



Living a normal life? Follow-up study of women who had been in opioid maintenance treatment during pregnancy

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ABSTRACT

Background: There are few longitudinal follow-up studies of patients in opioid maintenance treatment (OMT). For this reason we performed a follow-up study of a cohort of 67 women who had used OMT-medications during pregnancy an average of ten years earlier. The aim of our study was to explore how the women were doing over time regarding OMT medication adherence and use of other legal and illegal substances, as well as to evaluate the mortality for the women and custody situation for the children in the cohort.

Methods: Participants were recruited from two cohorts in our previous pregnancy study covering women who gave birth from 2004 to 2009. Sixty-seven women agreed to be interviewed, which is 73% of the eligible women from our original study. We developed a questionnaire, which we used in the interview, that focused primarily on these women's current life situation (custody of child they had delivered, the use of medications in OMT and other legal and illegal substances, and several other health and social aspects of the participants' lives).

Results: Two women had died prior to the follow-up. Eighty-one percent of the women had custody of the child they had delivered in our pregnancy study and half the women were single parents. Fifty-four percent of the women were employed. At follow-up, 42% of the women were in methadone maintenance treatment (MMT), 39% were in buprenorphine maintenance treatment (BMT), and 19% had left OMT. One-third of the women had changed their OMT medication during the follow-up period. The majority (77%) were satisfied with their current OMT medication. The women in MMT seemed to be more severe substance dependent than the rest of the participants. There was little use of legal and illegal substances at follow-up, especially among women with custody of their child. The frequency of substance use was low. Fourteen percent of the women were in the process of leaving OMT and another half of the women wanted to leave OMT, but had no plan for how and when.

Conclusion: This follow-up study describes a predominantly well rehabilitated cohort of women who had given birth while in OMT ten years earlier. The majority of the women had custody of their children and used very few legal and illegal drugs. Our findings may be explained partly from a life course perspective, with the women having experienced turning points when starting OMT or becoming mothers.

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1. Introduction

Although opioid maintenance treatment (OMT) has become the treatment of choice for opioid dependent individuals, including pregnant women (Jones et al., 2008; WHO, 2009, 2014), there is a scarcity of research focusing on longitudinal outcomes for OMT patients in general and for women who have been in OMT during pregnancy, specifically.

OMT is efficient in reducing mortality (Bukten, Stavseth, & Clausen, 2019), improving physical and mental health (Fingleton, Matheson, & Jaffray, 2015; Skeie, Brekke, Lindbæk, & Waal, 2008), and reducing criminality (Bukten et al., 2012) and illicit opioid use (Mattick, Breen, Kimber, & Davoli, 2014). In a recent meta-analysis of mortality during and after OMT, Sordo reports mortality rates of 11 and 36 per 1000 person years (PY) in and out of methadone treatment and similarly 4 and 10 per 1000 PY in and out of buprenorphine treatment, respectively (Sordo et al., 2017).

Hser reviewed the literature on the long-term course of opioid addiction (Hser, Evans, Grella, Ling, & Anglin, 2015). Twenty-three of the 28 studies included patients in treatment and fourteen of the studies included patients in opioid maintenance treatment (MMT). Hser's main finding was that opioid addiction was associated with increased mortality, morbidity, and other adverse outcomes. Stable abstinence from illegal opioid use was reported among less than 30% of study participants after 10–30 years of observation. Hser found that abstinence from illegal opioid use was associated with longer retention in treatment, family and social support, and participating in rewarding, nondrug activities such as employment, relationships, and parenting.

Soyka described a 6-year naturalistic outcome study of 1493 OMT patients from Germany (Soyka 2017). The 6-year retention rate in OMT was 77%. Three hundred and forty-nine of 1493 (23%) patients had left OMT and 140 (40%) of the patients who had left OMT were opiate free.

We have not identified any longitudinal studies that report patients' changes in the type of the OMT medication. A qualitative U.S. study reported that 22% of its 283 participants had used both methadone and buprenorphine during different treatment periods (Yarborough et al., 2016). In a peer-to-peer survey of more than 1000 Norwegian patients in OMT, 64% of patients reported that they were satisfied with methadone and 68% reported that they were satisfied with buprenorphine as their OMT medication (Muller, Bjørnstad, & Clausen, 2018). Their mean methadone dose was 97 ± 39 mg and their mean buprenorphine dose was 17 ± 7 mg. Eighty-four percent of the participants reported at least one adverse effect. Fifty-seven percent of respondents regarded OMT as a life-long treatment (more men than women) (Brun, Vestergaard, Holum, & Bjørnstad, 2016).

In a U.S.-based paper on parents in MMT, 24% reported use of opioids other than the OMT medication, 26% reported use of amphetamines, 10% reported use of benzodiazepines, and 13% reported marijuana use during the last 30 days (Skinner, Haggerty, Fleming, Catalano, & Gainey, 2010). In a paper based on the prospective part of the current study, 4% of the mothers reported use of other opioids, 13% reported use of benzodiazepines, and none reported use of cannabis or amphetamines during the last 30 days when their children were 4 years old (Lund, Brendryen, & Ravndal, 2014).

