Research Paper

Inadequate prenatal care utilization among women with and without methadone-treated opioid use disorders in Taiwan

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ABSTRACT

Aims: The present study aims to investigate the utilization pattern of prenatal care and correlates for women with opioid use disorders (OUD) in Taiwan.
Method: Using the data linkage between the Methadone Maintenance Treatment (MMT) register with national health insurance, national birth notification system, and birth registration system, we identified 1712 pregnancies with 20 or more gestational weeks from women enrolled in the MMT (heroin-exposed: receiving no methadone treatment during pregnancy, n = 1053 by 882 women; methadone-treated: receiving methadone for at least one day during pregnancy, n = 659 by 574 women) and their 1:10 matched pregnancies from 17,060 women without substance use disorder in the period of 2004-2013. The generalized linear mixed models with negative binomial and logit distributions were performed to evaluate the relationship between individual sociodemographic, health, and addiction treatment characteristics with the number of prenatal visits and receiving prenatal care in the first trimester (i.e., early entry).
Findings: Eighteen percent of pregnancies by women with OUD received no prenatal services and 21% had started prenatal care in the first trimester as compared with 1% and 46% in pregnancies by women without substance use disorders. For pregnancies by women with OUD, methadone treatment was not linked associated with prenatal care visits (adjusted relative risk [aRR] = 1.02; 95% = 0.92, 1.12). For methadone-treated pregnancies, treatment enrollment before pregnancy and spousal methadone treatment elevated prenatal visits by 8% and 18% (0.48 and 1.08 visits, respectively). Additionally, HIV infection (adjusted odds ratio [aOR] = 0.30, 95% CI = 0.10, 0.83) and prior delivery (aOR = 0.05, 95% CI = 0.01, 0.19) significantly reduced the odds of early entry into prenatal care.
Conclusion: Integrating addiction treatment programs with prenatal care is urgently needed to increase adequate prenatal care for pregnant women with OUD, especially the multiparous ones.

Introduction

Prenatal visits have been indicated as a window of opportunity to deliver care and to reduce obstetric and fetal complications (Beeckman, Louckx, Downe, & Putman, 2013; Kershaw, Magriples, Westdahl, Rising, & Ickovics, 2009), which is particularly crucial for high-risk pregnancies. Lack of prenatal care has been linked with increased risk of labor problems and adverse birth outcomes (e.g., preterm delivery and neonatal death)(Herbst, Mercer, Beazley, Meyer, & Carr, 2003;

Vintzileos, Ananth, Smulian, Scorza, & Knuppel, 2002). Although adequate prenatal care should be conceptually framed on the basis of utilization, content, and quality (Alexander & Kotelchuck, 2001; Beeckman et al., 2013; Phelan, 2008), "utilization" is the most common approach for assessing, through at least two indicators, such as number of prenatal visits and timing of prenatal care initiation (Alexander & Kotelchuck, 2001). Prior studies investigating low-frequency and late initiation of prenatal care utilization among women in high-income countries have identified important individual-level determinants,

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ranging from sociodemographic characteristics (e.g., younger maternal age, non-marital status, unemployment, no regular income, uninsured status, and lower educational attainment), medical conditions (e.g., infection with human immunodeficiency virus [HIV] and substance use problems), to the experience with healthcare system (e.g., prior interaction with service providers and access to child care) (Delvaux, Buekens, Godin, & Boutsen, 2001; Feijen-de Jong et al., 2012; Lia-Hoagberg et al., 1990; Roberts et al., 1998).

How women in subpopulations characterized by socially disadvantaged backgrounds and high-risk conditions utilize prenatal care is of critical concern to medical communities (Hollowell, Kurinczuk, Oakley, Brocklehurst, & Gray, 2009; Kershaw et al., 2009; Lia-Hoagberg et al., 1990; Vintzileos et al., 2002). Women using substance, a high-risk subgroup at elevated risks of delivery complications and adverse birth outcomes (Burns, Mattick, & Cooke, 2006; Chen, Lien, Yeh, Su, & Ho, 2015; Lester et al., 2002), are disproportionately represented in prenatal care clients (Funkhouser, Butz, Feng, McCaul, & Rosenstein, 1993; Jessup, Humphreys, Brindis, & Lee, 2003; Roberts & Pies, 2011; Schempf & Strobino, 2009). Earlier studies on pregnant women in inner cities areas of the U.S. reported that frequent substance users were 2.5 times more likely to have low utilization of prenatal care (Funkhouser et al., 1993). The phenomenon of receiving no or little prenatal care appeared more prevalent in pregnant women with opioid dependence (48%), two-fold greater than the urban-dwelling low-income women (i.e., one-fifth)(Schempf & Strobino, 2009). It should be noted that the observed inadequate prenatal service utilization in substance-using women may reflect not only the consequences of substance involvement (e.g., addiction stigma or unemployment), but also the antecedents or precipitating factors (e.g., lower educational attainment or unsupportive family).

