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Opioid substitution treatment in Ukraine: review of the peer-reviewed literature

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OBJECTIVE: To review published peer-reviewed papers regarding opioid substitution treatment (OST) in Ukraine and to describe the research agenda that has been in parallel with the development of opioid substitution treatment program in Ukraine. Further, to understand research gaps and future directions of scientific efforts concerning the OST implementation in Ukraine.

METHODS: Literature search using standardized research terms of PubMed, Science Direct, and Google Scholar was supplemented with consultations with relevant in-country researchers to identify any additional publications that were not found through on-line search. Original literature search has been conducted during August, 2013, two refreshment searches were conducted during October, 2013 and February, 2014. The literature search and eligible papers selection were conducted applying PRISMA guidelines.

RESULTS: Eight papers were published in peer reviewed journals specifically scrutinizing the features of the OST program or patients' outcomes in Ukraine. Demonstrating the feasibility of buprenorphine and methadone maintenance treatment in Ukraine was core aim of majority of the papers.

Few discussed TB and HIV treatment outcomes and health-related quality of life (QoL). Program description and cost-effectiveness of OST in Ukraine were the topic of two other papers. Decreased injection risk behavior and high retention rates were reported for Ukrainian methadone and buprenorphine patients. Other treatment indicators (TB treatment outcomes, HIV initiation, and services utilizations) have been higher among those on substitution treatment compared to those who were not. QoL besides health-related indicators have been understudied among Ukrainian OST patients.

CONCLUSION: Published papers provide evidence to conclude that OST in Ukraine is effective in terms of patients' retention on treatment and decreasing self-reported HIV-related risk behaviors and also provides a background for wide scale-up of the program. Further research is needed to understand how the program could be improved to better meet the needs of the opioid dependent drug users accounting for Ukrainian context.

KEYWORDS: opioid substitution treatment; OST; Ukraine.

INTRODUCTION

Substitution treatment with methadone as a full opioid agonist has been considered since 1965 in the US (Dole & Nyswander, 1965) and buprenorphine as a partial opioid agonist has become widely used for this purpose in France since 1995 (Carrieri et al., 2003). Treatment with opioid substitutes for drug using population serves several pub-

lic health goals besides the dependence management, such as (1) replacement of injected, illicit drugs with non-injected medication, therefore reducing risk of HIV transmission; (2) patient retention on treatment, which opens a 'window' for psychosocial interventions; (3) treatment delivery under observation of medical specialists, who may act as a gatekeeper for

other medical services and enabling opioid drug users to stabilize their social life (Mattick, Breen, Kimber, & Davoli, 2009).

In Ukraine, opioid substitution treatment (OST) was introduced as a means of HIV prevention through efforts of several international agencies (Bruce, Dvoryak, Sylla, & Altice, 2007). Initially, buprenorphine maintenance treatment

(BMT) was introduced in Ukraine in 2004 (Bruce et al., 2007) followed by introduction of methadone maintenance treatment (MMT) as more cost-effective option in 2007 (Schaub, Chtenguelov, Subata, Weiler, & Uchtenhagen, 2010). Initial accents within OST program were put on the need to facilitate the expansion of ARVs among HIV-infected people who inject drugs (PWIDs) and to prevent new cases of infection by reducing injection behavior among opioid dependent PWIDs. This context has shaped the research efforts as well as program delivery and its scale up. After advocacy of the necessity to introduce OST in Ukraine and scale up of the program, the next sound question was to understand how it works within Ukrainian healthcare system and

how it influences the lives of those who receive this treatment in Ukraine.

This literature review of published peer-reviewed papers regarding OST in Ukraine aims to describe the research agenda that have been in parallel with the development of opioid substitution treatment in Ukraine. This paper also aims to understand research gaps and future directions for scientific efforts concerning OST implementation in Ukraine.

