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Characteristics and quality of life of opioid-dependent pregnant women in Austria

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Introduction

Substance use disorders have undergone a paradigmatic shift in the scientific and clinical community and have increasingly been considered chronic conditions (e.g. as reflected in DSM-V, APA 2013). Along with this shift and the growing demand and subsequent importance of taking into account patients' views in health care evaluation (Armstrong and Caldwell 2004), the concept of quality of life (QoL) has received more attention, further development and increasingly broader application.

Currently, two QoL approaches are prevailing in medical research, targeting either an individual's perception of his/her health and associated functioning and well-being (health-related quality of life, HRQoL), or a more comprehensive, multi-dimensional overall subjective satisfaction with life, simply referred to as "Quality of Life" (see also Laudet 2011). The WHO (1998) endorses the latter, much broader concept, defining QoL as an "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (p.3). This definition stresses the subjective evaluation of QoL, which is embedded in a socio-cultural context that seems to be crucial in the perception of health, illness and recovery, particularly in psychiatrically ill patients. Moreover, psychiatric patients are frequently disadvantaged, having fewer or worse resources to cope with their everyday life, e.g. fewer social and cognitive skills, environmental assets, family support, and money; hence, a more comprehensive assessment covering different specific life domains seems more appropriate for psychiatric patients (Katschnig 2006).

Addiction research has made efforts to increasingly incorporate and address QoL, with a greater focus on HRQoL (Laudet 2011) and legal substance use disorders (e.g., alcohol) rather than targeting overall QoL and illegal substance use disorders (e.g., heroin). Systematic QoL assessment in patients with illegal substance use disorders is still scarce, and thus data on specific subgroups with special needs is widely lacking. Among patients

with substance use disorders, pregnant women have been identified as a sub-population with special needs, and clinicians and researchers agree that a multi-disciplinary comprehensive treatment approach seems most appropriate in addressing those needs. Specifically, interventions for pregnant opioid-dependent women and their newborns have been studied, so medical as well as psychosocial treatment recommendations have been developed and elaborated for mothers and children (e.g. Jones 2013, Shainker et al 2012, Unger et al 2012, Osborn et al 2010). However, little is known about the overall QoL of this special patient group. We only found two studies investigating comprehensive QoL in pregnant opioid-dependent women. One study was conducted by Fischer et al (2000) who evaluated quality of life in a sample of 43 opioid-dependent patients in Austria postpartum; the second analysis was published by Daley et al (2005) who created a QoL index (for economic comparison purposes) out of Addiction Severity Index (McLellan 1980) ratings from 439 pregnant substance-dependent women in the United States, who underwent different treatment modalities (these women could be dependent on different drugs, so they were not necessarily opioid dependent). Hence, to our knowledge, no study has been published to date that reports comprehensive QoL data during pregnancy and the postpartum period in opioid-dependent women, taking into account different time points and medications.

In the frame of a project evaluating the treatment outcome of pregnant opioid-dependent women undergoing opioid maintenance therapy in a multi-disciplinary setting at the Medical University of Vienna, Austria, QoL data had been collected routinely at treatment initiation and postpartum. This study is the first to analyze comprehensive QoL in opioid-dependent women maintained on buprenorphine, methadone, or slow-release oral morphine (SROM), taking into account two critical time points; i.e. treatment initiation during pregnancy and end of treatment postpartum, allowing an evaluation of the patients' satisfaction with different treatment conditions. Moreover, characteristics of pregnant opioid-dependent women in Vienna, Austria are depicted in order to obtain a complete picture of the "field population" in this area.

Materials and Methods

A multi-disciplinary, comprehensive treatment model applying standardized interventions for opioid-dependent pregnant women was established in November 1994 at the Addiction Clinic at the Medical University of Vienna, Austria. In 2008, a project aimed at evaluating the treatment approach was initiated, including systematic compilation and analysis of all data collected until January 2009.

Since no specific interventions for study purposes were undertaken, the basic treatment procedures are described below.

Upon treatment initiation (through voluntary engagement or referral by obstetricians, addiction clinics, or general practitioners), the women were informed about treatment interventions at the Addiction Clinic as well as about the intended purpose, risks and (side) effects of opioid maintenance treatment during pregnancy. If the women opted for (outpatient) treatment at the Addiction Clinic, they signed a contract explaining all treatment

modalities and expectations. All patients declared that they would adhere to the contract until the end of treatment in the postpartum phase.

The treatment team consisted of medical doctors, psychologists, nurses, and social workers who closely collaborated with the Department of Obstetrics and Gynecology (Ob/Gyn), and the Departments of Pediatrics and Adolescent Medicine at the Medical University of Vienna, other hospitals in Vienna treating neonates with prenatal opioid exposure, and other relevant institutions (e.g. child welfare services, criminal justice system etc.). Assessments and interventions followed standard operating procedures (SOPs), although treatment decisions such as choice and daily dose of maintenance medication (methadone, buprenorphine (Subutex®) or slow-release oral morphine (SROM; Substitol® retard/ Compensan® retard)) and frequency of visits (weekly up to daily, on average 2–3 times a week) were individualized and determined by the patient and the treating physician together, based on the patient's preferences, previous treatment experiences, current addiction stability and life circumstances. Thus, a case-management approach was applied using standardized methods. Women were in treatment for 21 weeks on average (including a 2–6 weeks postpartum period when they were referred to other treatment institutions or continued their pre-pregnancy treatment), and underwent the following assessments:

