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The Potential Benefits and Risks of Antidepressant, Antipsychotic and/or Mood Stabilizing Medications Use in Pregnancy: A Critical Review of the Literature

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THE POTENTIAL BENEFITS AND RISKS OF ANTIDEPRESSANT, ANTIPSYCHOTIC, AND/OR MOOD STABLIZING MEDICATION USE IN PREGNANCY: A CRITICAL REVIEW OF THE LITERATURE.

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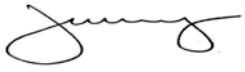
Second Reader Signature: ___  _____

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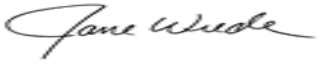
Director of Graduate Nursing Program Signature: ____  _____

Abstract

Background: Medication use in pregnancy walks a fine line between safety of the mother and adverse effects in the developing fetus. Medications are prescribed to either help the mother maintain mental stability or they are discontinued out of fear of fetal harm. Many providers hope that the shift in hormones during pregnancy will fulfill the medications requirement in the non-pregnant state but this is not always the case. Is a discontinuation in medications upon a positive pregnancy test warranted?

Purpose: To determine if antipsychotics, mood stabilizers, and antidepressants should be continued or discontinued during pregnancy or if they negatively impact the fetus/neonate development, maternal wellbeing, and/or maternal-fetal interactions.

Results: Continuation of medications has a high correlation with adverse fetal effects as well as adverse maternal metabolic syndromes. Discontinuation of medications has a high correlation with maternal relapse and adverse fetal effects due to maternal illness. More research is needed to be able to fully assess the safety of antidepressants, antipsychotics and mood stabilizers in pregnancy.

Conclusion: Midwifery care is helpful to patients in understanding all their options while taking medications in the antidepressant, antipsychotic, and mood stabilizing families during pregnancy. Each situation and patient need to be treated individually and care needs to be patient based. Midwives must educate patients and help them to make an informed choice as to continuing or discontinuing psychotropic medications during pregnancy.

Implications for Research and Practice: Careful consideration needs to be given based on each diagnosis and situation. Some situations may call for a discontinuation of medications while

others indicate continuation for best outcomes. Education and current research is more important than fear of liability and current trends.

Keywords: antipsychotics, antidepressants, mood stabilizers, pregnancy, maternal effects, fetal effects, neonatal effects, adverse effects, drug use, fetal outcomes, maternal outcomes, mental illness, medications

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Chapter I: Introduction

Pregnancy can be one of the most meaningful and life fulfilling experiences for a woman and family when they are ready for a child and even sometimes when they are not. However, pregnancy and fetal development can also be an overwhelming experience even for a healthy, mentally stable woman. For a woman with mental illness, the experience can be much more complicated. Unfortunately the onset of mental illness most commonly occurs in women ages 20-30 (National Alliance of Mental Illness, 2015), which coincides with a woman's child bearing and child rearing years. With the added complication of mental illness and the high risk medications that women may be required to take daily, pregnancy can be an overwhelming, terrifying, and unpredictable experience.

Many women with mental illness do not understand the medications that they are required to take each day nor do they understand the possible effects that these medications could have on their developing fetus. Individuals with mental illness such as bipolar disorder, schizophrenia (paranoid and nonspecific), and personality disorders, are required to take medications daily to actively decrease their symptoms and reduce the risk of a threat of harm to themselves or others within the community. However the medications that are most commonly prescribed to effectively treat these disorders by keeping the patient symptoms under control have the ability to negatively affect the developing fetus while benefitting the mother's mental health status. In past decades physicians have routinely taken pregnant women off of antipsychotics, mood stabilizers, and even some antidepressant medications at the woman's first perinatal visit hoping that pregnancy hormones would take over and stabilize the woman during pregnancy, thereby protecting the fetus from adverse medications side effects (Galbally, Snellen, Walker, & Permezel, 2010). Unfortunately, relying on pregnancy hormones alone does not

always keep the mother's symptoms at bay, leading some women to find themselves in a destructive, decompensating spiral and the medical community wondering: how can we treat mental illness during pregnancy? And most importantly how do we do this safely? Perinatal care is primarily focused on keeping mother and baby happy, healthy, and safe. For patients suffering from mental illness, how can we ensure a continued focus on happiness, health, and safety?

Statement of Purpose

Although the popular assumption by many physicians and midwives is to discontinue antipsychotics, mood stabilizers, and some forms of antidepressants to prevent fetal harm, there are no definitive sources to support this approach. On the other hand there are also no definitive sources to show that it is better to allow women to decompensate causing many more complications. The purpose of this critical review of the literature is to determine if antipsychotics, mood stabilizers, and antidepressants should be continued or discontinued during pregnancy or if they negatively impact the fetus/neonate development, maternal wellbeing, and/or maternal-fetal interactions.

Need for the Critical Review of the Literature

Use of antipsychotic medication prescriptions are on the rise within the pregnant population (Vigod, Gomes, Wilton, Taylor, & Ray, 2015). This increase is most notably due to an increased "use of atypical antipsychotics in the treatment of bipolar and major depressive disorder" (Vigod et al, 2015, p 1). With this increase that has effects on both mother and the developing fetus, there is a need to review and understand the evidence surrounding the use of these medications in pregnancy. Most studies have spent the majority of their focus on older generation antipsychotic medications, however, many psychologists are now prescribing atypical

antipsychotics. This change has made previous research less applicable as providers are not reviewing the risks and teratogenic effects these medications have on a developing fetus and maternal complications in pregnancy (Petersen, McCrea, Osborn, Evans, Pinfold, Cowen, Gilbert & Nazareth, 2014). This lack of guidance and education for women of child bearing age is concerning as many individuals with mental health disorders tend to participate in high risk behaviors. Such behaviors could include sexual promiscuity, prostitution, or even illegal drug use making sexuality and contraceptive education a priority. The lack of education by the psychiatric providers to their patients may be the first gap in care, leaving the bulk of education to the midwife after pregnancy has occurred. The decision then needs to be that of a mutual one between the patient and the midwife. Finding the best balance between keeping the mother from relapse and keeping the fetus healthy is key to overall care when looking at antepartum women with mental health disorders using antipsychotics, mood stabilizers, and antidepressant medications.

The midwife's overall goal is to help healthy low risk women to maintain their health and mental wellbeing in order to have a healthy pregnancy and raise a healthy baby. Medications need to be evaluated but not necessarily discontinued or changed. Evaluating the woman for mental stability and insight into her mental health disorder is an important factor in determining what steps need to be taken to maintain the patient's physical and mental wellbeing and ensure healthy fetal growth and development. Midwives need to be knowledgeable about what adverse effects antipsychotics, mood stabilizers, and antidepressants can have on fetal growth and development, but also what negative impacts the discontinuation of these medications could have on the mother during both antepartum and postpartum period.

In addition to the knowledge of the midwife and collaboration with the patient, more research on how antipsychotics, mood stabilizers, and antidepressants impact fetal wellbeing in humans is needed to be able to accurately determine if and how these medications are negatively impacting fetal development and maternal-fetal interactions. Or, is mental illness itself a main contributing factor to pregnancy and fetal complications and development?

Significance to Nurse-Midwifery

Nurse midwives are at the forefront in obstetric and gynecological care of low risk healthy women; "midwives can offer a cost-effective way of providing safe and excellent maternity care" (Budin, 2015, p.76). This population includes women with mental illness and other disorders. Unfortunately, for women many mental illnesses and their symptoms occur in the mid-to-late 20's. At this point in a woman's life they may not fully understand their mental illness, lacking insight to the situation that presents itself, thus making pregnancy and treatment of symptoms difficult and trying. Women are going to continue to get pregnant while on medications to treat schizophrenia, bipolar disorder, and depression. Women are going to continue to present in clinic with a viable pregnancy and an active prescription of antipsychotics, mood stabilizers, and antidepressants. It is ultimately up to the midwife to refer to the psychiatrist, reevaluate medications, or adjust antepartum cares accordingly.

An example includes the medication, lithium which is used to treat mania and bipolar disorder. According to James et al. (2009), lithium "increases the risk of the cardiac defect Ebstein's anomaly; approximately one in 500 births are affected, a 40-fold increase over the background rate" (p. 137). Midwives should be just as knowledgeable about medications for mental health as physicians because mental health patients are not classified as high risk and fall into the population of clients that midwives treat. Midwives are fully capable of caring for

pregnant women with a mental health diagnosis. Furthermore, midwives caring for women before pregnancy should be "taking steps to warn patients of the teratogenic risks, prescribing folate when appropriate, and discussing contraception" (James et al., 2009, p. 138) to ensure awareness in this patient population. Mental illness is and will continue to be a complication of pregnancy. Understanding when it is best to discontinue medications or continue medication in pregnant women is key to maintaining effective patient care. Midwives must weigh the benefits and risks for both mother and child when looking at negative fetal effects, negative maternal effects, and negative effects after birth.

Theoretical Framework

The theoretical framework that was chosen for this critical review of the literature is the Theory of Human Caring/Caring Science by Jean Watson. This theory looks at how effective antepartum care medically, psychologically, and fetal surveillance can prevent complications in the fetus and developing child after birth in regards to physical and mental development. Jean Watson's Theory of Human Caring/Caring Science shows how adequate care of patients can help both the patient and unborn child prosper in growth and development.

Jean Watson's Theory of Human Caring/Caring Science is based on the love and moral values of the healthcare professional showing that one must go past themselves – giving above and beyond to ensure the best possible outcome for their patient (Wagner, 2010). This applies mainly to the prescriber. When a prescriber is recommending antipsychotics/mood stabilizers/antidepressants to women of child bearing age they need to ensure that adverse effects to fetal development are reviewed as well as a full understanding of pregnancy prevention and contraceptive use. The Theory of Human Caring/Caring Science has seven main components that make up the theory overall, including 1: moral commitment to protect and enhance human

dignity, 2: respect/love for the person, 3: caring consciousness of the situation, 4: heart centered care of mind body and spirit, 5: inner harmony, 6: caring conscious intention, and 7: authentic presence (Wagner, 2010, p. 1). Once pregnancy has occurred the mother needs to be adequately informed of all her options and she needs to understand the situation in full (component one). Once all decisions have been made, the nurse midwife is to continue to support and encourage the mother to her full potential (component two and four). Many mental health patients lack the insight into their illness and may not understand what is required for child bearing and rearing. Ensuring the mental health diagnosis is in the forefront of a patient's antepartum care is important when making decisions to continue or discontinue medications that could negatively impact the developing fetus (component three, four, and five). Decisions such as these need to be made with the patient's input and understanding of both the benefits and risks of discontinuing or continuing a medication regime that includes antipsychotics, mood stabilizers and or antidepressants (components five, six and seven).

Summary

As the use of atypical antipsychotics, mood stabilizing, and antidepressant medication increases, further investigation is required to ensure the best possible outcome for the mother and developing fetus. Preventing maternal decompensation and ensuring proper fetal development is the ultimate objective of both the midwife and all other professionals involved. Midwives must be knowledgeable regarding risks and benefits to both the mother's metal health and fetal wellbeing when faced with the decision to either discontinue or continue high risk medications such as antipsychotics, mood stabilizers, and antidepressants.

