BRIEF REPORT OF THE TIPVAL STUDY
An Integrated Biological Behavioral Surveillance Survey among People Who Inject Drugs (PWID)
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INTRODUCTION

We are pleased to present this Brief Report of the South African TipVal Study, a biological behavioral survey (BBS) among People who Inject Drugs (PWID). The study was conducted in two metropolitan municipalities of South Africa, the city of Cape Town and the city of Tshwane. The TipVal study was sponsored by the US President's Emergency Plan for AIDS Relief (PEPFAR) through a cooperative agreement between the US Centers for Disease Control and Prevention (CDC) in South Africa and TB HIV Care (Cooperative Agreement # GH000257). Technical assistance for the surveillance activities was provided by the University of California, San Francisco (UCSF). In its capacity as technical advisors, UCSF collaborated with Anova Health Institute and the National Institute for Communicable Diseases (NICD) as implementing academic partners for the field and laboratory research and analysis contained within this report. Through this collaboration, the TipVal study has helped to further the South African capacity and infrastructure in the health services sector to conduct HIV surveillance with PWID and other key populations, towards fulfillment of Goal 8 of the National Strategic Plan (NSP) 2017-2022: Strengthening strategic information to drive progress towards achievements of NSP goals by enhancing South African institutions' technical capacity to conduct key population BBS surveillance, mapping, and size estimation among PWID [1].

As a component of a strengthened second generation national HIV surveillance system for key populations, this surveillance survey joins the South African Health Monitoring Survey (SAHMS) with Female Sex Workers (FSW) and the South African Men's Health Monitoring Survey (SAMHMS) with men who have sex with men (MSM) in strengthening South Africa's overall approach focusing efforts on key populations at high risk for HIV in part by delivering robust scientific data on the health and social welfare needs of PWID communities in South Africa and contributes necessary data that will inform the overall calculation of the NSP Impact indicator, namely the HIV prevalence in key populations. Population size estimations also assist with advocacy efforts to provide appropriate levels of funding and types of interventions for PWID communities. Additionally, survey data has already been used to inform the South African Key Population HIV Treatment Cascades, which identifies treatment gaps within key populations as South Africa targets the UNAIDS 90-90-90 targets [1,2]. Finally, the NSP recommends viral hepatitis services for PWID, in the light of available data (which this study presents and confirmed). South Africa has adopted the WHO commitments to end Viral Hepatitis 2030.
In September 2018 the National Department of Health approved the South African National Guidelines for the Clinical Management of Viral Hepatitis and the South African National Viral Hepatitis Action Plan. The guidelines and the Action Plan highlight the need for viral hepatitis services to address the needs of PWID, and to take co-infection risks of HIV into account.

Data from the survey itself, the formative assessment and mapping phase, and the size estimation efforts will further our understanding of PWID and their specific health needs within the South African context.

The specific aims of the TipVal study were:

1. To measure the prevalence of HIV and HCV and associated risk behaviors among PWID in selected South African cities and surrounding geographic areas.

2. To estimate the population size and distribution of PWID within selected South African cities*.

3. To identify and assess current prevention and treatment program coverage, and to identify social and behavioral factors associated with access to and utilization of health and social

* As noted, the study was conducted within the two metropolitan municipalities of Cape Town and Tshwane.

welfare programs in South Africa among PWID within selected South African cities[†].

4. Additionally, through the inclusion of a set of survey questions, the study aims to provide TB HIV Care with an evaluation of their PWID demonstration project (Step Up Project) conducted at the aforementioned proposed survey sites.

BACKGROUND

Globally there are an estimated 15.6 million (10.2 – 23.7 million) persons who inject drugs (PWID) of which approximately 17.8% (10.8 – 24.8%) are HIV-positive [3]. Recent studies regionally within sub-Saharan Africa suggest an even higher burden of HIV among this population. A study in Kenya estimates HIV prevalence ranging from 36-43% among PWID [4] while Tanzania estimated 42% of PWID are infected with the virus [4]. In neighboring Mozambique, a multi-city IBBS recently found HIV prevalence of 50% in Maputo and 20% in Nampula/Nacala [5]. Practices potentially contributing to the epidemic in Mozambique include sharing of needles or syringes (ever was 50% in Maputo and 42% in Nampula/Nacala; in the last month was 26% in Maputo and 29% in Nampula/Nacala), and condomless sex during the last sexual encounter (48% in Maputo; 71% in Nampula/Nacala). Sharing of equipment used for injecting drugs is a substantial risk for transmission of blood-borne virus, including HIV, HBV, and HCV. Globally, the disease burden of viral hepatitis and HIV are elevated among PWID. Global estimates of HCV and HBV prevalence among PWID are 52.3% (42.4-62.1%) and 9.1% (5.1-13.2%), respectively[3]. In addition to the burden of HIV, there is a relationship between HIV and Hepatitis C infection (also known as co-infection) in this population. Co-infection can result in more rapid progression of both diseases [6]. PWID account for more than half of all global HIV/HCV coinfections [7].

South African Context

Historically, there has been a dearth of regional information on how the HIV epidemic among PWID contributes to the overall South African HIV epidemic. The TipVal report builds upon fairly recent studies, both in South Africa, and the abovementioned studies within the Southern African region. Primarily, it follows a 2013 rapid assessment in five-South African cities, which found an HIV prevalence of 14%, with the highest burden on women PWID (18%) [6]. Of note, the study found high prevalence of risk behaviors, including not using sterile needles for injecting or effectively cleaning needles for re-use. Although their numbers appear to be small, female PWID bear the burden of multiple intersecting risks. The same study found over 50% of women PWID reporting a history of sex work; FSW are another key population with very high HIV prevalence [8]. Women PWID are highly susceptible to gender-based violence through which they may experience pressure that may compound their HIV vulnerability.

HIV prevention programming specifically designed for PWID in South Africa has been geographically limited. Services have mainly targeted PWID residing in metropolitan areas, beginning in the 2010s with Cape Town and in Tshwane. These services have mainly focused on clean drug injection equipment (i.e. needle and syringe exchange) and HIV testing services, with only a very limited demonstration project on providing opioid substitution therapy to 60 PWID in Cape Town and 892 in Tshwane[9]). Currently, there is a lack of hepatitis services for South African PWID. The high burden of HIV on PWID particularly in regional Southern Africa, cross membership some PWID have with other key populations (e.g., sex work, MSM) with established high HIV prevalence, and the high rates of risk-taking practices observed in recent studies provide context for the need for comprehensive bio-behavioral surveillance within this population to monitor practices and trends and provide crucial

[†] Under this specific aim, the BBS specifically assessed the reach of the TB-HIV Care (THC) of South Africa's targeted PWID health programming, and the social and behavioural factors associated with PWID's uptake of THCA and other programming in each metro.

strategic information to the public and private sector working with this vulnerable population.

The TipVal Study adds significant value to the epidemiological and programmatic evidence for South African PWID in several ways. First, this is the first undertaking of a methodologically robust surveillance study of its kind for PWID in South Africa. As such, the data serve as a useful baseline for understanding the future trajectory of the HIV and HCV epidemic among PWID. It will also serve as a baseline measure of the programmatic reach of several key initiatives being implemented under the NSP, including needle and syringe programs and opioid substitution therapy that specifically aim to halt and reverse the course of the epidemic among PWID. These goals include increasing HIV testing uptake to improve case finding and referral to care among PWID under South Africa's Universal Test and Treat (UTT) guidelines, as well as referral of the uninfected to biomedical Pre-Exposure Prophylaxis (PrEP) prevention services. The data also speak to the current reach and uptake of peer-based prevention programming. And finally, the TipVal Study reports PWID population size estimates (PSE) for both of the survey cities. These PSEs were calculated from multiple methods embedded in the BBS survey methodology, vetted by the UCSF technical advisory team, and South African key population civil society stakeholders, and adopted as consensus PSEs in two workshop meetings in September 2016 and February 2017 [10]. These PSEs ultimately are critical strategic information for programmatic planning, monitoring, and evaluation at national and sub-national levels.

This report presents results from the two metropolitan municipalities of Cape Town and Tshwane, surveyed in 2017. And while this report substantially closes the knowledge gap of the HIV epidemic among PWID, given the scope of the study was limited to two metropolitan municipalities, there still remain significant swaths of the country for which PWID data simply does not yet exist. Extrapolations of the data presented here to other municipalities and districts within South Africa is not recommended.

METHODS

An initial formative assessment phase of the study was conducted through rapid assessment, including the use of qualitative research techniques using key informant interviews (KII), focus group discussions (FGD), and ethnographic mapping [11-14]. The formative assessment was primarily done to aid in identifying the operational and logistical needs of conducting respondent-driven sampling (RDS) research among PWID, including HIV testing and data collection, in each location; determining appropriate location for study offices and participant compensation; identifying the initial RDS seeds (6-8 per study site) among the KII and FGD participants to launch RDS recruitment.

Participants in the IBBS phase of the study were recruited at two large urban metropolitan municipalities (>1.0 million residents). Both sites implemented an identical RDS recruitment protocol. Seed participants at both sites were identified based on key demographic and behavioral characteristics, determined in the abovementioned pre-survey formative assessment phase. Seeds were strategically "planted" both during the initial launch of recruitment and across the study implementation, based on ongoing monitoring of sample composition for geographic and demographic characteristics to ensure diversity within the developing sample to achieve a representative sample informed by formative assessment and the understanding of key stakeholders. These key indicators included age, gender, educational attainment, socioeconomic status, participation in sex work, geographic place of residence within the study site, race/ethnicity, known HIV serostatus, sexual behavior, drug injection practices, and non-injection related risk behaviors. The study issued up to three recruitment study coupons to each participant, including seeds, and provided instructions and guidance on how to recruit other PWID within their networks to participate in the BBS.