- *Prepartum assessment of basic clinical and demographic data* (family status, educational background, living conditions, prior pregnancies and births, data on opioid dependence and prior treatment, cigarette consumption) were completed during the first visits to the Addiction Clinic.
- *Supervised urine toxicologies* were conducted regularly throughout the treatment period, but at least once a week in order to assess concomitant consumption of cocaine, benzodiazepines and opioids (concurrent opioid consumption rates are only available for methadone- and buprenorphine-maintained patients since opioids cannot be distinguished from the maintenance medication in urine toxicology results for SROM-maintained patients). THC was not routinely tested with urine samples; due to the generally long period of positivity in urine toxicology results which can last several weeks or even months with chronic cannabis consumption (e.g. Westin et al 2009), these results would be of limited clinical relevance. For the present analysis, results were only counted if the woman provided at least one valid urine sample per week during the last trimester of pregnancy. Additionally, alcohol use disorders were monitored through breath analyses, i.e. regular breathalyzer tests were conducted in women with a history of alcohol use disorders, self-reported alcohol consumption, or if deemed necessary by any staff member.
- *Laboratory tests* were performed at least twice during the treatment period (at the first visit and at the time of delivery) to monitor various parameters during pregnancy (e.g. hormone status, infectious diseases like HIV, HCV, anemia markers).
- *Information about the delivery* (gestational age, delivery mode, anesthesia, etc.) was documented in the patient's records at the Department of OB/Gyn.

- During a *postpartum assessment*, basic data on delivery (date, place and mode of delivery) was assessed by means of a standardized questionnaire. Additionally, current maternal medication dose and further proceedings regarding treatment continuation and childcare matters (foster parents, mother-child care facility, adoption etc.) were documented.
- Assessment of *Quality of Life* was made with the *Berliner Lebensqualitätsprofil (BeLP) questionnaire* (Priebe et al 1995), which is a German adaptation of the Lancashire Quality of Life Profile (Oliver 1991/1992). It assesses an individual's satisfaction with 8 domains of life (general life satisfaction; satisfaction with employment/education, leisure time, financial status, housing, legal status and safety, family, friends and acquaintances, health) on a 7-point scale (1=could not be worse, 7=could not be better). This questionnaire was administered prepartum (at treatment initiation) and within 6 weeks after delivery in order to assess overall life satisfaction and changes over the course of the treatment period.

The *study sample* consisted of all opioid dependent women (DSM-IV 304.0, APA 1994) who underwent opioid maintenance therapy during pregnancy and the postpartum period at the Addiction Clinic between November 1994 and January 2009 (time of treatment initiation). Patients had to be at least 18 years old, have a single-fetus pregnancy and take their prescribed opioid medication at time of delivery to be included in this complete case analysis. Patients who had an abortion, a miscarriage, a multiple-fetus pregnancy, or decided to complete their treatment at another clinic/hospital (including the delivery and postpartum phase) were excluded because insufficient data were available to evaluate their treatment outcome. Thus, the final sample for analysis consisted of 390 cases (out of 478 cases in total). Of the 478 women who attended the Addiction Clinic at some point during their pregnancy, there were 416 live births (2 of these women had twin pregnancies, and 24 were not taking any opioid medication at time of delivery, i.e. did not follow the treatment regimen, and therefore also were not included in our analysis), 15 miscarriages, 12 abortions, and 4 stillbirths. Thirty-one women could not be tracked after they refused or stopped treatment at the Addiction Clinic; thus, 390 mother-infant pairs could be included in our analysis.

The main *outcome measures* were the QoL scores pre- and postpartum, i.e. at treatment initiation (around week 20–25 of their pregnancy) and at the end of treatment (2–6 weeks after delivery).

Statistical analyses

Statistical analysis was conducted by using SPSS for Windows (version 16 and 17), assuming interval scale level, and applying two-tailed testing as well as a level of significance of $\alpha=0.05$.

Demographic and clinical characteristics were depicted using descriptive statistical methods (frequencies, means, standard deviations and ranges); for inter-group comparisons of characteristics, ANOVAs were applied for continuous variables and crosstabs with Chi-

square tests/Fisher's Exact tests for categorical data. Homogeneity of variances was tested with Levene tests; in case of heterogeneous variances, the Welch method was used.

T-tests for paired samples were applied for comparing maternal QoL scores prepartum versus postpartum in the whole sample.

A mixed-model ANOVA with within-subject factors (time point/item) and a between-subject factor (medication group) was used to test for prepartum-postpartum maternal QoL differences in the 3 opioid medication groups (buprenorphine, methadone, slow-release oral morphine).

Ethical standards

The study was approved by the IRB of the Medical University of Vienna (IRB-number 514/2008) and was conducted in accordance with the Declaration of Helsinki (WMA 1964–2008) and its later amendments.

The women were asked to give informed consent to have their data, which would be collected within the context of their treatment at the Medical University of Vienna, anonymously analyzed and used for publication.

Results

General demographic and clinical characteristics

The final sample consisted of 390 women, whereof 265 (67.9%) indicated at time of treatment initiation (at the Addiction Clinic) that they were in current opioid maintenance therapy (n=111 women (28.5%) were maintained on methadone (mean dose=57mg, SD=34mg), n=52 (13.3%) on buprenorphine (mean dose=8mg, SD=5mg), n=102 (26.2%) on SROM (mean dose=411mg, SD=213mg), and n=125 women (32.1%) did not report being currently in treatment and were acquiring their opioids by other means, e.g. illegally).

At time of delivery, 184 women (47.2%) were maintained on methadone (mean dose at time of delivery=64mg, SD=36mg), 77 (19.7%) on buprenorphine (mean dose=10mg, SD=6mg), and 129 (33.1%) on slow-release oral morphine (SROM; mean dose=455mg, SD=207mg). Figure 1 shows self-reported opioid medication use at treatment entry (around 20th week of pregnancy) and following assignment to methadone, buprenorphine or SROM. Please note that all participants included in this (complete case) analysis followed the prescribed regimen, i.e. they were maintained on the medication they had been prescribed throughout the last trimester of pregnancy, including delivery.

