is typically attended by IBCLCs, dietitians, providers (MD, DO, ND, NP, CNM) and the lay public that cares for nursing mothers and infants. The DNP student will continue to be in contact with the Alaska State Department of Health and Social Services medical director to facilitate dissemination of information to other pediatric providers in the state.

National and international dissemination will be achieved by publishing this project on the Ohio State University database as well as submitting an abstract to appropriate medical publications. Additionally, an abstract of these findings was submitted and accepted and the DNP student will be presenting at the annual conference of International Board Certified Lactation Consultants to be held in August of 2019.

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Appendix A

Provider PowerPoint Training

Breastfeeding and Marijuana Use: A Provider Counseling Guide

Jennifer McKinnon, MSN, FNP, IBCLC

Prevalence of Marijuana Use

- Most commonly used illicit drug in the United States (National Institute on Drug Abuse [NIDA], 2018)
- Legal in 30 states and District of Columbia (State marijuana laws in 2018, 2018)
- 6% of pregnant women and 5% continue marijuana use while breastfeeding (Crume et al., 2018)
- 15-18 % of socioeconomically disadvantaged women (ACOG, 2015)
- Adolescent pregnancy- use rose in first 6 months postpartum (Gilchrist, Hussey, Gillmore et al, 1996)

Pharmacology of Marijuana

- Delta-9-tetrahydrocannabinol (THC) is the active component in marijuana
- THC is an agonist of cannabinoid (CB) receptors (Fride, 2001)
- CB receptors make up endocannabinoid system which are active by 19th week of gestation (Campolongo, Trezza, Ratano et al, 2001)
  - essential for attention, cognition, memory, emotion, movement, immune system (Jutras-Aswas, DiNieri, Harkany et al, 2009)
- THC action on anterior pituitary
  - promotes corticotropin secretion
  - Inhibits secretion of gonadotropin, thyroid-stimulating hormone, prolactin and growth hormone (Murphy, Munoz, Adrian et al, 1998)

Pharmacology of Marijuana

- Half Life (Smith-Kielland, Skuterud & Morland, 1999)
  - 1.3 days for one marijuana cigarette
  - 5-13 days for heavy user
- THC Routes
  - Smoking
    - plasma peak in 1-2 hours (Hollister et al., 1981)
    - 0.8% of mother's dose of one marijuana joint transfers to infant (Djulus, Moretti & Koren, 2005)
  - Oral
    - Plasma peak in 2-4 hours (Hollister et al., 1981)
    - Reduced bioavailability by 4-12% (Owens, Reisner, & Perez-Reyes, 1981)
- THC in marijuana has risen from 3.96% to 11.84% from 1995 to 2014 (ElSohly et al 2010)

Pharmacology of Marijuana

- Low molecular weight (314 g/mol) (Hale &Rowe, 2017)
- High Volume of Distribution (4-19 L/kg) (Hale &Rowe, 2017)
- Long Elimination half-life (25-57 hours) (Kruez &Axelrod, 1973)
- Lipophilic- should readily transfer into breastmilk (Hale &Rowe, 2017 p. e1164-172)
  - Foremilk (milk produced in first 3 minute of feeding/pumping) has less fat
  - Hindmilk (remainder of milk produced during feeding/pumping)
    - Increased amounts of THC (Gardiner, 2001)

Effects of Marijuana Exposure on Infants

Human Studies

- **Sedation, poor growth reduced muscle tone, poor suckling** (Liston, 1998)
- **Lethargy, less frequent and shorter feedings** (Institute of Medicine, 1991)
- **No correlation between marijuana exposure and infant growth and development at 1 year of age** (Tennes et al, 1985)
- **Impaired motor function at 1 year of age** (Astley & Little, 1990)
- **No detectable mental delays at 1 yr** (Astley & Little, 1990)

Animal Studies

- **Behavioral and neuroendocrine changes** (Moreno et al, 2005; Navarro, 2005; Trezza et al, 2008)
- **Anxious behavior and altered social functioning** (Newsom& Kelly, 2008)

Maternal Effects of Marijuana

Human Studies

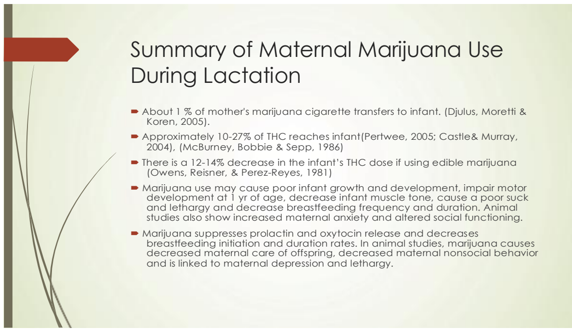
- **Suppresses prolactin production** (Murphy, Munoz, Adrian & Villanua, 1998; Mendelson, Ellingboe & Mello 1984; Ranganathan et al., 2009)
- **Decreased oxytocin release** (Tyrey, 1988)
- **Decreased breastfeeding initiation** (Crume et al, 2018)
- **Shorter breastfeeding duration** (Ko, Farr, Tong, Creanga & Callaghan, 2015)

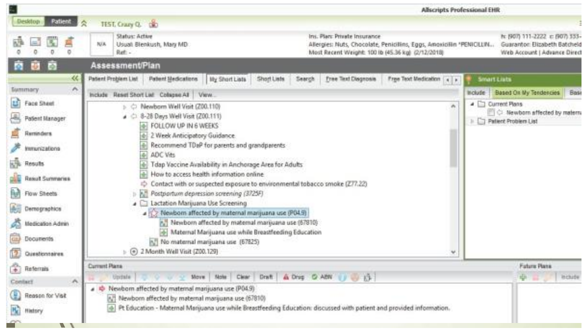
Animal Studies

- **Decreased oxytocin and prolactin release** (Tyrey & Murphy, 1988; Vilela & Giusti-Paiva, 2014; Bromley, Rabii, Gordon & Zimmerman, 1978; Asch, Smith, Siler-Khodr & Pauerstein, 1979)
- **Decreased care of offspring** (Bromley et al, 1978)
- **Decreased licking, retrieval and carry of pups** (Vilela & Giusti-Paiva, 2014)
- **Decreased maternal nonsocial activities** (Frischknecht, Sieber & Waser, 1980)
- **Maternal depression and lethargy** (Asch & Smith, 1986)

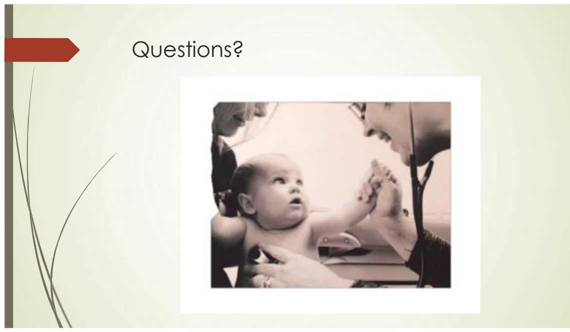
Recommendations for Marijuana Use While Breastfeeding

- AAP- "Street drugs such as PCP, cocaine, and cannabis can be detected in human milk, and their use by breastfeeding and their use by breastfeeding mothers is of concerns, particularly with regard to the infant's long-term neurobehavioral development and thus are contraindicated." (Garry et al., 2009)
- AAP-"Present data are insufficient to assess the effects of exposure of infants to maternal marijuana use during breastfeeding. As a result, **maternal marijuana use while breastfeeding is discouraged**". (AAP, 2018)
- ACOG- "There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, **marijuana use is discouraged.**" (ACOG, 2017)
- ABM- "**Breastfeeding mothers should be counseled** to reduce or eliminate their use of marijuana to avoid exposing their infants to this substance and advised of the possible long-term neurobehavioral effect from continued use." (Reece-Stremtan & Marinelli, 2015)
- ADHSS- "**continue to breastfeed** while making every effort to reduce the amount of marijuana consumed, whether smoked, vaped or eaten" (Butler, 2017)


Summary of Maternal Marijuana Use During Lactation
About 1 % of mother's marijuana cigarette transfers to infant. (Djulus, Moretti & Koren, 2005).
Approximately 10-27% of THC reaches infant(Pertwee, 2005; Castle& Murray, 2004), (McBurney, Bobbie & Sepp, 1986)
There is a 12-14% decrease in the infant's THC dose if using edible marijuana (Owens, Reisner, & Perez-Reyes, 1981)
Marijuana use may cause poor infant growth and development, impair motor development at 1 yr of age, decrease infant muscle tone, cause a poor suck and lethargy and decrease breastfeeding frequency and duration. Animal studies also show increased maternal anxiety and altered social functioning.
Marijuana suppresses prolactin and oxytocin release and decreases breastfeeding initiation and duration rates. In animal studies, marijuana causes decreased maternal care of offspring, decreased maternal nonsocial behavior and is linked to maternal depression and lethargy.


