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Medication-Assisted Treatment for Pregnant Women: A Systematic Review of the Evidence and Implications for Social Work Practice

Amber M. Holbrook West Chester University Viba H. Nguyen University of Pennsylvania

ABSTRACT Evidence-based practice with pregnant clients who are opioiddependent can be especially challenging because pregnant women are rarely included in clinical trials. The paper synthesizes systematic reviews on the outcomes of medication-assisted treatment for opioid dependent pregnant women and compares the effectiveness of methadone and buprenorphine. We explore evidence on maternal and neonatal outcomes, the safety of breastfeeding, and discuss the implications for social work practice. Searches were conducted in 6 databases. Ten reviews met the inclusion criteria. Results suggest medication-assisted treatment with either methadone or buprenorphine are equally effective in reducing maternal substance use, although methadone may offer slightly higher treatment retention rates when flexible dosing is implemented. Physical parameters and Apgar scores at birth show no significant differences in neonates exposed to methadone versus buprenorphine. Rates of treatment for neonatal abstinence syndrome also do not differ. However, when treatment is required burprenorphine may produce a shorter duration of withdrawal. Data on long-term developmental outcomes following in-utero exposure to opioid maintenance medications is inconclusive. Results suggest that there is minimal transmission of either methadone or buprenorphine to the neonate in breast milk. Conclusions are limited by missing data on broader psychosocial and maternal health outcomes. Evidence on long-term developmental outcomes for neonates is also confounded by prenatal drug exposure and environmental factors. Social workers engage with opioid-dependent pregnant women in many settings and can play an important role in ensuring access to treatment, and in addressing misconceptions around medication-assisted treatment for pregnant women with family members, peer supports, and other health care providers.

KEY WORDS: methadone, burprenorphine, pregnancy, systematic review, opioid abuse

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lence of opioid dependence during pregnancy are difficult to obtain, an estimated 2 million individuals in the United State abuse or are dependent upon opiates, including heroin or prescription opiates such as oxycodone and hydrocodone (Substance Abuse and Mental Health Services Administration [SAMHSA], 2012). Opiate dependence presents a major public health problem (Degenhardt et al., 2011; World Health Organization, 2009). As compared with the general population, illicit opiate users—especially injection drug users (IDUs)—have a higher incidence of infectious diseases such as hepatitis, HIV, and tuberculosis (Mathers et al., 2008; Nelson et al., 2011) and overdose is a significant cause of premature death (Degenhardt et al., 2011). In the United States, deaths related to opiate analgesic overdose now exceed those caused by heroin and cocaine combined (Centers for Disease Control and Prevention, 2011). The use of opioids during pregnancy significantly increases rates of preterm birth, spontaneous abortion, and infant mortality (Park, Meltzer-Brody, & Suzuki, 2012; Shainker, Saia, Lee-Parritz, 2012), resulting in a six-fold increase in obstetric complications and a 74fold increase in sudden infant death syndrome (Fajemirokun-Odudeyi et al., 2006; Ludlow, Evans, & Hulse, 2004).

The addiction liability of opiates is high (Bart, 2012), and longer term dependence on opiates can result in chronic alterations in dopaminergic, opioidergic, and stress responsive pathways, affecting the sensory, emotional, and impulse regulation centers of the brain (Bart, 2012). Medication-assisted treatment is intended to normalize aspects of stress responsiveness (Bart, 2012), relieve cravings, block the euphoric effects of illicit opioids, and prevent withdrawal symptoms (Center for Substance Abuse Treatment, 2005). Thus, medication-assisted treatment can be thought of as relapse prevention in that the medication corrects many of the disrupted neurobiological processes contributing to relapse. In pregnancy, medication-assisted treatment also serves to stabilize the uterine environment, protecting the fetus from the stress of repeated withdrawal (Jarvis & Schnoll, 1994). The intended patient outcomes of medication-assisted treatment with either methadone or buprenorphine are similar to those sought in substance abuse treatment overall: decreased drug use, reduced criminal behavior, and improved social functioning (Jackson, 2002). For pregnant women, improved maternal and neonatal outcomes are also a primary goal.

Medication-assisted treatment significantly reduces the risk of preterm birth (Shainker et al., 2012) as well as decreasing the risk of spontaneous abortion among women using heroin from 10%–20% to 3%–4% (Park, Meltzer-Brody, & Suzuki, 2012). Infant mortality rates among mothers receiving medication-assisted treatment are still higher than rates among women who have not used substances during pregnancy (Shainker et al., 2012). Nonetheless, when compared with outcomes of substance-using women who are not in treatment, it is clear that receipt of medication-assisted treatment lowers infant mortality rates and promotes fetal stability (Pritham, Troese, & Stetson, 2007).

Treatment retention is a strong predictor of long-term substance abuse treatment success, and therefore an important factor to consider in evaluating the efficacy of treatment (Terplan & Lui, 2007). Medication-assisted treatment is superior to psychosocial interventions alone or detoxification both in terms of treatment retention and reduction of substance use (Mattick, Breen, Kimber, & Davoli, 2009; Mayet, Farrell, Ferri, Amato, & Davoli, 2005). A flexible, individualized dosing regimen has been demonstrated to further improve treatment retention for nonpregnant patients (Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003; Mattick, Breen, Kimber, & Davoli, 2014). However, practitioners often raise concerns that higher doses of medication-assisted treatment used with pregnant patients might lead to neonatal abstinence syndrome (NAS), which is a constellation of symptoms of the gastrointestinal, respiratory, and autonomic and central nervous systems (Jansson, Velez, & Harrow, 2009). Estimates of the prevalence of NAS range from 48% to 95% in neonates born to mothers receiving opioid maintenance treatment (Konijnenberg & Melinder, 2011; Winklbaur et al., 2008). Although NAS symptoms are transitory and do not have long-term effects, extended hospital stays are often required for treatment of NAS in otherwise healthy infants.