METHODS

Research strategy comprised: (1) Literature search (research terms ‘Ukraine’ AND ‘opioid substitution treatment’) of PubMed, Science Direct, and Google Scholar. Additional search through

the same sources using similar terms (‘Ukraine’ AND ‘maintenance treatment’, ‘Ukraine’ AND ‘buprenorphine’, ‘Ukraine’ AND ‘methadone’) provided the same results. The search was conducted in August 2013. (2) Consultations with in-country researchers from the field of OST program delivery and Narcology to explore whether there were any additional publications that were not found through previous search. Fig 1. shows the PRISMA diagram for the search that led to the final set of papers included in this review. Brief overview of the search outcomes is provided in the Table 1. Numbers suggest that even though there are many publications that mention the topic of OST in Ukraine, the number of papers devoted specifically to this topic is limited given a 9-year history of OST in Ukraine.

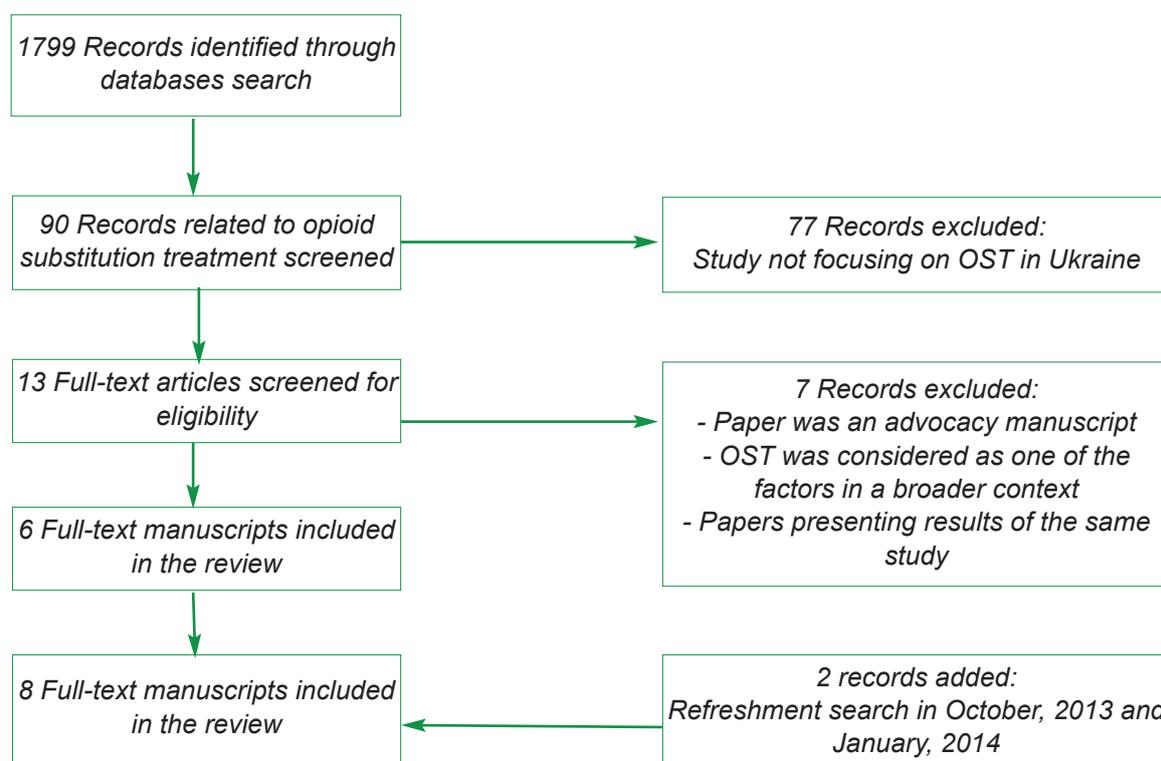


Fig 1. PRISMA diagram. Flow chart of studies identified through literature search reviewed for inclusion in the review (Final number of reviewed papers include 2 additional papers from refreshment search)

After removing all the duplicates and articles that have presented results from the same research (Dvoryak, 2008), six scientific peer-reviewed articles that specifically addressed OST program in Ukraine were included in the current review. Full texts of all papers were retrieved, thoroughly read and analyzed with the purpose to identify how the research community was following and reflecting the development of OST in Ukraine. Refreshment literature searches have been conducted in October, 2013 and January, 2014 to check on new papers that may have been published since the original search. Two additional papers that have not been previously identified were included in this review.