A study from Norway of 78 children prenatally exposed to substances found that 85% of the mothers had lost custody when the children were 3 years old (Moe & Slinning, 2001). In an Australian study of mothers in methadone treatment during pregnancy, 44% of the children were taken out of the mothers' home when they were 4.5 years old (Lean, Pritchard, & Woodward, 2013). When the children in the prospective part of our study were 4 years old, 86% were still living with their biological parents (Carolien Konijnenberg, Lund, & Melinder, 2015).

The aim of our research was to study the long-term outcomes for a cohort of women who had been in OMT during pregnancy, specifically their retention in OMT and the type of OMT medication used over time, as well as their use of other legal and illegal substances. We also evaluated the mortality of the women and whether they had custody of the children they had birthed. We also asked participants to evaluate their OMT medication and their future plans for OMT.

2. Materials and methods

Our study included a national cohort of women in OMT in Norway who delivered children between 2004 and 2009. The cohort is drawn from a previous study of women in OMT during pregnancy (G. K. Welle-Strand et al., 2013). One part of the original cohort is a prospective study where 36 women (Bakstad, Sarfi, Welle-Strand, & Ravndal, 2009; Lund et al., 2014) and their children were closely followed by our research group over time (Carolien Konijnenberg et al., 2015; C. Konijnenberg & Melinder, 2019; Sarfi, Martinsen, Bakstad, Roislien, & Waal, 2009; Sarfi, Sundet, & Waal, 2013). Of the 67 women included in the current study, 28 come from this prospective cohort.

2.1. Setting

The Norwegian OMT program started in the late 1990s with methadone, and buprenorphine was introduced in 2000. From 2000 on, the number of patients in OMT increased, as did the proportion of patients receiving buprenorphine as their OMT medication (Riksheim, Gossop, & Clausen, 2014).

We previously performed a pregnancy cohort study, focusing on maternal and neonatal outcomes related to exposure to methadone or buprenorphine in utero (G.K. Welle-Strand, 2015). Throughout the study period, the Norwegian OMT program had strict inclusion criteria and a high level of control, including take-home medication only for abstinent patients and regular urine drug screening of the patients to confirm self-reports of substance use (Welle-Strand et al., 2013). Inclusion criteria for receiving OMT included being older than 25 years, five or more years of opioid dependency, and prior attempts at abstinence-oriented treatment. When these regulations were issued, prior attempts were understood as treatment without agonist drugs. There were no numbers given for treatment attempts, but the younger the patient in question, the more treatment attempts of longer durations were required to qualify for OMT. Patients received coordinated care both during pregnancy and after the child was born, including pregnancy follow-up, psychosocial care, continuous OMT, and other specialized care needed for their substance use disorders and other health problems.

2.2. Participants

Participants for our study were recruited from our previous study of pregnant women using OMT medications. For a detailed description of the study, see G. K. Welle-Strand et al. (2013). In the consent form for the pregnancy study, we had permission to contact all the women who had given birth between 2004 and 2009. The first cohort of women was from a prospective study running from January 2005 to February 2007 (Bakstad et al., 2009). The second cohort was from a retrospective study, including the year 2004 and from February 2007 to March 2009 (Welle-Strand et al., 2013).

Ninety-two women from the two different cohorts were eligible for the follow-up study, of which sixty-seven (73%) were recruited. The eligibility criterion was that the women had given written consent during the pregnancy study to be contacted again for a follow-up study. Fig. 1 describes our participants from pregnancy to follow-up. Twenty-five women were not included in the final sample due to drop-out. Of the

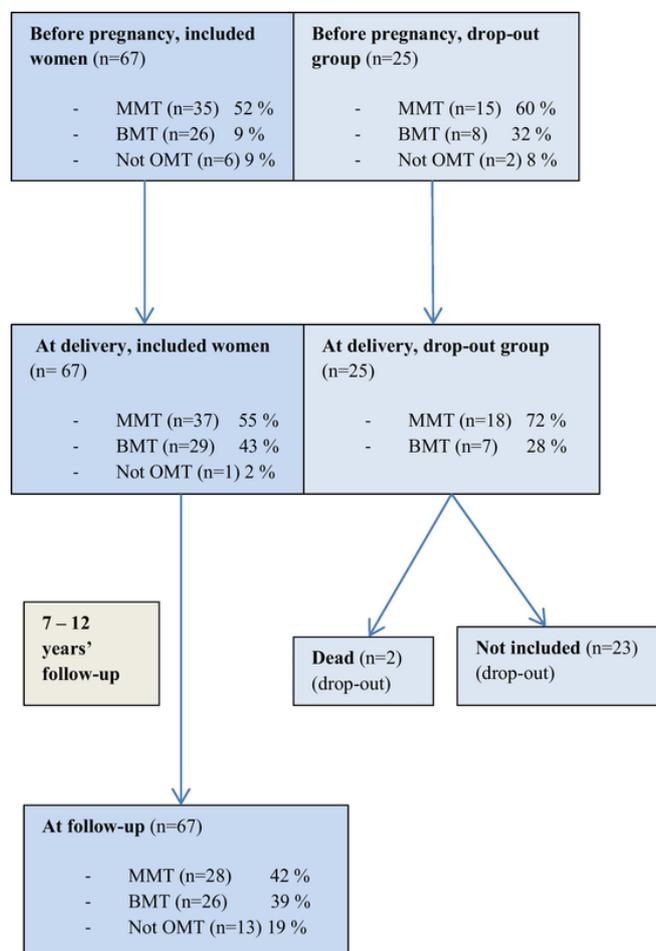


Fig. 1. Women included and the drop-out group in the follow-up study - prior to pregnancy being confirmed, at delivery, and at follow-up.