Inclusion criteria for survey participation were age of 16 years or older; self-reported drug injection for a non-medical purpose within 12 months preceding survey participation; possession of a valid study coupon; residing, working, or socializing within the geographic study area during the previous 6 months; consenting to having HIV testing results returned; and consenting to receiving hepatitis C test with results returned. Additionally, participants consented to providing contact information to the study in case of discrepant test results between rapid field testing and laboratory testing procedures. Participants who did not meet these criteria, or who were not able to provide informed consent, or who had previously participated in the study (determined by biometric data), or who were unable to demonstrate they had been voluntarily recruited by a known member of their social network (i.e. in possession of valid study coupon), were deemed ineligible through screening and excluded from enrollment. Once screened for eligibility, participants were guided by trained staff fluent in both English and local languages through the informed consent for behavioral survey, HIV testing and counseling, and Hepatitis C viral testing. Informed consent detailed all study procedures to participants (i.e. venipuncture for blood draw), risks, benefits, and contact information to report complaints or concerns. Staff were trained to provide eligible participants with the opportunity to have any questions answered by study staff. Participants were given the ability to consent to discrete portions of the study (behavioral data collect, venipuncture for sample preparation, laboratory and rapid field testing), though declining the return of HIV test results disqualified an otherwise eligible participant from study participation.

Behavioral data collection. Study staff administered a standardized interviewer-administered computer-assisted HIV surveillance questionnaire, adapted for South African PWID, programmed using the Questionnaire Development System (QDS) version 7.26.13. This behavioral data collection tool and technology has previously been successfully implemented in other key populations IBBS activities in South Africa and other PEPFAR countries by the UCSF Institute for Global Health Sciences/Global Strategic Information research unit and its local PEPFAR partners [5,8]. The questionnaire included information on demographics; knowledge of HIV and viral hepatitis transmission; sexual history; sexual behaviors during the 6 months preceding the survey; alcohol and drug use; HIV knowledge, HIV prevention, and testing history; HIV care and treatment; stigma, discrimination and violence; access and utilization of healthcare services; exposure to the Step Up[‡] or any other harm reduction program; and information regarding the participant's PWID social network. The questionnaire was developed and programmed in English, but the training of staff entailed a question by question discussion and consensus building process on how to phrase each survey item based on intent and current terms in common usage in each African vernacular language and local dialects so simultaneous translation into the regional languages and dialects would be consistent.

Biological Data Collection. Each site's staff were trained on venipuncture blood collection procedures for point of care testing (POCT) and surveillance testing for HIV and Hepatitis C Virus (HCV). The study's serological HIV antibody rapid testing and HCV rapid testing algorithms are shown in Figure 1. Whole blood specimens were collected via venipuncture with two x 8ml PST blood tubes. One tube was used for POCT, while the other was stored at 4-8° C and sent to the laboratory within in 24 hours of collection. Laboratory processing included preparation of dried blood spots, collection of plasma following centrifugation, and testing. Dried blood spots were prepared by spotting 5 x 100 µl spots on Whatman 903 cards. Cards were placed in gas impermeable bags containing desiccant packs and humidity cards and stored at -20° C. The DBS served as back-up specimens if required.

On-site POCT HIV rapid testing was conducted after completion of pre-test counseling by certified personnel. HIV Rapid testing was conducted using a serial testing algorithm as per the South Africa

[‡] Step Up is a TB/HIV Care program implemented by OUT, which aims to demonstrate the feasibility of providing a core package of evidence-based HIV prevention and harm reduction services to PWID in Cape Town, Durban (eThekwini), and Pretoria (Tshwane).

national testing guidelines and approved commercial kits. Participants were first screened for HIV using Advanced Quality Rapid anti- HIV (1&2) test (InTec Products INC). Non-reactive results were interpreted as HIV negative, and any reactive results was confirmed with Abon HIV 1/2/0 Tri-Line Rapid test kit (Abon BioPharm). If HIV rapid test results were discrepant (reactive screening test, and negative confirmatory test), the testing algorithm was repeated. If results remained discrepant participants were asked to visit an Anonymous Testing Site (ATS) or other facility for repeat testing.

On site testing for HCV infection was performed using the OraQuick HCV rapid antibody test (OraSure technologies), with reactive tests interpreted as HCV positive and nonreactive tests interpreted as HCV negative.

Laboratory HIV Antibody Testing: Whole blood specimens received by the laboratory were centrifuged to obtain plasma, which was tested for HIV antibodies using a 4th generation HIV ELISA (Biorad Genscreen Ultra HIV Ag-Ab) as the screen test (Test One). Non-reactive results on test one were regarded as negative. A 4th generation ELISA (Diasorin Murex HIV Ag/Ab Combo) was used to confirm any reactive ELISA result (Test Two) (see Figure 2). Due to the potential of false reactive results, a HIV-1 Western blot or similar confirmatory assay such as Geenius was performed.

HIV Viral Load Testing: HIV viral load testing was performed using the Abbott HIV Real Time M2000 platform. Cut-off viral load value for analysis were set at >500 copies/ml for detection of viral load and <500 copies/ml for undetectable viral load or virally suppressed on ART (see Figure 3).

Hepatitis C virus (HCV) antibody testing: HCV antibody tests used the Abbot ARCHITECT Anti-HCV assay, which is a chemiluminescent immunoassay (CMIA) for the qualitative detection of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to HCV in human adult serum and plasma. ARCHITECT Anti-HCV is designed to detect antibodies to putative structural and nostructural proteins of the HCV genome. The assay has 100% sensitivity and 98.8% specificity. Reactive samples were interpreted as HCV positive (see Figure 2 for flowchart for laboratory procedures for HCV). Thus, some of the HCV positive participants detected via antibody either may have cleared an infection or may be false positives.

HCV viral load testing: Viral load testing for HCV to confirm acute or chronic HCV infection was performed using the COBAS Ampliprep TaqMan (Roche), which is a nucleic acid amplification test for quantitation of HCV RNA in human serum or plasma. Specimen preparation was automated using the COBAS AmpliPrep Instrument with amplification and detection automated using the COBAS TaqMan 96 Analyzer. The COBAS AmpliPrep/COBAS TaqMan HCV test version 2.0 uses reverse transcription and PCR amplification primers that define a sequence within a highly conserved region of the 5'-untranslated region of the HCV genome. The nucleic acid sequence of the primers has been optimized to yield comparable amplification of the HCV genotypes 1-6. The test can quantitate HCV RNA over the range of 15 – 100,000,000 IU/ml. N.B. Due to the unanticipated high prevalence of HCV infection in the Tshwane population and the high cost of the the HCV viral load assay, the study was unable to perform this test on a small proportion of HCV antibody positive samples. Participants were able to receive this confirmatory test at any of the hospitals to which they study referred all HCV antibody positives. The HCV results reported in this study assumes HCV antibody-positive samples would have detected HCV RNA and thus acutely or chronically infected.