Aside of a descriptive paper (Bruce et al., 2007) and a cost-effectiveness paper (Alistar, Owens, & Brandeau, 2011), studies measured the feasibility of opioid substitution treatment among opioid-dependent individuals in general and by HIV status using such instruments as addiction severity index (ASI) scores, retention rates, changes in Blood Borne Virus Transmission Risk Assessment Questionnaire (BBV-TRAQ), Risk Assessment Battery (RAB), Time Line Follow Back by different follow up (1-, 2-, 3-, 6-, and 12 months) (Schaub et al., 2010; Schaub, Subata, Chtenguelov, Weiler, & Uchtenhagen, 2009), quality healthcare indicators (HIV, TB, addiction) (Bachireddy et al., 2013; Morozova, Dvoryak, & Altice, 2013). Quality of life has been measured with SF-36, ASI, WHO-QOL-BREF, and QALY instruments.

Besides the papers included in the review, we also came across seven publications that were to some extent related to the OST program in

Ukraine; however, they were focused on other research questions. We briefly report on topics of these papers in the results section, but data from these publications is not included into the Table 1 and discussion section.

RESULTS (PUBLISHED PEER-REVIEWED PAPERS)

Eight unique papers were published in peer reviewed journals specifically looking at the features of OST program or patients' outcomes in Ukraine (Alistar et al., 2011; Bachireddy et al., 2013; Bruce et al., 2007; Dvoriak et al., 2014; Lawrinson et al., 2008; Morozova et al., 2013; Schaub et al., 2010; Schaub et al., 2009).

Papers that have been included in this review were diverse in their research questions and methods used. Key characteristics of these research papers are presented in the Table 1. Research agenda ranged from description of program characteristics (Bruce et al., 2007), feasibility of buprenorphine and methadone maintenance treatment in Ukraine and specifically among people who use home-made opioids (Schaub et al., 2010; Schaub et al., 2009), viability of OST in Ukraine within a broader context of resource-poor settings (Lawrinson et al., 2008) to different treatment outcomes. MMT treatment outcomes by HIV status of participants (Dvoriak et al., 2014), TB treatment outcomes by receipt of MMT (Morozova et al., 2013) and quality healthcare indicators at different levels of services integration for PWIDs and health-related quality of life (QoL) (Bachireddy et al., 2013) have been reported and discussed in the most recent papers on OST in Ukraine. Cost-effectiveness

of OST in Ukraine was projected within context of HIV prevention efforts. The overall goal was to inform public health decisions on how to use the limited resources allocated for curbing the epidemic most effectively given that one of its driving forces in Ukraine is injection drug use (Alistar et al., 2011).

Studies reported OST retention ranging from 75% (Lawrinson et al., 2008) to 85% (Schaub et al., 2009) at 3 months of follow-up and from 70% (Lawrinson et al., 2008) to 84% (Schaub et al., 2009) at 6 months of follow-up.

Sample sizes varied from 50 (Dvoriak et al., 2014) to 331 (Schaub et al., 2010) participants for the papers looking at patient-level data (Bachireddy et al., 2013; Dvoriak et al., 2014; Lawrinson et al., 2008; Morozova et al., 2013; Schaub et al., 2010; Schaub et al., 2009). OST program key features description (Bruce et al., 2007) and mathematical modeling of country-level data (Alistar et al., 2011) were used in two other papers.

