Defining the mods of HIV transmission among young women registered in HIV Centers and their sexual partners in Ukraine (MOT2).

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Content

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Background

Surveillance is crucial element in global HIV response but presents many challenges in concentrated epidemics [1]. The populations most commonly considered at risk for infection are men who have sex with men, injection drug users, commercial sex workers and their clients. These populations also tend to be stigmatized which results in misclassification of the self-reported modes of HIV transmission due to underreporting of stigmatized risk behaviors [2].

Ukraine is the country with the second largest HIV epidemic in Europe where the most of new cases of HIV are officially registered with heterosexual transmission mode[3] [4]. According to official reported case registration data, heterosexual exposure was the dominant mode of HIV transmission in Ukraine since 2008 [5]. However, a triangulation study, combining all existing data sources, suggested that HIV transmission remained linked to PWID and their sexual partners [6]. Moreover, there is indirect evidence that heterosexual transmission among women in Ukraine remains largely linked to IDU partners which calls for additional investigation among newly registered non-IDU women to determine if the source of their infection is a male IDU[7]. In addition, available data suggest that among the group of young females, 46% reported ever having an IDU sexual partners.[8]

The national HIV surveillance system collects the data on the suspected mode of transmission (MoT); however, the registration form does not include fields for specific risk factors, and there are no guidelines for systematically collecting risk factor data. Healthcare providers individually interpret what the risk assessment algorithm should be, which may be affected by substantial stigma toward injecting drug use and MSM [9]. *As a result, the indirect evidence available in Ukraine indicated that modes of transmission were substantially misclassified as heterosexual transmission category* [10]. In particular, the 2013 surveys detected HIV prevalence in MSM reaching up to approximately 8% nationwide[11]. Given the number of estimated MSM population (175,750), these findings are supportive of the hypothesis that there is a significant underreporting and/or misclassification of MSM in the case reporting system, presumably as heterosexual men[12].

There was also indirect evidence on substantial misclassification cases in PWID population suggesting that as many as 35% of cases of men who reported as heterosexual could have been engaged in injecting drug use[13]. The most recent comprehensive study conducted by Dumchev et al. (2017) reviled that the proportion of new HIV cases likely caused by injecting drug use

based on the survey data was 59.7% compared to 33.2% in official reporting, and proportion of cases likely acquired through homosexual transmission was 3.8% compared to 2.8% [14].

To find out more on the role of the bridge populations in the HIV epidemic in Ukraine and define the weaknesses of the national HIV surveillance system we plan to conduct cross-sectional point prevalence assessment in population of Adolescent Girls and Yong Women (AGYW) who were registered as new HIV cases with heterosexual mode of HIV transmission. The chosen research design is a meaningful measure to obtain information on: 1) *the prevalence of new HIV cases* heterosexually infected from IDU partners 2) *the possible association* between the source of HIV infection and social and behavioral characteristics of the of AGYW and their sexual partners and…3) the magnitude of possible misclassification of the modes of HIV transmission in AGYW.

Study Goal

The main goal of this study was to identify the source of HIV infection among young HIV positive women registered in the healthcare with the heterosexual mode transmission and their sexual partners. By achieving the study goal, we planned to define the magnitude of the misclassification between heterosexual and IDU modes of transmission in newly infected AGYW and identify biological, social and behavioral factors associated with the misclassification; to classify AGYW's sexual partners as a source of HIV transmission based on their HIV risky behavior.

Study aims

Study goal was achieved by completing the following study aims:

Aim 1. To define the magnitude of the misclassification of the modes of HIV transmission in AGYW (15-25) registered in 2016-2019 as infected through heterosexual contact. The aim was achieved by calculating a share of HCV cases among newly identified HIV positive AGYW with registered heterosexual mode of HIV transmission or self-reported IDU.

Aim 2. To define the prevalence of IDU in HIV positive sexual partners of HCV negative AGYW (15-25 y.o.) diagnosed with HIV during 2016-2019. The aim was achieved by measuring self-reported IDU and by defining a share of HCV cases among HIV positive sexual partners of HCV negative AGYW with confirmed heterosexual mode of HIV transmission.

Aim 3. To measure sociodemographic and behavioral factors in AGYW (15-25 y.o.) diagnosed with HIV during 2016-2019 associated with confirmed heterosexual and injection modes of transmission.

Research Consortium

This project was designed and implemented by the consortium of the Alliance for Public Health (hereafter Alliance) and European Institute on Public Health Policy (EIPHP). Alliance and EIPHP have a longstanding relationship on topics related to HIV prevention and treatment, substance use, comorbid diseases, mental health and designing and implementing strategies to

improve medical services in Ukraine including correctional facilities, community-based health care, narcology and HIV programs, and primary care.

Alliance is the Principal Recipient of the Global Fund grant Rounds 1, 6 &10, responsible for prevention in key populations, MAT, community mobilization, etc. Multiple research studies were led by Alliance staff, including IBBS, various operational, formative and intervention studies. Alliance, as the main programmatic non-governmental entity providing international and domestic technical assistance to the government of Ukraine in the areas of HIV surveillance, HIV prevention and treatment programs monitoring and evaluation. In this research the Alliance's research team provided comprehensive organizational and technical support through all stages of the project implementation including but not limited to study planning, research protocol development, organizing regional research sites, data collection, data analysis and results dissemination. Key personnel had appropriate HSR training certification.

EIPHP is a leading Ukrainian organization in HIV and drug abuse research, with substantial portfolio of NIH-funded studies, including program evaluation, effectiveness and implementation studies, intervention costing assessments, etc. EIPHP has also served as an organizational and methodological resource center for MAT and Integrated Care scale up in Ukraine under GF rounds 1 through 10. EIPHP lead the development all project documentation including research protocol, standard operational procedures and data collection toolkit, IRB and administrative documentation packages. EIPHP was directly responsible for the research protocol implementation in the study regions, i.e. setting and activation of the regional research sites, respondents' recruitment, data collection, data quality control and assurance, reports development and dissemination of the results. All key personnel had appropriate HSR training certification.

Regional Partners

The consortium team has been collaboratively working with multiple domestic partners at national and regional level. Collaborating organizations worked with the research team and provided access to the target population to conduct the survey with the study respondents in 9 regions of Ukraine. Our implementing partner at a national level was the Ukrainian Public Health Center. At a regional level the collaborative network consisted of local HIV clinics where study research sites were established.

Key Members of the Research Team (KMRT)

Study Director – Oleksandr Zeziulin, MD, MPH. Senior Researcher at UIPHP. Currently PI of a large PEPFAR Population Implementation Science project (Grant # 114-CDC-15-A; 009-CDC-17-A) focusing on treatment linkage for people using drugs. His recent work concentrated on programmatic and scientific development and management of large projects covering multiple regions involving professionals in substance use, MAT, HIV prevention and treatment. He has a leading role in developing and creating data management and quality assurance plans, data exchange mechanisms, standard operational procedures, and multisite projects; working experience as a public health specialist for USAID, and is a member of a PEPFAR team in Ukraine providing technical assistance to the public health sector. In collaboration with the research team, he organized the processes of inter-organizational communication and decision-making, field personnel training and regional sites activation, data collection, management and

safety, multisite coordination mechanism, develop standard operational procedures as well administrative and financial algorithms including IRB approval, communication with the CSO, and reporting results.

Co-Investigator – Olga Varetska, Associate Director: Strategic Information, Monitoring and Evaluation at the Alliance for Public Health. Participated in the protocol, study procedures and study instruments development by providing the knowledge on the local programmatic context of the study conduct.

Co-Investigator – Marina Kornilova, MD, specializing in infectious diseases, Senior Project Manager at the Alliance for Public Heaths coordinating the research projects in HIV/AIDS supported by Alliance. Participated in the protocol, study procedures and study instruments development by providing the knowledge on the local programmatic context of the study conduct.

Co-investigator – Kostyantyn Dumchev, MD, MPH, is Scientific Director of the UIPHP and a physician specializing in Narcology. He has a degree in epidemiology with additional concentration in biostatistics and has been involved in NIH and PEPFAR funded research projects in Ukraine since 2004 including Site PI for the HPTN 074 trial that had high recruitment and retention rates. He is co-investigator on a NIDA implementation R01 DA043125 (Altice, PI) using the enrollment methodology (split PII and survey data) that is proposed in this project. He was primarily responsible for developing survey and qualitative data collection tools, data assurance procedures, and data management. In addition, Dr Dumchev provided methodological support on quantitative assessments, designed data collection and tracking forms, quality assurance and quality control mechanisms in REDCap, developed training materials, provided training sessions for regional teams, and wrote intermediate and final reports.

Central Survey Personnel (CSP)

Study Coordinator **–** Anastasia Taroyants. Was responsible for coordination of day-to-day protocol implementation activities, compliance with the SOP and administrative procedure, organizing research related logistics and communication.

Field Survey Personnel (FSP)

We established 9 assessment sites across Ukraine. We used rigorous procedures to select and hire field survey personnel based on our experience conducting large studies involving EIPHP based staff (Investigators, Data Manager and Survey Coordinator) and outsourced local field personnel. EIPHP has a large database of regional experts, including experienced Interviewers who worked with us in multiple studies with multisite design. The fundamental criterion for hiring local field personnel *performing data collection (Interviewers)* was not being an employee of HIV services providing organizations functioning in the area covered by the survey and not being a relative or friend of a local participant. Hiring local staff to perform data collection is not considered appropriate because of the obvious presence of conflict of interest in evaluating individuals who can be known by an Interviewer. In addition, there is the probability of triggering social desirability bias by respondents who could be influenced by an Interviewer status.

Each of the 9 Field Survey Teams consisted of an Interviewer and Regional Coordinator. Interviewers were hired in each of the 10 study regions based on the criteria of having basic data collection skills, using electronic devices, speaking Ukrainian and Russian, and willing to travel within the study region and organize data collection. Prior to starting fieldwork, key personnel

obtained demographic and professional information on Interviewer candidates that included home region, ethnicity, first language, second language (if any), level of education, and survey experience. Interviewers were required to collaboratively work with Regional Coordinators to perform survey screening and enrollment procedures.

Regional Coordinators were hired in each survey region among employees who had a position in an organization providing services to PLWH and ***had legal access*** to local HIV clinics data base. The Regional Coordinator were required to prepare a ***de-identified*** (containing HIV clinic code, age, gender - see enrollment section) list of potential survey participants, contact with Data Manager and Interviewer to screen and enroll survey participants.

All Interviewers and Regional Coordinators received training prior to performing procedures as described in the Study Specific Training section of this proposal. Final eligibility for field research personnel was determined by KMRT in collaboration with the Alliance.

The study Interviewers were responsible for:

- organizing the enrollment process in collaboration with a Regional Coordinator;
- creating a schedule for research activities in the survey area;
- performing survey screening procedures;
- obtaining Informed Consent from survey candidates before enrolling them;
- perform interviews with enrolled respondents;
- help manage the local survey data base;
- ensure that no personal identifiable information is collected;
- ensure data and equipment safety;
- arrange for safe-keeping of paper-based administrative and research documents and transfer of study documents to the CSP;
- timely reporting on administrative and financial procedures and outcomes.

The Regional Coordinator were responsible for:

- organizing the survey implementation at the regional level;
- working with HIV clinic records to prepare Recruitment Documentation;
- organizing screening and enrollment process by linking survey candidates with Interviewer;
- safe data transfer and timely reporting.

Methods.

Survey Approach and Methodology

The overall approach of this assessment was based on measuring the point prevalence of Hepatitis C and IDU as *outcomes* and probable *predictors* in the target population to calculate statistical associations. Therefore, the study used cross-sectional data collection to elicit self-reported data via self-administered assisted surveys and blood rapid tests to assess the prevalence of characteristics of interest.[15] The data were collected once from each survey participant during 4 month in each HIV clinic.

This study relied on self-report of risk behaviors, which is prone to recall bias and deliberate underreporting of stigmatized behaviors. To mitigate this limitation, we tested all respondents for biological markers assuming 100% specificity of positive anti-HCV results with regard to

injecting drug use exposure. HCV infection is a marker of IDU[13] as prime risk factors include re-use and sharing of needles/syringes and injection paraphernalia[16] and rarely can be transmitted heterosexually[17-19]. Therefore, we used rapid HCV tests to measure the prevalence of HCV and define the proportion of potential injection drug users in AGYW. As a result, we were able to desegregate AGYW into a group of cases with misclassified heterosexual mode of HIV transmission and cases with confirmed heterosexual mode of HIV transmission. Specifically, *those AGYW who was tested HCV positive or reported IDU prior to their HIV diagnosis* were defined as new HIV cases with IDU mode of transmission and were enrolled as *pre-Indexes*[1]. Those AGYW who tested HCV negative and *reported no IDU* prior to HIV diagnosis were defined as new HIV cases with ***confirmed*** heterosexual mode of transmission and were enrolled as *Indexes*.

