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# Prenatal Opioid Maintenance in the U.S. and its Effect on Neonatal Abstinence Syndrome: The Case of West Virginia's Opioid Epidemic

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# **PRENATAL OPIOID MAINTENANCE IN THE U.S. AND ITS EFFECT ON NEONATAL ABSTINENCE SYNDROME: THE CASE OF WEST VIRGINIA'S OPIOID EPIDEMIC**

## **ABSTRACT**

In 2017, West Virginia's opioid epidemic was the cause of about 1000 deaths. Opioid abuse has become an issue among pregnant mothers and has increased the effects of Neonatal Abstinence Syndrome (NAS) in infants. The purpose of this study was to evaluate the participation of prenatal opioid maintenance to determine if it has decreased the amount of treatment needed for NAS in infants in West Virginia. The methodology utilized a literature review complemented with a semi-structured interview. Thirty-six sources were referenced for this literature review. It was found that Buprenorphine Maintenance Therapy had the most positive effect on NAS after birth. This review also reported a lack of availability for addicted pregnant women to enroll in maintenance programs and a high drop-out rate. Opioid maintenance therapy has permitted pregnant women to refrain from illicit drug use without experiencing withdrawal symptoms and it has allowed the opportunity for their infants to have better health after birth.

**Key Words:** Infants, Maintenance, NAS, Opioid, Pregnant, and West Virginia.

## INTRODUCTION

The opioid epidemic in the United States (US) has led to 42,249 overdose deaths per year, and in West Virginia it was the cause of 52 per 100,000 deaths.<sup>1</sup> In 2017, more than 115 Americans died per day from opioid overdose: the CDC estimated a total of \$78.5 billion per year has been consumed on healthcare due to loss of productivity, addiction treatment, and criminal justice related to opioid abuse.<sup>2</sup> Excessive opioid abuse in the US has increased the occurrence of Neonatal Abstinence Syndrome (NAS) among infants, especially in West Virginia.<sup>3</sup>

NAS occurs in infants who have been exposed to opioid usage by drug dependent mothers throughout pregnancy.<sup>4</sup> NAS has been defined as an opioid withdrawal syndrome that has been found in 55% to 94% of newborns whose mothers have used opioid drugs while pregnant.<sup>5</sup> It has been caused by the use of Heroin, Codeine, Oxycodone, Methadone, and Buprenorphine, which has led to health complications that have commenced within one to three days after birth.<sup>6</sup> The WEST VIRGINIA state average of children born with NAS was 7.74 per 1,000 births in 2007 and increased to 31.56 per 1,000 births by 2013, which was three times the national average.<sup>7</sup>

Prenatal drug rehabilitation centers have used Methadone Maintenance Therapy (MMT) and Buprenorphine Maintenance Therapy (BMT) and has sustained opioid maintenance in addicted pregnant mothers.<sup>8</sup> The Maternal Addiction Recovery Center (MARC) Program in Huntington, West Virginia at Marshall Obstetrics & Gynecology has offered the combination of prenatal care and medication maintenance to opioid-addicted pregnant women.<sup>9</sup> Buprenorphine and Methadone have worked as opioid agonists and have contained chemicals that have linked to the brain's opioid receptors and have reduced withdrawal symptoms from Heroine or other opioids, managed pain, and have created a sense of well-being.<sup>10</sup> MMT and BMT during pregnancy has stabilized the amount of opioids within the fetus, decreased the risk of transmitting HIV to the fetus, and has improved overall neonatal health.<sup>11</sup> The use

of Suboxone has also been implemented during pregnancy, which has consisted of the combination of Buprenorphine and Naloxone.<sup>12</sup> Researchers conducted the Maternal Opioid Treatment: Human Experimental Research (MOTHER) project, which compared Buprenorphine and Methadone treatment among opioid addicted pregnant women, and concluded that Buprenorphine has been the most effective form of treatment for prenatal opioid dependence.<sup>13</sup>

The purpose of this research study was to evaluate the participation of prenatal opioid maintenance to determine if it has decreased the amount of treatment needed for Neonatal Abstinence Syndrome in infants in West Virginia.