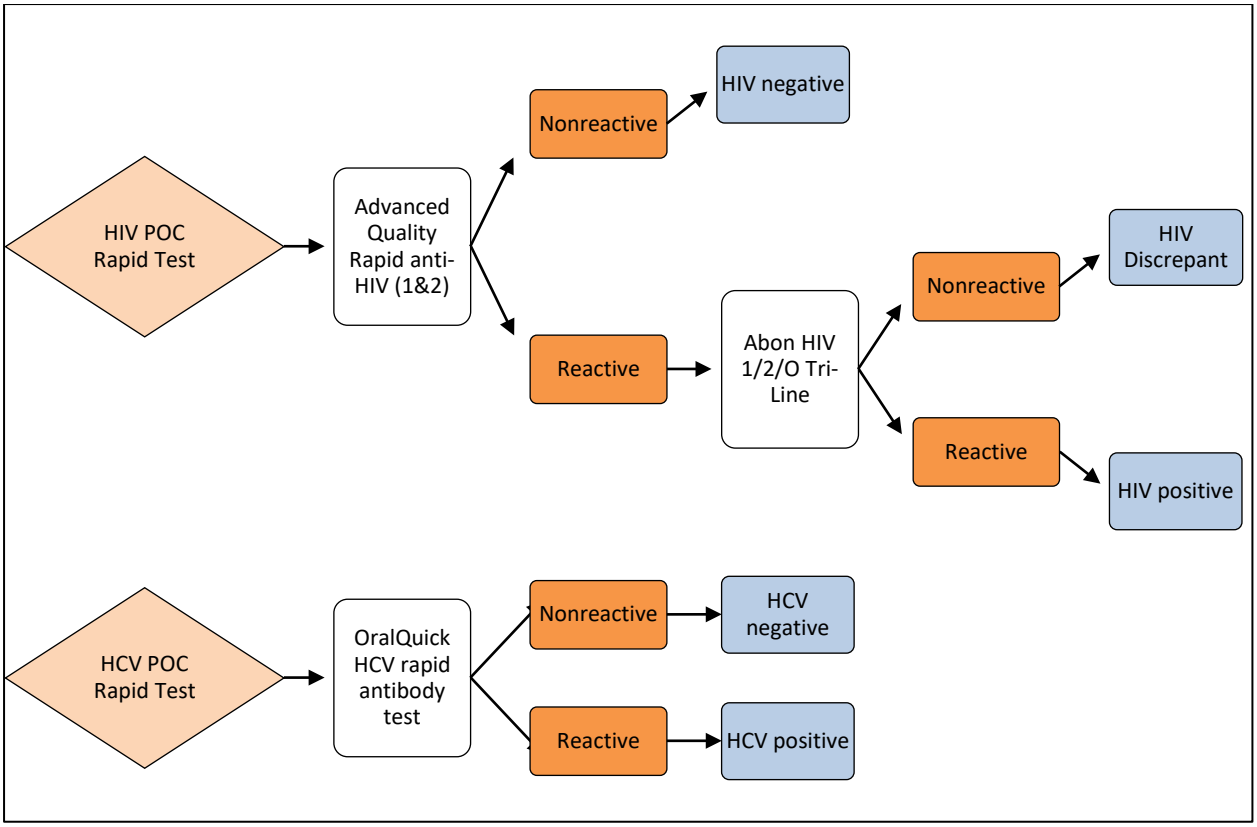


Figure 1: Flowchart of POCT for HIV and HCV, TipVal Study, 2017

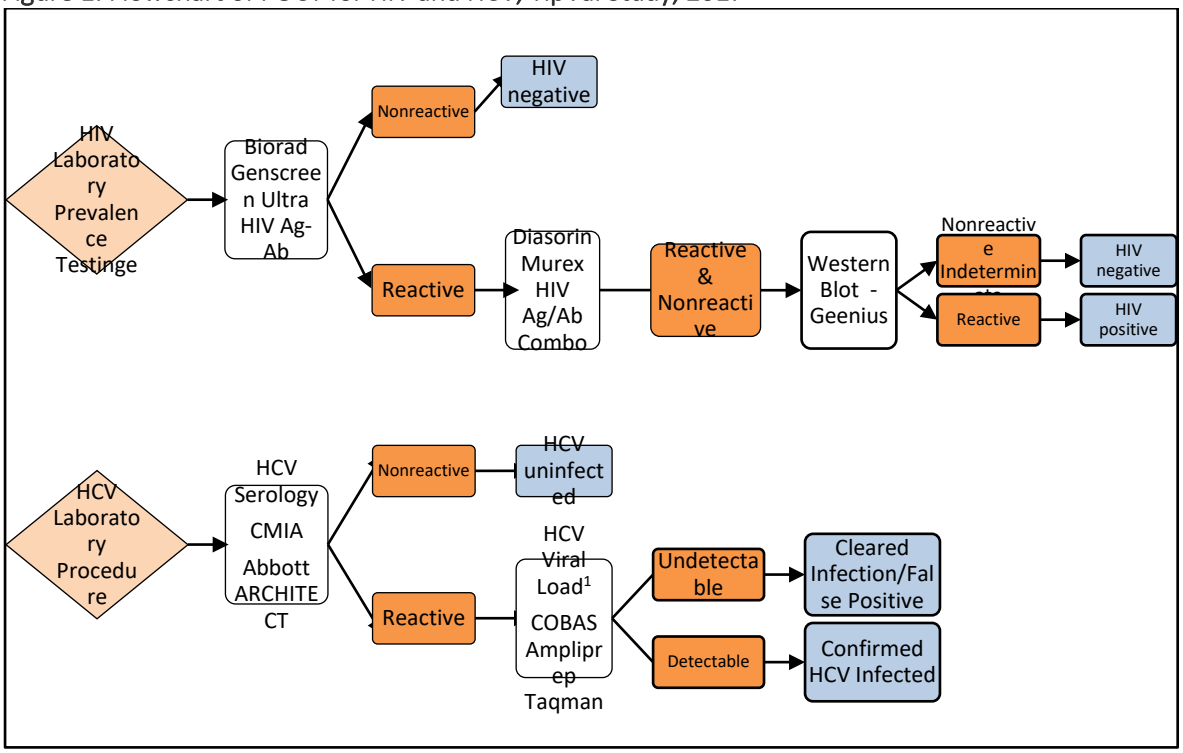


Figure 2: Flowchart of laboratory testing procedures for HIV and HCV, TipVal Study, 2017

1 - HCV prevalence within the sample was higher than anticipated. With the high HCV prevalence, budgetary constraints did not allow for HCV viral load testing on all reactive samples.

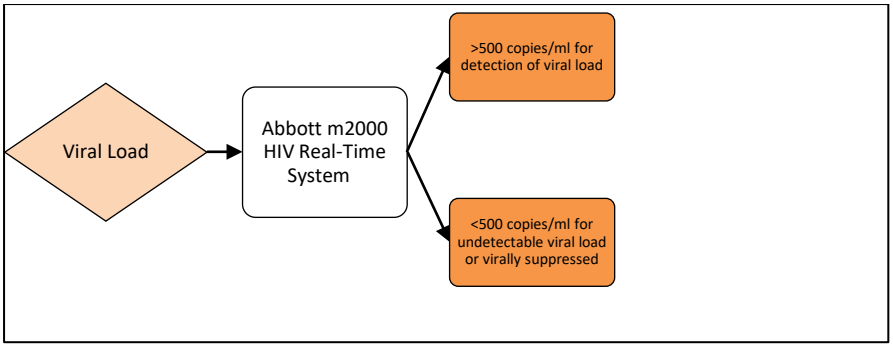


Figure 3: Flowchart for HIV viral load testing

All survey and laboratory data were anonymously collected and linked via study Identification numbers linked to the participant's coupon number. All PSE relied on the RDS-I (DS) estimator and were re-sampled with 15,000 bootstraps. Network size information was determined by asking participants, "Approximately how many people who inject drugs age 16 and over do you personally know who live in [study site]?" Biological and behavioral data were analyzed using RDS-A v 0.42 to calculate adjusted estimates of key surveillance indicators, including HIV and HCV infection, HIV treatment cascade, HIV testing behavior, and knowledge and uptake of HIV service indicators. (This data set is available from UCSF, CDC-South Africa, or any other partners to this surveillance survey for future analyses to explore selected adjusted and unadjusted bivariate associations between selected predictors and outcome indicators.)]

Population size estimation: we followed best practices for multiple methods for PSE, and a modified Delphi participatory process with key population stakeholders to achieve consensus on population size point estimates and a reasonable plausible range for each site[15]. We briefly detail this process below and present the results in the following Results section.

Unique Object Multiplier

The unique object multiplier involves the distribution of a large number of objects to PWID throughout the survey area. This component of the multiplier method meant the objects were distributed just prior to survey launch. The team ensured distribution of objects was thorough, including diversity in locations, dates and times. Each brief interaction with PWID was recorded including screening to ensure they were PWID and whether they previously received the object at another location or time. In the TipVal survey, participants were shown a picture of the object and asked if they received the object during the time of distribution. Below we present RDS-adjusted estimates of the population size using the unique object multiplier.

Service multiplier

The TipVal study collaborated with organizations providing health services to PWID in each survey city. To enable implementation of this method, each organization provided de-duplicated counts of PWID seeking services during a specified period (e.g. HTS between January 1st and April 30, 2017). In the survey participants were asked if they received the named service from the organization during the same time period. To limit recall bias, the survey question referenced holidays where applicable (i.e. New Year's Day). The proportion of those reporting receiving services was compared with service-provider data on total PWID served to form a population size estimate.

"Wisdom of the Crowds" (WOTC) Modified Delphi method

WOTC asks population members to estimate the size of the population based on their own perceptions and experiences in their communities. To accomplish this, we embedded within the survey, a question asking PWID to provide a best estimate of how many PWID there are in their location (i.e. Tshwane). To ensure response reliability, the question was asked twice within the survey.

(N.B. This question is also used per RDS methodology as the first question in an heuristic designed to enable participants to more accurately and precisely estimate their network size, e.g. "Of these, how many do you personally know and would consider giving a recruitment coupon to?" Network size estimation is used to calculate the probability of recruitment estimator upon which each RDS observation is weighted). Where there was difference between the two responses a mean of the two estimates was used to calculate a point WOTC PSE for that observation.

Successive sampling-population size estimation

Successive sampling-population size estimation (SS-PSE) along with network size imputation allows population size estimates to be made without relying on separate studies or additional data (unlike network scale-up, multiplier and capture-recapture methods), which may in themselves be biased. SS-PSE is a relatively new method and a potential alternative to estimate the size of hard-to-reach populations [16-19]. It relies primarily on data collected within the RDS study (participant's individual degree, recruitment patterns, and date of study participation). In addition, the method relies upon prior estimates, including modified Delphi expert opinions and guesses, about the population size. For this method, we followed the full description of the SS-PSE method as described elsewhere [20,21].

RESULTS

Population Size Estimates

We present point Population Size Estimates (PSEs) below. We followed best practice multiple multiplier estimation (MME)[15] and a modified Delphi consensus process to arrive at the February 2018 Key Population Consensus PSEs are detailed in the following section and summarized in Figure 4. A short summary of our consensus process has been described in detail elsewhere[8,10,22] and will be briefly reviewed below.

Unique Object Multiplier

The unique objects for the TipVal study were colored rubber bracelets. In Cape Town 680 objects were distributed; 202 PWID in the survey reported receiving one; resulting in an RDS-adjusted of 1,347. In Tshwane, 808 objects were distributed with 232 participants reporting having received one, for a point PSE of 1,972.

Service multiplier

In Cape Town service data from the Step Up Project counted 843 PWID receiving services of HIV testing or harm reduction packet; with 199 survey participants reported accessing services during the recall period, for a PSE of 1,688. In Tshwane, where the Step Up Project is also being implemented, OUT provided a count of 3,954 accessing services, with 279 survey participants reporting service uptake during the recall period, for a PSE of 7,827.

"Wisdom of the Crowds" (WOTC) Modified Delphi method

The WOTC method produced the following PWID size estimates: Cape Town 2000; Tshwane 7,000.

Successive sampling-population size estimation

In Table 1, we present the estimates and the results for SS-PSE method, which produced the following PWID size estimates: Tshwane 2,027, Cape Town 909.

