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The Effects of Opioid-Agonist Treatments on HIV Risk and Social Stability: A Mixed Methods Study of Women with Opioid Use Disorder in Ukraine

Emily Hoff, B.A.[1], **Ruthanne Marcus, Ph.D., MPH**[2], **Martha J. Bojko, Ph.D.**, **Iuliia Makarenko, MS, MPH**[2,3], **Alyona Mazhnaya, M.S., MPH**[3], **Frederick L. Altice, M.D., M.A.**[2,4,5], and **Jaimie P. Meyer, M.D., M.S.**[2]

[1]Yale School of Medicine, New Haven, Connecticut

[2]Yale School of Medicine, Section of Infectious Diseases, AIDS Program, New Haven, Connecticut

[3]ICP Alliance for Public Health, Kyiv, Ukraine

[4]Yale School of Public Health, Epidemiology of Microbial Diseases, New Haven, Connecticut

[5]University of Malaya, Kuala Lumpur, Malaysia

1.1 Introduction

Eastern Europe and Central Asia is the only global region where HIV incidence and mortality are increasing in the absence of adequately scaled HIV prevention (Joint United Nations Programme on HIV/AIDS (UNAIDS), 2016a, 2016b). HIV prevalence in Ukraine is among the highest in Europe, now 0.9–1.0% among adults (Joint United Nations Programme on HIV/AIDS (UNAIDS), 2016b). The HIV epidemic in Ukraine is concentrated in people who inject drugs (PWID), with HIV prevalence among them ranging from 21 to 50% (UNAIDS, 2015). Up to 86% of incident HIV in Ukraine is attributable to sexual risk and 24% to injection drug use (IDU), though one-third of HIV cases could be misclassified as sexually acquired because IDU is highly stigmatized and underreported (Cakalo et al., 2015; UNAIDS, 2015). Of an estimated 340,000 PWID in Ukraine, approximately 26% are women, who primarily inject a homemade liquid opioid (“shirka”) that is prepared in a shared container (Balakireva, 2014; “Results of Sociological Research: Estimation of the size of high risk groups for HIV transmission in Ukraine in 2016,” 2017; “Rhetoric and Risk: Human Rights Abuses Impeding Ukraine’s Fight Against HIV/AIDS,” 2006). Though essentially all opioids are injected, primarily because they are available as a liquid, they may also be combined with amphetamines, especially in Southern Ukraine (Booth, Kwiatkowski, Brewster, Sinitsyna, & Dvoryak, 2006; Chintalova-Dallas, Case, Kitsenko, & Lazzarini,

Corresponding Author: Jaimie P. Meyer, Yale AIDS Program, 135 College Street, Suite 323, New Haven, CT 06510, Jaimie.meyer@yale.edu, O: 203-737-6233, Fax: 203-737-4051.

2009). Women who inject drugs (WWID) are disproportionately infected with HIV: while women account for 27% of all PWID, they represent 45% of PWID who have HIV in Ukraine (Springer et al., 2015; Ukraine, 2014). In an analysis of PWID at three sites in Ukraine, being female was an independent predictor of HIV status (Booth et al., 2006) and in a study of 16 Ukrainian cities, women were more likely than men to have HIV (Taran, Johnston, Pohorila, & Saliuk, 2011). Women in Ukraine also report more sex- and injection-related risk behaviors than men despite having higher levels of HIV knowledge (Corsi et al., 2014).

In general and in Ukraine specifically, WWID experience increased HIV risk due to converging biological, social, cultural and economic factors (Des Jarlais, Feelemyer, Modi, Arasteh, & Hagan, 2012; Larney, Mathers, Poteat, Kamarulzaman, & Degenhardt, 2015). Women, particularly those who are dependent on partners for basic subsistence needs, may lack autonomy to effectively negotiate condoms, thereby increasing sexual risk (Jolley et al., 2012; Lambdin et al., 2013; Larney et al., 2015). Compared to their male counterparts, WWID inject more frequently, have overlapping sex and drug partners (Corsi et al., 2014), are more likely to be injected by someone else (often a partner) and to be “second on the needle,” increasing vulnerability to HIV (Springer et al., 2015). Increased stigma, discrimination and greater personal demands to care for others impede access to treatment programs (Des Jarlais et al., 2012; Lambdin et al., 2013; Simmonds & Coomber, 2009). Power imbalances predispose women to partner violence exposure, an independent risk factor for HIV infection (Campbell et al., 2008; Meyer, Springer, & Altice, 2011; Stockman, Lucea, & Campbell, 2013). For WWID, socioeconomic disadvantage may lead women to engage in transactional “survival” sex for drugs, money, or other goods, further increasing HIV risk (El-Bassel, Wechsberg, & Shaw, 2012; Iversen, Page, Madden, & Maher, 2015).

Following the dissolution of the Soviet Union, political upheaval in Ukraine resulted in poor socioeconomic conditions that exacerbated health disparities; thereby, fueling an explosive HIV epidemic especially among WWID. Political unrest is ongoing in Crimea and Donabas regions where opioid agonist therapies are now absent or extremely limited aggravating preexisting gender inequalities (Filippovych, 2015). Women’s lack of autonomy to negotiate condoms is particularly salient in Ukraine, where women often experience a lack of agency and power secondary to cultural norms (Burruano, 2009). WWID in Ukraine may also lack access to health services and resources to mitigate HIV risk (Balakireva, 2014; Busza et al., 2011; Malyuta, Newell, Ostergren, Thorne, & Zhilka, 2006). In general, however, there are limited epidemiologic data on HIV risk among WWID in Ukraine to inform policy or gender-sensitive interventions.