25 women who dropped-out, 2 had died, 13 women did not answer our attempts to reach them (phone or letter), 2 refused to take part in the follow-up, 4 wanted to take part, but dropped-out, and 4 women were unreachable (we did not have accurate, up-to-date contact information for them).

Table 1 shows that the background characteristics of all the participants in the pregnancy study were not significantly different between the women included in the follow-up study and the 25 women in the drop-out group (includes the two women who had died). The use of legal and illegal substances early and late in pregnancy did not differ between the two groups of women either.

2.3. Variables and procedures

We developed a questionnaire containing fixed-alternative, scale, and open-ended questions for this study. The questionnaire focused primarily on the women's current situation but also included questions covering the years after the child was born. Many of the questions were taken with permission from a questionnaire used in the Norwegian Cohort of Patients in Opioid Maintenance Treatment and Other Drug Treatment (NorComt) study (Skjaervo, Skurtveit, Clausen, & Bukten, 2017). Other questions were taken from a previous questionnaire developed for our pregnancy study.

The questionnaire covered employment, education, income, housing, physical and mental health, number of children (and for all children, the child's age, where they were living, if they were studying/working, and whether they were in contact with their biological

Table 1

Characteristics in the pregnancy study of the participants in the follow-up study and the women who were not included (drop-outs).

	All participants (n = 67)	Women not included (n = 25)	p-value
Opioid dependency prior to OMT (years), mean \pm SD (n = 92)	8,3 \pm 4,3	8,1 \pm 2,9	ns
Women's age at delivery (years), mean \pm SD (n = 92)	32,5 \pm 5,3	31,0 \pm 3,8	ns
In OMT when pregnancy was confirmed, % (CI) (n = 92)	91 (81-96) (61)	92 (73-99) (23)	ns
OMT length prior to pregnancy (months), mean \pm SD (n = 80)	30,9 \pm 25,4	29,1 \pm 22,8	ns
Methadone as OMT-medication in pregnancy, % (CI) (n = 92)	58 (46-70) (39)	68 (46-84) (17)	ns
Smoking last month before delivery, % (CI) (n = 91)	82 (70-90) (55)	92 (68-97) (22)	ns
Any opioids, benzodiazepines, cannabis and/or amphetamines last month before pregnancy was confirmed - self-reported, % (CI) (n = 91)	46 (34-59) (31)	46 (25-65) (11)	ns
Any opioids, benzodiazepines, cannabis and/or amphetamines last month before delivery - self-reported, % (CI) (n = 88)	10 (5-21) (7)	21 (8-41) (5)	ns

OMT = opioid maintenance treatment, SD = standard deviation, CI = confidence interval.

mother), nutrition, self-reported use of illegal/legal drugs and smoking, family and network, partner/biological father of the child, physical activity, experience of violence, criminality, OMT status and changes in OMT (type of medication, daily dosages, duration of treatment) since the last interview, control measures linked to OMT, and the custody status and development of the child since delivery. Self-report of licit and illicit substances was utilized since our earlier study had showed that self-report documented more substance use than the urine test did (G. K. Welle-Strand et al., 2013).

The women in the pregnancy study had reported their use of OMT medication (type of medication, daily dosage, duration of treatment) and the use of legal and illegal substances both one month prior to the confirmation of the pregnancy and one month prior to delivery. Likewise, the women in the current study reported their use of legal and illegal substances one month prior to the follow-up interview. With this information, we could account for the longitudinal use of OMT medications and legal and illegal substances (see Tables 3 and 4).

In this paper we report the characteristics of the participants, their use of OMT medications, their use of legal and illegal substances, who had custody of the child they had delivered, and the participants' future plans for OMT.

Most of the participants were interviewed via telephone; two were interviewed face-to-face. The interviews were conducted between December 2015 and May 2017.

The information regarding mortality in the drop-out group originated from the following sources: G.Welle-Strand (GWS) talked directly with eight of the women, for three women the information came from the child's biological father, for seven women it came from professionals in contact with the women and for the last seven women the information came from the principal investigator Monica Sarfi (co-author MS), who is in charge of the prospective part of our study.

Information regarding the custody situation of the children in the drop-out group was obtained in the following way: GWS received information directly from eight of the women, the child's biological father gave information about three of the women, professionals gave information about three other women, and MS provided the information for the last four women.

2.3.1.1. Ethics The study was approved by the Regional Committee for Medical and Health Care Research Ethics (REC-number: 2013/1606). All the women gave a separate written informed consent to take part in the follow-up study.

