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Prevalence of HIV and Hepatitis C and access to opioid substitution treatment among people who inject drugs in three cities in Croatia: findings from the second wave of respondent-driven sampling surveys

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Abstract

Background The second wave of integrated bio-behavioural surveys was conducted among people who inject drugs (PWID) in the cities of Zagreb, Split, and Rijeka in Croatia to estimate the prevalence of HIV and hepatitis C virus (HCV) antibodies and sexual and injecting risk behaviours.

Methods Respondent-driven sampling (RDS) was used to recruit a total of 301 PWID in Split, 130 in Rijeka, and 86 in Zagreb from March to July 2022. Participants provided biological specimens for HIV and HCV testing and completed a behavioural questionnaire. RDS-Analyst software was used to calculate weighted population estimates with 95% confidence intervals (95% CI).

Results Approximately one in four PWID were women (range from 24.3% in Zagreb to 29.9% in Rijeka). Overall, HIV prevalence was low, with no cases identified in Zagreb, and 0.6% and 0.8% in Split and Rijeka, respectively. HCV antibody prevalence was 37.2% among PWID in Zagreb and Rijeka, and as high as 59.5% in Split. Testing for HIV and HCV in the 12 months before the survey was reported by 11.3-19.8% and 17.3-21.6% of PWID across the cities, respectively. Use of needles and syringes in the past 30 days that had already been used by someone else was reported by 8.9-26.5% across the cities. A large proportion of PWID—54.0% in Zagreb, 31.0% in Rijeka and 29.9% in Split—never used needle and syringe exchange programmes. Being in drug addiction treatment at the time of the survey was reported by 50.8% in Split, 57.3% in Rijeka and 73.3% in Zagreb. Injecting cocaine in 30 days before the survey was common, ranging from 12.7 to 32.1% across the cities.

Conclusion HIV prevalence continues to be low among PWID in Croatia, whereas HCV prevalence is substantial. Due to low coverage of HIV and HCV testing and insufficient use of harm reduction services, there is a potential for further spread of drug-related infectious diseases in this population.

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Keywords HIV, Hepatitis C virus, Injecting drug use, Croatia, Opioid substitution treatment

Background

People who inject drugs (PWID) are disproportionally affected by HIV, hepatitis C virus (HCV) and other blood-borne and sexually transmitted infections (STIs) primarily due to unsafe drug injecting practices and high-risk sexual behaviours [1]. Furthermore, there are structural barriers that hinder their access to prevention and treatment of HIV and other blood-borne infections including the lack of health system's responsiveness to PWID-specific needs, incarceration, repressive policies regarding drug use, and widespread stigmatization [2]. This enforces some PWID to maintain hidden identities and avoid health care services, creating also challenges in obtaining representative data on the burden of HIV, HCV, and other infections in this population.

Effective response to HIV epidemics in PWID includes implementation of comprehensive harm reduction services— including needle/syringe exchange programmes (NSEP), opioid substitution treatment (OST) and naloxone distribution, and testing and treatment for HIV, viral hepatitis, tuberculosis and STIs [3]. These services should be provided with sufficient scale and quality to yield individual and population-level benefit and effect.

One of the targets of the WHO 2022–30 global health sector strategies for HIV/AIDS, viral hepatitis, and STIs is to decrease the number of new viral hepatitis and HIV infections globally from 4.5 million per year in 2020 to less than 500,000 in 2030 [4]. In PWID, the number of new HCV infections per year is targeted to decline from 8 per 100 in 2020 to 2 per 100 in 2030.

The European Union Drugs Agency (EUDA, formerly European Monitoring Centre for Drugs and Drug Abuse [EMCDDA]) estimates that the prevalence of injecting drug use in 18 European Union (EU) countries that had data for the 2015–2021 period is 1.8 per 1,000 population aged 15 to 64 years, while for Croatia it is estimated at 2.2 per 1,000 population [5]. HIV transmission due to injecting drug use remains at low level in the EU, accounting for 4.3% (993 persons) in newly reported HIV cases in 2022 [6]. Similarly, in Croatia, out of 113 HIV cases newly reported in 2022, 2.7% (three cases) were attributed to injecting drugs [7]. Among the 2017 HIV cases that were reported since the beginning of HIV reporting in Croatia, 4.0% were attributed to injecting drugs.

The first integrated bio-behavioural survey (IBBS) in PWID in Croatia was based on respondent-driven sampling (RDS) and carried out in 2014–2015 [8]. It found low prevalence of HIV in the three biggest cities in the country (0.2% in Zagreb and Rijeka and 0.3% in Split). Approximately a third of PWID tested positive for HCV antibodies (38.3% in Split, 31.5% in Rijeka and 29.1% in Zagreb).