With the gradual acceptance of a disease-based paradigm for addiction, some studies have documented increased utilization of prenatal care and potential beneficial outcomes among women who sought addiction treatment (Burns, Mattick, Lim, & Wallace, 2007; El-Mohandes et al., 2003; Wilson, Desmond, & Wait, 1981). A chart review study found that women enrolled in a methadone maintenance treatment [MMT] program utilized more prenatal visits than their non-treated polydrug using peers (Edelin et al., 1988). Also, one data linkage study in Australia reported that those who entered methadone treatment late (i.e., less than six months prior to delivery) were more likely to have the first prenatal visit after 20 gestational weeks and to arrive at the hospital for emergency delivery (Burns et al., 2007). Due to the ethical and legal concerns surrounding opioid misuse during pregnancy, enhancing access to addiction treatment has been recognized as a strategy to improve utilization of prenatal care. It is hypothesized that through engaging the OUD-affected women with treatment, barriers such as social stigmatization, fear of legal consequences, and difficulty in finding suitable prenatal care providers can be ameliorated (Kremer & Arora, 2015).

To this point, there are some gaps in the current state of knowledge toward prenatal care utilization of women with opioid use disorders. First, study samples in prior research often comprised women involved with a wide range of substances (e.g., opioid, marijuana, and cocaine) (Funkhouser et al., 1993; Schempf & Strobino, 2009). Given substance-related variation in scheduled status and treatment modality, it is important to focus on a sample with homogeneous substance experience in order to effectively devise needed healthcare and deliver appropriate intervention. Additionally, the determinants identified in previous studies were mostly focused on people from socially disadvantaged backgrounds (e.g., low income). With the increased access to addiction health services, it is important to understand how treatment experience may differentially shape the utilization of prenatal service.

In the background of the rising number of women with opioid use disorders in many parts of the world (Brogly et al., 2017; Chen et al., 2015; Martins et al., 2017), the present study first examined the association linking methadone treatment with the number of prenatal visits among pregnancies by women with opioid use disorders. Next, with a focus on those pregnancies with methadone treatment, we further investigated treatment characteristics associated with utilization of prenatal care and early entry into prenatal services.

Methods

The present study utilized four national administrative databases: (i) the 2006–2009 MMT program under the Centers for Disease Control and Prevention, (ii) the 2001–2013 National Health Insurance Database (NHID) under the National Health Insurance Administration, (iii) the 2001–2013 Birth Notification System (BNS) under the Bureau of Health Promotion, and (iv) the 2004–2013 Birth Registration System (BRS) under the Ministry of the Interior. In 2006, Taiwan initiated its MMT program to address a sharp rise in HIV cases associated with injecting drug use (mainly heroin). Methadone is dispensed only through oral formulation through daily clinic visits (Chen et al., 2015; Fang, Huang, Lin, Ho, & Chen, 2015; Lin et al., 2013). The NHID has been gathered and managed by the National Health Insurance Administration via the National Health Insurance program, which provides mandatory comprehensive and universal health care services coverage to all citizens and foreign residents since 1995. Although Taiwan's national health insurance plan does not cover "substance use disorders" *per se*, treatments for complications and injuries associated with substance use have generally been reimbursed (e.g., intoxication, infection, and accidents). Neonates, born with more than 500 g of weight or more than 20 gestational weeks, are mandatorily reported by medical facilities to the Bureau of Health Promotion BNS within 7 days after delivery. The BRS comprised live births with personal identification registration filed by their parents or other relatives within 60 days after birth.

Utilizing inpatient claim data within the NHID, in 2016 we initially identified a total of 1,931,121 delivery records (from 1,384,279 women) during the period of 2004–2013 (see Fig. 1). Through the linkage with the MMT dataset, all the deliveries were initially categorized into two groups: "opioid-dependent group" and "non-opioid-dependent group". After excluding the deliveries by women with substance-use disorders (International Classification of Diseases, 9th Version, Clinical Modification (ICD-9-CM) code: 291–292 and 304–305) in the "non-opioid-dependent group", we used maternal age at delivery, gestational weeks at delivery, and delivery year/month as matching criteria in a ratio of 1:10 to obtain 17,120 non-substance-exposed "deliveries" for comparison (n = 17,060 women). Finally, on the basis of estimated pregnancy period and records of daily methadone intake, we further subdivided the deliveries in the opioid-dependent group to (i) the heroin-exposed (i.e., receiving no methadone treatment during pregnancy: n = 1053, from 882 women. The deliveries ascertained in the years of 2004 and 2005 were all heroin-exposed) and (ii) the MMT-treated (i.e., having received methadone for at least one day during pregnancy: n = 659, from 574 women).

Measures

To assess adequate utilization of prenatal care during pregnancy, we obtained from the NHID the total number of prenatal visits and the utilization of prenatal care during the first trimester as two primary dependent variables. In Taiwan, the National Health Insurance program reimburses up to ten prenatal examinations scheduled in accordance with gestational weeks (i.e., once per month before 28 weeks, twice per month before 36 weeks, and four times per month after 36 weeks) (Edelin et al., 1988). The primary independent variable was maternal methadone exposure status during pregnancy, categorized as heroin-exposed, MMT-treated, and non-substance-exposed.