Papers mentioning OST in Ukraine not as the main focus of their research question reported participation in OST program as one of the independent variables (confounders), as a part of comprehensive approach towards treatment and care of people who inject drugs (Izenberg et al., 2013; Strathdee et al., 2010; Wolfe, Carrieri, & Shepard, 2010) and as a facilitator of entrance to HIV treatment and care for HIV-positive PWIDs (Mimiaga et al., 2010). Other papers were either a report, a letter or a case report, were aimed to put an advocacy statement regarding challenges that patients of substitution treatment face in everyday life

Table 1 Key characteristics of the published papers on opioid substitution treatment (OST) in Ukraine

		Other papers on the same study	Year published	Data collection period	Methods	
1	HIV Treatment Access and Scale-up for Delivery of Opiate Substitution Therapy with Buprenorphine for IDUs in Ukraine-- Programme Description and Policy Implications	(Bruce, Dvoryak, Sylla, & Altice, 2007)	(Dvoryak & Grishaeva, 2008)	2007	October, 2005 – July, 2006	Description of key program characteristics
2	Key Findings from the WHO Collaborative Study on Substitution Therapy for Opioid Dependence and HIV/AIDS	(Lawrinson et al., 2008)		2008	Late 2003 and mid-2005	Longitudinal cohort study of OST patients
3	Feasibility of Buprenorphine Maintenance Therapy Programs in the Ukraine: First Promising Treatment Outcomes	(Schaub, Subata, Chtenguelov, Weiler, & Uchtenhagen, 2009)		2009	2007	Longitudinal cohort study of OST patients
4	Feasibility of Buprenorphine and Methadone Maintenance Programs Among Users of home Made Opioids in Ukraine	(Schaub, Chtenguelov, Subata, Weiler, & Uchtenhagen, 2010)		2010	2008	Longitudinal cohort study of OST patients
5	Effectiveness and Cost Effectiveness of Expanding Harm Reduction and Antiretroviral Therapy in a Mixed HIV Epidemic: A Modeling Analysis for Ukraine	(Alistar, Owens, & Brandeau, 2014)		2011	2010	Mathematical modeling using actual and estimated data
6	Integration of Health Services Improves Multiple Outcomes among HIV-infected People who Inject Drugs in Ukraine	(Bachireddy et al., 2014)		2013	2010	Cross-sectional survey
7	Methadone treatment improves tuberculosis treatment among hospitalized opioid dependent patients in Ukraine	(Morozova, Dvoryak, & Altice, 2013)		2013	December, 2011- April, 2012	Prospective, non-randomized observational study
8	Methadone Maintenance for HIV Positive and HIV Negative Patients in Kyiv: Acceptability and treatment response	(Dvoriak et al., 2014)		2014	Not indicated in the paper	Longitudinal observational study

Table 1 Key characteristics of the published papers on opioid substitution treatment (OST) in Ukraine (continued)