The only two drugs federally approved for medication-assisted therapy for opioid dependence in the United States are methadone and buprenorphine. In the United States, methadone has been used for more than five decades, but can be dispensed only through federally approved opioid treatment programs (OTPs; SAMHSA, 2013b). In 2002, buprenorphine was approved by the Food and Drug Administration (FDA) for the treatment of opioid dependence. Physicians must obtain specialized training to prescribe buprenorphine. Some of these trained physicians are in private, office-based practices, while others are affiliated with substance abuse treatment facilities (SAMHSA, 2013b).

Access to medication-assisted treatment, particularly for pregnant women is complicated by many persistent barriers, including physical access, cultural norms, and stigma. Social workers engage with opioid dependent pregnant women in a variety of service contexts, including criminal justice and health care settings, through child protective or mental health services, and in outpatient treatment. Despite this frequent contact, many service providers have an unfavorable perception of OTP treatment:

Unfortunately, many communities and social service providers view OTPs and their patients with antipathy or disdain. Often, they misunderstand opiate agonist therapy, consider OTPs little more than legalized drug dealers, and consequently want nothing to do with an agency or its patients. (Jackson, 2002, p. 24.)

This concern is magnified when the opioid dependent individual is a pregnant woman (Goddard, 2003). Patients themselves might also be reluctant to seek or

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continue treatment, fearing the disapproval of friends, family, and service providers, or due to fear of unknown medical and developmental consequences for the fetus (Alto & O'Conner, 2011). As key providers of services to vulnerable and stigmatized populations, social workers can play a crucial role in facilitating receipt and continuation of treatment for opioid dependent pregnant women.

Present Study

The number of social workers entering the field of addictions treatment has increased substantially over the past three decades, making social workers primary providers of both mental health and addiction services in the United States (National Association of Social Workers, 2014). However, adoption of empirically supported techniques has been uneven across practice areas, with a slower rate of implementation noted in the addictions field (SAMHSA, 2013a). One of the key factors in breaking through barriers to implementation of evidence-based practices in the field has been identified as agency practitioners' attitudes toward, and knowledge of, empirically supported approaches (Wolf, Maguin, Ramsey, & Stringfellow, 2014). Given the concerns and stigma surrounding medicationassisted treatment, social service professionals, clients, and their families often express a preference for detoxification followed by psychosocial treatments to address opioid dependence during pregnancy. Social workers might be unclear what outcomes can be expected from medication-assisted treatment, or whether methadone or buprenorphine is most appropriate for a pregnant client. Therefore, examining the literature on the effectiveness of medication-assisted treatments is particularly important.

Evidence-based practice with pregnant clients who are opioid dependent can be especially challenging because pregnant women are rarely included in clinical trials. This means that the current state of knowledge is based largely on case studies, retrospective chart reviews of women who received treatment, and studies with small sample sizes and no comparison groups (Johnson, Jones, & Fischer, 2003). Systematic reviews and meta-analyses are one way of sifting and synthesizing this evidence to offer guidance to practitioners. However, although many review articles have been published on the topic of treating opioid dependence during pregnancy, their quality varies widely. In addition, many published reviews were written with a medical audience in mind rather than a social work audience, and thus focus on the clinical and pharmacological management of the pregnancy instead of evaluating treatment effectiveness. As Winklbaur et al. (2008, p. 1430) stated, "Guidance is scarce and published reviews tend to deal only with one aspect of the patient's challenges." The purpose of this paper is to critically review and synthesize information from the available systematic reviews and meta-analyses on medication-assisted treatment in opioid dependent pregnant women. Where available, we have examined evidence comparing the effectiveness of methadone and buprenorphine maintenance. We explore the evidence available on maternal and neonatal outcomes, the safety of breastfeeding, and discuss the implication of these findings for social work practice.

Method

This study is a systematic review of previously published meta-analyses and systematic reviews on the treatment of opioid dependence during pregnancy. We conducted four searches of the PubMed, EMBASE, Cochrane, SocAbs, WorldCat, and EBSCO databases, using the following sets of key words: (a) methadone, pregnancy; systematic review; (b) buprenorphine, pregnancy, systematic review; (c) methadone, pregnancy, meta-analysis; and (d) buprenorphine, pregnancy, meta-analysis. Search range was from January 2000 to August 2013.

The SocAbs, WorldCat, and EBSCO databases returned no results on all four searches. Results of from the PubMed, EMBASE, and Cochrane databases yielded 158 articles for the first set of keywords, 66 articles for the second, 30 articles for the third, and 13 articles for the fourth set of key words. These results were then reviewed and edited for duplication, leaving 22 distinct articles, which were then reviewed for relevance. No articles were excluded on the basis of language criteria, and translations were sought when necessary. Abstracts were reviewed initially and full text was sought when relevance was not clear from the abstract. We excluded reviews that focused primarily on the effects of illicit drug use, pharmacological or pain management strategies, or those that did not include outcomes. Five articles focusing primarily on clinical management strategies rather than outcomes were excluded based on relevance.

The remaining 17 articles were reviewed for quality and methodological rigor, using the criteria established by the Cochrane Collaboration and the PRISMA guidelines. Seven reviews were excluded because the articles did not meet these criteria (Higgins & Green, 2011; Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2009). For example, we excluded articles that failed to provide information on the search criteria used in the review. These exclusions yielded a total of nine systematic reviews and one meta-analysis that were included in our review.

Results

The majority of the systematic reviews meeting the inclusion criteria focused on neonatal rather than maternal outcomes of medication-assisted treatment. Two reviews examined maternal outcomes of treatment retention and concomitant substance use, whereas three reviews examined breastfeeding safety evidence and outcomes. Among the eight reviews addressing neonatal outcomes, the majority of the focus was on the length and severity of NAS symptoms. This limited scope indicates that although key outcomes have been addressed, data on many important maternal and neonatal outcomes might still be limited. In addition, most systematic reviews available on medication-assisted treatment during pregnancy did not provide concrete data on effect sizes, p values, or confidence intervals for the findings.