In Croatia, NSEPs for PWID were established in 1996 and are run by non-governmental organizations (NGOs) and continuously funded by the Ministry of Health. As part of services, NGOs also provide voluntary and anonymous testing for HIV and HCV. OST is available free of charge, with methadone treatment introduced in 1991, while the treatment with buprenorphine has been available since 2004. Family physicians are the main providers of OST. According to the National register on people treated for substance use disorders, the number of people who are on treatment for opioid abuse was continuously declining from 6,155 in 2015 to 5,338 in 2019, and further declined during the COVID-19 pandemic in 2020 when 4,431 individuals were on treatment. A slight increase was observed since 2021 (4,605 in 2021 and 4,741 in 2022); however, despite this rise, the number of treated individuals did not reach pre-pandemic levels recorded in 2019 [9]. From 2015 to 2022, a total of 13 NGOs implementing harm reduction programs were funded in Croatia, of which nine operated in Zagreb, Split and Rijeka. There were disruptions in the provision of the harm reduction programs in the capital city of Zagreb due to the COVID-19 pandemic and the earthquake that occurred in 2020. Due to the earthquake, the drop-in centre at the Croatian Red Cross in Zagreb had to be relocated and that made these services less accessible geographically, which could have affected service coverage.

This paper aims to describe key biological, behavioural and coverage with HIV and HCV prevention indicators collected in the second round of the IBBS using RDS among PWID in Split, Rijeka, and Zagreb in 2022, and correlates of not being on OST at the time of the survey. OST was selected as the outcome in the multivariate analysis because it is effective in the reduction and cessation of opiate use and reduces injecting risk behaviours and risks of HIV and HCV acquisition.

Methods

Sampling and survey procedures

RDS, a widely used sampling method for recruiting in surveys populations at high risk of HIV, was used to recruit PWID in three cities in Croatia. Zagreb is the capital city of Croatia while Split and Rijeka are large coastal port cities. RDS relies on peer-driven recruitment from participants' social networks, and the fieldwork starts with the participation of purposefully selected members of the target population [10].

Sample size calculations were designed to detect a 35% increase in Zagreb and Split and a 20% increase in Rijeka

in ever being in treatment for drug addiction, with 90% power and an error of 5%. The baseline values found in the 2015 survey were 56% in Zagreb, 57% in Split and 77% in Rijeka. A sample size calculation was set at 300 participants in Split, and 250 in Zagreb and Rijeka each, and recruitment was initiated with *seeds* (initial participants) in each of the cities. Seeds were diverse with respect to age, gender, and place of residence in the city. All participants, including seeds, who completed the survey received three coupons, which they used to recruit a maximum of three other participants from their social networks. Participants received a primary incentive (US$14 supermarket coupon) for their participation and a secondary incentive (US$7 supermarket coupon) for each person whom they recruited and who successfully participated in the survey. Inclusion criteria were being 18 years of age or older, residence in the survey city for at least 12 months before the survey, injecting drugs for non-medical purposes in the month before recruitment, being able and willing to provide an informed consent, and having a valid recruitment coupon. Prior to enrolment, participants were described the objectives and processes of the survey and were asked for a verbal consent to participate. To ensure all respondents met eligibility criteria and to prevent multiple enrolment, persons attending the study sites were screened by a trained staff member with experience in working with PWID.

Eligible participants received pre-test counselling and provided biological specimens for rapid HIV and HCV testing. Then they completed the behavioural questionnaire together with the interviewer. Finally, participants were given post-test counselling and, in the case of reactive test results, were referred to a further clinical assessment. They were also given coupons for recruiting their peers. A unique study identification number was used on all behavioural and biological data collection forms to ensure data anonymity and confidentiality.

The RDS study sites were in the premises of the organisations that provide harm reduction services to PWID, and these were the City Office of the Red Cross in Zagreb, the NGO Terra in Rijeka, and the NGO Help in Split. All survey procedures were conducted by the staff of these organisations who were trained in RDS methods and biological specimen taking, and all information that participants provided was kept anonymous and confidential. Ethical Approval was granted by the Ethical Board of the Croatian National Institute of Public Health.

Behavioural questionnaire

With minor modifications, we used the behavioural questionnaire from the first wave of the survey, conducted in 2014–2015. The questionnaire was administered in a face-to-face interview, and it collected data for the calculation of the indicators recommended by the EUDA and the Global AIDS Monitoring of the Joint United Nations Programme on HIV and AIDS (UNAIDS). Data were also collected on the parameters important for RDS data analysis, including the size of each participant's social network. Social network size was defined as the number of PWID the participant knows by name, who are 18 years of age or older, who live in the survey city and whom they have seen in the past three months.