Potential confounders comprised sociodemographic, health, and methadone treatment characteristics. Sociodemographic characteristics in this study were primarily retrieved from two sources: (i) the NHID, for maternal age at delivery (≤25, 26–30, 31–35, or ≥36), year of
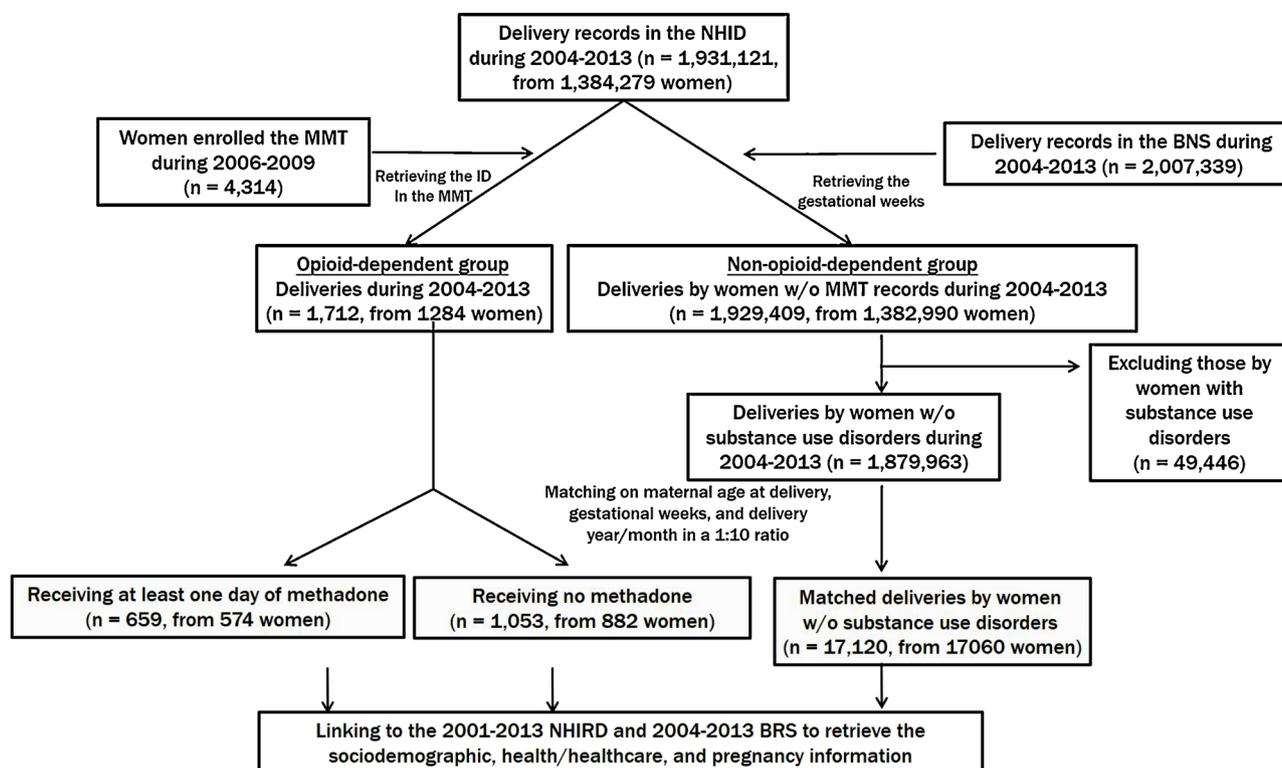
Fig. 1. Study population and data linkage process.

delivery (2004–2013), employment during pregnancy (yes or no), and urbanization of insured region during pregnancy (rural, suburban, or urban region)(Liu, Hung, & Chuang, 2006); and (ii) the BRS: maternal educational attainment (elementary/junior high school, senior high school, or college or above) and marital status (married or unmarried). Pregnancy-related characteristics were obtained from the BNS, including birth plurality and gestational weeks. All the variables concerning medical condition and healthcare utilization were retrieved from the NHID, including maternal mental disorders (ICD-9-CM: 290–319, excluding 291–292 and 304–305)(yes or no), as well as past-year utilization of non-pregnancy related outpatient (0, 1–10, or > 10) and emergency room visits (0 or ≥1). To reflect the recent experience with obstetric care, we also obtained "having any delivery within three years of the index delivery (yes or no)" from the NHID.

As to methadone treatment characteristics, we obtained two variables concerning each individual's first methadone treatment from the MMT database, including maximum dose within the first month (a proxy of addiction severity: i.e., < 60/mg and ≥60/mg)(Lin et al., 2013) and MMT enrollment before pregnancy. Spousal opioid use disorder was defined using linked records between the BNS and MMT. HIV infection status was confirmed by the NHID (ICD-9-CM codes: 042–043).

Statistical analyses

We descried sociodemographic, health, and treatment characteristics for deliveries and examined differences in relation to methadone treatment status by Chi-Square test. Since the number of prenatal care visits (count data) was over dispersed and its variance is not equivalent to the mean (see Table 1)(Covington, Churchill, & Wright, 1994; Gardner, Mulvey, & Shaw, 1995), we decided to turn to the negative binomial distribution to accurately assess factors associated with prenatal care visits. A series of the generalized linear mixed model (i.e., PROC GENMOD) with negative binomial (i.e., number of prenatal visits) and logit (i.e., early entry) distributions were performed. To avoid biased estimation due to multiple deliveries from the same

woman, intra-individual correlation was taken into account by specifying the subject encrypted identification number in the analyses exclusively for pregnancies by women with opioid use disorders. The association estimates were presented by relative risks (RRs) and odds ratios (ORs), with 95% confidence interval (CI); the predicted differences in prenatal care visits on the basis of association coefficients were also obtained as aid for interpretation. All the data preparation analyses were carried out via SAS 9.4 (SAS Institute Inc., Cary, NC) at the Department of Statistics of the Ministry of Health and Welfare. The protocol of this study has been approved by the Institutional Review Board (IRB) of the National Health Research Institutes (IRB No. EC10409010).

