An 11-year nationwide registry-linkage study of opioid maintenance treatment in pregnancy in Norway

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ABSTRACT

Aim: We aimed to describe opioid maintenance treatment (OMT) to pregnant women in Norway and study the background characteristics of the pregnant women compared to the general population of pregnant women and to a previous clinical cohort study of OMT in pregnancy.
Methods: Population-based cohort study with linked data from the Norwegian Medical Birth Registry, the Norwegian Prescription Database, the Norwegian Patient Registry, and Statistics Norway. The study population consisted of women giving birth between 2005-2015 in Norway. We defined OMT pregnancies as pregnancies where the woman was dispensed OMT medications (methadone, buprenorphine, or buprenorphine/naloxone) at least once during pregnancy.
Results: The study population consisted of 420,808 women with 645,440 pregnancies ending in a live birth in Norway in 2005-2015 (the general pregnant population). Of these, 261 women (0.6‰) had altogether 306 OMT pregnancies. The mean number of pregnancies was 28 OMT pregnancies per year and quite stable during the study period. Women with OMT pregnancies were older, smoked tobacco more frequently, had lower education, and fewer of them had a partner, compared to the general population of pregnant women. In most pregnancies, the women were treated with buprenorphine (n=183 (59.8%)), while in 120 (39.2%) pregnancies, the woman received methadone. From 2008, buprenorphine replaced methadone as the most frequently used drug. In only 38 (12.4%) pregnancies, OMT treatment was initiated in pregnancy. In 201 (66%) pregnancies, the woman used OMT medications in all trimesters. For these women, the mean amount of dispensed drug was 3.4 DDD/day (85 mg/day) in pregnancy for methadone and 1.9 DDD/day (15.2 mg/day) for buprenorphine.
Conclusion: The number of OMT pregnancies per year has been low and stable in the period 2005-2015. Following Norwegian recommendations, there has been a shift from treatment with methadone towards buprenorphine. The women receiving OMT during pregnancy had more risk factors for adverse outcomes than the general pregnant population but were quite similar to the previous clinical cohort.

INTRODUCTION

Opioid maintenance treatment (OMT) has been recommended as the standard care for opioid use disorder since the late 1990s in Norway (1). OMT combines pharmacological treatment with a variety of supportive psychosocial measures which has previously been described in detail (1). In a Norwegian setting, OMT has been shown to reduce mortality, morbidity, criminality, and improve the patients' quality of life (2-5).

About 30% of the individuals with an opioid use disorder are women, many in childbearing age (6). Maternal opioid use disorder during pregnancy is associated with a range of adverse obstetric and neonatal outcomes (7). The introduction of methadone maintenance treatment in the late 1960s in the US resulted in fewer obstetric complications, neonatal morbidity, and mortality compared to illicit heroin use during pregnancy (8-10). The World Health Organization (WHO) recommends that methadone or buprenorphine should be maintained during pregnancy if a woman in OMT becomes pregnant (11).

In 2011 the first Norwegian national treatment guideline for pregnant women in OMT was published (12). The guidelines recommend that the woman should continue using the OMT medication that she used before becoming pregnant. For new patients, buprenorphine without naloxone is recommended as the first drug of choice. This contrasts with WHO's guidelines that recommend methadone as the drug of choice for pregnant women (11). The Norwegian guideline has recently been revised, emphasizing that tapering of OMT medication during pregnancy should be considered as an equivalent treatment option to continued OMT medication (13).

Even though OMT has been shown to reduce adverse outcomes in the neonate compared to heroin exposure, OMT during pregnancy is not without risk if compared to neonates of women in the general population not using any opioids (14,15). In addition to opioid exposure, the socioeconomic factors associated with opioid

use also play an important role in the adverse outcomes (16).

In their guidelines, WHO emphasizes the need for descriptions of current clinical practice (11). From an earlier national clinical cohort study in Norway, we have knowledge about characteristics of pregnant women in OMT as well as the OMT treatment that was provided to these women until 2009 (17). OMT treatment of pregnant women in the period 2004-2010 has previously also been reported from a national registry study (18), as has the background characteristics of the women until 2013 (14), but we lack knowledge on a national level from later years about the OMT treatment that is provided to these women. Using the unique nationwide registry data in Norway, we aimed to describe the pharmacological part of OMT given to this patient group focusing on initiation of OMT in pregnancy, type and amount of OMT medication, and timing according to trimesters. We also aimed to compare the results, both with respect to OMT treatment and background characteristics, in the present study with results in the previous clinical cohort study of OMT in pregnancy from Norway (17).