Effective treatment for substance use disorders is also effective HIV prevention. Opioid agonist treatments (OAT) with buprenorphine or methadone is a mainstay of treatment for opioid use disorders, and secondarily prevents HIV. OAT decreases incident HIV by nearly 60%, increases adherence to antiretroviral therapy (ART), decreases opioid use, injection frequency and unsafe injection, reduces criminal activity, improves physical and mental health and reduces all-cause mortality among PWID by more than 50% (Degenhardt et al., 2014; El-Bassel et al., 2012; Lawrinson et al., 2008; MacArthur et al., 2012; Malta, Magnanini, Strathdee, & Bastos, 2010; Zaller et al., 2015). OAT scale-up is the most cost-

effective strategy to curb the HIV epidemic in Ukraine (Alistar, Owens, & Brandeau, 2011). In spite of the well documented benefits of OAT along the HIV care continuum (Low et al., 2016) and the potential to reduce HIV risk among WWID, few OAT programs focus specifically on women's needs, resulting in limited access to potentially life-changing treatment programs.

To evaluate differences in health and risk behaviors between Ukrainian WWID on or not on OAT, we conducted a mixed methods analysis. We hypothesized that OAT would provide a stabilizing force that decreases sexual risk, violence exposure, depressive symptoms and frequency of injection among women currently on OAT. The overarching objective was to inform the development of women-specific OAT and other HIV prevention interventions for WWID in Ukraine.

2.1 Methods

2.2 Structured Survey Sample

As a formative part of a study integrating OAT and HIV care for PWID in Ukraine, described elsewhere, structured surveys were administered to 1,613 PWID in five Ukrainian cities (Kyiv, Odesa, Mykolaiv, Lviv, Dnipro) between January 2014 and March 2015 (M.J. Bojko et al., 2015; Kutsa et al., 2016). OAT personnel contacted randomly selected participants with current or prior OAT experience and referred them for study participation; 99% of selected participants agreed to the study. PWID never on OAT were recruited using respondent driven sampling (RDS), where initial participant "seeds" were recruited by research assistants and from community outreach sites that engage with and/or provide services to PWID. Seeds referred their peers through RDS, thus recruiting participants with no lifetime exposure to OAT. Participants were included in the study if they were ≥18 years old, lived or worked in the study city, met ICD-10 criteria for opioid use disorder, were able to give informed consent, agreed to undergo HIV and HCV rapid testing and were willing to complete a structured survey (Makarenko et al., 2016). IDU in the past 30 days was an inclusion criteria for participants recruited through RDS and all study participants had a lifetime history of opioid injection. To evaluate women's specific needs and risks, only female participants (N=380) were included in the present analysis, though this is a secondary analysis of data from a study whose quantitative measures were not designed to be women- specific. During informed consent process, informational sheets were distributed to all participants. Institutional review boards at Yale University, the Ukrainian Institute on Public Health Policy and the Gromashevskiy Institute at the National Academy of Medical Sciences approved the study.

2.3 Study Survey

After meeting with research assistants for study enrollment, all eligible participants provided informed consent and completed a single structured survey; no eligible participants declined study enrollment. The survey was a computer assisted, self-administered survey (CASI), written in Ukrainian or Russian, and delivered via a Qualtrics web-based platform. The survey included measures of basic demographics, self-reported HIV status, HIV testing and treatment experience, drug use severity, psychiatric and other medical comorbidities, OAT

exposure and experience, sexual health, violence exposure and criminal justice system involvement. Participants were compensated 100UAH (~$4) for survey completion.

2.4 Survey Measures

The survey was first constructed in English and translated and back-translated to ensure understanding (Brislin, 1970).

Demographic and social characteristics included self-reported age, ethnicity, education, housing status, employment status, and sources of income (including social payment, transactional sex, and selling drugs.)

Social factors were assessed in terms of marital status, housing stability, and perceived role of religion in one's life.

Substance use severity was measured using the 10-item Drug Abuse Screening Test-10 (Gavin, Ross, & Skinner, 1989) and current opioid craving scale, a modification of the cocaine craving scale (Weiss et al., 2003). The survey also inquired about frequency of opioid overdoses in the prior 6 months, injection drug use in the past month, alcohol use in the past month, and other drug use in the past year. For the purposes of analysis, we defined severe drug use as the highest tercile of injection days (≥28 injection days in the past month). Women who fell between terciles were placed in the higher grouping resulting in slightly uneven sample distribution among categories.

Sex-related risk was assessed in terms of lifetime (transactional sex, sexual violence exposure) and past-90 day (number of regular and casual sex partners, transactional/exchange sex, and condomless sex) behaviors.

HIV and HCV were measured in terms of self-reported testing, diagnosis, and treatment outcomes of HIV, chronic Hepatitis B, and chronic Hepatitis C infection. Although the parent study tested for HIV and HCV, we included here only the self-reported measures because we were interested in self-perception of status that might drive health behaviors. We defined "currently taking ART" as those offered ART by their health care providers and taking it (as opposed to those not offered ART or those offered, but not taking ART). Mean last CD4 count was available only for those HIV+ participants who recalled and reported it; medical records were not available for verification.

Criminal justice involvement was evaluated in terms of lifetime incarcerations and past 6-month exposure to physical or sexual violence by police.

Depression was measured in terms of current depressive symptoms by the 10-item Center for Epidemiological Studies Depression Scale (Eaton, Smith, Ybarra, Muntaner, & Tien, 2004). Subjects were considered depressed if they scored >10 on the CES-D (Eaton et al., 2004).

