

Research Paper

Divergent estimates of HIV incidence among people who inject drugs in Ukraine

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ABSTRACT

Background: Divergent estimates of HIV incidence among people who inject drugs (PWID) in Ukraine have been reported in modeling studies, longitudinal cohort studies, and recent infection assays used in cross-sectional surveys. Estimates range from 0.65 to 24.8 infections per 100 person-years with substantial regional variation. In this paper, we study the sources of this discrepancy.

Methods: We compared baseline characteristics of study subjects recruited in the cross-sectional integrated bi-behavioral surveillance surveys (IBBS) in 2011 and 2013, with those from the longitudinal network intervention trial (network RCT) conducted between 2010 – 2013, the study that found a remarkably high incidence of HIV among PWID in Ukraine. The analysis was conducted for two cities: Mykolaiv and Odesa.

Results: Significant differences were found in the characteristics of study subjects recruited in the IBBS surveys and the network RCT, in particular in Odesa, where the mismatch in the estimates of HIV incidence is greatest. In Odesa, recent syringe sharing was about three times as prevalent in the network RCT as in the IBBS; 39% of the network RCT and 16–18% of the IBBS participants indicated stimulants rather than opiates as their drug of choice; 97% of respondents in the network RCT and 45% in the IBBS-2013 reported injecting in a group over half of the time; and the average monthly number of injections in the network RCT was about twice that in the IBBS studies.

Conclusions: Differences in study designs and sampling methodologies may be responsible for the substantial differences in HIV incidence estimates among PWID in Ukraine. The potential sources of selection bias differed between the studies and likely resulted in the recruitment of lower risk individuals into the IBBS studies compared to the network RCT. Risk stratification in the population of PWID may have implications for future surveillance and intervention efforts.

Introduction

The prevalence of HIV in Ukraine is among the highest in Europe and Central Asia, estimated to be around 1% in people 15–49 years old. The HIV epidemic is primarily concentrated in three high-risk groups: people who inject drugs (PWID), female sex workers, and men who have sex with men (UNAIDS, 2018). Recent studies of key risk groups in Ukraine show consistently high HIV prevalence estimates of about 20%

among PWID nationwide (Dumchev, Sazonova, Salyuk, & Varetska, 2018; Rozanova et al., 2018; Vitek et al., 2014) with substantial geographic heterogeneity (Zaller et al., 2015). At the same time, several studies conducted in Ukraine in the last decade have found remarkably divergent estimates of HIV incidence among PWID (Barska et al., 2016; Booth et al., 2016; Denisiuk et al., 2014; Dumchev, Varetska, Sazonova, & Smyrnov, 2017; Ompad et al., 2017; Public Health Center of the Ministry of Health of Ukraine, 2018).

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Direct estimates of HIV incidence require longitudinal research designs, which can be difficult to conduct in key HIV risk populations. Several methods have been used to estimate HIV incidence in Ukraine, including recent infection testing assays (Sazonova & Salyuk, 2018), studies of harm reduction program clients (Barska et al., 2016; Denisiuk et al., 2014; Dumchev et al., 2017; Ompad et al., 2017), and modeling studies (Public Health Center of the Ministry of Health of Ukraine, 2018). Estimates of the HIV incidence rate among PWID in 2010–2015 from these studies range between 0.65–3.2 infections per 100 person-years nationwide. Parameters in modeling studies are primarily informed by the cross-sectional integrated bio-behavioral surveillance (IBBS) surveys that have been conducted in Ukraine since 2007 every two years (Dumchev et al., 2018). National IBBS surveys are an integral component of the second-generation HIV surveillance in Ukraine. The objective of IBBS surveys is to estimate trends in HIV prevalence and risk behavior among key risk populations. The IBBS surveys use respondent-driven sampling (RDS) to recruit PWID (Heckathorn, 1997). Starting 2011, the IBBS surveys have included rapid testing for Hepatitis C virus (HCV) in addition to the rapid HIV test. Regional modeling studies based on data from IBBS estimate the annual cumulative incidence among PWID in Mykolaiv to be 11.5% in 2010, 9.8% in 2011, and 8.2% in 2012; and in Odesa – 6.3% in 2010, 5.4% in 2011, and 4.7% in 2012 (Neduzhko, Bolshov, Novak, & Salyuk, 2017).

