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People Who Inject Drugs and have tuberculosis: Opioid Substitution Therapy improves treatment outcomes in Ukraine

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Abstract

Introduction: Opioid substitution therapy is one of the pillars of harm reduction strategies for People Who Inject Drugs (PWID). OST should be an integral part of tuberculosis (TB) care to increase the uptake, compliance and effectiveness of treatment and also curtail risk behaviours. We aimed to compare TB treatment outcomes in relation to OST among PWID in six regions of Ukraine.

Methodology: A retrospective cohort study using routine programmatic data from centres offering integrated TB and OST (December 2016 – May 2020). OST involved use of methadone or buprenorphine. TB treatment outcomes were standardized.

Results: Of 228 PWID (85% male) diagnosed with TB, 104 (46%) had drug sensitive and 124 (64%) drug-resistant TB. The majority had pulmonary TB (95%), 64 (28%) were HCV-positive and 179 (78%) were HIV-positive, 91% of the latter were also on ART. There were 114 (50%) PWID with TB on OST. For drug-sensitive TB (n-104), treatment success was significantly higher (61%) in those on adjunctive OST than those not on OST (42%, $p < 0.001$). Similarly, for drug resistant TB (N -124) treatment success was also significantly higher when individuals were on OST (43%) compared to when not on OST (26%, $p < 0.001$).

Conclusions: This operational research study shows that OST is associated with significantly improved treatment success in PWID and can contribute to achieving Universal Health Coverage and the WHO Flagship Initiative "Find. Treat. All. #End TB". We advocate for the scale up of this intervention in Ukraine.

Key words: Tuberculosis; people who inject drugs; opioid substitution therapy; drug sensitive TB; drug resistant TB; Ukraine.

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Introduction

Opioid substitution therapy (OST – using methadone or buprenorphine) is one of the pillars of harm reduction strategies for People Who Inject Drugs (PWID). OST should be an integral part of tuberculosis (TB) care so as to increase the uptake, compliance and effectiveness of treatment and at the same time, curtail risk behaviours [1–6]. PWID are considered a "key population" group who are often socially marginalized and have limited access to health services [7]. They are at a 20 to 50 times higher risk of contracting HIV infection than the general population and contribute to about 10% of all new HIV infections globally [8]. Outbreaks of drug-susceptible and multi-drug resistant TB (MDR-TB) are also common in this group [9]. Finding ways of improving the detection of TB among PWID is important and aligns well with the Sustainable Development Goal (SDG) of achieving Universal Health Coverage for TB and also the WHO Flagship Initiative "Find. Treat. All. #End TB" [10]. Two of the three targets in the WHO and Stop TB Partnership Plan to end TB involve key populations such as PWID. One of these targets aims to ensure that TB diagnostic and treatment services reach at least 90% of all key population groups, while the other aims to achieve a minimum of 90% treatment success [11]. The International Charitable Foundation "Alliance for Public Health" (the Alliance), a Non-Governmental Organization (NGO) in Ukraine, coordinates HIV and TB prevention and care services working with PWID in Ukraine. A unique aspect of their work is the integrated delivery model of "OST with TB care" offered at the same health facility. This overcomes the barrier or vertical and disconnected delivery of such services, which is common in countries of the former Soviet Union [12]. A PubMed search revealed no studies that

have described TB treatment outcomes from NGO health facilities that have integrated OST and TB care among PWID in East Europe and Central Asia. There is very limited research on TB/OST programs implementation available from Ukraine. The study conducted in Kyiv oblast regarding predictors of poor TB treatment outcomes revealed that the country is experiencing and urgent need in programmatic interventions, especially aimed at patients with the highest risk of poor outcomes such as PWID [13]. Another study showed that methadone treatment improves TB treatment among hospitalized opioid dependent patients in Ukraine [14]. Those PWID on OST might have better compliance with TB treatment [15]. On the other hand, there are known drug-drug interactions between methadone and rifampicin and OST is known to reduce cell mediated immunity, all of which might influence TB treatment outcomes [16,17]. The subject of OST for PWID with TB is a recognized research priority in Ukraine and the wider European region. Our experience may thus guide operational strategies to improve integrated TB care for PWID in Ukraine and beyond. Taking into account very limited research on the topic, the authors believe that this paper will play a very important role in provision and scaling up both TB treatment and OST services for PWID. This study aims to compare TB treatment outcomes in relation to being on OST among PWID in six regions of Ukraine. Among PWID, the specific objectives were to determine the a) socio-demographic and clinical characteristics of TB patients who were and were not on OST, and b) TB treatment outcomes in relation to OST.