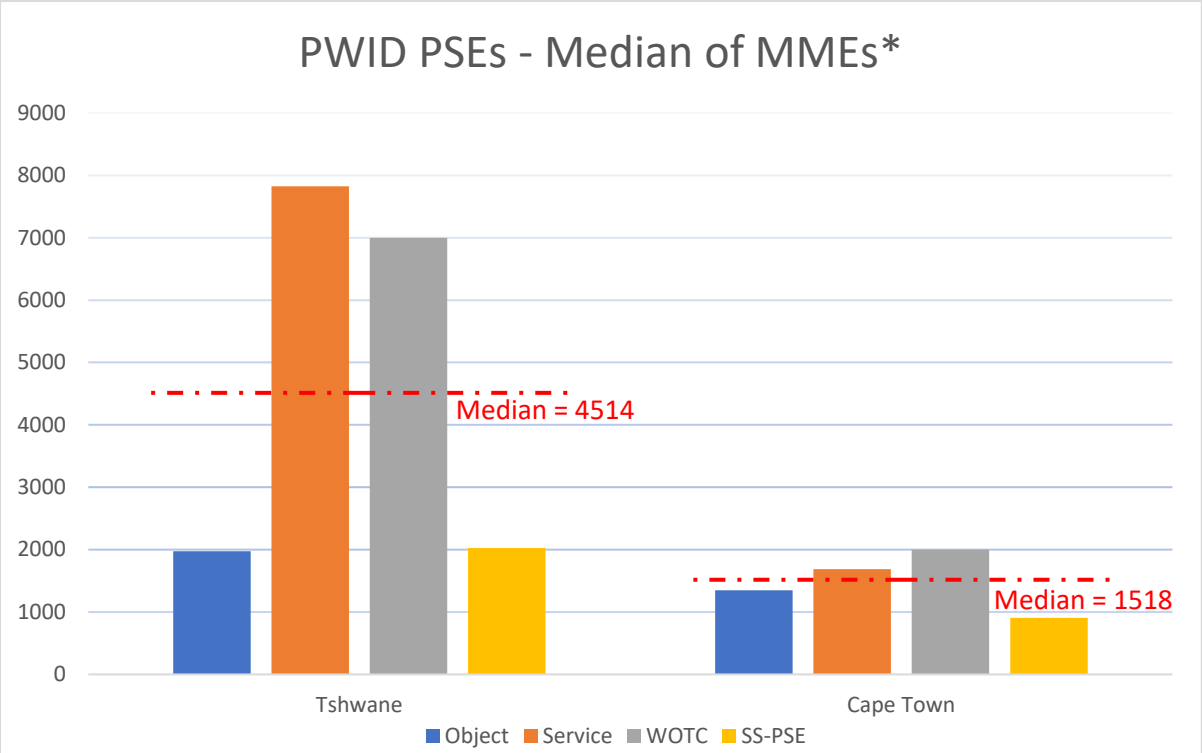
Table 1: Population size estimates using successive sampling, TipVal 2017.

	Prior[1]	Posterior Median	Posterior Median (flat prior)
Tshwane	3000	2041	2027
Cape Town	1300	789	909

1 – Prior used conservative estimates of previously known population sizes for both Tshwane and Cape Town.

Stakeholder vetting of median plausible estimates, and February 2018 Consensus PSEs

These population size figures were thoroughly vetted with stakeholders in light of programmatic experience: in general, they believed they were low compared to their service uptake numbers, but they acknowledged their service numbers had not been systematically deduplicated. They concluded that while these may be conservative estimates, they were backed up by empirical data and recommended to the entire group, with the highest and lowest point estimates representing a reasonable plausible range (PR): Tshwane 4,514 (PR 1,970-7,800), and Cape Town 1,518 (PR 909-2,000). These results are displayed in Figure 4.



* Multiple Multiplier Estimates, Abdul-Qader 2014; operationalized by SFDPH 2015, UCSF, 20

Figure 4. PSE for PWID in TipVal Surveillance Sites, 2017

Demographics and transactional sex

An overwhelming majority of our sample from both surveillance sites was male; South African; and single (e.g. never married or committed to a man or woman as if married). Similar to many RDS studies, the sample was young, with a majority being under age 35 (see Table 2). RDS adjustments did little to change the population estimates within those metropolitan areas. Transactional sex, both receiving and giving money or goods in exchange for sex, was not common (see Figure 5).

Table 2: Demographic characteristics of PWID, TipVal 2017

Measure	Tshwane (n=544)				Cape Town (n=348)			
	Crude		Adjusted		Crude		Adjusted	
	N	%	%	95% CI	N	%	%	95% CI
Sex								
Biological male	512	93.9%	93.8%	93.1-94.5%	303	87.1%	88.5%	85.1-91.9%
Citizenship								
South African	541	99.3%	99.7%	98.9->99.9%	346	99.4%	99.2%	99.1-99.2%
Marital Status								
Never married	528	96.9%	97.5%	97.4-97.6%	267	76.7%	77.2%	73.1-81.3%
Age								
18-24	111	20.4%	24.0%	19.0-29.0%	22	6.3%	7.5%	4.7-10.2%
25-29	212	38.9%	34.4%	32.6-36.2%	94	27.0%	22.8%	17.3-28.3%
30-34	151	27.7%	31.6%	27.3-35.8%	120	34.5%	34.0%	27.8-40.1%
35-39	49	9.0%	6.8%	4.0-9.6%	73	21.0%	24.8%	20.2-29.4%
40-49	20	3.7%	2.8%	<.01-7.4%	31	8.9%	8.8%	5.5-12.2%
50 and older	2	0.4%	0.4%	<.01-1.3%	8	2.3%	2.1%	0.4-3.8%

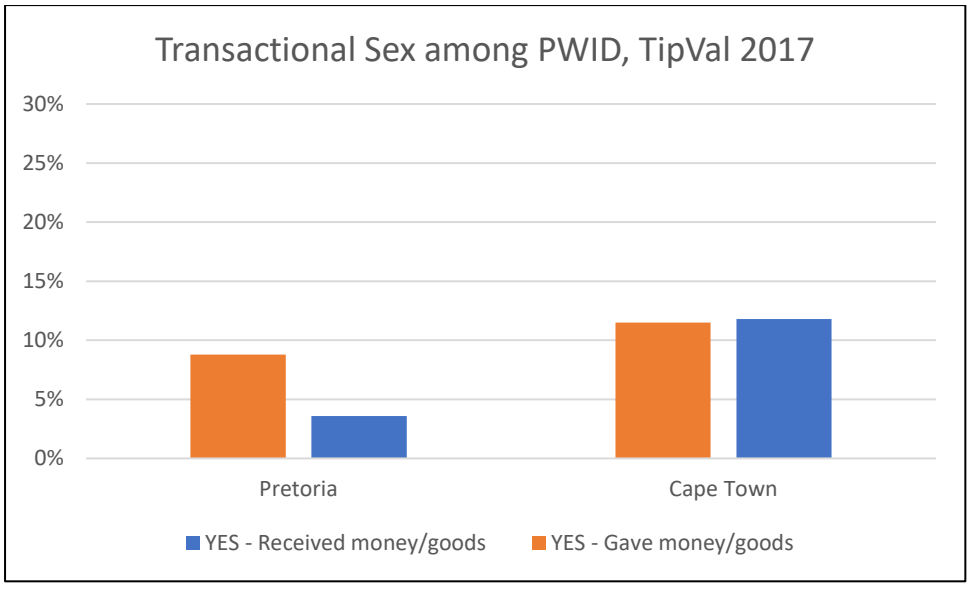


Figure 5. Proportion of PWID participants reporting transactional sex, TipVal 2017.

HIV Prevalence, and Treatment Cascade Indicators

Using the Population Size Estimates (PSEs) from above, we present HIV Prevalence estimates, and estimated PWID Persons Living with HIV (PLHIV) below in Table 3. The plausible range of population size estimates was used with the RDS-adjusted HIV prevalence and confidence interval to generate a range of estimated PWID living with HIV within the two metropolitan areas. Using the 2011 census data, we estimate the percent adult population (i.e. those over 15 years of age) who inject drugs.

Table 3: TipVal Population Size Estimates and HIV prevalence, 2017

Site Metro = Metropolitan Municipality	Point PSE (median plausible estimate, range)	% population ≥ 15 (2011 census)	RDS-Adjusted HIV prevalence (95% CI)	Estimated PWID PLHIV (estimate, range)
Tshwane Metro	4,514 (1,970 – 7,800)	0.20%	58.4% (52.9 - 63.8%)	2,637 (1,043 – 4,977)
Cape Town Metro	1,513 (909 – 2,000)	0.05%	11.4% (7.7 - 15.2%)	173 (70 – 304)

We observed high HIV prevalence Tshwane Metro, where approximately 6 in 10 PWID are estimated to be HIV infected. In Cape Town, around 1 in 10 PWID are HIV infected. Based on the HIV prevalence and population size estimates, we calculate 2,637 PWID living with HIV in Tshwane Metro and 173 in Cape Town Metro.

Hepatitis C infection and coinfection with HIV

This study found extremely high HCV prevalence among PWID: 94.1% in Tshwane and 64.1% in Cape Town are estimated to be infected with hepatitis C. Over half of PWID in Tshwane (56.6%) are estimated to be coinfected with HIV and HCV; in Cape Town, we estimate HIV-HCV coinfection prevalence at 8.3 %. We present these results in full in Table 4.

Table 4. HCV infection and coinfection with HIV, TipVal 2017.