### METHODOLOGY

The primary hypothesis for this study was that opioid maintenance therapy among pregnant women has decreased the occurrence and severity of NAS in infants. The methodology for this research analysis utilized a literature review of academic sources. The conceptual framework, illustrated by Figure 1, showed an adaptation of the research framework by Brogly, Hahn, Diaz, & Werler<sup>14</sup>, which demonstrated the benefits and barriers to opioid maintenance treatment during pregnancy. The use of this framework was appropriate because it demonstrated the adoption of MMT and BMT within prenatal drug treatment programs. It was similar to any project development in that the process was circular; it began with identification and definition of the opioid crisis and included development solutions. In this case, the solution has been preventing illicit drug usage or withdrawal during pregnancy through the use of maintenance medications to reduce NAS severity. Through process assessment, the use of opioid maintenance among pregnant women was researched, and the statistics showed positive effects on the infants after birth. Once prenatal drug treatment programs implemented the usage of medicated-maintenance therapy, benefits and barriers were addressed (Figure 1).

The literature review was conducted in three individual stages involving: (1) developing a search strategy and gathering data for the case study; (2) determining and analyzing the relevant literature; (3) delegating literature to appropriate categories.

### *Step 1: Literature Identification and Collection*

The electronic databases used include JAMIA, Elibrary, PubMed, Medline, and Google Scholar. The terms searched within each database were: “prenatal drug programs” AND “opioid maintenance” OR “opioid therapy” AND “Neonatal Abstinence Syndrome” OR “NAS” OR “neonatal withdrawal syndrome” AND “West Virginia” OR “US”. Journals cited included: The Journal of the Medical Library Association, West Virginia Medical Journal, The Journal of Rural Health, Journal of Addiction Research & Therapy, and other reliable medical and government websites. The searched identified 117 applicable citations and articles were excluded (N=81) if they did not meet inclusion principles. Articles were included (N=36) if they described prenatal opioid maintenance treatment protocol or the opioid epidemic in the US and West Virginia. These 36 articles were subject to full-text review and all 36 were included in the data abstraction and analysis (Figure 2).

### *Step 2: Literature Analysis*

As the US and WEST VIRGINIA opioid crisis has continued to rise, it has become important to know its impact on pregnant women and their infants. Therefore, the literature analyzed focused on the following key areas: the utilization MMT and BMT, opioid maintenance completion, and severity of NAS after treatment has been administered. In attempt to collect the most recent data, sources preceding years 2008-2018 were removed from the search and only sources written in English were used. Primary and secondary data from articles, literature reviews, research studies, and reports written in the US were

included in this research. The literature review included 36 references which were assessed for information pertaining to this research project. Furthermore, a semi-structured interview with an expert Nurse Coordinator of prenatal opioid maintenance, (N.Lindsey) supplemented information to the data collected (See Appendix A: Questions Asked in Semi-Structured Interview of an Expert in Prenatal Opioid Maintenance). The Nurse Coordinator will be referred to as Expert in Prenatal Opioid Maintenance throughout the review. The interview was tape recorded with IRB approval prior to execution, and only relevant answers were used to supplement the information found in this literature review. The literature search was conducted by MR and validated by AC, who acted as second reader and also double checked if references met the research study inclusion criteria.

### *Step 3: Literature Categorization*

The following subheadings were included in part of the following research framework: Illicit Opioid Use During Pregnancy in the US and West Virginia, Infants with NAS in the US and West Virginia, MMT and BMT During Pregnancy, and Prenatal Opioid Maintenance Programs.

## RESULTS

### **Illicit Opioid Use During Pregnancy in the US and West Virginia**

From 2008-2012, approximately 39.4% of female Medicaid patients and 27.7% of privately insured patients that were of childbearing age (15-44 years old) received opioid prescriptions each year.<sup>15</sup> These researchers also stated that out of more than 1 million Medicaid patients, 21.6% of pregnant women filled an opioid prescription and 2.5% of prescriptions exceeded 30 days. In 2011, 5% of women ages 15-44 years old in the US used illicit drugs while pregnant.<sup>16</sup> In addition, 138,224 out of 55,781,965 hospitalizations among pregnant women were due to opioid abuse. More than 35% of

opioid dependent women have also tested positive for marijuana, cocaine, benzodiazepines, and 77%-95% and have smoked tobacco.<sup>17</sup>