Methodology

This was a retrospective cohort study using routine programmatic data managed by the Public Health Center of the Ministry of Health of Ukraine.

Study population and study period

The study population included PWID diagnosed with TB and who started TB treatment in six regions of Ukraine. The inclusion criteria were: (a) age 18 and older; (b) having a history of injecting drug use (IDU). The study period was December 2016 to May 2020.

Settings

General setting

Ukraine is the largest country in Eastern Europe with a population of 42 million, and an HIV prevalence of 0.9% [18]. There are an estimated 324,300 PWID in the country: HIV prevalence is 22.6% in this sub-group and 63.9% have concomitant Hepatitis C [19]. The TB incidence rate in PWID is 80 (52-115) per 100,000 population [20]. In Ukraine only 4.25% of the total estimated number of PWID receive OST [12].

The Alliance oversees, supervises and monitors all activities including TB care and harm reduction activities, of non-governmental organizations (NGOs) who work with PWID. Within the Global Fund and PEPFAR grants, the Alliance is the principal recipient and provides sub-grants and ensures regular reporting to donors. There are formal agreements between the Alliance and Ministry of Health of Ukraine. Alliance is a principal recipient of the Global Fund for supervision and implementation of activities conducted by over 100 NGOs involving with PWID in Ukraine. Alliance collaborates closely with the Government and links up closely with existing health facilities.

Specific setting and study sites

The study sites included six TB centres offering integrated TB and OST in six regions (Chernihiv, Dnipro, Donetsk, Kherson, Kyiv, Zhytomyr) of Ukraine. The most frequently used injectable drugs include in graded order are: opium, street methadone, amphetamine type stimulants, hypno-sedatives and hallucinogens. Injection may be through intravenous, intramuscular and subcutaneous routes. Drugs are procured through peers and drug dealers. Self-made concoctions are also common. All NGOs offer a package of health interventions according to WHO guidelines [21], including the provision of sterile injecting equipment through needle and syringe exchange programs.

Management of tuberculosis

The management of TB is according to National and World Health Organisation (WHO) guidelines [22]. Both drug-sensitive and drug-resistant TB are managed at TB clinics by dedicated TB doctors. The Alliance provides integrated services of OST at the selected six TB sites. However, HIV/AIDS management is only available in separate HIV/AIDS clinics. As of now, HCV treatment is not available within the national public health programmes. TB treatment outcomes are standardised and categorized into favourable outcomes (cured + treatment completed) and unfavourable outcomes (lost to follow up, died, failed, not evaluated and not recorded) [22].

Opioid Substitution Therapy

Opioid Substitution Therapy (OST) is also known as “agonist replacement therapy” or “opioid agonist therapy”. OST is defined as the administration under

medical supervision of a prescribed psychoactive substance, pharmacologically related to the one producing dependence. Agents suitable for substitution therapy are those with some opioid properties so that they have the capacity to prevent the emergence of withdrawal symptoms and reduce craving. The available agents for OST include methadone and buprenorphine which are administered orally. The objectives of OST are broad and include: reduction of dependence on illicit drugs; a decrease in morbidity and mortality caused by illicit opioids; reduction in the risk of infectious diseases; improvement of physical and mental health; reduction in criminal behaviour; facilitation of the reintegration of PWID into the workforce and education system and a general improvement in social functioning as a whole [1]. All PWID with active TB are first offered inpatient TB treatment and counselled for OST. The patient can start OST only after discharge from inpatient TB care when he/she is registered with the Narcology service and subsequently the patient can receive OST drugs in the TB facility. When the patient is receiving inpatient TB treatment and OST, the psycho-social support and counselling is provided by NGOs working within the TB clinics under the supervision of the Alliance. TB treatment regimens remain unchanged with OST.

