

The Ukrainian SORT IT Course

People with high HIV viral load within risk networks: who are these people and who refers them best?

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Abstract

Introduction: Viral load is one of the most important determinants for HIV transmission. Identification of people with high viral load (PHVL) can be effective in limiting onward HIV transmission. In order to improve the identification of these individuals within risk networks, we determined a) the number of PHVL recruited through risk networks b) their socio-demographic, behavioural and clinical characteristics and c) the characteristics of individuals who referred these PHVL to the study.

Methodology: From November 2013 to March 2016, in Odessa, Ukraine, Transmission Reduction Intervention Project (TRIP) was implemented to identify people recently infected with HIV within the risk networks of “seeds” and “venues” where they engaged in risk behaviour.

Results: TRIP identified 53 PHVL, of whom 32 (60%) injected drugs; 42 (79%) were unaware of their HIV status; 25 (47%) had more than one sex partner, and only 14 (26%) were using condoms. There were 164 people who referred individuals into the study; 33 of them (20%) referred PHVL. In terms of referrers, those with lower than secondary level of education, not living with a sex partner, and reporting regular condom use were significantly more likely ($p < 0.05$) to refer PHVL. Most PHVL (38, 72%) and their referrers (27, 82%) were found through venues.

Conclusions: In Odessa city, PHVL are at high risk of transmitting HIV as the majority inject drugs, do not know their HIV status, and have unprotected sex and/or multiple partners. Targeting these individuals for HIV prevention, harm reduction and initiation of antiretroviral treatment (ART) is urgent.

Key words: people with high viral load; PHVL; risk network; high viral load; Ukraine; venues.

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Introduction

In 2017, an estimated 37 million people were living with HIV (PLWH) worldwide of whom 1.8 million were newly infected [1]. In Ukraine, there were an estimated 240,000 PLWH and 13,000 new HIV infections in 2017. Of the PLWH in Ukraine, only 56% were aware of their HIV status, which implies that the remaining 44% might transmit the virus without recognising that they are themselves infected. In 2017,

40% of known PLWH in Ukraine were on antiretroviral treatment (ART) and viral load suppression was at a low 23% [1].

Globally, about half (47%) of all new HIV infections occurred among key populations (KP) and their partners, emphasising their importance in global HIV control. These populations engage in behaviours that increase their risk of acquiring and transmitting HIV. Additionally their access to HIV testing as a

gateway to prevention and care is limited [2]. In 2017, KPs in Ukraine included an estimated 350,000 people who inject drugs (PWID), 80,000 sex workers (SW), and 180,000 men who have sex with men (MSM) [3]. HIV prevalence in these groups was respectively 22.6%, 5.2% and 7.5% [3], but varied greatly by region.

The National HIV Programme of Ukraine has aligned its targets with the UNAIDS 90-90-90 strategy [4]: 1) to detect 90% of all HIV positive individuals, 2) to ensure that 90% of PLWH are placed on ART and 3) to achieve 90% suppressed viral load among those on ART. Even though KPs are included in HIV testing and prevention services through NGOs and state health facilities, the gap in reaching the first 90 target is large [5-6]. It is thus critical to explore innovative strategies to identify new HIV positive cases among KPs.

Viral load (VL) is one of the most important determinants for HIV transmission. Several studies have demonstrated that high VL is associated with significantly higher HIV transmission than lower VL [7-12]. In this paper high VL is defined as 90,000 copies/mL [12] and higher based on literature review [13-14].

From November 2013 to March 2016, in Odessa, Ukraine, the Transmission Reduction Intervention Project (TRIP) was implemented to identify PLWH using network-based contact tracing techniques. The main aim of TRIP was to increase the detection of people who were recently infected with HIV (in the last 6 months), and then to initiate them on ART and prevent further HIV transmission within their risk networks [14]. The results of TRIP confirmed that, in contrast to other conventional HIV testing techniques, recruiting through social risk networks was more effective in identifying recently infected individuals [15-16].

This is the first TRIP-based paper to focus on identifying people with high viral load (PHVL) or to study who referred individuals with high viral load for the study. This information may be useful in locating potential HIV transmitters, helping them protect their health, and reducing HIV transmission. Specific objectives of this study are to determine a) the number of PLWH with high VL recruited through the risk networks b) their socio-demographic, behavioural and clinical characteristics and c) the characteristics of individuals who referred PHVL.

Methodology

Study design

A cross-sectional analysis of TRIP data.