Results

No opioid group-related differences were found in the linkage rate with the BNS (opioid-dependent: 98.49%; non-opioid-dependent: 98.23%)(see the upper panel of Fig. 1). Further analyses of the 2,007,339 delivery records in the BNS datasets during 2004–2013 found that 1.4% of opioid-dependent deliveries and 5.5% of non-opioid-dependent deliveries could not be identified in the inpatient delivery records through data linkage with the NHID, with higher maternal age at delivery and urban residence as non-linkage correlates ($p < 0.001$ by chi-square tests).

With matching criteria of delivery year, age, and gestational weeks, individual sociodemographic, health, and healthcare utilization characteristics were different across two groups defined by "pregnancies of women with opioid use disorders" and "pregnancies of women without substance use disorders" (see Table 1). A higher percentage of socially disadvantaged background (e.g., unmarried status: 36.9%; unemployment: 69.6%) and healthcare under-utilization (e.g., none outpatient visit: 24.8%) was shown in the pregnancies by women with OUD. Within the opioid-dependent group, differences emerged in year of delivery (since the MMT was launched in 2006), age at delivery, marital status, and employment status. The average number of prenatal care visits in methadone-treated pregnancies was significantly higher than heroin-exposed ones (5.99 vs. 4.94, $p < 0.001$), yet such methadone

Table 1
Selective characteristics for pregnancies, by women's methadone treatment status, 2004–2013.

Characteristics	Pregnancies of women with opioid use disorder (Opioid-dependent group)			Pregnancies of women w/o substance use disorder
	Heroin-exposed No. (%)	MMT-treated No. (%)[a]	Total No. (%)	No. (%)[b]
Total	1053 (61.5)	659 (38.5)	1712 (100.0)	17,120 (100.0)
Calendar year of delivery		***		
2004–2005	413 (39.2)	0 (0.0)	413 (24.1)	4130 (24.1)
2006–2007	336 (31.9)	22 (3.3)	358 (20.9)	3580 (20.9)
2008–2009	107 (10.2)	294 (44.6)	401 (23.4)	4010 (23.4)
2010–2011	96 (9.1)	205 (31.1)	301 (17.6)	3010 (17.6)
2012–2013	101 (9.6)	138 (20.9)	239 (14.0)	2390 (14.0)
Age (years)		***		
≤ 25	255 (24.2)	46 (7.0)	301 (17.6)	3010 (17.6)
26–30	413 (39.2)	222 (33.7)	635 (37.1)	6350 (37.1)
31–35	276 (26.2)	259 (39.3)	535 (31.3)	5350 (31.3)
> =36	109 (10.4)	132 (20.0)	241 (14.0)	2410 (14.0)
Gestational weeks at delivery				
20–25	7 (0.7)	6 (0.9)	13 (0.8)	130 (0.8)
26–36	205 (19.5)	145 (22.0)	350 (20.4)	3500 (20.4)
> 36	841 (79.8)	508 (77.1)	1349 (78.8)	13,490 (78.8)
Educational attainment				***
Elementary / junior high school	715 (67.9)	422 (64.0)	1137 (66.4)	1859 (10.9)
Senior high school	272 (25.8)	179 (27.2)	451 (26.4)	5256 (30.7)
College or above	20 (1.9)	16 (2.4)	36 (2.1)	7701 (45.0)
Missing	46 (4.4)	42 (6.4)	88 (5.1)	2304 (13.4)
Marital status		**		***
Married	586 (55.6)	407 (61.8)	993 (58.0)	14,202 (83.0)
Unmarried	422 (40.1)	210 (31.9)	632 (36.9)	628 (3.7)
Missing	45 (4.3)	42 (6.4)	87 (5.1)	2290 (13.3)
Maternal employment[c]		*		***
Yes	297 (28.2)	223 (33.8)	520 (30.4)	14,529 (84.9)
No	756 (71.8)	436 (66.2)	1192 (69.6)	2411 (14.1)
Urbanization				***
Urban	151 (14.3)	103 (15.6)	254 (14.8)	4838 (28.3)
Suburban	792 (75.2)	485 (73.6)	1277 (74.6)	11,050 (64.5)
Rural	110 (10.5)	71 (10.2)	181 (10.6)	1193 (7.0)
Prior delivery in the past three years[d]				***
Yes	199 (18.9)	106 (16.1)	305 (17.8)	4184 (24.4)
No	854 (81.1)	553 (83.9)	1407 (82.2)	12,936 (75.6)
Mental disorders[e]				***
Yes	197 (18.7)	134 (20.3)	331 (19.3)	852 (5.0)
No	856 (81.3)	525 (79.7)	1381 (80.7)	16,268 (95.0)
Number of outpatient visits before pregnancy[f]				***
0	273 (25.9)	151 (22.9)	424 (24.8)	1516 (8.9)
1–10	391 (37.1)	245 (37.2)	636 (37.2)	9146 (53.4)
> 10	389 (36.9)	263 (39.9)	652 (38.0)	6458 (37.7)
Number of emergency room visits before pregnancy[f]				***
0	719 (68.3)	464 (70.4)	1183 (69.1)	13,792 (80.6)
≥1	334 (31.7)	195 (29.6)	529 (30.9)	3328 (19.4)
Birth plurality				***
Singleton	1,033 (98.1)	641 (97.3)	1674 (97.8)	16,398 (95.8)
Twin or multiple births	8 (0.8)	6 (0.9)	14 (0.8)	475 (2.8)
Missing	12 (1.1)	12 (1.8)	24 (1.4)	247 (1.4)
Number of prenatal visits		***		***
0 visit	205 (19.5)	106 (16.0)	311 (18.2)	181 (1.0)
1-3 visits	220 (20.9)	115 (17.5)	335 (19.6)	704 (4.1)
4-6 visits	256 (24.3)	117 (17.8)	373 (21.8)	2667 (15.6)
7 visits or more	372 (35.3)	321 (48.7)	693 (40.4)	13,568 (79.3)
Mean (SD)	4.94 (4.16)	5.99 (4.51)	5.34 (4.33)	8.33 (2.69)
Prenatal visit in the first trimester				***
Yes	224 (21.3)	133 (20.2)	357 (20.9)	7825 (45.7)