A study conducted in 2009 reported that 146 out of 759 pregnant women in WEST VIRGINIA, or 19.2% tested positive for drug or alcohol abuse.<sup>18</sup> In 2010, 1 out of 3 pregnant women positively tested for opioid abuse at Charleston Area Medical Center's (CAMC) Women's Medicine Center in Charleston, West Virginia, but increased to 37% percent during the first quarter of 2011. Furthermore, CAMC tested 706 pregnant mothers between July 2010 and July 2011, which showed usage of 74% marijuana, 20% opioid, 12% Benzodiazepines, and 6% Methadone.<sup>19</sup>

### **Infants with NAS in the US and West Virginia**

Infants that have been born with NAS in the US more than doubled between years 2009 and 2013, with an increased rate of 3.6 per 1,000 infants to a rate of 7.3 per 1,000.<sup>20</sup> One study stated that in 2012, US hospitals expended \$316 million on infants with NAS, whose average length of stay was 16.6 days, or 3.5 times more than a non-NAS infant.<sup>21</sup> Drug dependent infants in the US have had a 150% greater chance of being readmitted into the hospital within 30 days after birth than infants born without any health complications.<sup>22</sup> Medicated-maintenance has been utilized to treat withdrawal symptoms in 50%-70% of infants born with NAS.<sup>17</sup>

In 2016, the frequency of NAS among infants In West Virginia was approximately 5% of total births.<sup>23</sup> This author also stated an increase from the two previous years, with 32.1% of infants born with NAS in 2014 and 34.4% in 2015. Another report in 2017 suggested that newborns with NAS were born every 25 minutes in West Virginia.<sup>24</sup> In 2013, 18% of infants in Huntington, West Virginia, were born with NAS, compared to the statewide rate of 37% and the nationwide rate of 7%.<sup>25</sup> Four years later

at Cabell Huntington Hospital in Huntington, West Virginia, 14% of infants were born with NAS, compared to the national average of 6% newborns.<sup>26</sup>

According to West Virginia perinatal collaborative officials, 33.3% of infants with NAS have been treated in well newborn nurseries, while the remaining 66.7% have been treated special care nurseries or the Neonatal Intensive Care Unit (NICU). Furthermore, drug dependent infants have cost an average daily charge of \$400 in West Virginia's neonatal withdrawal centers, \$2,600 in a special care nursery, and \$4,000 in a NICU.<sup>27</sup> A study conducted by West Virginia University suggested that the average length of stay for newborns with NAS was 18 days, which resulted in an overall hospitalization cost of \$9,000-\$12,600.<sup>28</sup> Lily's Place, an extended NAS treatment facility in Huntington, West Virginia, has kept infants for 2 weeks to 12 months for addiction withdrawal treatment but only has 12 available beds: they have treated 91 infants since opening in 2014.<sup>25</sup>

### **Methadone and Buprenorphine Maintenance Therapy During Pregnancy**

According to the MOTHER project, infants whose mothers participated in MMT during pregnancy had a hospital stay extent of 15-20 days and NAS treatment duration of 10 days, whereas infants whose mothers used BMT had a hospital stay of 10 days and NAS treatment duration for less than 5 days.<sup>29</sup> Researchers have suggested that within 4 weeks of the being transitioned from MMT to BMT, 15% of women showed illegal drug usage in urine screening, 90% continued follow-up appointments until delivery of the child, and 38.9% did not use drugs illicitly at the time of delivery.<sup>30</sup> Furthermore, there were fewer cases of NAS and shorter hospitals stays after birth when transitioned from MMT to BMT.

A recent study showed that BMT, rather than single-methadone treatments, has shown a 10% lower chance of NAS, 8.4 fewer days of neonatal treatment, and 3.6 mg less Morphine treatment.<sup>31</sup>



BMT has shown a longer duration of movements and less suppression in motor activity in infants.<sup>32</sup> Researchers from West Virginia University reported that 81% of infants who have been exposed to MMT still needed treatment for NAS, while only 26% who were exposed to BMT required NAS treatment.<sup>33</sup> In a study that involved 716 women participating in MMT or BMT, infants whose mothers were exposed to MMT showed a 65% incidence of NAS, whereas those exposed to BMT showed 49%.<sup>34</sup> This study also showed 17 more cases of NAS when mothers participated in MMT rather than BMT.

