HHS Public Access

Author manuscript

Curr Psychiatry Rep. Author manuscript; available in PMC 2023 June 27.

Published in final edited form as:

Curr Psychiatry Rep. ; 21(12): 118. doi:10.1007/s11920-019-1110-4.

Opioid Use in Pregnancy

Amalia Londono Tobon, MD,

Erin Habecker, MD,

Ariadna Forray, MD

Yale School of Medicine, Department of Psychiatry

Abstract

Purpose of review: Perinatal opioid use is a major public health problem and is associated with a number of deleterious maternal and fetal effects. We review recent evidence of perinatal outcomes and treatment of opioid use disorder (OUD) during pregnancy.

Recent findings: Opioid exposure in pregnancy is associated with multiple obstetric and neonatal adverse outcomes, with the most common being neonatal opioid withdrawal syndrome (NOWS). Treatment with buprenorphine or methadone is associated with NOWS, but neither medication appears to have significant adverse effects on early childhood development. Buprenorphine appears to be superior to methadone in terms of incidence and severity of NOWS in exposed infants. The long-term effects of opioid exposure in-utero have been inconclusive, but recent longitudinal studies point to potential differences in brain morphology that may increase vulnerability to future stressors.

Summary: Maintenance therapy with methadone or buprenorphine remains the standard of care for pregnant women with OUD given its consistent superiority to placebo in terms of rates of illicit drug use and pregnancy outcomes. New non-pharmacologic management options for NOWS appear promising. Future research is needed to further evaluate the effects of opioid exposure in utero and determine the optimal delivery model for maintenance therapy.

Keywords

pregnancy; drug; opioids; opioid; perinatal; antenatal; postpartum

Introduction

Opioid use has increased dramatically over the last two decades, including use among reproductive-age women. The number of pregnant women with opioid use disorder (OUD) presenting to the hospital at labor and delivery quadrupled between 1999 and 2014 [1]. During this time the prevalence of OUD in the U.S. increased from 1.5 per 1,000 delivery hospitalizations in 1999 to 6.5 per 1,000 delivery hospitalizations in 2014 [1]. Opioid use in pregnancy includes both heroin and prescription opiates. Anywhere from 14% [2] to 22% [3] of pregnant women are prescribed an opioid. In 2017, 6.5% of pregnant women reported

Please direct all correspondence regarding this manuscript to Ariadna Forray, MD at the Yale School of Medicine, 40 Temple Street, Suite 6B, New Haven, CT 06510. Phone: (203) 764-8620. ariadna.forray@yale.edu.

illicit use of prescription opioids or heroin in the past year, and 1.3% reported use in the last month [4].

According to recent data from the Centers for Disease Control and Prevention, of the 13,365 deaths from opioid overdose among women in 2016, 56% occurred in reproductive-age women [5]. In addition to the risk of death by unintentional opioid overdose, opioid use in the perinatal period is associated with a number of deleterious effects in the mother and her offspring. The impact of opioid use in pregnancy may vary depending upon the point of exposure, extent of use, type of use (therapeutic vs. illicit) and engagement in treatment. The adverse effects of opioid use are further complicated by the frequency of concurrent substance use and comorbid psychiatric illness [6, 7]. As many as 35% of pregnant women with OUD have concurrent cannabis, cocaine and benzodiazapien use [8, 9], while tobacco smoking is as high as 95% [10, 11]. Pregnant women with OUD are also much more likely to have a history of trauma, and comorbid psychiatric diasnosis, including depression, anxiety, posttraumatic stress disorder, bipolar disorder and personality disorders [12, 7, 13, 14]. In addition, women with OUD frequently experience poor nutrition, inadequate prenatal care, poverty, chronic medical problems and domestic violence [15, 16]. Untreated OUD can also lead to disrupted parental care, and early dysfunctional maternal-infant interactions that can compound the negative effects of prenatal opioid exposure [17, 18].

This review will examine the recent literature on the maternal and neonatal consequences of opioid use during pregnancy, available treatments and special considerations.

Obstetric, Neonatal, and Long-term Childhood Effects of OUD

Opioid use in pregnancy, both illicit use and prescribed, has been associated with a number of obstetric, neonatal, and childhood adverse effects. Of note, before the use of opioid replacement treatment for opioid use disorder, studies primary focused on the effects of illicit opioid use (i.e. heroin). However, with increasing use of methadone and buprenorphine, studies are focusing on the differential effects of these two treatments on pregnancy and infant outcomes, in order to assess the risks and benefits of these treatments. However, disentangling the effects of illicit and treatment opioid use has been challenging. Pregnant women taking methadone and buprenorphine may relapse, use heroin and other substances during pregnancy, as well as have health behaviors which may interfere with prenatal care, or other psychiatric comorbidities which may confound the risk estimates. For example, 77% to 95% women with opioid use disorder also smoke cigarettes during pregnancy, and this can confound risk estimates of adverse outcomes [10, 11]. Thus, this portion will summarize the literature on the effects of opioid use in pregnancy on obstetric, neonatal and long-term childhood outcomes, with emphasis on the most recent literature, and in the context of the limitations of studies in this area.

Obstetric and Neonatal Outcomes

Opioid use in pregnancy has been associated with a significant increased risk of the following obstetric complications: toxemia, third trimester bleeding, maternal mortality, preterm birth [19, 20]. Adverse neonatal outcomes that have been associated with opioid use during pregnancy include small for gestational age, low birthweight, reduced

head circumference, sudden infant death, respiratory complications, and neonatal opioid withdrawal syndrome (NOWS) or neonatal abstinence syndrome (NAS) [20, 19]. NOWS affects anywhere from 45% to 94% of infants exposed opioids in utero and will be discussed in more detail later in this manuscript [19, 20].

Recent large administrative and populations-based studies continue to confirm some of the previously identified obstetric and neonatal complications of opioid use during pregnancy. A recent study utilizing data from the Nationwide Inpatient Sample, consisting of over 56 million American women, demonstrated that women with any opioid use had a significant increase in the odds of in-hospital maternal death (adjusted odds ratio (aOR) 4.6, 95% Confidence Interval (CI): 1.8–12.1), cardiac arrest (aOR 3.6, 95% CI: 1.4–9.1), intrauterine growth restriction (aOR 2.7, 95% CI: 2.4–2.9), placental abruption (aOR 2.4, 95% CI: 2.1–2.6), preterm labor (aOR 2.1, 95% CI: 2.0–2.3), oligohydramnios (aOR 1.7, 95% CI: 1.6–1.9), transfusion requirement (aOR 1.7, 95% CI: 1.5–1.9, stillbirth (aOR 1.5, 95% CI: 1.3–1.8), premature rupture of membranes (aOR 1.4, 95% CI: 1.3–1.6), and cesarean delivery (aOR 1.2, 95% CI: 1.1–1.3) when compared with those with no opioid use [21•]. This study adjusted for age group, race, payer, previous pregnancy complications, and preexisting conditions, such as tobacco and other substance use, depression, anxiety, and HIV. Additionally, a recent Danish population-based study of any opioid use in pregnancy, also demonstrated increased risk for preterm birth, low-birth weight and small for gestational age, and still births in women with opioid use, including those with prescribed opioids [22]. This study also showed that some of the risk could be partially explained by concomitant smoking during pregnancy [23].

