



Medication assisted treatment discontinuation in pregnant and postpartum women with opioid use disorder



Christine Wilder^{a,b,*}, Daniel Lewis^a, Theresa Winhusen^a

^a Addiction Sciences Division, Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, 3131 Harvey Avenue, Cincinnati, OH 45229, USA

^b Department of Veterans Affairs Medical Center, 3200 Vine Street, Cincinnati, OH 45220, USA

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ABSTRACT

Background: Increasing use of opioids has led to an increase in the number of pregnant and postpartum women in medication assisted treatment (MAT) for opioid use disorder.

Methods: We (1) conducted a systematic review of published literature on MAT discontinuation (methadone and buprenorphine) in pregnant and postpartum women and (2) determined methadone discontinuation rates in a retrospective cohort (2006–2013) of pregnant and postpartum women in a university affiliated methadone clinic.

Results: We found limited generalizable literature reports of discontinuation rates, with a range of prenatal discontinuation rates from 0 to 33% and rates which spanned various prenatal and postnatal periods from 26 to 64%. In our cohort of 229 women, 251 pregnancies were reported, with a prenatal methadone discontinuation rate of 11.0%. Based on a Cox proportional hazards model controlling for age, pregnancy outcome, and duration of treatment prior to delivery, the probability of methadone discontinuation at or before 6 months postpartum was 56.0%. Duration of methadone treatment prior to delivery was inversely associated with risk for postpartum discontinuation of treatment (HR = 0.98, 95% CI (0.96, 0.99)).

Conclusions: We conclude that the postpartum period is a time of increased risk for discontinuation of MAT. More accurate assessment of rates of pre- and postpartum MAT discontinuation, as well as further investigation of factors affecting these rates, is warranted. Development and testing of interventions to encourage early prenatal enrollment in MAT and improve postnatal retention in MAT would benefit pregnant women and new mothers with opioid use disorder.

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1. Introduction

The percentage of pregnant women who use opioids has tripled in the last ten years, with 1.2% of all pregnant women reporting opioid use in 2012 (Substance Abuse and Mental Health Services Administration, 2003, 2013). Pregnant women face severe, long-term consequences of drug use, including an increased likelihood of assault and abuse, contracting HIV or hepatitis, miscarriage, delivering infants with physical and behavioral impairments, postpartum depression, and loss of custody of their children (Dakof et al., 2003; Dansky et al., 1999; Holbrook and Kaltenbach, 2012; Kissin et al., 2001). Pregnant women using illicit opioids expose themselves and their fetuses to additional risks specific to

opioid use, including pregnancy complications, premature labor, low birth weight, and spontaneous abortion (American Congress of Obstetricians and Gynecologists, 2012; Hulse et al., 1998; Kandall et al., 1999; Ludlow et al., 2004). Medication assisted treatment (MAT) with methadone or, more recently, buprenorphine is the most effective treatment for opioid use disorder (OUD) in pregnant women (American Congress of Obstetricians and Gynecologists, 2012; Jones et al., 2012; Minozzi et al., 2013) and those in MAT have better maternal and fetal outcomes than those not enrolled in treatment (Burns et al., 2007; Fajemirokun-Odudeyi et al., 2006; Welle-Strand et al., 2013). Some studies have also shown a relationship between length of time in methadone treatment and improved fetal outcomes (Burns et al., 2007; Peles et al., 2012). Although the effectiveness of MAT exclusively in postpartum women has not been studied, MAT is considered a highly effective treatment for OUD in the general non-pregnant population (Mattick et al., 2009), which includes postpartum women.

Because MAT has such strong evidence for improved treatment outcomes, retention of patients in MAT is critical. Treatment

* Corresponding author at: Addiction Sciences Division, Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, 3131 Harvey Avenue, Cincinnati, OH 45229, USA. Tel.: +1 513 585 8285; fax: +1 513 585 8278.

E-mail address: Christine.wilder@uc.edu (C. Wilder).

retention in MAT has been studied extensively in the non-pregnant population. Women (Kelly et al., 2011; Newman et al., 1976), older patients (Deck and Carlson, 2005; MacGowan et al., 1996; Magura et al., 1998; Newman et al., 1976), individuals who do not use other drugs during treatment (MacGowan et al., 1996; Magura et al., 1998), and individuals with no criminal justice involvement (Cox et al., 2013; Deck and Carlson, 2005; Greenfield et al., 1996; Magura et al., 1998; McGuire, 1979) are more likely to remain in methadone treatment for 90 days or more. Additionally, treatment with higher doses of methadone (≥ 60 mg per day) has been associated consistently with better treatment retention (Bao et al., 2009; Brady et al., 2005; Faggiano et al., 2003).

Surprisingly, however, there has been limited focus on MAT retention in pregnant or postpartum women, despite the fact that substance-using pregnant women can be difficult to retain in treatment (Haller et al., 1997; Jones et al., 2002). Studies of interventions to improve MAT retention in pregnant and postpartum women are also limited. In this article, we first review the published literature on MAT discontinuation rates in pregnant and postpartum women and on interventions to improve treatment retention in this group. We then present new data on treatment discontinuation from a methadone program treating pregnant and postpartum women. Finally, we synthesize these findings with previously published results and make recommendations for future research.

2. Materials and methods

2.1. Review of currently published literature

We completed a systematic review of the published literature to answer the following questions:

1. For pregnant and or postpartum women with opioid use disorder on MAT with methadone or buprenorphine, what are the discontinuation rates of MAT during pregnancy and in the immediate postpartum period?
2. What interventions improve treatment retention compared to standard care for pregnant and postpartum women on MAT with methadone or buprenorphine?