Note. Columns may not add up to 100% due to missingness.
[a] Comparisons of between heroin-exposed and MMT-treated pregnancy groups by chi-square tests. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.
[b] Comparisons of between opioid-dependent group and non-substance exposed group by chi-square tests. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.
[c] Having been employed during pregnancy.
[d] During the three years before the index delivery.
[e] Within one year before pregnancy, excluding substance use disorders.
[f] Within one year before index pregnancy.

treatment-related differences were not found in early entry into pre-natal care (20.2% vs. 21.3%).

An increase in prenatal visits was observed associated with metha-done-treated pregnancies as compared with heroin-exposed pregnancies (crude RR = 1.21, $p < 0.001$) as we included the non-substance exposed pregnancies in the analyses (Table 2, the left panel). With simultaneous adjustment for individual sociodemographic and health-related char-acteristics, the risk estimates associated with MMT treatment remained

Table 2
Methadone treatment, sociodemographic, health, and pregnancy characteristics associated with number of prenatal visits.

Characteristics	All pregnancies (n = 18,832)		Pregnancies of women with opioid use disorder (n = 1712)	
	Bivariate Crude RR[a]	Model 1 aRR (95% CI)[a]	Bivariate Crude RR[a,b]	Model 1 aRR (95% CI)[a,b]
Maternal methadone treatment status (ref = heroin-exposed pregnancy, n = 1053)[b]				
MMT-treated (n = 659)	1.21***	1.07 (1.02, 1.11)**	1.19***	1.02 (0.92, 1.12)
Non-substance exposed (n = 17,120)	1.69***	1.40 (1.35, 1.44)***	–	–
Prior deliveries[c] (ref = none)				
Yes	0.97***	0.95 (0.94, 0.96) ***	0.89*	0.77 (0.70, 0.86)***
Calendar year at delivery (ref = 2004–2005)[d]				
2006–2007	1.34***	1.30 (1.28, 1.32)***	1.18**	1.18 (1.06, 1.31)**
2008–2009	1.36***	1.32 (1.30, 1.34)***	1.25***	1.26 (1.10, 1.44)***
2010–2011	1.39***	1.35 (1.32, 1.37)***	1.46***	1.45 (1.26, 1.66)***
2012–2013	1.43***	1.36 (1.34, 1.39)***	1.73***	1.63 (1.42, 1.87)***
Age (ref= ≤ 25 years old)[d]				
26–30	1.13***	1.01 (0.99, 1.03)	1.01	0.87 (0.79, 0.97)**
31–35	1.19***	1.00 (0.98, 1.02)	1.10	0.82 (0.74, 0.92)***
≥36	1.15***	0.97 (0.95, 0.99)**	1.03	0.77 (0.67, 0.89)***
Educational attainment (ref = elementary / junior high school)				
Senior high school	1.23***	1.05 (1.03, 1.07)***	1.35*	1.19 (0.89, 1.60)
College or above	1.34***	1.06 (1.04, 1.08)***	1.05	1.04 (0.96, 1.13)
Marital status (ref = unmarried)[d]				
Married	1.56***	1.22 (1.18, 1.25)***	1.52***	1.35 (1.24, 1.47)***
Maternal employment (ref = no)				
Yes	1.33***	1.08 (1.06, 1.10)***	1.41***	1.19 (1.10, 1.28)***
Urbanization (ref = rural)				
Suburban	1.09***	1.02 (0.99, 1.04)	1.07	1.05 (0.90, 1.22)
Urban	1.14***	1.03 (1.00, 1.05)*	1.05	1.04 (0.92, 1.18)
Mental disorders (ref = no) [d,e]				
Yes	1.07***	1.11 (1.08, 1.13)***	1.44***	1.14 (1.03, 1.26)*
Number of outpatient visit before pregnancy (ref = 0) [d,f]				
1–10	1.37***	1.21 (1.19, 1.24)***	1.47***	1.44 (1.29, 1.60)***
> 10	1.46***	1.30 (1.27, 1.32)***	2.06***	1.92 (1.72, 2.14)***
Number of emergency room visits before pregnancy (ref = 0) [d,f]				
≥1	1.03***	1.02 (1.01, 1.04) ***	1.19***	1.00 (0.92, 1.08)
Birth plurality (ref = single birth)[d]				
Twin or multiple births	0.94***	1.07 (1.03, 1.11)***	1.02	1.42 (0.98, 2.06)
Gestational weeks at delivery (ref = 20–25)[d]				
26–36	2.23***	2.25 (2.04, 2.48)***	1.96**	2.08 (1.27, 3.42)**
≥37	2.86***	2.87 (2.61, 3.16)***	2.99***	3.26 (2.02, 5.26)***