MATERIALS AND METHODS

Data sources

Pregnancies were identified from the Medical Birth Registry, which contains information about the pregnant woman, pregnancy, birth, and neonates for all deliveries from gestational week 12 in Norway (19). Data on filled prescriptions were retrieved from the Norwegian Prescription Database (NorPD), which contains information on all filled prescriptions to patients in ambulatory care since 2004 (20). Data on drugs administered in hospitals or outpatient specialist care were therefore not captured. Drugs were classified according to the Anatomic Therapeutic Chemical (ATC) classification system (21). The amount of drug dispensed was provided as defined daily doses (DDDs). The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults (22). One DDD of methadone administered orally is 25 mg, while one DDD of buprenorphine administered sublingually is 8 mg. The recommended dose range to OMT patients, in general, is 80-110 mg/day for methadone and 12-24 mg/day for buprenorphine (23). Data on hospitalizations in multidisciplinary specialized substance treatment (TSB) were retrieved from the Norwegian Patient Registry and were available from 2008. Data on education were retrieved from Statistics Norway. All data were linked via the unique personal identifier.

Study population

The study population consisted of 420,808 women with 645,440 pregnancies ending in a live birth in Norway in 2005-2015 (the general pregnant population) (Figure 1). Among these, 558 women filled at least one prescription of opioids used in OMT any time during the study period. Women with no OMT exposed pregnancies were excluded (n=297). Thus, the final study population consisted of 261 women receiving OMT in at least one of their pregnancies.

Study drugs

Opioids used for OMT included methadone oral solution (ATC code N07BC02) and high-dose buprenorphine tablets (≥2 mg sublingual tablets, N07BC01 (buprenorphine) or N07BC51 (buprenorphine-naloxone)), which all are almost solely prescribed for the treatment of opioid use disorder in Norway.

Exposure definition

Exposure during pregnancy was defined as filling at least one prescription of OMT opioids between the start of pregnancy until birth. The start of pregnancy was defined as the first day of the last menstrual period (LMP, day 0) primarily based on prenatal ultrasound. Timing of exposure during pregnancy was defined according to filled prescriptions in the various trimesters (1st trimester: 0-97 days, 2nd trimester: 98-202 days, and 3rd trimester: 203 days until birth). Initiation of OMT in pregnancy was defined as filling at least one prescription of OMT medications during pregnancy and having no filled prescriptions ever before LMP (since 2004 when NorPD was established).

Characteristics of pregnancies

Characteristics of pregnancies were described according to information from the various data sources, on

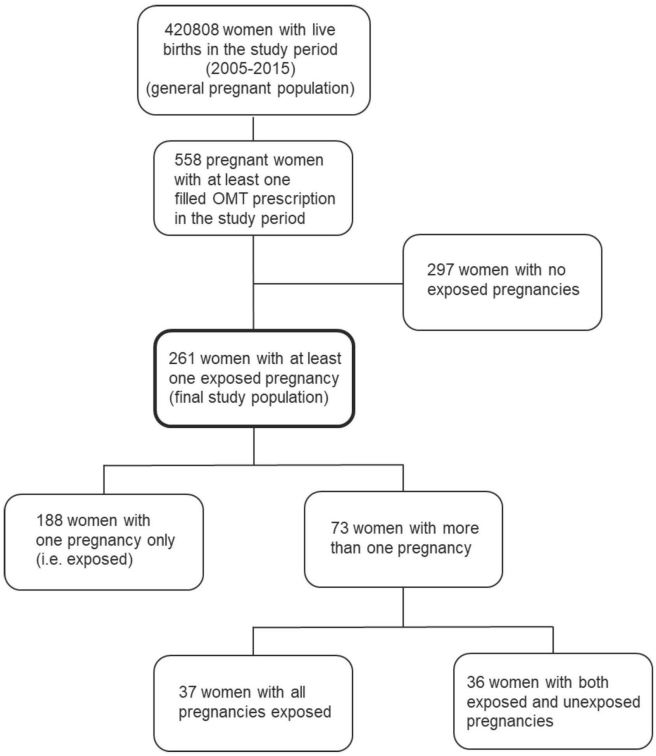

Figure 1. Flow chart of the study population. OMT: Opioid Maintenance Treatment.