More recently, there has also been concern with potential teratogenicity of opiates, in particular the risk of congenital malformations including oral cleft, ventricular and atrial septal defects, and clubfoot [22, 24, 25]. A systematic review of this topic including case-control and cohort studies, revealed mixed results with regards to congenital malformations and particular challenges with designs of the primary literature [24]. Despite mixed results, some studies do report increased risk of congenital abnormalities with opioid exposure in pregnancy. Therefore, there is a need for adequately powered studies to clarify the extent to which opioids may be associated rare congenital malformations.

Childhood Long-term Effects of Opioid Exposure In-utero

The long-term effects of opioid exposure in-uterine have been inconclusive [26, 27]. Some studies have revealed mixed evidence on long-term effects in infant vision and motor problems [27]. However, a more recent meta-analysis reported impairments with small to medium effect sizes for infants and medium to larger effect sizes for preschoolers' exposed to opioids in-utero compared to non-exposed, in cognitive, psychomotor, and behavioral domains [28•, 29]. Additionally, a recent, small longitudinal study of 17–21-year-old individuals exposed to opioids in-utero, demonstrated that although they performed within normal range of the population in cognitive testing, they had overall lower cognitive scores than the non-exposed comparison group [30]. Furthermore, these in-utero opioid-exposed young adults had smaller neuroanatomical volumes, smaller cortical surface areas and

thinner cortices than the non-exposed group [31]. These neuroanatomical characteristics partially mediated group differences in cognitive function [31].

Although much remains to be understood regarding the long-term effects of opioid use in pregnancy, recent studies indicate that there may be long-term effects of intrauterine opioid exposure. Several limitations of these studies include comorbid polysubstance exposure in-utero, variability in exposure and outcome measurements, and confounding factors including exposure to high-risk environments. It may be possible that intra-uterine opioid exposure not only directly affects development, but it may also increase vulnerability to future environmental adversities, and cause later impairments through indirect pathways.

Neonatal Opioid Withdrawal Syndrome Management

NOWS is characterized by several signs and symptoms including increased irritability, hypertonia, tremors, feeding difficulties, emesis, loose stools, respiratory difficulties and can lead to seizures [32]. NOWS incidence has continued to increase with the opioid epidemic from 1.20 per 1000 births in 2000 [19] to up to 20 per 1000 births per year in 2016 [33]. NOWS is highly prevalent in neonates exposed to opioids in utero and can result in significant neonatal morbidity and high healthcare utilization [19, 20].

There is considerable variability in the diagnosis and treatment of NOWS. Pharmacologic approaches including opioid replacement therapy with morphine or methadone starting in Neonatal Intensive Care Units (NICUs) have been the standard of care for the past decades. However, there has been increasing concern about the side effects of opioid use in infants including prolonged withdrawal symptoms, long hospital stays, and the short- and long-term effects of opioid treatments on development. Therefore, recently studies, including several retrospective cohorts and quality improvement studies, have examined novel, non-pharmacologic alternate options for the treatment of NOWS. These interventions, also known as the Eat, Sleep, Console model, include variations of environment (e.g. reduced light and noise, rooming-in instead of NICU), feeding (e.g. encouraging breastfeeding), soothing (e.g. swaddling, and skin to skin), and social techniques (e.g. encouraging caregiver interaction with infants) to treat withdrawal symptoms [34, 35••].

The results of these interventions are encouraging. One study showed that with non-pharmacologic interventions, the average opioid-exposed infant’s length of stay decreased from 22.4 to 5.9 days, infant treatment with morphine decreased from 98% to 14%, and there was a significant decrease in hospital costs, from $44,824 to $10,289 [36, 37]. Furthermore, no infants were readmitted for treatment of NOWS and no adverse events were reported [36]. A recent critical review of the available research on the Eat, Sleep, Console model supports the use of this approach to decrease length of stay, need for pharmacologic agents, and cost of treatment [38]. Although promising, these studies need to be considered in the context of their design limitations, and more rigorous trials comparing specific treatment strategies evaluating the short and long-term outcomes of these modalities are needed [39].

Buprenorphine vs. Methadone: Pregnancy and Infant Outcomes

More recently, multiple studies have focused on comparing the obstetric, birth, and long-term outcomes of methadone vs. buprenorphine given the increase use of these agents during pregnancy for opioid use disorders. A recent meta-analysis of unadjusted results of both randomized-controlled trials and observational cohort studies, showed that buprenorphine was associated with lower risk of preterm birth, greater birth weight, and larger head circumference compared to methadone treatment [40]. There were no differences between buprenorphine and methadone for spontaneous fetal death, fetal/congenital anomalies and other fetal growth measures [40]. These results are consistent with prior meta-analytic results [20, 41].

Additionally, a recent meta-analysis and a population-based cohort, showed that buprenorphine treatment during pregnancy was associated with lower NOWS treatment risk, mean length of hospital days for NOWS, shorter NOWS treatment, and lower morphine dose compared to methadone treatment during pregnancy [41, 22]. Although these results appear to indicate less NOWS and comorbidity with the use of buprenorphine in pregnancy, they need to be interpreted with caution given that the meta-analysis utilized data that had not controlled for potential confounders. Thus, some of the differences between treatments may be related to demographic differences between methadone and buprenorphine treated women and other confounding factors.

A recent study evaluating NOWS in women with OUD treated with buprenorphine found that maternal buprenorphine dose and exposure to other substance use were independently associated with NOWS, and that comorbid substance use was associated with more severe NOWS expression after controlling for buprenorphine dose [42••]. Similar findings have been reported with methadone treatment studies in which cigarette use and use of serotonin reuptake inhibitors were associated with more severe NOWS [43, 44, 10]. These findings highlight the role factors other than maintenance treatment have on expression of NOWS.