Note. RR = relative risk; aRR = adjusted relative risk; CI = confidence interval.
[a] Generalized linear model in negative binominal distribution; *p < 0.05; **p < 0.01; ***p < 0.001.
[b] Generalized linear model in negative binominal distribution, with specifying the subject to take intra-individual correlation into account; *p < 0.05; **p < 0.01; ***p < 0.001.
[c] Within three years of index delivery.
[d] Pregnancy-dependent variables.
[e] Within one year before index pregnancy, excluding substance-use disorders.
[f] Within one year before index pregnancy.

significant (Model 1: aRR = 1.07, 95% CI = 1.02, 1.11, increased by 0.35 visit). For the pregnancies by women with opioid use disorders (n = 1712), bivariate analyses showed that methadone treatment was linked with increased prenatal visit (RR = 1.19, 95% CI = 1.11, 1.29; p < 0.001, nearly 0.94 visit) when we took intra-individual correlation within multiple deliveries into account. However, such an association estimate was no longer significant when individual sociodemographic, health, and healthcare characteristics were simultaneously adjusted (Model 1: aRR = 1.02, 95% CI = 0.92, 1.12). Meanwhile, having at least one delivery within three years of the index delivery was linked with reduced prenatal care visits by 23% (95% CI = 0.70, 0.86); the association estimate was 0.8 (95% CI = 0.73, 0.87, p < 0.001) when prior delivery was defined on a 5-year basis.

For the 659 methadone-treated pregnancies (Table 3), 81.6% of conceptions occurred after enrollment in methadone treatment and 25.5% had a spouse with heroin problems. Having enrolled in the MMT before pregnancy and having a spouse enrolled in MMT increased prenatal visits by 46% and 26%, whereas having HIV infection and prior delivery reduced prenatal visits by 25% and 17% (Model 1), respectively. The association estimates were attenuated (e.g., MMT-before pregnancy: aRR = 1.08; 95% CI = 0.90, 1.31, increased by 0.48 visit) after statistical adjustment for maternal sociodemographic and health characteristics. Similar association estimates emerged when prior delivery was defined on a 5-year basis (e.g., Model 2: MMT-before pregnancy: aRR = 1.09; 95% CI = 0.90, 1.32). As to entry into prenatal care in the first trimester, HIV infection, the only significant MMT characteristic, reduced the odds of by 70%. The remarkable reduction in the odds was also noticed for having a delivery within three years (aOR = 0.05, 95% CI = 0.01, 0.19). Having 10 or more outpatient visits in the year preceding the index pregnancy elevated the odds of early entry into prenatal care by 246% (95% CI = 65%, 626%) whereas the emergency room visit may lower such odds by 51% (95% CI = 19%, 70%).

Table 3

Characteristics associated with prenatal visits and first trimester prenatal care utilization in methadone-treated deliveries (n = 659).

Characteristics	Number of prenatal visits			Receiving prenatal care in the 1st trimester		
	Crude RR[a]	Model 1 aRR (95% CI) [a]	Model 2 aRR (95% CI) [a]	Crude OR[b]	Model 1 aOR (95% CI) [b]	Model 2 aOR (95% CI) [b]
Methadone treatment characteristics						
Maximum methadone dose during the first month treatment (ref = < 60/mg)						
≥60/mg (n = 194, 29.44%)	1.05	1.03 (0.89, 1.18)	1.05 (0.93, 1.18)	0.86	0.88 (0.58, 1.34)	0.91 (0.57, 1.47)
MMT before pregnancy (ref = no)						
Yes (n = 538, 81.64%)	1.46[***]	1.48 (1.23, 1.78)[***]	1.08 (0.90, 1.31)	1.48	1.42 (0.82, 2.46)	1.40 (0.73, 2.68)
HIV status (ref = negative)						
Positive (n = 57, 8.65%)	0.75[*]	0.76 (0.60, 0.95)[*]	0.75 (0.61, 0.93)[**]	0.27[*]	0.39 (0.15, 0.98)[*]	0.30 (0.10, 0.83)[*]
Spousal opioid use during pregnancy (ref = no)						
Non-methadone-treated (n = 25, 3.79%)	1.01	0.96 (0.67, 1.38)	0.90 (0.65, 1.24)	1.03	1.01 (0.38, 2.68)	0.85 (0.29, 2.50)
Methadone-treated (n = 143, 21.70%)	1.26[***]	1.29 (1.10, 1.52)[**]	1.18 (1.02, 1.36)[*]	1.21	1.25 (0.80, 1.95)	0.80 (0.46, 1.38)
Individual sociodemographic and health characteristics						
Prior deliveries within three years (ref: none)[c,d]						
Yes	0.83[*]		0.66 (0.57, 0.76)[***]	0.07[***]		0.05 (0.01, 0.19)[***]
Age (ref = ≤ 25 years old)[c]						
26–30	1.48[***]		1.38 (1.09, 1.75)[**]	0.94		0.85 (0.33, 2.19)
31–35	1.40[**]		1.19 (0.93, 1.53)	1.02		0.94 (0.37, 2.38)
≥36	1.30		1.13 (0.87, 1.47)	0.73		0.83 (0.30, 2.31)
Educational attainment (ref = elementary / junior high school)						
Senior high school	1.08		1.08 (0.96, 1.22)	1.27		0.99 (0.61, 1.61)
College or above	1.49[**]		1.27 (0.95, 1.69)	0.71		0.42 (0.10, 1.72)
Marital status (ref = unmarried) [c]						
Married	1.49[***]		1.25 (1.08, 1.44)[**]	2.51[***]		2.31 (1.30, 4.11)[**]
Maternal employment (ref = no) [c]						
Yes	1.40[***]		1.20 (1.07, 1.34)[**]	2.25[***]		1.95 (1.25, 3.04)[**]
Urbanization (ref = rural)						
Suburban	1.22		1.17 (0.97, 1.41)	1.70		1.49 (0.68, 3.25)
Urban	1.21		1.12 (0.91, 1.39)	1.35		1.21 (0.46, 3.14)
Mental disorders (ref = no) [c,e]						
Yes	1.40[***]		1.06 (0.93, 1.21)	1.05		0.85 (0.47, 1.53)
Number of outpatient visits within before pregnancy (ref = 0) [c,f]						
1–10	1.56[***]		1.52 (1.27, 1.82)[***]	3.28[***]		3.56 (1.83, 6.91)[***]
> 10	2.11[***]		1.99 (1.66, 2.39) [***]	2.41[**]		3.46 (1.65, 7.26)[**]
Number of emergency room visits within before pregnancy (ref = 0) [c,f]						
≥1	1.22[**]		1.03 (0.92, 1.15)	0.68		0.49 (0.30, 0.81)[**]
Calendar year at delivery (ref = 2006–2009)						
2010–2011	1.16[*]		1.10 (0.96, 1.27)	0.93		0.76 (0.45, 1.27)
2012–2013	1.33[***]		1.29 (1.12, 1.49)[***]	0.57[*]		0.48 (0.25, 0.93)[*]