Target population

HIV positive women who have been tested and registered for the first time in 2016-2019 was a primary study population. Only those females who were diagnosed at the age of 15 to 25 years were considered for inclusion into the study. Specifically, AGYW diagnosed in 2016 were selected if they were born no earlier than in 1991, 2017 - in 1992, etc.

Pre-Indexes

AGYW were surveyed and examined for HCV. Those who were tested HCV positive OR reported IDU prior to their HIV diagnosis were enrolled as pre-Indexes (see Selection Criteria).

Indexes

Indexes were selected among screened AGYW based on their negative HCV status (see Selection Criteria). Those who reported heterosexual mode of HIV transmission during the assessment and no IDU prior to HIV diagnosis and have HCV negative test result were enrolled as Indexes and requested to identify and refer up to 5 of their sexual partners for assessment.

Partners

Partners were identified by Indexes as HIV positive men or men with unknown HIV status with whom the Indexes had sexual relationships prior to their HIV diagnosis *AND* indicated them as a potential source of HIV infection. The Partner should be identified and referred (recruited) by the enrolled Index (see Selection Criteria). Partners and Indexes in this study considered as a unique network, i.e. a partner could be referred *only by one Index* in this study. All referred partners were screened for HIV and those with positive HIV result were screened for HCV using rapid tests at study entry. Partners who have one reactive/positive HIV tests were eligible for enrollment. Eligible partners were assessed and referred to HIV/HCV care (if the diagnosis is not established at the time of the study entry), as well as substance use treatment (if applicable).

Selection Criteria

Pre-Indexes - Individuals who met all of the following criteria were eligible for inclusion in this study as a pre-Index participant:

- Female sex;
- Able to provide informed consent;

[1] Those AGYW who tested positively for HCV were not excluded from study as their data was used to define the factors associated with heterosexual misclassification.

- Diagnosed with HIV in 2016-2019;
- Being HCV positive OR reported IDU prior to HIV diagnosis;
- Age no older than 25 at HIV diagnosis;
- Being registered at a HIV clinic with heterosexual mode of HIV transmission.

Indexes - Individuals who met all of the following criteria were eligible for inclusion in this study as an Index participant:

- Female sex;
- Able to provide informed consent;
- Diagnosed with HIV in 2016-2019;
- Being HCV negative AND reported no IDU prior to HIV diagnosis;
- Age no older than 25 at HIV diagnosis;
- Being registered at a HIV clinic with heterosexual mode of HIV transmission;
- Had sexual partner/s or sexual partners with known HIV positive or unknown HIV status prior to HIV diagnosis;
- Agreed to indicate sexual partners with known HIV positive or unknown HIV status who could serve as a probable source of their HIV infection (optional);
- Agreed to partner notification procedure and referral (optional).

Partners - Individuals who met all of the following criteria were eligible for inclusion in this study as a Partner participant:

- Male sex;
- Able to provide informed consent;
- Being HIV positive at screening or being registered client of HIV clinic.

Network criteria of eligibility:

- Partner had to be confirmed (able to present referral identification cards) sexual partner of the Index;
- Partner could be referred by multiple Indexes but…;
- … be enrolled only once and associated with only one enrolled Index;
- Enrolled Index could have up to 5 enrolled Partners.

Analytic approach

Research question - Our analytic approach was based on the main research question:

Is IDU present among sexual Partners of Indexes who were diagnosed with HIV during 2016-2019 in Ukraine with the confirmed heterosexual mode of HIV transmission?

Hypotheses - Data analysis was driven by the next hypotheses:

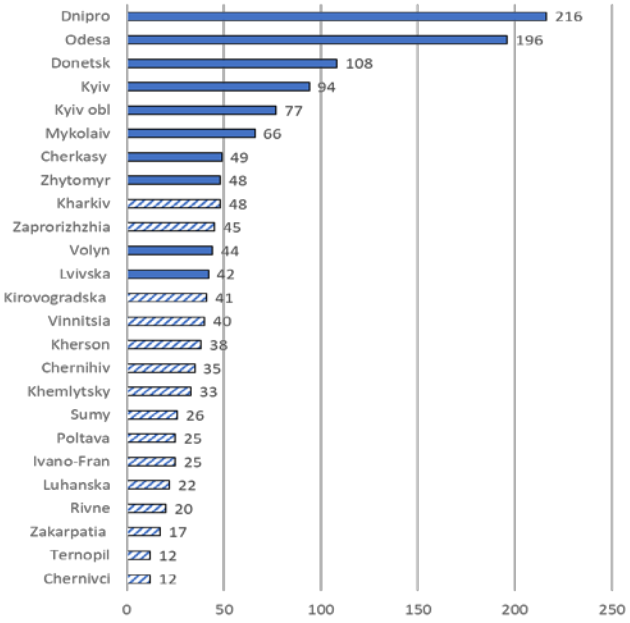
1) The proportion of HCV infected *in HIV positive Partners* is no less than 50%;
2) HCV positive AGYW are more likely to report IDU, and Pre-Indexes have more risky sexual practices than Indexes;
3) Partners with HCV are more likely to report IDU, risky sexual practices than Partners without HCV;
4) At least 30% of the AGYW sample enrolled are misclassified heterosexual HIV cases as have HCV positive test result and reported injection drug use;
5) Indexes reporting having IDU partner are more likely to report risky sexual practices;

6) Indexes reporting having IDU partner are more likely to report lower socioeconomic status.

Geographical Coverage **–** In order to assure effective study sample accrual priority was given to the regional HIV clinics where the number of the newly registered HIV cases in the AGYW is no less than 40 per 2017-2019 years[2] (see Figure 1)[3]. Therefore, the study team established local research sites in nine regions with optimal study population size and represent principal geographic areas of the country:

1. North regions: Kyiv city and Kyiv Oblast;
2. Eastern regions: Dnipro, Donetsk;
3. Southern regions: Odesa, Mykolaiv
4. Central regions: Cherkasy, Zhytomyr
5. Western regions: Lviv, Volyn.

Figure 1. Study Regions



Sample size **–** In this cross-sectional study the aim was to estimate the prevalence of unknown parameter (HCV in partners) from the target population using a random sample. So an adequate sample size is needed to estimate the population prevalence with a good precision[20]. *It is assumed that one Index could have been infected by only one sexual Partner*. The number of AGYW 15-24 diagnosed during 2017-2019 in the study regions was 940 individuals. Respectively, the number of the sexual partners considered as a source of HIV transmission is also 940.

Therefore, for the unknown prevalence of the factor of interest in the finite population of 940 individuals with the precision level of 5% and 95% confidence interval we needed to accrue minimal sample size of 274 partners[21]. This sample would provide sufficient statistical power to detect more than 50% prevalence of HCV in partners' population.

It was expected that response rate in Indexes would be no less than 63% as suggested by the prior study[14]. Indexes were asked to identify and refer their partners to participate in the study. Based on the available literature HIV positive index patients on average name 2 partners but this varied dramatically between studies (range 0.58-5.58)[22]. The ratio of partners who tested for HIV per index patient was on average 0.45 (range 0.01-1.19) for passive referral and 0.85 (range 0.19-1.81) for assisted partner notification. In this study, we plan to apply notification by an Index and enhanced referral algorithm that was expected to improve Partners and Indexes

[2] Data on new HIV cases in 2019 among females 15-24 y.o.a. are not yet available therefore the data for 2019 were extrapolated from past trends.
[3] Study regions in blue solid fill.

response rate. However, the notification and referral partners cascade is unknown in Ukraine. In addition we expected to observe up to 50% of new HIV cases with injection mode of transmission misclassified as heterosexual [14]. That means that half of the sample was expected to be comprised of AGYW who contracted HIV through IDU and would be enrolled as pre-Indexes. Only Indexes (see Index selection criteria) were expected to refer their sexual Partners to the study. Following the scenario with the Partners' response rate of 0.85 it was anticipated that at least ***n=275 (85%) of Indexes would successfully refer their Partners*** who reach the study site, agree to participate in the study and would be eligible for enrollment. Therefore, up to ***n=650*** AGYW were planned to be enrolled to allow testing the study hypotheses taking into account 50% heterosexual misclassification probability.

Enrollment **–** The regional electronic Medical Information System (MIS) have been actively used across the country regions to manage a big number of clinical records at local HIV clinics. The MIS, electronic clinical data management platform with online access, had fundamental application in our assessment as it proved to be an effective tool in patients' identification for screening and enrollment into our previous studies. However, the ability of the research team to use these registries was complicated because the HIV clinic patient contact information within this dataset has patient personally identifying information (PII), and thus cannot not be shared outside a HIV service provider. To tackle this problem, we used ***'Split PII and Survey Data' (SPSD)*** enrollment methodology to meet the requirement to maintain patients' PII within a HIV service provider, while producing a dataset that would be accessible to our study team. This method was successfully applied and described by Vogt at al.[23] and is similar to methods we used in large multisite implementation science and evaluation projects. This methodology has allowed us to disassociate patients' PII from survey data by splitting our outreach and data collection efforts. This enrollment strategy was successfully used in several of our studies. The SPSD enrollment allows for quick random selection of respondents and provides information on the potential amount of study participants, number interested and agreed to participate, number who successfully complete the survey, and reasons for refusal to participate. Using this methodology, along with the semi-automatic instruments integrated into REDCap, allowed our team to generate reports on response and completion rates with disaggregation by variables of interest.

Laboratory Testing **–** All AGYW were screened for HCV using rapid test system at the research sites located at a local HIV clinic before completing the survey.[4] All Partners were tested for HIV and HCV *before* completing the survey. Those Partners who tested negatively for HIV *were not enrolled* . The testing was performed by the staff medical nurse. The safety and legal procedures of blood testing was described in detail in the respective SOP.

Indexes Enrollment Procedures

Step 1 - Preparing Recruitment Documentation - In *each study region* the local Regional Coordinator used all types of HIV clinic data bases (HDB) to prepare the **P**rimary **E**lectronic **L**ist (PLE) of ***all*** AGYW meeting selection criteria to participate in the survey. The PLE did not include any personal identifiable information (PII) and contained HIV clinic patients' HDB *number, year of birth, gender, date of registration, date of discharge (if applicable) and reason of discharge, dates of HIV tests used for diagnosis and the registered mode of transmission*. Regional Coordinator shared the PLE via secure data transfer mechanism with Data Manager. Data Manager checked the compliance with the selection criteria and assigned Participant

[4] Those AGYW candidates who has HCV+ status indicated in their clinical records were not tested with rapid tests.

Identification number (PTIDs) to each HDB number aggregating them into the Electronic **L**ist of **Pre-S**elected (LPS) respondents. Data Manager sorted the PTIDs in LPS in *random order* to establish the sequence for the *First Contact* procedure.

Step 2 - First Contact - Data Manager shared LPS with Regional Coordinators who used HDB numbers to contact selected respondents via all allowable means of communication and offer them to participate in the survey by reading the survey Information Leaflet. If a candidate was interested and agreed to participate in the survey, the Regional Coordinator organized a meeting with an Interviewer. If a candidate was not interested in participating in the survey, the Regional Coordinator indicated it in LPS and contacted the next candidate.

Step 3 - Screening and Enrollment - Regional Coordinator met with a survey candidate, visually checked her ID and verified that the candidate was a registered HIV patient. After verification procedure, the Regional Coordinator referred the candidate to Interviewer. Interviewer offered to participate in the survey by reading or handing the Written Informed Consent Form. If the candidate agreed, the Interviewer recorded it in the LPS and started the interview. If the candidate did not give consent to participate, the Interviewer thanked the candidate, asked about the reason for not participating, and put the response into the LPS indicating the *reason of refusal* to participate.

Step 4 - HCV Testing - Blood test was performed BEFORE the respondent completed the survey by the authorized HIV clinic personal in safe conditions in HIV clinic. Once the test was complete, the Interviewer enrolled the respondents into the study either as Index or pre-Index based on the respective selection criteria. The HCV testing procedures were in details described in the specific SOPs. SOPs were developed in the stringent compliance with the established national blood testing guidelines following biological and information safety.