Measure	Tshwane (n=544)				Cape Town (n=348)			
	Crude		Adjusted		Crude		Adjusted	
	N	%	%	95% CI	N	%	%	95% CI
Hepatitis-C Antibody Lab Results[1]								
HCV Positive	508	93.4%	94.1%	91.4-96.8%	210	60.3%	64.1%	57.8-70.4%
HCV Negative	28	5.1%	5.9%	3.2-8.6%	133	38.2%	35.9%	29.6-42.2%
Missing	8	1.5%			5	1.4%		
Coinfection								
Coinfected with HIV & HCV	287	52.8%	56.6%	51.2-62.1%	28	8.0%	8.3%	6.3-10.3%
Not coinfected	247	45.4%	43.4%	37.9-48.8%	317	91.1%	91.7%	98.7-93.7%
Missing	10	1.8%			3	0.9%		
Previously known HCV status								
Known HCV infection	57	11.3%	11.6%	9.2-13.9%	57	27.1%	29.6%	15.7-43.4%
Newly diagnosed	448	88.5%	88.4%	86.1-90.8%	151	71.9%	70.4%	56.6-84.3%
Missing	1	0.2%			2	1.0%		

1 – Hepatitis C Lab results are based on the laboratory CMIA tests and do not include viral load tests to rule out false positives or cleared infection (see Figure 2).

Perceived HIV status among PWID

Across both sites, the HIV prevalence is higher than the proportion of PWID who perceive themselves positive. Over half of those testing HIV-positive misperceive themselves to be HIV negative (Tshwane 54.1%; Cape Town 50.0%). Most PWID who test HIV negative correctly perceive their status (Tshwane 81.8%; Cape Town 97.1%) (see Table 5). Note that a survey programming error inadvertently introduced an incorrect skip pattern into the survey. As a consequence, participants were not asked if they were aware of their HIV status. To create the HIV treatment cascade (e.g. UNAIDS 90-90-90

treatment targets) we triangulated the first 90: HIV positive individuals who correctly know their HIV positive status.

Because participants were not asked if they knew of their HIV status, a subsequent follow up question on ART use was also skipped. Laboratory tests for ART analytes was not conducted, so the results lack self-reported and laboratory-verified data on ART uptake among PWID. The study did conduct viral suppression analysis on all positive samples, so the final piece of the HIV treatment cascades, viral suppression, is represented in Figure 6. In stakeholder consultations from February, 2018, the consensus was that the number of PWID on ART is very low. Reported PWID programmes to provide HIV testing and linkage to care are funded, but at the time few PWID were known to access ART in the public sector.

Table 5. Perceived HIV status among PWID in Tshwane and Cape Town, TipVal, 2017.

Measure	Tshwane (n=544)				Cape Town (n=348)			
	Crude		Adjusted		Crude		Adjusted	
	N	%	%	95% CI	N	%	%	95% CI
Perceived HIV Status								
HIV Negative	360	66.2%	68.4%	63.5-73.3%	316	90.8%	91.3%	91.2-91.5%
HIV Positive	184	33.8%	31.6%	26.7-36.5%	26	7.5%	7.5%	6.4-8.7%
Don't Know		0.0%			6	1.7%	1.10%	0.01-2.2%
Perceived HIV Status among HIV-positive								
HIV Negative	164	54.1%	56.1%	46.1-66.2%	18	50.0%		
HIV Positive	139	45.9%	43.9%	33.8-53.9%	15	41.7%		
Don't Know					3	8.3%		
Perceived HIV Status among HIV-negative								
HIV Negative	189	81.5%	81.8%	71.3-92.3%	295	95.5%	97.1%	97.0-97.2%
HIV Positive	43	18.5%	18.2%	7.7-28.7%	11	3.6%	2.2%	1.9-2.5%
Don't Know					3	1.0%	0.70%	0.5-1.0%

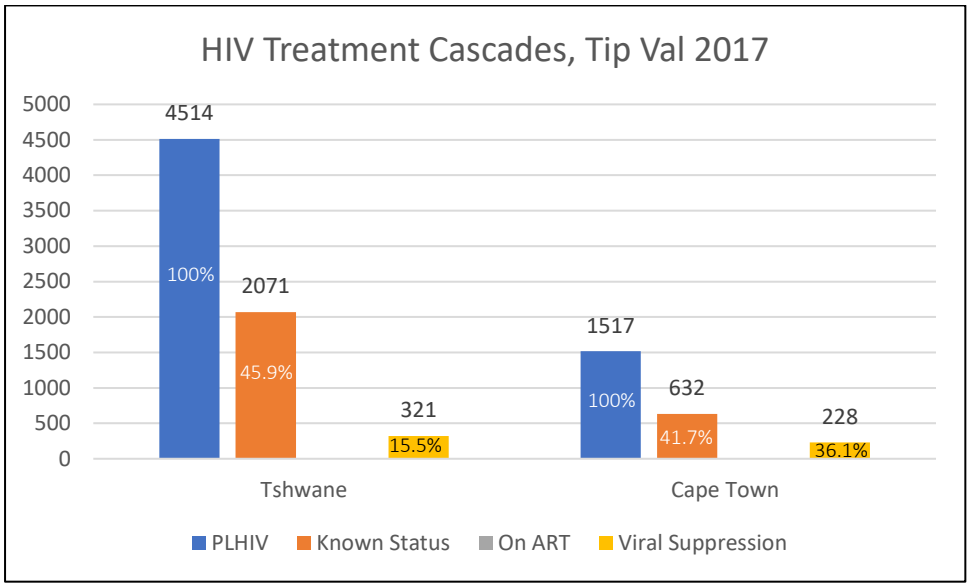


Figure 6. Tshwane and Cape Town Metro PWID Estimated HIV Treatment Cascades, TipVal 2017.

HIV viral suppression for all samples testing HIV positive was low. Of the 303 HIV positive samples from Tshwane, 47 samples were virally suppressed (15.5%). Of the 36 HIV positive samples from Cape Town, 13 were determined to be virally suppressed (36.1%). Using the population size estimates, we projected that in Tshwane among the 2,637 PWID living with HIV, XX have reached viral suppression; and of the 173 PWID living with HIV in Cape Town, XX have reached viral suppression.

HIV testing, stigma, and health seeking behaviors

An overwhelming majority of participants at both surveillance sites has tested for HIV (72.4% (95% CI: 67.7 - 77.2%) in Tshwane; 97.5% (95% CI: 97.0 - 97.9%) in Cape Town). Among HIV negative PWID in Tshwane few tested within the past 3 months [11.4% (95% CI: 5.1-17.7%)] with similar proportions testing in the last 3 to 6 months [12.5% (95% CI: 1.6-23.3%)]. HIV negative PWID in Cape Town report more recency of testing with half testing within 3 months (95% CI: 43.1-56.8%) and another one in five testing in the last 3 to 6 months [20.9% (95% CI: 13.5-28.3%)].

With the past 12 months, approximately a quarter PWID across both metropolitan areas sought medical care (27.2% (95% CI: 22.4 – 32.1%) in Tshwane; 25.7% (95% CI: 20.0 - 31.3%) in Cape Town); with fewer visiting health care centers with PWID-specific information. (17.9% (95% CI: 14.2 – 21.5 %) in Tshwane; 21.4% (95% CI: 16.0 - 26.7%) in Cape Town). Within healthcare settings, reports of discriminating behavior in the healthcare settings are low (8.7% (95% CI: 6.2 - 11.3%) in Tshwane; 6.2% (95% CI: 3.0 - 9.3%) in Cape Town). Most of the stigmatizing behavior reported was verbal insults; from police authorities; and when seeking employment or housing (see table 6).

Table 6. Stigmatizing behavior reported in previous 12 months, TipVal 2017

Measure	Tshwane (n=544)				Cape Town (n=348)			
	Crude		Adjusted		Crude		Adjusted	
	N	%	%	95% CI	N	%	%	95% CI
Report of Stigmatizing Behavior in Previous 12 Months								
Healthcare	38	7.0%	8.7%	6.2-11.3%	29	8.3%	6.2%	3.0-9.3%
Employment	115	21.1%	19.3%	14.4-24.2%	122	35.1%	32.8%	27.0-38.6%
Church/religious services	24	4.4%	3.4%	0.5-6.2%	22	6.3%	5.1%	2.3-7.9%
Restaurant/bar	133	24.4%	23.2%	18.3-28.0%	51	14.7%	10.8%	6.8-14.9%
Housing	73	13.4%	15.2%	11.5-18.9%	77	22.1%	19.8%	14.2-25.3%
Police Assistance	140	25.7%	25.9%	21.1-30.6%	125	35.9%	29.7%	23.8-35.6%
Verbal insults	267	49.1%	45.5%	40.0-51.0%	239	68.7%	57.0%	50.7-63.4%

Physical and sexual assault against PWID

PWID report suffering physical assaults within a 12-month period (see table 7). In Tshwane, approximately 3 in 20 have been kicked or beaten while almost a quarter in Cape Town have been similarly assaulted. No sexual assaults or rapes were reported in the Tshwane metro area, rendering RDS adjustments impossible, and very few Capetonian PWID have been sexually assaulted or raped in the past year (2.3%, 95% CI: 0.4 – 4.%).

Table 7. Physical and sexual assault within the preceding 12 months, TipVal 2017

Measure	Tshwane (n=544)				Cape Town (n=348)			
	Crude		Adjusted		Crude		Adjusted	
	N	%	%	95% CI	N	%	%	95% CI
Kicked or beaten because PWID in Previous 12 Months								
Yes	80	14.7%	14.7%	11.7-17.6%	94	27.0%	23.2%	17.6-28.8%
No	464	85.3%	85.3%	82.4-88.3%	254	73.0%	76.8%	71.2-82.4%
Sexually Assaulted or Raped in Previous 12 Months								
Yes	0	0.0%	--	--	10	2.9%	2.3%	0.4-4.1%
No	544	100.0%	--	--	338	97.1%	97.7%	95.9-99.6%

Knowledge (HIV and viral hepatitis)

Table 8 presents United Nations General Assembly (UNGASS) Knowledge Indicators. (A) includes the seven indicator questions generally asked in national AIDS Indicator Surveys, including the South African National Household Survey, as a marker of general HIV knowledge. (B) is an abridged version of these with the question "Can People reduce their chances of getting HIV by not having sexual intercourse at all." The reason for analyzing knowledge indicators as (B) is that with a key population, a question about abstinence is simply not useful knowledge upon which to assess general population knowledge or build any meaningful programmatic intervention to prevent sexual transmission. We also present in (C) the proportion who answered correctly to the question, "does sharing needles when injecting drugs
increase the risk of getting HIV?" and (D) the proportion who answered correctly to the question, "does cleaning needles and syringes between injections reduce the risk of getting HIV?" We note two trends in this data. Almost two-thirds of PWID in Cape Town demonstrate correct general knowledge of HIV but under half of PWID in Tshwane rovide correct answers to general HIV knowledge, even after the removal of the abstinence indicator. This said, it is encouraging that the one of the two indicators on injection behaviors was answered correctly by an overwhelming majority of PWID at both sites, showing optimal knowledge regarding "sharing needles" as a transmission risk. However, the proportions answering correctly to cleaning needles and syringes displays less than optimal knowledge on that indicator.