The women were on average 25.5 years of age at the time of delivery, 337 (86.4%) were Austrian, 204 (52.3%) had completed only compulsory education, and 218 (55.9%) were living with a partner. They were pregnant on average the second time, and were smoking approximately 14.6 cigarettes per day (range=0–80 cigarettes per day; only 18 (4.6%) were non-smokers) in the prepartum phase; the average self-reported nicotine consumption postpartum was 13.25 cigarettes per day (range 0–60 cigarettes per day; 17 women were non-smokers). Two-hundred and thirty one women (59.2%) were hepatitis C antibody positive,

and 23 (5.9%) were prescribed an antidepressant drug, 12 (3.1%) a benzodiazepine, and 7 (1.8%) another psychotropic drug. Two-hundred and eighty seven women (73.6%) could take their newborn home after discharge from hospital; 40 (10.3%) of the children went to foster parents, 5 (1.3%) were adopted, and in 58 (15% of the) cases, child care decisions were pending or data could not be retrieved at the time of assessment shortly after delivery.

Table 1 gives an overview of maternal demographic and clinical characteristics in each patient group.

Regarding general demographic and clinical characteristics, no significant medication inter-group differences were revealed. Therefore, no variable had to be used as a covariate for further analyses.

Concomitant consumption of opioids, benzodiazepines and cocaine

Concomitant consumption of opioids, benzodiazepines and cocaine during the last trimester of pregnancy was tested with regular supervised urine toxicologies (at least once a week). If a woman tested positive at least once during the 3rd trimester, she was included in the category for concomitant consumption. Alcohol consumption was verified with regular breathalyzer tests in women with a history of alcohol use disorders, self-reported alcohol consumption, or if deemed necessary by any staff member involved in treatment. Two women in the methadone group had low alcohol consumption during the last trimester; no alcohol consumption was confirmed for women in the buprenorphine and SROM groups.

Table 2 shows concomitant consumption rates during the last trimester of pregnancy (concomitant opioid consumption cannot be reported for the SROM group since it is indistinguishable from the opioid medication in the urine toxicology).

Concomitant consumption of benzodiazepines was significantly lower in the buprenorphine-medicated group compared to the women receiving methadone or SROM. Cocaine consumption seemed to be highest in the SROM group, followed by the methadone group, and lowest in the buprenorphine group, although the inter-group differences were not statistically significant. However, significantly more women maintained on methadone showed concomitant consumption of opioids in the third trimester of pregnancy than women in the buprenorphine group.

Quality of Life

Table 3 depicts prepartum and postpartum BeLP QoL scores for the whole sample.

All patients had mean satisfaction scores around 5, indicating satisfaction in the respective domain. Only the items “finances” and “prospect of staying in that living situation” had lower mean scores, indicating poorer satisfaction in these domains (see also Figure 2).

Satisfaction between the prepartum and postpartum assessments improved significantly with regard to life in general, finances, living situation, relationships with children and other family members, number of friends, health in general and mental health.

A mixed model ANOVA for testing *medication group differences over the BeLP QoL items and both time points* (prepartum/postpartum assessment) yielded significant results for the inter-item comparison, inter-time point (prepartum versus postpartum) comparison, and a significant result for the item-time point interaction; however, neither the inter-medication group differences nor the item-medication group interaction were significant. In addition, neither the time point-medication group interaction nor the item-time point-medication group interaction were significant (see Table 4). Thus, prepartum and postpartum QoL profiles differed significantly regarding time point and on the item level, but they did not differ among the 3 medication groups.

The following two figures show the prepartum (Figure 2) and postpartum (Figure 3) quality of life profiles according to the maternal opioid medication at time of delivery.

The items are shown in the same order as in Table 3 (error bars are omitted for better visibility).

Similar profiles were observed for prepartum and postpartum QoL. Average satisfaction scores ranged for all three medication groups between 5 and 6, indicating satisfaction in the domain; satisfaction with financial status and prospect of staying in the same living/housing situation showed lower mean scores compared to the other domains.

The QoL items are shown in the same order as in Table 3 (error bars are omitted for better visibility).

Discussion and Conclusion

The present study evaluated outcome parameters of opioid-dependent pregnant women undergoing pharmacological maintenance therapy in a multi-disciplinary outpatient setting in Vienna, Austria. Since all adult pregnant opioid-dependent women with single-fetus pregnancies who completed treatment were included in the analysis, the findings depict those of the “field population” in this region and thus have high external validity. A myriad of parameters were assessed in order to gain a comprehensive picture of this especially vulnerable population.

The analysis revealed that the women are young mothers, with low educational level, as well as a higher rate of adverse pregnancy outcomes (e.g. stillbirth rate, 0.84% versus 0.37% (in 2009) - 0.44% (in 1995) in the general population) and a lower rate of multiple births (0.48% versus 1.72% (in 2009)) compared to the general population of Austria (Statistik Austria 2011a and 2011b). However, the smoking and hepatitis C rate, as well as the prescription rate of psychotropic medications in the sample were high, and comparable to those of other opioid-dependent pregnant populations (Kashiwagi et al 2005, Vucinovic et al 2008, McCarthy et al 2005, Jones et al 2010, Seligman et al 2010, Mayet et al 2008).

The average daily opioid dose of the patients in this study was in between the dose ranges indicated by other studies, reporting higher (e.g. Seligman et al 2010) and lower methadone doses (e.g. Kashiwagi et al 2005) and higher (e.g. Jones et al 2005) and lower buprenorphine doses (e.g. Simmat-Durand et al 2009, Bartu et al 2012), respectively. In regard to average

daily SROM doses at time of delivery, no data from other treatment centers are available for comparison.