Chapter II: Methods

This chapter will address the critical review of the literature and the methods used in the review process. Literature includes studies related to antipsychotics, mood stabilizers, and antidepressant use in pregnancy, adverse effects on birth outcomes with medication use, and relapse in pregnancy after discontinuation of medications during pregnancy were all included. Criteria for exclusion or inclusion of research will be considered. The studies that were used will be reviewed and lastly, the evaluation process will be explained.

Search Strategies

The purpose of this critical review of the literature was to understand the maternal and neonatal complications in relation to the continuation or discontinuation of maternal antipsychotic, mood stabilizer, and or antidepressant use during pregnancy. Research was found for this topic using search engine databases including the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Elton B Stephens Company (EBSCO) and The National Center for Biotechnology Information (NCBI) that led to PubMed.

The initial search through CINAHL used key words such as “antipsychotics” and “pregnancy” and “antipsychotics” and “fetal development.” The results showed 52 items published between the years of 2000 and 2015. The second search through CINAHL used keys words such as “mood stabilizers” and “pregnancy.” This search showed 23 items published between the years of 2000 and 2013. The final search on CINAHL used key terms such as “antidepressants” and “pregnancy” along with “antidepressants” and “fetal development.” This search showed 270 items between the years of 1995 and 2015. The next search engine database that was used was EBSCO. Key terms used to limit the number of information sources were

terms such as “Maternal Antipsychotic Use” and “Pregnancy”; “Maternal Antipsychotic Use” and “Fetal Development”; “Maternal Mental Illness” and “Fetal Development”; “Maternal Mental Illness” and “Pregnancy”. These searches revealed a total of 513 items between the years of 1975 and 2015. The final search engine database that was used was NCBI which led to PubMed database. Key words such as “Mental Health” and “Pregnancy”; “Antidepressants” and “Pregnancy”; “Mood Stabilizers” and “Pregnancy”; “Schizophrenia” and “Pregnancy”; and “Schizophrenia” and “Fetal Development.” These searches revealed a total of 9,609 items between the years of 1959 and 2015 overall. This time frame was then limited to more current research for years 2000-2015.

After reviewing and searching the literature found on CINAHL, EBSCO, and PubMed subject terms such as “Maternal Mental Health”, “Fetal Development”, “Pregnancy”, “Antipsychotic Use”, “Mood Stabilizers”, “Antidepressants”, and “Schizophrenia Drug Therapy”, were the main subject terms used to reduce the amount of items by almost half on all search databases. The search year was also limited to the year 2000 to 2015, greatly reducing items to a total of 348 items on CINAHL, 349 items in EBSCO and 5,403 items in PubMed. In addition to the research search engine databases that were used, the reference lists within the research items analyzed generated additional items for review. Research was then limited to research that focused on maternal and fetal outcomes after exposure or continuation of medications such as antidepressants, antipsychotics and mood stabilizers. Research that focused on maternal conditions treated with these medication for other reasons besides mental health complications were excluded thus limiting the research found. This criteria limited search within the databases to 98 items on CINAHL, 116 items in EBSCO and 124 items in PubMed.

Exclusion or Inclusion of Research

When reviewing the literature, many articles did not pertain to the purpose of this critical review nor to the critical review question. Articles that referred to epileptic medications and fetal complications were excluded as this did not pertain to the review question. Other items that were excluded were items that referred to only maternal complications as they did not answer the review question such as comorbidities that need additional medical treatments. Lastly, research that was not of relevant timing was excluded in the matrices as it is no longer applicable to the integrity of this critical review. Items that were included in the matrices for this critical review of the literature are non-experimental, meta-analysis, non-randomized controlled, quantitative, and qualitative research studies that were categorized in the high or good quality of research according to the *John Hopkins Level and Quality* review (Dearholt, & Dang, 2009). Studies that considered maternal and perinatal outcomes with maternal antipsychotic use, antipsychotic use in pregnancy and safety, SSRI antidepressant use and fetal effects, mood stabilizers and the teratogenic effects on fetal development and maternal wellbeing, antenatal monitoring for bipolar and schizophrenic women and relapse in mothers with antidepressant or antipsychotic discontinuation during pregnancy were included in the final matrix as seen in chapter 3.

Studies Selected

The initial search yielded 6,100 studies and the final search after the exclusion criteria was implemented yielded 388 studies that related to maternal antipsychotic or mood stabilizer or antidepressant use in pregnancy, maternal antipsychotic or mood stabilizer or antidepressant use and fetal development, mental illness and pregnancy or fetal development, and discontinuation of schizophrenia medications during pregnancy. These studies were reviewed and sorted by

relevance and current data. Studies were sorted in reference to the type of research, quality and expert opinion, the John Hopkins level of research and lastly how the study pertained to the review subject question thus obtaining the final 25 studies used in this capstone. Each study was assessed for its relevance to the review question: to determine maternal and neonatal complications in relation to the continuation or discontinuation of maternal antipsychotic, mood stabilizer, and/or antidepressant medication use during pregnancy. Of the 25 items that were included for the final review of the literature, fifteen were non-experimental, four were experimental, and six were grounded theory.

The 25 final items that were chosen for this critical review of the literature are organized by matrix in chapter three. The matrices are organized by headings which include: citation, sample, purpose, design, measurement, result/conclusion, recommendations and John Hopkins level and quality. Each item was carefully chosen and appropriately organized to ensure the critical literature review could be effectively obtained.

Evaluating the Research

In order to accurately evaluate the research used in this critical review of the literature, the *Johns Hopkins Nursing Evidence-Based Practice: Model and Guidelines* (2012) were used. With this model, research evidence was graded by both quality and level. According to the *Johns Hopkins Nursing Evidence-Based Practice* quality and levels, quality is categorized by high, good and low/poor.

High quality is defined as research that has "consistent results, sufficient sample size, adequate control, and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence" (Dearholt & Dang,

2012, p. 108). Good quality is defined as "reasonably consistent results, sufficient sample size, some control, and fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence" (Dearholt & Dang, 2012, p. 108). Low or poor quality is defined as "little evidence with inconsistent results, insufficient sample size, and conclusions cannot be drawn" (Dearholt & Dang, 2012, p. 108). According to *Johns Hopkins Nursing Evidence-Based Practice* the strength is given a rating determined by levels.

The level of research evidence is broken down into three levels (I, II, III). Level I is "Evidence obtained from an experimental study, randomized controlled trial (RCT), or systematic review of RCTs, with or without meta-analysis" (Dearholt & Dang, 2012, p. 108). Level II is "evidence obtained from a quasi-experimental study or systematic reviews of a combination of RCTs and quasi-experimental studies, or quasi-experimental studies only, with or without meta-analysis" (Deerholt & Dang, 2012, p. 108). And lastly Level III is defined as "evidence obtained from a quantitative non-experimental study; systematic review of a combination of RCTs, quasi-experimental, and non-experimental studies, or non-experimental studies only with or without meta-analysis; or qualitative study or systematic review of qualitative studies, with or without a meta-synthesis" (Deerholt & Dang, 2012, p. 108).

The evidence that was used for this critical review of the literature was based upon the purpose of the evidence, the data collection method, the evidence sample size, the design of the study, and the quality of evidence based on the *John Hopkins Nursing Evidence-Based Practice* quality and level. They evidence in the matrices hold 14 items of good quality and 11 items of high quality. Evidence of low or poor quality was excluded from the critical review of the literature.

Summary

The effects of antipsychotics, mood stabilizers, and antidepressants on fetal development and maternal wellbeing are not fully understood. It is difficult to understand the effects of medication use in pregnant women as many times this can be unethical and complicated research to complete. The 25 studies used for this critical review of the literature in the final matrix focus on understanding and determining the best recommendations from both obstetrician/gynecological, midwifery and psychiatrists' point of view. This chapter reviewed evaluation and search strategies that were used to determine the most accurate and up to date information for this critical review of the literature.

Chapter III: Literature Review and Analysis

This chapter illustrates a review and analysis of the literature related to determining maternal and neonatal complications in relation to the continuation or discontinuation of maternal antipsychotic, mood stabilizer, and or antidepressant medication use during pregnancy. Mental illness in child bearing age is very common and an ongoing concern with psychiatrists, obstetricians, and gynecological professions. Determining the best treatment for the most optimal outcome for the mother and fetus and /or infant is the ultimate goal in mental illness and pregnancy.

Matrix Results

For this critical review of the literature, 25 pieces of evidence in the form of research were used. The evidence was organized via matrix. The form of maternal and/or neonatal complications in relation to the continuation or discontinuation of maternal antipsychotic, mood stabilizer, and/or antidepressant medication use during pregnancy and its evidence were included in this review. The Matrix shows information that was deemed beneficial to answer the research question. The research purpose is: to determine if antipsychotics, mood stabilizers, and antidepressants should be continued or discontinued during pregnancy or if they negatively impact the fetus/neonate development, maternal wellbeing, and/or maternal-fetal interactions. Below the information is summarized based on maternal and fetal effects with maternal continuation or discontinuation of the medications chosen.

Maternal Effects

The research found that with continuation of antipsychotic medications during any stage of pregnancy it put mothers at an increased risk of roughly 50% to obtain gestational diabetes

(Boden & et al., 2012). It was also shown that continuation of antipsychotics put mothers at a significantly higher increase for instrument vaginal delivery and cesarean sections (Sadowski & et al., 2013). Antipsychotic use in pregnancy was also greatly linked to higher incidence of maternal hypertensive disorders, preterm deliveries, placental abruption, induction of labor, and readmission to the hospital for medical purposes after delivery (Vigod & et al., 2015). The only benefit to discontinuing medications during pregnancy is that the teratogenic risk to the fetus is avoided. There were no other benefits for the mother if medications were discontinued during pregnancy. Multiple studies (Hanley & et al., 2014, Kulkarni & et al., 2008 and Galbally & et al., 2010) showed that maternal discontinuation of antipsychotics was not proven to be safe as mothers were at higher risk for decompensation of mental health and a relapse of symptoms would occur. Mothers had a very significant incidence of readmission to the hospital for psychiatric decompensation in about 12 months after delivery; it is unclear when mental health symptoms began to reappear in these cases (Kulkarni & et al., 2014).

Mothers that continued to use mood stabilizers had no significant complications in pregnancy in the evidence for this critical review. Mothers with bipolar disorder, regardless of medication continuation or discontinuation showed higher rates of preterm delivery, cesarean section instrumental vaginal delivery and induction (Boden & Et al., 2012). However mothers that discontinued medication for mood stabilization had a very high risk of maternal decompensation or deterioration in mental stability resulting in the lack of ability to care for child after birth (Galbally, Roberts, & Buist, 2010).

When looking at antidepressant use during pregnancy at any stage the evidence revealed no significant maternal complications if the medications were continued. However when looking at discontinuation of medications mother were found to be five times more likely to experience

mental health decompensation that required hospital admission (Cohen & et al., 2006). Over all the evidence suggest that with mothers using antipsychotics, mood stabilizers, or antidepressants the provider should examine each benefit and risk to either continuing or discontinuing the medications.