Note. RR = relative risk; aRR = adjusted relative risk; CI = confidence interval; OR = odds ratio; aOR = adjusted odds ratio.

[a] Generalized Linear Model in negative binomial distribution, with specifying the subject to take intra-individual correlation into account; [*]$p < 0.05$; [**]$p < 0.01$; [***]$p < 0.001$.

[b] Generalized Linear Model in logit distribution, with specifying the subject to take intra-individual correlation into account; [*]$p < 0.05$; [**]$p < 0.01$; [***]$p < 0.001$.

[c] Pregnancy-dependent variables.

[d] Within three years of index pregnancy.

[e] Within one year before pregnancy, excluding substance-use disorders.

[f] Within one year before index pregnancy.

Discussion

This register-based retrospective cohort study found that nearly one in five pregnancies of women with opioid use disorders utilized no prenatal care and 79% had not entered prenatal service in the first trimester. For pregnancies by women with opioid use disorders, when we took socially disadvantaged background, health condition, and intra-individual multiple deliveries into account, methadone treatment was not associated with prenatal care utilization whereas having prior delivery reduced prenatal care visits by 23%. Among the methadone-treated pregnancies, treatment enrollment before pregnancy and spousal methadone treatment accordingly increased prenatal visits by 8% and 18% (increased by 0.48 and 1.08 visits). HIV-positive status and prior delivery emerged as strong negative correlates for the number of prenatal visit and receiving prenatal care in the first trimester.

Although variation exists in the indicators of prenatal care utilization, type of substance involvement, and source of sample ascertainment (Burns et al., 2007; Schempf & Strobino, 2009; Shieh & Kravitz, 2006), by and large the prevalence of inadequate prenatal care utilization among pregnancies by women with opioid use disorder in our study fell between estimates previously reported in Australia and the United States, regardless of methadone treatment status. Since the barriers relevant to health insurance are substantially reduced under Taiwan's universal health care system as compared with the United States, the observation that 20% of heroin-exposed and 16% of methadone-treated deliveries received no prenatal care throughout pregnancy underscores potential influence of non-health insurance barriers, such as socioeconomic barriers and poor health conditions. In addition, it is possible that the effects of substance-related barriers — such as concern of being arrested, fears of drug disclosure, and associated discrimination (especially from health service providers) — were more prevalently embedded in this study population, in which heroin use is also considered as a criminal behavior.

Incongruent with earlier studies (Edelin et al., 1988; Wilson et al., 1981), results from this population-based study have showed no beneficial effects of methadone treatment, in terms of increasing the number of prenatal visits throughout. Although methadone treatment was associated with 7% increase in prenatal care visits in the whole

sample (n = 18,832), such association was not observed for the pregnancies by women with OUD only (n = 1772). This observation can be due to (i) less variation in prenatal care visits between heroin-exposed and methadone-treated pregnancies (mean: 4.94 vs. 5.99); (ii) the salience of prenatal care-seeking barriers associated with individual's socially disadvantaged backgrounds (e.g., being unmarried or unemployed); and (iii) that women enrolled in the national methadone treatment during the period of 2006–2009 represented a select subgroup of patients with OUD (e.g., those who cared more about their pregnancies or children were those who had higher motives to engage in treatment in early-phase). Nevertheless, it is also probable that receiving methadone treatment alone was not enough to increase prenatal care utilization among women with opioid use disorders. Since methadone is dispensed only on a daily basis and most methadone clinics were neither affiliated with (nor close to) obstetric clinics or general hospitals in Taiwan, for some pregnant women receiving long-term and stable doses of methadone, daily visits to methadone clinics may make access to prenatal care difficult, in terms of transportation time and cost. To increase adequate prenatal care utilization for women with OUD, our results suggest the urgent needs to integrate or link enhanced services with opioid treatment programs, such as on-site prenatal care or therapeutic childcare (Carroll, Chang, Behr, Clinton, & Kosten, 1995; Chang, Carroll, Behr, & Kosten, 1992; Sweeney, Schwartz, Mattis, & Vohr, 2000).