Step 5 - Partner Referral - Indexes were asked to identify, recruit (if possible) and refer up to 5 partners to a study site. The index participants were asked to prioritize recruitment of the sexual partners with whom they have risky sexual practices (unprotected sex|). At the end of the enrolment procedures (during the survey), Index were asked to refer their Partners in close collaboration with research personnel and the affiliated staff of a HIV clinic. Our partner referral mechanism was build based on the WHO Guidelines on HIV self-testing and partner notification[24]. All Indexes were provided with the assistance to refer Partners. This step included identification of an eligible Partner and screening all identified eligible Partners for Intimate Partner Violence (IPV). Only Indexes willing to contact and refer their eligible Partners (with no IPV identified – see below) received instructions on the Partners referral (use printed or send electronic referral cards to refer indicated Partners). Specific SOP guided the procedures of partners' enrolment.

Alternative Distant Indexes Enrollment Procedures

Due to the various complications in the regional context caused by the COVID 19 (see **Study conduct in COVID-19 context**), which has affected day-to-day life, businesses, disrupted local economies and citizen movements, the research sites used alternative distant enrollment of Indexes and pre-Indexes and data collection procedures in addition to visit-to-clinic scenario described above (see Indexes Enrollment Procedures). Distant enrollment algorithm involves steps 2, 3, 5 conducted via telephone and safe online communication between candidates and study team and the step 4 as online clinical information exchange within the study team. *The*

alternative enrollment was applicable only for those women who have documented HCV status in the local HIV clinic database. In this way, we expected to eliminate the participation steps involving travel to a local research site using public transportation, contact with the study staff and possible contact with other people including clinical and non-clinical staff in a local HIV clinic (COVID 19 at risk groups). First contact, screening, enrollment and data collection was performed by Regional Coordinators and Interviewers who communicated with a respondent via telephone or any other mean of available telecommunication as described below.

Alternative Step 1 - Preparing Recruitment Documentation - In *each study region* the local Regional Coordinator used all types of HIV clinic data bases (HDB) to prepare the **P**rimary **E**lectronic **L**ist (PLE) of ***all*** AGYW meeting selection criteria to participate in the survey and ***having documented HCV status as positive or negative***. Records with ***unknown*** HCV status were not considered for further processing for distant enrollment mode. The PLE did not contain any personal identifiable information (PII) but HIV clinic patients' HDB *number, year of birth, gender, date of registration, date of discharge (if applicable) and reason of discharge, dates of HIV tests used for diagnosis and the registered mode of transmission*. Regional Coordinator shared the PLE via secure data transfer mechanism with Data Manager. Data Manager checked the compliance with the selection criteria including the ***presence of HCV status*** and assigned Participant Identification number (PTIDs) to each HDB number aggregating them into the Electronic **L**ist of **Pre-S**elected (LPS) respondents. Data Manager sorted the PTIDs in LPS in *random order* to establish the sequence for the *First Contact* procedure. *Importantly, without indicated HCV status in the LPS the subsequent study procedures were not performed by the Interviewer as Index and pre-Index respondents status was defined by the respondents' HCV status.*

Alternative Step 2 - First Contact - Data Manager shared LPS with Regional Coordinators who used HDB numbers to contact selected respondents via all allowable means of communication and offered them to participate in the survey by reading the survey Information Leaflet for Distant Participation (Annex 2) or send the respective text via internet based messengers. If a candidate is interested and agrees to participate in the survey, the Regional Coordinator verifies the respondent by asking them to indicate full date of birth, approximate date of first positive HIV screening or date of registration in HIV clinic and ***their HCV status***. After a candidate verification, Regional Coordinator offered to participate in the survey by reading a Verbal Informed Consent Form for Distant Participation. In the Verbal Informed Consent Form for Distant Participation, it was clearly articulated *that it is required to share with an Interviewer the candidate's telephone number to conduct distant interview and a number of the bankcard with a study administrative personnel (Regional Coordinator and EIPHP administrative assistant) to wire participation compensation for distant interview and Partners referral.* If candidates agreed to participate in the study, the Regional Coordinator entered respective record in the LPS indicating that informed consent was obtained and the date of the verbal informed consent procedure. After that the Regional Coordinator organized the candidates' contact with the Interviewer via safe data transfer mechanism indicating participant phone number in the LPS. The Interviewer had an online access with a user rights to review the LPS without the right to amend the entered information. If a candidate was not interested in participating in the survey, the Regional Coordinator recorded it in LPS and contacted the next candidate.

Alternative Step 3 - Screening and Enrollment – The Interviewer worked with the LPS to identify those candidates who were verified by the Regional Coordinator, agreed to participate and provided their contact information. Interviewer contacted a candidate and conducted data collection in accordance with the established SOPs. At the beginning of the survey, the

Interviewer additionally clarified if a candidate gave verbal informed consent to participate to the Regional Coordinator. If the candidate did not give the consent to participate before interview or refused to patriciate during the interview the Interviewer thanked the candidate, indicated the refusal to participate in the electronic data capturing form and dismissed the candidate.

Alternative Step 4 - HCV Testing – Blood test was skipped in Alternative Distant Indexes Enrollment Procedures, as only Index candidates with documented HCV status were eligible for alternative distant data collection. Importantly, Interviewer payed particular attention during the enrollment procedure and interview to information regarding HCV status of the candidate indicated in the LPS. *The Interviewer was required to fill in the obligatory field in the electronic data capturing form with a respondent HCV status information.* Without the indication of the HCV status of the respondents, the enrollment procedures was not allowed by the data quality control mechanisms in the study data base in REDCap.

Alternative Step 5 - Partner Referral - Indexes were expected to identify, recruit (if possible) and refer up to 5 partners to a study site using the partner notification system. The index participants were asked to prioritize recruitment of the sexual partners with whom they have risky sexual practices (unprotected sex|). At the end of the enrolment procedures (during the survey), Index was asked to refer their Partners in close collaboration with research personnel and the affiliated staff of a HIV clinic. Our partner referral mechanism was based on the WHO Guidelines on HIV self-testing and partner notification[25]. All Indexes were provided with the assistance to refer Partners. The assistance included identification of an eligible Partner and screening all identified eligible Partners for Intimate Partner Violence (IPV). Only Indexes willing to contact and refer their eligible Partners (no IPV identified – see below) received instructions on the Partners referral (use electronic referral card to refer indicated Partners). Specific SOP guided the procedures of partners' enrolment.

Of note, Partners Distant Enrollment could be performed for indicated Partners who were registered patients of local AIDS Centers and had established HCV status. See below Alternative Distant Partners Enrollment Procedures.

Partners Enrollment Procedures

Step 1 - First Contact and Partner Verification - Partners referred by Indexes were expected to present at the study site where Interviewer performed SOP on Partner verification to assure that a Partner was referred by a respective Index to prevent violation of the network criteria of eligibility. Each Partner was required to demonstrate the paper referral card or electronic referral card that he received from his Index (in case if distant Index enrollment procedures undertaken) to the study personnel. If partnership was verified and the network criteria were preserved (each Partner could have only one Index but Index could have up to 5 Partners) the Interviewer offered Partners to participate in the survey by reading the survey Written Informed Consent From for Partners (Annex 5).

Step 2 - Screening and HIV/HCV testing - Once potential partner consented to participate the Interviewer performed screening for eligibility and HIV/HCV testing. For those partners who were not aware of their HIV status pre-test and post-test counselling was provided by HIV clinic staff in accordance with the national and local regulations (HIV screening consent, referral to HIV services, etc.).

Step 3 - Survey and Enrollment - After completion the self-administered assisted survey a Partner was enrolled into the study.

Alternative Distant Partners Enrollment Procedures

Step 1 - First Contact and Partner Verification - Partners referred by Indexes were expected to contact Coordinator who would perform SOP on Partner distant verification to assure that a Partner was referred by a respective Index to prevent violation of the network criteria of eligibility. Each Partner was required to demonstrate the electronic referral card that he received from his Index (in case if distant Index enrollment procedures undertaken) to the study personnel. If partnership was verified and the network criteria were preserved (each Partner could have only one Index but Index could have up to 5 Partners) the Interviewer would offer Partners to participate in the survey by reading the survey Verbal Informed Consent From for Partners.

Step 2 - Screening and HIV/HCV testing – HCV testing was omitted in Distant Enrollment as all Partner eligibility criteria had been checked by Coordinator during Partner verification procedure using HIV clinic database. After verification was complete, Coordinator organized the communication between Partner and Interviewer.

Step 3 - Survey and Enrollment - After completion the telephone survey with Interviewer a Partner was enrolled into the study.

Survey Data Collection – Data collection was performed by a respondent with the assistance of an experienced Interviewer using a laptop or tablet for direct data entry into the online participant Questionnaire using a REDCap data platform (see REDCap section). The data collection was confidential and performed in a private place without any third party being present. Enrollment of respondents continued until the LPS is exhausted or the national sample is reached.

In case of Distant Enrollment Procedures application, the data collection was undertaken via telephone or internet interview by an Interviewer.

Study Instruments – The KMRT has developed a comprehensive Study Toolkit to systematize and standardize implementation of the survey across all study regions. The research parts of the survey was developed in English included data collection generic forms and standardized instruments organized into the Survey Participant Questionnaire (thereafter Questionnaire). The Questionnaire was uploaded into electronic REDCap platform or administered on a paper-based form in accordance with the survey Data Management procedure (see section Data Management). The Study Toolkit included but not be limited to the Primary Electronic List, List of Randomly Selected respondents, Study Information Leaflet, Enrollment Checklist and Enrollment Log, Written Informed Consent Form and Standard Operational Procedures (SOP).

During the interviews, we collected data from Indexes and Partners on their sexual behavior[5], drug use history[5], STI history[5], parenteral exposures[5], self-reported way of HIV infection, alcohol use[5] (AUDIT-C), criminal history[5] and demographical information[5].

[5] During 10 years before finding out about HIV positive status of Index

Pre-Test **–** The Questionnaire was translated into Ukrainian before piloting. The Questionnaire was pilot-tested ***without*** participation of the FSP. KMRT pre-tested the Questionnaire in Odessa with 10 respondents. We tested both *Interviewer assisted* and respondent *self-administered* data collection mechanisms to identify the most convenient and time efficient data collection mode for respondents. Of note, particular attention was paid to the average time needed to complete the Questionnaire as data collection from one respondent was expected to take *no longer than 30 minutes*. Pre-test feedback and recommendations shaped the final version of the Questionnaire which was reviewed and approved by the Alliance before data collection started.

Study Specific Training **–** All Regional Coordinators and Interviewers went through a one-day research online training (see COVID-19 pandemic implications for the study conduct) prior to beginning procedures in the field. Training was conducted in accordance with the study implementation plan by the EIPHP study personnel (Drs. Zeziulin and Dumchev). The training included modules on In-Depth Research Protocol Review, Collaborative Communication with CSP, Data Management Plan, study SOP and administrative and financial procedures. The training agenda covered eligibility screening, informed consent, data collection tools, data entry and data security. Finally, all FSP staff underwent training on Research Ethics and Human Subject Protection and Good Clinical Practices. *Of note, pre-testing of the Questionnaire was not being part of interviewer training.* Training attendance and certification by EIPHP trainers was the obligatory prerequisite to contracting for all members of FSP.

Data Management **–** In this study, we collected personal data such as sex and date of birth, education, health issues and risky HIV experience. Since this information might lead to knowing the identity of a participant, all patients' study records were labeled by an automatically assigned PTID. Using coded participants identifiers was dictated by the necessity to create and maintain the quality of the large number of unique records in the study database through preventing duplications and linking irrelevant data to a participant record. *Of note, the phone numbers and names, and other information deemed sensitive was not collected by an Interviewer.* Nevertheless, all sensitive information (including phone numbers and e-messaging accounts) was used by Regional Coordinators who had authorized access to MIS records and could maintain contact with them as a part of their daily programmatic routine to organize meetings with Interviewers but NOT to enter it into ANY of the survey documents.

All completed electronic forms were managed by Interviewers in each region and submitted to the EIPHP using the online data management platform REDCap (see below) with reliable firewall defend and backup capabilities. We expected to deal with some cases when electronic forms could not be used (no internet connection in rural areas). Therefore, a specific SOP for ***paper-based documentation*** *application* was developed. All completed paper-based Questionnaire forms were entered immediately (usually on the same day) into REDCap to allow for real time data quality control (see section Survey Data Quality Control). At the end of the data collection, all complete research and administrative survey documentation was aggregated by Regional Coordinators in each region and submitted as scanned copies to the EIPHP using online file exchange platforms with reliable firewalls and backup capabilities. All hard copies of the research documentation and completed administrative forms were temporarily stored by Interviewers in locked cabinets and/or an office without access to unauthorized individuals. Once data collection was completed, the paper-based forms were posted to the EIPHP via secure postal services.