Table 1. Baseline characteristics of OMT pregnancies and pregnancies ending in live birth among the general pregnant population in the period 2005-2015.

	OMT pregnancies			General pregnant population		
	n	%	95% CI	n	%	95% CI
Total	306	100		645440	100	
Maternal age at delivery						
<18	0	0		2321	0.4	(0.3-0.4)
18-19	0	0		10216	1.6	(1.6-1.6)
20-24	28	9.2	(5.9-12.4)	90888	14.1	(14.0-14.2)
25-29	86	28.1	(23.1-33.1)	203292	31.5	(31.4-31.6)
30-34	118	38.6	(33.1-44.0)	214663	33.3	(33.1-33.4)
35-39	51	16.7	(12.5-20.8)	103836	16.1	(16.0-16.2)
≥40	23	7.5	(4.6-10.5)	20224	3.1	(3.1-3.2)
Parity						
0	135	44.1	(38.6-49.7)	272694	42.2	(42.1-42.4)
1	92	30.1	(24.9-35.2)	232563	36.0	(35.9-36.2)
2	41	13.4	(9.6-17.2)	99574	15.4	(15.3-15.5)
≥3	38	12.4	(8.7-16.1)	40609	6.3	(6.2-6.4)
Early pregnancy BMI						
<18.5	15	4.9	(2.5-7.3)	10906	1.7	(1.7-1.7)
18.5 - <25	66	21.6	(17.0-26.2)	160670	24.9	(24.8-25.0)
25 - <30	14	4.6	(2.2-6.9)	57887	9.0	(8.9-9.0)
≥30	7	2.3	(0.6-4.0)	31468	4.9	(4.8-4.9)
Missing	204	66.7	(61.4-72.0)	384509	59.6	(59.5-59.7)
Caesarean section						
Yes	72	23.5	(18.8-28.3)	96033	14.9	(14.8-15.0)
Elective	37	12.1	(8.4-15.7)	36571	5.7	(5.6-5.7)
Acute	35	11.4	(7.9-15.0)	59118	9.2	(9.1-9.2)
Unspecified	0	0		344	0.1	(0.1-0.1)
Smoking in pregnancy						
No	34	11.1	(7.6-14.6)	483648	74.9	(74.8-75.0)
Yes	216	70.6	(65.5-75.7)	63029	9.8	(9.7-9.8)
Missing	56	18.3	(14.0-22.6)	98763	15.3	(15.2-15.4)
Cohabitant						
Not married/cohabitant	132	43.1	(37.6-48.7)	48137	7.5	(7.4-7.5)
Married/cohabitant	174	56.9	(51.3-62.4)	597303	92.5	(92.5-92.6)
Country of birth						
Nordic countries	292	95.4	(93.1-97.8)	506279	78.4	(78.3-78.5)
Outside Nordic countries	10	3.3	(1.3-5.3)	133769	20.7	(20.6-20.8)
Unknown	4	1.3	(0.03-2.6)	5392	0.8	(0.8-0.9)
Education						
Lower secondary school	221	72.2	(67.2-77.2)	113165	17.5	(17.4-17.6)
Upper secondary school	75	24.5	(19.7-29.3)	258908	40.1	(40.0-40.2)
Higher education	7	2.3	(0.6-4.0)	236427	36.6	(36.5-36.8)
Missing	3	1.0	(0.3-3.1)	36940	5.7	(5.7-5.8)

OMT = opioid maintenance therapy. CI = confidence interval. BMI = body mass index.

maternal age at delivery (categorized as <18, 18–19, 20–24, 25–29, 30–34, 35–39, ≥40 years), parity (categorized as 0, 1, 2, ≥3), early pregnancy body mass index (BMI) (categorized as <18.5, 18.5–<25, 25–<30, ≥30 kg/m^2), caesarean section (yes (acute/elective/unspecified)), smoking in pregnancy (yes/no), cohabitation with a partner (yes/no), country of birth (Nordic countries/outside Nordic countries), and education (lower secondary school (includes individuals with lower secondary school or less)/upper secondary school/higher education).