2.4. Analysis strategy and statistics

Descriptive statistics were used to compare the women we included with those who were in the drop-out group. We further evaluated the mortality and child custody situation for all eligible women ($n = 92$). The mortality rate was calculated per 1000 person years (PY). We looked at the characteristics of the participants and compared them according to their OMT status. Then we proceeded to examine the longitudinal use of the different OMT medications; we also analyzed the current use according to the participant's child custody status.

The analyses also included the patients' view on their OMT medication and their future plans for OMT. We evaluated the longitudinal use of substances the month preceding confirmed pregnancy, the month before delivery, and the month before follow-up, including an analysis of substance use prior to follow-up according to participants' child custody status. Finally, we described type and frequency of substance use the last year prior to follow-up, analyzing it according to the current OMT status of the women.

Continuous variables were compared using independent sample t -tests. Discrete variables were compared using χ^2 tests. A significance level of 5% was applied for all tests of significance. Data analyses were carried out using SPSS 25 for Windows.

3. Results

3.1. Mortality

During the recruitment process we received information confirming that 21 of the 25 women in the drop-out group were alive. Two of the

four women had died, whereas the status for the other two was unknown. This gives a crude mortality rate (CRM) of 2.32 ($2/861 \times 1000$) per 1000 person year (PY) ($n = 88$, deaths = 2, PY = 861).

3.2. Participants' characteristics and their custody situation

Table 2 shows that the women were 42 years old on average at the time of the follow-up interview, and had been in OMT for a mean of 12 years. Their children's mean age was nearly 10 years. Fifty-four percent of the women were working or studying and 48% of the women were single parents. Thirteen women had one additional child and two women had delivered two more children during the follow-up period.

The women using methadone as the OMT medication at follow-up differed significantly from the women who were using buprenorphine or who had left OMT during the follow-up period: they were older, had longer opioid dependency prior to OMT, had fewer parental responsibilities, and were less often employed.

3.3. Longitudinal outcome of OMT

Table 3 shows the women's OMT status prior to the pregnancy through to the follow-up interview. Ninety-one percent of the women were already in OMT when the pregnancy was confirmed, while all but one woman were in OMT at the time of delivery. At follow-up, approximately 10 years later, 19% (13) of the women had left OMT.

Thirty-four percent (23) of the women had changed their OMT medication at some point after the birth of their child. Eight women had changed medication from methadone to buprenorphine, while three women had changed medication from buprenorphine to methadone. Seven women had switched between different buprenorphine formulations/preparations. Last, five women had changed to either methadone or buprenorphine, but eventually resumed the OMT medication they had used initially.

Of the women using methadone at follow-up, 75% reported that they were satisfied with their OMT medication and 79% experienced one or more side effects. Of the women using buprenorphine, 88% reported that they were satisfied with their OMT medication and 56% reported side effects.

Table 2
Characteristics of the participants in the study, divided into their current OMT-status.

	All participants (n = 67)	MMT (n = 28)	BMT (n = 26)	Not in OMT (n = 13)	p MMT vs BMT	p MMT vs not in OMT	p BMT vs not in OMT
Mother's age at interview (years), mean \pm SD (n = 67)	42,0 \pm 5,8	44,6 \pm 5,3	40,9 \pm 5,3	38,8 \pm 5,7	0,013	0,003	ns
Opioid dependency prior to OMT (years) mean \pm SD (n = 67)	8,3 \pm 4,3	10,4 \pm 4,7	7,2 \pm 3,6	6,0 \pm 2,9	0,008	0,004	ns
Total time in OMT (years), mean \pm SD (range) (n = 66)	11,7 \pm 3,3 (1,3 – 18,3)	13,0 \pm 2,7	12,2 \pm 2,3	7,9 \pm 3,8	ns	0,000	0,000
Age of child at follow-up interview (years), mean \pm SD (range) (n = 67)	9,7 \pm 1,7 (7,3 – 12,2)	10,3 \pm 1,6	9,8 \pm 1,6	8,4 \pm 1,3	ns	0,001	0,011
Biological mother custody of child % (CI) (n) (n = 67)	81 (69-89) (54)	61 (41-78) (17)	92 (73-99) (24)	100 (75-100) (13)	0,007	0,008	ns
Working/studying % (CI) (n = 67)	54 (41-66) (36)	29 (14-49) (8)	73 (52-88) (19)	69 (39-90) (9)	0,001	0,014	ns
Live with the other biological partner % (CI) (n) (n = 67)	30 (20-42) (20)	14 (5-34) (4)	46 (27-66) (12)	31 (10-61) (4)	0,010	ns	ns
Having another partner % (CI) (n = 67)	22 (13-35) (15)	30 (14-49) (8)	15 (5-36) (4)	27 (6-54) (3)	0,017	ns	ns
Total number of biological children), mean \pm SD (range) (n = 67)	2,2 \pm 1,1 (1-6)	2,3 \pm 1,2 (1-6)	2,0 \pm 1,1 (1-6)	2,4 \pm 1,0 (1-4)	ns	ns	ns

OMT = opioid maintenance treatment, MMT = methadone maintenance treatment, BMT = buprenorphine maintenance treatment, SD = standard deviation, CI = confidence interval.