All completed paper-based study research and administrative forms are being stored in EIPHP safe storage (archive) for five years after study completion or for the period indicated by

Alliance after which all paper documents will be destroyed. Only authorized personnel have an access to the archive.

Online Data Management Platform REDCap – All administrative and research electronic forms were completed by Interviewers and managed by the EIPHP staff via the Research Electronic Data Capture [26] platform (REDCap), a web-based application for building and managing online surveys and databases. This platform has no hard requirements with regard to server processing power, memory or hard drive space since it is not resource-intensive and requires little initial drive space by either the web server or database server. The application employs various methods to protect against malicious users who may attempt to identify and exploit any security vulnerabilities in the system. REDCap users have access only to data and information that they are supposed to have within the application by identifying user privileges. Each user had their own account and the user account only had access to REDCap projects that they created themselves or to projects which other users have granted them access. REDCap contains an auto-logout setting, which is customizable (default auto-logout time is 30 minutes), and automatically logs a user out of the system if they have not had any activity (e.g. typing, moving the pointer) on their current web page for the set amount of time. This prevents someone else from accessing their account and project data if they leave a workstation without properly logging out or closing their browser window. *REDCap maintains a built-in audit trail that logs all user activity and pages viewed by every user, including contextual information (e.g., the project or record being accessed). Therefore, a REDCap project administrator was able to monitor any activity in the project, e.g. entering data, exporting data, modifying a field, running a report, or add/modifying a user.* REDCap has been regularly used by the EIPHP since 2014 as its main data collection and data quality control tool as well as its administrative research database for timely and precise study subject documentation tracking. In addition, we have developed general approaches and respective SOPs in organizing and providing remote technical support to REDCap users form distant research sites.

Survey Data Quality Control – Quality Control is a daily process of checking for errors and making corrections to assure data precision and completeness, which is regulated by established Quality Control procedures (Data Management SOP). Quality Control was implemented at the local level (survey site) by the FSP, and central level (in EIPHP) by the Data Manager. ***At the local level***, Regional Coordinators and Interviewers were responsible for assuring data completeness and integrity. ***At the central level,*** the Data Manager was responsible for monitoring regional research sites by performing every day and periodic data quality procedures.

We used a two-stage approach to control data quality in this survey.

First, we applied the REDCap integrated Data Quality module to find discrepancies ***immediately after data entry.*** We created custom rules that REDCap executed to determine if a specific value is discrepant or not. Custom rules included mathematical operations and advanced logic functions to validate data. Last, but not least, we activated ***the real time execution of data quality rules*** to ensure that data integrity and completeness in the survey Questionnaire were preserved. For example, if an Interviewer tried to submit an uncompleted form or a form with incorrect values, a message generated by REDCap would appear on the type and source of the error. ***Interviewers were held responsible for performing all corrective measures*** to assure data quality and completeness.

Second, once a week, a Data Manager performed descriptive analyses using the REDCap statistical module and Data Quality module with administrative privileges to check for inconsistent data. A Data Manager assigned 'Unverified' status to the records with errors and via

email sent a quality query to an Interviewer. Examples include confirmation of participant codes, re-review of inconsistent or extreme values in the records, validating selection criteria, consultation with a Regional Coordinator having access to respondents PII to correct inconsistent participants' information. Once all data quality queries were resolved, the Data Manager accepted the record by assigning 'Verified' status. *In addition, using REDCap activity logs Data Manager monitored Interviewers activities in order to prevent any deviations and violations of Data Management Plan.*

Paper based forms - As we used electronic data entry and data exchange mechanisms, most inconsistencies or missing data are expected to be detected immediately. Through the study implementation period, there were circumstances when use of REDCap was not possible.

General Information

Communication and Administration – We established and activated nine regional study sites to conduct this study. EIPHP worked closely with the Alliance and local HIV service providers in each region to establish a collaborative research network that was agreed via official Memorandums of Understanding (MoU). MoU's included language stipulating willingness and agreement to implement the study at HIV clinic in full compliance to the protocol and detailed information on the outputs and activities which included organization of research sites, personnel training, access to HIV clinic patients registries, facilitating respondents recruitment, data collection and data management, adherence to the study procedures and principles of Good Clinical Practice, and timely reporting.

***Standard Operating Procedures* –** KMRT developed the assessment SOP in Ukrainian language that defined, step by step, research and administrate activities to assure the common understanding of the complex process of a research project implementation. SOPs are uniformly written procedures, with detailed instructions to record routine operations, processes and practices followed within a research project. In research, SOPs help define the research group's standard practices and daily processes conducted to assure execution of research tasks in accordance with institutional, state and national guidance. SOPs contain adequate detail to clearly guide research staff through a particular procedure and thereby establish uniformity in the everyday functions of the multisite study project. Each SOP was written in a general format that can be easily followed by local field research personnel. By laying out defined processes, the primary function of an SOP was to specifically avert procedural deviations. The Study SOPs received initial approval by the Project Director and were distributed among FSP.

Human Subjects Protection

***Ethical Review* –** All investigators had research ethics training certification. The study protocol was submitted for ethical review to the Institutional Review Board (IRB) at the Ukrainian Institute on Public Health Policy (Kiev, Ukraine).

***Informed Consent* –** For conducting screening, assessment and rapid HIV/HCV testing the respective Information Leaflets were handled/sent to each eligible candidate by study personnel and Written Informed or Verbal Consent was obtained. All questions that the candidate may have were clarified and explained. Potential subjects were informed that their participation is voluntary and that they have a right to withdraw their consent and stop participation at any time. Refusal or withdrawal from the study would have no effect on the participant's access to health facilities and treatment. Participants were informed that any information they disclose during the course of the study was considered confidential (i.e., no personal identifiers were used and only

aggregated information across all participants would be reported). Participants had the potential risks and benefits of the study explained to them as well.

Respondents' Compensation – For participation in the assessments, Indexes, pre-Indexes and Partners received compensation for their time in the amount of 250 in Ukrainian Hryvnas (UAH) for survey and blood testing. Indexes received 250 UAH for the referral of the eligible partner who was successfully enrolled into the assessment. The proposed compensation is based on our enrollment experience in other studies and comparable to the hourly salary rate of a mid-level employee in the Ukraine.[27] The rationale for this level of compensation is as follows: 1) a lower rate is likely to oversample individuals from lower socioeconomic strata who also tend to have higher medical and psychosocial needs, biasing the sample towards this segment of the HIV patient population. 2) higher rates would be prohibitively expensive and could encourage misrepresentation of non-partners as partners. 3) no compensation would bias the sample toward a narrow segment of the target population with unusually high levels of altruism and high levels of disposable time.

In case of Distant Enrollment Procedures application, for participation in the assessments, Indexes and pre-Indexes received compensation for their time in the amount of 150 in Ukrainian Hryvnas (UAH) for survey. Indexes received 250 UAH for the referral of the eligible partner who was successfully enrolled into the assessment. Partners received up to 550 of compensation if referred by the Indexes who were enrolled distantly including the cost of transportation to the study site from distant areas. Partners enrolled via Distant Enrollment received 150 in Ukrainian Hryvnas (UAH) for survey.

Benefits **–** There were no immediate benefit to study subjects. However, knowledge obtained in this study can help improve programmatic objectives and benefit the community by helping to improve HIV surveillance system and HIV services provision.

COVID-19 pandemic implications for the study conduct

The first cases of infection and death from COVID-19 were reported in March 2020. [28] The monthly number of new cases of COVID-19 has steadily increased: from 418 in March to 351,414 in December 2020. The total number of cases in 2020 was 1,074,093. 18,854 deaths from COVID-19 were registered. In order to prevent the spread of coronavirus, the Government introduced lockdown throughout Ukraine from March 12 to April 30, 2021. It was not allowed to visit educational institutions and organize and participate most of public events; the work of a number of various businesses and agencies was suspended. Since mid-March, Ukraine has closed international air transportation, rail and bus services, as well as intercity and interregional passenger transportation. Restrictions affected the medical services sector in the form of a temporary suspension of planned hospitalization measures and planned operations, except for urgent cases. [28] In addition, many medical institutions have been reformed to receive and treat COVID-19 infected patients in serious conditions.

On 4 May, the Ukrainian government extended the quarantine until 22 May.[29] On 1 June, railway connections between a number of Ukrainian cities were re-opened. After the government eased restrictions, the number cases began to rise sharply from July reaching 10,000 cases a day by November. On 11 November, the government approved weekend lockdowns were non-essential businesses would close for the weekend for three weeks starting from 14 November.

Regional HIV clinic were overloaded with the work related to COVID-19 pandemic. It was required by the Government to reduce the number of the clinical visits to regional HIV clinics and introduce telemedicine to conduct clinical appointments with patient and ART medication delivery to patients using courier or postal services. Therefore, since March 2020 the number of clinical visits to HIV clinics was substantially reduced.

Study sample accrual

As our research strategy was based on the using the regional HIV clinics facilities with the officially employed clinical staff to prepare enrollment documentation, contact study candidates, conduct informed consent and laboratory testing the entire chain of study procedures was disrupted by the COVID-19. The inability of HIV clinics allocate their resources for the study conduct during the COVID-19 pandemic resulted in the initial delay in the research sites activation and continuous participants accrual delay throughout the entire enrollment period. In addition, study accrual was complicated by the high rate of the refusal to participate due various patient related reasons (absence of the patient contact information in the HIV clinic data base, no willingness to discuss health related issues by phone) and factors related to COVID-19 pandemic. Importantly, predominant part of the study key population at the time of data collection were young females having children and the need to travel to the study site was the main reason to refuse to participate in the study.

As we performed quasi-random selection of respondents, we assumed that our sample would include a substantial number of AGYW with full time employment or/and having little children, thus making enrollment into a face-to-face survey challenging. In addition, we were aware about the 60% response rate among this population in Ukraine. To substitute those who refused to participate or did not meet selection criteria at any stage of the enrollment and data collection stages local research teams would need to re-run time-consuming procedures of recruitment documentation generation. We also expected that enrolling Indexes from distant areas especially in large Eastern regions (Dnipro, Donetsk) entails traveling by a respondent to research site. Therefore, it was anticipated that organizing and conducting of 925 interviews for 9 Interviewers would approximately take up to 4 business months. In accordance with the original study timeline, we planned to start participants' accrual in March 2020 and close all research sites in June 2020. Instead, due to various contextual issues caused by the COVID-19 pandemic described above, the accrual and enrollment started in August and ended in December 2020. To manage all the restrictions caused by the pandemic the study protocol was modified and agreed with the Alliance to introduce distant enrollment and assessment procedures. These modifications implied distant enrollment of the participants having the information on HCV status in their clinical records. Therefore, those candidates who did not have this information recorded where excluded from the participants lists for distant enrollment, which additionally reduced the size of the study target population.

Instruments

Analytic approach

Descriptive analysis was performed to characterize the sampled participants, separately for Indexes/Pre-indexes and Partners. Frequencies and proportion for socio-demographic and behavioral variables were used to describe the sample.

For each HIV risk factor, we created a dichotomous variable based on one or more questions in both samples. Some participants were not consistent in responding to different questions addressing the same risk factor; therefore, we constructed logical formulas defining absence or presence of the factor (Panel 1). Both in descriptive analysis and in hypothesis testing we treated these variables as not mutually exclusive, recognizing that one person may be exposed to more than one factor at the same time.

Panel 1. Logical formulas for risk behavior definitions.