However, in a social network randomized clinical trial (network RCT) conducted between 2010 and 2013 in three cities of Ukraine, Booth et al. (2016) found a remarkably high HIV incidence rate of 24.8 infections per 100 person-years (Booth et al., 2016). The main objective of the network RCT was to compare the effectiveness of a social network intervention combined with HIV testing and counseling, to HIV testing and counseling alone, in reducing the risk of HIV infection among PWID. The structure of the trial intervention required sampling of small clusters of PWID. The trial was not designed to recruit a representative sample of PWID: it used convenience sampling to recruit “index participants”, who were required to bring two members of their injecting network to be eligible. “Index” participants were recruited from the streets and injecting venues known to the outreach workers, the majority of whom were former PWID themselves. In this study, the annual cumulative incidence was 13.9% among PWID in Mykolaiv (Booth et al., 2016 refers to Mykolaiv using the Russian translation Nikolayev), and 24.7% in Odesa.

Booth et al., 2016 note the discrepancy between the IBBS-based estimates and those from the network trial, and suggest that the finding could be partially explained by the selection of regions most severely affected by the HIV epidemic. In this paper, we study the sources of this apparent discrepancy, and find that profound differences in baseline HIV risk characteristics of study subjects may explain the mismatch.

These differences may be the result of differences in the study designs and sampling methodologies between IBBS and the network RCT, which had different objectives and possibly different sources of selection bias. This analysis has the potential to elucidate HIV risk factors in Ukraine, and has implications for future surveillance, as well as the design and implementation of intervention campaigns.

Methods

Overview

We compare the characteristics of study subjects recruited into the cross-sectional IBBS surveys in 2011 and 2013 (Balakirieva, Bondar, Sereda, & Sazonova, 2012; Balakirieva, Bondar, Loktieva, Sazonova, & Sereda, 2014; Dumchev et al., 2018) with the baseline characteristics of subjects in the social network intervention trial (network RCT) by (Booth et al., 2016), conducted between 2010–2013. The duration of recruitment in network RCT motivated our inclusion of both IBBS-2011 and IBBS-2013 as comparison datasets. Due to substantial regional variation in HIV prevalence (Zaller et al., 2015), the comparison is performed separately in two cities: Mykolaiv and Odesa. The network RCT was conducted in three regions. We excluded Donetsk from this analysis, because the Donetsk sample in the network RCT was geographically restricted to Makiivka - the satellite town 15 km away from Donetsk, while IBBS surveys were conducted in Donetsk itself, and because regional-level HIV incidence modeling study was not conducted in this region.

The network intervention trial was approved by the Colorado Multiple IRB at the University of Colorado Denver and by the IRB at the Ukrainian Institute on Public Health Policy (Booth et al., 2016). The 2011 and 2013 IBBS studies were approved by the IRB at the Gromashevsky Institute of Epidemiology and Infectious Diseases, Ukraine (Dumchev et al., 2018). All datasets analyzed in this study were de-identified.

Design and implementation of the studies

Table 1 describes the main design features of the network RCT, the IBBS-2011, and the IBBS-2013. While a detailed description of the study methods is available from (Balakirieva et al., 2012, 2014; Booth et al., 2016; Dumchev et al., 2018), here we highlight several differences in recruitment procedures and verification of participant eligibility used in the three studies.

The IBBS studies used RDS, a social network link-tracing procedure, to recruit PWID (Heckathorn, 1997). RDS recruitment in the IBBS surveys started with the recruitment of 4–6 “seeds”, who were invited

Table 1
Main characteristics of study designs.

