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Feasibility of Buprenorphine Maintenance Therapy Programs in the Ukraine: First Promising Treatment Outcomes

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Key Words

Buprenorphine • Human immunodeficiency virus • Injection drug use • Opiate substitution therapy • Ukraine

Abstract

Background: Opiate substitution therapy (OST) in the Ukraine was not provided until 2004. As part of the introduction of OST, the first feasibility study was conducted in 2007. Six clinics in 6 cities were involved in providing OST and collecting data. **Methods:** A total of 151 opiate-dependent patients were given buprenorphine as a substitute, and a survey of substance use, HIV transmission risks, and legal and social status was conducted at baseline and at 6 and 12-month follow-up. **Results:** Illegal substance use and illegal activities and incomes were highly reduced, whereas employment rates and psychiatric problems improved. Retention was comparatively high (79.5%) after 12 months. No significant adverse events were reported. **Conclusion:** A successful implementation of OST in the Ukraine is feasible.

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Introduction

Opiate substitution treatment (OST) has recently been shown to achieve similar positive outcomes in numerous countries with incomes ranging from low to high. Outcomes include the reduction of heroin and other illicit opiate use, the reduction of HIV exposure-risk behaviors associated with injection drug use, the decrease of criminal activities and the improvement of physical and mental health [1]. As part of this international study a first feasibility study was performed in Ukraine, whose 12-month treatment data will be described in detail in the current report.

According to a recent WHO estimation [2, 3] there are between 325,000 and 425,000 injection drug users (IDUs) in Ukraine, of whom 144,000 are estimated to be HIV positive. To our knowledge, there are currently no estimations or exact numbers for the mortality rate among IDUs.

Despite this high prevalence of IDUs, until 2004 drug treatment programs relied on detoxification and abstinence-based rehabilitation in so called ‘narcological centers’ [4]. Because of political and clinical mistrust of OST,

buprenorphine was the only medication available for OST between 2004 and 2007. With the collaboration of the World Health Organization (regional office for Europe), the International HIV/AIDS Alliance, the Ukrainian Institute for Public Health Policy and the management and staff of existing treatment sites, the implementation of 6 buprenorphine maintenance treatment (BMT) sites started at the beginning of 2006. In June 2007, methadone was approved by the Ukrainian Ministry of Health and will now also be made available for maintenance treatment. Nevertheless, the number of IDUs receiving agonist maintenance is still very low and the vast majority of IDUs have not yet been reached by OST [4].

There are several specific aspects of opioid use patterns in the Ukraine that have to be kept in mind. Most Ukrainian IDUs do not use heroin but a self-made opioid called 'shirka', which is prepared from poppy straw in a common container shared among several users. A contaminated needle can result in contaminating the whole shirka and infecting other users. Also, ready-made shirka is available in preloaded unsterile syringes. These tend to be re-used and carry a high risk for contamination as they have usually been already used by the drug dealers themselves [5, 6].

In addition to the low availability of agonist maintenance in the Ukraine, access to antiretroviral therapy (ART) for IDUs was and still is low, and clinicians have tended to refuse ARTs to active IDUs, believing that they would be poorly adherent [4]. However, recent evidence has emerged that integrating ART and OST in HIV-positive IDUs can optimize outcomes for both opiate addiction and HIV infection status [7].

This publication reports the first year treatment data of the first 6 buprenorphine treatment sites in the Ukraine (Kiev City AIDS center and Sociotherapy clinic, Donetsk Narcological Dispensary, Odessa Oblast Narcological Dispensary, AR Crimea Republican Narcological Dispensary, Dnijpropetrovsk Narcological Dispensary and Mykolaiv Narcological Dispensary). More precisely, it focuses on the description of the outcomes of opiate-dependent patients in this BMT program at baseline and at 6- and 12-month follow-up.