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 Summary of Published Reviews: Outcomes of Methadone Treatment During Pregnancy

Published Review	Articles Included	Number of Participants	Maternal Outcomes	Neonatal Outcomes	Breastfeeding
Bandstra et al., 2010	6	ΝΑ	None	Growth parametersNeonatal abstinence syndrome (NAS)	N _O
Cleary et al., 2010	29	5139	None	• NAS	No
Jansson et al., 2004	8	47	None	None	Yes
Konijnenberg & Melinder, 2011	35	NA	None	PrematurityCognitiveNeurologicalGrowth parameters	No
Minozzi et al., 2013	15	150–223	• Substance use treatment retention	Apgar scoreBirth weightNAS	No
Muller et al., 2011	11	72	None	None	Yes
Thajam et al., 2010	10	1092	None	• NAS	No
Winklbaur et al., 2008	N/A	NA	• Substance use treatment retention	None	No

Breastfeeding Neonatal abstinence Growth parameters Growth parameters Growth Parameters Neonatal Outcomes syndrome (NAS) Neurological Apgar Score Birth weight Prematurity Cognitive • NAS • NAS NAS • NAS • NAS None treatment retention treatment retention Maternal Outcomes Substance use Substance use Summary of Published Reviews: Outcomes of Buprenorphine Treatment During Pregnancy None None None None None None Participants Number of 150-223 1017 309 150 N/A N/A N/A 6 Articles Included N/A 6 ∞ 21 35 15 11 10 Winklbaur et al., 2008 Goodman et al., 2011 Bandstra et al., 2010 Johnson et al., 2003 Minozzi et al., 2013 Thajam et al., 2010 Muller et al., 2011 Published Review Melinder, 2011 Konijnenberg & Table 2

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Maternal Outcomes

Two of the systematic reviews included maternal outcomes, with a focus on concomitant substance use and treatment retention (Minozzi, Amato, Vecchi, & Davoli, 2013; Winklbaur et al., 2008). However, these reviews did not examine other important indicators of psychosocial functioning and health risk, such as engagement in criminal activity, transmission of infectious diseases, or compliance with prenatal care.

Substance use. Methadone and buprenorphine appear to be equally efficacious in reducing use of opioids during pregnancy (RR 1.81, 95% CI [0.70, 4.69]; Minozzi et al., 2013; Winklbaur et al., 2008). This efficacy appears to increase when medication-assisted treatment uses a flexible dosing regimen that is not capped at a lower dosage (Mattick et al., 2014).

Treatment retention. Although one of the two studies examining maternal outcomes reported no differences in treatment retention between pregnant patients maintained on methadone versus those maintained on buprenorphine (Winklbaur et al., 2008), evidence from the remaining study suggested that when flexible dosing was implemented, maintenance with methadone achieved slightly better retention rates (RR 0.64, 95% CI [0.41, 1.01] (Minozzi et al., 2013).

Neonatal Outcomes

Preterm birth and infant mortality. Currently, only limited evidence is available comparing the effects of methadone with the effects of buprenorphine on improving rates of preterm birth, spontaneous abortion, and infant mortality (Minozzi et al., 2013).

Apgar scores. The Apgar test is a brief assessment of an infant's breathing, heart rate, muscle tone, reflexes, and skin color performed at 1 minute and 5 minutes after birth to assess how well the infant tolerated the birth process and how well the infant is doing outside the womb. Only Minozzi et al. (2013) examined scores on the Apgar test, and their review reported no significant differences between infants whose mothers who received methadone during pregnancy and those who had received buprenorphine (MD 0.00, 95% CI [0.03, 0.03]).

Birth weight and head circumference. Three of the included reviews examined infant head circumference (Bandstra, Morrow, Mansoor, & Accornero, 2010; Goodman, 2011; Konijnenberg & Melinder, 2011), and four analyzed the available evidence on birth weight (Bandstra et al., 2010, Goodman, 2011; Konijnenberg & Melinder, 2011; Minozzi et al., 2013). All four reviews noted a scarcity of studies reporting on these neonatal outcomes, as well as the failure of the available studies to control for maternal nicotine use, which is a significant confounding factor for low birth weight.

The results suggested that infants exposed to opiates exhibit significantly lower birth weights and head circumferences as compared with their counterparts who were not exposed to opiates during gestation (Konijnenberg & Melinder, 2011). Receipt of maternal substance abuse treatment was correlated with higher birth weights in, opioid-exposed infants when compared to infants born to women not receiving treatment (Bandstra et al., 2010). Overall, medication-assisted treatment was shown to increase the duration of gestation, birth weight, and head circumference of opioid-exposed infants with no significant differences found between the benefits of methadone versus buprenorphine (mean difference [MD] –365.45 g, 95% CI [–673.84, –57.07]; Goodman, 2011; Minozzi et al., 2013;).

Neonatal abstinence syndrome. Although one large-scale clinical trial (Jones et al., 2010), and one systematic review (Johnson et al., 2003) reported lower rates of NAS treatment with buprenorphine versus methadone other studies found no difference in incidence of NAS between the two medications (Welle-Strand et al., 2013). The systematic review conducted by Minozzi et al. (2013) found methadone and buprenorphine did not differ in the rate of NAS resulting from maternal treatment (RR 1.22, 95% CI [0.89, 1.67]); however, the authors did find that maternal treatment with buprenorphine not only resulted in shorter duration of infant treatment for NAS, when required (MD 4.01, 95% CI [1.29, 9.30]) but also necessitated a lower total dose of morphine to control symptoms in the neonate (MD 5.06, 95% CI [-3.36, 13.47]). A recent meta-analysis and systematic review also suggested that neither average prenatal dose nor maternal methadone dose at delivery were correlated with the emergence of NAS in the neonate (Cleary et al., 2010; Thajam, Atkinson, Sibley, & Lavender, 2010). No evidence was found in the literature on the impact of buprenorphine dosage during pregnancy on the rates or severity of NAS.