Allscripts Professional EHR
Assessment/Plan
Newborn Well Visit (Z00.110)
8-28 Days Well Visit (Z00.111)
FOLLOW UP IN 6 WEEKS
2 Week Anticipatory Guidance
Recommend TDaP for parents and grandparents
ADC Vits
Tdap Vaccine Availability in Anchorage Area for Adults
How to access health information online
Contact with or suspected exposure to environmental tobacco smoke (Z77.22)
Postpartum depression screening (3725F)
Lactation Marijuana Use Screening
Newborn affected by maternal marijuana use (P04.9)
Newborn affected by maternal marijuana use (67810)
Maternal Marijuana use while Breastfeeding Education
No maternal marijuana use (67825)
2 Month Well Visit (Z00.129)
Current Plans
Newborn affected by maternal marijuana use (P04.9)
Newborn affected by maternal marijuana use (67810)
Pt Education - Maternal Marijuana use while Breastfeeding Education: discussed with patient and provided information.


Handout to Parents
You should limit or stop using marijuana (weed, pot) while breastfeeding.
There is no safe time to nurse your baby after using marijuana.
Marijuana may:
Decrease your breastmilk supply
Affect your baby's brain
Affect your baby's behavior


Questions?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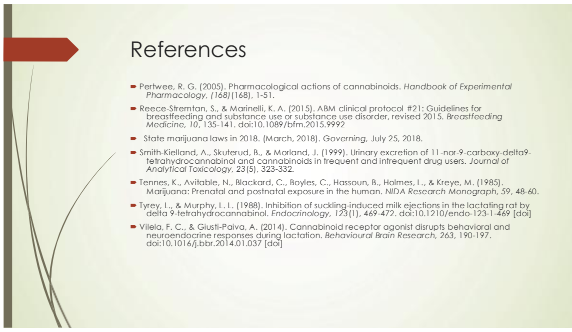
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Appendix B