	Follow up period	Measured outcomes
1 (Bruce, Dvoryak, Sylla, & Altice, 2007)	-	Retention rate and dosage were not specifically measured but discussed as main indicators
2 (Lawrinson et al., 2008)	6 months	1. Treatment retention; 2. Change in substance use; 3. Changes in BBV risk-taking behavior; 4. Quality of life (WHOQOL-BREF)
3 (Schaub, Subata, Chtenguelov, Weiler, & Uchtenhagen, 2009)	12 months	1. Treatment retention; 2. Substance use (last 30 days); 3. Changes in BBV risk-taking behavior; 4. ASI: occurrence of somatic disorders; employment; legal status; family problems; 5. Percentage of HIV positive patients who received ART
4 (Schaub, Chtenguelov, Subata, Weiler, & Uchtenhagen, 2010)	6 - months	1. Treatment retention; 2. Substance use (last 30 days); 3. Changes in BBV risk-taking behavior; 4. ASI: occurrence of somatic disorders; employment; legal status; family problems; 5. Percentage of HIV positive patients who received ART
5 (Alistar, Owens, & Brandeau, 2014)	-	1. HIV prevalence among PWIDs; 2. HIV prevalence among non-DUs; 3. Number of HIV infections averted over 20 years among PWIDs; 4. Number of HIV infections averted over 20 years among non-PWIDs; 5. QALYs
6 (Bachireddy et al., 2014)	-	1. 8 self-reported quality healthcare indicators (HIV, addiction and TB treatment outcomes); 2. HIV: receipt of ART, receipt of ART when CD4<200; CD4 monitoring within past 6 months; 3. Addiction: receipt of WHO-recommended OST dosing, no previous 30-day drug injection, less than daily drug injection; 4. TB: TB screening in the past 12 months; receipt of isoniazid preventive therapy (IPT); 5. SF-36
7 (Morozova, Dvoryak, & Altice, 2013)	90 days	1. % of patients completing 90 days of TB treatment and continuing with treatment at the end of the study; 2. Time to discontinuation of TB treatment; 3. Percentage of dosage of TB medications taken over the 90 days of observation; 4. Disposition of study participants
8 (Dvoriak et al., 2014)	20 weeks	1. ASI; 2. Time Line Follow-Back; 3. Risk Assessment Battery
Footnotes		BBV - Blood borne viruses

Table 1 Key characteristics of the published papers on opioid substitution treatment (OST) in Ukraine (continued)

	Main exposure	Sample size	Setting for sample enrollment
1 (Bruce, Dvoryak, Sylla, & Altice, 2007)	-	207 patients on BMT	
2 (Lawrinson et al., 2008)	Time on OST: BMT (baseline vs. 3 months vs. 6 months)	726 participants from Australia, China, Indonesia, Iran, Lithuania, Poland, Thailand and Ukraine (N=72 in Ukraine)	Drug addiction treatment centers or drug clinics
3 (Schaub, Subata, Chtenguelov, Weiler, & Uchtenhagen, 2009)	Time on OST: BMT (baseline vs. 6 months vs. 12 months)	151 patients on BMT	Existing drug addiction treatment places
4 (Schaub, Chtenguelov, Subata, Weiler, & Uchtenhagen, 2010)	Time on OST: BMT and MMT (baseline vs.6 months)	331 opioid dependent patients (191 of them received buprenorphine; 140 received methadone)	Existing drug addiction treatment places
5 (Alistar, Owens, & Brandeau, 2014)	Different strategies : 1. Status quo; 2. Moderate methadone coverage; 3. High methadone coverage; 4. Moderate mixed (methadone + ART); 5. High treatment coverage; 6. High methadone High treatment coverage	-	-
6 (Bachireddy et al., 2014)	Levels of healthcare integration: 1. Integrated &co-located sites (ICL); 2. Non-co-located sites; 3. (NCL), harm reduction and outreach (HRO).	296	OST sites* Harm reduction and outreach
7 (Morozova, Dvoryak, & Altice, 2013)	Prescription and receiving MMT	90	TB dispensary
8 (Dvoriak et al., 2014)	HIV status	50	Kyiv outpatient drug addiction treatment sites
Footnotes	OST - opiate substitution treatment BMT - buprenorphine maintenance treatment MMT - methadone maintenance treatment		* OST sites - Integrated &co-located and non-co-located

Table 1 Key characteristics of the published papers on opioid substitution treatment (OST) in Ukraine (continued)