Data management, analysis and statistics

The data were collected from two sources – a national register of TB patients managed by the Public Health Center of the Ministry of Health of Ukraine and a national OST patient register managed by the

Table 1. Characteristics of People Who Inject Drugs (PWID) and with Tuberculosis stratified by use of Opioid Substitution Therapy (OST) in Ukraine (December 2016 – May 2020, N = 228).

	Total	**OST N**	**No-OST N**	**p-value**
N	*228*	*114*	*114*	
Age group				*0.3*
≤ 35 years	36 (15.8)	19 (16.7)	17 (14.9)	
36-40 years	33 (14.5)	34 (29.8)	33 (28.9)	
41-45 years	67 (29.4)	21 (18.4)	34 (28.9)	
46-50 years	55 (24.1)	20 (17.5)	17 (14.9)	
≥ 51 years	37 (16.2)	20 (17.5)	13 (11.4)	
Gender (Female)	36 (15.8)	25 (21.9)	11 (9.6)	*0.02*
Employment status				*0.001*
Employed	9 (4.1)	4 (3.6)	5 (4.5)	
Unemployed of working age	150 (67.6)	78 (70.3)	72 (64.9)	
Pensioner	1 (0.5)	0	1 (0.9)	
Disabled	27 (12.2)	22 (19.8)	5 (4.5)	
Unknown	35 (15.3)	7 (6.1)	28 (24.6)	
Region				*1.0*
Chernihiv	94 (41.2)	47 (41.2)	47 (41.2)	
Dnipro	22 (9.6)	11 (9.6)	11 (9.6)	
Donetsk	26 (11.4)	13 (11.4)	13 (11.4)	
Kherson	30 (13.2)	15 (13.2)	15 (13.2)	
Kyiv	42 (18.4)	21 (18.4)	21 (18.4)	
Zhytomyr	14 (6.1)	7 (6.1)	9 (6.1)	
HIV status (positive)	179 (78.5)	87 (76.3)	92 (80.7)	*0.5*
On ART	163 (91.1)	84 (96.6)	79 (85.9)	*0.03*
HCV status (positive)	64 (28.1)	33 (28.9)	31 (27.2)	*0.9*
TB type				*0.1*
Pulmonary	216 (94.7)	107 (93.9)	109 (95.6)	
Extrapulmonary	12 (5.3)	7 (6.1)	5 (4.4)	
TB diagnostics				*0.6*
Laboratory	157 (68.9)	76 (66.7)	81 (71.1)	
X-ray	67 (29.4)	36 (31.6)	31 (27.2)	
Histologically	1 (0.4)	0 (0.0)	1 (0.9)	
Unspecified	3 (1.3)	2 (1.8)	1 (0.9)	
TB drug resistance type				*0.3*
Drug sensitive	104 (45.6)	56 (49.1)	48 (42.1)	
Mono- + Poly-	15 (6.6)	8 (7.0)	7 (6.1)	
MDR-TB	13 (5.7)	4 (3.5)	9 (7.9)	
XDR	96 (42.1)	46 (40.3)	50 (43.9)	

MDR-TB: Multi-drug resistant TB; XDR: extensively drug-resistant tuberculosis.

Alliance. The variables collected included socio-demographic variables, clinical data on TB, HIV and HCV status, OST related data and TB treatment outcomes. These data were double-entered and analyzed using SAS statistical software (Cary, North Carolina, USA).

We summarized the results using descriptive statistics (numbers, proportions). Differences between groups were assessed using the chi-square test with 95% confidence intervals. Levels of statistical significance were set at $p \leq 0.05$.

Ethical considerations

Permission to use the data was obtained from the Alliance and the National TB Control programme of Ukraine. Ethical approval was received from the Institutional Review Board of the Alliance (Kyiv, Ukraine) followed by the Union Ethics Advisory Group of the International Union against the TB and Lung disease (Paris, France). As we used secondary data, the issue of informed consent did not apply.