2.5 Qualitative Data

Focus groups (FGs) were conducted with 199 PWID during February–April 2013 in the same Ukrainian cities as the survey with one exception: FGs were initially held in Donetsk

in eastern Ukraine. In 2014, Dnipro replaced Donetsk as the study city for survey implementation due to the unstable political situation in Donetsk. Local research assistants familiar with each site selected a convenience sample of PWID in each city from OAT and community-based outreach sites (e.g., needle/syringe programs, non-governmental organizations). Eligibility criteria for all FG participants included: 1) ≥18 years old; 2) prior or current intravenous drug use of opioids; 3) able to give informed consent; and 4) living, working or studying in one of the 5 study cities. In each city, separate FGs were conducted based on OAT experience (current, previous or never), such that each session was comprised of male and female participants with the same OAT experience. A women-only FG (with mixed OAT experiences) was conducted in each city to explore gender differences related to OAT entry and retention in care. The OAT experience of the women-only participants was included in the transcription of each FG. There were a total of 25 FG sessions: 20 mixed gender sessions with 5–11 participants per session and five women- only FGs with 5–8 participants per group. Every mixed gender session had at least two women. In the present analysis, we used data from female participants in both the mixed gender and women-only FGs (n=67), where gender of the speaker was identified by audiotape, chosen pseudonym, and field notes.

FGs were facilitated by trained qualitative researchers fluent in Ukrainian and Russian. Groups were audio-recorded and lasted between 60 and 90 minutes. The FG guide explored access to OAT and medical and social services for substance abuse treatment, experiences with and attitudes toward OAT, recommendations for improving access to and experiences with OAT, and knowledge and attitudes toward the use of extended release naltrexone (XR-NTX) as an alternative medication assisted treatment. All FGs were conducted in private settings in each city. Participants were paid 80 UAH (~US $10) for their time. The audio-recorded interviews were transcribed and translated into English to ensure content (Brislin, 1970) could be consistently and thoroughly reviewed by all researchers. Files were uploaded into MAXQDA (Version 11; MAXQDA, 1989-53 2013, VERBI Software - Consult - Sozialforschung GmbH, Berlin, Germany) software for qualitative data analysis. More detailed information about the recruitment process, informed consent procedures and focus group implementation have been discussed previously (Bojko et al., 2015; Bojko et al., 2016).

2.6 Analysis

Although there are many valid approaches to a mixed methods analysis, we chose to analyze quantitative and qualitative data separately, evaluating the central hypothesis that OAT is broadly stabilizing. Results were then integrated so that the qualitative results explored possible explanations for the quantitative findings.

2.6.1 Quantitative—The demographic characteristics, risk behaviors and healthcare utilization patterns of current OAT recipients were compared to participants not currently (either never or previously) on OAT. Individuals currently on OAT were defined as those who were actively receiving OAT (with buprenorphine or methadone) for opioid use disorder at the time of the survey. Participants previously on OAT were grouped with participants never on OAT because once participants stop OAT, behaviors may revert to pre-

OAT patterns. Composite variables were created to assess ongoing sexual risk and violence exposure. Women with recent sexual risk-taking behavior were defined as having a casual sex partner, exchanging sex for money, rent, or drugs and/or not using a condom with an HIV+ partner, having a casual partner and/or a partner with whom they also used drugs in the past 90 days. Violence exposure was defined as women who had been beaten, slapped and/or hit before or during sex in the past 90 days, physically assaulted by police in the last 6 months or forced to have sex by police in the past 6 months. We compared current and notcurrent OAT recipients, using Pearson's chi-squared and Fisher's exact test where appropriate for categorical variables and independent sample t-tests for continuous variables, with $p<0.05$ defined as statistically significant. We used bivariate logistic regression to model correlates of currently receiving OAT. We then constructed a multivariate logistic regression model of currently receiving OAT with basic demographics and significant variables with $p<0.05$ on bivariate analysis weighted by location to account for a skewed geographical distribution of PWID in the local population. We additionally developed and tested other multinomial logistical regression models to assess fit with minimal change in model fit by AIC/BIC and Pearson's goodness of fit testing (not shown). All analyses were performed using SPSS (IBM, V24.0.0.0).

2.6.2 Qualitative—Each translated transcript was coded by two qualitative researchers (RM, MJB, AM, IM). Content was examined using a modified grounded theory approach to identify themes (Glaser & Strauss, 1967). While we use the term OAT throughout our analysis as a medically accurate way to define various forms of treatment of opioid use disorder, the FG participants referred to it as opioid substitution therapy (OST) or substitution maintenance therapy (SMT). We focused our analysis on the codes related to women-specific issues and identified by the female FG participants as relevant to women with an emphasis on the factors identified as significant in the quantitative survey data analysis.

3.1 Results

3.1.1 Quantitative survey data

As shown in Table 1, the study sample was comprised of 380 women from five Ukrainian cities who were currently on OAT (n=93) or not currently on OAT (n=287). Of the non-current OAT users, 79 were formerly on OAT and 208 were never on OAT. Women had been on OAT for a mean 3.4 years (SD= 2.36 years) with nearly 75% on methadone and the remaining on buprenorphine. Those currently on OAT were significantly older (37.9 years vs. 35.7 years; $p=0.03$ and more often ranked the role of religion as extremely important compared to those not currently enrolled in OAT. While 4.9% of women not currently on OAT reported selling drugs as a source of income, no woman currently on OAT reported selling drugs ($p=0.03$). There were no differences in ethnicity, education, housing, employment, marital status or housing stability between the two groups.

Table 2 presents drug use severity, sexual risk, STI history, incarceration history and composite variables of women on OAT compared to women not currently on OAT. Subjects in both groups reported relatively equivalent lifelong drug use severity scores, but subjects

currently on OAT reported significantly lower opioid craving scores (3.16 vs. 6.53; $p<0.001$), fewer injection days in the past month (2.89 vs. 18.62; $p<0.001$) and any drug use in the past year (78.5% vs. 92.7%; $p<0.001$). Fewer women on OAT had ever exchanged sex for money, rent or drugs (11.8% vs. 20.9%; $p=0.05$), while women currently and not currently on OAT experienced equivalent rates of lifetime violence exposure (15.1% vs. 16.0%; $p=0.82$) and forced sex (26.9% vs. 25.4%; $p=0.78$). In the previous three months, 44.1% of women currently on OAT had sex compared to 54.4% of women not on OAT ($p=0.08$). In the prior 90 days, women on OAT reported significantly fewer casual partners (0.01 vs. 0.09; $p<0.001$), less transactional sex (2.4% vs. 15.4%; $p=0.01$) and less frequent drug use with condomless sex (36.7% vs. 72.1%; $p=0.004$). There was no significant difference in mean number of sex partners or condom use between the two groups in the past 3 months.