Table 8. HIV Knowledge indicators, TipVal 2017

(A) All UNGASS Knowledge Indicators; (B) PWID-Abridged UNGASS Indicators; (C) Sharing Needles' (D) Cleaning Needles and Syringes

	Tshwane	Cape Town
A	35.7% (30.3-41.0%)	60.4% (54.1-66.8%)
B	47.4% (41.9-53.0%)	61.7% (55.5-67.8%)
C	99.2% (99.0-99.3%)	99.0% (97.4-99.9%)
D	67.7% (62.6-72.8%)	64.4% (58.2-70.5%)

Injection Behaviors

In Tshwane, the drug most often injected in heroin, while in Cape Town, PWID inject heroin as well as methamphetamine. In Tshwane, a majority of PWID report ever sharing needles, while roughly one third of PWID in Cape Town report ever sharing needles. An overwhelming majority of PWID report access to safe injection materials [89.3% (95% CI: 84.9-93.7%) and 85.7% (95% CI: 81.1-90.3%) in Tshwane and Cape Town respectively]. Sharing injection equipment and ineffective risk reduction strategies are prevalent within the community despite accurate awareness of HIV transmission risk and viral hepatitis (see Table 9).

Table 9. Drug injection behaviors and viral hepatitis knowledge, TipVal, 2017.

Measure	Tshwane (n=544)				Cape Town (n=348)			
	Crude		Adjusted		Crude		Adjusted	
	N	%	%	95% CI	N	%	%	95% CI
Drug Injected Most Often								
Brown heroin	305	56.07%	56.90%	51.4-62.4%	88	25.29%	21.10%	15.5-26.8
White heroin	408	75.00%	71.30%	66.6-76.1%	304	87.36%	86.30%	82.6-90.0
Cocaine	1	0.18%	--	--	0	0.00%	--	--
Methamphetamine	1	0.18%	--	--	89	25.57%	23.80%	18.1-29.6
Speedball	2	0.37%	--	--	4	1.15%	--	--
Other*	10	1.84%	--	--	2	0.57%	--	--
Ever Share Needles								
Yes	428	78.7%	83.2%	78.3-87.7%	139	39.9%	34.4%	28.1-40.7%
Access to new, unused needle anytime participant needs one								
Yes	479	88.1%	89.3%	84.9-93.7%	293	84.2%	85.7%	81.1-90.3%
The last time injected with someone…								
…used a new unused needles	274	50.4%	51.5%	46.1-57.0%	2	79.0	81.7	76.0-87.4%
…used a needle only previously used by participant	289	53.1%	53.0%	47.6-58.4%	1	53.7	58.4	52.0-64.8%
…used a needle and/or syringe after someone else had used it	386	71.0%	69.2%	64.4-74.0%	5	14.7	14.0	9.4-18.5%
…passed a needle to others after using it	368	67.7%	69.2%	64.0-74.3%	5	15.8	14.4	10.1-18.7%
What do you usually use to clean the needle/syringe?**								
Bleach	4	0.7%	--	--	2	5.7	4.5	1.7-7.3%
Can a person get…[below] …through sharing needles/syringes								
…Hepatitis C…	218	40.1%	35.9%	30.4-41.5%	2	73.6	65.4	59.8-71.1%
…Hepatitis B…	294	54.0%	51.7%	42.7-53.8%	2	74.1	68.4	63.1-73.6%

* Other includes crack, yellow heroin, cream white heroin, and Tik.
** Other response options included cold water, hot water, soap, saliva, urine, soda/soft drinks, alcohol, and cotton.

Pre-Exposure Prophylaxis and Post-Exposure Prophylaxis

Across both surveillance sites, roughly one in ten PWID have heard of either post-exposure (PEP) or pre-exposure prophylaxis (PrEP), and a tiny fraction of PWID have used either PEP or PrEP as a strategy for HIV prevention (see table 9).

Table 10. Post-exposure (PEP) and Pre-exposure prophylaxis (PrEP) awareness and usage, TipVal, 2017.

Measure	Tshwane (n=544)				Cape Town (n=348)			
	Crude		Adjusted		Crude		Adjusted	
	N	%	%	95% CI	N	%	%	95% CI
Has heard of PEP								
Yes	65	11.9%	13.8%	10.4-17.2%	51	14.7%	13.3%	8.8-17.7%
PEP Usage[1]								
Yes	0	0.0%	---	---	3	0.9%	2.1%	1.0-3.3%
Has heard of PrEP								
Yes	54	9.9%	10.0%	6.8-13.2%	55	15.8%	12.3%	7.0-17.6%
Has Used PrEP[1]								
Yes, currently	0	0.0%	---	---	1	0.3%	0.2%	0.2-0.3%
Yes, but stopped	1	0.2%	---	---	4	1.2%	0.8%	0.7-0.9%
No	543	99.8%	---	---	343	98.6%	99.0%	98.9-99.0%

1. Small cell sizes in the Tshwane sample prevented meaningful RDS adjustments.

Peer Education and Step Up Program Reach

A large majority of PWIDs have heard of the Step Up Project at both surveillance sites. Those PWID within Tshwane utilize the services frequently, with more than three fourths using services at least once a week, whereas over one third of Capetonian PWID do (note that half of the crude sample in Cape Town reported using services at least once a week). In general, both surveillance sites report similar services used when visiting Step Up, mainly needle and syringe services (e.g. clean needles/syringes; alcohol swabs; return used needles), but also health screening and safe sex education & materials. The exception is that roughly a quarter of Cape Town PWID report a history of testing for viral hepatitis[§] through Step Up services whereas less than 1 in 10 PWID in Tshwane do.

[§] Testing for viral hepatitis was only provided to PWID at one time as part of hepatitis surveillance research. This is not part of a comprehensive package of ongoing services offered to PWID.

Table 11. Exposure to and utilization of services from Step Up Project, TipVal, 2017.

Measure	Tshwane (n=544)				Cape Town (n=348)			
	Crude		Adjusted		Crude		Adjusted	
	N	%	%	95% CI	N	%	%	95% CI
Has heard of Step Up Project								
Yes	466	85.7 %	86.5 %	82.2-90.7%	218	62.6 %	56.4 %	49.7-63.1%
Frequency of using services from Step Up								
At least once a week	431	79.2 %	79.6 %	75.2-84.1%	177	50.9 %	39.0 %	32.5-45.5%
Services used by participant from Step Up (top five at each site)								
Clean needles/syringes	458	84.2 %	98.5 %	92.9->99.9%	205	58.9 %	47.6 %	41.2-54.0%
Alcohol swabs	403	74.1 %	88.3 %	83.8-92.8%	177	50.9 %	42.5 %	36.0-49.0%
Returned used needles	191	35.1 %	36.0 %	29.3-42.8%	130	37.4 %	32.8 %	26.9-38.7%
Health screening	79	14.5 %	12.8 %	7.6-18.0%	57	16.4 %	14.2 %	9.6-18.9%
Safe sex education/materials	55	10.1 %	10.9 %	6.9-14.8%	40	11.5 %	10.2 %	6.5-12.9%
Testing for HBV/HCV	52	9.6%	8.7%	4.5-13.0%	100	28.7 %	23.9 %	18.3-29.4%

DISCUSSION

The TipVal Study was the first of its nature among South African PWID, and further enhances the capacity of South African partners to conduct IBBS, mapping, size estimation, and data analysis as a component of a strengthened second generation national HIV surveillance system for key populations. The study successfully demonstrated the feasibility of using RDS within urban South African PWID communities to estimate HIV and HCV prevalence as well as reach population size estimates of PWID in the two metropolitan areas of Tshwane and Cape Town. The main findings from this survey are identified as a high burden of infection; significant inroads into community with PWID programming; low levels of PrEP/PEP knowledge and uptake; high levels of risk behaviors; and a significant gap to achieve 90-90-90 targets with this key population group.

High burden of HIV and HCV infection

HIV prevalence is estimated to be 58.4% and 11.4% among PWID in Tshwane and Cape Town, respectively. In Tshwane, this is five times higher than the city's overall HIV prevalence estimate (11.7%),[23] and in Cape Town, more than twice the overall HIV prevalence estimate (5.2%) [23]. The high level of HIV prevalence detected in Tshwane parallels estimated HIV prevalence in Maputo, Mozambique [5] and the Republic of Mauritius [24]and are higher than estimates from Zanzibar [estimated to be 11.3% in 2012[25]] and from Nairobi, Kenya [estimated to be 18.7% in 2011[26]].