Fetal Effects

When examining fetal health and risks, the evidence is much more concerning. When looking specifically at maternal antipsychotic use during any stage of pregnancy the evidence shows there is a great increase in risk of fetal harm. Lithium, carbamazepine, and lamotrigine were shown to cause major structural abnormalities in the fetus such as neural tube, cardiac, facial, and urogenital defect (Galbally & et al., 2010). Other complications with higher rates of incidence with fetal exposure to antipsychotics of any classification are floppy infant syndrome, severe neonatal hypoxemic encephalopathy, neural tube defects, fetal malformation typology and limb malformation (Gentile, 2010). Neonates had higher rates of admission to the NICU for respiratory complications and or failure to thrive after exposure in pregnancy (Kulkarni & et al., 2014). Exposure in pregnancy also showed an increase rate of infants that were large for gestational age, had withdrawal symptoms such as seizures and even higher rates of intraventricular hemorrhage (Vigod & et al., 2015). Infants that were followed after birth showed developmental delay in the social, cognitive, and emotional regard (Wichman, 2009). If mothers discontinued medications there were no adverse fetal effects.

Mood stabilizing medication showed a significant increased risk for congenital malformations, infants that are large for gestational age, microcephaly, withdrawal symptoms such as seizures, hypertonic, hypoglycemia, and an increased risk for Ebstrin anomaly (Galbally, Roberts & Buist, 2010). Infants also showed increased risk for cardiac defects and severe

weakness and developmental delays (Kallen & et al., 2013). The evidence showed that with discontinuation of mood stabilizing medication before pregnancy or after pregnancy has been confirmed, there was an increased risk of low APGARS, increased fetal hypoglycemia and infants found to be small for gestational age (Boden & et al., 2012).

For antidepressant use in pregnancy and fetal complications the evidence was conflicting. Discontinuation of antidepressants during pregnancy was not found in the research. One piece of evidence discussed continuation and discontinuation of antidepressants in the first trimester of pregnancy and showed no difference in the major congenital anomalies found in infants born to women with major depressive disorders or severe anxiety (Ban & et al., 2014). SSRI's or selective serotonin reuptake inhibitors (SSRIs) are commonly used in pregnancy; however this medication family is shown to have adverse fetal effects. SSRIs used in the first trimester of pregnancy has been linked to a small increased risk for omphalcele, craniosynotosis, congenital heart defects, conotruncal defects (Louik & et al., 2007). SSRIs have also been linked more significantly to congenital malformations and cardio vascular defects (Reis & Källén, 2013). There is no increase in the risk of spontaneous abortion but there is a significant risk in preterm deliveries, infants that are small for gestation age, intrauterine growth restriction and low APGAR scores (Ross & et al., 2013). These risks need to be known and risk needs to be assessed when decisions regarding medication regimen during pregnancy are assessed.

Matrix Synthesis

The 25 research articles used as evidence for this critical review of the literature are found in the matrix below and are categorized with the following headings: citation, purpose, sample, design, measurement, results/conclusions, recommendations, Johns Hopkins quality and level. The research evidence was evaluated by purpose and major findings as well as its

relevance to the review questions: to determine if antipsychotics, mood stabilizers, and antidepressants should be continued or discontinued during pregnancy or if they negatively impact the fetus/neonate development, maternal wellbeing, and/or maternal-fetal interactions. Research evidence was not included if it was determined to be non-peer reviewed, had a small sample size, and/or had low or poor quality rating.

Critique of Strengths & Weaknesses

While performing a critical review, strengths and weaknesses of the literature become apparent. One of the strengths noted in this critical review were large sample sizes. Many research studies were guided by chart review of mass data bases putting sample size in the one to ten thousands making the study more reliable and of better quality. Other strengths included surveying psychiatrists and patients, obtaining personal information from the source such as doctors and patients in order to better determine factors such as cognitive effects and patient understanding. Multiple levels of research were used such as qualitative and quantitative, non-experimental, meta-analysis, randomized, non-randomized, and cohort studies. All research evidence was of high or good quality based on the *Johns Hopkins Nursing Research Evidence* quality guide (2012). Most research evidence was published within the past five years with the exception of 7 out of 25 studies, however, all research evidence was published within the last ten years. The determination for inclusion of the research evidence was that of clarity, knowledge, effectiveness, and accuracy of the information each study provided.

Weaknesses of the studied literature lay mainly in the results and recommendations of much of the research evidence. Many studies ended with inconclusive results. It is accurate to state that more research is needed to determine if an antipsychotic, mood stabilizing, or antidepressant medication is safe during pregnancy or if it will have adverse effects on the

mother or fetus. Many showed adverse effects on the mother if medications were discontinued or adverse effects in the fetus if medications were continued. However, many individuals with mental health disorders also have co-occurring disorders such as health and hygiene neglect, drug abuse, use of tobacco and/or alcohol, promiscuous behaviors, history of or current sexually transmitted infections/diseases which could be the cause of poor outcomes and or adverse fetal effects. These stipulations and co-occurring illnesses were not always covered or addressed in the research evidence. When medications were discontinued, many women stopped receiving prenatal care making them hard to follow for this particular research. Also many women stopped refilling their prescriptions on their own without informing their physician in fear of fetal harm. This lack of self-care made it hard to continue to follow women making gaps in a starting and finishing sample sizes when research was completed.

Matrix

Below is the research evidence used for this critical review of the literature to answer the topic question of determining if antipsychotics, mood stabilizers, and antidepressants should be continued or discontinued during pregnancy or if they negatively impact the fetus/neonate development, maternal wellbeing, and/or maternal-fetal interactions as discussed above in the form of a matrix with 25 articles included.

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Ban L., West J., Gibson J. E., Fiaschi L., Sokal R., Doyle, P., Hubbard, R., Smeeth, L., & Tata, L. J. (2014) First trimester exposure to anxiolytic and hypnotic drugs and the risks of major congenital anomalies: a United Kingdom population-based cohort study. *PLOS ONE 9*(6): e100996. doi:10.1371/journal.pone.0100996	To determine if anxiolytic and hypnotic drugs during the first trimester of pregnancy increase the risk of major congenital anomalies (MCA).	Singleton live births from women ages 15-45 y/o between 1999-2010. 495 general practices were used from THIN database to find the sample population. All patients were anonymizes and data was retrieved from retrieval sites. Ethical approval from medical research ethics committee. This excluded women with serious mental illness and women that used antiepileptic drugs leaving total of 3,218 children.	Cohort-study Meta-analysis Non-experimental	Data retrieved from The Health Improvement Network (THIN) (mother and children's' medical records including, health, pregnancy, pharmacology etc.) Over all looking at benzodiazepine and non – benzodiazepine used during the first trimester of pregnancy (first 12 weeks of pregnancy)	Of the total 374,196 live singleton births 2.7% had major congenital anomalies 19,193 children born to mothers with anxiety or depression but not medicated and 3,128 children with first trimester exposure to anxiolytic or hypnotic drugs. Major congenital anomalies (MCA) was consistent across the groups. Mothers with anxiety/depression that took medications had 2.7% MCA Mothers without medications with the same diagnosis had 2.7% rate No finding suggest that early antenatal exposure to anxiolytic/hypnotic medication increase MCA.	With no evidence of increased risk of MCA after exposure to diazepam, temazepam, zopidone or other anxiolytic or hypnotic drugs it would be suggested that these medications are safe during the first trimester of pregnancy in regards to MCA.	Quality: good Level: 2

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Bodén, R., Lundgren, M., Brandt, L., Reutfors, J., Andersen, M., & Kieler, H. (2012). Risks of adverse pregnancy and birth outcomes in women treated or not treated with mood stabilisers for bipolar disorder: population based cohort study. *BMJ : British Medical Journal*, *345*, e7085. doi:10.1136/bmj.e7085	Looking at the outcome between treating bipolar women with mood stabilizing medications vs non medicated bipolar women during pregnancy. Also understanding the difference between pregnancy, labor, and child development between medicated bipolar, non-medicated bipolar and non-bipolar women.	332,137 women that gave birth between July 1st 2005 and December 31st 2009 320 women had two bipolar diagnoses that were actively being medically treated with mood stabilizers (lithium, antipsychotics, or anticonvulsants) during pregnancy and 554 women who were untreated. Both bipolar groups were compared to all other women that gave birth.	Random Non - Experimental	All data retrieved from three Swedish nationwide registers maintained by the National Board of Health and Welfare: Swedish prescribed drug register, medical birth register, national patient register.	Women with bipolar disorder were more often smokers, overweight, and more likely to have substance abuse issues over non bipolar women. Bipolar women (treated or untreated) had higher incidence of preterm delivery, C-section delivery, instrumental delivery, non-spontaneous start. Untreated = low Apgar scores, increased fetal hypoglycemia, small for gestational age, Treated = congenital malformations risk was higher Regardless of treatment women with bipolar are at an increased risk for preterm, instrumental and/or C-section deliveries.	Risks and benefits to both mother and fetus must be weighed when deciding to treat women with mood stabilizers. Untreated women showed a variety of complications showing that medications are not the only cause of adverse pregnancy, birth and neonatal complications	Quality: good Level: 2

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Boden, R., Lundgren, M., Brandt, L., Reutfore, J., & Kieler, H. (2012). Antipsychotics during pregnancy: relation to fetal and maternal metabolic effects. *Archives of General Psychiatry, 69* (7):715-721. doi:10.1001/archgenpsychiatry.2011.1870	To understand the effects of maternal use of antipsychotics (olanzapine and/or clozapine) during pregnancy on both gestational diabetes and fetal growth	There was a total of 358,203 singleton births 507 of the mothers used a form of antipsychotics during pregnancy 169 used olanzapine or clozapine while 338 used a different antipsychotic and they were compared to the 357,696 mothers that did not use antipsychotics during pregnancy	Random Non - Experimental Qualitative	The Swedish Prescribed Drug Register, the Medical Birth Register, and the National Patient Register is where information was obtained during July 2005-December 2009 to obtain medications, medical history, and fetal well-being and physical health. Then groups of exposed were compared to the non-exposed group	Both groups (antipsychotic users and non-users) 0.4% were stillborn 0.2% neonatal deaths Gestational diabetes twice as common in antipsychotic users Preterm rate of 5% in non-users and 8% in users Large for gestational age was greater in olanzapine and clozapine over any other antipsychotic users Small for gestational age greater in users of other antipsychotics over non-users.	Antipsychotics such as olanzapine and/or clozapine hold the highest risk of gestational diabetes regardless of maternal comorbidities. Proposed to divide antipsychotics according to their adverse effects, such as the propensity to cause weight gain and metabolic syndrome when looking at pregnancy Further investigation needed when determining drug safety and pregnancy.	Quality: good Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Cohen, A. S., Altshuler, L. L., Harlow, B. L., Nonacs, R., Newport, J., Viguera, A. C., Suri, R., Burt, V. K., Hendrick, V., Reminick, A. M., Loughead, A., Vitonis, A. F., & Stowe, Z. N. (2006). Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. *JAMA: Journal of the American Medical Association. 295* (5): 499–507. doi: 10.1001/jama.295.5.499	To understand the risk of relapse in pregnancy when women discontinue their antidepressant medications compared to women that continued to use and follow treatment.	201 pregnant women with a diagnosis of major depressive disorder. Women were selected from Perinatal and Reproductive Psychiatry Clinical Research Program,; Women's Mood Disorders Research Program, and the Women's Mental Health Program,	Longitudinal Non-experimental Non-randomized	Between 1999 - 2003 assessments were used to describe pregnant women who elected to discontinue or maintained drug use. All participants were informed and given information regarding the study patients gave consent and self-identified race and ethnicity. Women were followed only and not encouraged either way by the study to continue or discontinue medications.	13 women missed carried and 5 terminated their pregnancies. 12 women were lost due to follow up before completion of pregnancy and 8 choose to discontinue the study. SSRI's were the most commonly used overall 26% of women that maintained their medication regimen relapsed compared to 86% that discontinued their medications Women that discontinued their medications had a 5x higher relapse rate 61% of women that discontinued there medications restarted medications after relapse.	The common belief that pregnancy is a protective hormonal states is incorrect when deal with underlying mental illness. Weighing risks and benefits is key when prescribing medications during pregnancy, women need to be adequately informed of each risk and benefit and relapse of depression is a risk just as fetal malformation.	Quality: good Level: 2