Patient Handout

Table 1

Evaluation Table

Citation	Design/Method	Sample /S	Major Variables Studies and their defi	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
American Academy of Pediatrics [AAP] (2018). Marijuana use during pregnancy and breastfeeding: Implications for neonatal and childhood outcomes. *Pediatrics.* 142(3). 1-8	Policy Statement/ Expert Opinion	N/A	Reviews of 1. Pharmacokinetics of cannabinoids during pregnancy 2. Adverse effect of MJ on pregnancy, neonate, infant, child and adolescent 3. Mechanisms used to explain underlying effects on the developing fetus 4. Linkages of the endocannabinoid system to other neurotransmitter systems 5. Issues for the clinician 6. Breastfeeding and MJ use 7. Epidemiology 8. Pharmacokinetics of MJ in human milk 9. Published recommendations from other organizations	N/A	N/A	Specific to MJ use while breastfeeding: 1. THC is 99% protein bound, lipid soluble and has molecular weight of 314 which allows transfer into milk 2. Effect of MJ on breastfed infant: cited Tennes, Astley and Little article (individually reviewed later in this table) 3. Recommendations: encourage mother to breastfeed while strongly encouraging mom to abstain from using MJ as well as alcohol, tobacco and other drugs as well as effects of passive MJ smoke exposure to infants	Counsel all breastfeeding mothers who use MJ and encourage MJ abstinence while nursing.	IV Quality: hig Strength: high	Strength: Well known professional body Clarifies 2012 position on MJ use and breastfeeding Limitation: Does not address prenatal and postnatal MJ exposure separately Essentially contradicts 2012 position on MJ use while breastfeeding Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /S	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
American Academy of Pediatrics [AAP] (2012). Breastfeeding and the use of human milk. *Pediatrics.* 129(3). 598-601.	Policy Statement/ Expert Opinion	N/A	Reviews of: 1.epidemiology of breastfeeding rates 2.Infant outcomes of breastfeeding (methodologic issues, respiratory tract infections and otitis media, GI tract infections, necrotizing enterocolitis, sudden infant death syndrome and infant mortality, allergic disease, celiac disease, inflammatory bowel disease, obesity, diabetes, childhood leukemia and lymphoma, neurodevelopmental outcomes) 3. Preterm infants 4. Maternal outcomes 5. Economic Benefits 6. Duration of exclusive breastfeeding 7.Contraindications to breastfeeding 8. Maternal diet 9. Maternal medications 10. Hospital routines (pacifier use, vitamins and mineral supplements) 11. Growth 12. Role of the pediatrician 13. Business case for breastfeeding	N/A	N/A	Groups MJ with other “street drugs” (PCP, cocaine) and states MJ use by breastfeeding mothers is of concern, particularly with regard to the infant’s long-term neurobehavioral development. .	MJ use while breastfeeding is contraindicated	IV Quality: high Strength: medium	Strength: Well known professional body that is frequently cited as a clinical benchmark Limitation: Bases MJ as a contradiction to breastfeeding on one research article (Garry, 2009) Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /S	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
American College of Obstetrics and Gynecology [ACOG] committee opinion summary number 722 (2017). Marijuana use during pregnancy and lactation. *Obstetrics & Gynecology*. 130 (4), 931-932.	Position paper/expert opinion	N/A	Strength: Well known professional body that is frequently cited as a clinical benchmark Limitation: Does not address prenatal and postnatal MJ exposure separately Clinically feasible to include in provider counseling	Recommendations for marijuana use in breastfeeding women	N/A	Women reporting marijuana use should be counseled regarding potential adverse effects. Women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use, whether recreational or medicinal. Insufficient data available for review to evaluate effects of MJ on infants during lactation	In absence of sufficient published data to evaluate the effects of MJ use on infants during lactation and breastfeeding, MJ use should be discouraged	IV Quality: high Strength: high	Strength: Well known professional body that is frequently cited as a clinical benchmark Limitation: Does not address prenatal and postnatal MJ exposure separately Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Asch, R.H., Smith, C.G. (1986). Effects of delta-9-THC, The principal psychoactive component of marijuana, during pregnancy of the rhesus monkey. *Journal of Reproductive Medicine*. 31(12). 571-575.	Quasi-Experimental Pre and Post Test Design	Female rhesus monkeys receiving THC 2.5mg/kg during gestation from pregnancy diagnosis to day 155 (group 1, n=5), gestation day 55-109 (group 2, n=5), gestation day 110-155 (group 3, n=5) with corresponding control groups receiving vehicle (n=5) in each group. Postnatal treatment of THC 2.5 mg/kg during lactation (experimental group n=5) or vehicle (n=5)	Blood concentration of THC (2.5ng/ml) in mothers during pregnancy and lactation	Examine effects of THC treatments during different periods of gestation	Descriptive statistics Paired t-test	THC crossed placenta at term and peaked 8 hrs after THC administration to nursing mother. Blood distribution half-life of THC about 2 hrs Long milk half-life > 24 hrs Milk THC concentrations peaked several hrs after blood THC concentrations	THC transfers to nursing monkey through breastmilk THC in mother's milk associated with lethargic maternal behavior toward nursing.	II Quality: high Strength: high	Strength: Good review of literature of similar previous studies Limitations: THC exposure both in pregnancy and lactation Results may not be transferrable to human milk and breastfeeding infant Age of study No power analysis to assess sample size Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Asch, R.H., Smith, C.G., Siler-Khodr, T.M., Pauerstein, C.J. (1979). Acute decreases in serum prolactin concentrations caused by delta 9-tetrahydrocannabinol in nonhuman primates. *Fertility and Sterility.* 32(5) 571-575.	Quasi-Experimental Pre and Post Test Design	Intact male rhesus monkey (n=4) oophorectomized female rhesus monkeys (n=5)	Nursing mothers received either THC (2.5mg/kg) IM or THC and TRH (5 UG IV) simultaneously or vehicle	Evaluate acute prolactin response to single injections of THC and to evaluate the possible site of action of THC in nonhuman primates	One-way ANOVA	THC lowered prolactin levels within 30-120 min after injection Simultaneous administration of TRH with THC did not mitigate prolactin drop Serum prolactin concentrations plotted over 0-180 minutes after IM injections	THC induces decreased prolactin levels. Site of THC action is predominately suprapituitary	II Quality: low Strength: high	Strength: Valid evidence to support provider recommendations Limitation: No power analysis to assess sample size Results may not be transferrable to human milk and breastfeeding infant Age of study Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Set	Major Variables Studies and their defi	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Astley, S.J., Little, R.E. (1990). Maternal marijuana use during lactation and infant development at one year. *Neurotoxicology and Teratology*, 12(2), 161-168.	Cross Sectional Prospective Study	Breastfed children; (n=68) whose mothers used MJ, (n=68) Children whose mothers did not use MJ (n=136)	Dependent- Psychomotor Developmental Index (PDI)- Measures infant gross motor coordination and finer skills of hands and fingers. Mental Developmental Index (MDI) from the Bayley Scales of Infant Development- Measures infant problem-solving ability and verbal communication development. Independent- Number of days infant exposed to MJ Secondary independent variables- Maternal age, height, race, income level, education, marital status, pregnancy history and weight gain, tobacco, coffee, alcohol and psychoactive drug use during pregnancy and lactation and marijuana use during pregnancy Paternal alcohol and tobacco use before conception and during postpartum period 3. Infant gestational age and sex	Investigate the relationship between infant MJ exposure via breastmilk and infant motor and mental development at one year of age in predominately middle class, low-risk population MJ use and effect on PDI and MDI scores Differences in maternal characteristic between MJ using and not using mothers	Multiple regression analysis Chi square *t*-test	Daily infant exposure to MJ via mother's Postpartum month one associated with 14+/- poin decrease in MDI MJ exposure maore than half of days in first trimester or first month of lactation had lower PDI Moderate MJ exposure (no more than ½ of days in a period) affected PDI in first trimester. Mean score decreased with increasing MJ use	Daily infant MJ exposure via maternal breastmilk is associated with a decrease in infant gross motor, problem-solving and verbal communication and development at one year of age	III Quality: medium Strength: moderate	Strength: Tracks infant effects through 1 yr of age Limitation: Difficult to detect which period of exposure (prenatally or postpartum) had stronger effect on PDI score. Did not follow infants past one year of age Age of study Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Bertrand, K.A., Hanan, N.J., Honerkamp-Smith, G., Best, B.M., & Chambers, C.D. (2018). Marijuana use by breastfeeding mothers and cannabinoid concentrations in breast milk. *Pediatrics*. 142(3), 1-8.	Non-Experimental Single Variable Design	50 breastmilk samples (50 new samples and 4 repeat samples) from Mommy's Milk (research repository) from breastfeeding women who reported MJ use at any time since giving birth	Breastmilk concentrations of delta-9-THC (ng/ml), 11-OH-THC (ng/ml) and cannabidiol (ng/ml) reported in hours since last maternal use	Measured the amount of THC present in human breastmilk per hour after maternal ingestion of marijuana	Descriptive statistics Linear regression model R version 3.4.1 with 2 sided P value (<.05 significant	Most common route of maternal MJ administration was inhalation (64%) Most women in sample (88%) reported at least daily MJ use Median concentration of delta9-THC in breastmilk was 9.47ng/ml Each additional hour between last MJ exposure and milk sample collection caused a reduction of 0.03 in the log concentration of delta 9-THC (unlogged is 3%/hr) Longest duration between last use of MJ and measurable delta 9-Thc was approx. 140 hrs or 6 days	Delta 9-THC measurable in the breastmilk of MJ using mothers and lasted up to 6 days from last reported MJ use.	III Quality: moderate Strength: moderate	Strength: New research measuring THC in breastmilk Large sample size Limitations: Relied on maternal honesty and recall regarding MJ use Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Bromley, B.L., Rabii, J., Gordon, J.H., Zimmerman, E. (1978). Delta-9-tetracannabinol inhibition of suckling-induced prolactin release in the lactating rat. *Endocrine Research Communications.* 5 (4), 271-278.	Experimental Pre and Post Test Design	Lactating rats (n=14) and offspring (n=?)	Blood concentration of prolactin (ng/ml) Mothers received IV THC (1.25 or 4 mg/kg) or vehicle and then blood samples drawn 30,60, and 120 min after dose of THC	Primary: Study of THC on the regulation of prolactin release Secondary: Maternal behavior	Descriptive statistics t-test	THC caused decreased suckling-stimulated prolactin release ($P<0.01$) THC caused disruption in maternal behavior (continuous ambulatory movement or circling without regard for pups)	THC inhibits suckling-induced prolactin release in postpartum rats THC caused lack of care by mother for pups	III Quality: moderate Strength: moderate	Strength: Valid evidence to support provider recommendations Limitation: No power analysis to assess sample size Animal study may not translate into human lactation Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Brown, R.A., Dakkak, H.S., Seabrook, J.A. (2018). Is breast best? Examining the effects of alcohol and cannabis use during lactation. *Journal of Neonatal Perinatal Medicine*.	Literature Review	19 articles reviewed related to alcohol and breastfeeding 4 articles reviewed specific to cannabis (n=2 original papers; n=2 systematic reviews)	Search Engines: PubMed, CINAHL, Nursing and Allied Health, Google Scholar. Search terms: marijuana, cannabis, THC, alcohol, ethanol, breastfeeding, lactation and breastmilk Restricted to papers published since 2000	To examine the risks associated with alcohol and cannabis use among breastfeeding mothers Make recommendations to healthcare professionals regarding substance use in lactation	N/A	No association between maternal MJ use and SIDS Lactation professionals' recommendations vary, 44% depend on severity, 41% state benefits outweigh risks, 15% recommend stopping breastfeeding if mom using MJ Harm to infant exposed to MJ is prenatally. No clear risk associated with MJ during lactation. Breastfeeding mothers should be advised to reduce or cease MJ use while breastfeeding	Maternal outcomes related to cannabis consumption included panic attacks, delayed response time, increased heart rate, reduce short-term memory, dizziness, and impaired motor performance.	V Quality: high Strength: High	Strength: Comprehensive and current literature review Limitation: Small review of 4 articles specific to MJ Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /S	Major Variab Studies and th definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Butler, J.C., (2017). Memorandum: Breastfeeding mothers reporting marijuana use are encouraged to continue breastfeeding.	Policy Statement	N/A	N/A	Memorandum to Alaskan healthcare providers to encouraged mothers who use MJ to continue breastfeeding	N/A	N/A	Continue to breastfeed while making effort to reduce amount of MJ consumed, whether smoked, vaped or eaten.	V Strength: moderate Quality: moderate	Strength: Alaskan focus Opinion based on current professional guidelines Limitation: Opinion of elected official may change Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Sett	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Campolongo, P., Treeza, V., Ratano, P., Palmery, M., & Cuomo, V. (2011). Developmental consequences of perinatal cannabis exposure: Behavioral and neuroendocrine effects in adult rodents. *Psychopharmacology*. 214 (1). 5-15.	Literature Review	Did not list number of articles reviewed, search engines or search criteria	Review of relevant rodent studies examining long-term behavioral consequences of exposure to cannabinoid compounds during pregnancy and/or lactation Search engines and search terms not identified.	Reviewed rodent studies examining long-term behavioral consequences of exposure cannabinoids during pregnancy and/or lactation	N/A	Review of animal studies show CB receptors active by 19 wks gestation. Cannabis exposure in utero and/or lactation caused hyperactivity, cognitive impairments, altered emotionality.	Cannabinoid drugs are neuroteratogens causing abnormalities in exposed offspring.	V Strength: moderate Quality: moderate	Strength: Current literature review Reviewed neurobehavioral abnormalities Limitation: blends prenatal and postnatal cannabis exposure. Difficult to extrapolate solely breastmilk cannabis exposure. Clinically feasible to include in provider counseling.