The rates of concomitant consumption of other drugs of abuse during the last trimester of pregnancy, assessed by supervised urine toxicologies (benzodiazepines, cocaine and opioids), breathalyzer test (alcohol) and self-report (nicotine) are in the range of those found in other studies of pregnant women as well; e.g. Bakstad et al (2009) reported lower rates of concomitant benzodiazepine consumption, i.e. 23.0% of methadone maintained patients and 8.3% of buprenorphine maintained patients during the last trimester of pregnancy compared to 41.5% and 17.2% in this sample, respectively. Concurrent opioid consumption in her sample was lower as well (7.7% and 0.0% versus 47.7% and 30.4% in methadone- and buprenorphine-maintained women, respectively, in the present study). Simmat-Durand et al (2009) reported a higher rate of concomitant benzodiazepine use (22%) and a lower rate of cocaine use (5%) in the four weeks prior to delivery in buprenorphine-maintained patients compared to the current study sample in the last trimester (17.2% benzodiazepine use and 13.6% cocaine use in the buprenorphine group). Dryden et al (2009) reported concomitant benzodiazepine use by 60.4% of pregnant methadone-maintained patients, and cocaine, heroin, and cannabis use by 7.1%, 51.1%, and 18.2% of the patients, respectively. These rates are higher than those found in the present study, with the exception of cocaine (20.6%). The difference in outcomes between the present study and the study conducted by Dryden and colleagues (2009) may have been due to the fact that Dryden et al (2009) measured concomitant drug use for a longer period of time (throughout the entire pregnancy) whereas drug use was assessed only during the last trimester in the present analysis.

The methadone and the SROM group showed comparably high rates of concomitant benzodiazepine consumption in the third trimester of pregnancy (41.5% and 40.5%, respectively), whereas the buprenorphine-maintained women had a significantly lower rate (17.2%). Additionally, the SROM and the methadone-medicated groups had more missing urine samples compared to the buprenorphine group – these data could reflect more relapses, suggesting greater addiction severity (and subsequent choice of medication). In general, buprenorphine has been preferentially prescribed to more stable patients, and methadone or SROM to more severely addicted persons who are less likely to respond well to buprenorphine and thus, more likely discontinue treatment (Welle-Strand et al 2013, Jones et al 2010, Schindler et al 2002). Other authors, e.g. Bakstad et al (2009) also reported higher rates of concomitant benzodiazepine consumption in methadone- compared to buprenorphine-medicated pregnant women (23.0% versus 8.3%).

Similar results could be shown in regard to concomitant consumption of opioids in the third trimester, which was significantly more frequent in the methadone group, compared to the buprenorphine group (47.7% versus 30.4% of the patients had positive samples). This finding seems as well in line with that of Bakstad et al (2009) whose methadone-maintained pregnant patients also showed a higher rate of concomitant opiate consumption (7.7%) compared to buprenorphine-maintained pregnant women (0.0%), although her rates were considerably lower than in the present study. However, the result is not consistent with those reported by Jones et al (2005) and Winklbaur et al (2009), who found no differences between the two medication groups regarding concomitant opioid consumption rates.

Fischer et al (2006) reported an even higher rate of opioid positive urine samples in a buprenorphine-medicated group (35.3%) compared to a methadone-treated group (4.4%) in a small pilot study (N=14 study completers, whereof 6 were maintained on methadone and 8 on buprenorphine).

Our findings on inter-medication group QoL comparisons are not directly comparable to those reported by other studies because no other study comparing pre- and postpartum overall QoL in opioid-dependent women is available in the current literature. However, previous studies comparing opioid-dependent patients in maintenance therapy found inconsistent results. Giacomuzzi et al (2001, 2006) stated that opioid-dependent patients receiving SROM had lower QoL compared to buprenorphine- or methadone-maintained patients, whereas in another study (2003) they did not find significant differences between methadone- and buprenorphine-medicated opiate-dependent patients; Winklbaaur et al (2008) also found no significant differences between patients maintained on SROM and patients maintained on methadone. Our results suggest that there is no medication-related difference in QoL, but that QoL improves significantly soon after giving birth to a child. Thus, it is possible that for the patient's satisfaction the opioid maintenance medication is not crucial. De Maeyer et al (2011) who investigated QoL in 159 male and female opiate-dependent individuals in a methadone program in Belgium, found that the patient's QoL was mainly determined by their psychological well-being and a number of psycho-social variables, rather than physiological or drug-related variables.

Generally, the patients in this study reported a (very) good quality of life, with the majority of scores being around 5 or higher (maximum score per item = 7), indicating satisfaction within the domain. The self-reported QoL found in our sample seems to be quite high as it corresponds to the highest QoL profile that De Maeyer et al (2013) reported in their study on (non-pregnant) opiate-dependent individuals, using the same assessment instrument. The highest satisfaction scores in our study (at both time points) were those referring to the relationship with children, followed by (intimate) relationship satisfaction. The only areas of life with lower satisfaction scores were finances and the prospect of staying in the same living/housing situation with scores indicating poor to fair satisfaction only. These poor satisfaction scores could reflect the frequently rather low socio-economic status of this patient group, especially when considering that the housing situation is linked to the financial situation of an individual. At this point, we would like to mention that all women received (according to the laws in Austria) at least social assistance in form of a minimum income and maternity/child-care allowance, respectively; this minimum income would not allow them to maintain a high standard of living, but cover their basic everyday costs.

Quality of life significantly improved between prepartum and postpartum assessment in most of the measured domains by an average of 0.5 points in our study; satisfaction with leisure activities, personal safety, relationship with partner, the way of getting along with others, and the frequency of physician appointments did not change significantly between the two time points. These findings are comparable to those of Fischer et al (2000) who investigated postpartum quality of life with the same instrument in a sample of 43 opioid-dependent patients; she also found the lowest satisfaction scores in the finances domain and the highest scores regarding satisfaction with relationships with children and with partners.