Biological data collection methods

Participants gave a sample of oral fluid that was tested using rapid tests for HIV (*OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test*, *OraSure Technologies*, *USA*) and HCV antibodies (*OraQuick® HCV Rapid Antibody Test*, *OraSure Technologies*, *USA*). Those with an initial reactive HIV test result were further tested using a serial testing algorithm, which included *INSTI HIV-1/HIV-2 Antibody Tests*, *BioLytical Laboratories*, *Canada* and *Toyo anti-HIV 1/2/0 test*, *Turklab*, *Turkey* on blood specimens collected via finger sticks.

Analytical strategy

To calculate weighted population estimates with 95% confidence intervals (95% CIs), RDS-Analyst (RDS-A) version 0.86 software was used for univariate data analysis [11]. Data were analysed using the Gile's sequential sampler estimator which produces population estimates using data on the sizes of respondents' networks, recruitment patterns and estimated population size for each city in 2022. The estimated size of the PWID population, obtained via the multiplier method using these survey data, was 757 persons in Rijeka, 1,454 in Split and 2,805 in Zagreb. Initial respondents were included in the analysis. Homophily, convergence/equilibrium, and bottlenecks were analysed for the following nine key indicators: age, gender, anti-HCV status, using a sterile needle and syringe at last injection, using a condom at last sex in the past 30 months, testing for HIV in the 12 months before the survey, receiving two or more HIV prevention interventions in the three months before the survey, being in OST at the time of the survey, and comprehensive knowledge about HIV [12].

Only among PWID who had used opioids in the month before the survey, bivariable and multivariable logistic regression analyses were carried out using *svy* module in Stata (v17) statistical package. Weights were exported from RDS-A to adjust for sample biases and calculate population estimates [13, 14]. Weighted multivariable logistic regression analysis was used to assess correlates of not being on OST at the time of the survey. In addition to potential confounders (age and gender) independent variables included injecting-related behaviours, access to harm reduction services, history of imprisonment, anticipated stigma (avoidance of health care services

in the 12 months before the survey because of stigma and discrimination), and experienced stigma (experience of stigma and discrimination in healthcare setting in the last 12 months). Bivariable analyses were used to screen independent variables and their associations with the outcome. Age, gender, and variables associated with the outcome at $p<0.20$ in the bivariable analysis were included in the multivariate logistic regression model. The higher significance level was set to increase the chance of detecting actual relationships, which could otherwise be deemed not significant due to small sample sizes across many of the levels of independent variables. Statistical significance in the multivariable analysis was set to $p<0.05$. Participants with missing values were excluded casewise. Due to the small sample size, Zagreb data was omitted from the logistic regression analysis. Results are presented as odds ratios (ORs) with 95% CI.

Results

Recruitment patterns

Data collection was conducted from March to July 2022. A total of 526 PWID were enrolled: 301 in Split, 139 in Rijeka and 86 in Zagreb, with the pre-determined sample size reached only in Split. Several attempts were made to make recruitment more effective, particularly in Zagreb, such as engagement of an additional NGO that provides harm reduction services to PWID in Zagreb, dissemination of information about the survey via health care staff from the Clinical Hospital in Zagreb that provides OST to PWID, and several general practitioners and pharmacists that have a larger number of PWID as patients.

The maximum recruitment chain length was 15 in Rijeka, 16 in Split and six in Zagreb. Convergence was reached on all nine key indicators in all three cities. The average social network size was 10 in Zagreb, 14 in Split, and 20 in Rijeka.

Socio-demographic characteristics

Across all cities, most PWID were 35 years of age or older (80.1% in Rijeka, and 73.8% in Split, and 70.7% in Zagreb). The survey recruited many women who inject drugs, ranging from 24.3% of PWID in Zagreb to 29.9% in Rijeka, and being employed or self-employed at the time of the survey ranged from 24.4% in Split to 35.4% in Rijeka (Table 1). The majority of PWID (78.0-81.3%) completed at least secondary education. Few PWID were born outside of Croatia (ranging from 2.8% in Zagreb to 8.7% in Split). Finally, experience of imprisonment was common, ranging from 47.2 to 52.6% across the cities.

Injecting drug use behaviours

The median age at the first drug injection was 20 to 21 years across the cities, with the majority of PWID injecting drugs for longer than 10 years (75.8–90.7%). Injecting daily or more frequently in the past 30 days ranged from 14.3% in Rijeka to 23.2% in Split. The median number of injecting episodes in the month before the survey was four in Zagreb (the average value was 27), 15 in Split (average of 24) and seven in Rijeka (average of 22).