Long-term developmental outcomes. Limited data were found on the long-term developmental outcomes of children who were exposed to methadone or buprenorphine in utero, with only one systematic review meeting the criteria for inclusion. The few longitudinal studies available on human subjects have offered
conflicting results regarding cognitive development and performance, with some
reporting no differences between opiate-exposed and non-exposed children and
others finding lower cognitive performance among opiate-exposed children (i.e.,
exposed to either methadone or buprenorphine; Konijnenberg & Melinder, 2011).
When differences were noted between exposed and non-exposed children, such
differences were observed in cognitive and language functions, but not in nonverbal performance (i.e., motor skills and sensory) tasks as evidenced by scores on
the Bayley Scales of Infant and Toddler Development and Stanford-Binet Intelligence Scale (Konijnenberg & Melinder, 2011).

Breastfeeding. Three reviews examining the outcomes for breastfeeding with either methadone or buprenorphine maintenance met the inclusion criteria. Although several studies have examined the transmission of methadone in breast milk and found minimal levels of the drug (Jansson, Velez, & Harrow, 2004),

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all studies to date appear to have used small sample sizes (Muller, Lange, Paul, & Seeliger, 2011). Further, the existing literature examining the transmission of buprenorphine to the neonate via breast milk primarily consists of case reports. The limited pharmacologic data available suggest that low oral bioavailability of buprenorphine contained in breast milk may minimize potential effects on the neonate (Goodman, 2011).

Discussion

Our results suggest that once flexible dosing is implemented in medicationassisted treatment during pregnancy, both methadone and buprenorphine offer similar results with regards to reduction of substance use; however, better treatment retention might be achieved with methadone. This finding is consistent with the literature on non-pregnant substance use patients among whom greater treatment attrition is noted in patients receiving buprenorphine, but both medications are found equally effective in reducing opioid and other illicit drug use (Mattick et al., 2014).

Our review noted a lack of evidence for the efficacy of medication-assisted treatment on a broader range of indicators of psychosocial functioning and maternal health outcomes. Although the receipt of medication-assisted treatment is widely thought to improve both the rate of transmission of infectious diseases and compliance with prenatal care (Carrieri et al., 2006; Roberts, 2011; Ruger & Lazar, 2012), we did not find any studies addressing these outcomes. Moreover, none of the studies included in this review measured reductions in criminal activity even though criminal activity has been shown to be substantially reduced in non-pregnant patients receiving either methadone or buprenorphine treatment for opioid dependence (Faggiano et al., 2008; Mattick et al., 2014). None of the included reviews examined the impact of treatment on relationship quality or parenting.

The limited evidence available suggests that methadone and buprenorphine have similar effects on Apgar scores, head circumference, and birth weight. Birth weight and head circumference are considered important indicators of fetal development, predictors of newborn well-being, and etiological indicators that determine the need for additional surveillance of newborn health. Birth weight is associated with infant mortality during the first year of life and provides an estimate of the rate of small-for-gestational age and preterm births in a population (Wilcox, 2001). Head circumference is used by pediatricians an indicator of brain size and growth. The mechanism by which medication-assisted treatment achieves these outcomes is not clear, but researchers have posited the medication-assisted treatment yields positive outcomes through the stabilization of the uterine environment, improved nutrition, consistent receipt of prenatal care, and/or reduction in rates of preterm births (Fajemirokun-Odudeyi et al., 2006; Ludlow et al., 2004).

Although some research has suggested buprenorphine offers reduced incidence of NAS (Jones et al., 2010; Winklbaur et al., 2008), similar rates of treatment for NAS were found among neonates exposed to methadone and buprenorphine in utero. However, our findings suggest that, when treatment for NAS is required, infants exposed to buprenorphine may require a shorter duration of treatment.

The evidence found on the safety of breastfeeding during medication-assisted treatment was limited, but suggests that only low levels of either methadone or buprenorphine are transmitted to infants through breast milk. Breastfeeding has been associated with significant benefits in the form of superior infant nutrition, improved immunity, promotion of mother-infant bonding, and support of the infant's cognitive development (Hilton, 2012; Ip et al., 2007). Given the risk of poor health and developmental trajectories for children exposed to abused drugs in utero (Behnke et al., 2013), and the challenges in mother-infant attachment that often occur in this population, the benefits that breastfeeding might provide are considerable (Glatstein, Garcia-Bournissen, Finkelstein, & Koren, 2008). On the other hand, little is known regarding the transmission of opioid maintenance medication via breast milk or its potential effects on the neonate. In addition, breastfeeding may be complicated by a number of factors. Symptoms of NAS, such as nasal stuffiness, irritability, hypertonicity, and an uncoordinated sucking response can interfere with the infant's ability to nurse easily (Jannson et al., 2004). The mother of an infant who is hospitalized for NAS treatment for an extended length of time might find it difficult to visit their treatment provider daily, care for other children, and visit the neonate multiple times per day for feeding. Despite these challenges, the American Academy of Pediatrics has recommended that mothers maintained on either methadone or buprenorphine should be encouraged to breastfeed their infants (Hilton, 2012), provided no other contraindications are present, such as continued concomitant drug abuse, HIV positivity, or maternal use of certain prescribed psychotropic medications. Notably, hepatitis C infection is not necessarily a contraindication if a woman wishes to breastfeed (Winklbaur et al., 2008).