Statistical analysis

Pregnancies were the unit of measurement for all the analyses. Maternal background characteristics were expressed as numbers and proportions for the OMT pregnancies and all pregnancies in Norway (the general pregnant population). The number and proportions of OMT pregnancies initiating OMT in pregnancy or using OMT both before and during pregnancy were calculated according to type of OMT medication (methadone or buprenorphine). Pregnancies exposed to buprenorphine-naloxone were grouped with buprenorphine. Further, we performed descriptive statistical analysis of the pharmacological treatment the women received during their OMT pregnancies. Timing of OMT in pregnancy was expressed as numbers and proportions of pregnancies where the women filled OMT prescriptions in all trimesters, 1st or 2nd trimester (early in pregnancy), or 3rd trimester only (late in pregnancy).

For those women who did not fill any OMT prescriptions in the 3rd trimester, we studied whether these women had been hospitalized (overnight stay) in multidisciplinary specialized substance treatment and thus likely receiving their OMT medications in inpatient care (not captured by the NorPD). As the information on hospitalizations was available from 2008, pregnancies before 2008 could not be assessed for hospitalizations. The amount of OMT medications were studied both as the number of filled prescriptions during pregnancy and the number of DDDs per pregnancy day. The duration of pregnancy in days was calculated based on the date of birth and date of LMP. Since all women in OMT did not fill prescriptions in all trimesters, the amount of OMT medications were studied for the pregnancies where the woman filled OMT prescriptions in all trimesters. Mean and median are presented with corresponding standard deviation (SD) and interquartile range (IQR), respectively. When appropriate, proportions were presented with 95% confidence intervals using the corrected version of the score (24). Statistical analyses were conducted using Stata version 16 (Stata Corp, TX, USA).

RESULTS

Study population

In the final study population, 261 women (0.6‰ of all pregnant women) had in total 306 OMT exposed pregnancies in the study period, out of which 188 women (72%) had one pregnancy, and 73 women (28%) had more than one pregnancy (Figure 1). For women with more than one pregnancy, 37 women (50.7%) were exposed to OMT medications in all pregnancies, whereas 36 women (49.3%) had pregnancies both with and without the use of OMT medication.

Characteristics of OMT pregnancies

Table 1 shows the maternal characteristics of the OMT exposed pregnancies (n=306) and the pregnancies of the total general pregnant population (N=645,440). Women with OMT pregnancies were older, had lower BMI in early pregnancy, more frequently gave birth by caesarean section (23.5% vs. 14.9% in the general pregnant population), smoked more frequently (70.6% vs. 9.8%), were less frequently living with a partner (56.9% vs. 92.5%), and had lower education (72.2% vs. 17.5% had low education) compared with the general pregnant population. The majority (95.4%) of women with OMT exposed pregnancies were born in the Nordic countries.

Patterns of OMT medication use

In total, there were 306 OMT exposed pregnancies in the period 2005-2015 (Table 2). The average number of OMT exposed pregnancies per year was 28, ranging from 18 to 41 pregnancies. The most frequently used drug substance was buprenorphine, alone or in combination with naloxone (n=186) followed by methadone (n=120). Less than five pregnancies were exposed to buprenorphine-naloxone. Most pregnancies were exposed to methadone in the period 2005-2007, and from 2008 buprenorphine was the most frequently used drug substance (Figure 2).

Table 3 shows the pattern of initiation and timing of medication use in the 306 OMT exposed pregnancies. In 38 pregnancies, OMT was initiated in pregnancy, i.e., the woman did not fill any prescriptions of OMT medications before pregnancy start. Among these pregnancies, buprenorphine was initiated in 25 pregnancies and methadone in 13 pregnancies. Buprenorphine-naloxone was not used in any pregnancies where OMT was initiated after pregnancy start.