Types of drugs used, drug use patterns, and risk behaviours are shown in Table 1. The most commonly injected drug in the month before the survey was methadone and/or buprenorphine in Rijeka and Zagreb, and heroin in Split. Approximately one in three PWID in Split and one in four in Zagreb injected cocaine in the month before the survey. Importantly, injecting cocaine was much more prevalent in 2022 compared to 2015 in Split and Zagreb (Fig. 1).

The majority of PWID reported using a sterile needle and syringe at last injection episode but at a somewhat lower level than in 2015 (Fig. 1). However, as many as 26.5% of PWID in Zagreb, 14.7% in Rijeka and 8.9% in Split used needles and syringes in the past 30 days that had already been used by someone else. There was a large variation in reported use of injecting equipment (cooker, cotton, water, acid) in the past 30 days that had already been used by someone else, ranging from 6.8 to 43.8% across the cities (Table 1). The median number of persons with whom needles and syringes were shared in the past 30 days was two in all three cities.

Among those who ever were imprisoned, 0.5% in Zagreb, 14.2% in Split and 17.1% of PWID in Rijeka injected drugs while in prison. The use of non-sterile needles and syringes in the prison setting was common in Split (65.6%) and in Rijeka (67.3%). Although approximately every other PWID had ever experienced an overdose with opioid drugs, this was relatively uncommon in the past 12 months, ranging from 2.7 to 5.5% across the cities.

Sexual behaviours

In the 12 months before the survey, a majority of PWID (76.7% in Rijeka, 74.8% in Split, and 81.5% in Zagreb) had regular and non-regular sexual partners, including those who paid them for sex. The median number of partners was two in Rijeka and Split and one in Zagreb. A small proportion of male PWID (respectively 1.1% and 1.2% in Rijeka and Zagreb and 4.1% in Split) had same-sex partners in the past 12 months. Having partners who injected drugs in the past 12 months was reported by 39.1% of PWID in Rijeka, 48.4% in Split, and 61.4% in Zagreb. Receiving money or drugs for sex in the past 12 months was relatively uncommon in Rijeka and Zagreb (0.4% and 2.3%, respectively) but at a higher level in Split (reported overall by 11.8% of PWID, although much more prevalent among women (33.0%) compared with men (2.9%). Reported condom use at last sex with a non-regular

Table 1 Socio-demographic characteristics and drug injecting behaviours among PWID in Rijeka, Split and Zagreb, weighted by the network size, integrated bio-behavioural survey, 2022

	Rijeka		Split		Zagreb		
	n/N	% (95% CI)[a]	n/N	% (95% CI)	n/N	% (95% CI)	
Age groups							
18–24	0/130	/	17/300	11.1 (3.7, 18.3)	6/86	14.6 (3.2, 25.9)	
25–34	18/130	19.9 (8.5, 31.3)	49/300	15.1 (9.7, 20.6)	12/86	14.8 (6.0, 23.6)	
35–44	80/130	51.7 (36.8, 67.3)	87/300	26.4 (19.8, 33.1)	49/86	52.7 (38.9, 66.4)	
≥ 45	32/130	28.4 (11.5, 44.7)	147/300	47.4 (39.4, 55.4)	19/86	18.0 (8.6, 27.4)	
Women	30/130	29.9 (15.6, 43.9)	81/300	29.3 (21.8, 36,8)	17/86	24.3 (1.6, 35.7)	
Employment							
Employed	28/130	33.6 (15.2, 51.3)	61/300	21.9 (14.9, 29.0)	17/86	26.3 (13.2, 39.3)	
Self-employed	4/130	1.8 (0.1, 3.4)	11/300	2.5 (0.6, 4.4)	5/86	4.1 (0.3, 8.0)	
Used sterile needle and a syringe at last injection	122/130	86.7 (>63.6)	264/299	88.6 (83.3, 93.9)	77/ 86	90.0 (83.1, 96.9)	
Never used needles or syringes that were already used by someone else in the past 30 days	106/129	85.3 (76.4, 94.4)	264/298	91.1 (86.2, 95.9)	60/ 86	73.5 (62.2, 84.9)	
Never used equipment (cooker, cotton, water or acid) that was already used by someone else in the past 30 days	112/125	93.2 (87.7, 99.2)	186/238	82.4 (75.8, 89.3)	21/37	56.2 (35.3, 77.0)	
At least once gave, rented or sold needles or syringes after injecting in the past 30 days	16/ 129	10.8 (2.6, 18.9)	31/ 298	8.7 (3.6, 13.8)	30/ 86	31.2 (19.4, 43.2)	
Type of drugs injected in the past month[b]							
Heroin	39/127	25.6 (13.3, 377)	184/300	65.2 (57.2, 73.2)	32/86	42.2 (28.5, 55.7)	
Methadone	63/127	46.1 (28.0, 64.3)	138/300	31.6 (24.6, 38.3)	52/86	62.8 (50.3, 75.3)	
Buprenorphine	32/127	32.5 (18.3, 47.0)	27/300	8.5 (3.7, 13.3)	10/86	16.0 (4.3, 27.8)	
Amphetamine and/or methamphetamine	17/127	8.3 (2.8, 13.8)	25/300	4.3 (2.4, 6.3)	5/86	2.3 (<4.6)	
Cocaine	24/127	12.7 (4.4, 20.9)	81/300	32.1 (23.7, 40.5)	34/86	29.9 (17.5, 41.9)	
Frequency of injecting (on days when injecting)							
1 time per day		85/128	62.5 (47.7, 77.1)	197/300	67.2 (59.9, 74.5)	39/86	51.4 (38.6, 64.1)
2 times per day		15/128	8.7 (3.5, 13.7)	65/300	20.2 (13.7, 26.7)	17/86	20.0 (9.9, 30.3)
3 times per day		17/128	16.1 (5.1, 27.6)	27/300	10.2 (6.0, 14.5)	16/86	13.9 (5.6, 21.7)
≧4 times per day		11/128	12.7 (< 26.0)	11/300	2.4 (0.7, 4.1)	14/86	14.7 (5.7, 24.0)
Ever experienced drug overdose	76/130	43.2 (29.4, 57.0)	158/300	42.3 (34.4, 50.4)	49/85	47.2 (33.9, 60.9)	