Characteristic	Network RCT	IBBS-2011	IBBS-2013
Study design	Cluster randomized clinical trial with a 12-months follow-up	Cross-sectional study	Cross-sectional study
Timeframe (baseline recruitment)	July, 2010 – September, 2013	June – October, 2011	April – October, 2013
Recruitment strategy	Convenience sampling to recruit “index” subjects, each bringing two network members, who in turn could bring up to two other network members	Respondent-driven sampling	Respondent-driven sampling
Sample size: Mykolaiv	1285 (255 indexes)	500 (6 seeds)	500 (5 seeds)
Sample size: Odesa	1522 (256 indexes)	500 (4 seeds)	400 (5 seeds)
Eligibility criteria	16 years of age or older; injected drugs in the last 30 days; not planning to leave the area in the next 6 months and not under investigation that may result in the incarceration; “index” subjects were required to bring two members of injecting network	14 years of age or older; injected drugs in the last 30 days; residence in the study city	14 years of age or older; injected drugs in the last 30 days; residence in the study city
HIV test used in the study	HIV I + II One-Step Test finger-stick rapid test (Origenics Ltd, Yavne, Israel)	One Step Rapid Anti-HIV 1/2 Test Cards Captive, whole blood/serum/ plasma (InTec Products Inc, China)	CITO TEST HIV 1/2/0 (Acon Biotech Co, Ltd, China)

IBBS, integrated bio-behavioral surveillance; RCT, randomized controlled trial.

to recruit their peers into the study. This process continued in several waves until the target sample size of 400–500 participants was achieved. In both IBBS surveys, the seeds were selected to represent a wide range of important characteristics of the PWID target population, including residence in different parts of the city, demographics, and behavioral characteristics related to drug use. Importantly, all seeds were required to be either HIV-negative or not know their HIV status, as indicated by self-report. Individuals aware of their HIV-positive status were permitted at later stages of participant recruitment. In the network RCT, “index” participants were recruited using convenience sampling and constituted a substantial proportion of the final sample (20% in Mykolaiv and 17% in Odesa). Eligibility criteria for index subjects did not include HIV status. Instead, in order to be eligible for the study, index subjects were required to bring two members of their injecting network. According to all study protocols, visual inspection of recent venipuncture was used to verify recent injecting drug use, but the network RCT also performed urine testing for opiates and amphetamines.

Comparison of study subjects

We analyzed structured questionnaires administered in the three studies to find matching questions. Overlapping baseline characteristics included demographics, drug use history, risky drug use practices, history of opioid agonist therapy, history of incarceration, and infectious diseases testing and diagnosis. These characteristics were compared using the chi-squared test for categorical variables and ANOVA or independent sample Student *t*-test for continuous or integer-valued variables. Statistical analysis was performed in R statistical computing environment (R Development Core Team, 2013).

Recruitment of the network RCT participants was done between 2010 and 2013 with most people being recruited in 2011 and 2012. The Supplementary Appendix provides separate comparisons of IBBS-2011 and IBBS-2013 samples with the sub-samples of network RCT participants recruited during the same years, comparison of IBBS-2011 to IBBS-2013 samples, and comparison of network RCT sub-samples recruited during different years.

To visualize differences in multiple baseline characteristics simultaneously across studies, we used a principal component analysis (PCA) method that accommodates both continuous and categorical variables (Chavent, Kuentz-Simonet, Labenne, & Saracco, 2014). PCA is a dimension reduction technique that transforms a given set of variables into a new set of variables (called principal components) that are ordered by the proportion of the total variance in the data explained by these variables. Each principal component is a linear combination of the original variables.