In most pregnancies (n=201), the women filled prescriptions of OMT medications in all three trimesters (Table 4). In 75 pregnancies, the women did not fill prescriptions of OMT medications after the 2nd trimester. Among these pregnancies, the women were hospitalized in multidisciplinary specialized substance treatment care during the 3rd trimester in 42 pregnancies. For the remaining pregnancies, two pregnancies ended preterm (at 171 days and 210 days), and nine pregnancies ended with birth between 2005-2007 which is before data on hospitalizations from the patient registry was available. Thus, it was only in 22 pregnancies that we could have found data on filled prescriptions and where the woman was not dispensed OMT medications after the 2nd trimester. In 30 pregnancies, the women filled prescriptions of OMT medications in the 3rd trimester only.

Amount of OMT medications dispensed during pregnancy

In the OMT pregnancies where the woman was dispensed OMT medication in all trimesters, the women filled a mean of 36 prescriptions of methadone (median 22) and 46 prescriptions of buprenorphine (median 28) during pregnancy (Table 5). The median number of

Table 2. Number of OMT pregnancies and pregnancies ending in live birth among the general pregnant population in the period 2005-2015.

	OMT pregnancies n (%)	General population n (%)
Total	306 (100)	645440 (100)
Year of birth		
2005	18 (5.9)	55831 (8.7)
2006	27 (8.8)	57552 (8.9)
2007	26 (8.5)	57509 (8.9)
2008	41 (13.4)	59628 (9.2)
2009	21 (6.9)	61036 (9.5)
2010	30 (9.8)	60617 (9.4)
2011	32 (10.5)	59474 (9.2)
2012	28 (9.2)	59419 (9.2)
2013	31 (10.1)	58147 (9.0)
2014	27 (8.8)	58212 (9.0)
2015	25 (8.2)	58015 (9.0)
Average number of pregnancies per year	28	58676

OMT = opioid maintenance therapy

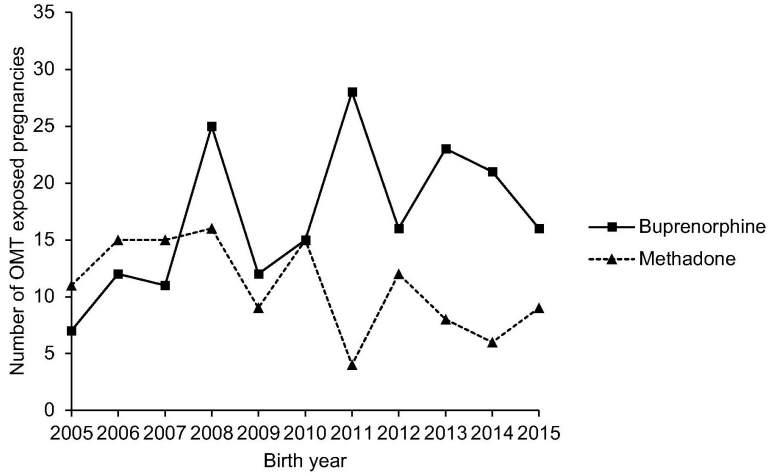

Figure 2. Number of OMT exposed pregnancies per year according to drug substance (buprenorphine or methadone). OMT pregnancies exposed to buprenorphine-naloxone (<5 pregnancies) were grouped with buprenorphine. OMT = opioid maintenance therapy.

Table 3. Number of OMT pregnancies by type of OMT medication and timing of treatment initiation among 261 Norwegian women from 2005-2015.

	methadone	buprenorphine[a]	Total
Pregnancies, n (%)			
OMT treatment before and during pregnancy	107 (39.9)	161 (60.1)	268 (100)
OMT initiated in pregnancy	13 (34.2)	25 (65.8)	38 (100)
Total	120 (39.2)	186 (60.8)	306 (100)

[a] In <5 pregnancies, the woman received buprenorphine with naloxone (bup/nal) and these pregnancies were grouped with buprenorphine pregnancies. The women who used bup/nal had been in OMT treatment before pregnancy.

Table 4. Timing of opioid maintenance treatment (OMT) in pregnancy among 261 Norwegian women (2005-2015).