Regarding longer term outcomes, a recent follow-up study of the original MOTHER study, a randomized controlled trial of opioid-agonist pharmacotherapy during pregnancy, did not show major differences between in long-term outcomes in children exposed to methadone vs. buprenorphine in utero [45••]. Specifically, at follow-up children with in-utero exposure to buprenorphine compared to methadone were both within normal ranges of physical, cognitive, and language development assessments, and there were no differences between treatments with regards to these outcomes [45]. Although these results appear promising, larger, longer-term follow up studies are needed to determine if there are ongoing effects of opioid treatments in pregnancy, and if there are differential effects between different treatment option.

OUD Treatment During Pregnancy

Methadone

Since the 1970s, use of methadone for stabilization in pregnant women with opiate use disorder has been recommended due to the fact that a steady concentration of opioid in the maternal bloodstream protects the fetus from the adverse effects of repeated withdrawals

common in the setting of opioid abuse [46]. Compared to no opioid replacement therapy in OUD, it has been shown to retain patients in treatment more effectively and decrease heroin use [47]. In pregnant women who are using opiates illicitly, methadone provides the additional benefits of increasing number of prenatal visits, decreasing HIV infection rates, and decreasing rates of preeclampsia [48, 49]. Women treated with methadone for OUD generally must present for daily visits to a treatment center where they consume their dose under supervision, in accordance with federal law [50]. This can present limitations, particularly in working populations and in geographical areas without easy access to a treatment center (patients and providers can locate treatment centers at https://findtreatment.samhsa.gov/).

Another potential drawback to methadone use is the number of drug-drug interactions with other agents also metabolized through the CYP2B6 and CYP3A4 pathways in the liver, such as antiretrovirals. Methadone can accumulate in slow metabolizers and can place patients at risk for respiratory depression and long QT arrhythmias (Toursade des Pointes) at high systemic concentrations. However, safety profiles in pregnancy are overall reassuring [51, 52]. In addition to the previously mentioned maternal benefits, benefits for the fetus include lower rates of preterm delivery, lower rates of fetal loss, and lower rates of low birthweight infants when compared to infants of mothers who continue to use illicit opioids such as heroin [53–56]. Options for women in pregnancy include continuation of an already established dose of methadone vs. methadone initiation during the pregnancy. Maternal and fetal morbidity outcomes appear to be similar in these scenarios, although one recent population-based study showed that there was a significantly higher rate of infants being discharged directly into the care of social services from the hospital in women who initiated methadone during pregnancy [57].

Physiologic changes during pregnancy include increased volume of distribution and creatinine clearance, which increases the rate of drug metabolism and can necessitate incremental dose titration. Most pregnant women require twice daily dosing due to increased rate of clearance [58, 59]. Mean dose at delivery was 93 mg in one retrospective case series [58]. Strategies for methadone initiation and dosing have remained relatively stable over the past twenty years. More recent research has focused on outcomes associated with co-location of addiction, mental health and obstetrical treatment and the potential impact of wraparound services in women receiving medication assisted treatment (MAT), but due to the regulations surrounding the dispensing of methadone these studies generally involve women receiving buprenorphine, and will be discussed below.

Buprenorphine

Buprenorphine has been approved for medical maintenance treatment and medically supervised withdrawal since 2002 [51]. Although a licensed and trained provider is required to dispense buprenorphine, its distribution for OUD is not limited to treatment centers allowing for flexible office-based dosing schedules, which improves treatment access among pregnant and parenting women. Traditionally, buprenorphine alone has been recommended in pregnancy to avoid fetal exposure to naloxone, but more recent studies have shown no increase in adverse effects in women treated with buprenorphine and naloxone. A

small retrospective study involving ten women treated with buprenorphine and naloxone in pregnancy found that maternal and fetal outcomes were not significantly different than those of women treated with buprenorphine alone [60]. Neonatal ICU admission rates, length of hospital stay, and days of treatment for NOWS were comparable in both groups. Another retrospective study found that among 62 mother-infant dyads, 31 of whom were treated with methadone and 31 of whom were treated with buprenorphine and naloxone, the buprenorphine and naloxone group had significantly lower rates of NOWS, shorter hospitalizations, and lower peak NOWS scores in those infants affected compared with the methadone-exposed infants [61•]. There were no other significant differences between the groups.

When compared to placebo, buprenorphine has been shown to be more effective at retaining patients in treatment and suppressing illicit drug use at doses of 16 mg daily or higher [62]. Several head-to-head trials have compared methadone and buprenorphine for MAT in pregnant women [63, 64], and since the publication of the MOTHER trial [65], buprenorphine treatment has become more common in pregnancy. The MOTHER trial was a double-blind, double-dummy, flexible-dosing, randomized controlled study which randomized 175 women to either methadone (n=89) or buprenorphine (n=86) and compared rates of NOWS between the groups of exposed neonates [65]. The attrition rate was significantly higher in the buprenorphine group, perhaps attributable to the discomfort involved in needing to be in mild opiate withdrawal before starting partial agonist therapy with buprenorphine. Neonates exposed to buprenorphine who were treated for NOWS required 89% less morphine and left the hospital an average of 7.5 days sooner than those exposed to methadone [65]. A recent Cochrane review noted that the overall body of evidence is small and that although methadone appeared more likely overall to retain patients in treatment, buprenorphine appeared to have more favorable outcomes with regards to neonatal withdrawal [46].

Naltrexone

Naltrexone is a competitive agonist at opiate receptors and blocks the euphoric effects of opioids, which can decrease the perceived gains of using opiates illicitly [66]. Data are limited on its use in pregnancy, although safety profile at this time appears favorable [67]. Naltrexone is not associated with NOWS. However, oral dosing of naltrexone has not been shown to be superior to placebo outside of treatment centers where medication adherence is compulsory [68, 69]. Injectable and long-acting implantable forms of the medication have shown efficacy in helping women maintain abstinence in pregnancy [51, 66]. Initiation of naltrexone in pregnancy is limited by the fact that complete detoxification from opioids must be achieved prior to initiation. Detoxification can place pregnant women and their fetuses at risk for withdrawal symptoms, which can precipitate fetal stress and adverse pregnancy outcomes. Women undergoing detoxification outside a supervised facility are also more likely to relapse to illicit opiates. The American College of Obstetricians and Gynecologists (ACOG) accordingly does not recommend naltrexone initiation in pregnancy, and recommends the decision of whether to continue preexisting naltrexone therapy during pregnancy be individualized [70]. Women on naltrexone therapy may have more difficulty

with anesthesia options and pain control during childbirth, particularly in the event of an operative delivery.