Best et al (2013), who analyzed QoL in 10,470 drug users in England, found that individuals engaging in “meaningful activities” that generate opportunities for developing personal “recovery capital” factors such as self-esteem and self-efficacy or providing opportunities to extend social networks, showed significantly higher QoL than patients without meaningful activities. Giving birth to a child and thus motherhood and associated activities, could of course be considered “meaningful activities.” Moreover, it is well known that the present affective state of an individual highly influences self-assessments of satisfaction (Schwarz et al 1983). Hence, it is very likely that the happiness of having a baby distorted our results in a positive direction. However, the treatment approach we were applying also could have contributed in a positive way to the patients’ satisfaction. Slade et al (2004), who investigated QoL in mentally ill patients in Italy, found a robust (inverse) relationship between the number of unmet needs and QoL. Considering this argument, we could infer that a multi-disciplinary approach that tailors interventions to our patients’ needs was quite effective. This would be in line with findings from other studies on substance-dependent pregnant women; continuous care for the women seems to be beneficial. Daley et al (2005) investigated quality of life in 439 pregnant substance dependent women in the United States, who underwent different treatment modalities (inpatient/outpatient/detoxification) and found significant improvements in QoL after 6 months of treatment, with higher improvements in patients with outpatient or inpatient treatment compared to detoxification. Passey et al (2007) investigated QoL in 63 substance-dependent women (whereof 27 were in methadone maintenance treatment) living in rural areas of Australia, receiving treatment by a case management approach, and showed that psychological quality of life improved significantly after 6 months of treatment. Given these findings and our results, it could be inferred that women’s quality of life improves within a case management treatment approach, particularly after giving birth to a child.

Although our study yielded a great deal of interesting information, we would like to stress that there are major limitations that should be considered when interpreting the findings and drawing conclusions from the results of our study. In general, the ability to compare our results with other studies using different experimental designs is limited, since randomized allocation to a medication group yields different results and cannot take into account the patient’s clinical condition and personal preferences. Another potential problem with the current study is that time effects due to the long period of time evaluated cannot be ruled out, in addition to other characteristics inherent to the analysis, e.g. inclusion of self-reported data (e.g. nicotine consumption), and a lot of missing data.

However, we believe that our study provides valuable insight into treatment aspects for this patient group that has various needs that should be addressed in order to improve treatment outcome. For example, our analysis shows for the first time results from a larger group of patients maintained on SROM throughout pregnancy, which seemed to be safe and effective as well. At least in regard to QoL where no significant medication inter-group differences could be found, SROM does not seem to be inferior. Of course more (controlled) studies would be needed to draw clear conclusions on SROM administration during pregnancy. Moreover, our observed patients reported improved quality of life post-partum, which suggests the application of a multi-disciplinary treatment approach was beneficial throughout pregnancy, independently of the opioid medication prescribed. Finally, we hope

that our findings inspire future research, particularly in regard to aspects that have not yet received adequate attention in the scientific community, such as the overall QoL of the mothers throughout pregnancy and after delivery. Specifically, it would be interesting to study maternal overall QoL at a later point and to examine whether the positive impact of giving birth changes over time, as well as possible associations with child-care matters.

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References

- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5. APA; Washington, DC: 2013.
- American Psychiatric Association. Diagnostic and statistical manual of mental health disorders. 4. American Psychiatric Association; Washington, DC: 1994.
- Armstrong D, Caldwell D. Origins of the concept of quality of life in health care: A rhetorical solution to a political problem. *Social Theory & Health*. 2004; 2:361–371.
- Bakstad B, Sarfi M, Welle-Strand GK, Ravndal E. Opioid maintenance treatment during pregnancy: occurrence and severity of neonatal abstinence syndrome. A national prospective study. *Eur Addict Res*. 2009; 15(3):128–34. [PubMed: 19332991]
- Bartu AE, Ilett KF, Hackett LP, Doherty DA, Hamilton D. Buprenorphine exposure in infants of opioid-dependent mothers at birth. *Aust N Z J Obstet Gynaecol*. 2012; 52(4):342–7. [PubMed: 22428721]
- Best D, Savic M, Beckwith M, Honor S, Karpusheff J, Lubman DI. The role of abstinence and activity in the quality of life of drug users engaged in treatment. *J Subst Abuse Treat*. 2013; 45(3):273–9. [PubMed: 23706622]
- Daley M, Shepard DS, Bury-Maynard D. Changes in quality of life for pregnant women in substance user treatment: developing a quality of life index for the addictions. *Subst Use Misuse*. 2005; 40(3): 375–94. [PubMed: 15776984]
- De Maeyer J, Vanderplasschen W, Lammertyn J, van Nieuwenhuizen C, Sabbe B, Broekaert E. Current quality of life and its determinants among opiate-dependent individuals five years after starting methadone treatment. *Qual Life Res*. 2011; 20(1):139–50. [PubMed: 20740316]
- De Maeyer J, van Nieuwenhuizen C, Bongers IL, Broekaert E, Vanderplasschen W. Profiles of quality of life in opiate-dependent individuals after starting methadone treatment: A latent class analysis. *Int J Drug Policy*. 2013; 24(4):342–50. [PubMed: 23127664]
- Dryden C, Young D, Hepburn M, Mactier H. Maternal methadone use in pregnancy: factors associated with the development of neonatal abstinence syndrome and implications for healthcare resources. *BJOG*. 2009; 116(5):665–71. [PubMed: 19220239]