Table 3

The use of OMT medication when pregnancy was confirmed, at birth, and at follow-up (both for biological mothers without and with custody).

	When pregnancy was confirmed n = 67	At birth (n = 67)	At follow-up – total group n = 67	At follow-up (no custody) n = 13	At follow-up (custody of child) n = 54
Methadone, % (CI) (n)	52 (40-64) (35)	55 (43-67) (37)	42 (30-54) (28)	85 (54-97) (11)	32(20-46) (17)
- Methadone dose, mean ± SD	110 ± 44	88 ± 56	104 ± 48*	92 ± 42	113 ± 52*
Buprenorphine, % (CI) (n)	39 (27-52) (26)	43 (31/56) (29)	39 (27-52) (26**)	15 (3-46) (2)	44 (31-59) (24)
- Buprenorphine dose, mean ± SD	16 ± 6	15 ± 8	15 ± 8	16 ± 0	15 ± 8
No OMT-medication, % (CI) (n)	9 (4-19) (6)	2 (0-9) (1)	19 (11-31) (13)	0 (0-25)	24 (14-38) (13)

*Outlier of 420 mg methadone is excluded **two of the women used buprenorphine/naloxone, 24 used buprenorphine OMT = opioid maintenance treatment, SD = standard deviation, CI = confidence interval. All participants have answered all the questions.

3.4. The use of legal and illegal substances

Table 4 shows the self-reported use of drugs and alcohol and smoking one month prior to the pregnancy confirmation, as well as one month prior to delivery and one month prior to the follow-up interview. During the month before delivery, the use of illegal or legal drugs or alcohol was low (0–6%), but 82% smoked cigarettes.

Table 5 shows the self-reported use and frequency of use of legal and illegal substances the last year before the follow-up interview. The women in MMT reported significantly more use of benzodiazepines (50% vs 15%) and cigarette smoking (89% vs 62%) than women who were not in any OMT. However, among participants who reported any use, the frequency of opioid use (other than the OMT medication, benzodiazepines, cannabis, and amphetamines) was typically one to three times a month. The majority of women reported drinking alcohol one to three times a month; few women reported drinking alcohol more often.

Table 4

The self-reported use of illegal and legal substances in the month prior to confirmation of the pregnancy, the month before birth, and the month before the interview (both for biological mothers without and with custody).

	Last month before pregnancy was confirmed (n = 67)	Last month before birth (n = 67)	Last month before interview – total group (n = 67)	Last month before interview – no custody (n = 13)	Last month before interview – custody of child (n = 54)
Used opioids other than OMT-medication % (CI) (n)	13 (7-24) (9)	0 (0-5) (0)	5 (1-13) (3)***	0(0-25) (0)	6 (1-16) (3)
Used benzodiazepines % (CI) (n)	36 (25-49) (24)	6 (2-15) (4)	17 (9-28)(11)****	54*(26-80) (7)	8 (2-19) (4)
Used amphetamines % (CI) (n)	18 (10-30) (12)	0 (0-5) (0)	5 (1-13) (3)	17*(3-46) (2)	2 (0-11) (1)
Used cannabis % (CI) (n)	19 (11-31) (13)	0 (0-5) (0)	5 (1-13) (3)	17*(3-46) (2)	2 (0-11) (1)
Smoking % (CI) (n)	96 (87-99) (64)	82 (70-90) (55)	84 (72-91) (56)	100 (75-100) (13)	80 (66-89) (43)
Alcohol use % (CI) (n)	12 (6-23) (8)**	3 (1-11) (2)	55 (41-66) (36)*****	58 (32-85) (8)	54(40-67) (29)

OMT = opioid maintenance treatment, *p significantly different from women who had custody of their child, CI = confidence interval, **n = 59, ***n = 63, ****n = 66, ***** n = 64.

3.5. Custody situation

Eighty-one percent of the women had custody of the child born to them during our pregnancy study (Table 2). Two biological fathers (both in OMT) had sole custody of their child, meaning that 84% of the children in our study were living with one or both of their biological parents. During the recruitment process we received information about the custody situation for 18 of the 25 children of the women in the drop-out group: Nine percent (2) of the children were living with their biological mother, 12% (3) were living with their biological father alone, and 52% (13) were not living with either of their biological parents. We have no information about the custody situation for the remaining seven children.

Eighty-five percent (11 of the 13) of the women who had lost custody were using methadone (Table 3). Of the 54 women who retained custody of their child, 31% (17) were in MMT, 44% (24) were in buprenorphine maintenance treatment (BMT) and 24% (13) had left OMT.

Use of legal and illegal drugs the month prior to the follow-up interview was still low among the women with custody (0–8%), but 80% were still smoking cigarettes (Table 4). Women without custody reported significantly more use of benzodiazepines, amphetamines, and cannabis the month before follow-up compared to women with custody of their child.