Women on current OAT were more likely to have been tested (93.5% vs. 81.9%; $p<0.001$), but not diagnosed (59.5% vs. 54.2%; $p=0.60$), with HIV. There was no difference in ART use (96.7% vs 88.1%; $p=0.172$) and past CD4 count (mean 453 cells/pL (SD=210) vs 454 cells/pL (SD=269); $p=0.970$) between WWID on OAT and those not engaged in OAT. Rates of HCV testing (87.1% vs. 65.2%; $p<0.001$) and diagnosis (69.9% vs. 50.7%; $p=0.004$) were higher in those on current OAT. The groups experienced similar rates of incarceration, forced sex by police and lifetime threats of physical violence by police, but those currently on OAT were less likely have experienced physical assault by the police in the last six months (0.0% vs. 7.3%; $p=0.007$).

Composite variables for depression, risky sexual behavior and violence exposure are depicted in Table 2. Depression was less prevalent in subjects currently on OAT compared to those not on OAT (53.3% vs. 71.4%; $p=0.001$). Women currently on OAT exhibited less lifetime (28.0% vs. 43.6%; $p=0.008$) and recent (19.4% vs. 35.9%; $p=0.003$) risky sexual behavior. Both groups experienced similar lifetime rates of violence exposure, but those currently on OAT experienced less recent violence (4.3% vs. 14.3%; $p=0.01$). In bivariate modeling, there was an association between current OAT use and the interaction between recent violence and sexual risk (OR=0.125; CI: 0.017–0.937; $p=0.04$).

Table 3 depicts the best fit multivariate model of current OAT use, weighted by location. After controlling for age, education, and marital status, current OAT use remained significantly protective against recent risky sex (aOR=0.49; CI: 0.31–0.76; $p=0.001$), recent violence (aOR=0.22; CI: 0.08–0.56; $p=0.002$), injection severity (aOR=0.10; CI: 0.06–0.17; $p<0.001$) and depression severity (aOR=0.52 CI: 0.37–0.73; $p<0.001$). Interestingly, marriage and cohabitation were associated with decreased odds of current OAT (aOR=0.64; CI: 0.43–0.95; $p=0.027$) and those who described religion as not important had lower odds of being on OAT (aOR=0.52; 95% CI: 0.32–0.85; $p=0.009$).

3.1.2 Qualitative

The 67 women who participated in FGs emphasized the stabilizing effects of OAT such as access to healthcare and reproductive health services, decreased sexual risk, and improved quality of life. Women's experiences with access to healthcare services varied, with some identifying challenges to receiving care while others felt OAT involvement improved their

access to other healthcare services. There was a mixture of experiences ranging from “They don’t give us anything. No free medications. Even if you’ve got AIDS or something…” (Katya, Donetsk, on OAT) to those women who felt OAT improved access to treatment. For example, Tania in Odesa who was on OAT said:

> … If you look at the way drug addicts live. We underwent medical examination by all doctors every year; we are obligated to do so. And if not for the program [OAT], who would be going to these medical examinations? Where would a drug addict go to receive healthcare services?
>
> Moderator: And by what doctors are you obligated to be examined?
>
> Tania: All doctors. We undergo all tests. Blood and urine tests, cardiogram, HIV, TB tests.

HIV testing was primarily conducted in specialized AIDS Centers that provided both HIV and OAT services and the women’s experience with testing and treatment was often positive as discussed by Yana from Kiev who was on OAT:

> In regular outpatient clinics, where ordinary doctors practice, their attitude would immediately change as soon as they find out about it [one’s HIV+ status]. But if you get to a specialized clinic, for example, where we do HIV tests and [receive] ARV therapy, you will come across a different attitude. When I came there and said that I needed to do the tests, they would ask: “What do you need them for?” I would answer: “For the program”. “For which program?” I would say: “For the substitution therapy program”. I thought that having told it to them they would treat me with animosity, but it was just on the contrary. They would ask me: “Really? Have you quit using street drugs?” I would say: “Yes. It’s finished”. “You are doing a good job! Take care!” And so on and so forth. The HIV tests are free of charge there. And they do the tests properly with a good attitude.

Access to reproductive health services, including obstetrics, was improved for clients on OAT. Although there were conflicting opinions on the use of OAT during pregnancy, most women supported the use of OAT when pregnant and some attributed positive outcomes of childbirth to their use of treatment. In Kyiv, Anya credited her experience on OAT with her successful pregnancy:

> As the girls have said already… I joined the substitution therapy [program] in my 5th month of pregnancy. And I am sure that had I not been enrolled into the [program] I would not have been able to keep the pregnancy.

The topic of decreased sexual drive, as a consequence of methadone treatment, affected sexual activity and risk for men and women, and was frequently discussed by the women. Women explained, “the desire for sex vanishes”, “libido disappears”, and according to Sveta from Mykolaiv, referencing her attitude towards her sexual partner while she was previously on methadone, “…it happens that when you sleep; and he looks like your brother, mother, father. Nothing at all…like anyone but your husband… no feelings.” Tania, currently on OAT in Odesa, discussed that contraception is available, but often unnecessary due to decreased sexual desire:

> I know that contraception, in my opinion, isn't a very relevant issue for drug addicts. Well, in principle, I, it seems to me that contraception can be performed with the gynecologist free of charge, if one wants to. Whoever wants to take care of their own health, do so accordingly…

The effect of OAT on family life and quality of life was confirmed by Yana from Kyiv who had experience with OAT.