Results

Table 2 compares baseline characteristics of study subjects, showing that most are significantly different in the three studies. In particular, substantial differences are observed in characteristics related to the risky drug use practices. In 2011, 11% and 9% of IBBS study subjects reported prior participation in similar surveys in Mykolaiv and Odesa, respectively. In the sub-sample of network RCT study subjects recruited during the same months as IBBS-2011, only 4% of participants in Mykolaiv and 1% in Odesa reported having this kind of experience, suggesting that IBBS and network RCT samples were likely drawn from different sub-populations of PWID.

While screening and eligibility requirements were the same across cities, sample differences across studies on several important characteristics are much larger in Odesa than in Mykolaiv, including the drug of choice, injecting frequency, sharing of drug paraphernalia, recent syringe sharing, history of incarceration, history of HIV testing, and access to HIV treatment.

Fig. 1 shows subjects' characteristics plotted on the first two principal components, with points colored by study (both IBBS studies are represented by the same color), in Mykolaiv and Odesa. The Supplementary Appendix provides the details about the relative contribution of each variable included in the PCA to the first two principal components. The most influential variables in the first principal component include various measures of high risk injection practices and employment, and in the second principal component – age, history of incarceration, HIV status and receipt of antiretroviral therapy, history of tuberculosis, and the drug of choice. The first two principal components explain 23.6% of the variance in the data. In Mykolaiv, subjects from the IBBS and the network RCT studies appear similar, though some clustering by study is evident. In Odesa, subjects from the network RCT exhibit near separation from those of the IBBS studies.

Additional comparisons presented in the Supplementary Appendix are qualitatively similar to those presented in Table 2 and Fig. 1. There is evidence of minor clustering across studies, but not years in Mykolaiv, and major clustering across studies in Odesa with the same pattern observed in 2011 and 2013 sub-samples. There are no major differences on the first two principal components between IBBS-2011 and IBBS-2013 or across network RCT sub-samples recruited during different years.

Discussion

Reliable HIV incidence estimates among high risk populations, such as PWID, are essential to inform intervention planning and resource allocation, as well as the design of future studies. But when high-quality studies like IBBS and the network RCT reach different conclusions about HIV incidence, the available evidence may be insufficient to guide future prevention and research efforts. In this study, we explored the potential sources of divergence in the estimates of HIV incidence among PWID in Ukraine by analyzing the differences between the samples of PWID recruited in 2011 and 2013 IBBS surveys, and the network RCT conducted between 2010–2013 in Mykolaiv and Odesa.

Substantial differences are evident in characteristics that may predict HIV infection, including frequency of injecting in a group, practicing front or back loading, and antiretroviral treatment among injecting peers (Jolley et al., 2012; Strathdee et al., 2010). Separate comparison of IBBS-2011 to IBBS-2013 samples and sub-samples of network RCT recruited during different years suggests that some of the differences may be explained by temporal changes in the characteristics of PWID during this interval. The most substantial differences are observed between the IBBS and network RCT studies, in particular in Odesa. These differences persist when participants are stratified by their date of recruitment. The IBBS and network RCT studies had different objectives and employed starkly differing designs and sampling strategies, which may have led investigators to reach distinct sub-populations of PWID, with different distributions of HIV risk factors, in Odesa.

Both IBBS studies and the network RCT used peer referral mechanisms to recruit participants, but this design was implemented in different ways that may have affected the composition of the samples. The IBBS studies used RDS (Heckathorn, 1997) to recruit study subjects. The properties of seeds in RDS studies may play a role in the distribution of the characteristics of the final sample (Gile & Handcock, 2010), and the representativeness of samples obtained by RDS is controversial (Gile, Johnston, & Salganik, 2015; Mills, Johnson, Hickman, Jones, & Colijn, 2014; Rocha, Thorson, Lambiotte, & Liljeros, 2017; Rudolph, Fuller, & Latkin, 2013). Recent empirical studies provide evidence of recruitment bias in RDS among PWID (Crawford, Aronow, Zeng, & Li, 2018; Li et al., 2018; Zeng, Li, & Crawford, 2019). In the IBBS studies, seeds were required to be either HIV-negative or unaware of their HIV status, which might have biased the final sample toward lower risk individuals. In the network RCT, “index” participants were recruited by outreach workers using convenience sampling and were

Table 2
Characteristics of study subjects.