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Chao, F.C., Green, D.E., Forrest, I.S., et al. (1976). The passage of 14C-delta-9-tetrahydrocannabinol into the milk of lactating squirrel monkeys. *Research Communications in Chemical Pathology and Pharmacology*. 15 (2), 303-317.	Quasi Experimental Pre and Post Test design	Lactating squirrel monkeys (n=11) and their young (3-4-month-old) infants (n=6) received 2 mg/kg THC orally 2 times a week (n=6) or 5 times a week (n=5) followed by 2 doses of 14C-THC (tracer) A third group (n=6) mothers were controls. Maternal milk, maternal and infant urine and feces collected 1-24 hrs after THC administration	Milk concentration of THC Maternal and infant urine and feces concentration of THC	Transfer of THC into mammalian milk, urine and feces THC's effect on milk production	Analysis of variance t-tests	Slight but nonsignificant difference in milk volume between THC and control group ($P<0.10$) Compared milk production and amount of THC in milk (0.19%), urine (1%) and feces (42%). Within 24hrs, mothers had 0.19% of labeled drug in their milk. . .	No difference in maternal milk volume. Slower rate of THC excretion in urine and feces with 5 times/week THC exposure	II Strength: moderate Quality: moderate	Strength: Valid evidence to support provider recommendations Limitations: No power analysis to assess sample size Possible species variation in THC content in milk. Animal study may not translate into human lactation Clinically feasible to include in provider counseling.

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Crume, T.L., Julh, 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. *Journal of Pediatrics*, 197, 90-96	Cross Sectional study	Colorado PRAMS (Pregnancy Risk Assessment Monitoring System) data to measure prenatal and postnatal MJ use (n=3207) Exclusions: nonresidents, out of state births, adopted out infants, multiple births (4 or more), maternal age < 15 yrs	MJ use pre (3 months prior to pregnancy, first 3 months of pregnancy and last 3 months of pregnancy) and postnatally (2-4 months postpartum)	state-level prevalence of prenatal and early postnatal MJ use Association of maternal MJ use with adverse neonatal outcomes	Pearson $\chi 2$ tests (alpha of 0.05)	Decreased breastfeeding initiation with prenatal MJ use ($P<0.02$) Prenatal and postnatal MJ use =shorter duration of breastfeeding ($P<0.001$)	Prenatal cannabis use decreases breastfeeding initiation Pre and post-natal cannabis use results in shorter breastfeeding duration	III Strength: moderate Quality: moderate	Strength: Large sample size Study from legalized MJ state Limitation: Confounding variable of prenatal MJ use as well as postnatally Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setti	Major Variables Studies and their defin	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
D'Apolito, K. (2013). Breastfeeding and substance abuse. *Clinical Obstetrics and Gynecology*. 56(1). 202-211	Literature Review	Did not list number of articles reviewed, search engines or search criteria N/A	Review of: 1. Formation of breast milk 2. Mechanism of drug transfer into breast milk 3. Factors associated with passage of drugs into breastmilk (molecular weight, acid-base dissociation constant, protein binding, lipid solubility and oral bioavailability, maternal factors, infant factors) 4. Methods of estimating infant drug exposure (milk-to-plasma ratio) 5. Concentration of drugs in the breast milk (methadone, marijuana, cocaine, alcohol, heroin, buprenorphine)	Review the mechanisms involved in the formation and transfer of licit (alcohol) and illicit drugs (methadone, MJ, cocaine, and heroin) into breastmilk. Review breastfeeding recommendations	N/A	MJ Pka 10.6 , molecular wt 314.46, lipid soluable MJ 97% bound to albumin Foremilk (first 3 min of pumping/nursing) has less fat than hindmilk Contrasts moderate to heavy THC users Possible neurodev't delay at 1 yr	Regular MJ use not recommended with breastfeeding Occasional MJ use should be evaluated on case by case basis	V Strength: moderate Quality: high	Strength: Excellent pharmacokinetics review of MJ Limitation: 6 yr old data Contradicting study findings, recommendation based on pharmacokinetics Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Varia Studies and definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Frischknecht, H.R., Sieber, B., Waser, P.G. (1980). Behavioral effects of hashish in mice. II. Nursing behavior and development of the sucklings. *Psychopharmacology*. 70(2) 155-161.	Quasi Experimental Pre and Post Test Design	Newborn mice (n=8) with a body wt of 1.4 g along with both parents were gavage fed 20 mg THC/kg or control of 2ml olive oil/kg on days 1,3,6,8,10,13,15,17 and 20. Parent nursing behaviors tested 1.5-2h after 2nd and 5th treatment on days 3 and 10. Spontaneous pup behavior noted on day 21. Pups were weaned, and mothers separated from pups until they gave birth to second litter. Those pups were then weighed and days between 1st and 2nd litters recorded	Pup suckling Pup weight Maternal behavior	Evaluate THC effects on nursing behavior of parents and the consequences on the development of the pups.	Descriptive mean +/- standard error Wilcoxon's rank-ordered test, two-tailed	THC group had reduced maternal nonsocial behavior and locomotion initially. Resumed usual care level after 5th dose of THC on day 10 postpartum. Weight of pups (offspring of dams and males given THC) significantly lower ($P \leq 0.05$) at ages 6 and 10 days by about 15% compared to controls. Parent mice given THC had decreased Locomotion ($P \leq 0.1$) and decreased latency until all pups retrieved ($P \leq 0.005$)	Maternal THC during lactation causes decreased weight gain in pups Hashish decreases lactation Hashish causes transient impairment in maternal behavior (locomotive activity, nonsocial activities and pup retrieval)	III Quality: high Strength: high	Strength: Valid evidence to support provider recommendations Limitation: No power analysis to assess sample size Animal effects may not translate into human lactation Age of study Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Settin	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Garry, A., Rigourd, V., Amirouche, A., Fauroux, V., Aubry, S., & Serreau, R. (2009). Cannabis and breastfeeding. *Journal of Toxicology*. 596149.	Literature Review	Search engines and search terms not identified.	Review of 1. Definition and epidemiology of MJ u 2. Pharmacology data and side effects of MJ 3. MJ and breastfeedir 4.Polyintoxications	To assess if MJ could be used during breastfeeding	N/A	Clinical and pharmacokinetic data indicated that MJ use is dangerous during breastfeeding for the child.	Mothers who use MJ should stop breastfeeding	V Quality: moderate Strength: moderate	Strength: Highlights differences in two studies of effects of MJ on motor development Limitation: Small number of studies reviewed Age of Study