	Inclusion criteria	Measures of association
1 (Bruce, Dvoryak, Sylla, & Altice, 2007)	HIV positive; Opioid dependent PWIDs; 18+; 2+ non-pharmacological drug treatment attempts; Interested in buprenorphine	-
2 (Lawrinson et al., 2008)	Being on OST less than 2 weeks	F = repeated-measures analysis of variance test statistics; χ^2 -Friedman test statistics
3 (Schaub, Subata, Chtenguelov, Weiler, & Uchtenhagen, 2009)	Willing to start a BMT; Dependence diagnosis for opiates according to ICD- 10; 18+; No signs of severe cognitive impairment, mental retardation, severe behavior, disturbances or psychotic syndrome. Living in permanent residence in the study city	F = repeated-measures analysis of variance test statistics; χ^2 -Friedman test statistics
4 (Schaub, Chtenguelov, Subata, Weiler, & Uchtenhagen, 2010)	Willing to start a BMT; Dependence diagnosis for opiates according to ICD- 10; 18+; No signs of severe cognitive impairment, mental retardation, severe behavior, disturbances or psychotic syndrome. Living in permanent residence in the study city	F = repeated-measures analysis of variance test statistics; χ^2 -Friedman test statistics
5 (Alistar, Owens, & Brandeau, 2014)	Projections were made both for PWIDs and non PWIDs	Cost effectiveness of different strategies (Incremental cost-effectiveness ratio)
6 (Bachireddy et al., 2014)	HIV infected patients/harm reduction clients	Chi-square tests or independent t-tests, multivariate linear regression
7 (Morozova, Dvoryak, & Altice, 2013)	Opioid dependent persons with confirmed pulmonary TB diagnosis who were prescribed at least 90 days of inpatient TB treatment from baseline enrollment 18+	Chi-square test or independent T-test for sample characteristics; Kaplan – Meier analysis with Log rank (Mantel-Cox) test of equality of survival distributions; Binary logistic regression
8 (Dvoriak et al., 2014)	1 year and more opioid addicted individuals seeking outpatient treatment in Kyiv 18+ Not planning to move Willing to participate in daily observed dosing	ANOVA Differences within group across time

Footnotes

Table 1 Key characteristics of the published papers on opioid substitution treatment (OST) in Ukraine (continued)

	Main result	Message
1 (Bruce, Dvoryak, Sylla, & Altice, 2007)	The existing infrastructure allows for further scale-up of and administration of BMT (buprenorphine maintenance treatment) and the possibility of co-administration with ARV.	Despite the barriers and obstacles, implementation of opioid substitution treatment is both feasible and achievable.
2 (Lawrinson et al., 2008)	Treatment retention at 6 months was uniformly high (70% for Ukraine)	The study showed that OST can be as effective in low-and middle-income countries as in the developed countries.
3 (Schaub, Subata, Chtenguelov, Weiler, & Uchtenhagen, 2009)	Substance use decreased significantly for opiate use (p<0.001)	Successful and adequate implementation of OST in Ukraine is feasible, therefore scale-up is recommended.
4 (Schaub, Chtenguelov, Subata, Weiler, & Uchtenhagen, 2010)	Use of other opioids decreased significantly (p<0.001).	Data supports successful implementation of OST in Ukraine among drug users who mainly use self-made opioids. Results advocating for feasibility of both BMT and MMT.
5 (Alistar, Owens, & Brandeau, 2014)	Offering methadone substitution therapy to 25% of PWIDs - the most cost-effective strategy in averting infections (4,700 and adding QALYs (76,000) compared with no intervention at cost US\$530/QALY gained.	Methadone substitution therapy is a highly cost-effective option for the epidemic that is currently described in Ukraine.
6 (Bachireddy et al., 2014)	Participants from integrated and co-located sites (ICL) had significantly higher QHI composite score compared to participants from non-located and harm reduction sites (NCL and HRO): 71.9% vs 54.8% vs 37.0%, p <0.001) after controlling for potential confounders.	OST alone improves health-related quality of life. Integration of services improves healthcare quality indicators.
7 (Morozova, Dvoryak, & Altice, 2013)	In multivariate analysis receipt of MMT was uniquely associated with completing 90 days of TB treatment	MMT integrated into inpatient TB treatment greatly improves retention in TB treatment and TB adherence among PWIDs
8 (Dvoriak et al., 2014)	Significant reductions in the use of heroin and other opiates for both HIV positive and HIV negative (p<0.0001)	Methadone maintenance was well accepted by both HIV+ and HIV – opioid dependent individuals and was associated with reduction of drug use and HIV risk behaviors