Results

Number of PWID with tuberculosis on OST and their characteristics

There was a total of 228 PWID with TB from six regions of Ukraine, 84% were male in the age group 40-50 years (54%) and unemployed (68%). The great majority (216, 95%) had pulmonary TB, 179 (78%) were HIV-positive and 64 (28%) were HCV-positive. 163 (91%) of those HIV-positive (n-179) were also on ART (Table 1).

A total of 114 (50%) studied TB patients were on OST. The characteristics of those who were, and were not, on OST are shown in Table 1**.** Between those on OST and those not on OST, females, employment status and ART showed significant differences. The HIV prevalence among OST patients was 76% while among non-OST this was 81% and 97% of those on OST were on ART while this was 86% for those not on OST (P-0.03). The prevalence of HCV in the cohort was 28%.

TB treatment outcomes in relation to OST

Drug-sensitive TB

Of the 228 PWID with TB, 104 (46%) had drug sensitive TB. Standardized TB treatment outcomes for drug sensitive TB are shown in Table 2a. Overall treatment success was 52%. Treatment success was significantly higher (61%) in those on adjunctive OST than those not on OST (42%, $p < 0.001$).

Drug-resistant TB

There were 124 (54%) PWID with drug resistant TB (96 XDR-TB, 13 MDR-TB and 15 with mono/poly resistance, Table 1). The overall treatment success for drug resistant TB was at a low 34% (Table 2b), but significantly higher when individuals were on OST (43%) compared to when not on OST (26%).

Table 2a. Drug-sensitive tuberculosis treatment outcomes in People Who Inject Drugs stratified by Opioid Substitution Therapy (OST) in Ukraine (December 2016 – May 2020, N = 104).

TB treatment outcomes	Drug sensitive TB (N = 104)			
	Total N (%)	OST N (%)	No-OST N (%)	p -value[1]
Favorable outcomes[2]	54 (52)	34 (61)	20 (42)	< 0.001
Unfavorable outcomes	50 (48)	22 (39)	28 (58)	
- Failure	24 (23)	12 (21)	12 (25)	0.03
- LTFU	10 (10)	4 (7)	6 (13)	< 0.004
- Died	16 (15)	6 (11)	10 (21)	< 0.001
Total	**104**	**56**	**48**	

LTFU: Lost to Follow up; [2] Includes cured and treatment completed.

Table 2b. Drug-resistant** Tuberculosis treatment outcomes in People Who Inject Drugs stratified by Opioid Substitution Therapy (OST) in Ukraine (December 2016 – May 2020, N = 124).

TB treatment outcomes	Drug resistant TB (N=124)			
	Total N (%)	OST N (%)	No-OST N (%)	p-value[1]
Favorable outcomes[2]	42 (34)	25 (43)	17 (26)	< 0.001
Unfavorable outcomes	72 (66)	33 (57)	49 (74)	
- Failure	30 (24)	13 (22)	17 (26)	< 0.001
- LTFU	22 (18)	8 (14)	14 (21)	0.002
- Died	30 (24)	12 (21)	18 (27)	0.03
Total	**124**	**58**	**66**	

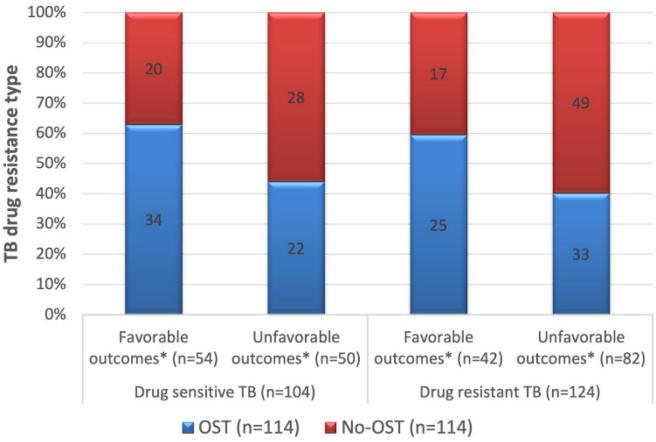
LTFU: Lost to Follow up; [1] X^2 test for categorical variables; [2] Includes cured and treatment completed.