### **Prenatal Opioid Maintenance Programs**

The MARC Program in Huntington, West Virginia has the capacity to treat 36 patients, which have ranged from ages 22-34 years of age.<sup>35</sup> However, upon the occasion that MARC has been unable to treat anymore patients, they have contacted an alternate facility and placed them on their waiting list. The Expert in Prenatal Opioid Maintenance stated that drug tests, which have included urine and blood screenings, have been performed weekly. Furthermore, if drugs screenings were not clear, a breach in contract has occurred, and patients must discontinue treatment. The Expert reported that Buprenorphine has been administered to MARC patients during the term of pregnancy at a maximum dose of 16 mg per day. After delivery, however, patients have been prescribed Suboxone, which also has a maximum dose of 16 mg per day. Each patient has been prescribed a different dose depending on each individual's level of addiction and have experienced minimal side effects such as nausea or headaches.<sup>35</sup> In addition to medication, the Expert also stated that patients have been required to attend group counseling, monthly individual meetings, and two Narcotics Anonymous meetings per month. The Expert reported that there have not been any cases of overdose while participating in the MARC Program.

One study in 2017 stated that only 16% of drug dependent pregnant women have successfully completed an opioid maintenance program and sustained from illicit drug use until the time of delivery.<sup>36</sup> Researchers have found that the dropout rate of mothers who used Buprenorphine as maintenance medication was 33%, which was significantly higher than the 18% dropout rate of pregnant women who used Methadone during maintenance therapy.<sup>36</sup> Between the years of 1992-2012, the number of pregnant women who were admitted into prenatal opioid therapy facilities due to prescription opioid drug usage increased from 2% to 28%.<sup>15</sup> Finally, a study that consisted of 95 women showed that 44% relapsed and resorted to illicit drug use before giving birth.<sup>17</sup>

## DISCUSSION

The purpose of this research study was to evaluate the participation of prenatal opioid maintenance to determine if it has decreased the amount of treatment needed for Neonatal Abstinence Syndrome in infants. The primary hypothesis for this study was that opioid maintenance therapy among pregnant women has decreased the occurrence and severity of NAS in infants. This analysis showed that prenatal opioid maintenance, especially with the use of Buprenorphine, has decreased the need for NAS treatment after birth and increased overall health in infants born to mothers who have participated in medication maintenance therapy.

One study showed that 5% of women within child bearing ages illicitly used opioids during their term of pregnancy.<sup>16</sup> In West Virginia, the amount of opioid-addicted pregnant women has continued to increase each year: this has resulted in more than twice as many cases of NAS. Hospitals have expended over \$300 million to treat infants with NAS, which have required 3.5 longer hospital stays than healthy newborns due to medicated-maintenance and health complications.<sup>21</sup> Holdren<sup>23</sup> suggested that NAS occurred in 5% of total births in West Virginia in 2016, which has shown a continual increase

each year. Cabell Huntington Hospital in Huntington, West Virginia, had 8% more cases of NAS than the remainder of hospitals in the state.

Studies have shown that BMT throughout pregnancy has been more effective for NAS after delivery than MMT. Johnson & Martin<sup>30</sup> reported less cases of NAS and a shorter length of stay with BMT. Furthermore, another study found that a significant amount of MMT exposed infants still needed treatment, compared to those who were exposed to BMT.<sup>34</sup> The MARC Program in Huntington, West Virginia has had a 100% completion rate using BMT, with minimal side effects. After delivery, MARC patients have been prescribed Suboxone for maintenance. Patients have also attended counseling and meetings as supplementary forms of treatment (Expert in Prenatal Opioid Maintenance, 2018). On the contrary, Klamon, et. al.<sup>35</sup> reported only 16% of women have completed a program without returning to illicit drug use. Furthermore, the need for prenatal opioid maintenance has continued to increase. Between 1992-2012, the need for medication maintenance increased by 26%.<sup>15</sup>

A positive component of opioid maintenance therapy throughout the term of pregnancy in West Virginia and the US has been the decrease in necessary treatment and severity of NAS in infants after birth. BMT has decreased the occurrence of NAS in infants to 49% and has decreased treatment needed for those born with NAS.

A negative component to prenatal opioid maintenance has been the dropout or relapse rate of pregnant mothers. Prenatal opioid maintenance programs also have not had the capacity to treat every opioid-addicted pregnant mother that has been seeking medication maintenance therapy.