Methods

Study Population

Since BMT started in 6 already existing treatment places, patients were asked if they were willing to start a BMT during a recruitment period of 2–3 months. At the beginning of the recruitment, this new treatment possibility was demanded by almost ev-

ery patient (n = 176). A patient recruitment list was prepared for documenting the basic characteristics of persons applying for OST at the sites, for documenting their eligibility and their eventual admittance to the program by treatment staff at their sites. Patients with signs of severe cognitive impairment, mental retardation, severe behavior disturbances or psychotic symptoms were excluded from the study. Furthermore, patients who were expecting hospitalization or imprisonment were also excluded. In order to be eligible for participation in the study, patients had to fulfil dependence diagnosis for opiates according to ICD-10, be at least 18 years old, be living in permanent residence within commuting distance of the respective OST clinic and provide informed consent to treatment and the treatment regime, including blood testing, and to their participation in the study follow-up interviews. 153 eligible patients were recruited for the OST program and the study. Only 2 patients refused to give informed consent. Finally, a total of 151 patients were included in the study.

Patients had to ingest their individual dose of buprenorphine at the OST site on a daily basis. According to the Ukrainian guidelines for good practice in BMT, higher buprenorphine doses were prescribed at the beginning of treatment to suppress withdrawal syndromes (typically 12–14 mg). The doses were then gradually reduced to the maintenance dose, which usually was from 2 to 8 mg. For the most part, this was on the initiative of the patients, who usually had plans to leave the program in the long run due to the inconvenience of coming each day to be supervised while they took the BMT. Patients were also tested for HIV in the first 2 weeks of the BMT study. Hepatitis B and C status were taken from the medical records at the beginning of the study. Care was provided to seropositive patients outside the OST sites by AIDS centres (further HIV testing, laboratory monitoring and ART provision). All OST and HIV/AIDS services were free of charge.

Treatment Staff and Monitoring

At all sites, relevant professionals (doctors, psychiatrists, nurses, psychologists, and social workers) were in the team taking care of the somatic, psychiatric, psychological and social needs of patients. In all teams at all project sites, competence to work with drug-dependent persons was assured by recurring training according to the Ukrainian guidelines for good practice in BMT, as well as by supervision on request. The monitoring and evaluation protocol and plan was developed at the Research Institute for Public Health and Addiction at Zurich University, in consultation with the WHO Euro-office, the International HIV/AIDS Alliance, the OST program managers and the Ukrainian Institute of Public Health Policy. An international consultant from Vilnius University visited all OST sites.

Data Collection

Patient descriptions, baseline and follow-up data (6 and 12 months after intake) were collected by use of a clinical record form. An external interviewer assessed history and patterns of substance use with the Addiction Severity Index (ASI) [8] at baseline and follow-up. Furthermore, the external interviewer administered the Blood-Borne Virus Transmission Risk Assessment Questionnaire BBV-TRAQ [9] at baseline and follow-up to determine risk behaviors. The Ukrainian Institute of Public Health Policy translated both questionnaires into Ukrainian. Data on status, regime, treatment received, adverse events, compliance and termination were entered daily by OST treatment staff into

standardized patient records prepared by the same institute. Patients who dropped out of the study were contacted if possible in order to find out more about their reasons for dropping out and to motivate them to participate in the nearest follow-up interview. Reasons for dropout were noted on the patients' clinical report forms.

Data Management and Analyses

Data were transmitted electronically to the Ukrainian Institute of Public Health Policy and entered into a relational database. All patient data were coded and recorded anonymously. Differences between baseline and follow-up data were tested by repeated-measures analysis of variance test statistic for those patients who stayed in treatment. In case of categorical variables, applicable data percentages were specified and χ^2 tests for dependent and independent samples were applied, respectively. The reasons why patients dropped out of the study were reported on the clinical report form. Finally, a Cox regression analysis for months in treatment was performed to investigate effects of baseline characteristics, mean buprenorphine dose, baseline HIV status, and baseline ASI and BBV-TRAQ scores as predictors. Dropouts' baseline data were further compared with baseline data of those patients who reached the 12 month follow-up. $P < 0.05$ was considered statistically significant. All data were analyzed with the statistical software package SPSS, version 15.