Footnotes

Table 1 Key characteristics of the published papers on opioid substitution treatment (OST) in Ukraine (continued)

	First author's institution
1 (Bruce, Dvoryak, Sylla, & Altice, 2007)	Yale University AIDS program, USA.
2 (Lawrinson et al., 2008)	World Health Organization Collaborating Centre for Research in the Treatment of Drug and Alcohol Problems, Australia.
3 (Schaub, Subata, Chtenguelov, Weiler, & Uchtenhagen, 2009)	Research Institute for Public Health and Addiction, Switzerland.
4 (Schaub, Chtenguelov, Subata, Weiler, & Uchtenhagen, 2010)	Research Institute for Public Health and Addiction, Switzerland.
5 (Alistar, Owens, & Brandeau, 2014)	Department of Management Science and Engineering, Stanford University, USA .
6 (Bachireddy et al., 2014)	Yale University School of Medicine, Department of Medicine, Section of Infectious Diseases, AIDS Program, New Haven, USA
7 (Morozova, Dvoryak, & Altice, 2013)	Ukrainian Institute on Public Health Policy
8 (Dvoriak et al., 2014)	Ukrainian Institute on Public Health Policy

Footnotes

(Cohen, 2010; Golovanevskaya, Vlasenko, & Saucier, 2012; Filipovych et al., 2013).

DISCUSSION

Numerous previous studies, literature reviews, and systematic reviews have documented the effect of opioid substitution treatment on drug-related behaviors. Among the documented outcomes are injection risk behaviors (injecting use and sharing of equipment) which were shown to be statistically significantly lower for those who were on opioid substitution treatment (Amato et al., 2005; Clausen, Waal, Thoresen, & Gossop, 2009; Gowing, Farrell, Bornemann, Sullivan, & Ali, 2011; MacArthur et al., 2012). Studies from Ukraine have reported similar outcomes, showing statistically significant reduction in injection risk behaviors using BBV-TRAQ (Lawrinson et al., 2008; Schaub et al., 2010; Schaub et al., 2009), RAB (Dvoriak et al., 2014) and measures of 'drug injection' and 'less than daily drug injection' (Bachireddy et al., 2013).

Given the risk of HIV epidemic generalization in Ukraine (Des Jarlais et al., 2012; Mazhnaya et al., 2014), sexual behavior among PWIDs should be considered as an important outcome when studying any intervention related to reducing HIV risk. However, Ukrainian studies on OST have not been much oriented at reporting and discussing risky sexual behaviors change, some of which (multiple sexual partners and commercial sex) were reported in the systematic review to be lower for those on OST (Gowing et al., 2011). The results from Ukrainian studies for risky sexual be-

havior are somewhat mixed showing no difference for methadone and statistically significant reduction for buprenorphine (Schaub et al., 2010; Schaub et al., 2009) in one study and reduction among methadone patients in another study (Dvoriak et al., 2014). These mixed results could be explained by small sample size in the latter study or by differences in instruments used to measure sexual risk behavior.

One of the most frequently discussed outcomes that have been reported in the studies of OST is the retention in treatment which considered a primary outcome and a proxy of treatment effectiveness. Ukrainian studies have reported high retention in treatment in line with the findings from the Cochrane reviews which have shown that methadone and buprenorphine are effective in retaining patients in treatment (Mattick et al., 2009; Mattick, Kimber, Breen, & Davoli, 2008). Ukrainian studies did not find differences in retention for those on methadone vs. buprenorphine, which is different from the previous findings showing that buprenorphine in flexible doses is less effective in retaining patient on treatment (Mattick et al., 2008).