Detoxification from Opioids versus Maintenance Therapy

Due to the risks to the fetus posed by in utero exposure to opiates and the risk for development of NOWS, ongoing debate continues over whether detoxification from opiates should be considered for pregnant women. Many women on maintenance opioid replacement therapy desire detoxification upon learning that they are pregnant. However, abrupt opioid withdrawal has been associated with a host of complications such as preterm labor, fetal withdrawal symptoms leading to fetal distress, and increased rates of miscarriage in older studies [67]. More recent research has not supported an association between withdrawal and preterm labor or withdrawal and pregnancy loss. One retrospective analysis involving 301 patients failed to show any adverse fetal outcomes related to detoxification [71]. However, most studies addressing detoxification in pregnancy are underpowered, lack control groups, and have a significant portion of participants lost to follow up [72•]. Pregnant patients with opioid use disorder on MAT demonstrate improved rates of abstinence from illicit drugs and better engagement with treatment than patients who undergo detoxification [48]. Women who chose to discontinue MAT are vulnerable to cycles of relapse and withdrawal due to the high rates of relapse associated with opioid use. Additionally, illicit use in the context of relapse is associated with a multitude of other risks, such as exposure to blood-borne pathogens, soft tissue infections, endocarditis, incarceration, and overdose death [51, 73]. A Cochrane review concluded that methadone maintenance is superior to no opioid replacement therapy based on the current body of research due to improved treatment retention and better suppression of heroin use in those treated with MAT [47]. Current ACOG and Substance Abuse and Mental Health Services Administration (SAMHSA) [74] guidelines support MAT as first line treatment in pregnant women with active opioid use.

Non-pharmacologic Treatments

While opioid agonist pharmacotherapy is the recommended therapy for OUD in pregnancy by ACOG [70], SAMHSA also recommends psychosocial support that at a minimum includes an assessment of the mother’s needs and referral to more intensive psychosocial treatment services [75]. Unfortunately, the literature regarding benefit of behavioral interventions alone or in addition to MAT in pregnant women is limited and mixed. Contingency management (CM), a behavioral interventions based on the principle of positive reinforcement (e.g. monetary vouchers) to modify behavior in a positive and supportive manner, has been the most frequently studied. CM initially appeared to be efficacious for pregnant women with OUD. Jones et al., found that CM was effective in treating opioid use in pregnancy, by significantly increasing abstinence and treatment attendance compared to controls [76]. However, more recent findings have found no benefit of fixed or escalating incentives in drug abstinence rates and days retained in treatment compared to non-incentive control condition [77]. Similarly, in a study evaluating CM with escalating incentives to improve birth weight among pregnant women on MAT, found that infants born to women in the CM condition did not differ from those receiving standard care condition [78].

Other Treatment Considerations

The multiple barriers experienced by pregnant women in seeking treatment for substance use, including fear of social stigma, involvement in violent relationships, lack of adequate child care during treatment and high rates of coexisting mental health issues, such as posttraumatic stress disorders and depression, led to the creation of women-centered treatment [79, 80]. Women-centered care among women with an OUD, often includes prenatal care, MAT, care coordination, behavioral health services, family planning and breastfeeding support [81–83]. The impact of multidisciplinary care in the outcomes of pregnant women with opioid use disorders has been investigated in recent years. One study compared women receiving opiate replacement therapy at a treatment center (methadone or buprenorphine), women receiving buprenorphine in a community program, and women receiving buprenorphine with an obstetric provider with co-located MAT services; there were no significant differences between the groups [84]. The OPTI-Mom study investigated the use of a patient navigation intervention, and although only a feasibility study it found that pregnant women with opioid use disorder receiving buprenorphine who completed the intervention reported improved abstinence from illicit opioids and other drugs [85•]. Another feasibility study on a model of embedded care for MAT and mental health care in an obstetric clinic demonstrated high retention rates (13/14 enrolled women remained engaged through delivery) and continued engagement (81% of patients continued buprenorphine treatment after delivery) [86]. Initial data on wraparound and collaborative care models appear encouraging, but more research is needed to determine the best model for treatment delivery.

Breastfeeding—Breastfeeding is an important intervention for women on maintenance therapy and opioid-exposed newborns. Breastfeeding has been demonstrated to decrease NOWS severity, reduce the need for pharmacotherapy and shorten hospital stay for the infant [87–89]. In addition, breastfeeding enhances attachment between a mother and her infant, facilitates skin-to-skin care, and provides immunity to the infant. As noted earlier it is one of the mainstays for the non-pharmacologic interventions for the management of NOWS. The American Academy of Pediatrics recommends breastfeeding for women who are stable on methadone or buprenorphine regardless of maternal dose [90]. Breastfeeding should also be encouraged in women who are not actively using illicit drugs and have no other contraindications, such as HIV [91]. Women should also be advised to suspend breastfeeding in the event of a relapse.

Conclusion

Over the last two decades opioid use in pregnancy has increased dramatically. With this increase in opioid use there has been a corresponding increase in NOWS. In addition, opioid use in pregnancy is associated with a number of adverse pregnancy outcomes, including maternal death at delivery, intrauterine growth restriction, placental abruption, preterm labor, oligohydramnios, stillbirth, premature rupture of membranes, and cesarean delivery when compared with no opioid use. Fortunately, MAT in pregnant women is an effective treatment that has been demonstrated to retain patients in treatment, decrease ilicit opioid use and improve birth outcomes. While methadone maintenance has been the standard of care for pregnant women with OUD for several decades, buprenorphine has

emerged as an effective alternative treatment. The recent literature supports buprenorphine as having a more favorable risk profile with respect to neonatal outcomes compared to methadone. Of note, recent evidence has demonstrated that exposure to MAT in pregnancy is not associated with cognitive or behavioral problems in offspring. The literature on the neurocognitive effects of prenatal opioid exposure provides conflicting results, pointing to the need for further studies that control for confounding factors, such as comorbid substance use and exposure to high-risk environments. There have been recent innovations in the management of NOWS, with the Eat, Sleep, Console approach, that have led to improved infant outcomes, with decreased length of stay and exposure to pharmacologic agents. The literature also supports the delivery of MAT via women-centered care that involves a wide range of health-care, social, and behavioral services to address the complex needs of pregnant women with OUD. While collaborative care and co-localized care are currently the main models to provide this type of care, further research is needed to determine the optimal model.

Declarations of Interest:

A.LT. is supported by NIMH T32 (MH MH018268-34), the Ariella Ritvo Grant.