Citation	Design/Method	Sample /Settir	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Hill, M., Reed, K. (2013). Pregnancy, breast-feeding, and marijuana: A review article. *Obstetrical and Gynecological Survey*. 68(10). 710-718.	Literature Review	Search engines and search terms not identified	Review of 1. incidence of use 2. Use in pregnancy 3. Physiologic and psychological effects 4. Effects in women 5. Levels of MJ transferred via placenta and breastmilk 6. MJ effects on fetal, childhood and adolescent outcomes 7. MJ effects during breastfeeding 8. Legal implications	Effects of MJ exposure during pregnancy and breastfeeding	N/A	Heavy MJ use (> 5 joints/week) may cause difficulty with reasoning and attention in breastfed infants	Discourage MJ use but encourage breastfeeding Mandatory reporting of MJ use during pregnancy and punitive measures during pregnancy or breast-feeding are not medically warranted	V Strength: moderate Quality: moderate	Strength: 5 yr old literature review Limitation: Difficult to address legal implication of MJ use due to varying state laws Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Set	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Hollister, L.E., Gillespie, B.A., Ohlsson, A., Lindgren, J.E., Wahlen, A. & Agurell, S. (1981). *Journal of Clinical Pharmacology.* 21. 171s-177s.	Quasi-experimental Study	Men who use marijuana (a 35) (n=11) Smoking MJ (joint with 19 mg THC) IV MJ (5 mg THC) Oral MJ (20mg THC cookie)	Self-rating of intoxication Conjunctival injection Pulse rate	Relate plasma concentrations of THC to self-ratings of decree of intoxication.	Log concentrations of THC (ng/ml) P values of THC exposure and perceived "high"	Smoked route caused lower peak plasma THC than IV route (P<0.01) Oral route caused slower absorption than smoked or IV route (P, 0.01)	Oral ingestion of THC slower than smoked or injected route. Could not establish relationship between plasma concentration of THC and "high" Oral THC "high" and plasma THC concentration paralleled each other	III Quality: low Strength: low	Strength: Good comparison of routes of administration on peak THC content Limitation: Subjective "high" reporting Results based on honest word of participants No power analysis to assess sample size Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Se	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Jaques, S.C., Kingsberry, A., Henshcke, P., Chomchai. C., Clews, S., Falconer, J, …Oei, J.L. (2014). Cannabis, the pregnant woman and her child: weeding out the myths. *Journal of Perinatology*, 34(6), 417-424.	Literature Review	Search engines and search terms not identified	Reviewed cannabis 1. Definition 2. Pharmacodynamics 3. Genetic susceptibility to effects 4. Prevalence of use in pregnancy 5. Detecting use in pregnancy 6. Impact on fetus and newborn 7. Longer-term growth and neurodevelopment 8. Medical cannabis 9. Lactation 10. Recommendations for management of pregnant women using	Provide health practitioner with guidance for advising women who use cannabis in pregnancy on the potential effects of cannabis use on their unborn baby and future child development	N/A	See next page	Advise women to stop using marijuana or decrease use while breastfeeding MJ may adversely affect neurodevelopment, impacting neuropsychiatric, behavioral and executive functioning.	V Quality: moderate Strength: moderate	Strength: Reviews multiple areas regarding cannabis use during pre and post-natal period Limitation: Study heavily looked at prenatal MJ exposure Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Se	Major Variabl Studies and the definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Jaques con't						Susceptibility to adolescent cannabis user may be influenced by heredity 5% UK pregnant women use cannabis Use detected early in pregnancy by maternal and newborn toxicology, maternal hair samples, meconium testing, neonatal urine testing, questioning mother In utero cannabis exposure= increased risk of prematurity, growth restriction in mid to late pregnancy, low birthweight, smaller head circumference In utero cannabis exposure may impair long-term growth and neurodev't, impair visual memory, learning problems, impulse control problems, increased depressive symptoms, attention problems, increased risk of delinquency Unknown effects of medical vs recreational use of cannabis during pregnancy Cannabis and metabolites pass into breast milk in variable concentrations depending on maternal ingestion THC inhibits gonadotropin, prolactin, growth hormone and thyroid-stimulating hormone release and stimulated corticotropin release No safe threshold limits for cannabis use in pregnancy and post natally- advise moms to limit or stop using cannabis			

Citation	Design/Method	Sample /Set	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Justras-Aswad, D., DiNieri, J.A., Harkany, T., & Hurd, Y.L. (2009). Neurobiological consequences of maternal cannabis on human fetal development and its neuropsychiatric outcome. *European Archives of Psychiatry and Clinical Neuroscience*. 259 (7). 395-412	Literature Review	Search engines and search terms not identified	Reviewed 1. Neurobiology of endocannabinoid system and relevance to developing brain 2. Impact of cannabinoid exposure on the maturation of neurotransmitter systems 3. Consequences of developmental cannabis exposure on behavior and cognition 4. Prenatal cannabis exposure in relation to neuropsychiatric disorders	Overview of endocannabinoid system and examines neurobiological consequences of cannabis exposure in pregnancy and early life	N/A	Endocannabinoid system impacts CNS patterning by modulating cell fate decisions in neural progenitor cells and also influences migration, survival and differentiation of committed neurons	Endocannabinoid system is primary molecular target of THC	V Quality: moderate Strength: moderate	Strength: In depth review of endocannabinoid system development and effects of THC on the system Limitations: Did not address post-natal THC exposure on endocannabinoid system Age of study Heavy focus on prenatal exposure