Discussion

To our knowledge, this is the first study from an NGO setting in Eastern Europe that has assessed TB treatment outcomes in relation to OST among PWID with a high HIV and HCV prevalence. Half of all PWID were placed on OST and in this group, TB treatment outcomes were significantly better for both drug-sensitive and drug resistant TB (Figure 1). Moreover, to our knowledge this is the first study conducted in Ukraine to compare the TB treatment outcomes among PWID on and not on OST, and our findings are compliant with the results of very limited previously conducted in Ukraine research on the topic [14]. Our results are also in line with similar studies conducted worldwide [23,24]. This study is an important step towards achieving the STOP-TB target of ensuring that TB diagnostic and treatment services reach at least 90% of key populations. Reaching out to those left out of the health system is also pivotal for achieving equity and Universal Health Coverage under the WHO flagship initiative "Find.Treat.All" #End TB" [10]. This study also addresses a recognized national and global health research priority. The study strengths are that we covered six regions (including rural settings) of Ukraine, and the findings are likely to mirror the operational reality on the field. All consecutive PWID with TB were included and there was no missing data on TB treatment outcomes. The Alliance also has a dedicated monitoring and evaluation unit that ensures data quality and we thus believe our data is robust. To improve reporting quality, we also adhered to STROBE guidelines [25].

The findings from this study have some important policy and practice implications. First, in both drug-sensitive and drug-resistant TB, OST made a significant difference to treatment outcomes. This is supportive evidence for further integration and scale up of OST as a basic package of care for PWID in Ukraine. The fact that considerable proportions of PWID in our cohort were also HIV and HCV positive brings to imagination, the clinical and programmatic complexity of managing these individuals. That not-withstanding, collaborative linkages were successfully established with all involved programs, all patients were followed up and monitored and 91% of the cohort were also placed on ART. This demonstrates that in terms of joint collaboration "it can be done". The role of an NGO in bridging services and fostering a patient-centered approach involving "many diseases, one patient" merits recognition. Second, although OST improved TB treatment outcomes, the treatment success levels remain far from the desired 90% mark. An added consideration is that 96 (77%) of

Figure 1. Tuberculosis treatment outcomes in people who inject drugs in relation to Opioid Substitution Therapy in Ukraine (December 2016 – May 2020).



the 124 individuals with drug-resistant TB had extensively drug-resistant TB (XDR-TB). Global data involving 9528 patients with XDR-TB from 57 countries revealed a treatment success of 39% [20]. Despite being focused on a much more difficult cohort of PWID, our results compares well with this figure. A way forward to improve the lot of MDR-TB patients is to embark on the use of more effective shorter-term MDR-TB regimens designed on the basis of the latest evidence coupled with more patient-centered models [26–29]. Shorter MDR-TB regimens will facilitate TB management both from the health system and patient perspectives. Third, we need to make efforts to increase the number of OST patients among PWID. We believe there are several structural and patient-related factors that hamper further gains. For example: to access OST, all PWID need to be formally registered as "drug addicts" which curbs social liberties such as freedom to drive a car or be employed in certain livelihoods. This is likely to be perceived as a punitive measure and will only serve as a disincentive to those who desire to benefit from OST. There are also established quotas for OST which limits the overall number that can benefit. Further qualitative research into the structural and patient centered barriers to OST would be very useful for informed-decision making and re-orienting policy and practice. OST services also need to be provided in an integrated package of TB-HIV-HCV and OST in a "One-Stop-Shop" approach. The "how to" of this approach would benefit from operational research. Another limitation is that several variables had small sample sizes which did not allow performing adjusted ORs to verify if OST is independently associated with treatment success. Finally, despite being screened for HCV, none of the PWID had access to treatment. The

once-daily pill, which is a combination of the already approved drug sofosbuvir and a new drug called ledipasvir can cure HCV [30]. The cost of one tablet of sofosbuvir is $1,000 (many times the value of its weight in gold!). A full 12-week course of treatment with this drug costs $84,000 and with the current state of affairs, this practically remains unavailable in Ukraine. We strongly advocate for wider access to generic treatment. Differential access for PWID who are at highest risk of acquisition and transmission of HCV and who at the same time, are the most vulnerable is merited. The main study limitation is that due to sample size limitations, we were unable to perform a sub-analysis of the HCV cohort. This merits specific research.