> Life in drug use leads to a dead end. A person is always in need of something – in need of money, in need of getting something else. It's a dead end in family relations because a person simply lacks time for that, especially when she has children. And this thing [OAT] helps, because you know that you do not have to do anything special and you can devote your time, which in the past you would spend for searching around, for the necessary things, namely, the family, work or something else.

OAT improved family relationships as Ira from Kyiv said after initiating OAT, "I began a new life. I have a mutual understanding in the family, and my relations with my child were improved". A unique aspect of the women's experience with drug use and OAT revolved around issues of power and intimate partner violence. Tania from Odesa who was on OAT relayed her story of her husband's influence on her drug use:

> Then I met someone… Women usually get hooked because of men; this "shouldn't have happened". And so I fell in love with a drug addict six years ago. And living with him, because he wants to shoot drugs, and a woman, as a rule, ends up doing what her husband does. And so I returned to my old ways.

Her friend Natasha, who was also on OAT, confirmed that "Her husband got her hooked. She loved him very much." Women seemingly interpreted their drug use in terms of their relationships, equating shared use to loyalty. In this way, the gendered power dynamic negatively impacted women's motivation to engage in treatment for their substance use. This social dynamic was further reinforced by partner violence exposure, both physical and emotional. Tania, another Odesa FG participant who was on OAT, identified her drug use as a means by which her husband exerted control:

> He morally choked me, not physically grabbed by throat, but made me suffocate morally. Then he hit me once. After we had lived about a year and a half together he hit me. We had an argument, he just slapped me. But we had a deal with him that when. yeah. I say, I have not been beaten even as a child. I do not understand what it is to be beaten. I do not forgive such things. He slapped me, I was ready to leave, and he lay there at the door and said, "I am not letting you out of the apartment." He began saying he was sorry. I said, "Alright". I pretend going to bed. I wait while he falls asleep, and then I leave. He wakes up two hours later, calls me asking where I am.
>
> I tell him, "Good-bye my boy". He goes, "Tania, please come back, come back. I will hang myself." He was going to hang himself, it was simply ridiculous. So I come back. There's a hook in the ceiling, you know, driven into a dowel. I am

asking, “why is there a hook in the ceiling?” And he says, “I was trying to hang myself.” “Why are you still alive then?”

Women described a lack of power and control within their relationships, perpetuated by mutual drug use, that are additional barriers to seeking treatment. This is particularly poignant in the patriarchal culture in Ukraine. Taken together, quantitative and qualitative findings demonstrate a broadly stabilizing effect of OAT on risk behaviors, depression, and other social factors. Women’s relationships with men who use drugs; however, were a major barrier to engaging in OAT.

4.1 Discussion

In this mixed methods study of 380 women with opioid use disorder in Ukraine, we found that ongoing engagement in OAT represented a stabilizing influence in women’s lives. One might have anticipated, based on prior studies in Ukraine and elsewhere, that OAT would be protective against drug- and sex-related HIV risk behaviors (Degenhardt et al., 2014; Lawrinson et al., 2008; MacArthur et al., 2012; Malta et al., 2010; Zaller et al., 2015), but little has been studied about the broader benefits of OAT, specifically for women. To our knowledge, this is the only study that investigates the effects of OAT engagement among women in Ukraine. We found OAT was broadly associated with reductions in depression and violence exposure and improvements in healthcare engagement. This finding is particularly powerful considering the overall 50% prevalence of self-reported HIV, and the fact that women currently and not currently on OAT experienced similar lifetime prevalence of violence exposure and drug use severity. Qualitative findings suggest that the broadly stabilizing effects of OAT on women’s lives were not merely secondary to women’s reduced drug use, but rather directly attributable to improved quality of life and OAT systems of care.

Previous studies suggest that unlike men, women primarily derive satisfaction from OAT through improved familial relationships and relationships formed with healthcare personnel and other clients (Marchand et al., 2015). Our qualitative findings confirm that women may trust in and engage with OAT-affiliated providers because they experience less stigma about their substance use. Moreover, women identified that OAT allowed them to devote time and energy towards improving relationships with family and friends, rather than the all-consuming demands of active substance use. These factors improve overall quality of life among women on OAT, while reducing depression and partner violence exposure, which has been shown to disrupt engagement in care, resulting in lower rates of viral suppression and higher rates of AIDS among people living with HIV (Schafer et al., 2012). In another study, women with HIV reported depression as a barrier to entering and remaining in care (Messer et al., 2013). Notably, marriage and cohabitation were potential barriers to engagement in OAT. While marriage is often seen as a protective factor representing social connection, women may continue to use when they lack power or control in relationships or are involved with men who also use drugs. This phenomenon was emphasized in the qualitative analysis. One study on relapse among people with substance use disorders reported marriage as a protective factor against relapse for men, while being a risk factor for relapse among women (Walitzer & Dearing, 2006). We found that women who ranked religion as extremely important were more likely to be on OAT. Prior research has identified religion as a positive

influence on care enrollment and retention, or conversely, a barrier to care for those with a negative relationship to religion (Puffer, Skalski, & Meade, 2012). In a 5-year analysis of patients who recovered from opioid use disorder, nearly half stated that religion was very important in abstaining from opioids (Flynn, Joe, Broome, Simpson, & Brown, 2003). This finding is important to the Ukrainian context, where engagement in organized religion is commonplace (Bremer, 2016).

