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#### Research paper

# Comparison of adverse obstetric outcomes and maternity hospitalization among heroin-exposed and methadone-treated women in Taiwan



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#### ABSTRACT

Aims: To identify sociodemographic and clinical factors predicting the overall risk of adverse obstetric outcomes and the length of maternal hospital stay among heroin-exposed and methadone-treated women in Taiwan

Methods: Using the retrospective matched cohort study design, 396 births to women on methadone treatment during pregnancy (the methadone-treated group) and 609 to women who started methadone treatment after childbirth (the heroin-exposed group) were identified in the National Methadone Maintenance Program. Adverse pregnancy outcomes were assessed by still birth, low birth weight and preterm delivery. We used multivariate methods and zero-truncated negative binomial regression to evaluate association estimates.

Finding: Both heroin-exposed and methadone-treated women had 2–4-fold greater risk of adverse pregnancy outcomes. HIV infection increased the overall risk of adverse pregnancy outcome in the methadone-treated group, whereas being unmarried and having treatment history of substance use disorders increased such risk in the heroin-exposed group. Maternal ages at delivery and healthcare facility used had moderate effects on the length of maternal hospital stay; HIV infection significantly increased the length of hospital stay for women in the heroin-exposed group (adjusted relative risk = 1.32, 95% CI = 1.05–1.68).

Conclusions: Our results showed no appreciable differences in the occurrence of adverse obstetric outcomes and the length of maternity hospitalization between the methadone-treated and the heroin-exposed women; the profile of sociodemographic and clinical predictors was similar as well. Coordination of addiction treatment and prenatal care may help reduce unfavorable obstetric outcomes among female heroin addicts seeking substitution treatment.

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#### Introduction

Activities related to illegal drugs have broken down sociodemographical boundaries and taken an increasingly heavy toll on different societies. Within drug-using populations, special attention concerning negative consequences has been paid to certain

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subgroups given their minority or vulnerability status, including pregnant women. In the case of opioid exposure, pregnant women with untreated dependence disorders or misuse problems may have greater risk of obstetric complications, ranging from toxemia, third trimester bleeding to low birth weight (Greenfield, Manwani, & Nargiso, 2003; Keegan, Parva, Finnegan, Gerson, & Belden, 2010; Kuczkowski, 2007; Narkowicz, Plotka, Polkowska, Biziuk, & Namiesnik, 2013). Adding to the concerns are the burdens this puts on the health care system and the rising medical cost (Dryden, Young, Hepburn, & Mactier, 2009; Fajemirokun-Odudeyi et al., 2006; Johnson, Greenough, & Gerada, 2003).

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Growing evidence supports the use of substitution (or replacement) therapy during pregnancy for women addicted to opioid (Benningfield et al., 2012; Holbrook et al., 2012). A meta analysis of 18 studies looking at the association between infant birth weight and maternal use of heroin and methadone during pregnancy found that the mean birth weight of infants born to mothers who used heroin is 489 g lower than the un-exposed control (95% CI: 284-693 g), whereas the mean birth weight of those born to mothers in methadone program is 279 g lower (95% CI: 229–328) (Hulse, Milne, English, & Holman, 1997). Some researchers have examined factors accounting for the excessive risk and severity of adverse obstetric outcomes among methadone-treated women. For example, on the basis of more than 2500 births to women in methadone programs identified in the 1992-2002 New South Wales Midwives Data Collection and Inpatient Statistics, a study compared neonatal outcomes in relation to mother's entry time at methadone program (i.e. late entry, early entry and previous treatment)(Burns & Mattick, 2007). The results showed that infants born to mothers who entered the program late in pregnancy were more likely to have a less than 37 weeks gestation (Odds Ratio [OR] = 2.6), suggesting that continuous methadone treatment during pregnancy may encourage early utilization of antenatal service, thus improves neonatal outcomes (Burns, Mattick, & Cooke, 2006). Other than MMT entry timing, several sociodemographic and clinical factors were also found to affect, directly or indirectly, the beneficial effects of methadone treatment on maternal and neonatal health, including racial/ethnic minority, unmarried status, financial hardship, tobacco smoking, continued use of illegal heroin or other illegal drugs during pregnancy, medical condition and methadone dose (Bakstad, Sarfi, Welle-Strand, & Ravndal, 2009; Burns, Mattick, Lim, & Wallace, 2007; Choo, Huestis, Schroeder, Shin, & Jones, 2004; Dryden et al., 2009; Hulse et al., 1997; Kuczkowski, 2007; Wouldes & Woodward,