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Evidence-based review assesses safety of antipsychotics during pregnancy. (Cover story). (2009). *Brown University Child & Adolescent Psycho pharmacology Update*, *11*(8), 1-6.	To determine if antipsychotic use during pregnancy increase the risk for birth defects or other adverse events	Data analysis from 1966-2008 that report on safety of antipsychotics in human pregnancy Antipsychotic use in 710 pregnant women using antipsychotics. Most women were 20-24 years of age.	Qualitative Non experimental	They monitored the pregnancy to term or if the pregnancy was terminated then determined if the fetus had deformation psychical and or mental.	Some antipsychotics such as chlorpromazine, loxapine, promethazine = no effects on the fetus other antipsychotics such as flupenthixol, fluphenazine, haloperidol perphenazinem prochlorperazine, thioridazine and trifluoperazine = negative effects on the fetus More research is warranted Need to prioritize the maternal antipsychotic use vs potential risk to the newborn.	Antipsychotics may be prescribed during pregnancy for various reasons discontinuing current antipsychotics can seriously negatively affect the mother Much assessment of the risks of non-treatment of the mother and her ability to interact with her newborn, against a potential risk to the fetus much be considered.	Quality: good Level 3

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Galbally, M., Snellen, M., Walker, S., & Permezel, M. (2010). Management of antipsychotic and mood stabilizer medication in pregnancy: recommendations for antenatal care. *Australian & New Zealand Journal Of Psychiatry*, *44*(2), 99-108. doi:10.3109/00048670903487217	To develop recommendations for antenatal care and monitoring for women with bipolar disorder and schizophrenia who are on lithium carbonate, antipsychotic or anti-epileptic medication during pregnancy	A review of published research review articles and guidelines for the psychiatric and pharmacological management of women with bipolar disorder and schizophrenia. Including a computerized search of the electronic databases Medline, EMBASE and PsychInfo for articles that were relevant to clinical assessment of risk and care in pregnancy for schizophrenia, bipolar, mood stabilizers and antipsychotic medications	Qualitative grounded theory	Searches were also undertaken of relevant guidelines, reference books and bibliographies of identified articles	Increase in teratogenic risk associated with the use of sodium valproate, carbamazepine, lamotrigine and lithium. majority of the structural abnormalities are central nervous system anomalies, particularly neural tube defects, as well as cardiac, facial and urogenital malformations postpartum period comes with a high risk of maternal relapse regular assessments and ongoing monitoring of the woman's mental state through this high-risk period.	Therapeutic drug monitoring is necessary for medications such as lithium, Carbamazepine, sodium valproate and lamotrigine Stop lithium 24–48 h prior to delivery or at delivery, a lithium level when admitted for delivery, ensuring adequate hydration during labor and deliver is important It is important for these women to avoid sleep deprivation during the initial postpartum period Infant withdrawal should be monitored closely Discharge planning should also include the mother–infant relationship and, ideally, support for the partner or family involved in supporting the mother–infant dyad	Quality: good Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Galbally, M., Roberts, M., & Buist, A. (2010). Mood stabilizers in pregnancy: a systematic review. *Australian & New Zealand Journal Of Psychiatry*, *44*(11), 967-977. doi:10.3109/00048674.2010.506637	To undertake a systematic review of the effects of exposure to mood stabilizer medication in pregnancy, evaluating teratogenicity and other outcomes for mother and child.	A review of published research review articles and guidelines for the psychiatric and pharmacological management of women with bipolar disorder and schizophrenia. Including a computerized search of the electronic databases Medline, EMBASE and PsychInfo for articles that were relevant to clinical assessment of risk and care in pregnancy for schizophrenia, bipolar, mood stabilizers and antipsychotic medications	Qualitative grounded theory	Multiple studies and case studies looked at the medication duration and then type of outcome the infant had if living at birth. Children in he studies where then followed up to 7 years. (this looked at the studies themselves they did not do the actual study)	All mood stabilizers were found to be associated with a risk of malformation and perinatal complications.	More research needed as most research they found related more epilepsy All four mood stabilizers reviewed may affect fetal growth and length of gestation. = fetal growth surveillance is recommended all exposed infants be observed for sedation, withdrawal and toxicity Maternal drug levels should be monitored in pregnancy and, in particular, in the third trimester If possible the patient should make a conscious decision with their provider before actively trying to get pregnant	Quality: good Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Gentile, S. (2010). Antipsychotic therapy during early and late pregnancy. A systematic review. *Schizophrenia Bulletin, 36*(3): 518-544. doi: 10.1093/schbul/sbn107	To determine the effects of antipsychotic medications during early and late stages of pregnancy on the developing fetus. Main focus diagnosis is schizophrenic women pregnant women.	2189 articles were found when searching MEDLINE/PubMed, TOXNET, EMBASE, and The Cochrane Library. 2nd generation antipsychotics were amisulpride, aripiprazole, clozapine, olanzapine, quetiapine, sertindole, ziprasidone, risperidone 1st generation antipsychotics were Butyrophenone, Diphenylbutylpiperidine, and Thioxathene Derivates. Haloperidol	Meta- analysis Non-experimental Qualitative	Literature review Medical literature information published in any language since 1950 was identified using MEDLINE/PubMed, TOXNET, EMBASE, and The Cochrane Library Search terms used were pregnancy, psychotropic drugs, (a)typical-first-second generation antipsychotics, and neuroleptics Last search updated on 7/24/08	Antipsychotics have a significant increased risk with birth defects overall. With no human data amisulpride, ziprasidone, and sertindole are considered as unknown. **Aripiprazole** has unwanted effects on neonatal cardiac rhythm so this should be avoided during pregnancy. **Clozapine** = neonatal and perinatal complications including floppy infant syndrome and severe neonatal hypoxemic encephalopathy **Olanzapine** = SG, neural tube defects, **Risperidone**= fetal malformation typology & perinatal complications **Haloperidol**= limb malformations All others in study had minimal risk.	Further information is needed before prescribing antipsychotic medications during pregnancy. Each situation is different. MD should weigh pro's and con's prior to discontinuing or prescribing medications	Quality: good Level: 2

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Gentile, S. (2010). Neuro developmental effects of prenatal exposure to psychotropic medications. *Depression & Anxiety (1091-4269)*, *27*(7), 675-686. doi:10.1002/da.20706	To determine the neurodevelopmental effects on children that were exposed to psychotropic medications at any time in the womb.	Available data from studies investigating developmental outcome of children exposed prenatally to psychotropics. A computerized Medline/PubMed / TOXNET/ENBASE search between 1960–2010 Data were extracted from 41 articles (38 identified electronically and 3 non electronically	Qualitative grounded theory	They used 41 articles total looking at the neuro effects of psychotropics on the fetus and developing infant/child after exposure.	Antidepressants showed no significant changes in the infant. Lithium showed severe weakness Valproate induces developmental delays Detrimental effects on psychomotor and neurocognitive effects has been associated with exposure both throughout and during late pregnancy no conclusions can be drawn about the potential risk of neurodevelopmental delay in children whose mothers need antipsychotic therapy while pregnant mood stabilizers are still very controversial .	Further investigation needs to be done as this looked at only past research articles. Many of the past articles lumped medication together and did not take the time to look at each medication specifically.	Quality: good Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Hanley, G. E., Mintzes, B. (2014). Patterns of psychotropic medicine use in pregnancy in the United States from 2006 to 2011 among women with private insurance. *BMC Pregnancy Childbirth, 242(*14), 1-12. doi: 10.1186/1471-2393-14-242.	To determine the rate of use of antipsychotic medications during pregnancy	Overall 343,299 women had live births from 1/106 to 12/31/11 and of these women 10.3% were on one or more psychotropic medications during their pregnancy	Meta-analysis Non-experimental cohort study	Inpatient and outpatient information was retrieved using the Truven Health MarketScan database (population base 70 million).	There were 33,995 women on psychotropic medications 6 months preconception then 24,776 continued use in the first trimester. 15, 883 continued use in the second trimester. And 18,161 continued use in the third trimester.	Psychotropic medications seem to be overly prescribed. Providers must weigh the risks and benefits of psychotropic medications on both the mother and fetus prior to starting, changing, and/ or discontinuing medications during any stage of pregnancy. Further investigation regarding safety of medications is still required.	Quality: high Level: 3

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
James, L., Paton, C., Lelliott, P., Barnes, T., & Taylor, D. (2009). Mood stabilizers and teratogenicity-prescribing practice and awareness amongst practising psychiatrists. *Journal Of Mental Health*, *18*(2), 137-143.	To evaluate the knowledge and stated practice of consultant psychiatrists with respect to the prescribing of these drugs to women of child-bearing age	52 psychiatrists	Qualitative controlled non experimental	Semi-structured interviews with 52 consultant psychiatrists Using questionnaires, face to face interviews	Most psychiatrists did not talk about contraceptives as they did not believe their patients to be mentally competent. Across the board there were no guidelines followed for women of childbearing ages and monitoring their current medications levels. majority of psychiatrists report that they are more cautious about using teratogenic mood stabilizers in women of child-bearing age, knowledge of specific teratogenic potential is poor.	It's encouraging that so many psychiatrists claimed to exercise prudence in prescribing mood stabilizers to younger women. If psychiatrists are treating younger women of childbearing (or before childbearing) years they should be better versed in the drug information using the best medications possible.	Quality: good Level: 3