3.6. Future plans regarding OMT: should I stay or should I leave?

Of the 54 women who were in OMT at follow-up, 14% (n = 7) said that they were in the process of tapering their OMT medication dose and planned to leave OMT (four respondents missing). Fifty percent (n = 25) of the women said they wanted to leave OMT, but had no current plans for when and how. Thirty-six percent (n = 18) wanted to stay in OMT, but most of them said they wanted a dose reduction. There were no significant differences between women in MMT and BMT regarding their future plans for their OMT medication.

4. Discussion

4.1. Mortality

Two of the women in our cohort had died during the follow-up period of 10 years, and mortality status was unknown for two women in the drop-out group. CMR was calculated to be 2.32 per 1000 PY in the cohort. In comparison, Bukten reported an all-cause CMR of 13.0/1000 PY in OMT, and 33.7/1000 PY after OMT (Bukten et al., 2019) in a cohort of almost 7000 Norwegian OMT patients. While our study had a

Table 5

The self-reported use of illegal and legal substances the last year before the follow-up in interview, divided into present OMT status.

	All participants (n = 67)	MMT (n = 28)	BMT (n = 26)	Not in OMT (n = 13)
Used opioids other than OMT-medication % (CI) (n) (n = 63)	11 (5-21) (7)	12 (3-29) (3)	8 (1-27) (2)	17 (3-46) (2)
-1-3 times/month (%)	11	12	8	17
Used benzodiazepines % (CI) (n) (n = 66)	34 (22-46) (22)	50* (31-69) (14)	24 (10-44) (6)	15 (3-46) (2)
-1-3 times/month (%)	21	29	16	15
-1-3times/ week (%)	3	4	4	0
-daily/nearly daily (%)	9	18	4	0
Used amphetamines % (CI) (n) (n = 67)	12 (6-23) (8)	18 (7-38) (5)	8 (1-27) (2)	8 (0-38) (1)
-1-3 times/month (%)	10	18	8	0
-1-3times/ week (%)	2	0	0	8
Used cannabis % (CI) (n) (n = 67)	13 (7-24) (9)	21 (9-42) (6)	4 (0-22) (1)	15 (3-46) (2)
-1-3 times/month (%)	10	14	4	15
-1-3times/ week (%)	2	4	0	0
-daily/nearly daily (%)	2	4	0	0
Smoking % (CI) (n) (n = 67)	84 (72-91) (56)	89* (71-97) (25)	89 (69-97) (23)	62 (32-85) (8)
Alcohol use % (CI) (n) (n = 67)	81 (69-89) (54)	79 (59-91) (22)	77 (56-90) (20)	92 (62-100) (12)
-1-3 times/month (%)	70	64	69	85
-1-3times/ week (%)	9	11	8	8
-daily/nearly daily (%)	2	4	0	0

OMT = opioid maintenance treatment, MMT = methadone maintenance treatment, BMT = buprenorphine maintenance treatment, *p significantly different from "not in OMT", CI = confidence interval.

lower mortality rate compared to other studies, the lower hazard rate of all-cause mortality for opioid dependent women compared to men must be taken into account (Evans et al., 2015; Sordo et al., 2017). A recent register study focusing on mortality in Norwegian OMT found that female deaths constitute 26% of all reported deaths (Bech, Clausen, Waal, Saltyte Benth, & Skeie, 2019). Women constitute approximately 30% of the patients in OMT in Norway (Waal et al., 2017); therefore, in Bech's paper the women in OMT had almost the same mortality rate as the men.

The low mortality rate in our cohort may be due to the low rate and frequency of licit and illicit substance use among the women in our study.

4.2. Retention in OMT

Eighty-one percent of the women we interviewed at follow-up were still in OMT 12 years after they entered OMT, which is a high retention rate over a longer follow-up period compared to other studies of OMT patients. Eastwood from the UK reported 60% retention after seven years (Eastwood, Strang, & Marsden, 2018), Soyka from Germany reported a 6-year retention rate of 77% (Soyka, Strehle, Rehm, Bühringer, & Wittchen, 2017). Teesson from the Australian Treatment Outcome Study reported that 47% of patients were in treatment after 11 years (Teesson et al., 2015) and the retention rate after 11 years in MMT reported by Peles from Israel was approximately 40%

for participants who had children (Peles, Schreiber, & Adelson, 2006).

The one-year retention rate for all OMT patients in Norway in 2018 was 96% (Waal et al., 2019). There may be several reasons for these high retention rates. Norway is an affluent country with high quality treatment. It follows individual patients closely and has a generally high threshold to discharge patients from treatment despite concurrent use of illicit drugs. Many patients prefer to continue treatment to avoid troublesome withdrawal symptoms. There is also a well-known risk of relapse to illicit opioid use if one were to leave OMT.

4.3. OMT medication

Approximately one-third of the respondents had changed their OMT medication between the birth of their child and follow-up; the majority had changed from methadone to buprenorphine or between different buprenorphine formulations. More patients changed from methadone to buprenorphine, than the other way around, consistent with findings from two U.S.-based studies (Gryczynski et al., 2013; Yarborough et al., 2016). Oral reports from the participants during the follow-up interviews confirmed that they changed from methadone to buprenorphine because they feared getting dependent on a full opioid agonist, wanted to have a "clear head" as a caregiver, and experienced adverse effects from and the stigma associated with methadone.