[a] Weighted population estimates and 95% confidence intervals (CI); [b] Response percentages exceed 100% because the question allowed respondents to select multiple answers

		Rijeka	Split	Zagreb
		%	%	%
Ever used needle and syringe exchange programmes	2015	63,8	97,4	36,5
	2022	69,0	70,1	46,0
Ever been treated for drug addiction	2015	76,9	56,7	55,5
	2022	75,0	69,4	78,6
Used sterile needle and syringe at last injection	2015	93,7	99,7	95,1
	2022	86,7	88,6	90,0
Injected heroin in the past 30 days	2015	40,4	50,8	40,1
	2022	25,6	65,2	42,2
Injected cocaine in the past 30 days	2015	5,9	8,5	8,7
	2022	12,7	32,1	29,9
Tested for HIV in the past 12 months	2015	20,2	6,8	13,1
	2022	18,2	11,3	19,8
Tested for HCV in the past 12 months	2015	21,5	7,0	13,5
	2022	21,6	17,3	21,5
HIV positive	2015	0,2	0,3	0,2
	2022	0,8	0,6	0,0
HCV antibody positive	2015	31,5	38,3	29,1
	2022	37,2	59,5	37,2
Had sexual partner/s in the past 12 months	2015	91,4	85,3	81,5
	2022	76,7	74,8	91,2
Used a condom at last sex	2015	27,9	33,2	38,7
	2022	25,5	45,0	37,1

Fig. 1 Coverage with needle and syringe exchange programmes, opioid substitution treatment, drug use patterns and testing for HIV and viral hepatitis C, and sexual behaviour, weighted by network size, integrated bio-behavioural surveys, 2015 and 2022

partner in the past 12 months ranged from 29.6% in Rijeka to 58.9% in Split.

Except for the higher prevalence of transactional sex among mostly women in Split who inject drugs (4.7% in 2015 compared with 11.8% in 2022), the data do not suggest there has been an increase in sexual risk behaviours since 2015. In fact, compared to 2015, fewer PWID in 2022 reported any sexual partners in the previous year (decrease from 91.4% in Rijeka and 85.3% in Split, but an increase to 91.2% in Zagreb). Condom use at last sex remained stable in Zagreb and Rijeka (respectively 25.5% and 37.1% in 2022) and increased in Split from 33.2% in 2015 to 45.0% in 2022.

HIV and HCV antibody prevalence and prior testing for HIV and HCV

In the survey, less than 1% of PWID in Rijeka and Split were found to be HIV infected and these individuals knew that they were HIV positive, while no cases of HIV were identified in Zagreb (Fig. 1). The highest prevalence of HCV antibody positivity was found in Split (59.5%, 95% CI 51.2–67.8) while in Rijeka and Zagreb it was 37.2% (95% CI 22.1–52.2) and 37.2% (95% CI 25.0-49.6), respectively. As can be seen from Fig. 1, since 2015 anti-HCV prevalence increased in all the cities, but significantly so in Split. Testing for HIV in the past 12 months ranged from 11.6 to 19.6%, while for HCV, testing ranged from 17.3 to 21.6%. Of those PWID with reactive anti-HCV test results, 43.2% in Rijeka, 77.1% in Split and 21.9% in Zagreb knew that they were HCV antibody positive from prior testing.