Future Directions for Research

Although researchers have conducted numerous reviews of medication-assisted treatment during pregnancy, the majority of these reviews have focused on clinical management of the pregnancy rather than the effect of treatment on substance use, treatment retention, delivery complications, and transmission of infectious disease. In addition, a number of methodological concerns pose serious limitations regarding the evidence on maternal outcomes for methodone and buprenorphine, including infrequent inclusion of pregnant women in clinical trials, small sample sizes, and failure to control for concomitant substance use. Substantial differences in methodology have also prevented the synthesis of results across

studies (Winklbaur et al., 2008). Even though it is clear that medication-assisted treatment offers improved outcomes over detoxification or behavioral interventions alone, more research is needed on the role of flexible dosing regimens in improving treatment retention and reducing concomitant substance use.

The majority of reviews on neonatal outcomes of medication-assisted treatment have focused on the occurrence and severity of NAS. Many of the studies included in the systematic reviews did not control for confounding factors such as maternal nicotine use or the use of psychotropic medications. Failure to account for the impact of maternal nicotine use is a significant oversight because approximately 90% of opioid dependent women are also heavy smokers (Winklbaur et al., 2008). Given that a large number of substance abusing women also have cooccurring psychiatric disorders for which they require treatment (Fitzsimmons, Tuten, Vaidya, & Jones, 2007), it is critically important that studies control for maternal use of psychotropic medications, particularly benzodiazepines and serotonin selective reuptake inhibitors (SSRIs) that are used in the treatment of anxiety and depression. Moreover, symptoms of NAS can be mimicked by an infant's withdrawal from nicotine (Kaltenbach et al., 2012; Winklbaur et al., 2009), benzodiazepines (Prithim et al., 2007; Welle-Strand et al., 2013), and SSRIS (Kaltenbach et al., 2012), and withdrawal from these substances can impacting a broad range of other neonatal outcomes as well (Lattimore et al., 2005; Winklbaur et al., 2008). Although NAS is a significant issue that impacts health care costs and the quality of mother-infant bonding, it is important to note that NAS is transitory and does not have long-term effects on neonatal health and developmental outcomes. Further studies that address a broader range of neonatal outcomes are much needed.

Studies on long-term developmental outcomes are constrained by a number of methodological issues, including small sample sizes, failure to control for environmental factors, and poorly defined comparison groups (Bandstra et al., 2010). Current researchers in this area have found it especially difficult to delineate the effects of illicit prenatal drug exposure and the home environment on the developing child from the longer term effects of prenatal maintenance treatment. Issues of dosage and timing of exposure during pregnancy have yet to be explored. Integration of the animal and human research on opioid exposure have suggested several potential pathways by which opiate maintenance treatment might affect cognitive development, including fetal growth and maturity, myelination, endocrine function, and/or neurotransmitter content (Konijnenberg & Melinder, 2011).

Implications for Social Work Practice

Treatment for opiate addiction requires a long-term, comprehensive treatment approach. To date, no studies have supported the effectiveness of setting a fixed

limit on the duration of treatment (Minozzi et al., 2013). The recommended approach to medication-assisted treatment for pregnant women is to combine flexible dosing with individualized treatment plans that address financial, psychological, medical, legal, and social concerns (Winklbaur et al., 2008). In addition, treatment programs that include more frequent counseling contact and use of contingency management strategies, such as tying increased privileges to urinalysis results, might assist in reducing use of other drugs that are frequently abused by this population such as cannabis, cocaine, and benzodiazepines (Winklbaur et al., 2008).

Given that social workers are the main providers of substance abuse, mental health, and child welfare services in the United States, social workers are likely to encounter pregnant and parenting women who are opioid dependent in multiple settings. It is important that social workers offer these women accurate information on seeking treatment for opioid dependence, encourage them to access the full dose required for stabilization, and support informed decision making about breastfeeding. Many opioid-dependent women experience stigma and confront prejudice regarding medication-assisted treatment from their family members, hospital nursing staff, other social service providers, and even 12-step programs. Furthermore, if these women are recently released inmates, they are at particularly high risk for overdose and disease transmission (Rich, McKenzie et al., 2005). By providing women returning to the community with links to methadone treatment immediately upon release from incarceration, social workers have an opportunity to combat disease transmission, facilitate reentry into the community, and reduce recidivism (Rich, Boutwell, et al., 2005; Rich, McKenzie et al., 2005); however, this opportunity is frequently overlooked or neglected (Nunn et al., 2009). Social workers in correctional settings and community organizations that serve returning citizens could play a more active role in bridging gaps between criminal justice agencies and substance abuse facilities that offer medicationassisted treatment.

Social workers can also play a role in educating family members regarding the benefits of medication-assisted treatment as well as the commitment and support required for successful, long-term recovery. Facilitating family education groups can offer family members the opportunity to ask important questions about medication-assisted treatment, the recovery process, and long-term effects of drug use and medication-assisted treatment on the neonate. Family education groups can help repair and strengthen social supports that are critical for the mother's successful recovery.

Local 12-step groups can also play an important role in fostering recovery. Unfortunately, the culture of some 12-step meetings can be resistant to medication-assisted treatment for opioid-dependent individuals. Consequently, social workers

in substance abuse treatment programs can help to ensure a meeting climate in which opioid-dependent women will feel supported by partnering with a peer specialist and reaching out to 12-step groups to create a dialogue around medication-assisted treatment. Another way social workers can assist in building support in the community is through providing technical and organizational support to individuals wishing to organize a local Methadone Anonymous group in areas where such groups are not available.