Although methadone maintenance treatment has been used for more than 40 years, earlier studies examining the relationship between obstetric outcomes and methadone exposure during pregnancy came mostly from hospital chart reviews or clinical follow-ups in the western societies (Cleary et al., 2012; Greig, Ash, & Douiri, 2012; Kashiwagi, Arlettaz, Lauper, Zimmermann, & Hebisch, 2005; Wouldes & Woodward, 2010). Given that countryrelated heterogeneity exists in methadone treatment (e.g., program content, coverage rate and methadone dose) and treatment seekers (e.g., age, educational attainment, racial composition and addiction severity) (Baewert et al., 2012; Unger et al., 2010), the results may not be directly generalized to Asian countries. Recently, record linkage, an approach that connects records for the same individual across different data sources, has been used to study adverse obstetric outcomes related to illegal drug uses by bringing together the drug-related hospital admission and birth records (Burns et al., 2006, 2007; Lain, Algert, Tasevski, Morris, & Roberts, 2009). However, these studies often focus on outcome-specific excessive risks, thus obscuring the association between the overall risk of adverse obstetric outcomes and its explanatory factors. Consequently, it is hard to translate these findings to prevention programs. Finally, much of the early evidence on predictors of healthcare utilization was mainly on neonates (Burns et al., 2007; Pritham, Paul, & Hayes, 2012), and did not effectively address maternal needs for postpartum

To fill this knowledge gap, we used record linkage to establish a cohort of opioid-exposed pregnant women in Taiwan. By focusing on two groups of women (i.e., heroin-exposed and methadone-treated), the goal of this study was to identify sociodemographic and clinical predictors for the overall risk of adverse obstetric outcomes and for the length of maternity stay.

#### Materials and method

Study population and data sources

This is a retrospective matched cohort study using records from three national databases in Taiwan: the Birth Notification System (BNS), the National Health Insurance Database (NHID) and the Methadone Maintenance Treatment Program.

In Taiwan, all newborn with weight more than 500 g or a gestational age of more than 20 weeks, whether alive or dead, must be reported to the Bureau of Health Promotion (BHP) within 7 days of the birth. The National Health Insurance Program (NHIP) was launched in 1995 to provide comprehensive medical coverage (including prenatal and childbirth cares) to citizens and foreigners in Taiwan. The coverage rate is around 99%. The National Health Insurance Database contains the registration files and reimbursement claims from the NHIP. In Taiwan, street heroin was mostly administered via intravenous injection. The Center for Disease Control in Taiwan initiated the Methadone Maintenance Treatment (MMT) program in 2006 to prevent HIV infection in heroin users. Daily visit to the MMT clinics is mandatory for the participants and no take-home dose is allowed.

The record linkage procedures were performed by the Office of Statistics of the Department of Health. Both individual-level identifiers and linkage to identifiers were removed after the cross-linkage. On the basis of 881 women enrolled in the MMT between 2006 and 2009, we retrieved the records of (i) 396 "methadone treated" births — those who were delivered after methadone treatment, and (ii) 609 "heroin-exposed" births. Given empirical evidence in Taiwan indicated that average year of heroin history prior to MMT was 5 years (Lin et al., 2013), the present analyses defined the "heroin-exposed" births to those delivered during the three years preceding the MMT enrollment to assure in-uterus exposure to heroin (no earlier than 2003).

To gain the efficiency in analyses, this matched cohort study randomly sampled births to women never enrolled in MMT programs, using a ratio of 1:10. A total of 10,050 controls matched on maternal income level, age at childbirth and neonatal birth year/month were selected. The overall linkage rate for the BNS and the NHID was estimated to be greater than 98% in the assessment period of the present study (i.e., 2003–2009). The corresponding estimates for women in the heroin and methadone groups were 88.11% and 95.96%, slightly lower than 99.37% for control women.

#### Measures

For each birth, maternal sociodemographic and clinical characteristics such as the highest level of education, marital status and healthcare provider (i.e., hospital vs. clinic) were retrieved from the Birth Notification System (BNS). Maternal income level (estimated from the insurance premium), employment status and healthcare utilization were extracted from the National Health Insurance Database (NHID). Individual healthcare utilization records contained HIV status and treatment history for substance use disorders (ICD-9 CM codes of 291, 292, 303, 304, or 305) within the past two years. The use of benzodiazepines, the most commonly abused prescription drug among heroin users in Taiwan, in the past year was obtained from the prescription records.

For women giving birth while on the MMT (the methadone-treated), three methadone treatment variables were ascertained: (i) the date of the first enrollment: a woman who was using street heroin when conceived but gave birth while on MMT was coded as "MMT entry during pregnancy" (Fajemirokun-Odudeyi et al., 2006). The others were coded as "MMT entry prior to pregnancy"; (ii) the compliance rate during pregnancy: the rate was calculated as the

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