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Källén, B., Borg, N., & Reis, M. (2013). The use of central nervous system active drugs during pregnancy. *Pharmaceuticals*, *6*(10), 1221–1286. doi:10.3390/ph6101221	To determine if drugs that focus on the central nervous system such as opioids, anticonvulsants, drugs used for Parkinson's disease, neuroleptics, sedatives/ hypnotics, antidepressants, psychostimulants and a group of other CNS active drugs have an adverse effect on the fetus when used during early pregnancy.	Data retrieved from the Swedish Medical Birth Register from 1996-2011 1,552,382 women gave birth, 42,881 reported use purpose medications Non medicated and medicated women compared.	Non-experimental Qualitative Meta-analysis	Literature review used per each medication mainly the Swedish Medical Register regarding health, pharmacology, infant health, birth rates, adverse effects, birth defects.	70,339/1,575,849 infants born had congenital malformation and 49,499 were severe 16,145 were cardiovascular 11,157 were ventricular septum or atrial septum defect and 4,552 had hypospadias Congenital malformations per drug Opiods= 401/70,339 Anticonvulsants= 334/70,339 Anti-Parkinson's= 78/70,339 Sedatives/hypnotics= 358/70,339 Antidepressants= 1,048/70,339 Psychostimulating = more maternal complications	More research needs to be completed of drug use during pregnancy. Not only do medication effect the fetus in negative ways but they also can increase maternal risk of GDM, preterm labor, stillbirths, miscarriage, preeclampsia, placenta abruption, hemorrhage, and low Apgar's each case is different. One must weigh the benefits and risks of each medication during pregnancy.	Quality: high Level: 2

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Kulkarni, J., McCauley-Elsom, K., Marston, N., Gilbert, H., Gurvich, C., de Castella, A., & Fitzgerald, P. (2008). Preliminary findings from the National Register of Antipsychotic Medication in Pregnancy. *Australian & New Zealand Journal Of Psychiatry*, *42*(1), 38-44. doi:10.1080/0004867070 1732723	To outline the establishment of, and present preliminary data from, the National Register of Antipsychotic Medication in Pregnancy (NRAMP	Australian women,110 women with schizophrenia, there were a total of 257 pregnancies, resulting in 198 live births The inclusion criteria are necessarily broad because the basic question pertains to the relationship of the antipsychotic medication to maternal and baby health there is no exclusion criteria,	Non randomized Quantitative Controlled	Information regarding each woman and her infant is gathered every 6 weeks throughout her pregnancy, at the time of delivery, and at 6 weeks, 12 weeks, 6 months and 12 months after delivery Direct interview and medical records, and encompasses personal history, physical and mental health of the mother, psychiatric management and outcomes, and pregnancy and delivery details, as well as health and developmental outcomes for the infant	The establishment of NRAMP, focusing as it does on the broader needs and vulnerabilities of pregnant women requiring antipsychotic treatment, will enable us to develop guidelines for their optimal health-care interventions.	Further investigation to guidelines followed is needed. Drastic changes in medications for schizophrenia or other mental illness may cause decompensation leading to relapse of symptoms causing more complications for the patient's family dynamics. Providers need to be in contact with each other before such changes are made. Medications should never be stopped cold turkey.	Quality: high Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Kulkarni, J., Worsley, R., Gilbert, H., Gavrilidis, E., Van Rheenen, T. E., Wang, W., Fitzgerald, P. (2014). A Prospective cohort study of antipsychotic medications in pregnancy: the first 147 pregnancies and 100 One year old babies. *PLOS ONE*, *9*(5), e94788. doi:10.1371/journal.pone.0094788	To determine the effects on mother and child of antipsychotic use during pregnancy	Data collected from 205 to 2012 and a finalized number of 147 pregnancies were followed with142 live births out of these 100 babies were followed for one year after birth	Non-experimental Qualitative	Information was retrieved using the Australian National Register of Antipsychotic Medications in Pregnancy (NRAMP). Baseline interview involved social, medical, psychiatric, medication and obstetric history. Women were contacted every 6-8 weeks during pregnancy and asked questions pertaining to health. 6 weeks after birth depression and neonatal health were determined. Then contacted again at 12 weeks, 6 months and 12 months of infant age.	Quetiapine and Olanzapine were the most commonly prescribed 53 women were absent in antenatal care 138 women had gestational diabetes Instrumental vaginal delivery and caesarean delivery had higher rates in user group. 18% of infants were premature 37% had respiratory distress at birth 43% had to be admitted to NICU Over 50% of mothers were admitted to the hospital within 12 months of delivery for mental health decompensation.	Overall antipsychotic use during pregnancy is not warranted. Congenital abnormalities risk is of a higher rate than the general population, Maternal metabolic effects are also greatly increased showing many women to develop GDM and maternal decompensation of psychiatric state greatly increased after delivery. Mother-infant bonding was less likely to occur in mothers on antipsychotics. Some information is unclear if it is correlated with medications or mental illness.	Quality: high Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Louik, C., Lin, A. E., Werler, M. M., Hernandez-Diaz, S., & Mitchell, A. A. (2007). First-trimester use of selective serotonin-reuptake inhibitors and the risk of birth defects. *New England Journal of Medicine, 356*(26), 2675-2683.	To determine the risk of birth defects with maternal use of SSRI's during the first trimester of the antepartum period	Infants were identified by birth registries and calling new born nurseries and labor and delivery rooms. Mothers were interviewed in person and by phone after risk was determine. 9849 infants with malformation and 5860 control infants health records were used	Non – experimental Qualitative	This study looked at any birth defect but did pay closer attention to the main groups that SSRI's have been previously associated with such as craniosynostosis, omphalocele, and congenital heart defects. 1st trimester exposure included SSRI use from 28 days before the LMP through the 4th lunar month (112 days after the LMP)	Out of the 9849 infants with malformations 127 had omphalcele 115 had craniosynostosis, and 3724 had congenital heart defects (186 looping/laterality defects, 620 conotruncal defects, 164 atrioventricular defects, 363 right ventricular outflow tract obstruction defects, 482 left ventricular outflow tract obstruction defects, 1161 septal defects, and 17 had anomalous pulmonary venous return) Even though malformation were found the overall numbers were not statically significant.	There is no definitive connection between an increased risk of birth defects and SSRI use during pregnancy. Each situation is different and the provider must weigh the benefits v the risk of both the mother and fetus before prescribing new medications or discontinuing medications during pregnancy.	Quality: high Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
McCauley-Elsom, K., Gurvich, C., Elsom, S., & Kulkarni, J. (2010). Antipsychotics in pregnancy. *Journal Of Psychiatric & Mental Health Nursing*, *17*(2), 97-104. doi:10.1111/j.1365-2850.2009.01481.x	To presents literature surrounding the use of antipsychotic medications in pregnancy, providing an overview of the historical and contemporary perspectives which influence clinicians prescribing practices To summarizes the literature relating to the use of antipsychotics in pregnancy with a focus on the most commonly used atypical antipsychotics	Data were sourced from Medline, CINAHL, PsycINFo Articles were from 1967 to 2010. Papers were selected based on the abstracts	Qualitative grounded theory	The data was measured by medication effects on the fetus and or neonate after birth	This review identifies that the literature provides no clear answer for clinicians as to the risk associated with the use of antipsychotics in pregnancy Olanzapine had no major malformations but did have an incidence with stillbirths, and prematurity but the highest incidence was with spontaneous abortions Clozapine had no conclusive evidence Risperidone had adverse events during pregnancy and fetal anomalies were moderate Quetiapine had minimal to no adverse effects Aripirazole had high rates of neural tube defects resulting in miscarriage.	Withholding medications may be more detrimental to the mother then the possible teratogenic effect on the fetus. Breast feeding is okay with risperidone of any kind There are no conclusive adverse effects with other types of antipsychotic and breast feeding Taking multiple medications for mental health complications can cause more complications then if they were to just use one. Balancing of both the mental well-being of the woman and the safety of her baby remains a complex task for health professionals.	Quality: good Level: 2

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Peng, M., Gao, K., Ding, Y., Ou, J., Calabrese, J., Wu, R., & Zhao, J. (2013). Effects of prenatal exposure to atypical antipsychotics on postnatal development and growth of infants: a case-controlled, prospective study. *Psycho pharmacology*, *228*(4), 577-584. doi:10.1007/s00213-013-3060-6	To investigate the developmental effects of atypical antipsychotics on infants who were born to mothers taking an atypical antipsychotic throughout pregnancy	76 infants who experienced fetal exposure to atypical antipsychotics was compared to that of 76 matched control infants who had no fetal exposure to any antipsychotics	Non Experimental Case Controlled Qualitative	A newborn assessment and Apgar score at birth and followed up at 12 months of age. Infant development included body weight, height, and neuro behavioral development measurements at 2, 6, and 12 months of age. evaluated by the Bayley Scales of Infant and Toddler Development	Fetal exposure to atypical antipsychotics causes short-term delayed development in cognitive, motor, social–emotional, and adaptive behavior still by 12 months of age. The mothers of the exposed group had higher rates of factors known to increase the risk for a negative pregnancy. a higher % of newborns who were exposed to antipsychotics met the criteria for low birth weight.	Antipsychotic treatment should continue during pregnancy to prevent relapse although studies of the effects of antipsychotic exposure during pregnancy on infants' neurodevelopment with longer follow up period are warranted.	Quality: high Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Petersen, I., McCrea, R. L., Osborn, D. J. P., Evans, S., Pinfold, V., Cowen, P. J., Gilbert, R., & Nazareth, I. (2014). Discontinuation of antipsychotic medication in pregnancy: A cohort study. *Schizophrenia Research*, *159*(1), 218-225. doi: http://dx.doi.org/10.1016/j.schres.2014.07.034	To determine the effects of discontinuation of antipsychotics during pregnancy	Overall 495,953 pregnancies of 365,138 women were found. In this 1442 of the women had ongoing antipsychotic use	Meta-analysis Quantitative	Data was gathered from The Health Improvement Network (THIN) primary care database from 578 practices which covers the majority of the UK's population. Women were identified from 1/1/95 to 12/31/12 for 6 month before pregnancy and then there after that were on antipsychotic medications during that time	207 women on typical antipsychotics before pregnancy there was 1st trimester d/c 134/207 and by 3rd trimester 168/207 279 on atypical antipsychotics before pregnancy there was 1st trimester d/c rate of 129/279 and by 3rd trimester 172/279 Discontinuation rates depended on medication and dosage. Women prescribed in lower doses were less likely to d/c medications.	Providers need to be mindful of schizophrenia and bipolar surfacing around childbearing ages. Trends still show a strong link between the discontinuation of antipsychotic medications and pregnancy. Be this from the psych provider, primary provide, OB/GYN provider or by independent decision based solely on the pregnancy.	Quality: good Level: 3