Beyond building positive relationships with support networks and healthcare providers, OAT increased healthcare engagement because of the ways in which care was organized. For example, women in FGs identified that because OAT participation required completion of annual medical exams, they were more likely to be tested for HIV and Hepatitis C, and to then be referred to specialized treatment centers. Integrated treatment for medical, psychiatric, and substance use disorders is an evidence-based effective strategy to improve care engagement along the HIV care continuum (Hoang et al., 2009; Soto, Bell, Pillen, Hiv/Aids Treatment Adherence, & Cost Study, 2004; Volkow & Montaner, 2011) and has been documented to improve numerous quality health indicators in Ukraine (Bachireddy et al., 2014). In the BHIVES multisite demonstration project of integrated buprenorphine and HIV care, those retained on buprenorphine at 6 months were significantly more likely to be retained in HIV care, prescribed ART and achieve viral suppression (Altice et al., 2011). Interestingly, our study found no significant differences in mean CD4 count and ART use between women currently on OAT and not on OAT, perhaps due to the small numbers of women accessing ART and the potential for recall and social desirability biases inherent in self-reported measures. Additionally, the participants who knew CD4 counts or were using ART had already been linked to care; OAT often improves these measures by improving HIV+ PWID initial enrollment in care. Integrated systems of care and those with low barriers to entry, such as take-home doses of medication or the availability of prescriptions, are crucial for WWID (in Ukraine and elsewhere) because they often have limited resources to navigate complex systems of care and experience stigma both because of their sex and their drug use (Des Jarlais et al., 2012; Springer et al., 2015).

Although the quantitative survey did not specifically assess women's engagement in reproductive healthcare, participants in the FGs spoke about the importance of receiving free contraception through OAT sites. This is not only critical to harm reduction (reducing sexual risk of HIV through condom use), but also to empowering women to make their own reproductive choices. One study of 204 Australian women found that women on OAT had high pregnancy rates, high rates of adverse pregnancy outcomes, misunderstandings about contraception and a low use of contraceptive methods among sexually active women uninterested in pregnancy (54.7%) (Black, Stephens, Haber, & Lintzeris, 2012). Women also explained that OAT reduced sexual risk behaviors by reducing libido. Many studies have investigated the impact of OAT on male sexual dysfunction; however, literature looking at the relationship female sexual dysfunction and OAT is lacking (R. Brown, Balousek, Mundt, & Fleming, 2005; R. a. Z. Brown, M., 2007; Hallinan et al., 2008; Yee, Loh, Hisham Hashim, & Ng, 2014). Findings suggest that, with adequate resources, OAT clinics could be more important gateways to reproductive healthcare for women who experience extraordinary sexual risk related to their drug use. More data is needed on how OAT impacts other facets of reproductive healthcare, including completion of screening pap smears,

human papilloma virus (HPV) vaccination, screening and treatment for sexually transmitted infections, and pregnancy planning.

Women who inject drugs are often overlooked and underrepresented in HIV treatment and OAT despite their increased risk of HIV infection (Greenfield et al., 2007; Page et al., 2015). Women who inject drugs may be characterized as a “difficult to reach population” because of the multifactorial nature of their drug dependence and accordingly, are less likely to enter OAT (Greenfield et al., 2007). Our results indicate OAT in a mixed gender setting can provide wide- reaching benefits by decreasing risk behaviors and increasing well-being in WWID in Ukraine, but more studies are needed to evaluate the impact of women-specific OAT programs on women’s lives. Prior studies have explored the benefits of drug treatment that focus on the unique needs of women, including a community based HIV intervention among African American women that showed a reduction in sexual and injection risk behavior after a gender- specific education program (Sterk, Theall, Elifson, & Kidder, 2003). Another investigation of a HIV intervention in African American crack cocaine users demonstrated decreased sexual and injection risk behaviors in all women, but women in gender-specific groups also experienced improved employment and housing status (Wechsberg, Lam, Zule, & Bobashev, 2004). As women encounter greater barriers to treatment such as increased stigma/discrimination, fear of violence, higher rates of psychiatric disorders and loss of parental custody (El-Bassel, Gilbert, Witte, Wu, & Chang, 2011; Page et al., 2015), culturally-appropriate programs that take these barriers into account could improve enrollment, satisfaction and retention among women. Techniques such as women-only spaces, couple-enrollment, childcare and trauma-informed care are vital strategies to reach and improve outcomes among WWID who are disproportionately impacted by the Eastern European HIV epidemic.

Our study on the benefits of OAT in Ukraine highlights the continued importance of access to OAT in the face of Russia’s ongoing influence. Despite statements from the Joint United Nations Program on HIV/AIDS, the World Health Organization and the United Nations Office on Drugs and Crime that support OAT for HIV prevention, Russia explicitly bans OAT, perpetuating negative attitudes and impeding OAT access in the countries of the former Soviet Union (Cohen, 2010; World Health Organization, 2004). Ukraine has been a leader in OAT implementation in the region, but still struggles with individual, cultural and structural barriers to extensive implementation of OAT programming (Bojko, Dvoryak, & Altice, 2013; Martha J. Bojko et al., 2015; Bojko et al., 2016; Makarenko et al., 2016). Russia’s continued influence in Ukraine, particularly in Crimea and Donbas regions, threatens to reverse progress the Ukrainian government has made towards expanding access to OAT and HIV prevention and treatment services. In the regions currently not under Ukrainian government control, access to resources (and funding to support programs) are limited (Filippovych, 2015). Our results argue for the crucial protection and expansion of current OAT programs to improve and stabilize the lives of WWID in Ukraine and decrease HIV risk across the Ukrainian population.