Timing, n (%)	methadone	buprenorphine[a]	Total
all trimesters	80 (39,8)	121 (60.2)	201 (100)
1st or 2nd trimester	28 (37.3)	47 (62.7)	75 (100)
3rd trimester	12 (40.0)	18 (60.0)	30 (100)
total	120 (39.2)	186 (60.8)	306 (100)

[a] In <5 pregnancies, the woman received buprenorphine with naloxone (bup/nal) and these pregnancies were grouped with buprenorphine pregnancies. The women who used bup/nal were dispensed the drug in 1. and 2. trimester.

prescriptions had a wide interquartile range for both methadone and buprenorphine. In pregnancies with OMT medications dispensed in all trimesters, the interquartile range was 16-40 for methadone and 19-44 for buprenorphine. The median DDD/days in pregnancy was 3.3 (mean 3.4) for methadone equivalent to 82.5 (85) mg methadone per day. The corresponding numbers for buprenorphine were median 1.9 DDD (mean 1.9), equivalent to 15.2 mg buprenorphine per day.

DISCUSSION

In this study, we found that the number of OMT pregnancies per year in Norway has been relatively low and quite stable, with an average of 28 pregnancies per year

Table 5. Number of prescriptions and doses (DDD) of buprenorphine and methadone dispensed to women who were dispensed buprenorphine or methadone in all trimesters (n=201 pregnancies).

	Pregnancies with dispensed OMT medication in all trimesters	
	methadone	buprenorphine
Number of pregnancies	80	121
Number of prescriptions		
mean (sd)	36 (43)	46 (55)
median (IQR)	22 (16-40)	28 (19-44)
Number of DDDs/day		
mean (sd)	3.4 (1.7)	1.9 (0.8)
median (IQR)	3.3 (2.1–4.3)	1.9 (1.2–2.4)

1 DDD methadone O = 25 mg, 1 DDD buprenorphine SL = 8 mg
sd=standard deviation, IQR=interquartile range

during the study period. During this period, there has been a shift in the treatment of pregnant women from methadone towards buprenorphine. Most of the women in the study population had been in OMT before pregnancy, and most continued to use OMT medications throughout pregnancy. There seemed to be large differences in how often the pregnant women were dispensed their OMT medications at the pharmacy. However, the estimated doses per day during pregnancy were within the recommended dosage range for OMT patients in general. The women in OMT during pregnancy had more risk factors for adverse outcomes than women in the general pregnant population.

The first Norwegian national guideline for OMT treatment in pregnancy published in 2011, recommended buprenorphine without naloxone as the drug of choice in OMT patients who initiated treatment in pregnancy (12). However, buprenorphine had been available in Norway since 2000, and from 2005 it was recommended as the drug of choice for opioid dependent individuals in OMT in general (17). This may explain why we already from 2008 and onwards observed a shift from methadone to buprenorphine as the most frequently prescribed drug. Consequently, women were treated with buprenorphine in about 60% of the pregnancies during the entire study period. In a previous clinical cohort study of 139 pregnant women giving birth between 1996 to 2009 in Norway, only 35% were treated with buprenorphine (17). This was not unexpected since that study only included pregnancies until the beginning of 2009, and therefore mostly included pregnancies from the period before the shift towards buprenorphine as the most frequently used drug.

In only 12.4% of the pregnancies, OMT was initiated in pregnancy. In agreement with the national guidelines most of these women were dispensed buprenorphine instead of methadone. Also, only in very few pregnancies (<5) the woman used only buprenorphine in combination with naloxone, which is not recommended during pregnancy, and did not switch to buprenorphine. In these pregnancies, the women were not dispensed OMT medications in all trimesters. This might indicate that the women managed to taper the drug, or that they were hospitalized.

In approximately 90% of the pregnancies, the woman was already in OMT before pregnancy start, irrespective of whether she was treated with buprenorphine or methadone. Opioid use disorder and associated lifestyle reduce the probability of getting pregnant but after initiation of OMT, the probability of getting pregnant increases (25, 26). This might be one explanation for the high proportion of women already in OMT at the start of pregnancy. The supportive psychosocial measures that hopefully improve the women's total life situation compared to living with an untreated opioid use disorder might also increase the desire to get pregnant. In the previous cohort study from Norway, the proportion of women already in OMT at pregnancy start was in the same order of magnitude as found in this study (17).

Most of the OMT women in the present study continued treatment throughout pregnancy measured as filled prescriptions in all trimesters. The WHO guidelines recommend methadone as the drug of choice during pregnancy partly because of results that show higher retention in treatment in studies comparing methadone and buprenorphine (11). We did not observe any difference in retention measured as filled prescriptions in all trimesters between methadone (80/120, 67%) and buprenorphine (121/186, 65%).