	Indexes	Partners
Heterosexual exposure	admitting heterosexual contacts * OR having one or more partners of the opposite sex* OR self-reporting being infected through heterosexual contact	all partner participants were considered to have had heterosexual exposure
High-risk heterosexual exposure	having heterosexual exposure (defined above) AND (having more than 5 sexual partners* OR having had a sexual partner who injects drugs* OR having had sex with a bisexual man* OR having had sex with a HIV positive person* OR having a commercial male sex partner* OR giving or receiving money or drugs for sex*)	having more than 5 sexual partners* OR having had a female sexual partner who injects drugs* OR having had sex with a HIV positive woman* OR having a commercial female sex partner* OR giving or receiving money or drugs for sex*
Injecting drug use (IDU)	admitting injecting illicit drugs at least once* OR self-reporting the IDU as the most likely way of acquiring HIV OR self-reporting being treated for substance dependence OR self-reporting being treated for overdose	
Homosexual exposure		having one or more male sexual partners* OR having homosexual contact with a man who injected drugs* OR having homosexual contact with an HIV-positive man* OR self-reporting MSM as the most likely way of acquiring HIV
Nosocomial exposure	having had blood or blood product transfusion* OR having had organ or tissue transplantation* OR self-reporting being treated for substance dependence* OR self-reporting being treated for overdose* OR being hospitalized for any other reason* OR having had any surgery* OR having been on hemodialysis* OR having had conditions that required frequent injections* OR self-reporting being infected through medical procedures	
Accidental	Injecting or being injected any substance with a non-sterile needle* OR having been injected by not a medical worker* OR having been involved in practice related to blood, needles or knives (e.g. acupuncture, tattoo, scarring, other practices)* OR self-reporting being infected in a non-occupational accident with skin penetration	
Sexually transmitted infections (STI) Exposure	self-report on having gonorrhea OR syphilis OR genital herpes OR other STI at any time before finding out about HIV positive status	
HCV test	positive test for anti-HCV antibodies	

	Indexes	Partners
result		

*during 10 years before finding out about HIV positive status of Index

All risk factors were cross-tabulated to describe the overlap between them. We constructed a summary variable representing the most probable mode of transmission based on the survey responses (SMoT). Given the strong correlation between HCV and IDU, presence of anti-HCV antibodies was considered a marker of IDU-related transmission. If no anti-HCV antibodies were detected, but injecting drug use risk factor (defined above) was reported, SMoT was also assigned as IDU. Indexes/pre-indexes without HCV antibodies and not self-reporting IDU, were considered to be infected heterosexually. Partners, who did not have HCV or IDU, but reported homosexual contact, were considered to be infected through MSM exposure. The others were assigned the heterosexual transmission category.

Hypotheses testing

The analytic approach was based on the main research question:

> Is IDU present among sexual Partners of Indexes who were diagnosed with HIV during 2016-2019 in Ukraine with the confirmed heterosexual mode of HIV transmission?

The following analytic methods were used to analyze the hypotheses:

1) The proportion of HCV infected in HIV positive Partners is no less than 50%;

95% confidence intervals were computed for HCV prevalence among partners, and one-sample binomial test with two-sided p-value was used to determine significance of difference between the observed proportion and hypothesized 50% prevalence.

2) HCV positive AGYW are more likely to report IDU, and Pre-Indexes have more risky sexual practices than Indexes;

Pearson's chi-square test was used to test the association between the HCV status among indexes/pre-indexes and IDU, high risk heterosexual contacts, STI factors (defined above), and sexual practices such as having a PWID partner, MSM partner, HIV-positive partner, commercial sex partner, exchanging money or drugs for sex, and condom use.

3) Partners with HCV are more likely to report IDU, risky sexual practices than Partners without HCV;

Pearson's chi-square test was used to test the association between the HCV status among indexes/pre-indexes and IDU, high risk heterosexual contacts, STI factors (defined above), and sexual practices such as having a female PWID partner, HIV-positive female partner, commercial sex partner, exchanging money or drugs for sex, and condom use with female partners.

4) At least 30% of the AGYW sample enrolled are misclassified heterosexual HIV cases as have HCV positive test result and reported injection drug use;

One-sample binomial test with two-sided p-value was used to test the difference between the hypothesized and observed IDU mode of transmission prevalence.

5) Indexes reporting having IDU partner are more likely to report risky sexual practices;
6) Indexes reporting having IDU partner are more likely to report lower socioeconomic status;

Pearson's chi-square test was used to test the association between having an IDU partner among indexes/pre-indexes and IDU, high risk heterosexual contacts, STI factors (defined above), and sexual practices such as having a PWID partner, MSM partner, HIV-positive partner, commercial sex partner, exchanging money or drugs for sex, condom use, and socio-demographic characteristics.

7) The proportion of IDU mode of transmission among indexes/pre-indexes does not change over time (by year of registration).

Mantel-Haenszel test for trend was used to assess the linear trend in the proportion of cases attributed to IDU among AGYW across the years of HIV registration.

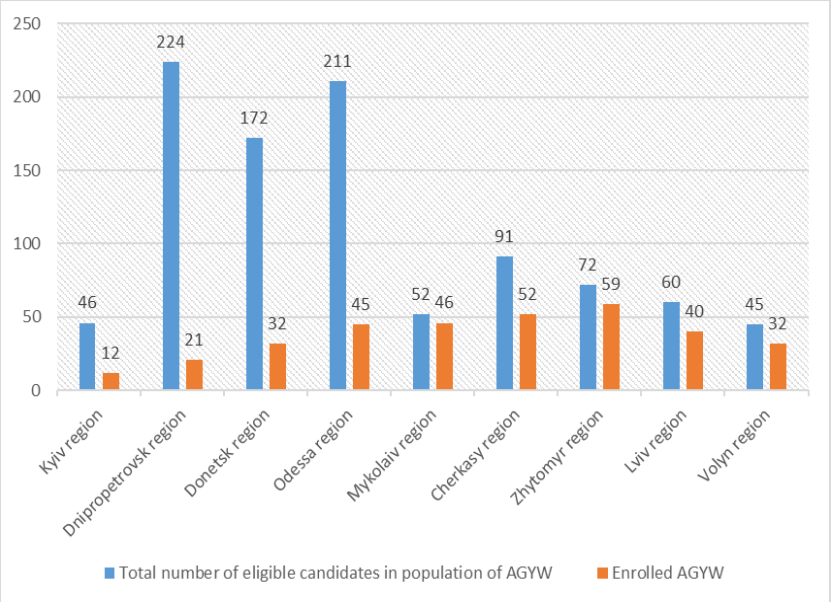
Statistical analysis was done using SPSS® for Windows version 23 (IBM Corporation, Armonk, New York, USA).

Results

Access to the target populations and participants response rate.

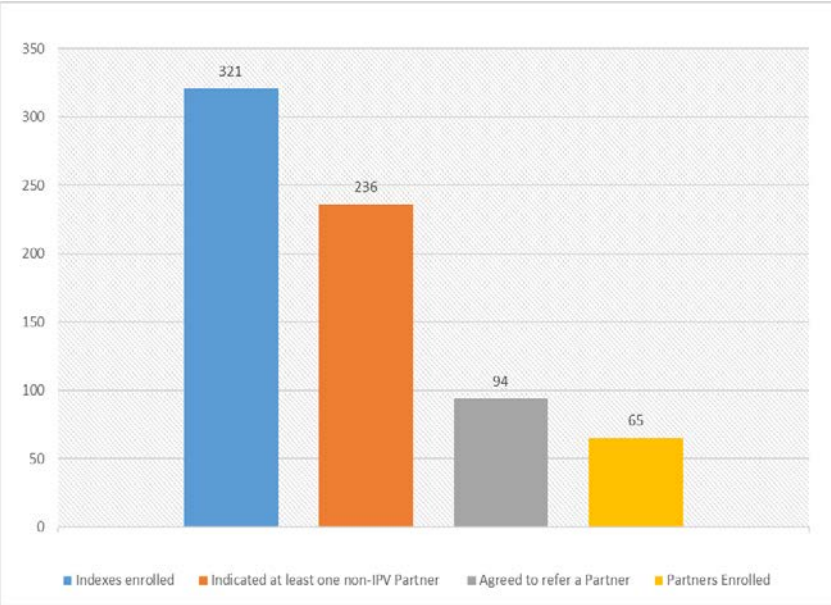
974 records of eligible AGYW candidates from HIV clinics registries in all study regions were entered into the study database and processed. In Kyiv region 46 (5%) of records were found to eligible and extracted into the candidates list, in Dnipropetrovsk region - 224 (23%), Donetsk region - 172 (18%), Odessa region - 211 (22%), Mykolaiv region - 52 (5%), Cherkasy region - 91 (9%), Zhytomyr region - 72 (7%), Lviv region - 60 (6%), Volyn region - 45 (4%) (Figure 2). 339 AGYW and 65 partners were enrolled during the study enrollment period from August to December 2020 resulting in 35% response rate among Indexes and Pre-Indexes. 12 (4%) of enrolled AGYW were recruited in Kyiv region, Dnipropetrovsk region - 21(6%), Donetsk region - 32(9%), Odessa region - 45(13.3%), Mykolaiv region - 46 (14%), Cherkasy region - 52 (15%), Zhytomyr region - 59 (17.4%), Lviv region - 40 (11.8%), Volyn region - 32 (9%).

Figure 2. The number of AGYW eligible and enrolled by region



Based on the study selection criteria (see Selection Criteria) enrolled AGYW were disaggregated into 321 Indexes and 18 Pre-Indexes (Table 1). Indexes were asked to identify and refer up to 5 of their sexual partners to the study site. Each potential partner indicated by Index was screened for IPV and those who was reported to have at least one IPV criterion was excluded from the Index sexual network and was not eligible for enrollment. 236 Indexes indicated at least one sexual partner who had negative IPV screening results and 94 (40%) of them agreed to refer their partners to the study site (Figure 3). 41 (13%) out of all Indexes reported IPV history.

Figure 3. Partners enrollment cascade



Sociodemographic characteristics of AGYW

The majority of AGYW were (53%) between 21 and 26 years of age at enrollment into the study (Table 1)(Figure 4). At the time of HIV diagnosis Pre-Indexes had numerically lower level of technical and college or university education (17% and 6%) compared to Indexes (29% and 15%) (Figure 5). For Indexes it was common to be employed at the time of HIV diagnosis (52%) while more than a half of Pre-Indexes (56%) were unemployed (Figure 6). At the time of HIV diagnosis more Indexes were married (27%) than Pre-Indexes (11%). Year of registration in HIV clinic was equally distributed among Indexes and was numerically different in Pre-Indexes but small number of observations does not allow making reasonable conclusion.

Figure 4. AGYW by age

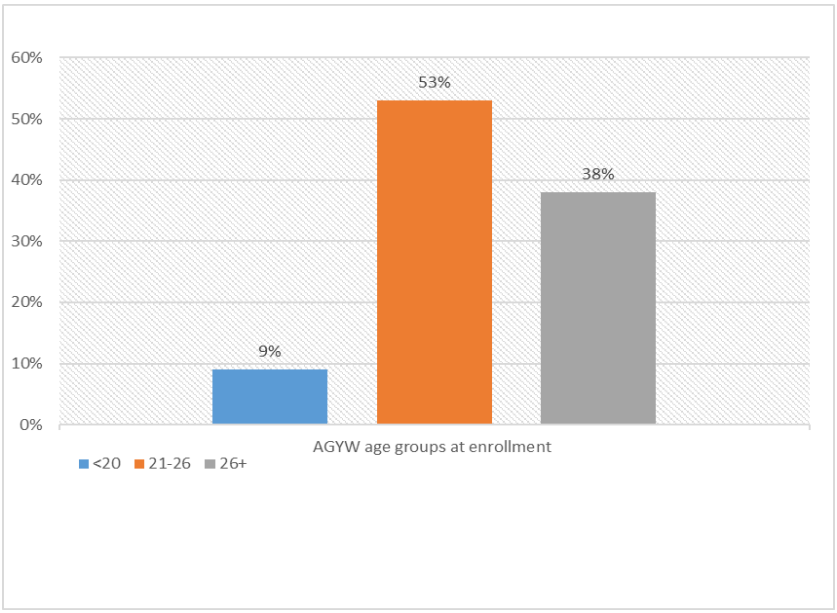


Figure 5. AGYW by education

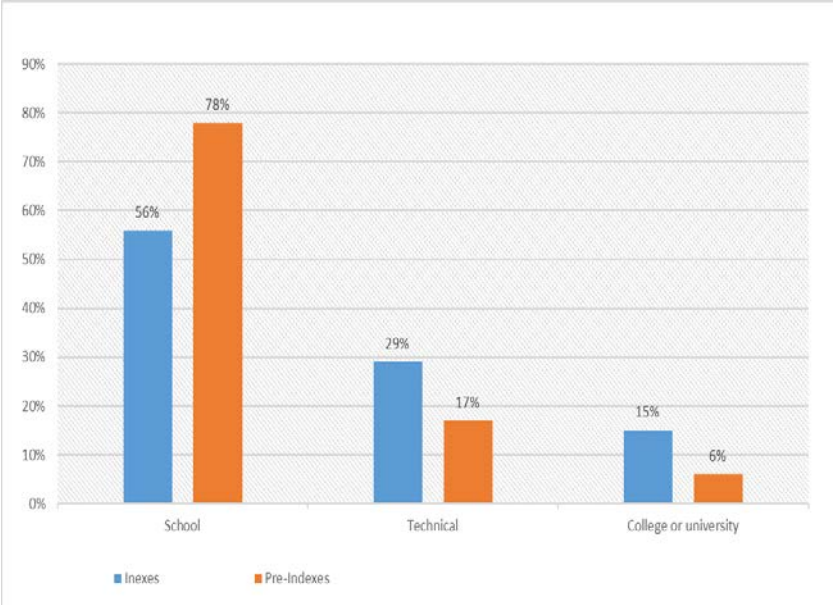
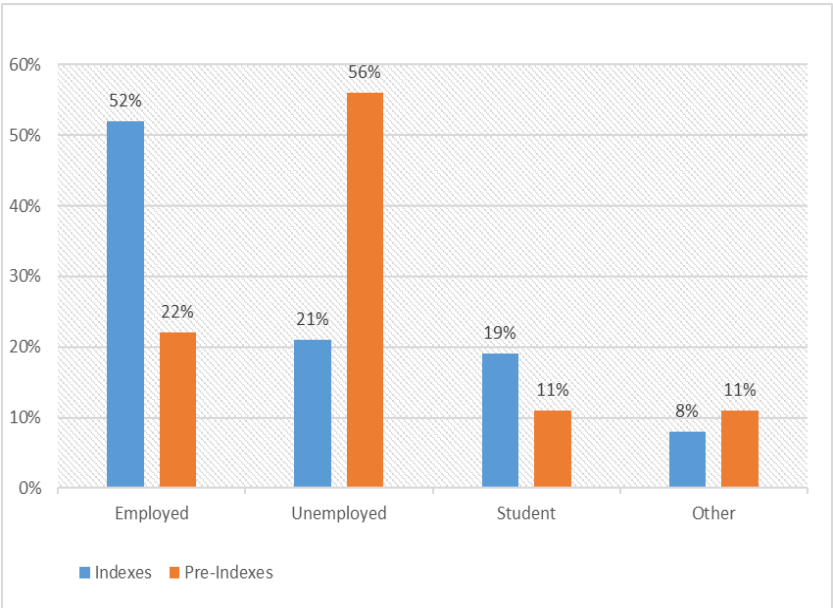