Access to sterile injecting equipment and enrolment in harm reduction programmes

Ever using services of NSEP was reported by 46.0% in Zagreb, 69.0% in Rijeka and 70.1% in Split. Although almost all PWID from Rijeka and Split were able to obtain sterile needles and syringes when they needed them, this was not the case with approximately one in four PWID in Zagreb. In Zagreb and Rijeka, the commonest source of sterile needles and syringes was a pharmacy (reported by 68.2% and 60.0%, respectively), while in Split it was a "drop-in" centre (by 43.5%). The total average number of obtained needles and syringes in the past 30 days was 44 in Rijeka, 79 in Split and 106 in Zagreb. Out of these, 38 in Rijeka, 67 in Split and 30 in Zagreb were obtained free of charge.

Over half of PWID were in drug addiction treatment at the time of the survey (50.8% in Split, 57.3% in Rijeka and 73.3% in Zagreb). However, a sizeable proportion of PWID—30.6% in Split, 25.0% in Rijeka and 21.4% in Zagreb—have never been included in any treatment programme for drug dependence. Most PWID were not in treatment because they "did not need treatment (32.7% in Zagreb, 61.0% in Rijeka and 80.0% in Split) and/or because they "were not ready to stop using drugs" (2.3% in Rijeka, 72.8% in Split and 56.1% in Zagreb).

Correlates of not being in OST

Factors associated with not being in OST were assessed among PWID in Split and Rijeka who reported using opioids in the 30 days before the survey (N_{Split} = 285; N_{Rijeka} = 115). The results of the multivariable analyses are shown in Table 2. PWID who experienced an opioid overdose were less likely to not be in OST at the time of the survey compared to those who never overdosed, both in Split (AOR = 0.5 (95% CI 0.2–0.9)) and in Rijeka (AOR = 0.3 (95% CI 0.11–0.97)). Although age was significantly correlated with OST in both cities, the odds of not being in OST decreased with age in Rijeka, while the reverse was true for Split. Only in Split, PWID who injected stimulant drugs and/or cocaine in the past 30 days were more likely to not be in OST compared to those who did not inject these drugs (AOR = 2.32 (95% CI 1.66–3.23)).

Discussion

We found that HIV prevalence among PWID remains low, whereas the substantial levels of HCV antibody prevalence found already in 2015 have further increased in all the cities, but significantly so in Split [8]. Given the persistently low level of testing for HIV and HCV and the presence of needle and syringe sharing among PWID across the three cities, there is a potential for further HIV and HCV spread in this population. Overall, PWID in the three largest cities in Croatia are marked by a predominantly long duration of drug injection. Coverage with NSEP and the use of harm reduction services was found to be below the UNAIDS target of 90%. The greatest decrease in service utilisation in 2022 compared with 2015 was found in Split and likely it is due to the sample composition (in 2015, one of the study limitations noted in Split was that almost all recruited PWID were clients of the city's NSEP). Importantly, aligned with findings from other EU countries, there are major shifts in Croatia towards a more frequent injecting use of cocaine and other stimulant drugs in the 2015–2022 period, especially in Split [5].

The UNAIDS target of 90% of PWID using a sterile needle and syringe at last injection has been reached in Zagreb and is close to be achieved in Rijeka and Split [15]. More than 90% of PWID reported having access to sterile needles and syringes in two of three cities surveyed, but their main sources are pharmacies and not community-based harm reduction programmes. The use of harm reduction services was found to be sub-optimal and far lower than the UNAIDS target of 90%.

Of particular concern are continuing low levels of testing for HIV and HCV in PWID in these three cities. Testing is the first step in accessing the continuum of HIV and HCV care. However, Croatia is among the few EU countries that have clinical restrictions on direct-acting antiviral agents (DAAs) for treatment of chronic HCV infection in PWID [16]. To be treated for chronic HCV infection in Croatia, persons who use drugs need to abstain from injecting drug use for at least 6 months prior to initiation of treatment and are then subject to toxicological assessment for drug use every three months during treatment [17]. ECDC and other agencies recommend treating HCV infection in PWID with DAAs as a cost-effective strategy along with provision of harm reduction interventions to reduce the risk of re-infection

Table 2 Factors associated with not being in opioid substitution treatment (OST) among PWID who reported using opioids in the past 30 days before the survey: bivariable and multivariable logistic regression with odds ratios (ORs) and adjusted ORs (aORs) with 95% confidence intervals (CIs), weighted by the network size, integrated bio-behavioural survey, 2022