### *Limitations and Practical Implications*

This research study was not conducted without its limitations. Prenatal opioid maintenance programs have not had the capacity for all pregnant mothers who have needed treatment, which has resulted in

NAS severity among infants. This literature review was restricted due to search strategy such as difficulty distinguishing generic drug names, number of databases or sources found, which may have affected the availability or accuracy of the research, and finally research and publication bias. Further research of Buprenorphine, Methadone, or new drugs is needed to ensure better results of NAS occurrence in the future. Continual participation in maintenance medication and cooperation of opioid-addicted pregnant women will help with further research regarding the occurrence and severity of NAS in newborns. BMT has decreased the need for opioid treatment in infants after birth and improved their overall health. The practical implications of prenatal opioid maintenance outcomes will need to be more heavily researched as more pregnant mothers continue to participate or drop-out of programs and new drugs come into the market.

## CONCLUSION

Participation in opioid maintenance therapy during pregnancy has shown a decrease in severity of NAS infants. This literature review has suggested that BMT has been the most effective form of treatment thus far.

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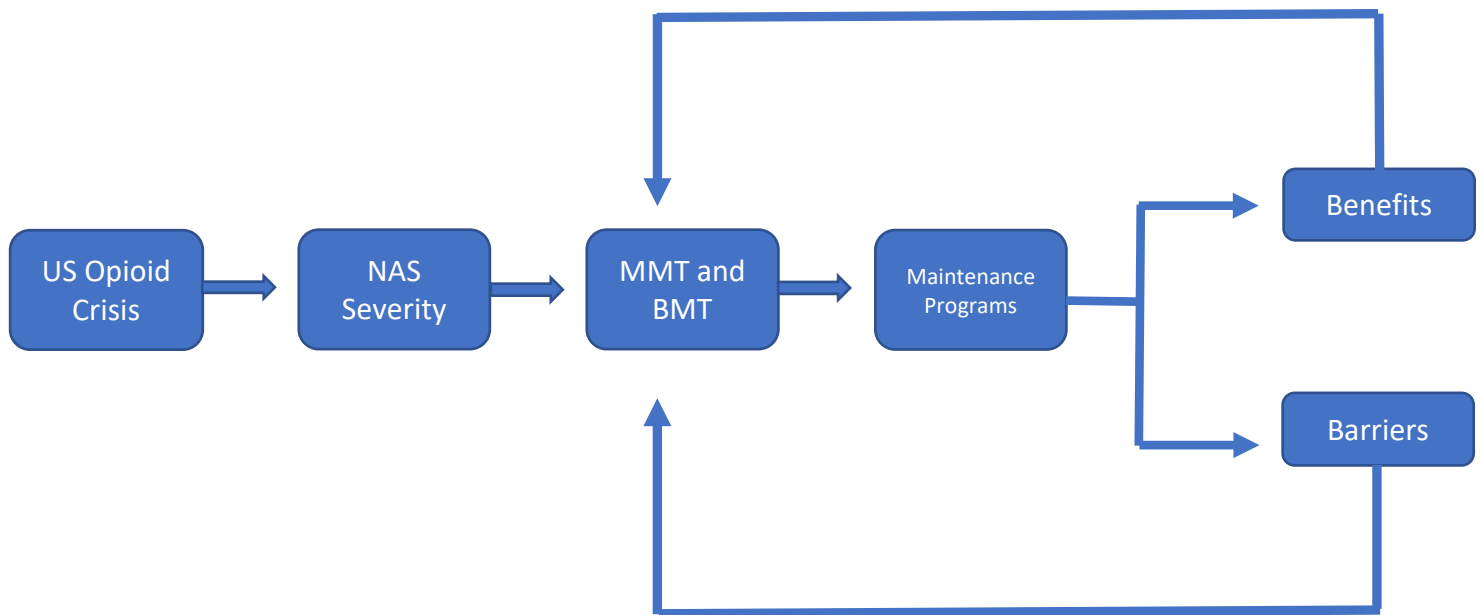
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Figures