Only two out of the 26 women on buprenorphine in our follow-up study used the buprenorphine/naloxone formulation. Unlike the preference for buprenorphine/naloxone preparation that was reported in a French study (Daulouede et al., 2010), Norwegian OMT patients most often prefer mono-preparations of buprenorphine, as reported by 1030 OMT patients who answered a questionnaire in a national peer-to-peer study (Muller et al., 2018).

More than 75% of the participants reported satisfaction with their OMT medication, a result in line with a Norwegian national peer-to-peer survey (Muller et al., 2018). The percentage of women reporting adverse effects from the OMT medication in our study is also in line with the results from the peer-to-peer survey.

In a recent study, 23 women in OMT (15 in MMT and 8 in BMT) from our prospective study group were compared to 30 healthy age-matched mothers. Self-reported responsiveness to nondrug rewards was high for both groups, yielding moderate evidence that subjective anhedonia did not exist in the OMT group. The mothers in OMT also displayed robust reward responsiveness in a behavioral task. The authors concluded that reduced sensitivity to rewards and anhedonia are not necessarily consequences of prolonged opioid use (Eikemo et al., 2019). These results support the women's reported satisfaction with their OMT medication.

Nationally there has been a gradual and steady shift from methadone to buprenorphine in OMT since the latter was introduced in 2000 (Riksheim et al., 2014). In Norway, the choice of both methadone and buprenorphine as OMT medication has consistently been regulated according to the same inclusion criterion and provided by the same health professionals. When the first patients in this study gave birth in 2004, 77% of the OMT patients in Norway used methadone (Waal, Clausen, Håseth, & Lillevold, 2009), whereas in 2016, when most of the follow-up interviews were conducted, 38% of the patients nationally used methadone (Waal et al., 2017). In the National Opioid Maintenance Treatment Guidelines issued in 2010, buprenorphine was recommended as the first line OMT medication (Blindheim & Johannessen, 2010).

In clinical practice in Norway, buprenorphine is typically the treatment on which most patients start out. However, many of the women in our cohort initiated OMT before buprenorphine was available in the country. More women, therefore, changed from methadone to buprenorphine, than the other way around. However, women with a

more severe opioid dependence might be better off with methadone, hence why some women changed from buprenorphine to methadone. These factors may have contributed to the reported changes in OMT medications in our study.

We found that women who used methadone as their OMT medication at follow-up were older, had longer opioid dependency prior to OMT, held custody of their child less, and had a lower employment rate. Eleven of the 13 women who had lost custody were using methadone. These findings, in line with our previous findings (G. K. Welle-Strand et al., 2013), may suggest that the women in MMT at follow-up is a more vulnerable subgroup who is suffering from a more severe substance dependence than the women in BMT or the women who had left OMT.

4.4. Longitudinal outcome for substance use

We found that participants' reported use of substances the month before pregnancy (see Table 4) was similar to the use reported in the annual status survey for OMT patients in Norway in 2008: opioids (15% vs 13%), cannabis (19% vs 32%), benzodiazepines (39% vs 42%) and amphetamines (18% vs 15%) (Waal et al., 2009). That is, before realizing they were pregnant, women in our cohort used licit and illicit substances to the same extent as other OMT patients in Norway. When comparing the reported substance use the last four weeks before follow-up for our cohort with the annual national report for 2016, another picture emerges: opioid use (5% vs 10%), cannabis use (5% vs 32%), benzodiazepine use (17% vs 39%), and use of amphetamines (5% vs 15%) (Waal et al., 2017). At follow-up, as well as in the last month before delivery, the women used substantially less substances than the average OMT patient in Norway. We believe that this significant reduction in the use of substances is primarily because these women had become pregnant/mothers while they were undergoing OMT.

4.5. Custody

Eighty-one percent of the children were living with their biological mother at follow-up. This is a higher percentage of custody for biological mothers than reported in other, shorter-term follow-up studies of women in OMT during pregnancy (Lean et al., 2013; Schaubberger, Borgert, & Bearwald, 2019; S. Taplin & Mattick, 2015). Even if we assume that all the women in the drop-out group, for which such information is lacking, had lost custody, at least 66% of the women in our study retained custody of their child at the 10 year follow-up. All thirteen women who had left OMT had custody of their child; they had higher employment rates, smoked less, and used benzodiazepines less than the women in the MMT-group.

Having custody of children may be considered a protective factor against using drugs, either due to an increased inner motivation to have a life without drugs or a fear of child protection services intervening (Taplin & Mattick, 2013; Taplin & Mattick, 2015).

The self-reported use of legal and illegal substances was even lower at follow-up among the women with custody; this finding is in line with what Lund reported for 26 of the women 4 years after delivery in a previously published study of the prospective part of our cohort (Lund et al., 2014). The women without custody in our cohort reported significantly more use of benzodiazepines, amphetamines, and cannabis than the women with custody. A study from Ireland reported that patients with children in their care used much less heroin and cocaine at 3-year follow-up than patients without children in their care (Comiskey, Hyland, Hyland, & Misuse, 2016).