Setting

General setting

Odessa is a port city located in the south of Ukraine with a population of approximately one million [17]. This region has one of the highest HIV prevalence rates in the country (830.2 per 100,000 population) [5]. According to the national estimates, the number of KP members in the city is high with 24,000 PWID, 5,500 MSM, and 5,900 SW [18]. More than half of them receive services from harm reduction programmes [5].

Specific setting

TRIP aimed to identify recently infected PLWH within the social networks of individuals referred to as “seeds”, mainly targeting PWID (who injected drugs during the past six months). All participants provided 18-millilitre blood samples. Blood samples were tested by New Vision Diagnostics Profitest Combo tests (Intec Products Inc., Haicang Xiamen, China). Viral load was measured with HIV-1 Abbott Real Time TM. Recent infection was determined with the LAg assay (SediaTM Biosciences Corporation, Portland, USA). LAg is based on antibody maturation and categorizes HIV infection as recent versus long-term [19].

A recently infected “seed” was defined as a newly diagnosed HIV-positive person with a documented negative result during the past six months or with a LAg Optical Density (ODn) ≤ 1.5 and viral load more than 1,000 copies/mL. Potential recently-infected “seeds” were referred to TRIP from the Odessa Regional Laboratory Center of the Ministry of Health of Ukraine, the Odessa City AIDS Center and The Way Home Charity Foundation. Other HIV positive individuals whom they referred that did not fulfil the aforementioned criteria were considered long-term infected “seeds” if they were matched to recently infected seeds in terms of gender, risk group, age (± 5 years) and the referring organization [14-16].

“Seeds” along with other referrers (identified in the network of the “seeds”) recruited network or venue members. Network members were direct sex and drug-using partners as well as partners’ direct sex and drug-using partners or people who were present when they did drugs (defined as acquaintances). Those who visited the same venues where they gather to use drugs, to have sex, or to meet new sex partners were defined as venue members. Network and venue members were recruited (interviewed and tested) regardless of their HIV status [14-16]. The interview collected data related to socio-demographic, clinical and behavioural characteristics. If a recently infected participant was found in networks

or venues of seeds, their risk networks were recruited for 2 additional steps.

Study population and period

All PLWH identified through TRIP between November 2013 and March 2016 with available viral load results (278, 75.3%) were included in the first part of the study population. The second part consisted of those who nominated at least one person or venue that led to the successful recruitment of someone who took part in the study. We refer to these as “referrers.” A comparison was made between the referrers of at least one PLWH with high viral load ($\geq 90,000$ copies/mL) versus the referrers of all other participants.

Data and statistical analysis

The data were cleaned and two subsets were made for analysis. Frequencies, proportions, measures of central tendency (mean), and variation (standard deviation) were used to present the results. Differences between groups were assessed with the use of Pearson’s χ^2 (Chi-squared test) or Fisher’s exact test for categorical variables. Student’s t-test was used for continuous variables (for normally distributed data). The level of significance was set at $p < 0.05$ and 95% confidence intervals (CI) were used throughout.

Ethics

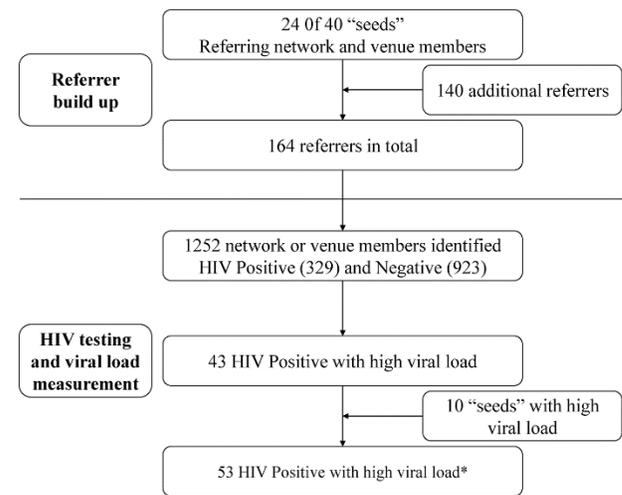
All TRIP participants gave informed consent for the use of their data under the protocol approved by the Medical Ethics Committee at Gromashevsky Institute of Epidemiology and Infectious Diseases, Kyiv, Ukraine and the Institutional Review Board of the National Development and Research Institutes in New York, NY.