- Fischer G, Eder H, Peternell A, Windhaber J. Lebensqualitaet gravider substanzabhaengiger Frauen unter oraler Erhaltungstherapie mit synthetischen Opioiden. *Nervenheilkunde*. 2000; 19:205–11. (German).
- Fischer G, Ortner R, Rohrmeister K, Jagsch R, Baewert A, Langer M, Aschauer H. Methadone versus buprenorphine in pregnant addicts: a double-blind, double-dummy comparison study. *Addiction*. 2006; 101(2):275–81. [PubMed: 16445556]
- Giacomuzzi S, Kemmler G, Ertl M, Riemer Y. Opioid addicts at admission vs. slow-release oral morphine, methadone, and sublingual buprenorphine maintenance treatment participants. *Subst Use Misuse*. 2006; 41(2):223–44. [PubMed: 16393744]
- Giacomuzzi SM, Riemer Y, Ertl M, Kemmler G, Richter R, Rössler H, Hinterhuber H. Substitutionsbehandlung und Lebensqualität: Methadon vs. retardiertes Morphinsulfat – eine Vergleichsstudie. *Suchtmed*. 2001; 3(1):89–95.
- Giacomuzzi SM, Riemer Y, Ertl M, Kemmler G, Rössler H, Hinterhuber H, Kurz M. Buprenorphine versus methadone maintenance treatment in an ambulant setting: a health-related quality of life assessment. *Addiction*. 2003; 98(5):693–702. [PubMed: 12751987]
- Jones HE. Treating opioid use disorders during pregnancy: historical, current, and future directions. *Subst Abus*. 2013; 34(2):89–91. [PubMed: 23577898]
- Jones HE, Johnson RE, Jasinski DR, O'Grady KE, Chisholm CA, Choo RE, Crocetti M, Dudas R, Harrow C, Huestis MA, Jansson LM, Lantz M, Lester BM, Milio L. Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on the neonatal abstinence syndrome. *Drug Alcohol Depend*. 2005; 79(1):1–10. [PubMed: 15943939]
- Jones HE, Kaltenbach K, Heil SH, Stine SM, Coyle MG, Arria AM, O'Grady KE, Selby P, Martin PR, Fischer G. Neonatal abstinence syndrome after methadone or buprenorphine exposure. *N Engl J Med*. 2010; 363(24):2320–31. [PubMed: 21142534]
- Kashiwagi M, Arlettaz R, Lauper U, Zimmermann R, Hebisch G. Methadone maintenance program in a Swiss perinatal center: (I): Management and outcome of 89 pregnancies. *Acta Obstet Gynecol Scand*. 2005; 84(2):140–4. [PubMed: 15683373]
- Katschnig H. Quality of life in mental disorders: challenges for research and clinical practice. *World Psychiatry*. 2006; 5(3):139–145. [PubMed: 17139340]
- Laudet AB. The Case for Considering Quality of Life in Addiction Research and Clinical Practice. *Addict Sci Clin Pract*. 2011; 6(1):44–55. [PubMed: 22003421]
- Mayet S, Groshkova T, Morgan L, MacCormack T, Strang J. Drugs and pregnancy--outcomes of women engaged with a specialist perinatal outreach addictions service. *Drug Alcohol Rev*. 2008; 27(5):497–503. [PubMed: 18696296]
- McCarthy JJ, Leamon MH, Parr MS, Anania B. High-dose methadone maintenance in pregnancy: maternal and neonatal outcomes. *Am J Obstet Gynecol*. 2005; 193(3 Pt 1):606–10. [PubMed: 16150249]
- McLellan AT, Luborsky L, O'Brien CP, Woody GE. An improved diagnostic instrument for substance abuse patients: The Addiction Severity Index. *Journal of Nervous & Mental Diseases*. 1980; 168:26–33.
- Oliver JPI. /1992) The social care directive: Development of a quality of life profile for use in community services for the mentally ill. *Soc Work Soc Sci Rev*. 1991; 3:5–45.
- Osborn DA, Jeffery HE, Cole MJ. Opiate treatment for opiate withdrawal in newborn infants. *Cochrane Database Syst Rev*. 2010; 6(10):CD002059. [PubMed: 20927730]
- Passey M, Sheldrake M, Leitch K, Gilmore V. Impact of case management on rural women's quality of life and substance use. *Rural Remote Health*. 2007; 7(3):710. [PubMed: 17683243]
- Priebe S, Gruyters T, Heinze M, Hoffmann C, Jaekel A. Subjective evaluation criteria in psychiatric care – assessment methods for research and general practice. *Psychiatr Prax*. 1995; 22(4):140–44. (German). [PubMed: 7675903]
- Schindler, S.; Ortner, R.; Fischer, G. Medizinische Grundlagen zur Therapie der Opiatabhängigkeit. In: Fischer, G., editor. *Therapie mit Opioiden*. Wien: Facultas Universitätsverlag; 2002. p. 31-77. German
- Schwarz N, Clore GL. Mood, misattribution, and judgments of well-being: informative and directive functions of affective states. *J Person Soc Psychol*. 1983; 45:513–23.