References

1. Haight SC, Ko JY, Tong VT, Bohm MK, Callaghan WM. Opioid Use Disorder Documented at Delivery Hospitalization - United States, 1999–2014. MMWR Morb Mortal Wkly Rep. 2018;67(31):845–9. doi:10.15585/mmwr.mm6731a1. [PubMed: 30091969]
2. Bateman BT, Hernandez-Diaz S, Rathmell JP, Seeger JD, Doherty M, Fischer MA et al. Patterns of Opioid Utilization in Pregnancy in a Large Cohort of Commercial Insurance Beneficiaries in the United States. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2014;120(5):1216–24. doi:10.1097/aln.0000000000000172.
3. Desai RJ, Hernandez-Diaz S, Bateman BT, Huybrechts KF. Increase in Prescription Opioid Use During Pregnancy Among Medicaid-Enrolled Women. Obstetrics & Gynecology. 2014;123(5):997–1002. doi:10.1097/aog.0000000000000208. [PubMed: 24785852]
4. Abuse Substance and Mental Health Services Administration. National Survey on Drug Use and Health, 2017., Rockville, MD. 2017. https://pdas.samhsa.gov/#/survey/NSDUH-2017-DS0001. Accessed May 6 2019.
5. Seth P, Scholl L, Rudd RA, Bacon S. Overdose Deaths Involving Opioids, Cocaine, and Psychostimulants - United States, 2015–2016. MMWR Morb Mortal Wkly Rep. 2018;67:349–58. doi: 10.15585/mmwr.mm6712a1. [PubMed: 29596405]
6. Tuten M, Heil SH, O'Grady KE, Fitzsimons H, Chisolm MS, Jones HE. The impact of mood disorders on the delivery and neonatal outcomes of methadone-maintained pregnant patients. Am J Drug Alcohol Abuse. 2009;35(5):358–63. doi:10.1080/00952990903108231. [PubMed: 20180664]
7. Benningfield MM, Arria AM, Kaltenbach K, Heil SH, Stine SM, Coyle MG et al. Co-occurring psychiatric symptoms are associated with increased psychological, social, and medical impairment in opioid dependent pregnant women. The American journal on addictions / American Academy of Psychiatrists in Alcoholism and Addictions. 2010;19(5):416–21. doi:10.1111/j.1521-0391.2010.00064.x.
8. Keegan J, Parva M, Finnegan M, Gerson A, Belden M. Addiction in pregnancy. Journal of addictive diseases. 2010;29(2):175–91. doi:10.1080/10550881003684723. [PubMed: 20407975]
9. Metz VE, Brown QL, Martins SS, Palamar JJ. Characteristics of drug use among pregnant women in the United States: Opioid and non-opioid illegal drug use. Drug and Alcohol Dependence. 2018;183:261–6. doi:10.1016/j.drugalcdep.2017.11.010. [PubMed: 29310077]

10. Jones HE, Heil SH, Tuten M, Chisolm MS, Foster JM, O'Grady KE et al. Cigarette smoking in opioid-dependent pregnant women: neonatal and maternal outcomes. Drug Alcohol Depend. 2013;131(3):271–7. doi:10.1016/j.drugalcdep.2012.11.019. [PubMed: 23279924]

11. Chisolm MS, Tuten M, Brigham EC, Strain EC, Jones HE. Relationship between cigarette use and mood/anxiety disorders among pregnant methadone-maintained patients. American Journal on Addictions. 2009;18(5):422–9. [PubMed: 19874163]

12. Chisolm MS, Tuten M, Strain EC, Jones HE. Screening for Mood Disorder in Pregnant Substance-dependent Patients. Addict Disord Their Treat. 2009;8(2):88–98. doi:10.1097/ADT.0b013e31817c331b. [PubMed: 21528109]

13. Benningfield MM, Dietrich MS, Jones HE, Kaltenbach K, Heil SH, Stine SM et al. Opioid dependence during pregnancy: relationships of anxiety and depression symptoms to treatment outcomes. Addiction. 2012;107 Suppl 1:74–82. doi:10.1111/j.1360-0443.2012.04041.x. [PubMed: 23106929]

14. Eggleston AM, Calhoun PS, Svikis DS, Tuten M, Chisolm MS, Jones HE. Suicidality, aggression, and other treatment considerations among pregnant, substance-dependent women with posttraumatic stress disorder. Comprehensive psychiatry. 2009;50(5):415–23. doi:10.1016/j.comppsych.2008.11.004. [PubMed: 19683611]

15. Havens JR, Simmons LA, Shannon LM, Hansen WF. Factors associated with substance use during pregnancy: results from a national sample. Drug Alcohol Depend. 2009;99(1–3):89–95. doi:10.1016/j.drugalcdep.2008.07.010. [PubMed: 18778900]

16. HUTCHINS E, DIPIETRO J. Psychosocial Risk Factors Associated With Cocaine Use During Pregnancy: A Case-Control Study. Obstetrics & Gynecology. 1997;90(1):142–7. [PubMed: 9207829]

17. Mansoor E, Morrow CE, Accornero VH, Xue L, Johnson AL, Anthony JC et al. Longitudinal effects of prenatal cocaine use on mother-child interactions at ages 3 and 5 years. J Dev Behav Pediatr. 2012;33(1):32–41. doi:10.1097/DBP.0b013e31823968ab. [PubMed: 22157442]

18. Strathearn L, Mayes LC. Cocaine Addiction in Mothers: Potential Effects on Maternal Care and Infant Development. Annals of the New York Academy of Sciences. 2010;1187:172–83. doi:10.1111/j.1749-6632.2009.05142.x. [PubMed: 20201853]

19. Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000–2009. JAMA : the journal of the American Medical Association. 2012;307(18):1934–40. [PubMed: 22546608]

20. Minozzi S, Amato L, Bellisario C, Ferri M, Davoli M. Maintenance agonist treatments for opiate-dependent pregnant women. Cochrane Database of Systematic Reviews. 2013(12).

21•. Maeda A, Bateman BT, Clancy CR, Creanga AA, Leffert LR. Opioid Abuse and Dependence during PregnancyTemporal Trends and Obstetrical Outcomes. The Journal of the American Society of Anesthesiologists. 2014;121(6):1158–65.This study assessed nationwide trends in opioid abuse or dependence during pregnancy including obstetric and birth outcomes in the United States.

22. Nørgaard M, Nielsson MS, Heide-Jørgensen U. Birth and neonatal outcomes following opioid use in pregnancy: a Danish population-based study. Substance abuse: research and treatment. 2015;9:SART. S23547.