Results

Sample Characteristics

A total of 151 BMT patients entered the study at baseline. Seventy-five percent of all patients were male, had an average age of $35.2 (\pm 7.7)$, declared on average $10.8 (\pm 2.0)$ years of education and $1.8 (\pm 1.9)$ years of professional education. More than half of all patients were married (54.3%), only 4.6% stated they lived in irregular housing conditions (homeless) and 38.1% stated they held a legally paid job. By far the longest history of substance use related to 'other opiates' (13.5 ± 7.6 years), followed by cannabis use (6.6 ± 8.8 years) and polydrug use (6.0 ± 6.3 years). In contrast, the use of other substances, and especially of heroin, was more recent. Barbiturate use went back 1.4 ± 3.0 years and the use of sedatives and tranquillizers 2.7 ± 4.5 years. Accordingly, the range of drug use history was greatest between use of other opiates (almost exclusively shirka) and use of heroin.

The large majority of former treatments received were for drug problems, with an average of $5.6 (\pm 7.8)$ treatments per patient. Previous treatments for alcohol problems (0.1 ± 0.6 episodes) and psychiatric problems (0.3 ± 0.9 episodes) were much less frequent. 75.3% of all patients had been arrested at least once. 15.2% of all patients had been participating in groups of Alcoholics Anonymous or Narcotics Anonymous.

More than half of all patients (51.7%) were found to be HIV positive at entry into the program. In regard to the infection stage, clinical AIDS syndrome was diagnosed in 12.3% of the HIV infected patients at baseline. Hepatitis C virus seropositivity was reported in 15.8% (17.2% missing) of patients and the rate for hepatitis B seropositivity was 3.3% (17.2% missing). There was a deficit in tuberculosis diagnosis (9.5% were tuberculosis positive but data were missing in 62.9% of patients).

Treatment Outcomes

Substance use (last 30 days) decreased significantly for other opiate use ($F_{120; 119} = 187.864, p < 0.001$), on the ASI alcohol ($F_{120; 119} = 5.451, p < 0.05$) and drug score ($F_{120; 119} = 197.265, p < 0.001$) between baseline, 6 and 12 month follow-up (table 1). Meanwhile, the mean buprenorphine dosage remained approximately the same ($F_{120; 119} = 0.423, n.s.$), but the prescription of ART medication increased ($\chi^2_{120; 2} = 44.912, p < 0.001$).

The occurrence of somatic disorders decreased for digestion ($\chi^2_{120; 2} = 9.234, p < 0.01$) and urination ($\chi^2_{120; 2} = 11.375, p < 0.01$) problems. Moreover, fewer patients were HIV positive ($\chi^2_{120; 2} = 102.282, p < 0.001$) and patients' ASI medical score improved ($F_{120; 119} = 6.831, p < 0.05$) after 12 months. Psychiatric problems were also less observed as measured by the ASI psychiatric problems score ($F_{120; 119} = 46.015, p < 0.001$).

Concerning the BBV-TRAQ (transmission risk behaviors), there were considerable decreases for injection virus transmission risk behaviors ($F_{120; 119} = 51.209, p < 0.001$) and somewhat less pronounced for sexual virus transmission risks ($F_{120; 119} = 8.165, p < 0.01$). The BBV-TRAQ skin penetration scores did not change over the 12-month period ($F_{120; 119} = 0.010, n.s.$).