Characteristic	MYKOLAIV			p-value	ODESA			p-value
	n (%) / mean (SD)				n (%) / mean (SD)			
	Network RCT (baseline N = 1285)	IBBS-2011 (N = 500)	IBBS-2013 (N = 500)		Network RCT (baseline N = 1522)	IBBS-2011 (N = 500)	IBBS-2013 (N = 400)	
Demographics								
Sex								
male	1005 (78)	361 (72)	395 (79)	0.0129	956 (63)	383 (77)	328 (82)	<0.0001
female	280 (22)	139 (28)	105 (21)		566 (37)	117 (23)	72 (18)	
Age: mean (SD)	34.95 (8.21)	36.01 (7.95)	35.05 (8.14)	0.0437	33.12 (7.96)	33.70 (9.54)	35.72 (9.03)	<0.0001
Education								
9 years or less	120 (9)	101 (20)	146 (29)	<0.0001	46 (3)	46 (9)	85 (21)	<0.0001
high school / some college	1125 (88)	374 (75)	332 (66)		1428 (94)	421 (84)	274 (68)	
bachelor and above	40 (3)	25 (5)	22 (4)		48 (3)	33 (7)	41 (10)	
Marital status								
single	850 (66)	258 (52)	282 (56)	<0.0001	939 (62)	231 (46)	259 (65)	<0.0001
married / has a partner	435 (34)	241 (48)	218 (44)		583 (38)	268 (54)	141 (35)	
Employment								
regular / student	387 (30)	75 (15)	130 (26)	<0.0001	110 (7)	95 (19)	104 (26)	<0.0001
day labor / seasonal / home	439 (34)	218 (44)	273 (55)		313 (21)	289 (58)	232 (58)	
disabled / retired	89 (7)	39 (8)	52 (10)		46 (3)	29 (6)	32 (8)	
unemployed	369 (29)	165 (33)	45 (9)		833 (55)	85 (17)	32 (8)	
other	1 (0)	3 (1)	0 (0)		220 (14)	2 (0)	0 (0)	
Drug use history								
Age of first injection: mean (SD)	19.70 (5.31)	19.55 (4.95)	18.61 (4.43)	0.0002	21.47 (4.71)	19.91 (5.68)	19.09 (4.62)	<0.0001
Drug of choice								
opiates / sedatives	1266 (99)	494 (99)	494 (99)	0.8495	926 (61)	422 (84)	329 (82)	<0.0001
stimulants	19 (1)	6 (1)	6 (1)		596 (39)	78 (16)	71 (18)	
Injected in the last 24 hours								
no	817 (64)	208 (42)	84 (17)	<0.0001	117 (8)	266 (54)	199 (52)	<0.0001
yes	468 (36)	291 (58)	415 (83)		1405 (92)	226 (46)	186 (48)	
Number of injections in the last 30 days: mean (SD)	21.69 (20.29)	21.66 (22.82)	33.62 (31.71)	<0.0001	44.42 (29.97)	21.55 (20.98)	19.59 (17.85)	<0.0001
Risky drug use practices								
Frequency of injecting in a group								
50% of time or more	984 (81)	–	263 (53)	<0.0001	1365 (97)	–	178 (45)	<0.0001
sometimes / rarely	193 (16)	–	173 (35)		38 (3)	–	113 (28)	
never	44 (4)	–	64 (13)		3 (0)	–	108 (27)	
Sharing cooking equipment or drawing drug solution from a common container in the last 30 days								
no	909 (71)	265 (53)	375 (75)	<0.0001	50 (3)	147 (29)	246 (62)	<0.0001
yes	376 (29)	235 (47)	125 (25)		1472 (97)	353 (71)	154 (38)	
Recent syringe sharing: use of syringes previously used by someone else in the last 30 days								
no	1243 (97)	465 (93)	481 (96)	0.0017	1275 (84)	476 (95)	380 (95)	<0.0001
yes	42 (3)	35 (7)	19 (4)		247 (16)	24 (5)	20 (5)	
Number of times unclean syringes were used in the last 30 days (among those, who used them): mean (SD)	5.50 (7.87)	3.09 (2.94)	2.44 (2.18)	0.0825	10.32 (11.04)	6.52 (12.48)	8.42 (7.08)	0.2833
Gave their used syringes to other people in the last 30 days								
no	1225 (95)	447 (89)	479 (96)	<0.0001	1360 (89)	470 (94)	379 (95)	0.0001
yes	60 (5)	53 (11)	21 (4)		162 (11)	30 (6)	21 (5)	
Practice of front or back loading in the last 30 days								
no	746 (58)	427 (85)	373 (75)	<0.0001	11 (1)	479 (96)	337 (84)	<0.0001
yes	539 (42)	73 (15)	127 (25)		1511 (99)	21 (4)	63 (16)	
Getting drugs in pre-loaded syringes in the last 30 days								
no	1242 (97)	163 (33)	261 (52)	<0.0001	1380 (91)	135 (27)	125 (31)	<0.0001
yes	43 (3)	337 (67)	239 (48)		142 (9)	365 (73)	275 (69)	
Treatment of substance use disorders								
History of opioid agonist treatment								
no	1222 (95)	458 (92)	423 (85)	<0.0001	1485 (98)	484 (97)	393 (98)	0.3734
yes	63 (5)	42 (8)	77 (15)		37 (2)	16 (3)	7 (2)	
Incarceration / detention								
History of incarceration / detention for at least one month								
no	667 (52)	275 (55)	272 (54)	0.4069	740 (49)	341 (68)	268 (67)	<0.0001
yes	618 (48)	225 (45)	228 (46)		782 (51)	159 (32)	132 (33)	
Infectious diseases								
HIV status (tested in the study)								
negative	730 (57)	281 (56)	338 (68)	<0.0001	953 (63)	342 (68)	292 (73)	0.0002
positive	555 (43)	219 (44)	162 (32)		569 (37)	158 (32)	108 (27)	
History of HIV testing								
no	281 (22)	125 (25)	99 (20)	0.1341	992 (65)	143 (29)	40 (10)	<0.0001
yes	1004 (78)	375 (75)	401 (80)		530 (35)	357 (71)	360 (90)	