Increase in ART initiation as a core initial goal of OST in Ukraine has been reported in several papers (Bachireddy et al., 2013; Schaub et al., 2010; Schaub et al., 2009), with some discussion of the in-country barriers that prevent full impact of OST on ART initiation. However, none of the Ukrainian papers have reported ART retention for those on OST, which limits comparison with international data (Malta, Strathdee, Magnanini, & Bastos, 2008).

Among other outcomes that have been reported but less discussed in

Ukrainian studies are the measures of quality of life, such as employment, legal status, and family problems (Schaub et al., 2010; Schaub et al., 2009) which have improved after entering the treatment. One paper has specifically discussed health-related quality of life and showed that integration of services improves the utilization of health care services related to HIV, TB and addiction (Bachireddy et al., 2013); however, general health, physical and mental scores were indistinguishable for different levels of integration. Statistically significant differences for health-related QoL scores were found between those who receive OST and those who do not receive OST. Improved TB treatment outcomes among those on MMT compared to those who are not have been specifically investigated and confirmed by another Ukrainian study (Morozova et al., 2013)

Quality of life of those entering OST program is widely discussed in international literature (Jessica De Maeyer, Vanderplasschen, & Broekaert, 2010; J. De Maeyer et al., 2011). This question is especially important within the context of scaling up the program which was greatly supported in the paper that modeled the impact of OST and ART programs on HIV epidemic in Ukraine (Alistar et al., 2011). Research that would allow going beyond the HIV prevention aim of the OST can add substantially to the development of the program. Recent review showed that QoL indicators measured by WHOQOL-BREF and ASI improved among OST patients regardless of the follow-up period (Feelemyer, Jarlais, Arasteh, Phillips, & Hagan, 2013). However, not all domains have shown improvement. Therefore, further

research is needed to investigate and understand how the OST program impacts the life of opioid dependent people through the complex concept of quality of life and different social factors that are at play for opioid-dependent people.

There are several limitations that should be noted with regard to the reviewed papers. Among the published papers, five used data from cohort studies, one from cross-sectional and one was descriptive. None of the studies assessed directly the impact of OST on the risk of HIV transmission and other related outcomes. Moreover, one study reported lower percentage of HIV infected OST patients after 12 months of follow-up in a defined cohort and did not address this issue in the discussion (Schaub et al., 2009). Among other limitations is that only one cross-sectional study (Bachireddy et al., 2013) used randomization process for participants selection. Furthermore, studies were limited to a few regions of Ukraine which were either OST pilot regions (Lawrinson et al., 2008; Schaub et al., 2010; Schaub et al., 2009) or the regions with the longest history of OST (Bachireddy et al., 2013; Dvoriak et al., 2014; Morozova et al., 2013) which limits the generalizability of results. We also understand that our review may be prone to the publication bias. It is important to notice that majority of the leading authors were of foreign background, therefore, results of the studies that were conducted by in-country scientific community are less presented in the peer-reviewed literature. To overcome this limitation, the academic community should be encouraged to publish on these topics in the peer-reviewed international literature. Another important observation is the evident gap between

the data collection and publishing the results of the studies (1–3 years). This delay have been shown for many research areas; however, it still prevents managers from using scientific data for their programmatic decisions.

Results from reviewed papers provide evidence to conclude that OST in Ukraine is a viable approach towards reducing injection risk behaviors and illegal activities both among HIV-positive and HIV-negative PWIDs, providing retention in treatment and improving health outcomes and therefore reducing risk of HIV infection as well as improving health related QoL. Published papers provide background for wider scale-up of the program, nevertheless, further research is needed to understand how the program could be more tailored to the needs of the opioid-dependent drug users applying the patient-oriented service provision within the Ukrainian context.

P.S.

At the moment of publication of this review we acknowledge that several important new papers, which were published after the final submission, have not been included in this review. These publications mainly explore discourses of desire within OST programs (Carroll, 2015), challenges to implementing OST in prisons (Polonsky et al., 2015), and geographic variability of OST programs (Zaller et al., 2015) in Ukraine.

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