Employment (paid working days) $F_{120; 119} = 14.767, p < 0.001$; ASI score employment ($F_{120; 119} = 5.295, p < 0.05$) and legal status (criminal activity last 30 days) $F_{120; 119} = 22.127, p < 0.001$; ASI score for legal problems $F_{120; 119} = 51.154, p < 0.001$; persons with illegal problems $\chi^2_{120; 2} = 35.121, p < 0.001$ improved consistently in all applied measures over time (table 1). The same was the case for the ASI family problems score ($F_{120; 119} = 16.223, p < 0.001$), emotional abuse ($F_{120; 119} = 16.266, p < 0.001$) and sexual abuse ($F_{120; 119} = 9.735, p < 0.01$).

Last but not least, the number of HIV-positive patients in treatment who received ART medication increased during the study period ($\chi^2_{42; 2} = 44.912, p < 0.001$).

Table 1. Baseline, 6- and 12-month follow-up of BMT

	Baseline	6 months	12 months	F/ χ^2	P
Patients, n (% of baseline)	151 (100.0)	129 (85.4)	120 (79.5)	–	–
Medication					
Buprenorphine dosage, mg/day	10.4 ± 3.7	9.9 ± 4.3	10.2 ± 4.3	0.423	n.s.
BMT treatment regime change, %	–	23.3	11.2	0.210	n.s.
Antiretroviral medication, %	10.6	18.9	28.3	19.143	<0.001
Substance use in last 30 days ^a					
Heroin	0.1 ± 0.6	0.0 ± 0.0	0.0 ± 0.0	2.818	n.s.
Other opiate	18.4 ± 12.7	0.1 ± 0.9	0.3 ± 1.7	187.864	<0.001
Sedative	5.5 ± 9.7	2.2 ± 5.9	2.5 ± 6.8	2.487	n.s.
Alcohol intoxication	0.6 ± 3.5	0.3 ± 1.7	0.4 ± 1.5	0.049	n.s.
Cocaine	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–	
Amphetamines	0.3 ± 2.5	0.0 ± 0.0	0.6 ± 2.7	0.388	n.s.
Inhalants	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–	
ASI score alcohol	0.1 ± 0.1	0.0 ± 0.1	0.0 ± 0.1	5.451	<0.05
ASI score drugs	0.3 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	197.265	<0.001
Somatic disorders					
Normal weight, %	55.8	59.8	58.1	3.407	n.s.
Trophic ulcer, %	7.5	3.3	2.7	4.571	n.s.
Digestion problems, %	28.6	13.9	19.8	9.234	<0.01
Urination problems, %	10.3	0.8	4.5	11.375	<0.01
Sexual problems, %	13.6	11.5	11.7	1.188	n.s.
HIV positive, %	51.7	51.7	27.2	102.282	<0.001
ASI score medical	0.3 ± 0.3	0.2 ± 0.3	0.2 ± 0.2	6.831	<0.05
Risk taking behaviour (BBV-TRAQ)					
Injecting score	12.4 ± 11.8	1.1 ± 2.5	2.4 ± 5.1	51.209	<0.001
Sexual score	7.8 ± 7.9	4.7 ± 6.6	5.0 ± 6.7	8.165	<0.01
Skin penetration score	2.6 ± 3.2	1.3 ± 2.2	2.6 ± 10.2	0.010	n.s.
Psychiatric problems (ASI score)	0.3 ± 0.2	0.1 ± 0.2	0.1 ± 0.2	46.015	<0.001
Employment and legal status					
Paid working days in last 30 days	8.4 ± 11.3	14.2 ± 11.8	14.4 ± 11.3	14.767	<0.001
ASI score employment	0.7 ± 0.2	0.7 ± 0.3	0.7 ± 0.3	5.295	<0.05
Criminal activity in last 30 days ^a	3.9 ± 8.6	0.3 ± 1.6	0.0 ± 0.0	22.127	<0.001
ASI score for legal problems	0.2 ± 0.2	0.1 ± 0.1	0.1 ± 0.1	51.154	<0.001
Persons with illegal income last 30 days, %	26.5	4.7	2.8	35.121	<0.001
Family problems					
ASI score family	0.2 ± 0.2	0.1 ± 0.1	0.1 ± 0.1	16.223	<0.001
Emotional abuse (last 30 days) ^a	1.3 ± 0.5	1.2 ± 0.4	1.1 ± 0.3	16.266	<0.001
Physical abuse (last 30 days) ^a	1.1 ± 0.3	1.0 ± 0.2	1.0 ± 0.1	9.735	<0.001

F = Repeated-measures analysis of variance test statistic; χ^2 = Friedman test statistic.