(continued on next page)

Table 2 (continued)

Characteristic	MYKOLAIV			p-value	ODESA			p-value
	n (%) / mean (SD)				n (%) / mean (SD)			
	Network RCT (baseline N = 1285)	IBBS-2011 (N = 500)	IBBS-2013 (N = 500)		Network RCT (baseline N = 1522)	IBBS-2011 (N = 500)	IBBS-2013 (N = 400)	
Receiving HAART (among those tested HIV positive)								
no	401 (72)	164 (75)	87 (54)	<0.0001	534 (94)	129 (82)	42 (39)	<0.0001
yes	154 (28)	55 (25)	75 (46)		35 (6)	29 (18)	66 (61)	
HCV status (tested in the study)								
negative	–	306 (61)	181 (36)	<0.0001	–	255 (51)	146 (36)	<0.0001
positive	–	194 (39)	319 (64)		–	245 (49)	254 (64)	
History of tuberculosis diagnosis								
no	1137 (88)	406 (82)	417 (83)	0.0002	1082 (73)	416 (83)	331 (83)	<0.0001
yes	148 (12)	91 (18)	83 (17)		399 (27)	84 (17)	69 (17)	
Sample overlap								
History of participation in similar surveys [†]								
no	132 (96)	445 (89)	–	0.0286	142 (99)	457 (91)	–	0.0050
yes	6 (4)	55 (11)	–		2 (1)	43 (9)	–	

HAART, highly active antiretroviral therapy; HCV, hepatitis C virus; IBBS, integrated bio-behavioral surveillance; RCT, randomized controlled trial; SD, standard deviation.