4.6. Future plans for OMT

One third of the participants in our study reported that they wanted to remain in OMT, while a peer-to-peer survey reported that 51% of the female responders considered OMT to be life-long treatment (Brun et al., 2016). Our study shows that a group of women were well rehabilitated (with approximately one-third having left or in the process of leaving OMT), after having spent a mean number of eight years in this treatment.

4.7. Turning points and life course perspectives

Hser (Hser, Longshore, & Anglin, 2007) and Teruya (Teruya & Hser, 2010) have offered a theoretical and practical framework for widening our understanding of how different points in the life course may influence people with opioid use disorders. Transitions like entering OMT, becoming a parent, or starting a job may generate turning points or a change in the life course. Trajectories might become long-term patterns of stability and change. Jessup reports in her qualitative study of significant life events that parenting responsibilities reinforce abstinence and are an aid to recovery (Jessup et al., 2014).

Most of the women in our study entered OMT before they became mothers or knew they were pregnant. Many of them were employed at follow-up, often after having finished education. Other women in our cohort experienced turning points in a different sequence; for example, entering OMT after realizing that they were pregnant. These multiple transitions help to explain these women's marked reduction in/cessation of substances and their sustained recovery. However, the degree of rehabilitation and how the patients benefitted from the turning points they experienced seemed to vary among the participants. Nevertheless, all women in our study shared the common turning points of entering OMT and becoming a parent.

On the other hand, those mothers who had lost custody may have experienced the painful loss of a child as a negative turning point, which may have increased the use of substances and reversed their recovery process.

Since 1996, Norway has had a law allowing substance-using pregnant women to be admitted to a specialized ward/institution without their consent (Söderström & Skolbekken, 2012). Parental substance use is considered child maltreatment by the Child Welfare Services in Norway (Burns, Pösö, & Skivenes, 2017; Juhasz & Skivenes, 2017). These legal measures may partly explain the lower use of substances among our participants after they realized that they were pregnant.

4.8. Strengths and limitations

To our knowledge, this is the first longitudinal study of a group of predominantly well-rehabilitated opioid-dependent women that focuses on changes in the use of OMT medication over time, the participants' use of other substances, and their future plans for OMT. Further, it is a national study, with patients recruited from all over Norway. Seventy-three percent of the eligible participants were interviewed, and information about mortality and custody was also obtained for most of the women in the drop-out group. This is a relatively high recruitment rate for an opioid-dependent cohort (Pombo & da Costa, 2018).

The fact that this is a selected group of OMT patients; women who used OMT-medication during pregnancy, can be viewed as a strength and a limitation. The strength is that the group of participants is well defined, and hence our results may be generalized to other groups of women who have used methadone or buprenorphine during pregnancy. The limitation is that our longitudinal results cannot be generalized to all patients (men and women) in OMT. It would be possible to test the

generalizability through linking our data to national registries. We did not have the permission to do so in this study. However, we plan to conduct another study and hope to link our data in that study to national registries.

The current study also has limitations. Norway is a rich country, with well-developed social services and welfare systems, which make it easier to enter education and the work force. These services are free and available to former substance users. Hence, our findings are not generalizable to less affluent countries, or countries with less well-established welfare states. The resources available for follow-up of patients in OMT in general, and pregnant women or parents in OMT specifically, are rich, as Norway is an affluent country. Further, the Norwegian legislation mentioned above, which applies both for women using substances in pregnancy and as parents (different law, but similar consequences), may influence our results. This study does not have sufficient power to detect significant differences in our relatively small groups. Finally, we do not have urinary drug tests to confirm self-reported drug use.

5. Conclusion

In a follow-up study of a cohort of women who used OMT medications during pregnancy, 73% of the eligible women agreed to be interviewed ten years after delivery. The majority of the women had custody of their child and the mortality rate in the cohort was low. The majority of the women were in recovery and half of them were employed. The ten-year retention rate in OMT was 81%. One of five women in our study had left OMT. There was little use of legal and illegal substances among the women, especially among the women with custody of their children. However, women using methadone at follow-up seemed to be a more substance-dependent and vulnerable group than the other women in the study.

CRedit authorship contribution statement

Gabrielle K. Welle-Strand: Conceptualization, Methodology, Validation, Formal analysis, Data curation, Resources, Investigation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration, Funding acquisition. **Svetlana Skurtveit:** Conceptualization, Methodology, Validation, Formal analysis, Resources, Writing - review & editing, Visualization. **Kristine Fiksdal Abel:** Conceptualization, Validation, Writing - review & editing, Visualization. **Fatemeh Chalabianloo:** Conceptualization, Validation, Writing - review & editing, Visualization. **Monica Sarfi:** Conceptualization, Methodology, Validation, Resources, Writing - review & editing, Visualization.

Declaration of competing interest

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GWS performed the interviews with the participants and analyses of the data from 2016 to 2018 as part of her job at the Norwegian Directorate of Health. From 2018 to June 2019 GWS did the analyses and writing as part of her job at Oslo University Hospital.

OMT = opioid maintenance treatment, MMT = methadone maintenance treatment, BMT = buprenorphine maintenance treatment.

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