Nursing staff in obstetric/gynecological clinics and neonatal hospital units who are unfamiliar with the evidence supporting medication-assisted treatment for pregnant opioid-dependent women might have reservations about particular aspects of the treatment. Nurses might be worried that the higher doses of methadone or buprenorphine during pregnancy will lead to poor neonatal outcomes, particularly a higher incidence and severity of NAS. In addition, poorly informed nursing staff might discourage breastfeeding in women receiving medicationassisted treatment out of concern for the impact of the medication on the neonate, or because they have reservations regarding other substances (such as nicotine or illicit drugs) that the patient might use. Multiple barriers to successful breastfeeding may occur, ranging from active discouragement by neonatal nursing staff to the physical symptoms of NAS that make breastfeeding challenging. Inclusion of social workers in the treatment planning process can help in addressing some of these issues. Social workers in health care settings can assist with counseling patients to alleviate fears of dose increases, and provide balanced information regarding the benefits and risks of breastfeeding for each patient. Social workers can also offer nonjudgmental information on the impact of nicotine use and the use of illicit drugs, especially benzodiazepines, on the neonate, and help to ensure the woman has the psychosocial supports needed for recovery and to pursue breastfeeding if she chooses.

Conclusion

Long-term medication-assisted treatment for opioid-dependent pregnant women has the potential to improve both immediate and long-term maternal and neonatal outcomes. Data on the safety of breastfeeding remains limited, but the available evidence suggests that transmission of methadone or buprenorphine to the neonate via breast milk is minimal. It is critically important that social workers provide direct support to opioid-dependent pregnant women in a variety of settings, as well as engage in advocacy and community education around the broad range of benefits that can be offered by medication-assisted treatment. Given that social workers are keenly concerned with social determinants of health and combating stigmatization that can function to reduce access to care, these professionals are positioned to play a leadership role in disseminating the evidence regarding the benefits to mother and child offered by medication-assisted treatment.

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References

*denotes article included in the review

- Alto, W. A., & O'Connor, A. B. (2011). Management of women treated with buprenorphine during pregnancy. *American Journal of Obstetrics and Gynecology*, 205(4), 302–308. http://dx.doi.org/10.1016/j.ajog.2011.04.001
- *Bandstra, E. S., Morrow, C. E., Mansoor, E., & Accornero, V. H. (2010). Prenatal drug exposure: Infant and toddler outcomes. *Journal of Addictive Diseases*, 29(2): 245–258. http://dx.doi.org/10.1080/10550881003684871
- Bart, G. (2012). Maintenance medication for opiate addiction: The foundation of recovery. Journal of Addictive Diseases, 31, 207—225. http://dx.doi.org/10.1080/10550887.2012.694598
- Behnke, M., Smith, V.C., Committee on Substance Abuse, & Committee on Fetus and Newborn. (2013). Prenatal substance abuse: Short- and long-term effects on the exposed fetus. *Pediatrics*, 131, e1009-e10024. http://dx.doi.org/10.1542/peds.2012-3931
- Carrieri, M. P., Amass, L., Lucas, G. M., Vlahov, D., Wodak, A., & Woody, G. E. (2006). Buprenorphine use: The international experience. *Clinical Infectious Diseases*, 43, S197—S215. http://dx.doi.org/10.1086/508184
- Center for Substance Abuse Treatment. (2005). Medication-assisted treatment for opioid addiction in opioid treatment programs. Treatment Improvement Protocol (TIP) Series 43 (HHS Publication No. SMA 12-4214). (Rev. ed.). Rockville, MD: Substance Abuse and Mental Health Services Administration. http://dx.doi.org/10.1037/e715712007-001
- Centers for Disease Control and Prevention. (2011). Vital signs: Overdoses of prescription opioid pain relievers—United States, 1998—2008. *Morbidity and Mortality Weekly Report*, 60, 1487—1492. Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6043a4 .htm
- *Cleary, B. J, Donnelly, J., Strawbridge, J., Gallagher, P. J., Fahey, T., Clarke, M., & Murphy, D. J. (2010). Methadone dose and neonatal abstinence syndrome—Systematic review and meta-analysis. *Addiction*, 105, 2071—2084. http://dx.doi.org/10.1111/j.1360-0443.2010.03120.x
- Degenhardt, L., Bucello, C., Mathers, B., Briegleb, C., Ali, H., Hickman, M., & McLaren, J. (2011). Mortality among regular or dependent users of heroin and other opioids: A systematic review and meta-analysis of cohort studies. *Addiction*, 106, 32–51. http://dx.doi.org/10.1111/j.1360-0443.2010.03140.x
- Faggiano, F., Vigna-Taglianti, F., Versino, E., & Lemma, P. (2003). Methadone maintenance at different dosages for opioid dependence. *Cochrane Database of Systematic Reviews*, 3, CD002208. http://dx.doi.org/10.1002/14651858.CD002208
- Fajemirokun-Odudeyi, O., Sinha, C., Tutty, S., Pairaudeau, P., Armstrong, D., Phillips, T., & Lindow, S. W. (2006). Pregnancy outcome in women who use opiates. European Journal of Obstetrics, Gynecology, and Reproductive Biology, 126, 170—175. http://dx.doi.org/10.1016/j.ejogrb.2005.08.010