- Seligman NS, Salva N, Hayes EJ, Dysart KC, Pequignot EC, Baxter JK. Predicting length of treatment for neonatal abstinence syndrome in methadone-exposed neonates. *Am J Obstet Gynecol*. 2008; 199(4):396.e1–7. [PubMed: 18928986]
- Seligman NS, Almario CV, Hayes EJ, Dysart KC, Berghella V, Baxter JK. Relationship between maternal methadone dose at delivery and neonatal abstinence syndrome. *J Pediatr*. 2010; 157(3): 428–33. 433.e1. [PubMed: 20472252]
- Shainker SA, Saia K, Lee-Parritz A. Opioid addiction in pregnancy. *Obstet Gynecol Surv*. 2012; 67(12):817–25. [PubMed: 23233054]
- Slade M, Leese M, Ruggeri M, Kuipers E, Tansella M, Thornicroft G. Does meeting needs improve quality of life? *Psychother Psychosom*. 2004; 73(3):183–9. [PubMed: 15031591]
- Simmat-Durand L, Lejeune C, Gourarier L. Groupe d' Etudes Grossesse et Addictions (GEGA) . Pregnancy under high-dose buprenorphine. *Eur J Obstet Gynecol Reprod Biol*. 2009; 142(2):119–23. [PubMed: 19058904]
- Statistik Austria. Durchschnittliches Gebaer- bzw. Fertilitaetsalter der Mutter nach Lebendgeburtenfolge seit 1991. 2011a; 2011a updated 2011 May 19. Available from: www.statistik.at/web_de/statistiken/bevoelkerung/geburten/index.html. German.
- Statistik Austria. [accessed 2011, June 3] Geborene seit 2000 nach ausgewaehlten demografischen und medizinischen Merkmalen. 2011b. updated 2011 May 19 Available from: www.statistik.at/web_de/statistiken/bevoelkerung/geburten/index.html. German
- Unger A, Metz V, Fischer G. Opioid dependent and pregnant: what are the best options for mothers and neonates? *Obstet Gynecol Int*. 2012; 2012:195954. [PubMed: 22496696]
- Vucinovic M, Roje D, Vucinovic Z, Capkun V, Bucat M, Banovic I. Maternal and neonatal effects of substance abuse during pregnancy: our ten-year experience. *Yonsei Med J*. 2008; 49(5):705–13. [PubMed: 18972589]
- Welle-Strand GK, Skurtveit S, Jones HE, Waal H, Bakstad B, Bjarkø L, Ravndal E. Neonatal outcomes following in utero exposure to methadone or buprenorphine: a National Cohort Study of opioid-agonist treatment of Pregnant Women in Norway from 1996 to 2009. *Drug Alcohol Depend*. 2013; 127(1–3):200–6. [PubMed: 22841456]
- Westin AA, Huestis MA, Aarstad K, Spigset O. Short communication: Urinary excretion of 11-nor-9-carboxy-Delta(9)-tetrahydrocannabinol in a pregnant woman following heavy, chronic cannabis use. *J Anal Toxicol*. 2009; 33(9):610–4. [PubMed: 20040136]
- WHO Division of Mental Health and Prevention of Substance Abuse. WHOQOL User Manual. WHO; Geneva, Switzerland: 1998.
- Winklbaur B, Baewert A, Jagsch R, Rohrmeister K, Metz V, Aeschbach Jachmann C, Thau K, Fischer G. Association between prenatal tobacco exposure and outcome of neonates born to opioid-maintained mothers. Implications for treatment. *Eur Addict Res*. 2009; 15(3):150–6. [PubMed: 19420947]
- Winklbaur B, Jagsch R, Ebner N, Thau K, Fischer G. Quality of life in patients receiving opioid maintenance therapy. A comparative study of slow-release morphine versus methadone treatment. *Eur Addict Res*. 2008; 14(2):99–105. [PubMed: 18334820]
- WMA. [Accessed 30 July 2013] The Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. 1964–2008. <http://www.wma.net/en/30publications/10policies/b3/17c.pdf>

Figure 1.

Opioid medication administration at treatment entry and during last trimester of pregnancy, including delivery

Numbers next to dashed arrows indicate the number of patients who remained on the opioid medication they were taking at treatment entry at the Addiction Clinic.

Numbers next to solid arrows indicate the number of patients who were switched to another medication at the Addiction Clinic.

Figure 2.
QoL profiles prepartum according to opioid medication group

Figure 3.
Postpartum QoL profiles according to opioid medication group

Table 1

Maternal characteristics in each patient group

Characteristic	Methadone group (n=184) Mean (SD)	Bupren. group (n=77) Mean (SD)	SROM group (n=129) Mean (SD)	F	df 1/df 2	P
Age at delivery (years)	25.63 (5.21)	25.14 (5.58)	25.61 (5.47)	0.248	2/387	0.781
Gravidity	2.32 (1.53)	2.07 (1.33)	2.31 (1.71)	1.402	2/384	0.247
Parity	1.67 (1.04)	1.47 (0.85)	1.50 (0.81)	1.802	2/387	0.166
Miscarriages	0.26 (0.66)	0.28 (0.56)	0.40 (0.83)	1.604	2/380	0.202
Abortions	0.39 (0.73)	0.30 (0.57)	0.54 (0.94)	2.498*	2/208	0.085
Cigarettes/day prepartum	14.68 (9.61)	12.65 (6.81)	15.72 (9.37)	2.636	2/354	0.073

Characteristic	Methadone group n (%)	Bupren. group n (%)	SROM group n (%)	χ^2	df	P
<i>Nationality (n=378)</i>						
- Austrian	162 (88.0%)	62 (80.5%)	113 (87.6%)	2.848	2	0.241
- other	22 (12.0%)	15 (19.5%)	16 (12.4%)			
<i>Education (n=371)</i>						
- <9 years	73 (42.0%)	24 (32.0%)	51 (41.8%)	3.686 ♣	-	0.450
- compulsory education	90 (51.7%)	48 (64.0%)	66 (54.1%)			
- higher education	11 (6.3%)	3 (4.0%)	5 (4.1%)			
<i>Relationship status (n=379)</i>						
- living alone	76 (42.9%)	30 (39.5%)	55 (43.7%)	0.367	2	0.832
- partner	101 (57.1%)	46 (60.5%)	71 (56.3%)			
<i>Current child's father's health (n=390)</i>						
- current/former addiction	80 (43.5%)	34 (44.2%)	66 (51.2%)	1.956	2	0.376
- no addiction known	104 (56.5%)	43 (55.8%)	63 (48.8%)			
<i>Maternal smoking status (n=357)</i>						
- smoker	160 (96.4%)	69 (93.2%)	110 (94.0%)	1.591 ♣	-	0.439
- non-smoker	6 (3.6%)	5 (6.8%)	7 (6.0%)			
<i>Analgesia during delivery (n=370)</i>						
- analgesia	121 (69.1%)	58 (79.5%)	90 (73.8%)	2.863	2	0.239