Conclusions

This study is an excellent example of relevant operational research conducted close to the supply and demand of health services and which can contribute to achieving Universal Health Coverage for TB in Ukraine and beyond. Our results show that access to OST significantly improves TB treatment outcomes in PWID as well as the effectiveness of treatment of MDR-TB in PWID, THUS we are advocating for the scale up of both interventions in Ukraine.

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Authors' contributions

All the authors contributed to the conception of the study and protocol development. Data collection and data entry were done by TF and LK. Data analysis was done by AM. Data interpretations were done by RZ, AM, TF. The first draft of the paper was prepared by TF, RZ, AM. All the authors reviewed the paper critically and gave final approval of the paper.

References

1. World Health Organization, United Nations Office on Drugs and Crime, Joint United Nations Programme on HIV/AIDS (2014) Substitution maintenance therapy in the management of opioid dependence and HIV/AIDS prevention. Available: https://www.who.int/substance_abuse/publications/en/PositionPaper_English.pdf. Accessed 24 January 2020.
2. Kermode M, Crofts N, Kumar MS, Dorabjee J (2011) Opioid substitution therapy in resource-poor settings. Bull World Health Organ 89: 243.
3. Mathers BM, Degenhardt L, Ali H, Wiessing L, Hickman M, Mattick RP, Myers B, Ambekar A, Strathdee SA (2010) HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. Lancet 375: 1014–1028.
4. Spire B, Lucas GM, Carrieri MP (2007) Adherence to HIV treatment among IDUs and the role of opioid substitution treatment (OST). Int J Drug Policy 18: 262–270.
5. Roux P, Carrieri MP, Villes V, Dellamonica P, Poizot-Martin I, Ravaux I, Spire B (2008) The impact of methadone or buprenorphine treatment and ongoing injection on highly active antiretroviral therapy (HAART) adherence: evidence from the MANIF2000 cohort study. Addiction 103: 1828–1836.
6. 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 (2008) Key findings from the WHO collaborative study on substitution therapy for opioid dependence and HIV/AIDS. Addiction 103: 1484–1492.
7. Getahun H, Gunneberg C, Sculier D, Verster A, Raviglione M (2012) Tuberculosis and HIV in people who inject drugs: evidence for action for tuberculosis, HIV, prison and harm reduction services. Curr Opin HIV AIDS 7: 345–353.
8. Joint United Nations Programme on HIV/AIDS (2017) Global AIDS Monitoring 2018. Available: https://www.unaids.org/sites/default/files/media_asset/2017-Global-AIDS-Monitoring_en.pdf. Accessed: 23 August 2020.
9. Deiss RG, Rodwell TC, Garfein RS (2009) Tuberculosis and Illicit Drug Use: Review and Update. Clin Infect Dis 48: 72–82.
10. World Health Organization (2018) Joint Initiative "FIND. TREAT. ALL. #ENDTB". Available: https://www.who.int/initiatives/find-treat-all-endtb. Accessed 23 August 2020.