^a Data are mean ± SD number of instances in last 30 days.

Dropouts

A total of 22 (14.6%) patients dropped out of the study after the 6-month follow-up and an additional 9 (5.9%) patients dropped out after the 12-month follow-up. Reasons for these 33 (20.5%) dropouts were: systematic non-attendance and intake of illegal drugs (11 patients); imprisonment (6 patients); treatment regime violation (2 patients); absence of euphoric sensations so the patient wished to stop treatment (8 patients); move to a '12-step'

rehabilitation program (1 patient), move to religious rehabilitation center (1 patient); admission to hospital (1 patient); move to another city (1 patient); unknown (1 patient), and hospitalization followed by death in hospital (1 patient). None of the dropout patients could be motivated for the next follow-up interview.

The Cox regression for month in treatment ($\chi^2_{148; 23} = 33.641$, n.s.) revealed no significant effects on patients who dropped out for the covariates age, sex, age of first

drug use, years of use of the assessed substances and poly-drug use, years of previous drug treatments, average buprenorphine dose, baseline HIV status, baseline ASI and BBV-TRAQ scores. Patients who dropped out differed at baseline from the patients staying in treatment on the ASI drugs domain score (dropouts 0.34 ± 0.13 , others 0.25 ± 0.13 , $t_{151; 149} = 3.491$, $p < 0.001$), family domain score (dropouts 0.29 ± 0.21 , others 0.19 ± 0.19 , $t_{151; 149} = 2.447$, $p < 0.05$) and the psychiatric domain score (dropouts 0.35 ± 0.18 , others 0.25 ± 0.20 , $t_{151; 149} = 2.676$, $p < 0.01$). Dropouts further differed on the baseline BBV track-score injecting practices (dropouts 16.55 ± 10.40 , others 11.30 ± 11.88 , $t_{151; 149} = 2.246$, $p < 0.05$) and sexual practices (dropouts 5.03 ± 6.80 , others 8.55 ± 8.07 , $t_{151; 149} = -2.230$, $p < 0.05$). There were no significant differences between the dropouts and the patients staying in treatment for buprenorphine dose at baseline (dropouts 10.98 ± 3.22 mg/day, others 10.31 ± 3.76 mg/day, $t_{151; 149} = 0.896$), mean buprenorphine dose (dropouts 10.97 ± 3.24 mg/day, others 10.10 ± 3.55 mg/day, $t_{151; 149} = 1.306$), HIV status at baseline (dropouts 1.55 ± 0.55 , others 1.45 ± 0.51 , $t_{148; 146} = 0.944$), in the duration of all assessed lifetime substance use (e.g. years of other opiates: dropouts 11.68 ± 7.77 , others 14.03 ± 7.47 , $t_{151; 149} = 1.548$) and in the numbers of previous addiction treatment stays (dropouts 5.46 ± 7.07 , others 6.13 ± 10.20 , $t_{151; 149} = 0.427$).

Discussion

The study outcomes during the 12 months of treatment were impressive. There were large reductions in use of illegal and non-prescribed substances, illegal activities, illegal incomes and risk-taking behaviors. Patients' employment rates increased and their psychiatric problems improved.

It also revealed that the target group of chronic Ukrainian opiate (shirka) users, who were relapsing after many previous drug-free treatments, were willing to enter OST and that the great majority remained in treatment during a 1-year observation period. This study also documented that almost all patients gave their consent to participate in an extensive data collection used for evaluation purposes. Getting their medication at the OST sites by daily supervised intake restricted their freedom to work and relaxation during weekends and vacations.