Citation	Design/Method	Sample /Setting	Major Variables Studies and thei definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Ko, J.Y., Tong, V.T., Bombard, J.M., Hayes, D.K., Davy, J., & Perham-Hester, K.A. (2018). Marijuana use during and after pregnancy and association of prenatal use on birth outcomes: A population-based study. *American Journal of Obstetrics and Gynecology*. 213 (2). P. 72-78.	Qualitative Case Study	PRAMS (Pregnancy Risk Assessment Monitoring System) data of prenatal and post-natal MJ use(n=9013). Survey questionnaire (mailed or telephonic) from 2-9 months after delivery	Infant birth weight Gestational age Maternal MJ use Socio-demographic characteristics	Correlated of MJ use during and after pregnancy, and examined the relationship between prenatal marijuana use and infant outcomes	Chi Square analysis to assess MJ prevalence T-tests to assess differences in birth weights and gestational age	Postpartum MJ use associated with depressive symptoms (P=0.03) and shorter breastfeeding duration (P<0.001	Monitor postpartum maternal use of MJ	V Quality: good Strength: moderate	Strength: Large US sample size Limitation: Focused on prenatal MJ exposure Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Kreuz, D.S., Axelrod, J. (1973). Delta-9-tetrahydrocannabinol: Localization in body fat. *Science*. 179, 4071, 391-393	Two-Group RCT with posttest design	Sprague-Dewley rats (n=4) injected SQ with 14 ml of 1 mg/ml THC after 1,3,6,9, or 13 doses.	Brain, lung, liver and perirenal fat pad concentration of THC	accumulation and retention of THC in body fat	mean and standard deviation	Tenfold greater concentration of THC in fat than other tissues (P values not reported)	THC localizes in body fat of rats	III Quality: poor Strength: low	Strength: Valid evidence to support provider recommendations Limitation: Poor description of study design and methods No power analysis to assess sample size Age of study Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setti	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Liston, J. (1998). Breastfeeding and the use of recreational drugs—alcohol, caffeine, nicotine and marijuana. *Breastfeeding Review*, 6(2), 27-30.	Literature Review	Search engines and search terms not identified	Reviewed recreational drug (alcohol, caffeine, nicotine and marijuana) use while breastfeeding	Reviewed breastfeeding and 1.Alcohol 2. Caffeine 3. Nicotine 4. MJ	N/A	Heavy MJ use showed 8x accumulation of THC in breastmilk compared to plasma Infant effects: sedation, weakness and poor feeding patterns Maternal effect: reduced prolactin levels	Mothers should be encouraged to restrict intake of MJ while nursing	V Quality: good Strength: moderate	Strength: Reviewed current research and AAP recommendation on maternal MJ use while breastfeeding Limitation: Did not define “heavy” MJ use Gives opinion that maternal MJ use can distort her reality and make it hard for her to handle emergency situations Older review Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Settir	Major Variables Studies and their defin	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Marchei, E., Escuder, D., Pallas, C.R., Garcia-Algar, O., Gomez, A., Friguls, B., Pellegrinia, M., and Pichini, S. (2011). *Journal of Pharmaceutical and Biomedical Analysis.* 55(2), pp 309-316.	Quasi experimental Cross-Sectional Study	Breastmilk samples from Spanish milk bank (n=400).	Determined if liquid chromatography tandem mass spectrometery (LC-MS-MS) was a reliable method to quantify amount of MJ in breastmilk	Development and validation of LC-MS-MS method for accurately measuring licit and illicit (opiates, methadone, cocaine, amphetamines and cannabinoids) in human breast milk. Applied method to screen samples from milk bank and identified 18 drugs and metabolites	Linearity determined by least-squares regression with $1/\chi 2$ weighting Linearity was acceptable when coefficient of determination was at least 0.99	LC-MS-MS is an accurate tool to measure MJ in breastmilk Identified 18 drugs and metabolites from Spanish milk bank samples	LC-MS-MS can accurately quantify the amount of THC in a breastmilk sample	I Quality: high Strength: high	Strength: High specificity of instrument tested (LC-MS-MS) Limitation: No power analysis to assess sample size Not clinically relevant to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Mendelson, J.H., Ellingboe, J., and Mello, N.K. (1984). Acute effects of marihuana smoking on prolactin levels in human females. (1985). *The Journal of Pharmacology and Experimental Therapeutics.* 20(1). 103-106.	Double-blind, randomized crossover design	Females (n=16) with MJ use 14.4 times/month of which: Follicular phase of menses (n=8) Luteal phase of menses (n=8	Smokes MJ cigarette with 1.83% THC or placebo. Collected blood samples at specific intervals and plasma prolactin levels during luteal and follicular phases of menses.	Assess acute effects of MJ smoking on prolactin levels in females	2-way analysis of variance with all prolactin levels decreased as a function of time	THC decreased serum prolactin levels during luteal phase ($P<0.05$)	MJ use while breastfeeding is contraindicated	II Quality: moderate Strength: moderate	Strength: Valid evidence to support provider recommendations Limitation: No control group No power analysis to assess sample size Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setti	Major Variables Studies and thei definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Merritt, T.A., Wilkinson, B., Chervenak, C. (2016). Maternal use of marijuana during pregnancy and lactation: Implications for infant and child development and their well-being. *Academic Journal of Pediatrics & Neonatology*. 2(1) 001-007.	Literature Review	Search engines and search terms not identified	Reviewed 1. MJ use during pregnancy 2. MJ and breastfeeding 3. MJ and epigenetic modifications 4. MJ and public health agencies 5. MJ and parenting skills	Reviewed MJ use during pregnancy, while breastfeeding and summarized ABM recommendations	N/A	Summarized ABM recommendations: 1. Counsel mothers who admit to MJ use 2. Counsel mothers with positive urine THC screen 3. Counsel on benefits of breastfeeding vs potential risk of TCH on developing infant 4. Lack of long term data but caution mothers ACOG recommendation to discourage MJ use due to lack of evidence. AAP recommendation that women using MJ should not breastfeed	ABM and ACOG counsel mothers and discourage use of MJ AAP- MJ using mothers should not breastfeed.	V Quality: high Strength: strong	Strength: Current review Limitation: Both pregnancy and lactation MJ exposure articles reviewed- difficult to analyze just lactation exposure Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variable Studies and the definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Metz, T.D., Stickrath, E.H. (2015). Marijuana use in pregnancy and lactation: a review of the evidence. *American Journal of Obstetrics and Gynecology*, 213(6), 761-778.	Systematic Review	Search Engines: PubMed and Embase database searches on 12/11/14 Search Terms: marijuana, marihuana, cannabinoids, pregnancy, lactation, outcomes, adverse perinatal outcomes, neurodevelopment MJ and fetal growth studies (n=20) MJ and preterm birth studies (n=3) MJ and congenital anomalies studies (n=7)	Reviewed 1. Effects of MJ legalization 2. Attitudes and beliefs 3. Screening and testing for MJ 4. Anesthetic considerations 5. Adverse perinatal outcomes 6. MJ and breastfeeding	Provide practicing clinicians with an understanding of existing literature and recommendations for managing women who use marijuana during pregnancy due to increasing prevalence	PRISMA	Several summary recommendations after literature reviewed Specific recommendations for breastfeeding mothers: MJ is passed to the neonate in breastmilk Possible adverse effects on early neurodevelopment Provide counseling but do not withdraw lactation support	MJ is passed to the neonate in breastmilk Possible adverse effects on early neurodevelopment Provide counseling but do not withdraw lactation support	I Quality= high Strength= strong	Strength: Current literature review Limitation: Reviews studies of varying methodological rigor Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Settin	Major Variables Studies and their defin	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Moreno, M., Escuredo, L, Munoz, R., Rodriguez, De Fonscca, F., Navarro, M., (2005). Long-term behavioural and neuroendocrine effects of perinatal activation or blockade of CB1 cannabinoid receptors. 16, 5-6. 423-430	Quasi-Experimental, randomized control study	Mother rats during pregnancy and lactation and their adult offspring. Mothers (n=17-24 per regimen) received oral dose of THC (0.1, 0.5, or 2 mg/kg) or vehicle (n=17-24) (0.1 mL of sesame oil)	1. Nursed offspring behavior (immobility, exploration. Grooming, locomotion). 2. Serum corticosterone, adrenocorticotrophin and prolactin levels	Extend previous results of on perinatal THC psychomotor activation and on alterations in dopamine agonist-induced motor behaviors in adulthood	One-way analysis of variance (ANOVA) for treatment and two-way ANOVA for treatment and sex interaction. Student-Newman-Keuls test for significant F values	Adult females exposed to THC had higher cortisol levels (P< 0.05), reduced locomotor behavior (P, 0.05) reduced at lower doses but increase with 2 mg/kg THC dose. Adult males exposed to THC had lower cortisol and mobility (P<0.05)	Long-term behavioral and neuroendocrine changes in adult animals exposed to cannabinoids perinatally	II Quality: high Strength: strong	Strength: Valid evidence to support provider recommendations Limitation: No control group No power analysis to assess sample size Cannot distinguish prenatal from postnatal THC exposure Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setti	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Mourh, J., Rowe, H. (2017). Marijuana and breastfeeding: Applicability of the current literature to clinical practice. *Breastfeeding Medicine*. 12(10). P 582-596.	Systematic Review	Maternal effects of THC (n=9) Transfer of THC into breastmilk and offspring (n=10) Effects of TCH on offspring (n=15) 34 articles reviewed: Maternal effects: 2 human, 7 animal. Transfer of THC: 4 human, 6 animal. Effects of THC on offspring: 3 human, 12 animal	Search was conducted 6/2017 Search engines: Google Scholar. University Library Search Engine, PubMed, Google, Elsevier Science-Direct, Springer Link Search terms: marijuana, CB, cannabis, breastfeeding, milk, human milk, breast milk, mother's milk, lactation, infant, prenatal effects, postnatal, development.	Review the available literature regarding marijuana use during lactation and to evaluate the risks of exposing infants to this medication in breastmilk	PRISMA	Cannabinoid (CB) receptors present by 19th week of gestation. THC prevents prolactin secretion. Cannabis suppresses immune system in adults. THC in MJ risen (1995-2014) from 3.96% +/- 1.82% to 11.84 +/- 6.66% for mother and child Conflicting data exists. 2-5% use during pregnancy. 15-28% of socioeconomically disadvantaged women in cities use. Increased use in first 6 months postpartum in adolescent pregnancy.	Human studies: THC transfers into milk. Current evidence for MJ use during lactation is limited and poor. MJ may have potential short and long-term consequence Mothers should refrain from MJ use while breastfeeding Impossible to make informed decision regarding MJ use while breastfeeding Counsel MJ using mother	I Quality: high Strength: strong	Strength: Recent review Valid evidence to support provider recommendations Limitation: Recommendation that it is impossible to make well-informed decision and that conservative approach is suggested however, then states that it is ultimately the mother's decision Clinically feasible to include in provider counseling and parental handout