Results

Characteristics of PLWH with high viral load

There were 24 recently infected and 16 long-term infected seeds. Figure 1 shows the build-up of the pool of referrers stemming from these 40 seeds and leading on to the identification of a total of 1252 network and venue members. The risk network members (including those recruited at venues) included 554 (44%) PWID, 17 (1.4%) MSM, and 4 (0.3%) SW. The rest were not from key populations. Of 1252 network and venue members, a total of 329 (26.3%) HIV positive individuals were identified, of whom 43 (13.1%) had a high viral load. 38 (88.4%) of the latter were identified through venues. There were also 10 seeds who had a high viral load making a total of 53 identified individuals with high viral load included in the study.

Figure 1. Flow chart of referrer recruitment and HIV testing in the Transmission Reduction Intervention Project (TRIP) in Odessa, Ukraine (November 2013 - March 2016).



* 91 People Living With HIV (PLWH) have no viral load data.

Among the infected (both seeds and network/venue members), for 91 people (24.7%) viral load data could not be obtained.

The socio-demographic, behavioural and clinical characteristics of those with high viral load are summarized in Table 1. The minimum level of viral load was 91,252 copies/mL and the maximum was 1,171,318 copies/mL; 17 (32%) of PHVL were recently infected, according to our definition of recency.

Among 53 persons with high VL, 42 (79%) were unaware of their HIV status, 32 (60%) were PWID and only one was on ART. Twenty-five (47%) had more than one sex partner during the last 6 months and only 14 (26%) were using condoms.

Characteristics of people who referred at least one PLWH with high viral load

Tables 2, 3 and 4 show the socio-demographic, clinical and behavioural characteristics of 164 “referrers”, respectively and the factors associated with having at least one person with a high viral load successfully recruited into the study as a result.

Of the 164, about half (83, 51%) did not have HIV infection. The total number of referrers (including “seeds” and their network/venue members) who helped the recruitment of PHVL was 33, of whom 27 (82%) were recruited from venues, 3 (9%) from networks, and 3 (9%) were seeds.

In terms of referrers, those with lower than secondary level of education (up to 9 years), those not living with a sex partner and those who reported regular

Table 1. Characteristics of People Living with HIV (PLWH) with high viral load in Odessa, Ukraine (November 2013 - March 2016).

Characteristics		PLWH with high viral load (n = 53)	
		n, mean	%, SD
Socio-demographic			
Age		35	8.5
Gender:	Male	40	75.5
	Female	13	24.5
Education level:	Up to 9 years	13	25.0
	Secondary (11 years)	38	73.0
	University level	1	2.0
Employment status:	Employed	23	43.4
	Occasional earnings	10	18.9
	Not employed	20	37.7
Living with sex partner:	Yes	26	49.1
	No	27	50.9
Accommodation type:	Place without renting	24	45.3
	Renting	21	39.6
	Homeless	8	15.1
Sexual orientation:	Straight	48	96.0
	LGBT	2	4.0
Clinical			
HIV load (copies/mL)		377178	295245
HIV Status:	Recent ¹	17	32.1
	Long Term	36	67.9
HIV testing prior to TRIP:	Yes	39	78.0
	No	11	22.0
Previous HIV test result:	Negative	27	71.1
	Positive	11	28.9
ART status:	Yes	1	8.3
	No	11	91.7
Behavioral			
Number of sex partners:	No partners	5	9.4
	One	23	43.4
	More than one	25	47.2
Using condoms:	Yes	14	26.4
	No	39	73.6
Sex worker:	Yes	2	3.8
	No	51	96.2
PWID:	Yes	32	60.4
	No	21	39.6
Duration of drug injection (years)		13	9.1
Addiction treatment:	Yes	3	9.4
	No	29	90.6
Linkage type:	Network	5	9.4
	Venue	38	71.7
	Seed	10	18.9
Connection type:	Sex partner	8	15.1
	Drug injection partner	18	33.9
	Acquaintance	17	32.1
	Seed	10	18.9

For some cases data was missing: Education level (1), Sexual orientation (3), HIV testing (3), and Previous HIV test result (1). ¹ - newly diagnosed HIV-positive persons with a documented negative result in the past six months or with LAg ODn ≤ 1.5 (on Sedia HIV-1 LAg-Avidity EIA) and viral load more than 1,000 copies/mL. ART: Antiretroviral treatment, LGBT: Lesbian, Gay, Bisexual, Transgender, PWID: People Who Inject Drugs, SD: Standard Deviation.

Table 2. Comparison of Socio-Demographic characteristics of referrers in the Transmission Reduction Intervention Project (TRIP), Odessa, Ukraine (November 2013 - March 2016).