Our analyses indicated that having prior delivery in the three years preceding the index pregnancy was associated with reduced prenatal care visits, and such reduction was especially prominent when the analyses were restricted to the women with OUD (i.e., 5% vs. 23%). Multiparous women were more likely to have underutilization or late initiation of prenatal care because they often perceived prenatal care as less important or other matters received more priority than prenatal visits (e.g., taking care of a young child)(Augustyn & Maiman, 1994; Roberts et al., 1998). For pregnant women involved in substance like opioids, the reduced adequate prenatal service utilization can be explained by at least two processes: (i) women may delay, skip, or avoid prenatal visits if prior encounters with obstetric care providers were negative experiences, such as through stigmatization, discrimination, or arrest (Roberts & Pies, 2011); and (ii) the majority of pregnancies by women with OUD were unintended or even unwanted (Heil et al., 2011). Indeed, the enrollment in addiction treatment may not completely reduce fears that obstetric health care providers would judge the mothers to have inadequate parenting capability or that child-protective services would be notified (Neale, Tompkins, & Sheard, 2008). Such fears can be exacerbated when the mother–child attachment is strong.

Earlier research has shown that, for substance-using women, a partner's substance use and violent behaviors were barriers in seeking care due to the partner's physical and financial dominance (Jessup et al., 2003). In our sample, nearly one third of MMT-treated pregnancies were from unmarried women and at least one quarter were fathered by opioid-using spouses. The observed increased prenatal visits associated with spousal methadone treatment highlights the need to assess and involve families (especially substance-using partners) when devising and delivering family-centered addiction treatment to pregnant women (Freda, Chazotte, & Youchah, 1995; Sutter, Gopman, & Leeman, 2017). Meanwhile, prior year's outpatient care utilization served an important role in elevating prenatal care visit and early entry into prenatal service. For pregnant women receiving methadone treatment, this association may be a result of (i) having fewer barriers in accessing to healthcare; (ii) enhanced positive experiences of encounters with healthcare providers and social workers in the treatment-seeking process, and (iii) elevated skills in navigating the healthcare system. Finally, positive HIV status was a strong predictor for inadequate prenatal care utilization (Hlarlaithe, Grede, de Pee, & Bloem, 2014; Lindau et al., 2006). Potential factors associated with low prenatal care utilization among HIV-affected women may involve social norms and knowledge, stigma, and partner relations. Future research can be developed to incorporate family- or community-based variables that reflect potential barriers to seeking prenatal service by this doubly marginalized population (opioid use and HIV positive).

Findings in the present study should be considered in light of several study limitations. First, the study population was defined only by the delivery records from medical claim data in the NHID. Deliveries that did not take place at medical facilities (hospitals or clinics) or that were paid out-of-pocket were not included. Similarly, pregnancies with gestational weeks less than 20 weeks or with neonates less than 500 g were not included in the analyses, which may lead to underestimate the association given that prenatal cares were rarely utilized in the first trimester for women with opioid use disorder. Second, owing to the limited variables in administrative data, information concerning (i) important factors of antenatal care utilization (e.g., maternal social support and network)(Augustyn & Maiman, 1994) and (ii) indicators of content and quality of prenatal care visits were therefore not included in the analytic model, which may restrain the interpretations of the present study. Third, data concerning opioid dependence and methadone treatment were identified through national methadone treatment data. Our sample characteristics hampered the generalization of results to those pregnancies by women who had opioid use disorder but never sought methadone treatment, at least during the period of 2006–2009. On a related note, generalization to other parts of the world is also constrained due to variations in health insurance plans and access to prenatal care. Finally, since the number of prenatal care visits had a relatively narrow range (0–10 visits), the statistical significance emerged in relative risk estimates may not be directly translated into clinical significance. However, some strengths arose despite the above-mentioned limitations. To this point, research in prenatal care utilization among opioid-involved women has been derived largely from a few single-hospital based studies. To our knowledge, this investigation is one of the first population-based studies to report the pattern of prenatal care utilization among women with opioid use disorder and to explore methadone treatment characteristics linked with adequate prenatal care (e.g., receiving methadone before conception). Finally, the nature of data allows us to explore this important issue in a marginalized and stigmatized population with a rather large sample size.

Our findings echoed the importance of integrating prenatal care and social services into existing addiction-treatment programs for women (Patrick, Schiff, & Committee on Substance Use and Prevention, 2017; Sweeney et al., 2000). Having methadone treatment programs pay special attention to those women with a recent delivery may be especially critical. Additional research is needed to explore how the experience of prior delivery or having a young child may affect one's access to prenatal care or one's willingness to utilize prenatal service in the first trimester. Service providers practicing in the specialties of addiction or obstetrics can be trained to raise awareness of potential barriers associated with disadvantaged socioeconomics, unsupportive networks, and medical condition (e.g., substance-using spouse and perceived discrimination against HIV), and to facilitate the seeking of adequate prenatal care based upon the special needs and resources available to women of reproductive age, mothers-to-be, and the mothers with young children in addiction-treatment programs (Schwartz et al., 2017; Sutter et al., 2017).

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