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Reis, M., & Källén, B. (2013). Combined use of selective serotonin reuptake inhibitors and sedatives/ hypnotics during pregnancy: risk of relatively severe congenital malformations or cardiac defects. A register study. *BMJ Open*, *3*(2), e002166. doi:10.1136/bmjopen-2012-002166	To determine the relation between SSRI's benzodiazepines and the adverse effects the fetus. Looking at both severe congenital malformations and or cardiac defects.	A total of 10,511 infants that were born to women that used SSRI medications only 1000 infants whose mothers used benzodiazepines only and 406 infants whose mothers used a combination of benzodiazepines and SSRI's No other CNS – active drugs were used in this study	Cohort – study Meta-analysis Quantitative	Information retrieved from Swedish Medical Birth register for women and children that were birthed from July 1995- December 2008. Midwifes interviewed patients at their first antenatal visit information was put into Anatomical, Therapeutic, Chemical classification system for data retrieval. Congenital malformation were identified by the medical birth register, birth defect register, and patient register.	(CM congenital malformations, CVD cardio defects) **SSRI** = 12195 exposed; 396 CM and 121 CVD **SSRI w/o sedative/ hypnotic** = 10,511 exposed; 337 CM and 103 CVD **Benzodiazepines w/o SSRI** = 1000 exposed; 37 CM and 13 CVD **HBRA w/o SSRI** = 776 exposed; 22CM and 2 CVD **Other sedative /hypnotics w/o SSRI** = 606 exposed; 21 CM and 5 CVD **SSRI w/ benzo's** = 822 exposed; 46 CM and 13 CVD **SSRI w/HBRA**= 309 exposed; 8 CM and 2 CVD **SSRI w/ sedative/ hypnotic** = 256 exposed; 10 CM and 3 CVA	Further studies are recommended before ongoing use during pregnancy.	Quality: high Level: 2

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Risk of congenital malformations linked to maternal use of antipsychotics. (2008). *Brown University Psycho pharmacology Update*, *19*(8), 1-7.	To determine the effects on the fetus of antipsychotics during pregnancy	Medical data of infants born to 2,908 women in Sweden who took antipsychotics or lithium during early pregnancy who gave birth between July 1995 and July 2005.	Qualitative non experimental control	Mothers were split into two group's 1 women who took either dixyrazine or prochlorperazine and 2 women who took any other antipsychotic during the first trimester.	benefit of pharmacological treatment must outweigh the possible risks in a short & long perspective for both the woman & the fetus Dixyrazine used by 2062 women Prochlorperazine used by 224 women and Congenital malformations were low Other antipsychotics had significant risk for congenital malformation, with increased odds when excluding mild and common malformations including an increased risk of low birth rate, preterm births, and intrauterine growth retardation.	Risk-benefit analysis concludes antipsychotic use during first trimester poses a moderate risk for congenital malformation, but when clinically indicated antipsychotics should not be withheld during pregnancy Over all further study is recommended	Quality: high Level: 3

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Ross, L. E., Grigoriadis, S., Mamisashvili, L., Vonder Porten, E. H., Roerecke, M., Rehm, J., Dennis, C., Koren, G., Steiner, M., Mousmanis, P., & Cheung, A. (2013). Selected pregnancy and delivery outcomes after exposure to antidepressants medication. *JAMA Journal of the American Medical Association Psychiatry. 70*(4) :436-443. doi:10.1001/jamapsychiatry.2013.684.	To determine if maternal antipsychotic use during pregnancy is associated with an increased risk of adverse pregnancy or delivery outcomes.	3074 citations identified 735 articles were reviewed in full and 51 articles reporting on outcomes of interest met the meta-analysis criteria.	Meta-analysis Quantitative	Information was reviewed from Databases that were searched. Databases that were searched include MEDLINE, PsychINFO, EMBASE, and scopus. Reference lists and meta-analysis were searched, studies were considered if they were published in English and had original data.	Spontaneous abortion is not conclusive of antidepressant use. Preterm delivery defined as <37 weeks showed a strong association with antidepressant use Neonates small for gestational age had a strong association with antidepressant use APGAR scores showed a decrease in neonates that were exposed to antidepressants in utero.	Antidepressants can have significant effects on fetal well-being. Weighting the pros and cons of medications is imperative when deciding to continue or discontinue treatments. More research and investigation needs to be completed on each drug class to determine the overall outcomes for both mom and baby.	Quality: good Level: 2

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Sadowski, A., Todorow, M., Yazdani Brojeni, P., Koren, G., & Nulman, I. (2013). Pregnancy outcomes following maternal exposure to second-generation antipsychotics given with other psychotropic drugs: a cohort study. *BMJ Open*, *3*(7), e003062. doi:10.1136/bmjopen-2013-003062	To examine reproductive safety of second generation antipsychotics and to compare pregnancy outcomes between second generation mono and polytherapy with psychotropic medications	133 women using second generation antipsychotic (SGA) medications (37 monotherapy and 96 polytherapy) and 133 healthy non medicated women (control group) 266 women total	Qualitative Experimental Control	Participants identified by a database from the motherisk program at the hospital for sick children from 2005-2009. Mothers that used SGA medications for 4 or more weeks during pregnancy were invited into the study Comparison group = healthy normal women and pregnancies from the same database Telephone interviewing 2009-2012 of both groups regarding children's health and Medical chart review of children at primary clinics	Exposed group had more C-section deliveries, higher preterm deliveries, LGA, and higher NICU presenting with poor neonatal adaptions signs: central nervous system, respiratory and gastrointestinal problems. <u>Polytherapy vs monotherapy</u> Poly = shorter gestational age, and major malformations. Higher admission to NICU for poor neonatal adaption signs also noted Exposed women pre pregnancy were heavier, smokers, breast fed less, less likely to take prenatal vitamins and had more comorbidities.	Polytherapy SGA poses more harm to the mother and fetus then monotherapy. Polytherapy should be seriously considers and taken into perspective in each individual case looking at the real risks and benefits for the mother and baby. Reproductive safety of polytherapy of antipsychotic medications needs to be studied more with a greater population size while taking into consideration the reality of comorbidities, genetic and environmental factors of the mother.	Quality good Level 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Toh, S., Li, Q., Cheetham, T., Cooper, W., Davis, R., Dublin, S., & ... Andrade, S. (2013). Prevalence and trends in the use of antipsychotic medications during pregnancy in the U.S., 2001-2007: a population-based study of 585,615 deliveries. *Archives Of Women's Mental Health*, *16*(2), 149-157. doi:10.1007/s00737-013-0330-6	estimate the prevalence of and temporal trends in prenatal antipsychotic medication use within a cohort of pregnant women in the U.S	Women ages 15-45 that gave birth between 2001-2007 in 11 US health plans totally 585,615 deliveries 4771 where to women on atypical antipsychotics at some time throughout pregnancy	Quantitative Grounded theory	Used data from the Medication Exposure in Pregnancy Risk Evaluation Program and the 11 health plans - affiliated research institution identifying when the antipsychotic was used and for how long it was used to determine frequency and symptoms of the medications for schizophrenia bipolar disorder or depression any time from 180 days before pregnancy through delivery	Prevalence of antipsychotic was highest at 0.5% during the first trimester decreasing to 0.3 % in the second trimester and 0.2% in the third trimester. 2.5-fold increase in the prevalence of prenatal use of atypical antipsychotics 81 % of the deliveries to women with atypical antipsychotic exposure any time from 60 days before pregnancy through delivery had a recorded diagnosis of depression, bipolar disorder, or schizophrenia.	Treating psychiatric conditions during pregnancy is generally recommended MD must weigh the benefits and risks of any medication use during pregnancy and possible adverse effects to the fetus and or mother.	Quality: high Level:1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Vigod, S. N., Gomes, T., Wilton, A. S., Taylor, V. H., & Ray, J. G. (2015). Antipsychotic drug use in pregnancy: high dimensional, propensity matched, population based cohort study. *BMJ : British Medical Journal*, *350*, h2298. doi:10.1136/bmj.h2298	To understand both maternal and perinatal effects/outcomes associated with maternal antipsychotic (quetiapine, olanzapine, risperidone) drug use in pregnancy	1021 women of any age/race that had delivered 1 child, between the years of 203-2012 in Toronto, Ontario. Mothers had to be on two or more antipsychotic medications during the first and second trimesters of their pregnancy and 1021 non medicated healthy mothers (control group) 2042 women total	Experimental Control	Health records of mother and baby were reviewed via ICES' MOMBABY datafile, Canadian Institutes of Health Information Discharge Abstract Database, ICD-10-CA codes, Ontario Mental Health Reporting System, Registered Persons Database, National Ambulatory Reporting System, Ontario Health Insurance Plan.	Antipsychotic use during pregnancy showed higher rates of gestational diabetes, hypertensive disorders of pregnancy, preterm birth, placental abruption, macrosomia, induction of labor, caesarean sections, operative vaginal delivery, and readmission to the hospital. Infants showed higher rates of preterm birth, intraventricular hemorrhage, seizures, sepsis, and neonatal adaptation syndrome.	Must weight risks and benefits of antipsychotic use during pregnancy Women that use antipsychotic medications during pregnancy put themselves, their pregnancy and child at higher risk for complications. Overall antipsychotic medications are not to be discontinued during pregnancy if maternal mental health warrants them.	Quality: high Level: 1

Citation	Purpose	Sample	Design	Measurement	Results/conclusions	Recommendations	Johns Hopkins Level & Quality
Wichman, C. L. (2009). Atypical antipsychotic use in pregnancy: A retrospective review. *Archives Of Women's Mental Health*, *12*(1), 53-57. doi:10.1007/s00737-008-0044-3	determine the prevalence of use of atypical antipsychotics in pregnancy and describe infant outcomes associated with these exposure	Retrospective chart review of all pregnant women presenting at our medical center, from the years 1993 to 2007. Of the 30,092 delivers 16 mothers were on atypical antipsychotics	Controlled Experimental	The obstetrical database listed all medications taken during pregnancy then confirmed by individual chart review. Infant outcomes were assessed by gestational age, birth weight, Apgar scores, NICU admission, congenital malformation or ongoing medical issues, and medical charts were reviewed from birth to Dec 31th 2007.	5/16 infants were female 3/16 male infants were premature Average APGAR score at 1 min was 6.9 and at 5 min was 8.2 4/16 infants required NICU admission after delivery. 6/16 infants showed 0 malformations, neurobehavioral difficulties, or feeding difficulties 1/16 infants had a major malformation 3/16 had heart murmurs that disappeared in 1 year 2/16 had behavioral concerns that initiated after age 3 years. 1/16 infants died at 5 weeks of age with an autopsy revealing positional asphyxia.	Populations group was small, further investigation needs to be done. Antipsychotics are not recommended to be stopped with pregnancy. Antipsychotic medication should be considered high-risk and both mother and fetus should be monitored appropriately	Quality: high Level: 1

Summary

It is difficult to effectively distinguish an appropriate maternal and neonatal balance when assessing the continuation or discontinuation of maternal antipsychotic, mood stabilizer, and or antidepressant medication use during pregnancy. This difficulty is due to clinical and moral obstacles that can arise. One obstacle is that mothers do not want to be a part of a research project during pregnancy when outcomes are unknown and possible lethal or gross adverse fetal effects may occur. Medical providers are taught that if medications are known to cross the placental barrier they should be avoided during pregnancy. However they do not always assess the effects of discontinuation on the mother's wellbeing.

The critical review of the literature shows that there is still much need for more in-depth research studies to be conducted in order to accurately determine the safety of continuing and/or discontinuing antipsychotic, mood stabilizing and/or antidepressant medications. Chapter four will give a final conclusion of the critical review by answering the practice question, identifying trends and gaps in the literature, implications for nurse-midwifery practice, and recommendations for practice in the future, integration and application of the theoretical framework and give a complete conclusion of all the information gathered.