Figure 6. AGYW by employment



Sociodemographic characteristics of Partners

At the study enrollment, 46% of Partners were younger than 29 years of age, 35% were no older than 35 years and the remaining 18% were 35 y.o. and older (Table 2)(Figure 7). 37% reported having only school education before the time of HIV diagnosis of Index and the rest of the

Partners reported technical (43%) and college or university level of education (20%) at that time (Figure 8). Most of them were employed (86%) and 22% were married.

Figure 7. Partners by age

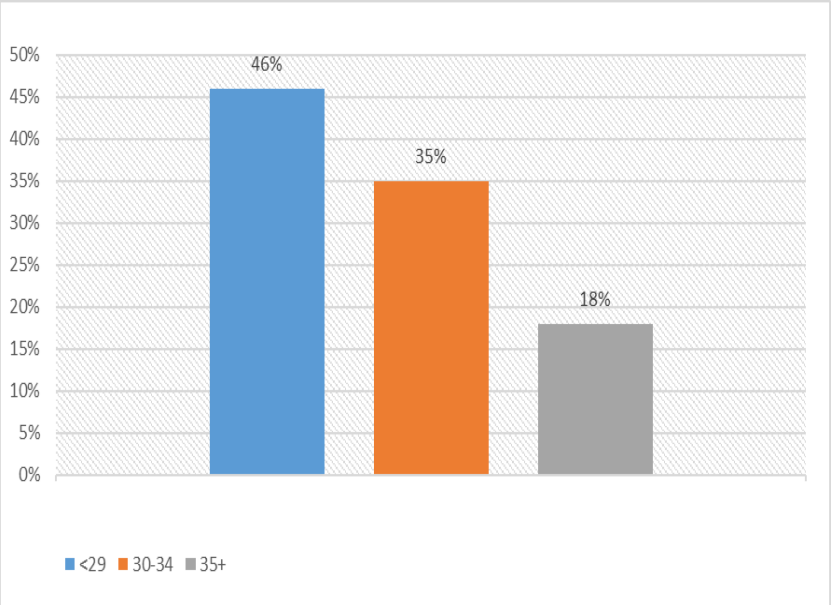
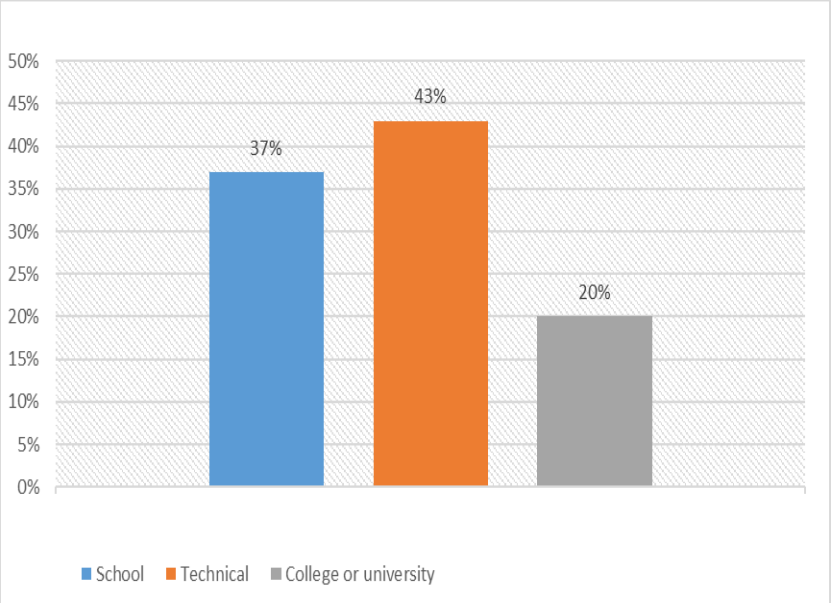


Figure 8. Partners by education

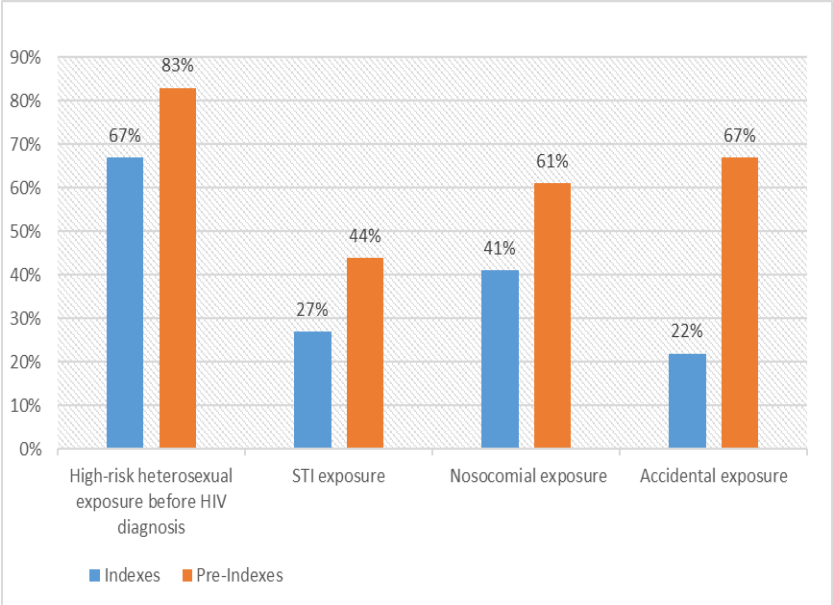


HIV risk factors among AGYW

IPV was queried only from Indexes and 13% have reported the history of IPV (Table 1). HCV positive test result had 89% Pre-Indexes and 11% of Pre-Indexes were negative. Injection drug

use (IDU) before HIV diagnosis reported almost half of Pre-Indexes (56%). 89% Pre-Indexes reported heterosexual exposure and 2 Pre-Indexes reported having no sexual partners before HIV diagnosis. High-risk heterosexual exposure before HIV diagnosis was reported by 83% of Pre-Indexes versus 67% in Indexes(Table 1). Similarly, STI exposure was more common in Pre-Indexes (44%) vs Indexes (27%) as well as nosocomial exposure was more frequent in Pre-Indexes (61%) compared to Indexes (41%). Accidental exposure was much more frequently reported by Pre-Indexes (67%) vs (22%) in Indexes.

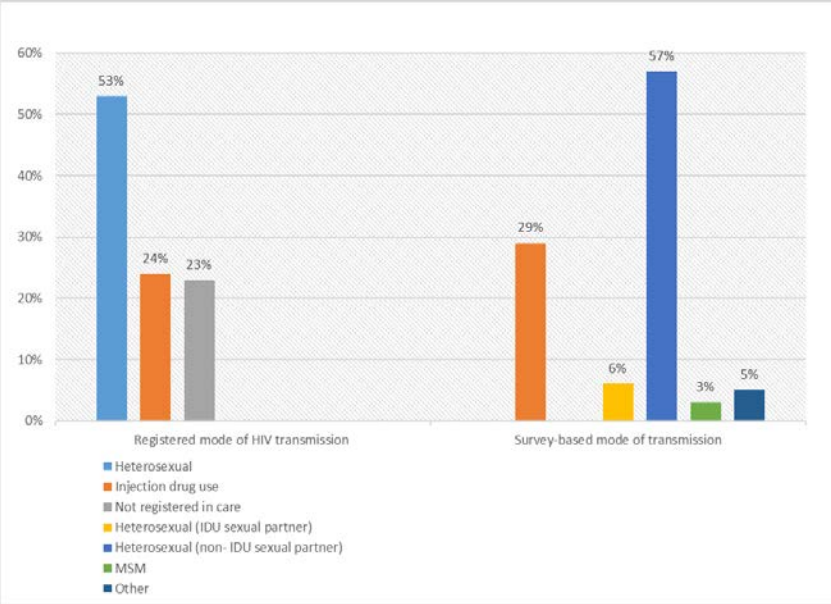
Figure 9. HIV exposures among AGYW



HIV risk factors in Partners.

22% reported problematic alcohol use before Index HIV diagnosis and 71% reported consuming alcohol and drugs before sex always or frequently (Table 2). More than a half of Partners (51%) never or rarely used condoms. 38% reported IDU exposure and 33% were had positive HCV status. 2 (3%) reported having MSM exposure, 62% had high risk heterosexual exposure and 49% - STI exposure. Nosocomial exposure was reported by 45% Partners and 35% had accidental exposure. At the time of the study enrollment 51 (77%) out of 65 partners were registered patients of HIV clinic and 53% of Partners were registered with heterosexual mode of transmission and 24% were registered as IDU (Figure 10). During the study survey 19 (29%) of Partners reported IDU as their mode of HIV infection, 2 (3%) reported MSM, 37 (57%) reported heterosexual transmission from non-IDU sexual partner and 4 (6%) reported heterosexual transmission from IDU sexual partner.

Figure 10. Registered vs survey-based mode of HIV transmission in Partners



Hypotheses testing

Hypothesis 1. *The proportion of HCV infected in HIV positive Partners is no less than 50%.*

At the alpha level of 0.05, we reject the null hypothesis (Panel 2). The proportion of HCV infected in HIV positive Partners detected in the study sample was 33% (CI 22%, 46%).

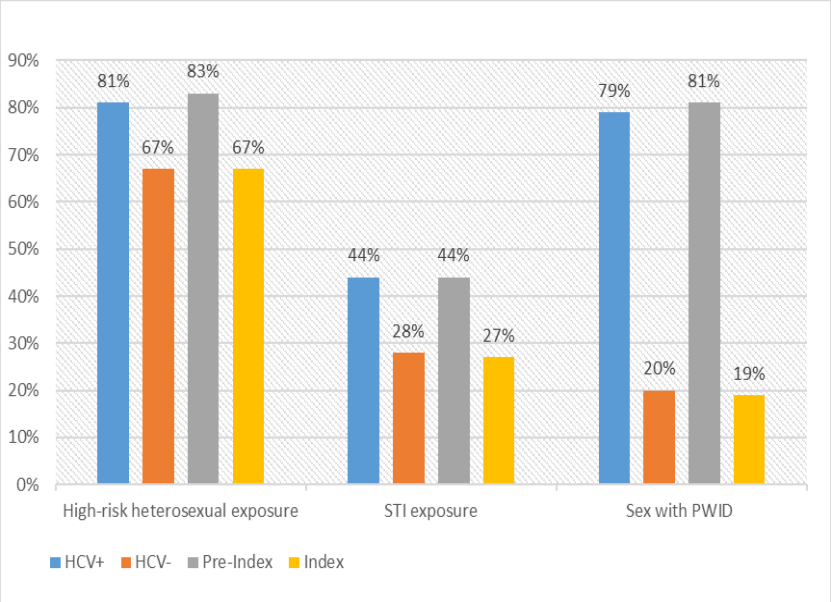
Panel 2. Hypothesis 1 testing results.