The reason why one fifth of patients dropped out of the study could be ascribed to the usual dropout reasons for these types of studies (systematic non-attendance and intake of illegal drugs, absence of euphoric sensations

and therefore the patient wishing to stop treatment) for patients who tended to carry a higher burden of drug, family and psychiatric problems at baseline. However, these dropout rates could also have emerged from specific Ukrainian OST prescription regulation problems (some patients had to be admitted to hospital, or were imprisoned within the 12 months, although patients who were expecting hospitalization or imprisonment were excluded from the study at baseline).

Thus, one of the biggest obstacles that emerged during the study period was that OST could not be continued for patients who had to be hospitalized. Hospitals had no license to store controlled medications. Likewise, imprisonments lead to interruption of substitution treatment. Another problem that emerged during the study was that although the provision of ART medication for HIV-positive patients at the AIDS centers increased during the 12 months, we must assume that not all patients who would profit from ART medication actually received it.

The main strength of the current study is that it provides the first systematically collected data on the feasibility of OST in Ukraine and in a comparatively large sample of specific homemade opiate (shirka) injectors. However, there are also some limitations to the current study: (1) it had to rely on self-declaration when assessing frequency of substance use, since systematic urine testing would have been too expensive; (2) patients were recruited within already existing (previously abstinence-oriented) treatment places what could have led to a selection bias; (3) there were some language restrictions (e.g. the ASI and the BBV-TRAQ had to be translated into Ukrainian but could not be validated as part of the current study).

In consideration of the current study results, we conclude that a successful and adequate implementation of OST in the Ukraine is feasible. Scale-up of OST in the Ukraine is highly recommended.

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References

- 1 Lawrinson P, Ali R, Buavirat A, Chiamwongpaet S, Dvoryak S, Habrat B, Jie S, Mardiati R, Mokri A, Moskalewicz J, Newcombe D, Poznyak V, Subata E, Uchtenhagen A, Utami DS, Vial R, Zhao C: Key findings from the WHO collaborative study on substitution therapy for opioid dependence and HIV/AIDS. *Addiction* 2008;103:1484–1492.
- 2 UNAIDS: AIDS Epidemic Update: December 2007. Geneva, WHO/UNAIDS.
- 3 WHO, UNAIDS, UNODC: Joint WHO/UNDAIDS/UNODC Mission on Opioid Substitution Therapy in Ukraine. 2005.
- 4 Bruce RD, Dvoryak S, Sylla L, Altice FL: HIV treatment access and scale-up for delivery of opiate substitution therapy with buprenorphine for IDUs in Ukraine: programme description and policy implications. *Int J Drug Policy* 2007;18:326–328.
- 5 Booth RE, Kennedy J, Brewster T, Semerik O: Drug injectors and dealers in Odessa, Ukraine. *J Psychoactive Drugs* 2003;35:419–426.
- 6 Booth RE, Kwiatkowski CF, Mikulich-Gilbertson SK, Brewster JT, Salomonsen-Sautel S, Corsi KF, Sinitsyna L: Predictors of risky needle use following interventions with injection drug users in Ukraine. *Drug Alcohol Depend* 2006;82:S49–S55.
- 7 Sullivan LE, Bruce RD, Haltiwanger D, Lucas GM, Eldred L, Finkelstein R, Fiellin DA: Initial strategies for integrating buprenorphine into HIV care settings in the United States. *Clin Infect Dis* 2006;43:191–196.
- 8 McLellan AT, Kushner H, Metzger D, Peters F: The fifth edition of the Addiction Severity Index. *J Subst Abuse Treat* 1992;9:199–213.
- 9 Fry CL, Lintzeris N: Psychometric properties of the Blood-Borne Virus Transmission Risk Assessment Questionnaire (BBV-TRAQ). *Addiction* 2003;98:171–178.