Our study is novel in its sex-specific and mixed methods analytic approach, but is not without limitations. This was a secondary data analysis that was women-specific, though the parent study was not. As a result, all treatment programs were mixed gender. Data were

limited to that collected for the parent study and not all key variables of interest were measured with validated instruments (e.g. violence exposure). Although we did attempt to correlate contemporaneous (and recent) risk behaviors with OAT receipt, causality cannot be implied in this cross-sectional study. This study is specific to the Ukrainian context and may not be generalizable to other populations of women who use drugs elsewhere, though we suspect that treatment needs overlap.

4.2 Conclusions

In this mixed methods study of women with opioid use disorder in Ukraine, engagement in OAT was beneficial in terms of reducing injecting drug use, sexual risk, depression, and violence exposure and improving quality of life. OAT also directly facilitated relationships with healthcare providers and engagement in care for HIV, reproductive health, and other medical comorbidities. The study highlighted the need for continued support and expansion of OAT services in the former Soviet region despite Russia's aggressive attempts to discredit evidence-based substance use treatment strategies. While more research is needed on the effect of OAT on other parameters of reproductive health, our findings support expansion of gender-sensitive OAT programs for women in Ukraine to combat the HIV epidemic.

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Highlights

- Women who inject drugs in Ukraine exhibit high rates of risk behaviors.
- OAT was associated with decreased sexual risk and violence exposure.
- Depression and injection frequency were also independent correlates of OAT use.
- Focus groups suggested improved social support for WWID on OAT.

Table 1

Characteristics of Study Sample by Current OAT Use and Correlates of Current OAT Use by Bivariate Logistic Regression (N=380)

	No Current OAT n=287	**Current OAT n=93**	***p*-value**	**OR (95% CI)**	***p*-value**
Demographics	Mean (SD) or n (%)	Mean (SD) or n (%)			
Mean Age, y	35.72 (8.54)	37.92 (8.37)	0.030	1.031 (1.00-1.06)	0.031
Location			0.001		
Kyiv	66 (23.0%)	41 (44.1%)		Referent	—
Odesa	37 (12.9%)	9 (9.7%)		0.39 (0.17–0.90)	0.026
Mykolaiv	56 (19.5%)	18 (19.4%)		0.52 (0.27–1.00)	0.050
Dnipro	89 (31.0%)	21 (22.6%)		0.38 (0.20–0.70)	0.002
Lviv	39 (13.6%)	4 (4.3%)		0.16 (0.06–0.50)	0.001
Ethnicity			0.346		
Ukrainian	226 (78.7%)	79 (84.9%)		2.44 (0.54–11.01)	0.243
Russian	47 (16.45)	12 (12.9%)		1.79 (0.26–8.96)	0.480
Other	14 (4.9%)	2 (2.2%)		Referent	—
Education			0.546		
High school completion or below	126 (43.9%)	35 (37.6%)		Referent	—
Completed some university	122 (42.5%)	45 (48.4%)		1.33 (0.80–2.20)	0.273
Completed university	39 (13.6%)	13 (14.0%)		1.20 (0.58–2.49)	0.635
Housing			0.647		
Own Place—rented or owned	101 (35.2%)	36 (38.7%)		Referent	—
Family or friend’s place or hotel	180 (62.7%)	54 (58.1%)		0.84 (0.52–1.37)	0.488
Shelter, homeless or other	6 (2.1%)	3 (3.2%)		1.40 (0.33–5.90)	0.644
Employment			0.602		
Full or part time	134 (46.7%)	42 (45.2%)		Referent	—
Temporary, seasonal or day laborer	37 (12.9%)	9 (9.7%)		0.78 (0.35–1.74)	0.538
Not Employed	116 (40.4%)	42 (45.2%)		1.16 (0.70–1.89)	0.568
Sources of Income					
Social Payment	130 (45.3%)	47 (50.5%)	0.379		
Sex for Money	12 (4.2%)	2 (2.2%)	0.366		

	No Current OAT n=287	Current OAT n=93	*p*-value	OR (95% CI)	*p*-value
Drug Sales	14 (4.9%)	0 (0.0%)	0.026		
Social Factors					
Marital Status			0.627		
Single	65 (22.6%)	17 (18.3%)		Referent	
Married/living together	129 (44.9%)	46 (49.5%)		1.36 (0.72–2.56)	0.336
Separated/divorced/widowed	93 (32.4%)	30 (32.3%)		1.23 (0.63–2.42)	0.542
Currently Live Alone	55 (19.2%)	17 (18.3%)	0.850		
Next Month-Housing Stability			0.164		
Very/somewhat Sure	239 (83.3%)	83 (89.2%)		1.67 (0.81–3.44)	0.168
Somewhat/very unsure	48 (16.7%)	10 (10.8%)		Referent	—
Religion Role			0.030		
Not Important	68 (23.7%)	15 (16.1%)		0.46 (0.23–0.90)	0.022
Fairly Important	134 (46.7%)	37 (39.8%)		0.57 (0.34–0.96)	0.036
Extremely Important	85 (29.6%)	41 (44.1%)		Referent	—

Table 2

Risk behaviors and Healthcare utilization of study sample by current OAT Use (N=380)