Chapter IV: Discussion and Conclusion

This chapter will discuss the critical review of the literature. This discussion will review the literature synthesis, current trends and gaps in the literature, implications for nurse-midwifery practice, recommendation for future research and finally integration and applications of the theoretical framework. This chapter will cover the information that was presented in the matrices in chapter three. The purpose for this critical review is to understand if antipsychotics, mood stabilizers, and antidepressants should be continued or discontinued during pregnancy or if they negatively impact the fetus/neonate development, maternal wellbeing, and/or maternal-fetal interactions. Nurse-midwives need to understand the importance of continuing or discontinuing these medications in pregnant patients. Having a good understanding of appropriate medication use in pregnancy and the potential effects on the mother and baby are very important to having a happy, healthy patient outcome.

Literature Synthesis

This critical review of the literature was completed to attempt to determine if antipsychotics, mood stabilizers, and antidepressants should be continued or discontinued during pregnancy or if they negatively impact the fetus/neonate development, maternal wellbeing, and/or maternal-fetal interactions, with the main focus of maternal/fetal outcomes with continuation or discontinuation of medications in pregnancy at any time. The purpose of this review was to evaluate the safety of these medications for maternal wellbeing and fetal outcomes. This synthesis will be continued in the recommendations paragraphs to follow.

Current Trends

Current trends in the literature discussed maternal and fetal wellbeing in regards to continuation or discontinuation of antidepressants, antipsychotics, and or mood stabilizing medications. To adequately answer the review purpose many factors must be considered. Providers must educate their patients with current information and make the best decisions possible in order to keep the mother mentally stable and the fetus physically and mentally viable and healthy.

It is important to understand how much progression healthcare has made over the years in regards to mental health medications and pregnancy. It is beneficial to understand history and progress when understanding why current trends are important. In the 1970's, antipsychotics were considered not only safe during pregnancy, but beneficial to offspring (Clues to preventing schizophrenia, 1979). In lab rats, the pups were determined to have less dopamine in their brains upon birth making them less susceptible to schizophrenia (Clues to preventing schizophrenia, 1979). This decreased risk of schizophrenia was the only fetal benefit for neuroleptic or antipsychotic medication use during pregnancy, and there were no negative impacts noted.

Antidepressants in pregnancy have been used for decades. Many studies were completed and most were in agreement that antidepressants such as SSRI's were deemed safe across all trimesters in pregnancy (Musa & Smith, 1979). However, tricyclic antidepressants have been linked to negative effects in the infant, such as drug withdrawal, malformation, neonatal morbidity, and hypothermia, making these medications a bad choice in pregnancy (Musa & Smith, 1979). The Musa & Smith study from 1979 showed that interest in maternal fetal safely was growing and better outcomes for both mom and baby were warranted.

Current literature supports the need for positive maternal/fetal outcomes. Literature suggests that medications during pregnancy can cause fetal harm; however, discontinuation of medications during pregnancy can cause significant maternal mental decompensation (McCauley-Elsom, Gurvich, Elsom, & Kulkarni, 2010). Finding the best treatment plan is the ultimate goal when providing care for pregnant mothers with mental health disorders. Studying pregnant women for medication use and fetal safety is difficult. Many women do not want to volunteer to participate in research related to the health of their unborn child. Current trends show research from large data bases from different countries or large hospital systems (Evidence-based review assesses safety of antipsychotics during pregnancy, 2009). Research looking at data bases with maternal consent shows maternal medication compliance and maternal outcome as well as fetal outcomes. This helps show the rates of adverse fetal effects with various medications and each maternal psychiatric diagnosis. It is important to note that maternal diagnosis and social economic behaviors/status were not taken into consideration during this critical review.

Gaps in the Literature

Several gaps exist in the literature. A significant research limitation is the sole focus on medication continuation or discontinuation and maternal/ fetal/ neonatal effects. Co-morbidities, medical diagnosis, psychological diagnosis and socio-economic status were not assessed or taken into consideration which may skew results. Issues such as maternal diabetes, illegal drug use, and tobacco use could impact the fetal/neonatal outcomes when medications were continued or discontinued during pregnancy.

Other gaps in the literature include the reliance on data from large databases. Data retrieval such as this can be difficult to determine to be completely accurate. Data retrieval from

large databases does not take anything into consideration except for numbers and outcomes. This source does not look at specifics in people and populations but more as numbers and outcomes. Another large gap in the literature is the psychiatrist, primary care provider's, and midwife's knowledge regarding medication safety in pregnancy and psychiatric disorders. "Decisions regarding the best form of treatment are complicated when there is a requirement to medicate women who are acutely psychotic in pregnancy" (McCauley-Elsom & et al., 2010. p.101). This challenge highlights the central purpose of this review regarding balancing maternal health with potential risks to the infant.

Implications for Nurse-Midwifery Practice

This critical review of the literature has a vast array of implications for the nurse midwife practice. Understanding the risks and benefits to both patients (maternal and fetal) when looking at their medication regime is key to outstanding practice. When determining if medications need to be discontinued or continued throughout pregnancy, the midwife needs to be able to provide pertinent information for both the patient and possibly the prescribing physician. Provider education is of utmost importance, but also an understanding of the midwifery scope. When is it appropriate for the midwife to take over psychiatric medication dosing during pregnancy and when would this become an inappropriate use of practice? Who should prescribe medication during pregnancy? Midwifery scope of practice does not usually include extensive psychiatric medications, but mental health patients benefit from midwifery cares (American College of Nurse-Midwifes, 2015). Midwives need to understand psychiatric medications effects, side effects, and potential harmful effects to both the mother and developing fetus to help protect women and ensure they get the care they deserve.

Knowing that the potential effects of medications on fetal development and maternal wellbeing is of greatest importance, midwives are advocates and leaders in best practices for women's health and fetal wellbeing. The decision to continue or discontinue medications needs to be driven by more than just fear of medication use in pregnancy. There needs to be supported and well documented research and information before decision of discontinuation or continuation of medications is applied. It is well known that discontinuation of antipsychotics can lead to a relapse of symptoms and mental health decompensation leading to "personal suffering and increased family and societal burden" (Peng & et al., 2013, p. 578). However, all psychotropic medications cross the placenta, thus exposing the fetus to the effects of the medications (Peng & et al., 2013).

It is important for midwives to understand that the psychiatrist may not have taken this patient's child bearing needs into consideration while prescribing medications. Many studies have shown that psychiatric providers focus more on the maternal side in managing symptoms, and focus less on the fetal realm of healthcare (Peterson et al, 2014). Studies on psychiatrists have shown that many do not discuss reproductive issues with patients, including contraceptive, pregnancy, and potential complications (James, Paton, Lelliott, Barnes, & Taylor 2009). The reality of this is that providers are prescribing young women medications but not fully educating them on life choices or safe sex practices. Midwives have the ability to see women of all ages and educate women at a young age, before life changing events occur. If mental instability occurs throughout a woman's life, education is needed prior to and during pregnancy to help women understand the risks associated with medications crossing the placenta barrier

Midwives need to understand that depression in pregnancy and postpartum is common. In fact, up to 20 percent of women without mental health complications develop depression

during pregnancy or within the first year postpartum (Midris, 2014). Women need to be educated and treated for mental health issues before, during, and after pregnancy (Midris, 2014). It is not only the psychiatric provider's role to treat women before pregnancy but also the midwives' role as well. Women in childbearing ages need education on medications, mental stability, and the risks a pregnancy could bestow upon them (Midris, 2014). Women need to understand that discontinuing an antidepressant, antipsychotic, or mood stabilizing medication could cause a depressive, manic, or psychotic relapse and truly impact them negatively during pregnancy or after delivery in the postpartum stage. This relapse could greatly impact the mother's ability to care for herself and her family and has the potential to cause a postpartum psychosis episode (Cohen et al., 2006). Midwives need to educate patients, physicians, and themselves about antidepressant, antipsychotic and mood stabilizing medication use in pregnancy in order to safely and effectively treat patients and obtain positive outcomes.

Recommendations

Recommendations for the research questions: to determine if antipsychotics, mood stabilizers, and antidepressants should be continued or discontinued during pregnancy or if they negatively impact the fetus/neonate development, maternal wellbeing, and/or maternal-fetal interactions; was divided into three main categories with the research assessed in the matrices above. Recommendations for all three medication family groups were divided equally into sub categories of continuation/discontinuation, provider education, and need for more research for recommendation.

Continuation vs discontinuation.

When discussing pregnant women, one is discussing the treatment of not only one patient, but two. Balancing the safety of the mother's mental health with the physical and mental health of the developing fetus is pertinent to appropriate care. Continuation of medication use during pregnancy needs to take many factors into consideration, maternal mental stability, fetal effects of continuation, trimester of use, and maternal/fetal effects of discontinuation need to be addressed and prioritized. Antipsychotics, antidepressants, and mood stabilizing medications can have negative adverse effects on the developing fetus at any stage of pregnancy, but discontinuation of medication can impact the mother and still cause negative impacts on the developing fetus. It is important to note that fetal/neonatal effects can not only be linked to medication use but also to maternal mental illness (Kulkarni et al., 2014). This factor should be of highest consideration when determining appropriate treatment during pregnancy.

Where should priority lie, with the patient before the midwife or the patient that is growing inside? Balancing maternal well-being with safety of the developing fetus soon to be neonate is a complex and trying task for healthcare professionals (McCauley-Elson, Gurvich, Elsom & Kulkarni, 2010). Discontinuation of medications can be more detrimental to the mother than continuation of medications and the teratogenic effects that can occur to the developing fetus (McCauley-Elson, Gurvich, Elsom & Kulkarni, 2010). Antipsychotics, antidepressants, and mood stabilizing medications have all been linked to adverse effects on the developing fetus no matter the time frame of maternal use, whereas discontinuation has been strongly linked to maternal decompensation and adverse fetal effects. Overall therapeutic medication monitoring and careful planning are recommend with continuation of medications for mothers with severe mental health disorders (Galbally, Snellen, Walker, & Permezel, 2010). Increasing fetal

surveillance, maintaining maternal sleep patterns, and promoting maternal mood stability with increase prenatal visits are helpful for effective medication dosing and fetal and maternal safety during pregnancy (Galbally, Snellen, Walker & Permezel, 2010). After delivery, maternal and fetal bonding needs to be closely monitored and active interventions are mandatory. Postnatally the infant needs to be assessed for medication withdrawal, toxicity, and sedation (Balbally, Roberts & Buist, 2010). Overall neonatal monitoring needs to occur as if the infant presented as high risk. The neonate needs to be closely monitored for neurodevelopmental complications for the first two years of life as adverse effects may not present until typical milestones are missed (Peng et al., 2013). Antipsychotic, antidepressant, and mood stabilizing medications need to be assessed as high risk for both maternal and fetal measures no matter how common the use of these medications become (Wichman, 2009). If medications are going to be prescribed more frequently, providers need to understand their potential for adverse effects when continued or discontinued, and closer monitoring needs to be implemented.

Provider education.