23. Nørgaard M, Nielsson MS, Heide-Jørgensen U. Birth and Neonatal Outcomes following Opioid Use in Pregnancy: A Danish Population-Based Study. Substance Abuse: Research and Treatment. 2015;9s2:SART.S23547. doi:10.4137/sart.S23547.

24. Lind JN, Interrante JD, Ailes EC, Gilboa SM, Khan S, Frey MT et al. Maternal use of opioids during pregnancy and congenital malformations: a systematic review. Pediatrics. 2017;139(6):e20164131. [PubMed: 28562278]

25. Broussard CS, Rasmussen SA, Reefhuis J, Friedman JM, Jann MW, Riehle-Colarusso T et al. Maternal treatment with opioid analgesics and risk for birth defects. American journal of obstetrics and gynecology. 2011;204(4):314. e1-. e11.

26. Behnke M, Smith VC, Abuse CoS. Prenatal substance abuse: short-and long-term effects on the exposed fetus. Pediatrics. 2013;131(3):e1009–e24. [PubMed: 23439891]

27. Maguire DJ, Taylor S, Armstrong K, Shaffer-Hudkins E, Germain AM, Brooks SS et al. Long-term outcomes of infants with neonatal abstinence syndrome. Neonatal Netw. 2016;35(5):277–86. [PubMed: 27636691]

28•. Baldacchino A, Arbuckle K, Petrie DJ, McCowan C. Erratum: Neurobehavioral consequences of chronic intrauterine opioid exposure in infants and preschool children: a systematic review and meta-analysis. BMC psychiatry. 2015;15(1):134. [PubMed: 26108949] This meta-analysis reports moderate effects of intrauterine opoid exposure on infant and preschool children's cognitive, psychomotor and observed behavioral outcomes.

29. Baldacchino A, Arbuckle K, Petrie DJ, McCowan C. Neurobehavioral consequences of chronic intrauterine opioid exposure in infants and preschool children: a systematic review and meta-analysis. BMC psychiatry. 2014;14(1):104. [PubMed: 24708875]

30. Nygaard E, Slinning K, Moe V, Walhovd KB. Cognitive function of youths born to mothers with opioid and poly-substance abuse problems during pregnancy. Child Neuropsychology. 2017;23(2):159–87. [PubMed: 26471942]

31. Nygaard E, Slinning K, Moe V, Due-Tønnessen P, Fjell A, Walhovd KB. Neuroanatomical characteristics of youths with prenatal opioid and poly-drug exposure. Neurotoxicology and teratology. 2018;68:13–26. [PubMed: 29679636]

32. Hudak ML, Tan RC. Neonatal drug withdrawal. Pediatrics. 2012;129(2):e540–e60. [PubMed: 22291123]

33. Milliren CE, Gupta M, Graham DA, Melvin P, Jorina M, Ozonoff A. Hospital variation in neonatal abstinence syndrome incidence, treatment modalities, resource use, and costs across pediatric hospitals in the United States, 2013 to 2016. Hospital pediatrics. 2018;8(1):15–20. [PubMed: 29263122]

34. Ryan G, Dooley J, Gerber Finn L, Kelly L. Nonpharmacological management of neonatal abstinence syndrome: a review of the literature. The Journal of Maternal-Fetal & Neonatal Medicine. 2019;32(10):1735–40. [PubMed: 29207895]

35••. MacMillan KDL, Rendon CP, Verma K, Riblet N, Washer DB, Holmes AV. Association of rooming-in with outcomes for neonatal abstinence syndrome: a systematic review and meta-analysis. JAMA pediatrics. 2018;172(4):345–51. [PubMed: 29404599] This systematic review evaluates the current evidence for non-pharmacologic treatment of neonatal abstinence syndrome as an alternative treatment.

36. Grossman MR, Berkwitt AK, Osborn RR, Xu Y, Esserman DA, Shapiro ED et al. An initiative to improve the quality of care of infants with neonatal abstinence syndrome. Pediatrics. 2017;139(6).

37. Grossman MR, Lipshaw MJ, Osborn RR, Berkwitt AK. A Novel Approach to Assessing Infants With Neonatal Abstinence Syndrome. Hosp Pediatr. 2018;8(1):1–6. doi:10.1542/hpeds.2017-0128. [PubMed: 29263121]

38. Grisham LM, Stephen MM, Coykendall MR, Kane MF, Maurer JA, Bader MY. Eat, Sleep, Console Approach: A Family-Centered Model for the Treatment of Neonatal Abstinence Syndrome. Advances in Neonatal Care. 2019;19(2):138–44. doi:10.1097/anc.0000000000000581. [PubMed: 30855311]

39. Wachman EM, Schiff DM, Silverstein M. Neonatal abstinence syndrome: advances in diagnosis and treatment. JAMA : the journal of the American Medical Association. 2018;319(13):1362–74. [PubMed: 29614184]

40. Zedler BK, Mann AL, Kim MM, Amick HR, Joyce AR, Murrelle EL et al. Buprenorphine compared with methadone to treat pregnant women with opioid use disorder: a systematic review and meta-analysis of safety in the mother, fetus and child. Addiction. 2016;111(12):2115–28. [PubMed: 27223595]

41. Brogly SB, Saia KA, Walley AY, Du HM, Sebastiani P. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. American journal of epidemiology. 2014;180(7):673–86. [PubMed: 25150272]

42••. Jansson LM, Velez ML, McConnell K, Spencer N, Tuten M, Jones H et al. Maternal buprenorphine treatment and infant outcome. Drug and Alcohol Dependence. 2017;180:56–61. doi:10.1016/j.drugalcdep.2017.08.001. [PubMed: 28869859] This study evaluates polysubstance use as a contributor to neonatal abstinence syndrome in buprenorphine-treated pregnant women.

43. Kaltenbach K, Holbrook AM, Coyle MG, Heil SH, Salisbury AL, Stine SM et al. Predicting treatment for neonatal abstinence syndrome in infants born to women maintained on opioid agonist medication. Addiction. 2012;107 Suppl 1:45–52. doi:10.1111/j.1360-0443.2012.04038.x.

44. Choo RE, Huestis MA, Schroeder JR, Shin AS, Jones HE. Neonatal abstinence syndrome in methadone-exposed infants is altered by level of prenatal tobacco exposure. Drug and Alcohol Dependence. 2004;75(3):253–60. doi:10.1016/j.drugalcdep.2004.03.012. [PubMed: 15283946]

45••. Kaltenbach K, O'Grady KE, Heil SH, Salisbury AL, Coyle MG, Fischer G et al. Prenatal exposure to methadone or buprenorphine: early childhood developmental outcomes. Drug and alcohol dependence. 2018;185:40–9. [PubMed: 29413437] This study is one of the first to show that both methadone and buprenorphine use in pregnancy for opiate use disoder do not seem to have major effects in early childhood developmental outcomes.