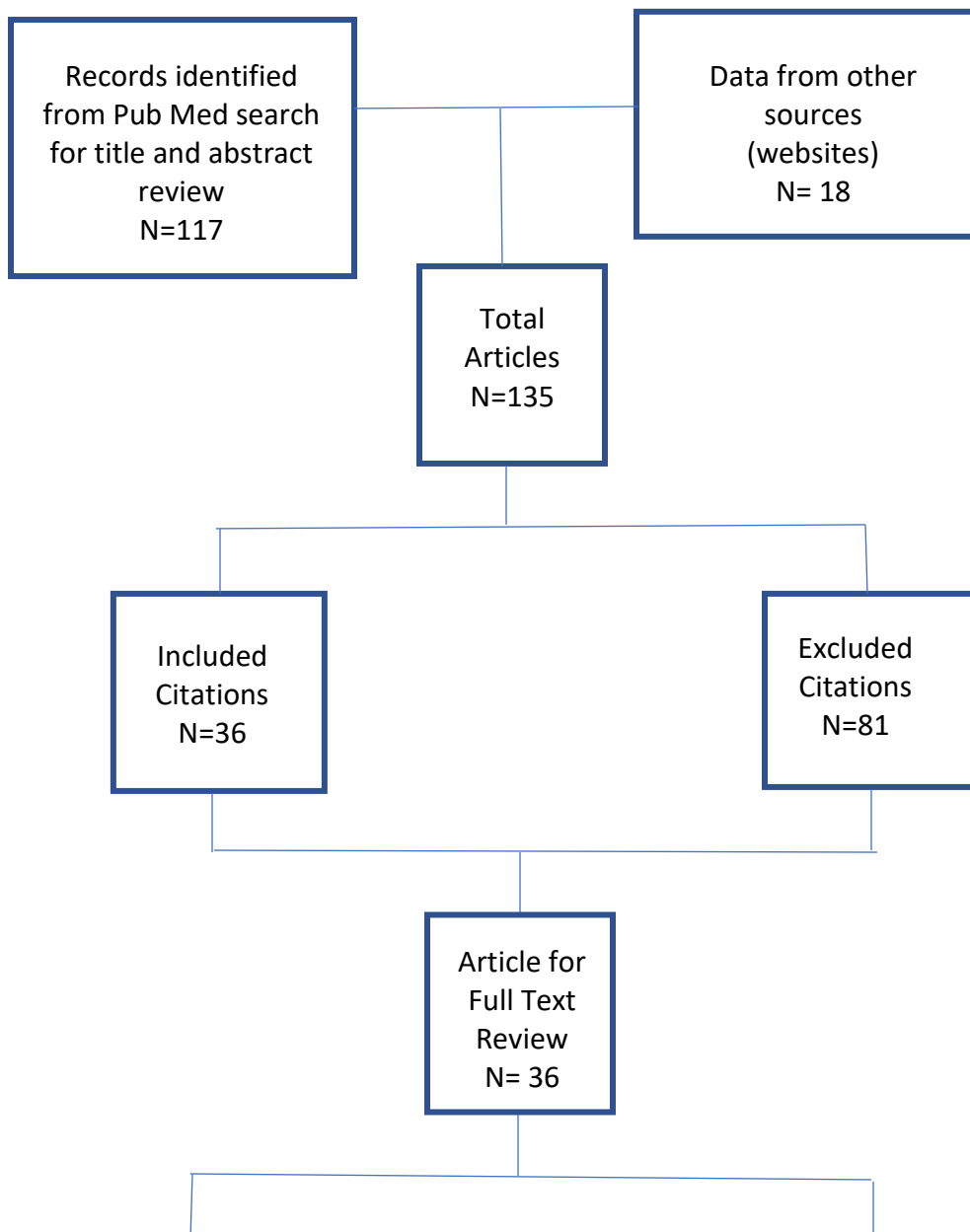
1. Promote Participation of Prenatal Opioid Maintenance Therapy



Source: Adopted from Brogly, Hahn, Diaz, & Werler<sup>14</sup>

Figure 1: Conceptual Research Framework

2. Overview of citation evaluation.



Articles included in  
The Data abstraction  
And Analysis  
N=36

Excluded Articles  
N= 0

## APPENDIX A

Questions Asked in Semi-Structured Interview of an Expert in Prenatal Opioid Maintenance on  
March 20, 2018

- What is your rate of relapse?
- How often have patients become opioid-free by the time of delivery? Why?
- How frequently do you perform drug tests?
- What is the range of ages currently enrolled? Why?
- Does a certain age group have a higher completion rate? Why?
- How many women can you have enrolled at once?
- How many women do you have to turn away? Why?
- What are the requirements/repercussions of staying in the program?
- What maintenance medication do you use? Why?
- How often is medication administered? Why?
- If more than one form of treatment is used, have you found one to be more effective than the other? Why?
- What are the side effects of medication used for treatment?
- How many miscarriages have been reported?
- Have any women overdosed while participating in your program?

- If known, how has your program impacted the infants of your patients? Why?