Providers need to be aware of the current trends in medication prescribing, and all providers that come into contact with childbearing women need to be able to provide education about safe pregnancy. Ideally providers need to understand mental illness and its development in women during childbearing ages. Schizophrenia, bipolar, and other mood disorders typically developing in a person's 20's (Petersen et al., 2014), a direct correlation to the social time frame for when women typically start families and have children. Education for preconception and family planning during this time is fragile and lacking in healthcare. Many women do not experience mental illness symptoms until pregnancy has occurred. Others don't have complications until the postpartum phase. This leaves mothers to believe this is normal in

pregnancy and they stay un-medicated and still show adverse effects with fetal development, maternal bonding and ultimately family development. These effects are due to mental illness and can greatly impact family relationships and infant needs.

For women that are medicated before pregnancy, there is a provider trend to discontinue medications out of fear of pregnancy, liability, and fetal harm (Petersen et al., 2014). No regard is given to the mother's mental stability if un-medicated. Providers need to be educated and feel safe when leaving mothers on medications for mental illness to provide effective care. Liability should not drive safety. Providers need more education but where are they to turn when in many cases studies report that for best outcomes more research is needed.

More research required.

How are providers going to be informed with many studies show a need for more research and patients aren't willing to be the guinea pig? Antidepressants are so commonly used in pregnancy, especially antidepressants in the SSRI family. However these medications have not been determined safe for fetal development during pregnancy (Ross et al., 2013). SSRI's have been shown to have significant negative fetal effects while used in pregnancy such as spontaneous abortion, preterm delivery, small for gestational age, low APGAR scores and flat affect (Ross & et al., 2013). Yet these medications are classified as safe for use during pregnancy making them the most commonly used mental health medication is pregnancy (Cohen et al., 2006). Overall more research is needed to determine if the adverse effects on the developing fetus are related to medications, maternal socioeconomic barriers, mental illness or all factors put together (Reis & Kallen, 2013). When looking at antidepressants the provider needs to also assess the situation. Yes SSRI's are a category B but they also show adverse effects to fetal

development. The degree of harm done if medications were continued vs if they were discontinued needs to be assessed and researched (Louik et al., 2007).

When looking at research for antipsychotic medication use in pregnancy there is much debate and more research is needed to make the murky water clear for providers. It may be beneficial to divided research into groups by maternal adverse effects when assessing safety in pregnancy. All in all pregnancy is not the time to experiment but if maternal use is already occurring medication effectiveness vs metabolic syndromes caused by medications should be taken into consideration with future studies (Boden et al., 2012). Patients that are using antipsychotic medications prior to pregnancy typically have co-morbidities that also need to be evaluated with research. Research focuses on medications and pregnancy but not other factors such as promiscuity, illegal drug use or behaviors, socioeconomic status, obesity, relationship status or other causative factors for poor outcomes (Gentile, 2010). Research needs to be finer turned to special consideration and separation of medications; maternal and fetal effects are just one factor (Hanley & Mintzes, 2014). Conclusively when looking at antipsychotics as a whole more research is needed with greater population size and the reality of co-morbidities, genetics, environmental factors and maternal situation bases to effectively give appropriate recommendations for antipsychotic use in pregnancy (Sadowski et al., 2013).

Mood stabilizing medications is a large category that needs to be separated into small categories. Ultimately medication use should be discussed prior to pregnancy (Galbally, Roberts, & Buist, 2010). Medications should not be used if a woman is actively trying to get pregnant but after pregnancy occurs medications may or may not be discontinued. It is a difficult line for providers to walk. Just as in the case of antidepressants and antipsychotics more research is needed to help providers make the best informed decision. Providers need to actively weigh the

risks, alternatives, and benefits to medications continuation or discontinuation with the limited research provided (Kallen, Borg, & Reis, 2013) while including women in the decision making process. More research is required to be able to safely take care of both patients during pregnancy when looking at continuation or discontinuation of maternal medications for mental health purposes. There is not enough research to adequately guide providers to educate patients effectively when looking at adverse fetal or maternal side effects. Medications, situations, and current research needs to be weighed to make the best patient outcome. Overall more research is required for mental health medications and pregnancy.

Application of Theoretical Framework

The theory chosen for this critical review of the literature was Jean Watson's theory of Human Caring/Caring Science. This theory has been implemented throughout in the discussion of provider and patient education and understanding of medication continuation or discontinuation during pregnancy. Jean Watson's theory of caring ultimately breaks down to the more antenatal care a woman receives in pregnancy the better the outcome of the fetus and maternal/neonatal bonding. This theory is set in the bases of love, compassion towards others and positive morals (Wagner, 2010).

The theory of Human Caring/Caring Sciences is specific to the recommendation for provider education and the need for research. Midwives need to be able to have the education to be able to balance the well-being of both the mother and the developing fetus to ensure the best outcome for both (McCauley-Elsom, Gurvinch, Elsom & Kulkarni, 2010). Midwives are bestowed with the ability to look at patients as patients not a disorder and to look at pregnancy as normal not a complications. This alone shows that midwives are more apt to practicing the theory of Human Caring/Caring Sciences over any other. Patients are at the forefront of

midwifery cares not the present illness or reason for their visit. This is important when looking at medication use in pregnancy.

In Jean Watson's Theory of Human Caring/Caring Science (Wagner, 2010), there are seven main components that truly define midwifery practice. Each of the components applies to midwifery practice and the decision to continue or discontinue medication. The first component is moral commitment to protect and enhance human dignity. Midwives show this by including women in care planning and in decision making. Also this is shown by the ultimate goal of protecting and serving others. The second component is respect/love for the person. This is the definition of midwifery care. Midwives care about people, and treat them as such. Listening to women under their care and planning treatment mutually shows respect for the individual patient. The third component is caring consciousness of the situation. This is shown by the knowledge that midwives have in regards to medications safety vs adverse effects for the mom and fetus. Midwives educate the women in their care about the adverse effects of medications and help them to weigh an exacerbation of symptoms with the risks associated with continuing medications. The fourth component is heart centered care of mind body and spirit. This is again shown by the midwifery care model. Midwifery care is not treating a diagnosis but instead treating a patient who happens to need treatment. Midwives have the special ability to care for the whole patient and educate them with the most up to date research so that they can make the best decisions about their healthcare and future. The fifth component is inner harmony, the sixth is caring conscious intention, and the seventh is authentic presence. These components are shown in midwifery care by the midwives' ongoing ability to not only listen to a patient but also given them the time and encouragement when making decision about their care. Midwives aren't grouping every patient with the same diagnosis the same way. Midwives treat each patient as an

individual and help that patient make the best decision that pertains to their specific situation. When midwives are given the ability to be a part of a patient's care they give that patient the best individualized care plan that helps them make the best decisions about their care. When looking at medications for mental health complications in pregnancy, the midwife has the ability to educate the mother and themselves on the risks, benefits and alternatives to continuing or discontinuing their medications. These concepts define midwifery practice when comparing them to the midwifery scope of practice. The midwifery scope of practice not only defines the roles of a midwife but also the caring and art of compassion that midwives uphold daily. "Midwives are uniquely placed to help ensure women receive high quality individualized care at a distressing time" (Lyus, Creed, Fisher, & McKeon, 2014. p. 336) or at any time when they are caring for women and newborns.

Mental health medications such as antidepressants, antipsychotics, and mood stabilizers are going to be used in pregnancy. Treatment and patient care needs to be considered from all angles and most importantly the mother's ability to take care of herself in pregnancy and then her ability to interact with her newborn after delivery vs the potential adverse fetal affects that could arise during medications use in pregnancy (Evidence-based review assesses safety of antipsychotics during pregnancy, 2009). The fear of liability needs to be minimized and the compassion for maternal and fetal well-being needs to be maximized. This is where the midwifery model of healthcare flourishes.

The midwifery philosophy of care is to "affirm the power and strength of women and the importance of their health in the well-being of families, communities and nations. We believe in the basic human rights of all persons, recognizing that women often incur an undue burden of risk when these rights are violated" (ACNM, 2016, paragraph 1). This plays a direct role with

Jean Watson's theory of Human Caring/Caring Sciences. Midwives are a key member in the independence of women and in the protection of their rights. In order for women to be independent in healthcare they need a healthy knowledge base that focuses on their well-being. Midwives are that caring informational source that woman can trust and with whom they can feel safe. Midwifery hold a role like no other in caring for women so that women can care for themselves.

Conclusion

Each and every patient is different. Each and every patient has their own thoughts, feelings, dreams, ambitions, motivating factors and disorders. Midwives understand this; thus making an individualized healthcare plan for each patient is of the utmost importance when implementing patient cares. It is not fully understood if medications such as antidepressants, antipsychotics, and mood stabilizers should be discontinued or continued during pregnancy. It is understood that maternal and fetal well-being is of the most importance when attempting to decide what steps should be taken before and after pregnancy has been confirmed. Midwives need to be aware that psychiatric providers may have not taken situational factors into consideration, such as, the woman being treated is of childbearing age (Petersen et al., 2014). This may fall into the hands of the midwife and this education of planning pregnancy over accidental pregnancy should be implemented with every woman no matter her potential mental health disorder.

Midwives need to be able to have the conversation with the patient to inform them of all the risks, benefits, and alternatives to continuation or discontinuation of mental health medications during pregnancy. Patients need to know that continuing medications can cause adverse fetal effects as well as adverse maternal effect but will keep the patient mentally stable

and she will be able to care for herself and her family, while discontinuation of the medications may cause mental health relapse and potential hospitalization while still causing adverse fetal effects related to mental illness (Boden et al., 2012). Midwives and patients need to collaboratively make the best decision for the best possible outcome for both the patient and her unborn child.

Understanding that fear should not drive decision making is the midwife's role. Knowing how to monitor patients at a therapeutic medication level, ensuring mothers have proper dietary and water intake along with a healthy sleep pattern is important for pregnancy and best outcomes for all (Galbally, Snellen, Walker & Permezel, 2010). Truly this is the foundation of midwifery care in pregnancy for all women, not just women on high risk medications during pregnancy. Discharge planning should follow suit as well. While midwives educate all mothers on self-care, fetal monitoring, safe environment, postpartum depression and routine follow up visits, special consideration must be taken for mothers with a diagnosed mental health disorder. Regardless of medication use in pregnancy, the postpartum period places all women in a fragile state; adding mental illness to the equation heightens the fragility and puts mothers more at risk. Mothers will need midwifery support, extra visits and additional supportive relationships to ensure maternal neonatal bonding and to reinforce the maternal/infant relationship (Galbally, Snellen, Walker & Permezel, 2010).

It is important for women to feel safe when receiving healthcare. Leaving them out of important decisions in their health care will make them become less responsive and less compliant. Midwives have the ability to bond with women on a personal level thus creating trust within the healthcare system leading to compliance and positive outcomes. To determine if antidepressants, antipsychotics, and mood stabilizing medications be continued or discontinued

in pregnancy is situational and in the hands of the provider/midwife and the patient. More research may be needed to be able to give a definitive yes or no but for now the importance of education for child bearing women prior to pregnancy as well as newly pregnant women is the foundation for the greatest outcome both for the mother and the developing fetus/neonate.

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