46. Minozzi S, Amato L, Bellisario C, Ferri M, Davoli M. Maintenance agonist treatments for opiate-dependent pregnant women. The Cochrane database of systematic reviews. 2013:CD006318. doi:10.1002/14651858.CD006318.pub3.

47. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. The Cochrane database of systematic reviews. 2009:CD002209. doi:10.1002/14651858.CD002209.pub2.

48. Jones HE, Kraft WK. Analgesia, Opioids, and Other Drug Use During Pregnancy and Neonatal Abstinence Syndrome. Clinics in perinatology. 2019;46:349–66. doi:10.1016/j.clp.2019.02.013. [PubMed: 31010564]

49. Jones H Specialty treatment for women. In: Strain E, Stitzer M, editors. Methadone Treatment for Opioid Dependence. Baltimore: Johns Hopkins University Press; 2006. p. 455–84.

50. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. Journal of addiction medicine. 2015;9:358–67. doi:10.1097/ADM.0000000000000166. [PubMed: 26406300]

51. Rodriguez CE, Klie KA. Pharmacological treatment of opioid use disorder in pregnancy. Seminars in perinatology. 2019. doi:10.1053/j.semperi.2019.01.003.

52. Mozurkewich EL, Rayburn WF. Buprenorphine and methadone for opioid addiction during pregnancy. Obstetrics and gynecology clinics of North America. 2014;41:241–53. doi:10.1016/j.ogc.2014.02.005. [PubMed: 24845488]

53. Forray A, Foster D. Substance Use in the Perinatal Period. Current Psychiatry Reports. 2015;17:91. doi:10.1007/s11920-015-0626-5. [PubMed: 26386836]

54. Hulse GK, Milne E, English DR, Holman CD. The relationship between maternal use of heroin and methadone and infant birth weight. Addiction (Abingdon, England). 1997;92:1571–9. [PubMed: 9519499]

55. Jones HE, O'Grady KE, Malfi D, Tuten M. Methadone maintenance vs. methadone taper during pregnancy: maternal and neonatal outcomes. The American journal on addictions. 2008;17:372–86. doi:10.1080/10550490802266276. [PubMed: 18770079]

56. Katrine Welle-Strand G Opioid maintenance treatment in pregnancy: Maternal and neonatal outcomes. 2015.

57. Guan Q, Sproule BA, Vigod SN, Cadarette SM, Greaves S, Martins D et al. Impact of timing of methadone initiation on perinatal outcomes following delivery among pregnant women on methadone maintenance therapy in Ontario. Addiction (Abingdon, England). 2019;114:268–77. doi:10.1111/add.14453. [PubMed: 30276907]

58. Albright B, de la Torre L, Skipper B, Price S, Abbott P, Rayburn W. Changes in methadone maintenance therapy during and after pregnancy. Journal of Substance Abuse Treatment. 2011;41:347–53. doi:10.1016/j.jsat.2011.05.002. [PubMed: 21741197]

59. Jansson LM, Dipietro JA, Velez M, Elko A, Knauer H, Kivlighan KT. Maternal methadone dosing schedule and fetal neurobehaviour. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians. 2009;22:29–35. doi:10.1080/14767050802452291.

60. Debelak K, Morrone WR, O'Grady KE, Jones HE. Buprenorphine + naloxone in the treatment of opioid dependence during pregnancy-initial patient care and outcome data. The American journal on addictions. 2013;22:252–4. doi:10.1111/j.1521-0391.2012.12005.x. [PubMed: 23617867]

61•. Wiegand SL, Stringer EM, Stuebe AM, Jones H, Seashore C, Thorp J. Buprenorphine and naloxone compared with methadone treatment in pregnancy. Obstetrics and gynecology. 2015;125:363–8. doi:10.1097/AOG.0000000000000640. [PubMed: 25569005] This study assessed the rates and characteristics of NOWS in women who were exposed to buprenorphine and naloxone versus those who were exposed to methadone.

62. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. The Cochrane database of systematic reviews. 2014:CD002207. doi:10.1002/14651858.CD002207.pub4.

63. Fischer G, Ortner R, Rohrmeister K, Jagsch R, Baewert A, Langer M et al. Methadone versus buprenorphine in pregnant addicts: a double-blind, double-dummy comparison study. Addiction (Abingdon, England). 2006;101:275–81. doi:10.1111/j.1360-0443.2006.01321.x. [PubMed: 16445556]

64. Jones HE, Johnson RE, Jasinski DR, O'Grady KE, Chisholm CA, Choo RE et al. Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on the neonatal abstinence syndrome. Drug and alcohol dependence. 2005;79:1–10. doi:10.1016/j.drugalcdep.2004.11.013. [PubMed: 15943939]

65. Jones HE, Kaltenbach K, Heil SH, Stine SM, Coyle MG, Arria AM et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. The New England journal of medicine. 2010;363:2320–31. doi:10.1056/NEJMoa1005359. [PubMed: 21142534]

66. Tran TH, Griffin BL, Stone RH, Vest KM, Todd TJ. Methadone, Buprenorphine, and Naltrexone for the Treatment of Opioid Use Disorder in Pregnant Women. Pharmacotherapy. 2017;37:824–39. doi:10.1002/phar.1958. [PubMed: 28543191]

67. Saia KA, Schiff D, Wachman EM, Mehta P, Vilkins A, Sia M et al. Caring for Pregnant Women with Opioid Use Disorder in the USA: Expanding and Improving Treatment. Current obstetrics and gynecology reports. 2016;5:257–63. doi:10.1007/s13669-016-0168-9. [PubMed: 27563497]

68. Jones HE, Chisolm MS, Jansson LM, Terplan M. Naltrexone in the treatment of opioid-dependent pregnant women: the case for a considered and measured approach to research. Addiction (Abingdon, England). 2013;108:233–47. doi:10.1111/j.1360-0443.2012.03811.x. [PubMed: 22471668]

69. Minozzi S, Amato L, Vecchi S, Davoli M, Kirchmayer U, Verster A. Oral naltrexone maintenance treatment for opioid dependence. The Cochrane database of systematic reviews. 2011:CD001333. doi:10.1002/14651858.CD001333.pub4.