We searched PubMed, MEDLINE, and PsycINFO online databases using the Boolean search query: ("medication assisted treatment" OR methadone OR buprenorphine) AND (pregnan* OR postpartum OR post-partum OR "post partum") AND (retention OR dropout OR drop-out OR "drop out" OR discontinu* OR attendance OR adherence OR compliance). This query yielded 88 unique citations which were imported into an electronic database (EndNote X5; Thomson Reuters, Philadelphia, PA). Titles and abstracts for each article were screened and articles were excluded if it could be determined from screening that they met one of the following pre-specified, sequential exclusion criteria:

1. Pregnant or postpartum women were not a significant focus of the article (studies for which there was only incidental inclusion of pregnant or postpartum women or studies which focused exclusively on neonatal outcomes were excluded).
2. MAT was not addressed as a treatment modality.
3. Article was a review or guidance article without presentation of new data, or a single case report.
4. Article did not report retention, discontinuation, or drop-out rate(s) of MAT or describe intervention(s) to improve treatment retention in MAT.

Forty-one articles could not be definitively excluded based on examination of title and abstract and were retained for full-text review. The reference lists for all articles selected for full-text review were manually searched for relevant citations. These were cross-referenced against our original search results and any additional potentially relevant citations were screened. Seven additional articles were added for full-text review based on manual search. We therefore reviewed a total of 48 full text articles using the same exclusion criteria above. Fifteen articles remained after applying all criteria and were included in this review.

2.2. Retrospective cohort study of methadone treatment discontinuation in pregnant and postpartum women

2.2.1. Clinic description. We conducted a retrospective chart review of a methadone treatment clinic affiliated with the University of Cincinnati. The clinic is not-for-profit but does not accept Medicaid or other public assistance. It has a census of approximately 450 individuals receiving methadone dosing, individual therapy, and group counseling. It has collaborative contacts with the maternal-fetal

centers of several of the city's main hospitals and therefore receives referrals for opioid dependent pregnant women wishing to enter methadone treatment. The clinic collaborates directly with prenatal treatment providers but no prenatal treatment occurs on site. Pregnant women receive treatment which includes methadone dosing, weekly individual counseling, biweekly physician appointments with dose adjustments, biweekly urine drug testing, and coordination of care with their prenatal care providers. Pregnant women are eligible for significantly reduced fees if they fulfill treatment requirements and provide drug-free urine tests, although these fee reductions continue only for the duration of the pregnancy and are not available postpartum. After hospital discharge following delivery, women are assessed every three days by the clinic physician for dose adjustment, based on clinical signs and symptoms, over the first two weeks postpartum.

2.2.2. Chart review. We queried the electronic medical record system of the clinic to identify all individuals who had been pregnant between 1/1/2006 and 10/1/2013. These charts were individually reviewed to obtain patient age, race, ethnicity, outcome of pregnancy (elective abortion, miscarriage, perinatal demise, or live birth), delivery or termination of pregnancy date, duration of treatment episode, discharge date, and reason for discharge (transferred to another clinic, moved out of area, incarcerated, relapsed and left treatment, tapered off methadone, cross-tapered to buprenorphine, or lost to follow up with no discharge plan). Treatment discontinuation was defined as stopping treatment with no plan for continued medication assisted treatment; as such, it included the following categories of discharge: incarcerated, relapsed and left treatment, tapered off methadone, or lost to follow up with no discharge plan. The beginning of a treatment episode was defined by the first methadone dosing record prior to (or on, if the patient was already pregnant when she began methadone) the date the pregnancy was first identified. The end of the treatment episode was defined as the last dosing record after which there was a break in dosing of at least 14 days or there were no further dosing records. The study was approved by the University of Cincinnati Institutional Review Board.

2.2.3. Statistics. We calculated demographic summary statistics and unadjusted prenatal and 6-month postpartum methadone discontinuation rates. For individuals who had multiple pregnancies during the trial period, only the first pregnancy for each individual was included for determination of discontinuation rates and other analyses. We conducted a Cox Proportional Hazard linear model for postpartum methadone discontinuation, controlling for maternal age, outcome of pregnancy (live versus non-live births), and number of days in treatment at the clinic prior to delivery. Race was not included as a covariate because the population was almost exclusively Caucasian. Outcome of pregnancy was included as a covariate because it was felt that early miscarriages or elective abortions might not be included in patient records, resulting in a sampling difference between the reported non-live births and live births. Individuals who left treatment prior to delivery were excluded from the postpartum Cox proportional hazard analysis and postpartum individuals who transferred to another clinic, moved from the area, or cross-tapered to buprenorphine were censored. One hundred eighty-seven women were included in the Cox proportional hazards model, of which 14 were censored.

3. Results

3.1. Review of currently published literature

Table 1 describes the 15 studies identified through our literature review. These studies included a total of 1125 women. Six studies followed women into the postpartum period (Chappel and Senay, 1973; Crandall et al., 2004; Fischer et al., 1998; Laken and Ager, 1996; Peles and Adelson, 2006; Silverman et al., 2001); none were focused exclusively on postpartum subjects. In addition to methadone or buprenorphine prescription, MAT in all studies included some level of group and individual psychosocial treatment at least weekly. Three studies included women treated with buprenorphine (Fischer et al., 1998; Jones et al., 2005, 2010), comprising less than 10% of the total sample reviewed. All other studies used methadone as the only MAT medication, although one study did include 29 women on a slow release formulation (Fischer et al., 1998).

3.1.1. Discontinuation rates of MAT. Four cohort studies reported discontinuation rates for the total population they examined; among these, DePettillo and Rice (1995) and McCarthy et al. (2005) reported discontinuation rates prior to delivery of 0 and 4% respectively. Two cohort studies included pregnancy and the postpartum period: Peles and Adelson (2006) reported a 1-year discontinuation rate of 22%, and Chappel and Senay (1973) reported a 2-year

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