Numbers may not sum to totals due to missing values, and percentages may not sum to 100% due to rounding. The p-value corresponds to the chi-squared test for categorical variables and the ANOVA F-test for continuous or integer valued variables.

[†] For the network RCT, this question uses a sub-sample of respondents recruited and interviewed during the same time frame (year and month) as the IBBS-2011 study. This sub-sample includes 138 subjects in Mykolaiv, and 144 subjects in Odesa.

required to bring two of their injecting network peers into the study. During the initial screening, outreach workers informed potential participants that urine testing and checking for signs of recent injection would be required to enter the study. While the outreach workers in the network RCT did not specifically target high-risk individuals, the requirement that index subjects bring two members of their injecting network necessarily resulted in a sample of individuals who are more likely to inject in a group. Knowledge of the requirement for various drug injection screening procedures may have discouraged some lower-risk PWID from participating.

HIV incidence estimates based on the IBBS studies were obtained using mathematical models of HIV transmission. The reliability of model-based projections depends on the accuracy of structural assumptions and unbiased estimates of the model parameters. Even if IBBS surveys recruited representative samples, model parameters that were not informed by the IBBS studies, in particular mortality rate, may be biased. This would have substantial implications for the HIV incidence estimates. In contrast, incidence estimates from longitudinal cohort studies do not require assumptions about HIV transmission

dynamics. To the best of our knowledge, the network RCT is the only trial conducted in Ukraine to estimate HIV incidence directly using the cohort study design that was not limited to PWID already participating in harm reduction programs. A longitudinal design, like that employed by the network RCT, may be subject to different sources of bias, including loss to follow-up and selection of people willing to enroll in a long-term study.

There are several plausible explanations for the substantial differences between studies observed in Odesa, but not in Mykolaiv. First, the population of PWID in Mykolaiv may be better connected and more homogenous with respect to risk behavior compared to Odesa, where there may be distinct high and low risk clusters that share few common members. Second, an estimated 6400 PWID lived in Mykolaiv, while 20000 lived in Odesa in 2011 (Berleva et al., 2012), so the proportion of the PWID population recruited in the survey samples is substantially larger in Mykolaiv. Regardless of the recruitment strategy employed, overlapping samples may be more likely in a smaller target population, as in Mykolaiv. Finally, in the IBBS studies, seed participants were required to self-report as either HIV-negative or with unknown HIV