Observed HCV proportion	95% CI LL	95% CI UL	Null hypothesis	p-value for difference
33%	22%	46%	50%	0.009

Hypothesis 2. *HCV positive AGYW are more likely to report IDU, and Pre-Indexes have riskier sexual practices than Indexes.*

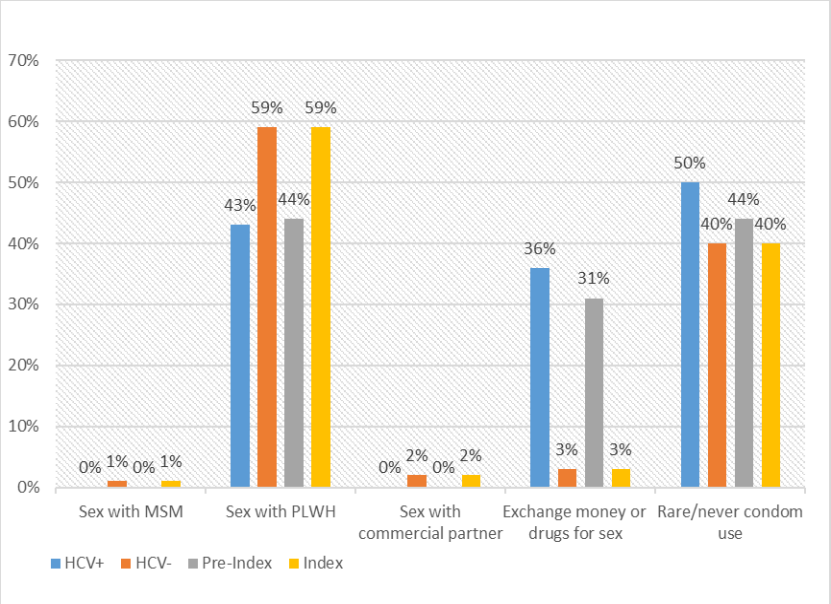
At the alpha level of 0.05, we accept the null hypothesis (Table 3) as we have sufficient evidence to conclude that HCV positive AGYW are more likely to report IDU. The proportion of AGYW with IDU exposure was significantly higher in HCV positive respondents compared to HCV negative respondents (HCV+ 50% vs HCV- 1%, p<.0001). High-risk heterosexual exposure was equally distributed across HCV status (HCV+ 81% vs HCV- 67%, p=.25) and among Pre-Indexes and Indexes (Pre-Indexes 83% vs Indexes 67% p=.17) (Figure 11). Similarly, STI exposure did not differ significantly between HCV positive and negative AGYW (HCV+ 44% vs HCV- 28%, p=.165) and among Pre-Indexes and Indexes (Pre-Indexes 44% vs Indexes 27% p=.17). Therefore, we do not have enough evidence to conclude that sexual practices are riskier in Pre-Indexes compared to Indexes.

Figure 11. High-risk sexual exposers by HCV status and Index status (part 1).



However, the sex with PWID was more common in HCV+ (HCV+ 79% vs HCV- 20%, p<.0001) and among Pre-Indexes (Pre-Indexes 81% vs Indexes 19%, p<.0001). Proportions of those who had sex with MSM and had sex with PLWH did not differ significantly across HCV status and between Pre-Indexes and Indexes (Figure 12). Similarly, we did not observe difference across the comparison groups in condom use and sex with commercial partner. Nevertheless, exchange money or drugs for sex was reported more frequently in HCV+ AGYW (HCV+ 36% vs HCV- 3%, p<.0001) and among Pre-Indexes (Pre-Indexes 31% vs Indexes 3%, p<.0001).

Figure 12. High-risk sexual exposers by HCV status and Index status (part 2).

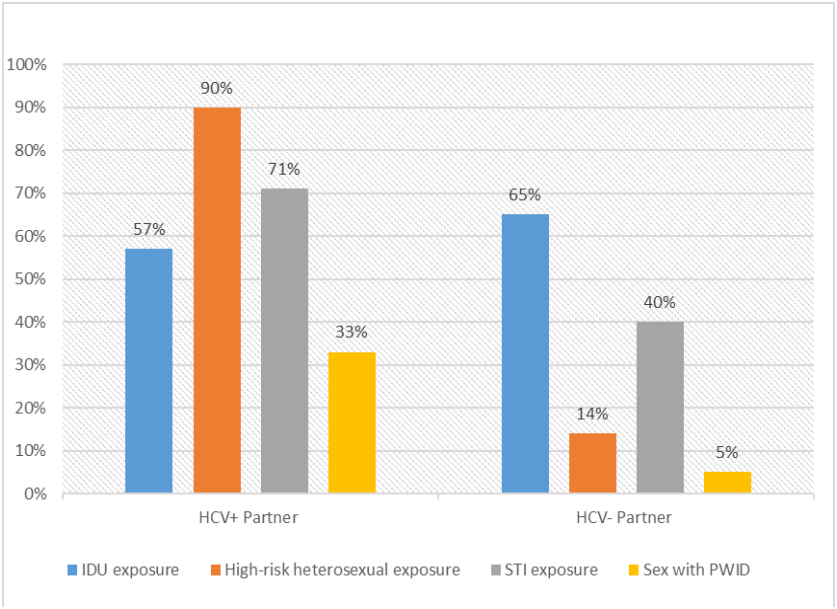


Hypothesis 3. *Partners with HCV are more likely to report IDU and risky sexual practices than Partners without HCV.*

The IDU exposure was not different between HCV+ and HCV- Partners (57% vs 65%, p=.53) (Table 4)(Figure 13). Therefore, at the significance level of 0.05, we do not have enough evidence to accept the null hypothesis. However, high-risk heterosexual exposure was

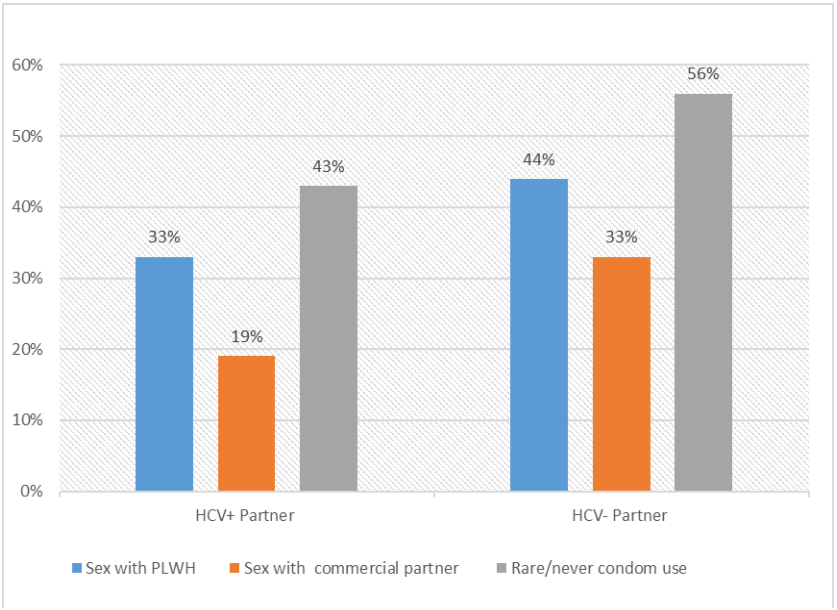
significantly higher in HCV positive Partners versus HCV- (90% vs 14%, p<.0001). Similarly, STI exposure (71% vs 40%, p=.017) and sex with PWID (33% vs 5% p=.0004) were substantially higher in HCV+ Partners.

Figure 13. HIV exposures by HCV status in Partners (part 1)



HCV negative Partners were prone to more often have sex with PLWH and have sex with commercial partner but the difference did not rich the level of statistical significance (33% vs 44%, p=.4 and 19% vs 33%, p=0.26 respectively)(Figure 14). Interestingly, using condoms always or frequently was numerically more prevalent in HCV+ Partners (38% vs 14%, p=.087).

Figure 14. HIV exposures by HCV status in Partners (part 2)



Hypothesis 4. *At least 30% of the AGYW sample enrolled are misclassified heterosexual HIV cases as have HCV positive test result and reported injection drug use.*

At the alpha level of 0.05, we reject the null hypothesis (Panel 3). The proportion of the AGYW sample who were enrolled in the study and misclassified heterosexual HIV cases as they had HCV positive test result or reported injection drug use is less 30%. The hypothesis testing revealed that the proportion of the misclassified cases is 3% (CI 1%, 5%, p<.0001).

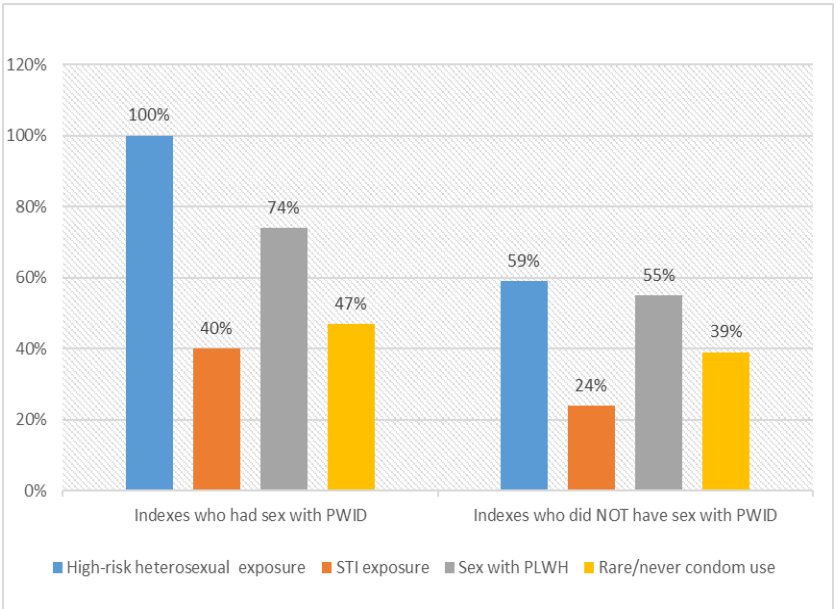
Panel 3. Hypothesis 4 testing results.

Observed HCV proportion	95% CI LL	95% CI UL	Null hypothesis	p-value for difference
3%	1%	5%	30%	0.000

Hypothesis 5. *Indexes reporting having IDU partner are more likely to report risky sexual practices.*

Indexes reporting having IDU partner (IP) had significantly higher frequency of high-risk heterosexual exposure than Indexes reporting having non-IDU partner (NIP) (100% vs 59%, p<.0001) (Table 5)(Figure 15). Hence, at the significance level of 0.05, we have sufficient evidence to accept the null hypothesis. In addition, IP were more likely to have STI exposure and sex with PLWH compared to NIP (40% vs 24%, p=.011 and 74% vs 55%, p=.005 respectively). Sex with MSM, sex with commercial partner and exchange money or drugs for sex were rare in both IP and NIP and did not differ significantly between these two groups (2% vs 1%, p= .476 and 2% vs 2%, p=1 and 3 vs 3%, p=1 respectively). Rare/never condom use was more likely to be reported by IP but did not differ significantly compared to NIP (47% vs 39%, p=.249).

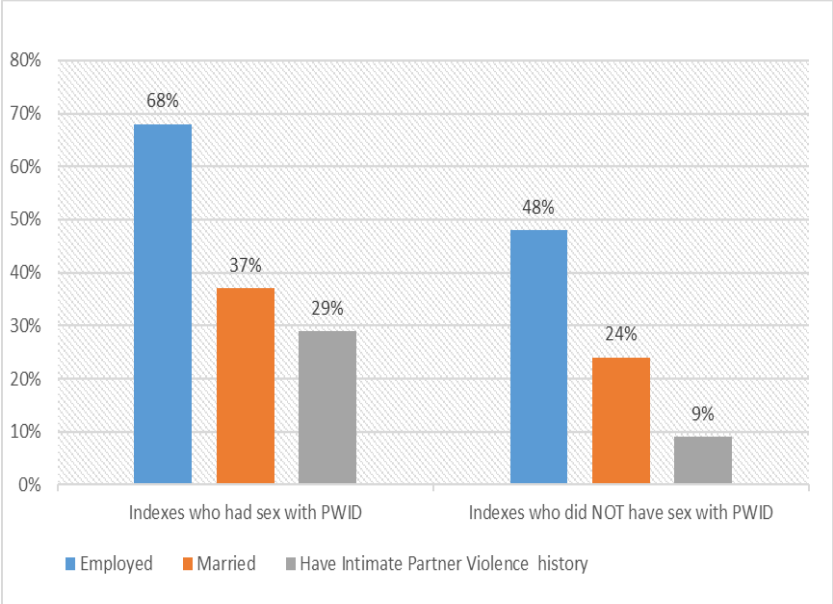
Figure 15. HIV exposures by having PWID sex partner in Indexes.