Citation	Design/Method	Sample /Setti	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Murphy, L.L., Munoz, R.M., Adrian, B.A, & Villanua, M.A. (1998). Function of cannabinoid receptors in the neuroendocrine regulation of hormone secretion. *Neurobiology of Disease.* 5. 432-446.	Literature Review	Search engines and search terms not identified	Reviewed 1. Cannabinoid effects on the hypothalamic-pituitary-gonadal axis 2. Mechanism of cannabinoid action on the hypothalamic-pituitary-adrenal axis 3. Cannabinoid effects on prolactin secretion 4. Sites and mechanisms of cannabinoid action on prolactin secretion 5. Cannabinoid effects on other hormone	Effects of cannabinoids on neuroendocrine regulation of the gonadotropins, prolactin, stress hormones, growth hormone and thyroid hormones Role of cannabinoid receptors in the neuroendocrine regulation of hormone secretion.	N/A	THC inhibits gonadotropin, prolactin, growth hormone and thyroid-stimulating hormone. THC stimulated release of corticotropin	THC decreases prolactin	V Quality: high Strength: strong	Strength: Valid evidence to support provider recommendations Limitation: Age of review Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and thei definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Newsom, R.J., Kelly, S.J. (2008). Effects of perinatal delta-9-tetrahydrocannabinol exposure disrupts social and open field behavior in adult male rats. *Neurotoxicology and Teratology*. 30(3). 213-219.	Randomized Control Experimental Study	Pregnant female rats and their male offspring. Rats received 2 mg/kg SQ THC or vehicle twice daily from gestation thru day 22 and postnatally day 2 through 10 Mothers (n=8) Male offspring (n=8) Mothers for each regimen (n=8). Male offspring for each regimen (n=8).	Behavioral testing, open field activity, active social interaction and forced swim test in THC exposed rats	Socioemotional behavior in offspring adult male rats Effects on offspring due to THC exposure across the period equivalent to all three trimesters in human gestation	Descriptive statistics with standard error of the mean for each regimen at gestational day s 5, 10 and 21 Pregnant dams weight daily from gestation day 1 to 22. Offspring weighed daily from day of live 2, 10, 21, 30, 60 and 90.	THC group: pups had increased anxiety (P> 0.10), greater anxiety risk in adulthood (P>0.010) No effect on weight gain (P<0.001)	THC exposed pups show increased anxiety as adults	I Quality: high Strength: good	Strength: Valid evidence to support provider recommendations Limitation: Small sample size Cannot distinguish prenatal from postnatal THC exposure Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Perez-Reyes, M., Wall, M.E., (1982). Presence of delta 9 tetrahydrocannabinol in human milk. *New England Journal of Medicine*. 307,819-820.	Non-Experimental Qualitative Study	Breastfeeding mothers (n=2)	Mother1-smoked MJ once per day for 7 months Mother2-smoked MJ 7 times a day for 8 months Compared maternal plasma concentration of THC to maternal milk concentration of THC	Assessed THC presence in milk of lactation mother and its transfer to nursing infant	Method of data analysis not identified	8x accumulation of MJ in breastmilk	THC present in mother's milk and absorbed and metabolized by the nursing infant	III Quality: low Strength: poor medium	Strength: Valid evidence to support provider recommendations Limitation: Small Sample size Unable to replicate results Old study- THC concentration has changed Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variable Studies and the definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Ranganatham, M., Braley, G., Pittman, B., Cooper, T., Perry, E., Krystal, J., and D'Souza, D.C. (2009). The effects of cannabinoids on serum cortisol and prolactin in humans. *Psychopharmacology*. 203(4), 737-744.	Experimental Double-Blind Study	IV doses of delta 9 THC (0.0357, 0.0286 or 0.0714 mg/kg) or placebo for both regular MJ users (n=40) and nonusers. (n=36). No mention of sex of participants in either group	Cortisol and prolactin levels after IV injection of THC on chronic users and nonusers	Tested two previous hypotheses: 1. THC produced dose-related increased in plasma cortisol levels and decrease in plasma prolactin levels 2. Frequent MJ users showed altered baseline levels of cortisol and prolactin and blunted THC - induced changes of the two hormones	Descriptive statistical analysis by mean and standard deviation. Normality testing by Kolmogorov-Smirnov statistics and probability plots created	Normal distribution of cortisol levels between users and nonusers (P<0.0001) Frequent MJ users had lower baseline prolactin levels (p=0.007	THC caused lower baseline prolactin and increase in cortisol	I Quality: good Strength: moderate	Strength: Compared chronic MJ users with nonusers Limitation: Did not address occasional MJ user Did not address male/female participants Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /S	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Reece-Stremtan, S., Marinelli, K.A. (2015). ABM clinical protocol #21: Guidelines for breastfeeding and substance use or substance use disorder, Revised 2015. *Breastfeeding medicine.*	ABM Clinical Protocol	N/A	Guidelines for breastfeeding and substance use (methadone, buprenorphine, other opioids, marijuana, alcohol and tobacco)	Provide literature-based guidelines for evaluation and management of women with substance use or substance use disorder who are considering breastfeeding.	N/A	Breastfeeding mothers should be counseled to reduce or eliminate use of MJ. Possible long-term neurobehavioral effects from continued use.	Breastfeeding mothers should be counseled to reduce or eliminate their use of marijuana to avoid exposing their infants to this substance and advised of the possible long-term neurobehavioral effects from continued use. Data not strong enough to recommend not breastfeeding with any marijuana use, urge caution. Cannot base recommendation s sole on legality of MJ since it differs from state to state.	IV Quality=high Strength=strong	Strength: Well known professional body Limitation: Biased towards breastfeeding Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Schauer, G.L., King, B.A., Bunnell, R.E., Promoff, G., & McAfee, T.A. (2016). Toking, vaping, and eating for health or fun: Marijuana use patterns in adults, U.S., 2014. *American Journal of Preventative Medicine*. 50(1). 1-8.	Nonexperimental Retrospective Case Study	Data from Summer Styles (n=4,269). Survey of adults aged 18 or over, collected in 2014.	MJ use in the past 30 day(current) or ever	Prevalence and modes of current and ever MJ use Prevalence of medicinal and recreational MJ use	Bivariate and multivariant logistic regression	7.2% current MJ use 34.5% every used MJ 10.5% medicinal only use 53.4% recreational-only use 36.1% both recreational and medicinal use	Combined use of MJ most prevalent in US adults. Majority of MJ use recreational	III Quality: high Strength: moderate	Strength: Large, cross sectional sample size Limitation: US adults only (18 yrs and older) No delineation if pregnant nor nursing No male/female delineation Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Se	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Smith-Kielland, A., Skuterud, B., & Morland, J. (1999). Urinary excretion of 11-nor-9-carboxy-delta9-tetrahydrocannabinol and cannabinoids in frequent and infrequent drug users. *National Institute of Forensic Toxicology*. 23(5). 323-332.	Quasi-Experimental Study	Prison inmates in Norway between 1991-1994 (n=22)	Urine excretion and concentration of THC (ng/ml) and THC/creatinine ratios	Evaluate urine excretion profiles of THC and the ration of THC/creatinine ratios in known drug users	XY scatter plots of screen vs confirmation result analyzed by linear regression using Excel.	Mean urinary ½ life 1.3 days for frequent and 1.4 days for infrequent MJ users	Positive THC found in urine 4-5 days (THC concentration cutoff 10.3ng/ml) after exposure in infrequent users and 17,22 and 27 days in frequent users.	III Quality: poor Strength: low	Strength: Valid evidence to support provider recommendations Limitation: Self-reported MJ use, unable to calculate THC dose Unsure when MJ exposure took place No mention of IRB approval and study used vulnerable prison population