Characteristic	Methadone group n (%)	Bupren. group n (%)	SROM group n (%)	χ^2	df	P
- no analgesia	54 (30.9%)	15 (20.9%)	32 (26.2%)	3.772	2	0.152
Cesarean section (n=386)						
- C-section	75 (41.0%)	28 (36.4%)	38 (30.2%)			
- no C-section	108 (59.0%)	49 (63.6%)	88 (69.8%)			

* Welch-corrected,

♣ Fisher's Exact test was applied

Since complete data could not be obtained for the whole sample for each category, sub-sample sizes are indicated in brackets.

Table 2
Concomitant consumption of opioids, benzodiazepines and cocaine in the last trimester of pregnancy

Concomitant consumption of	Methadone group n (%)	Bupren. group n (%)	SROM group n (%)	χ^2	df	P
<i>Benzodiazepines (n=206)</i>						
- yes	44 (41.5%)	10 (17.2%)	17 (40.5%)	10.618	2	0.005
- no	62 (58.5%)	48 (82.8%)	25 (59.5%)			
<i>Cocaine (n=211)</i>						
- yes	22 (20.6%)	8 (13.6%)	13 (28.9%)	3.702	2	0.157
- no	85 (79.4%)	51 (86.4%)	32 (71.1%)			
<i>Opioids (n=163)</i>						
- yes	51 (47.7%)	17 (30.4%)	-	4.528	1	0.033
- no	56 (52.3%)	39 (69.6%)	-			

Since complete data could not be obtained for the whole sample for each category (at least 1 urine sample per week during the last trimester was required for inclusion in this analysis), sub-sample sizes are indicated in parentheses.

Table 3

QoL scores pre- and postpartum

<i>Satisfaction with *</i>	Prepartum score Mean (SD)	Postpartum score Mean (SD)	Correlation	p	t	df	p
1 Life in general (n=212)	4.96 (1.41)	5.75 (1.24)	0.308	<0.001	-7.324	211	<0.001
2 Leisure activities at home (n=196)	4.99 (1.64)	5.23 (1.46)	0.364	<0.001	-1.911	195	0.057
3 Leisure activities outside (n=187)	5.03 (1.64)	5.22 (1.55)	0.401	<0.001	-1.552	186	0.122
4 Finances (n=186)	2.90 (1.86)	3.69 (1.80)	0.352	<0.001	-5.143	185	<0.001
5 Living situation (n=212)	4.73 (2.08)	5.29 (1.80)	0.294	<0.001	-3.528	211	0.001
6 Cohabitation with housemates (n=183)	5.78 (1.74)	6.17 (1.30)	0.346	<0.001	-3.004	182	0.003
7 Privacy at home (n=209)	5.40 (2.03)	5.86 (1.59)	0.349	<0.001	-3.164	208	0.002
8 Prospect of staying in living situation (n=203)	3.90 (2.41)	4.48 (2.22)	0.402	<0.001	-3.291	202	0.001
9 Safety in hometown (n=211)	5.18 (1.59)	5.01 (1.63)	0.563	<0.001	1.650	210	0.100
10 Safety at domicile (n=209)	5.75 (1.49)	5.67 (1.48)	0.311	<0.001	0.675	208	0.501
11 Relationship with partner (n=185)	5.94 (1.60)	5.99 (1.66)	0.629	<0.001	-0.523	184	0.602
12 Relationship with children (n=84)	5.81 (2.15)	6.30 (1.58)	0.555	<0.001	-2.440	83	0.017
13 Relationship with other family members (n=206)	5.39 (1.69)	5.75 (1.50)	0.572	<0.001	-3.520	205	0.001
14 Frequency of contacts with family (n=206)	5.20 (1.85)	5.62 (1.60)	0.460	<0.001	-3.352	205	0.001
15 Way of getting along with others (n=214)	5.84 (1.13)	6.00 (1.23)	0.391	<0.001	-1.889	213	0.060
16 Number of friends (n=210)	5.40 (1.66)	5.80 (1.39)	0.348	<0.001	-3.311	209	0.001
17 Health in general (n=214)	5.07 (1.51)	5.59 (1.31)	0.412	<0.001	-2.005	213	0.046
18 Mental health (n=213)	5.15 (1.51)	5.59 (1.17)	0.455	<0.001	-4.509	212	<0.001
19 Frequency of physician appointments (n=207)	5.01 (1.72)	4.92 (1.56)	0.385	<0.001	0.687	206	0.493

* since individual items were more or less applicable to individual patients, there is a high variability in the number of responses (as indicated in brackets for each item)

Table 4

Prepartum and postpartum QoL in the three medication groups

<i>Tested BeLP QoL parameters</i>	Type III Sum of Squares (Greenhouse Geisser)	F	df 1	df 2	p
<i>Inter-item differences</i>	1338.077	27.380	8.755	910.556	<0.001
<i>Inter-medication group differences</i>	66.420	1.763	2.000	104.000	0.177
<i>Item-medication group interaction</i>	58.394	0.597	17.511	910.556	0.900
<i>Prepartum-postpartum (time point) differences</i>	98.978	19.832	1.000	104.000	<0.001
<i>Time point-medication group interaction</i>	9.315	0.933	2.000	104.000	0.397
<i>Time point-item interaction</i>	58.569	2.812	10.377	1079.202	0.002
<i>Time point-item-medication group interaction</i>	41.569	0.998	20.754	1079.202	0.463