In as many as 75 pregnancies the woman was not dispensed OMT medications in the third trimester, but for most of these pregnancies there were explanations for why the woman was not dispensed the OMT medication in the third trimester. Either the woman had a pregnancy that did not last until the third trimester, she was hospitalized in multidisciplinary specialized substance treatment, or she gave birth before the patient registry was established. In only 22 (7.2%) of the 75 pregnancies, the women might have discontinued OMT medication after the second trimester. These women may have managed to taper the drug. However, we cannot rule out that these women were hospitalized in other hospital sectors for other reasons such as pregnancy complications and thereby not captured by the prescription registry. Some of the women who were hospitalized, either in multidisciplinary specialized substance treatment or other hospital sectors, may have tapered their OMT medication to zero. Tapering OMT medication was not recommended in the WHO guidelines (11). In a previous clinical cohort study, only 2% managed to taper their OMT medication completely during pregnancy (27).

Both the mean and median estimated doses per day for both buprenorphine and methadone were in the recommended dose range for OMT treatment (23). Compared to results from the clinical cohort study, our estimated doses per day for buprenorphine were close to the dose when pregnancy was confirmed (15.8 mg), and close to the dose at delivery for methadone (89.9 mg) (17). However, registry data is not an optimal data source to study changes in prescribed doses during pregnancy. Such changes are common since the distribution volume for OMT medications increases as the pregnancy progresses.

Maternal risk factors for adverse pregnancy outcomes, such as preterm birth, were more common in women with OMT pregnancies compared to the general population of pregnant women. Pregnant women in OMT were older, a higher proportion was in the lowest BMI category in early pregnancy, smoked more frequently, were less frequently living with a partner, and had lower education (28). Compared to the previous clinical cohort study, there were some differences in background characteristics (17). These differences might reflect the different ways in which the data were collected. First, while the results on education were not directly comparable, the women in the clinical study had a mean of 10.8 and 11.3 years of education for

methadone and buprenorphine, respectively, while in the present study as many as 72.2% had 10 years of education or less. Second, a higher proportion (43%) of the women in the present study did not have a partner, compared to 17% and 16% for methadone and buprenorphine treated women in the clinical study. Based on registry data, women who were registered as cohabitants or married were regarded as having a partner, while in the clinical study, the information is collected by questionnaires. In contrast, smoking during pregnancy was more frequently reported in the clinical study. Reporting of smoking in the medical birth registry is voluntarily and this might lead to underreporting of smoking which is a limitation with use of such data.

Strengths and limitations

Data on dispensed OMT medications were retrieved from the Norwegian Prescription Database (NorPD) with complete coverage of all filled prescriptions in Norway since 2004. Data on drugs administered in hospitals and outpatient specialist care clinics are not captured, but it has been estimated that approximately 90% of patients who are dispensed OMT medications are registered in the NorPD (23). For pregnant women in OMT, this figure might be somewhat lower as these women might be more inclined to enter in-patient treatment during pregnancy. Data on filled prescriptions eliminates primary non-compliance, i.e. that the patient do not fill the issued prescription (29). However, we do not know whether the patient consumed the drugs. In our study, we found that most women filled OMT prescriptions regularly throughout their pregnancies, so it seems likely that the drugs were consumed. Also, for some patients, intake of OMT medications is supervised at the pharmacy (1). In contrast to previous register-based studies on OMT treatment in pregnancy in Norway (14, 18, 30), information on hospitalizations in multidisciplinary specialized substance treatment was available in the current study.

CONCLUSION

The pharmacological part of OMT seemed mostly in agreement with the national guidelines for OMT in pregnancy. Using Norwegian registry data to a large extent confirmed the results from the previous clinical cohort studies both regarding the pharmacological treatment provided and the background characteristics of the pregnant women. Registry and clinical studies both yield important information and together gives us a broader understanding of OMT medication use in pregnancy.

Ethical approval

The use of data was approved by the Regional Ethical Research Board in Norway (2014/358/REK sørøst D). The publication has used data from the Norwegian Patient Register (NPR). The authors are solely responsible for the interpretation and presentation of the data provided.

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