In comparison to the global hepatitis infection rates among PWID from other countries, the hepatitis C seroprevalence detected in Tshwane is staggering (94%), and ranks among some of the highest detected [Estonia (92%), Lithuania (89%), Thailand (90%), Nepal (87%), Mauritius (97%), and Mexico (97%)[27]]. The high prevalence of HIV and hepatitis C coinfection detected in Tshwane (57%) is an additional and urgent concern as the clinical prognosis for coinfected individuals coinfection is worse than for those monoinfected with either disease[28]. Due to the relatively low HIV prevalence in Cape

Town, HIV/HCV coinfection prevalence remains low (8%), which may provide some level of optimistic caution that immediate efforts to prevent HIV and HCV transmission among PWID and other individuals that use drugs can prevent further HIV and HCV outbreaks among PWID. Based on reports from stakeholders with knowledge and experience with the PWID population in South Africa, we have previously described the culture of drug use within Cape Town as "transitioning", that is from smoking to injecting drugs[10]. If the culture is indeed transitioning, and if appropriate prevention programming does not keep pace with this transition, then as PWID as a proportion of the total population using drugs will increase, injecting networks will expand and become more intricate, and we may see an HIV-HCV outbreak Cape Town similar to what we observed in Tshwane.

Roughly half of HIV-positive PWID in both Tshwane (56%) and Cape Town (50%) misperceived their HIV status as negative. The misperception of HIV negative status among HIV-positive individuals is used here as a proxy for unknown HIV infection. Unknown infections contribute to onwards transmission [29-31]. Furthermore, viral suppression of HIV was low, among all HIV positive samples, 16% and 36% were virally suppressed in Tshwane and Cape Town, respectively. Additionally, survey findings indicate that most HCV infected individuals are unaware of their infections. As a result of the study, large proportions of undiagnosed HCV infection were identified and diagnosed. Of those who tested HCV positive, 89% and 73% reported no prior history of HCV infections in Tshwane and Cape Town, respectively.

Across the communities, HIV knowledge regarding to the transmission risk of drug injection is high, yet awareness of viral hepatitis is low. This is especially true for PWID in Tshwane where HCV awareness is roughly a third. The study detected a very high number of HCV infections among participants with no prior history of HCV, indicating that HCV remains an undiagnosed epidemic across both PWID communities.

Community reach of PWID programming

The Step Up Project's reach within the community is an encouraging finding. Step Up is the primary course for both needle distribution, collection and peer-based prevention programming for PWID, with 99% and 48% in Tshwane and Cape Town receiving clean needles and syringes from Step Up. A majority of PWID indicate not only some knowledge about the program, 87% and 56% in Tshwane and Cape Town, but also report frequent utilization of its services, with 80% Tshwane and 39% in Cape Town accessing services at least once a week (note the RDS adjustment for this indicator in Cape Town should be treated with caution as the crude prevalence was 51%). Beyond the self-reported utilization of specific Step Up services, PWID overwhelmingly indicate access to clean needles anytime needed [Tshwane 89.3% (95% CI: 84.9-93.7%), Cape Town 85.7% (95% CI: 81.1-90.3%)]. Despite these high levels of program engagement and access to needle and syringe services, PWID still acknowledge risk behaviors around drug injection behaviors (see below). Inconsistent use of clean needles despite high levels of program engagement, suggest further expansion of the program is warranted to facilitate greater access.

Few PWID indicated any contact with a HIV peer educator within the 6 months preceding the survey, 3% and 18% in Tshwane and Cape Town, respectively. Thus, there appears to be a disconnect within the community as to whether Step Up is viewed as having HIV peer education as a component of its program. Regardless, the reach of Step Up into the community is robust.

PWID report utilization of a wide range of harm reduction services, including needle and syringe services, through Step Up (i.e. clean injection equipment, alcohol swabs, return used needles, health screening, and safe sex education & materials). While this reach of services is encouraging, in light of the viral hepatitis C prevalence, the reported utilization of hepatitis testing for HBV and HCV does not appear to meet the need. Only 9% and 24% in Tshwane and Cape Town report prior testing for viral

hepatitis, and fewer report hepatitis B vaccination (around 5% in both sites)[**]. Given how coinfection with viral hepatitis leads to worse clinical prognosis for HIV infected individuals, these services need priority, including allocation of funding by agencies and prioritization by health departments. Once there is this commitment, community engagement and consultation need to promote utilization of hepatitis services (screening, diagnosis, vaccination and treatment) for PWID. In particular, implementation of viral hepatitis services for PWID, as included in the current draft South African National Viral Hepatitis Action Plan needs to be encouraged.

South African PWID use peer-based programming when and where it is available; inconsistent use of safe injection methods may be due to sporadic access to peer-delivered safe injection materials. The TipVal study has documented urgent unmet needs for South Africa PWID. We urge the rapid scale-up of evidence-based programming, particularly for HIV-HCV prevention and treatment, including referral and access to ART; and expanded, regular access to peer-based safe injection programming. Access to and awareness of opioid substitution therapy (OST) was not assessed as part of this study, however, OST with agonist are recommended by the WHO, UNODC, UNAIDS and PEPFAR as part of the core package of HIV services for PWID. OST services for PWID are limited to a handful of small demonstration projects, access to which should be reviewed for scale-up.

PrEP and PEP knowledge and uptake

Survey results demonstrated very little awareness or utilization of Post-Exposure Prophylaxis (PEP). This is not surprising given that PEP is premised on single "accidental" exposure events, such as needlesticks in medical settings, and condom failure (including failure to use a condom) involved in sexual transmission between discordant or status unknown partners. PWID are vulnerable to HIV acquisition through sex with infected partners, but primarily and much more efficiently through the repeated sharing of injection equipment over relatively long periods of time. It is this behavior that defines PWID both as a key population, and as a coherent community of shared identity and interests.

With PrEP, survey results also demonstrated relatively scant knowledge and minimal uptake. Unlike PEP, PrEP is designed for longer-term exposure, including through injection behaviors: the Bangkok Tenofovir Study, a clinical trial in Thailand, demonstrated its efficacy against HIV acquisition through shared injection equipment with infected partners [32]. With both PEP and PrEP, knowledge (and uptake) was slightly greater in Cape Town, though even there too low to achieve epidemic impact. At present, PWID are not considered a target population for the PrEP rollout in South Africa, although any individual could access PrEP at a designated roll-out clinic. Going forward we recommend that referral and access to PrEP for HIV-negative PWID should be considered as a component of comprehensive package for HIV prevention that also includes OST and access to clean drug injection equipment.

High levels of transmission risk behaviors

Over eight in ten PWID in Tshwane (83%) and roughly a third in Cape Town (34%) report ever sharing needles. Over two thirds in Tshwane (69%) and approximately 15% in Cape Town used a needle after someone else had used it, with similar proportions of people who reported sharing a needle at both sites report passing a needle onto others after injecting themselves. Among those sharing needles, roughly a quarter in Tshwane (28%) and approximately three fourths in Cape Town (71%) report cleaning the needle in some form every time when sharing. Cleaning injection equipment is an HIV harm reduction strategy; however, in order to be effective, a nine-step process is recommended with clean water and bleach. Realistically, this is not always possible in these two communities and for most PWID in South Africa. The survey did not assess whether PWID participants followed these evidence-based cleaning procedures, nor is bleach distributed as part of HIV prevention services

[**] Participants who report accessing these services were likely part of an earlier hepatitis surveillance study as Step Up does not currently provide hepatitis testing within its package of services.

provided by Step Up. Additionally, cleaning injection equipment is less effective at preventing Hepatitis C virus transmission. Although bleach has been shown to have some virucidal effect against HCV, HCV is more resilient than HIV, remaining virulent outside the body for a much longer duration. The best prevention for HCV transmission is to use new, sterile syringes and equipment for each injection.

The TipVal data indicate two seemingly contradictory results in this regard. An overwhelming majority of PWID at both surveillance sites, Tshwane and Cape Town (89% and 86%), report having access to new, unused needles anytime the participant needs one. This is consistent with high levels of peer-based program engagement. Yet they still acknowledge high rates of lifetime and recent sharing of injection materials. This may be indicative of prevention services that are in high demand by PWID, but whose providers may not have the capacity to deliver services in proportion to the needed coverage. These findings suggest further expansion of the program to new geographic areas and penetration into new networks is warranted to facilitate greater access by PWID. Increased frequency and intensity of services across both sites is also recommended to further promote harm reduction strategies, to increase HIV testing, to increase exposure to peer education, and to change norms around haring and reuse of drug injection equipment.

Additionally, access to OST requires intensification as current coverage is limited to 60 PWID in Cape Town including 230 PWID in Pretoria (at August 2018). In light of the TipVal survey's findings of high HIV and HCV prevalence, the implementation of the OST program may need to be fine-tuned, particularly regarding hepatitis. In addition to expansion of ART and intensification of OST, programs should emphasize hepatitis awareness, testing, treatment, and prevention, including hepatitis B vaccination for those eligible as part of a comprehensive combination prevention package for PWID. PrEP referrals for HIV negative PWID may also be considered.

Significant gap to achieving UNAIDS 90-90-90 targets

By definition, achieving the 90-90-90 treatment targets, requires 72.9% of people living with HIV to be virally suppressed (90% x 90% x 90%). An implementation error prevented the collection of self-reported data on the number of PWID who knew their status (the first 90), and budget constraints prevented the collection of laboratory-reported numbers of PWID LHIV currently taking ART (the second 90). (See "Limitations" below.) However, the data on viral suppression among HIV-positive PWID demonstrated a substantial gap between the two sites (16% and 36% in Tshwane and Cape Town), and indicating some distance at both to reach to the third 90. This study is unable to determine the reasons for such poor viral suppression outcomes. That is, we cannot ascertain whether the low viral suppression observed among PWID is attributable to a lack of engagement in HIV care, non-adherence to ARV, or genotypic resistance in the strain(s) of HIV virus infecting PWID.