70. ACOG. Opioid use and opioid use disorder in pregnancy. Committee Opinion No.711. Obstetrics and gynecology 2017;130:e81–94. [PubMed: 28742676]

71. Bell J, Towers CV, Hennessy MD, Heitzman C, Smith B, Chattin K. Detoxification from opiate drugs during pregnancy. American journal of obstetrics and gynecology. 2016;215:374.e1–6. doi:10.1016/j.ajog.2016.03.015.

72•. Jones HE, Terplan M, Meyer M. Medically Assisted Withdrawal (Detoxification): Considering the Mother-Infant Dyad. Journal of addiction medicine. 2017;11:90–2. doi:10.1097/ADM.0000000000000289. [PubMed: 28079573] This review critically evaluates medically assisted withdrawal compared to maintenance therapy. The authors found that the evidence does not support either benefit of medically assisted withdrawal or equivalence to opioid agonist pharmacotherapy.

73. Terplan M, Laird HJ, Hand DJ, Wright TE, Premkumar A, Martin CE et al. Opioid Detoxification During Pregnancy: A Systematic Review. Obstetrics and gynecology. 2018;131:803–14. doi:10.1097/AOG.0000000000002562. [PubMed: 29630016]

74. SAMHSA. A collaborative approach to the treatment of pregnant women with opioid use disorder. Rockville, MD: Substance Abuse and Mental Health Services Administration2016.

75. Kampman K, Comer S, Cunningham CO, Fishman MJ, Gordon A, Langleben D et al. National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. Chevy Chase, Md: American Society of Addiction Medicine2015.

76. Jones HE, Haug N, Silverman K, Stitzer M, Svikis D. The effectiveness of incentives in enhancing treatment attendance and drug abstinence in methadone-maintained pregnant women. Drug Alcohol Depend. 2001;61(3):297–306. doi:10.1016/S0376-8716(00)00152-6. [PubMed: 11164694]

77. Tuten M, Svikis DS, Keyser-Marcus L, O'Grady KE, Jones HE. Lessons Learned from a Randomized Trial of Fixed and Escalating Contingency Management Schedules in Opioid-Dependent Pregnant Women. The American Journal of Drug and Alcohol Abuse. 2012;38(4):286–92. doi:10.3109/00952990.2011.643977. [PubMed: 22352784]

78. Peles E, Sason A, Schreiber S, Adelson M. Newborn birth-weight of pregnant women on methadone or buprenorphine maintenance treatment: A national contingency management approach trial. The American Journal on Addictions. 2017;26(2):167–75. doi:10.1111/ajad.12508. [PubMed: 28191917]

79. Andrews CM, Cao D, Marsh JC, Shin HC. The impact of comprehensive services in substance abuse treatment for women with a history of intimate partner violence. Violence Against Women. 2011;17(5):550–67. doi:10.1177/1077801211407289. [PubMed: 21525014]

80. Laudet AB, Stanick V, Sands B. What could the program have done differently? A qualitative examination of reasons for leaving outpatient treatment. J Subst Abuse Treat. 2009;37(2):182–90. doi:10.1016/j.jsat.2009.01.001. [PubMed: 19339133]

81. Krans EE, Bobby S, England M, Gedekoh RH, Chang JC, Maguire B et al. The Pregnancy Recovery Center: A women-centered treatment program for pregnant and postpartum women with opioid use disorder. Addict Behav. 2018;86:124–9. doi:10.1016/j.addbeh.2018.05.016. [PubMed: 29884421]

82. Jones HE, Deppen K, Hudak ML, Leffert L, McClelland C, Sahin L et al. Clinical care for opioid-using pregnant and postpartum women: the role of obstetric providers. Am J Obstet Gynecol. 2014;210(4):302–10. doi:10.1016/j.ajog.2013.10.010. [PubMed: 24120973]

83. Saia K, Bagley SM, Wachman EM, Patel PP, Nadas MD, Brogly SB. Prenatal treatment for opioid dependency: observations from a large inner-city clinic. Addiction science & clinical practice. 2017;12(1):5. doi:10.1186/s13722-016-0070-9. [PubMed: 28086944]

84. Collier KW, MacAfee LK, Kenny BM, Meyer MC. Does co-location of medication assisted treatment and prenatal care for women with opioid use disorder increase pregnancy planning, length of interpregnancy interval, and postpartum contraceptive uptake? Journal of Substance Abuse Treatment. 2019;98:73–7. doi:10.1016/j.jsat.2018.12.001. [PubMed: 30665607]

85•. Cochran GT, Hruschak V, Abdullah W, Krans E, Douaihy AB, Bobby S et al. Optimizing Pregnancy Treatment Interventions for Moms (OPTI-Mom). Journal of Addiction Medicine. 2017;12:1. doi:10.1097/ADM.0000000000000370.This study investigated the feasibility of a targeted patient intervention during pregnancy and the postpartum period to improve abstinence from illicit opiates in mothers with opiate use disorder.

86. Mittal L, Suzuki J. Feasibility of collaborative care treatment of opioid use disorders with buprenorphine during pregnancy. Substance Abuse. 2017;38:261–4. doi:10.1080/08897077.2015.1129525. [PubMed: 26672650]

87. O'Connor AB, Collett A, Alto WA, O'Brien LM. Breastfeeding rates and the relationship between breastfeeding and neonatal abstinence syndrome in women maintained on buprenorphine during pregnancy. J Midwifery Womens Health. 2013;58(4):383–8. doi:10.1111/jmwh.12009. [PubMed: 23931660]

88. Welle-Strand GK, Skurtveit S, Jansson LM, Bakstad B, Bjarko L, Ravndal E. Breastfeeding reduces the need for withdrawal treatment in opioid-exposed infants. Acta Paediatr. 2013;102(11):1060–6. doi:10.1111/apa.12378. [PubMed: 23909865]

89. Bagley SM, Wachman EM, Holland E, Brogly SB. Review of the assessment and management of neonatal abstinence syndrome. Addiction science & clinical practice. 2014;9(1):19. doi:10.1186/1940-0640-9-19. [PubMed: 25199822]

90. Sachs HC. The Transfer of Drugs and Therapeutics Into Human Breast Milk: An Update on Selected Topics. Pediatrics. 2013;132(3):e796–e809. doi:10.1542/peds.2013-1985. [PubMed: 23979084]

91. Sarah R-S, A. MK, Medicine TAoB. ABM Clinical Protocol #21: Guidelines for Breastfeeding and Substance Use or Substance Use Disorder, Revised 2015. Breastfeed Med. 2015;10(3):135–41. doi:10.1089/bfm.2015.9992. [PubMed: 25836677]