	SPLIT			RIJEKA		
	***N* not in OST/ *N* total**	**OR (CI 95%)**	**aOR[a] (CI 95%)**	***N* not in OST /*N* total**	**OR (CI 95%)**	**aOR[a] (CI 95%)**
	104/284		*N*[b]=283	45/115		*N*[b]=115
Gender	69/212	1	1	33/89	1	1
Men						
Women	35/72	2.56** (1.33, 4.91)	1.95 (0.94, 4.04)	12/26	2.23 (0.53, 9.27)	1.65 (0.47, 5.70)
Experience of overdose (ever)						
No	58/131	1	1	24/46	1	1
Yes	46/153	0.39** (0.21, 0.71)	0.47* (0.24, 0.91)	21/69	0.25** (0.08, 0.77)	0.33* (0.11, 0.97)
Included in the NSP in the past 3 months						
No	55/116	1	1	14/29	1	1
Yes	49/168	0.63 (0.34, 1.17)	0.57 (0.30, 1.10)	31/86	0.34 (0.09, 1.25)	0.44 (0.12, 1.56)
Injected stimulants and/or cocaine in the past 30 days						
No	60/204	1	1	38/91	1	
Yes	44/80	2.15*** (1.50, 3.09)	2.32*** (1.66, 3.23)	7/24	0.85 (0.47, 1.55)	/
Used non-sterile needle/syringe in the past 30 days	87/249	1		37/94	1	
No						
Yes	16/33	1.05 (0.37, 3.01)	/	8/21	0.43 (0.11, 1.67)	/
Imprisoned in the past 12 months						
No	96/257	1	1	42/102	1	1
Yes	8/27	0.46 (0.17, 1.24)	0.40 (0.15, 1.06)	3/13	0.26 (0.06, 1.05)	0.34 (0.07, 1.69)
Anticipated stigma[c]						
No	88/250	1	1	34/90	1	
Yes	15/33	2.96* (1.15, 7.58)	1.28 (0.50, 3.32)	11/25	1.03 (0.31, 3.44)	/
Experienced stigma[d]						
No	90/231	1		34/79	1	/
Yes	14/53	0.71 (0.33, 1.49)	/	11/36	1.71 (0.48, 6.06)	
	Mean (SD) not in OST/ Mean (SD) total			Mean (SD) not in OST/Mean (SD) total		
Age	46.0 (8.12)/			39.0 (5.2)/		
	42.9 (10.8)	0.94*** (0.91, 0.97)	0.96* (0.93, 0.99)	40.5 (6.3)	1.09 (0.97, 1.22)	1.10* (1.01, 1.21)

[a] Controlling for sex, age and variables associated with the outcome at $p < 0.2$ in the bivariable analysis; [b] Number of respondents included in the final model; [c]Avoidance of health care in the last 12 months because of stigma and discrimination; [d] Experience of stigma and discrimination in healthcare setting in the last 12 months; / Not significant in the bivariable analysis and therefore not included in the multivariable logistic regression model; *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

[18]. In fact, a number of modelling studies did suggest that along with the provision of OST and NSP, a scale-up of anti-HCV treatment with DAAs could substantially reduce chronic HCV prevalence within the next 10 to 20 years [19, 20]. Both anti-HCV and HCV RNA testing and linkage to treatment for PWID not only are life-saving interventions for individuals but they also have the potential to reduce transmission at the population-level and as such are cornerstones of the HCV elimination strategy. Without making HCV diagnosis and HCV treatment available to PWID, Croatia cannot reach the WHO HCV elimination targets by 2030 that stipulate that 90% of those with chronic HCV should be diagnosed, and 80% of those diagnosed should be cured [21].

Of note is also a substantial increase since 2015 in injecting cocaine. These results are aligned with the findings from the analysis of the residual content of discarded syringes collected across seven European cities in the European Syringe Collection and Analysis Project Enterprise where cocaine was the most prevalent substance detected (31%), followed by heroin (24%), buprenorphine (21%), and synthetic cathinones, and amphetamines (both 17%) [22]. It is estimated that 3.9% of people aged 18–34 years in Croatia use cocaine, which is the third highest prevalence in the EU, after the Netherlands and Ireland [5]. Treatment options for cocaine and stimulant dependence are limited and mainly based on psychological interventions such as contingency management [23]. Although currently data from Croatia do not yet suggest an increase in risky sexual behaviours among PWID, injecting of cocaine and other stimulants was found to be associated with high-risk sexual behaviours that can facilitate HIV transmission [24, 25]. For example, high levels of injecting cocaine among PWID were found to be associated with HIV outbreak in Scotland in 2015, despite a high coverage with harm reduction, in Luxembourg, and with HIV transmission in the 2014–2020 period in Athens, Greece [26–28].