We used proxy measures to construct limited HIV treatment cascades for PIWD. Our proxy indicator for the first 90 is deduced through the perception among laboratory confirmed HIV infection participants. We see that among laboratory confirmed HIV cases, less than half correctly perceive themselves as positive (44% and 42% in Tshwane and Cape Town). While we don't know whether HIV-positive PWID are on ART, nor whether they had ARV analytes circulating in their blood, the survey demonstrated low engagement in health care. In consultation with stakeholders, it was noted that the number of PWID confirmed on ART is very low. PWID programs have been funded to provide HIV testing and linkage to care, but few PWID were known to access ART in the public sector. Additionally, few PWID seek health care in general. Roughly a quarter of PWID sought health care in the previous 12 months, 27% and 26% in Tshwane and Cape Town, with fewer visiting a health care center with PWID-specific information, 18% and 21% in Tshwane and Cape Town.

LIMITATIONS

The TipVal Study confirms many of the findings from earlier exploratory studies in South Africa[6,33], and is consistent with regional PWID surveillance studies including in Mozambique and Zanzibar[5,25]: South African PWID shoulder an enormous burden of HIV infection, Hepatitis C infection, and coinfection of HIV and HCV. In fact, the study detected higher HCV prevalence than anticipated, at levels which impacted the budget such that a decision was made to reduce the number of tests on HCV viral load. The study appears to have observed a possible outbreak of HCV in the PWID community of Tshwane what we've defined elsewhere as an "established" PWID population[10]. However, additional funding has been allocated to conduct more laboratory tests with regards to HCV, including HCV viral load testing. Currently, NICD has plans to conduct a sensitivity/specificity analysis of the HCV POCT used in the field for this surveillance study against laboratory-confirmed tests.

Within Tshwane, survey participants reported lower utilization of viral hepatitis testing services through Step Up in comparison to those from Cape Town. At the time of TipVal a different viral hepatitis surveillance study among key populations (including PWID) was being implemented in both cities, viral hepatitis services are not currently part of the service delivery packages of either sites. The hepatitis C burden among Tshwane PWID is an urgent public health concern requiring immediate intervention: awareness appears low, HCV testing is not funded by current program funders, commensurate with apparent need or reported risk behaviors; and HCV prevalence astonishingly high. Implementers should undertake intensive community engagement and consultation to understand how peer programming might further facilitate viral hepatitis testing, treatment, vaccination, and prevention. Unfortunately, the TipVal study was unable to conduct HBV surveillance testing, so we cannot provide estimates for a known significant viral infection among PWID through this study. Prevalence of HBV surface antigen among PWID conducted in a recent study was 5.3% and 5.7% in Tshwane (n= 296) and Cape Town (n=286) respectively.

As mentioned elsewhere, the implementation of the QDS behavioral survey contained errors. The simple errors was a skip pattern in the programming that failed to ask participants whether participants were aware of their HIV infection. As a result, a follow up question related to awareness of a HIV-positive diagnosis (i.e. whether or not the HIV-positive participant was on ART) was not assessed. While we are unable to report on some of the HIV treatment cascade indicators, we identified proxy measurement for known HIV status, and had laboratory-verified viral suppression to show the treatment gap within the 90-90-90 treatment cascade.

Beyond these site-specific limitations, there are the following limitations, typical to conducting respondent-driven sampling within key populations:

- Sampling, while scientifically sound, may not have captured certain categories of PWID (i.e. females, older aged PWID, non-South African citizens). However, service providers indicate that the PWID communities are predominantly male. Additionally, it is a common challenge in these surveys to reach older members of the population. Furthermore, PWID from other countries living in South Africa may not be networked to South African PWID, or may wish to remain hidden due to their immigration status.
- The sampling in both sites reached equilibrium on key variables. However, the sample size in Cape Town (N=348) did not reach the target of 500. We still remain confident in the reported estimates, but statistically, there was a limit to some analyses performed due to small cell sizes in Cape Town.
- Respondent-driven sampling methodology is subject to self-selection bias. Participants may have opted to participate due to a perceived benefit, such as hepatitis C testing, and these participants may have had a higher probability of being HIV-positive.

- We cannot rule out social desirability bias when conducting face-to-face interviews with individuals. Some participants may have answered survey items based on what they perceived to be socially desirable answers. For example, participants may have incorrectly reported on their risk behaviors in an attempt to demonstrate to the interviewers that they were adhering to harm reduction practices.
- Recall bias can be a problem in these surveys, especially when assessing drug injection behaviors among PWID. To overcome this, we reported on the last time a participant injected drugs, rather than behaviors conducted of the span of a month, or a year.
- As this is a cross-sectional survey, we are unable to infer any causality in associations between disease infections and any risk behaviors.
- The analysis within this report does not delve into multivariate modeling. Future analyses will take into account associations with predictor variables and specific outcomes, such as HIV, HCV, and HIV/HCV coinfection, and control for the complexity of effects within the variables. These will be conducted separately and a scientific manuscript will be prepared for a peer-reviewed journal.

RECOMMENDATIONS

Like other key populations in South Africa, PWID are currently experiencing a high-incidence, high prevalence HIV
epidemic. HIV transmission is concentrated in distinct geographic and social networks of PWID. There is an established evidence base for programming to offer OST to PWID as an effective tool in a comprehensive prevention package that would also include an intensification of safe access to syringes and needles. PrEP may also be considered for PWID though as yet, there are multiple unknowns regarding optimal implementation of PrEP within comprehensive programs throughout the world[32,34-38] related to the implementation and legal status, acceptability, and uptake of other evidence-based prevention programming. This survey did not ask about acceptability of PrEP (nor would the small number of responses have been useful); presumably as PrEP roll out in South Africa advances a future round will need to ask standard acceptability questions for the PWID population. It is important to note that implementation of PrEP would not have an influence on reduction of HCV risk, which from this study is of paramount importance.

We note that among South African PWID advocates, there is apparent tension between the imperative to deploy and scale up PrEP to reduce HIV incidence among PWID, and what may be perceived as less grudging support for access to safer injection materials—an evidence-based harm reduction intervention that is unfortunately much maligned as contributing to the problem of drug abuse and dependency supporting drug use and addiction in political discourse throughout the world. And advocates may feel pressure to prioritize HIV discussions over other pressing health needs– opioid substitution therapies, and Hepatitis C diagnosis and treatment. There are frequent discussions among advocates, implementers, and policymakers about how to address these issues through comprehensive programming; but the current distribution of resources for PWID in South Africa (and indeed in many PEPFAR countries) does not match the current disease burden of Hepatitis C nor PWIDs self-assessment of non-HIV needs.

Yet the survey shows that HIV is no small problem. Currently there exists both the evidence base and, increasingly, the resources to support reducing the burden of the HIV epidemic on PWID. We recommend that all stakeholders in these discussions continue to seek alignment on what is possible now (for example, intensification of access to clean drug injection equipment; provision of OST; and referrals or provision of PrEP and ART), and then build on the experience of these partnerships to improve all outcomes on the co-morbidities (i.e. hepatitis C) PWID continue to suffer greatly and disproportionately from in comparison to HIV, and hold each other accountable to iterative

development of healthy programming that delivers optimal health outcomes to the greatest number of PWID.

The data presented in this Brief Report support the following recommendations for HIV prevention, treatment, and other health and well-being needs among PWID in South Africa. This list is not exhaustive, and the authors hope that the data presented here will be understood and added to in the context of the rapidly growing knowledge base to which multiple academic research and health sector programming initiatives with PWID and other Key Populations in South Africa.

TipVal's results show that peer programming is highly acceptable to PWID, and that they access critical prevention services through peer outreach, including HIV testing, access to safer injection materials through needle and syringe services, and other population-specific clinical services. We recommend that the Step Up model be considered for adaptation and implementation in stakeholder-identified sites; particularly those on the cusp of transitioning from using drugs to injecting drugs.

However the data also point to several gaps that must be addressed with urgency in any peer-support model:

- Ensure peer staff capacity appropriate to the geographic breadth of required outreach activities, and allocate appropriate funding to ensure delivery of the daily peer outreach dose recommended as evidence-based prevention. Emerging PWID communities must have consistent and proportional access to clean syringes and other safer injection materials to avoid the human and financial costs of catastrophic HIV and viral hepatitis outbreaks.
- Scale up human rights affirming clinical care for PWID in the public sector to mitigate the burden of HIV, HCV, HIV-HCV coinfection, and other co-morbidities.
- Explore peer support models for HIV treatment to improve outcomes along the care continuum
- Increase knowledge and adoption of viral hepatitis prevention and treatment behaviors, including screening (HBV and HCV), referral to vaccination (HBV), and referral to treatment (HBV, HCV), per the National Hepatitis Action Plan 2018 and the National Guidelines for the Management of Viral Hepatitis; and ensure appropriate funding for PWID services under the Plan.
- Provide funding for viral hepatitis services for PWID, including screening, treatment and vaccination for hepatitis B.
- Ensure access to HCV treatment services and explore adaptation/implementation of peer treatment support models.

PrEP has the potential to greatly reduce HIV incidence, even in high-incidence key populations like PWID. We encourage continued engagement and dialogue among PWID stakeholders and advocates, implementers, health officials and global health program sponsors on the best way to implement PrEP into existing comprehensive PWID health programming. To begin, a PrEP acceptability study should be conducted among PWID to inform programs and funding agencies.

- We acknowledge that HIV is but one of multiple life-threatening illnesses for which PWID are a high-risk population, and recommend additional investment in screening, referral, and treatment of comorbid conditions, particularly alleviating addiction and supporting ART adherence through OST as well as screening for and treating viral hepatitis in the context of comprehensive PWID health programming.

- We encourage data-informed policy around PrEP, needle and syringe programmes, and opioid substitution therapy (OST) as components of an evidence-based and comprehensive HIV prevention plan for PWID[39,40]. This should include the collection, analysis, and utilization of PWID-specific feasibility, acceptability, and operational implementation science research to inform all behavioral and biomedical HIV and HCV prevention options for PWID.

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