Characteristics	Referred PLWH with high load ¹		Odds Ratio/ Mean difference (SD)	95% CI	p value	
	Yes, n = 33 n/mean (%/SD)	No, n = 131 n/mean (%/SD)				
Age	33.5 (9.4)	34.4 (8.7)	1.0 (1.8)	[-2.7, 4.6]	0.6	
Gender:	Female	7 (21.2)	26 (78.8)	1.1	[0.4, 2.8]	0.9
	Male	26 (19.8)	105 (80.2)	1.0		
Education level:	University level	4 (17.4)	19 (82.6)	0.5	[0.1, 1.8]	0.4
	Secondary (11 years)	16 (16.2)	83 (83.8)	0.4	[0.2, 1.0]	0.047*
	Up to 9 years	13 (31.0)	29 (69.0)	1.0		
Employment status:	Not employed	13 (20.0)	52 (80.0)	0.8	[0.3, 2.0]	0.7
	Occasional earnings	7 (17.1)	34 (82.9)	0.7	[0.2, 1.9]	0.5
	Employed	13 (23.2)	43 (76.8)	1.0		
Living with a sex partner:	No	23 (26.7)	63 (73.3)	2.5	[1.1, 5.6]	0.03*
	Yes	10 (12.8)	68 (87.2)	1.0		
Accommodation type:	Homeless	4 (21.1)	15 (78.9)	1.3	[0.5, 3.0]	0.7
	Renting	11 (21.2)	41 (78.8)	1.3	[0.3, 4.8]	0.6
	Place without renting	15 (17.4)	71 (82.6)	1.0		
Sexual orientation:	LGBT	1 (12.5)	7 (87.5)	0.5	[0.0, 4.6]	1.0
	Straight	31 (20.5)	120 (79.5)	1.0		

For some cases data was missing for following characteristics: employment status (2), accommodation type (7), and sexual orientation (5). 1 – Referrers in TRIP who recruited at least one PLWH with high viral load to the project, * statistically significant results. CI: Confidence Interval, LGBT: Lesbian, Gay, Bisexual, Transgender, PLWH: People Living With HIV, SD: Standard Deviation.

Table 3. Comparison of Clinical characteristics of referrers in the Transmission Reduction Intervention Project (TRIP), Odessa, Ukraine (November 2013 - March 2016).

Characteristics	Referred PLWH with high load ¹		Odds Ratio	95% CI	p value	
	Yes n = 33 n (%)	No n = 131 n (%)				
HIV Status:	HIV negative	18 (21.7)	65 (78.3)	0.8	[0.3, 2.0]	0.6
	HIV positive a long time	7 (13.7)	44 (86.3)	0.4	[0.1, 1.4]	0.1
	Recently HIV ⁺ ²	8 (26.7)	22 (73.3)	1.0		
High HIV load:	No	8 (17.0)	39 (83.0)	0.5	[0.1, 2.8]	0.4
	Yes	4 (28.6)	10 (71.4)	1.0		
HIV testing prior to TRIP:	No	8 (21.1)	30 (78.9)	1.1	[0.4, 2.7]	0.9
	Yes	24 (19.8)	97 (80.2)	1.0		
Previous HIV test result:	Negative	19 (22.1)	67 (77.9)	1.6	[0.5, 6.0]	0.5
	Positive	5 (15.2)	28 (84.8)	1.0		
ART status:	No	3 (15.0)	17 (85.0)	1.1	[0.1, 14.5]	1.0
	Yes	2 (14.3)	12 (85.7)	1.0		

For some cases data was missing: High HIV load (20), HIV testing prior to TRIP (5), and Previous HIV test result (2). 1- Referrers in TRIP who recruited at least one PLWH with high viral load to project, 2- newly diagnosed HIV-positive person with a documented negative result in the past six months or with LAG ODn ≤ 1.5 (on Sedia HIV-1 LAg-Avidity EIA) and viral load more than 1,000 copies/mL. ART: Antiretroviral treatment, CI: Confidence Interval, PLWH: People Living With HIV.

Discussion

This is one of the first studies in Ukraine that focused on identifying individuals posing a high risk for HIV transmission due to having a high viral load. Of 53 PHVL, the VL ranged from about 90,000 copies to over a million copies/mL suggesting “high-transmitters” [20]. In addition, about eight-in-ten of these individuals did not know their HIV status, six-in-ten were active PWID, about half of PHVL had multiple sexual partners and three-in-four were engaging in unprotected sex. Only one individual was on ART. Venues proved to be the best source for finding PLWH with high VL and their referrers.