11. World Health Organization (2013) The End TB Strategy. Available: https://www.who.int/tb/strategy/end-tb/en/. Accessed 23 August 2020.
12. ICF Alliance for Public Health (2019) 2018 Annual Report. Available: http://aph.org.ua/wp-content/uploads/2019/09/Annual-Report-2018_red_for-site.pdf. Accessed: 23 August 2020.
13. Aibana O, Slavuckij A, Bachmaha M, Krasiuk V, Rybak N, Flanigan TP, Petrenko V, Murray MB (2019) Patient predictors of poor drug sensitive tuberculosis treatment outcomes in Kyiv Oblast, Ukraine. F1000Res 6: 1873.
14. Morozova O, Dvoryak S, Altice FL (2013) Methadone treatment improves tuberculosis treatment among hospitalized opioid dependent patients in Ukraine. Int J Drug Policy 24: e91–e98.
15. Elk R, Grabowski J, Rhoades H, Spiga R, Schmitz J, Jennings W (1993) Compliance with tubercolosis treatment in methadone-maintained patients: Behavioral interventions. J Subst Abuse Treat 10: 371–382.
16. Gupta A, Kumar V, Natarajan S, Singla R (2020) Adverse drug reactions & drug interactions in MDR-TB patients. Indian J Tuberc 67: S69–S78.
17. Cisse Diallo VMP, Deguenonvo LF, Mbaye KD, Ka D, Lakhe NA, Ndiaye I, Thioub D, Diop Nyafouna SA, Massaly A, Dièye A, Diop M, Ndour CT, Seydi M (2017) TB/HIV co-infection associated with Kaposi's sarcoma under opioid substitution treatment using methadone: about a case. Pan Afr Med J 28: 43 [Article in French].
18. United Nations Development Programme (2019) Human Development Report 2019. Available: http://hdr.undp.org/sites/default/files/hdr2019.pdf. Accessed 23 August 2020.
19. Alliance for Public Health (2016) Monitoring of behavior and HIV prevalence among people who inject drugs and their sexual partners. Available: https://aph.org.ua/wp-content/uploads/2015/05/Monitoryng-povedinky-SIN__Eng__Na-RED.pdf. Accessed 23 August 2020.
20. World Health Organization (2020) Global Tuberculosis Report 2019. Available: https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf. Accessed 23 August 2020.
21. World Health Organization (2016) HIV Prevention, Diagnosis, Treatment and Care for Key Populations. Available: https://www.afro.who.int/sites/default/files/2017-06/9789241511124-eng.pdf. Accessed 23 August 2020.
22. State institution "Public Health Center of the Ministry of Health of Ukraine" (2019) National Tuberculosis Guidelines. Available: https://phc.org.ua/en/diseases-and-information/tuberculosis/guidelines. Accessed 23 August 2020.
23. Batki SL, Gruber VA, Bradley JM, Bradley M, Delucchi K (2002) A controlled trial of methadone treatment combined with directly observed isoniazid for tuberculosis prevention in injection drug users. Drug Alcohol Depend 66: 283–293.
24. Bruce RD, Lambdin B, Chang O, Masao F, Mbwambo J, Mteza I, Nyandindi C, Zamudio-Haas S, Buma D, Dunbar MS, Kilonzo G (2014) Lessons from Tanzania on the integration of HIV and tuberculosis treatments into methadone assisted treatment. Int J Drug Policy 25: 22–25.
25. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP (2014) The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg 12: 1495-1499.
26. World Health Organisation (2016) WHO treatment guidelines for drug-resistant tuberculosis. 2016 Update. WHO, Geneva, Switzerland. Available: https://apps.who.int/iris/bitstream/handle/10665/250125/9789241549639-eng.pdf. Accessed 23 August 2020.
27. Reuter A, Tisile P, Von Delft D, Cox H, Cox V, Ditiu L, Garcia-Prats A, Koenig S, Lessem E, Nathavitharana R, Seddon JA, Stillo J, Von Delft A, Furin J (2017) The devil we know: Is the use of injectable agents for the treatment of MDR-TB justified? Int J Tuberc Lung Dis 21: 1114.-1126.
28. World Health Organisation (2018) Rapid Communication: Key changes to the treatment of drug-resistant tuberculosis. WHO, Geneva, Switzerland. Available: https://www.who.int/tb/publications/2019/WHO_RapidCommunicationMDRTB2019.pdf. Accessed 23 August 2020.
29. World Health Organisation (2020) Consolidated guidelines on tuberculosis. Module 4. Treatment. Drug-resistant tuberclosis treatment. WHO, Geneva, Switzerland. Available: https://www.who.int/publications/i/item/9789240007048. Accessed 23 August 2020.
30. Mazhnaya A, Meteliuk A, Barnard T, Zelenev A, Filippovych S, Altice FL (2017) Implementing and scaling up HCV treatment services for people who inject drugs and other high risk groups in Ukraine: An evaluation of programmatic and treatment outcomes. Int J Drug Policy 47: 187–195.

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