Results of multivariable analyses indicate that there is a positive association between experiencing an opioid overdose and being in OST at the time of the study. Although we cannot establish the temporality of this relationship, it may be due to a greater willingness of PWID to enter treatment after experiencing life-threatening effects of an overdose, which was described in other studies [29–31]. In Split, but not in Rijeka, injecting cocaine and other stimulant drugs was associated with the higher odds of not being in OST.

The study findings reveal several gaps in community and health-system response to health care needs of PWID. Firstly, some components of comprehensive harm reduction services have suboptimal coverage, specifically, NSEP, HIV and HCV testing services, and prevention of overdose. In the context of the UNAIDS prevention targets, the opioid substitution programme seems to have achieved the largest coverage in comparison with other components of harm reduction. The effectiveness, particularly in terms of the reach, of community-based harm-reduction services should be improved as they can provide not only NSEP and counselling regarding injection-related harms and treatment options, as well as legal and social protection services, but also linkage to OST and other interventions that are health care facility-based in Croatia.

Due to the changing patterns in HIV and HCV epidemiology in PWID in Croatia, it is important to continue with bio-behavioural surveillance possibly using less costly approaches than RDS and that were successfully implemented elsewhere [32].

Study limitations

Since data were collected via face-to-face interviews, social desirability biases might have arisen due to the underreporting of risky drug use behaviours and sexual practices. Accuracy of responses about past events may have been affected by recall bias. Although the study results may be considered representative of the social network of the population from which respondents were recruited, recruitment might have missed important subgroups, such as PWID who were not willing to come to the study site, those for whom the financial incentive to participate was too low, or those who have small social networks. Furthermore, the fact that the RDS study sites were in the premises of the organisations that provide harm reduction services to PWID may have led to this study's overestimation of PWID's engagement in these services. It is of note, however, that in all three cities this study sampled many PWID who had previously not been in contact with these organisations. Finally, despite efforts to include young PWID, the survey in Rijeka failed to recruit any PWID younger than 25 years of age.

Another limitation of the study are the achieved sample sizes in Rijeka and Zagreb. Fewer PWID were recruited in the 2022 IBBS compared to 2015, and despite multiple attempts to achieve better recruitment, target sample sizes were not reached in these two cities. Slow recruitment could have been due to a decline in the number of PWID but also it could point to challenges with RDS implementation. The latter seems to be particularly relevant for Zagreb. Despite being the most populous city in Croatia with the highest estimated number of PWID, there have been barriers in Zagreb not only regarding recruitment into this survey but also regarding overall access to harm reduction services. Small sample sizes overall and small numbers of observations across some of the variables may have affected accuracy of estimates and reduced the power of the study. Finally, participants who were found to be HCV antibody-reactive were not

tested for HCV RNA, which prevents us from determining the prevalence of chronically infected PWID in Croatia. Given highly effective HCV treatment, it is essential to include HCV RNA testing in the next round of IBBS in order to estimate the burden of hepatitis C and treatment gaps in the PWID population.

Conclusion

Although we found a low HIV prevalence, anti-HCV prevalence has increased since 2015, particularly in Split. Given that anti-HCV prevalence is a proxy biomarker of the HIV epidemic potential among PWID, these findings indicate a need to strengthen harm reduction services in terms of their availability, access, and quality [33]. The growing stimulant drug use can additionally contribute to potential increases in the transmission of drug-related infectious diseases among PWID in Croatia.

Abbreviations

DAAs	Direct-acting antiviral agents
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
EU	European Union
EUDA	European Union Drugs Agency
HCV	Hepatitis C virus
NGO	Non-governmental organization
IBBS	Integrated bio-behavioural survey
NSEP	Needle and syringe exchange programme
OST	Opioid substitution treatment
PWID	People who inject drugs
RDS	Respondent-driven sampling
RDS	A-Respondent-driven sampling-Analyst
STIs	Sexually Transmitted Infections
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

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Author contributions

All authors participated in the planning and conception of the research questions and the study design. S.S., G.K., T.N.B., M.L.K.L., S.H. and I.B. contributed to the study design. S.S., G.K. and M.P.P. supported and supervised the study implementation and analysed the data. I.B. drafted the article, and all authors participated in interpreting the data and critically revising the manuscript. All authors read and approved the manuscript.

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Data availability

The datasets used and analysed during the study are available from the corresponding author on request.

Declarations

Ethics approval and consent to participate

Ethical Approval was granted by the Ethical Board of the Croatian National Institute of Public Health. All study participants were explained the purpose and the process of the survey, were given to read an informed consent form and provided an oral consent for participation.

Consent for publication

The manuscript does not contain any individual person's data.

Competing interests

The authors declare no competing interests.

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