Citation	Design/Method	Sample /Setting	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Tennes, K., Avitable, N., Blackard, C., Boyles, C., Hassoun, B., Holmes, L., Kreye, M. (1985). Marijuana: prenatal and postnatal exposure in the human. 59. 48-60.	Experimental Prospective study	Children whose mothers belonged to a low-income prenatal clinic Children whose mothers consumed marijuana while nursing (n=27) Children whose mothers either consumed or did not consume marijuana while nursing (n=35)	Effects of MJ exposure on fetal growth and development at birth and 1 year of age	Neonatal Assessment: Brazelton Neonatal Behavioral Assessment Scale At 1 yr of age: Bayley Infant Scale of Mental and Motor Development and Behavior Checklist	Multiple regression analysis	Weaning age similar among both groups. Developmental measures did not differ Heavy MJ use associated with increased male offspring Increased use of pain meds in labor for MJ users No increased pregnancy or deliver complications with MJ users Increased use of alcohol and MJ but not nicotine and MJ during pregnancy.	Comparing MJ users and nonusers: No difference in growth and development at one year of age No difference in infant age at weaning	III Quality: good Strength: moderate	Strength: Prospective study looking at MJ exposure after 1 yr of age Limitation: Only low income participates No power analysis to assess sample size Unable to differentiate prenatal from postnatal MJ exposure Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Set	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Trezza, V., Campolongo, P., Cassano, T., Macheda, T., Dipasquale, P., Carratu. M., Gaetani, S., Cuomo, V. (2008). Effects of perinatal exposure to delta-9-tetrahydrocannabinol on the emotional reactivity of the offspring: A longitudinal behavioral study in Wistar rats. *Psychopharmacology*. 198. 529-537.	Quasi-Experimental Study	Mother rats received an injection of THC (2.5-5mg/kg) or vehicle from gestation day 15 to postnatal day 9 (n= ?)	Emotional reactivity of infant adolescent and adult rats in 4 areas (body weight, isolation-induced ultrasonic vocalizations, social interaction, elevated plus maze)	Investigated whether perinatal exposure to moderate doses of THC influenced the emotional reactivity of rat offspring	One-way ANOVA and Tukey's post hoc test	With 5 mg/kg THC, male offspring had decreased play ($P< 0.05$) and social interactions ($P<0.01$) (during adolescence and increased anxiety in adulthood.($P<0.05$)	Moderate doses of THC perinatally can affect brain maturation and long-lasting neurodevelopmental alterations	III Quality: moderate Strength: moderate	Strength: Valid evidence to support provider recommendations Limitation: Unknown number of participant rats No power analysis to assess sample size Age of study Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /Setting	Major Variabl Studies and th definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Tyrey, L., Murphy, L.L. (1988). Inhibition of suckling-induced milk ejections in the lactating rat by delta 9-tetrahydrocannabinol. *Endocrinology*. 123(1), 469-472.	Two Group RCT with Posttest Only Design	Lactating rats (10-16 days postpartum) and pups THC (0.5mg/kg) exposed pups (n=8) Vehicle exposed pups (n=8) Oxytocin (0.5mU) after their dose of THC exposed pups (n=5)	Milk ejection intervals	Determined the effect of THC on suckling-induced oxytocin release	Analysis of variance and Scheffe test.	THC group had longer delay before initial ejection of milk ($P<0.01$) and between further ejections. ($p<0.05$)	THC interferes with oxytocin release in response to suckling Proposed that THC prevented oxytocin secretion via the posterior pituitary	I Quality: high Strength: moderate	Strength: Valid evidence to support provider recommendations Limitation: No power analysis to assess sample size Animal study-may not translate to humans Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /S	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
United States National Library of Medicine Drug and Lactation Database [Lactmed] (2018).	Systematic Review	N/A	34 articles peer reviewed Search engines: PubMed, EMBASE, Web of Science, BIOSIS Updated monthly	Summary of published literature for marijuana and breastfeeding	PRISMA	THC is excreted into breastmilk in small quantities. THC is very fat soluble and persistent in body fat of users. THC slowly released over days or weeks. THC estimated daily intake for infant was 8 mcg/kg or 2.5% of weight-adjusted maternal dose	1. Cannabis use should be minimized or avoided, may impair parental judgement and child care abilities. 2. Cannabis should not be smoked by anyone in the vicinity of infants due to secondhand exposure. 3. Encourage mothers who use cannabis to continue to breastfeed and reduce or abstain from cannabis use and minimize smoke exposure.	I Quality: high Strength: strong	Strength: Expert review Current comprehensive review Limitation: Updated monthly, data constantly changing and may miss information based on time of search Clinically feasible to include in provider counseling and parental handout

Citation	Design/Method	Sample /Settin	Major Variable Studies and thei definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
Vilela, F.C., Giusti-Paiva, A. (2014). Cannabinoid receptor agonist disrupts behavioral and neuroendocrine responses during lactation. *Behavioral Brain Research*. 263, 190-197.	Two Group RCT with Posttest Only Design	Nursing rats (n=?) received injection of cannabinoid receptor agonist (1 or 3 mg/kg) or vehicle 1ml/kg) pups (male n=4, female n=4)	Cannabinoid receptor agonist (WIN55,212-2) and its effect on maternal care, maternal aggression, open field test	Behavioral and neuroendocrine responses during lactation	Descriptive statistics with ANOVA Newman-Keuls post test	Cannabinoid receptor agonist group had lower maternal oxytocin concentrations (pp<0.05), reduced weight gain in pups (p<0.05) less maternal care (pup retrieval and latency to carry p<0.01, decreased licking time p<0.05) and reduced aggressive anxiety (pp<0.05) No difference in exploratory activity (P<0.001). .	Behavioral changes in lactating rats given cannabinoid receptor agonist may be related to disruption in neuroendocrine control of oxytocin secretion	I Quality=good Strength=moderate	Strength: Valid evidence to support provider recommendations Limitation: Small sample size Animal study- may not translate to humans Clinically feasible to include in provider counseling

Citation	Design/Method	Sample /S	Major Variables Studies and their definitions	Outcome Measurement	Data Analysis	Findings	Conclusion	Level of Evidence	Quality of Evidence: Critical worth to practice
American Academy of Pediatrics [AAP] (2012). Breastfeeding and the use of human milk. *Pediatrics.* 129(3). 598-601.	Policy Statement/ Expert Opinion	N/A	Reviews of: 1.epidemiology of breastfeeding rates 2.Infant outcomes of breastfeeding (methodologic issues, respiratory tract infections and otitis media, GI tract infections, necrotizing enterocolitis, sudden infant death syndrome and infant mortality, allergic disease, celiac disease, inflammatory bowel disease, obesity, diabetes, childhood leukemia and lymphoma, neurodevelopmental outcomes) 3. Preterm infants 4. Maternal outcomes 5. Economic Benefits 6. Duration of exclusive breastfeeding 7.Contraindications to breastfeeding 8. Maternal diet 9. Maternal medications 10. Hospital routines (pacifier use, vitamins and mineral supplements) 11. Growth 12. Role of the pediatrician 13. Business case for breastfeeding	N/A	N/A	Groups MJ with other “street drugs” (PCP, cocaine) and states MJ use by breastfeeding mothers is of concern, particularly with regard to the infant’s long-term neurobehavioral development. .	MJ use while breastfeeding is contraindicated	IV Quality: high Strength: medium	Strength: Well known professional body that is frequently cited as a clinical benchmark Limitation: Bases MJ as a contradiction to breastfeeding on one research article (Garry, 2009) Clinically feasible to include in provider counseling

Table 2

Synthesis Table

	Level I	Level II	Level III	Level IV	Level V
1				X	
2				X	
3				X	
4		X			
5		X			
6			X		
7			X		
8			X		
9					X
10					X
11					X
12		X			

13		X			
14					X
15			X		
16					X
17					X
18			X		
19					X
20					X
21					X
22			X		
23					X
24	X				
25		X			
26					X
27	X				
28		X			
29	X				

30					X
31	X				
32			X		
33	X				
34				X	
35			X		
36			X		
37			X		
38			X		
39	X				
40	X				
41	X				

Legend of Levels of Evidence

Level I

Experimental study, randomized controlled trial (RCT)

Systematic review of RCTs, with or without meta-analysis

Level II

Quasi-experimental study

Systematic review of a combination of RCTs and quasi-experimental, or quasi-experimental studies only, with or without meta-analysis

Level III

Non-experimental study

Systematic review of a combination of RCTs and quasi-experimental, or non-experimental, or non-experimental studies only, with or without meta-analysis.

Qualitative study or systematic review, with or without meta-analysis

Level IV

Opinion of respected authorities and/or nationally recognized expert committees/consensus panels based on scientific evidence.

Includes: clinical practice guidelines and consensus panels

Level V

Based on experimental and non-research evidence.

Includes: literature reviews, quality improvement, program or financial evaluation, case reports, opinion of nationally recognized expert(s) based on experiential evidence

From Johns Hopkins nursing evidence-based practice: Models and Guidelines

Dearholt,S., Dang, D., & Sigma Theta Tau International. (2012). *Johns Hopkins Nursing Evidence-based Practice: Models and Guidelines.*

Legend of Studies:

1. American Academy of Pediatrics [AAP] (2018). Marijuana use during pregnancy and breastfeeding: Implications for neonatal and childhood outcomes. *Pediatrics.* 142(3). 1-8

2. American Academy of Pediatrics [AAP] (2012). Breastfeeding and the use of human milk. *Pediatrics.* 129(3). 598-601.

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