- Fitzsimmons, H. E., Tuten, M., Vaidya, J., & Jones, H. E. (2007). Mood disorders affect drug treatment success of drug-dependent pregnant women. *Journal of Substance Abuse Treatment*, 32, 19–25. http://dx.doi.org/10.1016/j.jsat.2006.06.015
- Glatstein, M. M., Garcia-Bournissen, F., Finkelstein, Y., & Koren, G. (2008). Methadone exposure during lactation. *Canadian Family Physician*, 54, 1689—1690.
- Goddard, P. (2003). Changing attitudes towards harm reduction among treatment professionals: A report from the American Midwest. *International Journal of Drug Policy*, 14, 257–260. http://dx.doi.org/10.1016/s0955-3959(03)00075-6
- *Goodman, D. (2011). Buprenorphine for the treatment of perinatal opioid dependence: Pharmacology and implications for antepartum, intrapartum, and postpartum care. *Journal of Midwifery and Women's Health*, 56, 240–247. http://dx.doi.org/10.1111/j.15422011 .2011.00049.x
- Higgins, J.P.T., & Green, S. (Eds.). (2011). Cochrane handbook for systematic reviews of interventions version 5.1.0. Cochrane Collaboration. Retrieved from http://www.cochrane-handbook.org
- Hilton, T. C. (2012). Breastfeeding considerations of opioid dependent mothers and infants. MCN: American Journal of Maternal/Child Nursing, 37, 236—240. http://dx.doi.org/10.1097 /NMC.0b013e318251056c
- Ip, S., Chung, M., Raman, G., Chew, P., Magula, N., DeVine, D., . . . Lau, J. (2007). Breast-feeding and maternal and infant health outcomes in developed countries (AHRQ Publication No. 07-E007). Evidence Report/Technology Assessment, 153, 1–186. Retrieved from http://archive.ahrq.gov/downloads/pub/evidence/pdf/brfout/brfout.pdf
- Jackson, T. R. (2002). Treatment practice and research issues in improving opioid treatment outcomes. Science and Practice Perspectives, 1(1), 22–28. http://dx.doi.org/10.1151/spp021122
- *Jansson, L. M., Velez, M., & Harrow, C. (2004). Methadone maintenance and lactation: A review of the literature and current management guidelines. *Journal of Human Lactation*, 20(1), 62-71. http://dx.doi.org/10.1177/0890334403261027
- Jansson, L. M., Velez, M., & Harrow, C. (2009). The opioid-exposed newborn: Assessment and pharmacologic management. *Journal of Opioid Management*, 5, 47–55. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2729086/
- Jarvis, M. A., & Schnoll, S. H. (1994). Methadone treatment during pregnancy. Journal of Psychoactive Drugs, 26, 155—161. http://dx.doi.org/10.1080/02791072.1994.10472263
- *Johnson, R. E., Jones, H. E., & Fischer, G. (2003). Use of buprenorphine in pregnancy: Patient management and effects on the neonate. *Drug and Alcohol Dependence*, 70, S87—S101. http://dx.doi.org/10.1016/s0376-8716(03)00062-0
- Jones, H. E., Kaltenbach, K., Heil, S. H., Stine, S. M., Coyle, M. G., Arria, A. M., . . . Fischer, G. (2010). Neonatal abstinence syndrome after methadone or buprenorphine exposure. New England Journal of Medicine, 363, 2320—2331. http://dx.doi.org/10.1056/nejmoa1005359
- Kaltenbach, K., Holbrook, A. M., Coyle, M. G., Heil, S. H., Salisbury, A. L., Stine, S.M., . . . Jones, H. E. (2012). Predicting treatment for neonatal abstinence syndrome in infants born to women maintained on opioid agonist medication. *Addiction*, 107, 45–52. http://dx.doi.org/10.1111/j.1360-0443.2012.04038.x
- *Konijnenberg, C., & Melinder, A. (2011). Prenatal exposure to methadone and buprenorphine: A review of the potential effects on cognitive development. *Child Neuropsychology*, 17, 495—519. http://dx.doi.org/10.1080/09297049.2011.553591
- Lattimore, K. A., Donn, S. M., Kaciroti, N., Kemper, A. R., Neal, C.R. Jr., Vazquez, D. M. (2005). Selective serotonin reuptake inhibitor (SSRI) use during pregnancy and effects on

- the fetus and newborn: A meta-analysis. *Journal of Perinatology*, 25, 595–604. http://dx.doi.org/10.1038/sj.jp.7211352
- Ludlow, J. P., Evans, S. F., & Hulse, G. (2004). Obstetric and perinatal outcomes in pregnancies associated with illicit substances. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 44, 301–306. http://dx.doi.org/10.1111/j.1479-828x.2004.00221.x
- Mathers, B. M., Degenhardt, L., Phillips, B., Wiessing, L., Hickman, M., Strathdee, S.A., . . . Mattick, R. P. for the 2007 Reference Group to the UN on HIV and Injecting Drug Use. (2008). Global epidemiology of injecting drug use and HIV among people who inject drugs: A systematic review. *Lancet*, 372, 1733—1745. http://dx.doi.org/10.1016/S0140-6736(08)61311-2
- Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2009). Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database of Systematic Reviews*, 8(3), CD002209.pub2. http://dx.doi.org/10.1002/14651858.cd002209.pub2
- Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo versus methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews*, 2: CD002207. http://dx.doi.org/10.1002/14651858.CD002207.pub4
- Mayet, S., Farrell, M., Ferri, M., Amato, L., & Davoli, M. (2005). Psychosocial treatment for opiate abuse and dependence. *Cochrane Database of Systematic Reviews*, 25(1), CD004330. http://dx.doi.org/10.1002/14651858.cd004330.pub2
- *Minozzi, S., Amato, L., Vecchi, S., & Davoli, M. (2013). Maintenance agonist treatments for opiate dependent pregnant women. *Cochrane Database of Systematic Reviews*, 12, CD006318. http://dx.doi.org/10.1002/14651858.cd006318.pub3
- Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & The Prisma Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLOS Medicine, 6(7), e1000097. http://dx.doi.org/10.1371/journal.pmed.1000097
- *Muller, M. J., Lange, M., Paul, T., & Seelinger, S. (2011). Breast feeding during methadon and buprenorphin therapy. *Klinische Padiatrie*, 223(7), 408—413. http://dx.doi.org/10.1055/s-0031-1283193
- National Association of Social Workers. (2014). *Social work profession: General fact sheet.* Retrieved from http://www.socialworkers.org/pressroom/features/general/profession.asp
- Nelson, P. K., Mathers, B. M., Cowie, B., Hagan, H., Des Jarlais, D., Horyniak, D., & Degenhardt, L. (2011). Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: Results of systematic reviews. *Lancet*, 378, 571–583. http://dx.doi.org/10.1016/S0140-6736(11)61097-0
- Nunn, A., Zaller, N., Dickman, S., Trimbur, C., Nijhawan, A., & Rich, J. A. (2009). Methadone and buprenorphine prescribing and referral practices in US prison systems: Results from a nationwide survey. *Drug and Alcohol Dependence*, 105, 83–88. http://dx.doi.org/10.1016/j.drugalcdep.2009.06.015
- Park, E. M., Meltzer-Brody, S., & Suzuki, J. (2012). Evaluation and management of opioid dependence in pregnancy. *Psychosomatics*, 53, 424–432. http://dx.doi.org/10.1016/j.psym .2012.04.003
- Pritham, U. A., Troese, M., & Stetson, A. (2007). Methadone and buprenorphine treatment during pregnancy: What are the effects on infants? *Nursing for Women's Health*, 11, 558–567. http://dx.doi.org/10.1111/j.1751-486X.2007.00243.x
- Rich, J. D., Boutwell, A. E., Shield, D. C., Key, R. G., McKenzie, M., Clarke, J. G., & Friedmann, P. D. (2005). Attitudes and practices regarding the use of methadone in US stateand federal prisons. *Journal of Urban Health*, 82, 411—419. http://dx.doi.org/10.1093/jurban/jti072

