International Journal of Drug Policy 57 (2018) 11–17

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research Paper

Hepatitis C virus status awareness and test results confirmation among people who inject drugs in Ukraine

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ARTICLE INFO

Keywords:
HCV
Ukraine
People who inject drugs (PWID)
HCV testing
Cascade of care

ABSTRACT

Background: Among the estimated 340,000 people who inject drugs (PWID) in Ukraine, HCV prevalence is approximately 70%. As HCV treatment availability increases, an assessment of the HCV treatment cascade is needed to guide HCV prevention and treatment strategies.

Methods: Opioid dependent PWID were interviewed and tested for HIV and HCV in five Ukrainian cities from January 2014 to March 2015. Logistic regression was used to examine the independent correlates of two cascade steps: a) anti-HCV positive status awareness; b) chronic HCV confirmation; and of c) annual HCV testing for PWID.

Results: Among 1613 PWID, 1002 (62.1%) had anti-HCV positive test result, of which 568 (56.7%) were aware of it before the study and 346 (34.5%) reported previous confirmatory testing for chronic HCV. Independent correlates of being aware they had anti-HCV positivity included: current [AOR: 3.08; 95%CI: 2.16–4.40] or prior [AOR: 1.85; 95%CI: 1.27–2.68] opioid agonistic treatment (OAT) experience, relative to no prior OAT, living in Lviv [AOR: 0.50; 95%CI: 0.31–0.81] or Odesa [AOR: 2.73; 95%CI: 1.51–4.93] relative to Kyiv and being aware of having HIV [AOR: 4.10; 95%CI: 2.99–5.62]. Independent correlates of confirming HCV infection among those who were aware of their anti-HCV positive status included: current OAT [AOR: 2.00; 95%CI: 1.24–3.23], relative to prior OAT, the middle income category [AOR: 1.74, 95%CI: 1.15–2.63], relative to the lowest, and receiving ART [AOR: 4.54; 95%CI: 2.85–7.23]. Among 1613 PWID, 918 (56.9%) were either HCV negative or not aware of their HCV positive status, of which 198 (21.6%) reported recent anti-HCV test (during last 12 month). Recent anti-HCV test in this group was associated with current [AOR: 7.17; 95%CI: 4.63–11.13] or prior [AOR: 2.24; 95%CI: 1.32–3.81] OAT experience, relative to no prior OAT.

Conclusion: Encouraging PWID to participate in OAT may be an effective strategy to diagnose and link PWID who are HCV positive to care. Among HIV negative participants, regular HCV testing may be ensured by participation in OAT. More studies are needed to assess HCV treatment utilization among PWID in Ukraine and OAT as a possible way to retain them in treatment.

Background

Globally, an estimated 71 million people have viraemic hepatitis C virus (HCV) infection ("Polaris Observatory, H. C. V. Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study," 2017). Over the past 25 years, HCV-associated disability-adjusted life years have more than doubled and HCV-related mortality is increasing (Stanaway et al., 2016). People who inject drugs (PWID) account for most HCV cases in Eastern Europe and Central Asia with global prevalence of HCV among PWID exceeding 52%. (Degenhardt et al., 2017). Ukraine is home to Europe's most devastating drug injection epidemic, with 1.2% of the population injecting opioids (United Nations Office on Drugs and Crime (UNODC), 2016) The national estimate of HCV prevalence among PWID in Ukraine is approximately 70% (Hope, Eramova, Capurro, & Donoghoe, 2014), with more than 240,000 individuals infected with HCV and

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https://doi.org/10.1016/j.drugpo.2018.03.022
Received 9 December 2017; Received in revised form 11 March 2018; Accepted 19 March 2018

needing treatment. Despite evidence that HCV testing and treatment are increasing globally (Milne et al., 2015; Smith, Combellick, Jordan, & Hagan, 2015), PWID continue to lack access to effective treatment. Getting tested for antibodies to HCV (anti-HCV)and confirming chronic HCV infection are the necessary steps in the treatment cascade (Meyer et al., 2015). For most patients, the diagnosis is a two-step process: testing for anti-HCV using serological tests followed by confirmation of viremia with polymerase chain reaction (PCR) test that detects HCV RNA in the blood of the patient. Since 14–26% of infected patients clear their HCV and do not become chronically infected, the confirmation of viremia is needed to decide if treatment is necessary (Lauer & Walker 2001).

A 2013 cross-sectional survey of PWID in Ukraine reported that 50% of PWIDs were aware of their anti-HCV positive status (Salyuk & Sazonova, 2015). In this convenience sample, 9.4% of PWID with HCV reported receiving some treatment (Salyuk & Sazonova, 2015). Sub-optimal awareness and treatment availability coupled with high financial costs of treatment are among the main barriers to universal treatment of chronic HCV. In fact, pegylated-interferon and ribavirin treatment was introduced in Ukraine only in 2013 with some state funding which excluded PWID and funding by international donors for 100 PWID on opioid agonist therapy (Luhmann et al., 2015). Treatment with direct acting antiviral (DAA) medications was piloted in a group of 1500 patients starting in 2015 (Mazhnaya, Marcus et al., 2017; Mazhnaya, Meteliuk et al., 2017). This scale-up project of HCV treatment with DAA for PWID was implemented in community-based settings and was shown to be feasible even for actively injecting participants (Mazhnaya, Marcus et al., 2017; Mazhnaya, Meteliuk et al., 2017). While opportunities for better treatment coverage in Ukraine are being explored, it is critical for program planners to better understand factors related to the hepatitis C testing and treatment cascade in PWID.