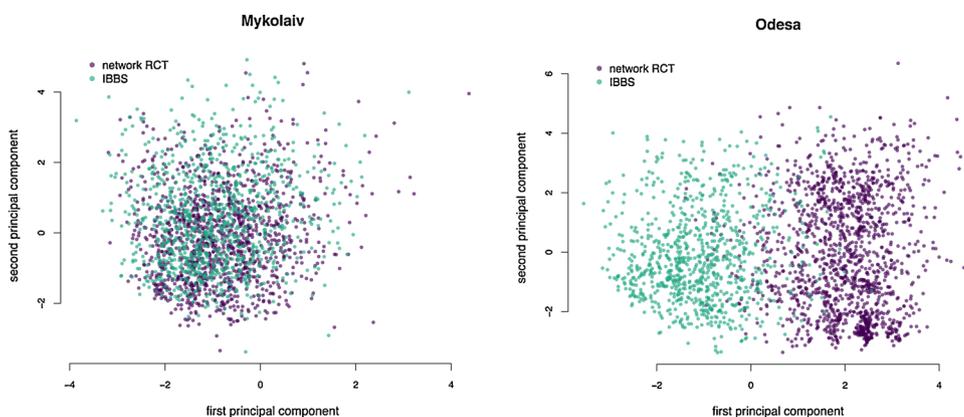


Fig. 1. Principal component analysis (PCA) in Mykolaiv and Odesa. Every point corresponds to a study subject, with the two integrated bio-behavioral surveillance (IBBS) studies merged into one category. Variables included in the analysis are: sex, age, education, marital status, employment, drug of choice, having injected in the last 24 h, number of injections in the last 30 days, injecting in a group in the last 30 days, syringe sharing in the last 30 days, giving own used syringes to others in the last 30 days, front or back loading in the last 30 days, getting drugs in a pre-loaded syringe in the last 30 days, history of opioid agonist treatment, history of incarceration/detention for at least one month, HIV status, history of HIV testing, receiving HAART, and history of tuberculosis

diagnosis. The values of the first principal component are plotted on the horizontal axis, and the values of the second principal component – on the vertical axis. The PCA was conducted on the merged dataset that included both cities.

status. In Mykolaiv, three of six seeds in 2011 and one of five in 2013 tested HIV-positive in the study. In Odessa, however, both in 2011 and in 2013 all of the seeds tested HIV-negative. This may explain why HIV incidence projections from the modeling studies (which are primarily informed by the IBBS surveys) in Mykolaiv are not dramatically different from the direct incidence estimates found by Booth et al. (2016). In Odessa, however, IBBS studies likely recruited low risk PWID, and network intervention trial recruited high risk individuals resulting in the annual cumulative HIV incidence of 24.7% among PWID – substantially higher than the annual cumulative incidence projections of 4.7%–6.3% from the modeling studies.

Conclusions

Effective public health responses to the HIV epidemic require reliable estimates of HIV incidence for the optimal scaling of effective prevention and treatment interventions, in particular opioid agonist treatment, antiretroviral treatment, and harm reduction programs. In order to implement interventions and harm reduction programs, policymakers need reliable estimates of risk, the distribution of risk factors, and the size of the target population. Likewise, investigators planning an intervention trial require reliable estimates of the incidence of the outcome of interest for sample size and power calculations. In Ukraine, these decisions are based on evidence from surveillance and clinical research among PWID, largely provided by the IBBS and modeling studies. When another study, such as the network RCT, provides starkly divergent estimates of HIV incidence, researchers, public health advocates, and policymakers may rightly question whether current resource allocations reflect the best available knowledge about PWID and HIV risk. In Ukraine and elsewhere, understanding the distribution and dynamics of HIV incidence and related risk factors is critical to guide public policy and program planning, and the investigators should strive for representativeness in the sampling procedures. When mismatches arise in key measures of HIV risk, critical evaluation of the strengths and weaknesses of study designs may help assess the potential sources of bias and differentiate between the actual changes in the risk behaviors of the target population and those resulting from the study design.

Authors' contributions

OM and FWC conceived the study, developed the methodology and wrote the first draft of the manuscript. OM conducted the data analysis. REB, SD, KD, YS and TS conceived, designed and implemented the parent studies. All authors contributed to the interpretation of the data, revisions, and approved the final version of the manuscript.

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Declaration of Competing Interest

None.

CRediT authorship contribution statement

Olga Morozova: Conceptualization, Formal analysis, Funding acquisition, Methodology, Software, Visualization, Writing - original draft. **Robert E. Booth:** Funding acquisition, Investigation, Resources, Writing - review & editing. **Sergii Dvoriak:** Conceptualization,

Investigation, Resources, Writing - review & editing. **Kostyantyn Dumchev:** Investigation, Writing - review & editing. **Yana Sazonova:** Data curation, Investigation, Writing - review & editing. **Tetiana Saliuk:** Funding acquisition, Investigation, Resources, Writing - review & editing. **Forrest W. Crawford:** Conceptualization, Funding acquisition, Methodology, Resources, Visualization, Writing - review & editing.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.drugpo.2019.07.023>.

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