The study highlights the importance of projects such as TRIP in identification of individuals who are likely to be involved in intense HIV transmission within social risk networks. The value of TRIP techniques for locating high-priority people for intervention has also been demonstrated for Chicago, Athens, and other papers about Odessa [15-16, 21]. This is in line with the Sustainable Development Goal of eliminating the HIV/AIDS epidemic by 2030 and opens opportunities for improving the “test and treat” strategy [22].

The study strengths were that VL measurements were done under research laboratory conditions and thus reliable. We also used a high cut-off threshold of ≥ 90,000 copies/mL for the definition of high VL [12]. Those with high VL in our study are thus relatively

likely to be high transmitters with considerable public health importance [23]. The main study limitations include the small number of referrers for people with high VL, which did not allow for adjusted statistical analysis. Furthermore, we had 24.7% of HIV positive individuals for whom we did not have VL data. This was due to operational challenges such as nurses being unable to draw blood, the samples being too small or ending up being coagulated before testing. In a setting where 44% were PWID, finding a good vein may be problematic even for a well experienced nurse. Furthermore, PWID on opioids and stimulants might have been less patient and cooperative when having to cope with multiple needle picks. We thus considered this an operational reality.

The findings from this study have some policy and practice implications. First, over half of those identified as being at risk within the social risk networks were not from key populations. There is thus “a mix” of KPs mostly drug users and those from the general population. The interaction between these two groups can transmit HIV infection in the general population outside the KPs. The TRIP project, which is embedded within these networks, provides a useful mechanism for limiting such spread. Second, those with high VL came mostly from venues and many had increased risk for acquiring and transmitting HIV since they did not know their HIV status, were drug users engaged in

Table 4. Comparison of behavioral characteristics of referrers in the Transmission Reduction Intervention Project (TRIP), Odessa, Ukraine (November 2013 - March 2016).

Characteristics	Referred PLWH with high load ¹		Odds Ratio/ Mean Difference (SD)	95% CI	p value	
	Yes, n = 33 n/mean (%/SD)	No, n = 131 n/mean (%/SD)				
Number of sex partners:	No partners	5 (25.0)	15 (75.0)	1.9	[0.4, 7.1]	0.3
	More than one	18 (23.1)	60 (76.9)	1.7	[0.7, 3.9]	0.2
	One	10 (15.2)	56 (84.8)	1.0		
Using condoms:	No	18 (14.6)	105 (85.4)	0.3	[0.1, 0.7]	0.002*
	Yes	15 (36.6)	26 (63.4)	1.0		
Sex worker:	No	31 (19.3)	130 (80.7)	0.1	[0.0, 2.4]	0.1
	Yes	2 (66.7)	1 (33.3)	1.0		
PWID:	No	15 (22.4)	52 (77.6)	1.3	[0.6, 2.7]	0.5
	Yes	18 (18.6)	79 (81.4)	1.0		
Addiction treatment:	No	15 (17.4)	71 (82.6)	0.6	[0.1, 3.7]	0.4
	Yes	3 (27.3)	8 (72.7)	1.0		
Linkage type:	Network	3 (9.7)	28 (90.3)	0.7	[0.1, 6.2]	1.0
	Venue	27 (24.8)	82 (75.2)	2.3	[0.6, 12.5]	0.3
	Seed	3 (12.5)	21 (87.5)	1.0		
Connection type:	Sex partner	7 (20.0)	28 (80.0)	0.9	[0.3, 2.8]	0.9
	Drug injection partner	11 (21.6)	40 (78.4)	1.1	[0.4, 2.7]	0.9
	Acquaintance	11 (20.8)	42 (79.2)	1.0		
Duration of drug injection		15.82 (1.0)	15.56 (9.6)	0.3 (1.9)	[-5.2, 5.8]	0.9

¹ – Referrers in TRIP who recruited at least one PLWH with high viral load to project, * statistically significant result. CI: Confidence Interval, PLWH: People Living With HIV, PWID: People Who Inject Drugs, SD: Standard Deviation.

unprotected sex, and/or had multiple partners. Few were on ART. Introducing targeted strategies for HIV testing, harm reduction and ART at known venue sites is urgently required. Further, it is likely that some of the 68% of participants with high viral load who were not recently infected were in the later stages of infection or co-infected with other pathogens. These participants would probably be in urgent need of antiretroviral therapy and perhaps other medical interventions. The fact that TRIP located these potential patients was an unexpected benefit of the intervention. Finally, we identified a few characteristics of those who referred PLWH with high VL.

Conclusion

Odessa venues that were located based on risk networks of HIV infected people are good sites to find cases with HVL. Programmes to locate them and provide care to PHVL should be implemented.

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