	No Current OAT n=287*	**Current OAT n=93***	***p*-value**	**OR (95% CI)**	***p*- value**
History of Drug Use	Mean (SD) or n (%)	Mean (SD) or n (%)			
Mean DAST Score	7.48 (1.96)	7.09 (2.35)	0.150	0.92 (0.82–1.02)	0.115
Mean age of Injection initiation, y	19.78 (5.84)	19.31 (4.72)	0.438		
Mean opioid craving scale	6.53 (3.43)	3.16 (3.32)	<0.001		
Mean # overdoses in past 6 months	0.10 (0.38)	0.04 (0.29)	0.149		
Mean # injection days in past month	18.62 (12.07)	2.89 (7.58)	<0.001	16.89 (9.58– 29.77)	<0.001
Frequency of Drug Injection			<0.001		
Mild (0–1 days/month)	48 (16.7%)	72 (77.4%)			
Moderate (2–27 days/month)	110 (38.3%)	15 (16.1%)			
Severe (28–30 days/month)	129 (44.9%)	6 (6.5%)			
Mean # of days using alcohol in past month	4.02 (7.10)	2.02 (4.71)	0.002		
Past Year					
Used drugs	266 (92.7%)	73 (78.5%)	<0.001		
Unable to stop using drugs	206 (71.8%)	59 (63.4%)	0.128		
Blackouts	166 (57.8%)	53 (57.0%)	0.885		
Experienced withdrawal	260 (90.6%)	73 (78.5%)	0.002		
Felt guilty about drug use	261 (90.9%)	75 (80.6%)	0.007		
Neglected family due to drug use	248 (86.4%)	71 (76.3%)	0.022		
Sexual Behavior					
Ever exchanged sex for money, rent or drugs	60 (20.9%)	11 (11.8%)	0.051		
Ever been forced to have sex against your will	73 (25.4%)	25 (26.9%)	0.782		
Ever been beaten, slapped or hit before or during sex	46 (16.0%)	14 (15.1%)	0.823		
In the last 90 days					
Had sex	156 (54.4%)	41 (44.1%)	0.085		
Of whom:	N=156	N=41			

	No Current OAT n=287*	Current OAT n=93*	*p*-value	OR (95% CI)	*p*- value
Had a regular sexual partner	143 (91.7%)	40 (97.6%)	0.308		
Mean # sex partners	1.03 (3.02)	0.44 (0.50)	0.063		
Casual sex partner	27 (17.3%)	1 (2.4%)	0.005		
Mean # casual sex partner	0.09 (0.29)	0.01 (0.10)	<0.001		
Exchanged sex for money/rent/drugs	24 (15.4%)	1 (2.4%)	0.014		
Beaten, slapped, hit before or during sex	22 (14.1%)	3 (7.3%)	0.155		
Without a condom	104 (66.7%)	30 (73.2%)	0.485		
Of whom:	N=104	N=30			
Mean # of partners	0.43 (0.79)	0.32 (0.47)	0.131		
with an HIV+ partner	33 (31.7%)	11 (36.7%)	0.931		
with a regular partner	84 (80.8%)	24 (80%)	0.520		
with a casual partner	9 (8.7%)	0 (0.0%)	0.120		
and exchanged money	4 (3.8%)	0 (0.0%)	0.252		
and used drugs	75 (72.1%)	11 (36.7%)	0.004		
Condom use with last sex	65 (22.6%)	17 (18.3%)	0.373		
History of HIV and HCV infections					
HIV/AIDS					
Ever tested	235 (81.9%)	87 (93.5%)	<0.001		
Ever diagnosed	155 (54.2%)	46 (59.5%)	0.604		
Currently taking ART	74 (88.1%); n=84	29 (96.7%); n=30	0.172		
Mean last CD4 count, cells/pL	454.4 (269); n=97	452.8 (210); n=37	0.970		
Ever tested for HCV	187 (65.2%)	81 (87.1%)	<0.001		
Diagnosed with chronic HCV	145 (50.7%)	65 (69.9%)	0.004		
Ever tested for HBV	122 (42.5%)	57 (61.3%)	0.002		
Incarceration History					
Ever incarcerated in prison	76 (26.5%)	20 (21.5%)	0.337		
Mean # times in prison	0.60 (1.344)	0.70 (1.756)	0.617		

	No Current OAT n=287*	Current OAT n=93*	*p*-value	OR (95% CI)	*p*- value
Mean # time needles confiscated by police	0.16 (1.071)	0.00 (0.00)	0.014		
Ever been threatened with physical violence by police	105 (36.6%)	38 (40.9%)	0.460		
Ever threatened with weapon by police	60 (20.9%)	15 (16.1%)	0.314		
Ever forced to have sex by police	40 (13.9%)	11 (11.8%)	0.604		
Ever physically assaulted by police	129 (44.9%)	42 (45.2%)	0.971		
Physically assaulted by police in last 6 months	21 (7.3%)	0 (0.0%)	0.007		
Last 6 months, forced to have sex by police	7 (2.4%)	1 (1.1%)	0.426		
Composite Variables					
Recent risky sexual behavior	103 (35.9%)	18 (19.4%)	0.003	0.43 (0.24–0.76)	0.003
Recent violence exposure	41 (14.3%)	4 (4.3%)	0.010	0.27 (0.09–0.77)	0.015
Severe drug use	129 (44.9%)	6 (6.5%)	<0.001	0.08 (0.04–0.20)	<0.001
Depressed	205 (71.4%)	49 (53.3%)	0.001	0.46 (0.28–0.74)	0.001

* Unless otherwise noted, based on survey skip patterns. Shading and indentation also reflects survey skip patterns.

Table 3

Independent correlates of currently being on opioid agonist therapies: Weighted by Location (N=380)

	aOR (95% CI)	p-value
Age	0.98 (0.95–1.00)	0.023
Education		
High school completion or below	Referent	
Completed some university	0.69 (0.40–1.20)	0.188
Completed university	1.03 (0.59–1.80)	0.921
Marital Status		
Single	Referent	
Married/living together	0.64 (0.43–0.95)	0.027
Separated/divorced/widowed	0.65 (0.39–1.06)	0.082
Religion Role		
Extremely Important	Referent	-----
Not Important	0.52 (0.32–0.85)	0.009
Fairly Important	0.72 (0.44–1.14)	0.108
Recent Risky Sex	0.49 (0.31–0.76)	0.001
Recent Violence	0.22 (0.08–0.56)	0.002
Injection Severity	0.10 (0.06–0.17)	<0.001
Moderate to severe depression	0.52 (0.37–0.73)	<0.001