- Rich, J. D., McKenzie, M., Shield, D. C., Wolf, F. A., Key, R. G., Poshkus, M., & Clarke, J. (2005). Linkage with methadone treatment upon release from incarceration: A promising opportunity. *Journal of Addictive Diseases*, 24, 49–59. http://dx.doi.org/10.1300/J069v24n03_04
- Roberts, S. (2011). Complex calculations: How drug use during pregnancy becomes a barrier to prenatal care. *Maternal and Child Health Journal*, 15, 333—341. http://dx.doi.org/10.1007/s10995-010-0594-7
- Ruger, J. P., & Lazar, C. M. (2012). Economic evaluation of drug abuse treatment and HIV prevention programs in pregnant women: A systematic review. *Addictive Behaviors*, 37, 1–10. http://dx.doi.org/doi:10.1016/j.addbeh.2011.07.042
- Shainker, S. A., Saia, K., & Lee-Parritz, A. (2012). Opioid addiction in pregnancy. *Obstetrical and Gynecological Survey*, 67, 817–825. http://dx.doi.org/10.1097/OGX.0b013e3182788e8c
- Substance Abuse and Mental Health Services Administration. (2012). Results from the 2011 National Survey on Drug Use and Health: Summary of national findings (NSDUH Series H-44, HHS Publication No. SMA 12-4713). Rockville, MD. Retrieved from http://www.samhsa.gov/data/NSDUH/2012SummNatFindDetTables/NationalFindings/NSDUHresults2012.pdf
- Substance Abuse and Mental Health Services Administration. (2013a). Report to Congress on the nation's substance abuse and mental health workforce issues (Pub. ID PEP13-RTC-BHWORK). Rockville, MD: Author. Retrieved from http://store.samhsa.gov/shin/content/PEP13-RTC-BHWORK/PEP13-RTC-BHWORK.pdf
- Substance Abuse and Mental Health Services Administration. (2013b). The N-SSATS report:

 Trends in the use of methadone and buprenorphine at substance abuse treatment facilities: 2003 to 2011. Rockville, MD: Author. Retrieved from http://www.samhsa.gov/data/
- Terplan, M., & Lui, S. (2007). Psychosocial interventions for pregnant women in outpatient illicit drug treatment compared to other interventions. *Cochrane Database of Systematic Reviews*, 4, CD006037. http://dx.doi.org/10.1002/14651858.CD006037.pub2.
- *Thajam, D., Atkinson, D.E., Sibley, C. P., & Lavender, T. (2010). Is neonatal abstinence syndrome related to the amount of opiate used? *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 39, 503—509. http://dx.doi.org/10.1111/j.1552-6909.2010.01174.x
- Welle-Strand, G. K., Skurtveit, S., Jones, H. E., Waal, H., Bakstad, B., Bjarko, L., & Ravndal, E. (2013). Neonatal outcomes following in utero exposure to methadone or buprenorphine: A national cohort study of opioid-agonist treatment of pregnant women in Norway from 1996-2009. *Drug and Alcohol Dependence*, 127, 200–206. http://dx.doi.org/10.1016/j.drugalcdep.2012.07.001
- Wilcox, A. J. (2001). On the importance—and the unimportance—of birthweight. *International Journal of Epidemiology*, 30, 1233—1241. http://dx.doi.org/10.1093/ije/30.6.1233
- *Winklbaur, B., Kopf, N., Ebner, N., Jung, E., Thau, K., & Fischer, G. (2008). Treating pregnant women dependent on opioids is not the same as treating pregnancy and opioid dependence: A knowledge synthesis for better treatment for women and neonates. *Addiction*, 103, 1429—1440. http://dx.doi.org/10.1111/j.1360-0443.2008.02283.x
- Winklbaur, B., Baewert, A., Jagsch, R., Rohrmeister, K., Metz, V., Aeschbach Jachmann, C., . . . Fischer, G. (2009). Association between prenatal tobacco exposure and outcome of neonates born to opioid-maintained mothers. Implications for treatment. European Addiction Research, 15, 150–156. http://dx.doi.org/10.1159/000216466
- Wolf, D.A.P.S., Maguin, E., Ramsey, A., & Stringfellow, E. (2014). Measuring attitudes toward empirically supported treatment in real-world addiction services. *Journal of Social Work Practice in the Addictions*, 14, 141–154. http://dx.doi.org/10.1080/1533256X.2014.902717

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World Health Organization. (2009). Global health risks: Mortality and burden of disease attributable to selected major risks. Geneva, Switzerland: Author. Retrieved from http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf

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