Opioid agonist therapy (OAT) with methadone or buprenorphine not only effectively reduces opioid use, but also reduces HIV and HCV transmission (Gowing, Farrell, Bornemann, Sullivan, & Ali, 2011; Roux et al., 2008), and improves engagement in treatment in the HIV cascade of care (Low et al., 2016; Roux et al., 2008). In Ukraine, buprenorphine maintenance treatment became available to a limited number of patients in 2004 and OAT using methadone was introduced in 2008 (Bruce, Dvoryak, Sylla, & Altice, 2007; Schaub, Chtenguelov, Subata, Weiler, & Uchtenhagen, 2010). Despite its documented benefits, OAT is under-scaled due to individual, structural and policy barriers (Bojko et al., 2015; Mazhnaya et al., 2016), resulting in only 2.7% of the estimated 340,000 opioid injectors in Ukraine being on treatment. OAT has demonstrated benefits on the HIV (Mazhnaya, Marcus et al., 2017; Mazhnaya, Meteliuk et al., 2017) and TB (Morozova, Dvoryak, & Altice, 2013) treatment cascades in Ukraine, but has yet to be studied for HCV.

This study aimed to examine the first steps in the HCV treatment cascade among PWID in Ukraine and look for the independent correlates associated with: 1) being aware of anti-HCV positive status; 2) receipt of confirmatory HCV testing; and 3) among those with negative or unknown status, the proportion who adhered to HCV testing recommendations (annual testing) ("AASLD and IDSA. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C," 2014–2017). Specifically, we hypothesize that, among other factors, OAT is related to higher level of anti-HCV positive status awareness, confirmatory HCV testing and annual anti-HCV testing among HCV negative participants or with unknown status.

Methods

Data collection

The methods for the cross-sectional biobehavioral study involving 1613 PWID in 5 cities in Ukraine (Kiev, Odesa, Mykolaiv, Dnipro, Lviv) conducted from January 2014 to March 2015 have been previously described (Makarenko et al., 2016). Eligibility included age 18 years or older, ICD-10 criteria for opioid dependence, lived/worked in the city where the survey was conducted, provided informed consent, and agreed to undergo rapid HIV and HCV testing. Three groups of opioid dependent PWID were included: (1) never on OAT; (2) previously on OAT; (3) currently on OAT. For the first group, respondent-driven sampling (RDS) was used, and random selection from the OAT registry was used for the second and the third group. "Seeds" for RDS were recruited at community outreach sites in each city and included at least one: female, individual aged 18–25, and an individual who had injected less than two years. After completing, a computer-assisted, self-administered instrument (CASI) using Qualtrics®, point-of-care HIV and HCV (CITO TEST HIV 1/2/0, *Pharmasco* and CITO TEST HCV, *Pharmasco*) testing was performed along with pre- and post-test counseling by trained staff. The study was approved by the institutional review boards at Yale University and the Gromashevsky Institute at the National Academy of Medical Sciences, Kyiv, Ukraine.

Measures

The dependent variables were assessed

1) being aware of having positive anti-HCV status (and confirmed using rapid onsite testing); 2) self-report of confirmatory testing for the subsample already aware of their anti-HCV positive status; and 3) compliance with recommendations for annual HCV testing ("AASLD and IDSA. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C," 2014–2017) for PWID who are unaware of their HCV status before the study or believe themselves to not have HCV.

Definitions of independent variables

Key among our hypotheses is that patients on OAT would have higher engagement in the HCV treatment cascade. Being on OAT was confirmed by chart review of patients randomly sampled at OAT sites. Participants who were previously on OAT were confirmed by chart review and could not have taken OAT in the previous 10 days. Based on the review of the previous studies of OAT implementation in Ukraine (Makarenko et al., 2016; Makarenko et al., 2017) in addition to standard socio-demographic characteristics we measured duration of injection drug use, rapid HIV test results and HIV status self-report, and current antiretroviral treatment based on self-report. Cohabitation with sexual partner, presence of children in the household, and importance of religion (measured in Likert scale) were characteristics indicating the presence of social support which was found to be an important correlate in previous studies of PWID (Artenie et al., 2015; Solomon et al., 2015; Ti et al., 2013). Income level was categorized into: $<$ 1200 UAH (150 USD), 1200–3500 (150–437 USD) and $>$ 3500 (437USD) based on minimum poverty level and average monthly wage for Ukraine in 2014. Educational attainment was categorized as (1) high school drop-out, (2) completion of high school (including vocational school), (3) some college or higher education. Alcohol use was assessed using the AUDIT, with scores $\geq$8 for men and $\geq$4 for women defining an harmful or hazardous drinking (Saunders, Aasland, Babor, De la Fuente, & Grant, 1993). Addiction severity was measured using the DAST-10 (Yudko, Lozhkina, & Fouts, 2007). Scores $\leq$5 were indicative of low to moderate addiction, whereas scores $>$ 5 indicated substantial to severe addiction. Depression was assessed using the CES-D-10, with scores $\geq$10 classified as moderate to severe depression (Zhang et al., 2012).

Statistical analysis

A diagram of the subject disposition for the analytical sample is displayed in Fig. 1. First, we examined the frequency distributions of categorical variables and mean (or median) of continuous variables. Then, we conducted bivariate analyses of the associations between the independent variables and study outcomes. Pearson's Chi-square tests were used to assess the statistical significance of associations between