Hypothesis 6. *Indexes reporting having IDU partner are more likely to report lower socioeconomic status.*

IP were less likely to have college or university education compared to NIP (11% vs 16%, p=.035)(Table 5). However, IP were more likely to be employed (68% vs 48%, p=.044) (Figure 16) and the proportions of unemployed and students were higher in NIP (16% vs 23% and 11% vs 20% respectively). Among IP were more respondents who reported being married at the time of HIV diagnosis (37% vs 24%, p=.041). Finally, the level of the self-reported intimate partner violence (IPV) was significantly higher in IP compared to NIP (29% vs 9%, p<.0001).

Figure 16. Sociodemographic characteristics and IPV by having PWID sex partner in Indexes.



Conclusion

In this study, we enrolled and assessed AGYW registered at HIV clinics in 2016-2019 in nine regions of Ukraine. At enrollment AGYW were disaggregated into Indexes and Pre-Indexes based on the current HCV status, injection drug use history and history of having sexual relationships before their HIV diagnosis. Indexes – AGYW with HCV negative test results, without the history of the injection drug use and reporting having sexual relationships before HIV diagnosis – were requested to identify and refer to the study their sexual partners who most probably infected them with HIV. Pre-Indexes – having HCV positive status or reporting IDU or having no sexual relationships prior to HIV diagnosis – were not required to refer their sexual partners but served as a comparison group for study hypotheses testing. Therefore, in this study Pre-Indexes were defined as ***misclassified*** new HIV cases with heterosexual mode of HIV transmission.

We enrolled and assessed HIV positive sexual Partners of the Indexes to find out if IDU is present among Partners population and weather the IDU in Partners is associated with HIV risky behavior in Partners and Indexes. We found that almost quarter of enrolled HIV positive Partners were not registered in HIV clinic and a third of all Partners were infected with HCV, which is indicative of the injection drug use.

53% of Partners were registered with heterosexual mode of transmission and 24% were registered as IDU. *However, almost 40% reported IDU at the time prior to Index HIV diagnosis, which may suggest about substantial level of heterosexual HIV transmission mode*

misclassification in Partners. During the study survey 29% of Partners reported IDU as their mode of HIV infection and 6% reported heterosexual transmission from female PWID sexual partners. In addition, 22% of partners reported problematic alcohol use and 29% reported consuming alcohol and drugs before sex before HIV diagnosis in Index. More than a half of Partners (51%) during the same period never or rarely used condoms. 62% of Partners had high-risk heterosexual exposure and 49% - STI exposure. Nosocomial exposure was reported by 45% of Partners and 35% of all Partners had accidental exposure. Surprisingly, the IDU was not associated with HCV status in the sample of Partners, which can be the result of the unwillingness of the respondents to disclose their IDU status during the survey. Therefore, over again, the prevalence of IDU in Partners may be higher than that we detected in our study. High-risk heterosexual exposure was associated with HCV positive status in Partners. Similarly, STI exposure and sex with PWID were substantially higher in HCV+ Partners.

The rate of *heterosexual HIV cases* misclassification (proportion of Pre-Indexes) in the studied group of AGYW (3%) was lower than in study conducted by Dumchev at al. (2017). That study reviled that up to 35% of cases of men who reported as heterosexual could have been engaged in injecting drug use[13] which is consistent with our results on the history of IDU in Partners – 40% reported injecting drugs before Index HIV diagnosis.

HCV positive AGYW were much more likely to report IDU compared to HCV negative AGYW. In general, high-risk heterosexual exposure before HIV diagnosis was higher in Pre-Indexes. Similarly, STI exposure as well as nosocomial and accidental exposures were more frequently reported by Pre-Indexes compared to Indexes. In addition, the sex with PWID and exchange money or drugs for sex were also significantly associated with the status of misclassified heterosexual HIV case.

In conclusion, our analysis revealed that 20% of newly registered confirmed heterosexual HIV cases among AGYW have IDU sexual partners. Indexes reporting having IDU sex Partner had significantly higher frequency of high-risk heterosexual exposure than Indexes reporting having no IDU partner. Having IDU sex partner was associated with higher probability of STI exposure and being more likely to have sex with PLWH. 13% out of all Indexes reported IPV history and those having IDU partner were three times more likely to report IPV than Indexes having no IDU sexual partner.

Recommendations

Based on the study results it is recommended to increase and maintain the coverage of index testing with the specific focus on AGYW and HIV key populations. All Partners should be screened for HCV and IDU with the subsequent referral to HIV/HCV/STI prevention and treatment services as well as drug treatment programs. As many of male and female Partners of Indexes may be active PWID the index testing services should be integrated with the programs linking to and retaining PWID in HIV care (case-management, peer-navigation models), substance use treatment programs (medication assisted treatment for opioid users) and harm reduction services (syringes/needles exchange and condoms distribution).

Our findings also suggest that Indexes and Partners should have the access to counselling and psychosocial support as a part of index testing program to reduce HIV risky behaviors, IPV and prevent further HIV transmission. Both HIV positive and negative Partners and Indexes having IDU partners should have access to and be actively involved into harm reduction services and counseling. Special attention should be payed to developing and implementing prevention

models of heterosexual way of HIV transmission in HIV key populations and their IDU and non-IDU sexual partners.

Prospective sexual and IDU network-based studies involving PLWH and their HIV positive and HIV negative partners are needed to better understand the role of IDU in HIV bridging into general population as well as the influence of sexual and IDU networks on the effectiveness of HIV prevention programs and HIV treatment cascade.

Tables

Table 1. Socio-demographic characteristics, HIV risk factors and mode of transmission among Indexes and Pre-Indexes

		Total		Pre-Indexes		Indexes	
		Count	Column N %	Count	Column N %	Count	Column N %
Total		339	100%	18	100%	321	100%
Age group	<20	32	9%	1	6%	31	10%
	21-26	179	53%	10	56%	169	53%
	26+	128	38%	7	39%	121	38%
Education	School	194	57%	14	78%	180	56%
	Technical	95	28%	3	17%	92	29%
	College or university	50	15%	1	6%	49	15%
Employment	Employed	170	50%	4	22%	166	52%
	Unemployed	79	23%	10	56%	69	21%
	Student	62	18%	2	11%	60	19%
	Other	28	8%	2	11%	26	8%
Family status	Single/separated	251	74%	16	89%	235	73%
	Married	88	26%	2	11%	86	27%
Time in HIV care	<1 years	30	9%	2	11%	28	9%
	1-2 years	80	24%	4	22%	76	24%
	2-3 years	94	28%	2	11%	92	29%
	3+ years	135	40%	10	56%	125	39%
Year of registration	2016	72	21%	6	33%	66	21%
	2017	89	26%	4	22%	85	26%
	2018	90	27%	5	28%	85	26%
	2019	88	26%	3	17%	85	26%
Intimate partner violence history	no					272	87%
	yes					41	13%
HCV test result	no	323	95%	2	11%	321	100%
	yes	16	5%	16	89%	0	0%
IDU exposure	no	329	97%	8	44%	321	100%
	yes	10	3%	10	56%	0	0%
Heterosexual exposure	no	2	1%	2	11%	0	0%
	yes	337	99%	16	89%	321	100%
High-risk heterosexual exposure	no	108	32%	3	17%	105	33%
	yes	231	68%	15	83%	216	67%
STI exposure	no	243	72%	10	56%	233	73%
	yes	96	28%	8	44%	88	27%
Nosocomial exposure	no	195	58%	7	39%	188	59%
	yes	144	42%	11	61%	133	41%
Accidental exposure	no	255	75%	6	33%	249	78%
	yes	84	25%	12	67%	72	22%

Table 2. Socio-demographic characteristics, HIV risk factors and survey-based mode of transmission in Partners

		Count	Column N %
Total		65	100%
Age group	<29	30	46%
	30-34	23	35%
	35+	12	18%
Education	School	24	37%
	Technical	28	43%
	College or university	13	20%
Employment	Employed	56	86%
	Unemployed	6	9%
	Other	3	5%
Family status	Single/separated	51	78%
	Married	14	22%
Alcohol problematic use	Not problematic	51	78%
	Problematic	14	22%
Alcohol or drug use before sex	Always/frequent	46	71%
	Rare/never	19	29%
Condom use	Always/frequent	14	22%
	50/50	18	28%
	Rare/never	33	51%
Time in HIV care	0-2 years	14	27%
	2-3 years	11	22%
	3+ years	26	51%
HCV test result	no	43	67%
	yes	21	33%
IDU exposure	no	40	62%
	yes	25	38%
MSM exposure	no	63	97%
	yes	2	3%
High risk heterosexual exposure	no	25	38%
	yes	40	62%
STI exposure	no	33	51%
	yes	32	49%
Nosocomial exposure	no	36	55%
	yes	29	45%
Accidental exposure	no	42	65%
	yes	23	35%
Registered Mode of HIV transmission	Heterosexual	35	53%
	Injection drug use	16	24%
	Not registered in care	15	23%
Survey-based mode of transmission	Heterosexual (IDU sexual partner)	4	6%
	Heterosexual (non- IDU sexual partner)	37	57%
	Injection drug use	19	29%
	MSM	2	3%
	Other	3	5%

Table 3. Hypothesis 2: HCV positive AGYW are more likely to report IDU, and Pre-Indexes have riskier sexual practices than Indexes.

		HCV test result					Pre-index				
		negative		positive			no		yes		
		Count	Column N %	Count	Column N %	p-value	Count	Column N %	Count	Column N %	p-value
IDU exposure	no	321	99%	8	50%	0.000					
	yes	2	1%	8	50%						
High risk heterosexual exposure	no	105	33%	3	19%	0.249	105	33%	3	17%	0.155
	yes	218	67%	13	81%		216	67%	15	83%	
STI exposure	no	234	72%	9	56%	0.165	233	73%	10	56%	0.175
	yes	89	28%	7	44%		88	27%	8	44%	
Sex with PWID	no	259	80%	3	21%	0.000	259	81%	3	19%	0.000
	yes	64	20%	11	79%		62	19%	13	81%	
Sex with MSM	no	320	99%	14	100%	1.000	318	99%	16	100%	1.000
	yes	3	1%	0	0%		3	1%	0	0%	
Sex with PLWH	no	134	41%	8	57%	0.245	133	41%	9	56%	0.241
	yes	189	59%	6	43%		188	59%	7	44%	
Sex with commercial partner	no	316	98%	14	100%	1.000	314	98%	16	100%	1.000
	yes	7	2%	0	0%		7	2%	0	0%	
Exchange money or drugs for sex	no	313	97%	9	64%	0.000	311	97%	11	69%	0.000
	yes	10	3%	5	36%		10	3%	5	31%	
Condom use	Always/frequent	85	26%	2	14%	.581	83	26%	4	25%	0.966
	50/50	108	33%	5	36%		108	34%	5	31%	
	Rare/never	130	40%	7	50%		130	40%	7	44%	

Table 4. Hypothesis 3. Partners with HCV are more likely to report IDU, risky sexual practices than Partners without HCV.

		HCV Result negative		positive		p-value
		Count	Column N %	Count	Column N %	
IDU exposure	no	15	35%	9	43%	0.536
	yes	28	65%	12	57%	
High-risk heterosexual exposure	no	37	86%	2	10%	.000
	yes	6	14%	19	90%	
STI exposure	no	26	60%	6	29%	.017
	yes	17	40%	15	71%	
Sex with PWID	no	41	95%	14	67%	0.004
	yes	2	5%	7	33%	
Sex with PLWH	no	24	56%	14	67%	0.407
	yes	19	44%	7	33%	
Sex with commercial partner	no	29	67%	17	81%	0.259
	yes	14	33%	4	19%	
Exchange money or drugs for sex	no	43	100%	21	100%	0.000
	yes	0	0%	0	0%	
Condom use	Always/frequent	6	14%	8	38%	0.087
	50/50	13	30%	4	19%	
	Rare/never	24	56%	9	43%	

Table 5. Hypothesis 5. Indexes reporting having IDU partner are more likely to report risky sexual practices. Hypothesis 6. Indexes reporting having IDU partner are more likely to report lower socioeconomic status.

		Did you have sex with a man who injected drugs?				
		no		yes		p-value
		Count	Column N %	Count	Column N %	
Total (Indexes)		259	100%	62	100%	
High-risk heterosexual	no	105	41%	0	0%	.000
exposure	yes	154	59%	62	100%	
STI exposure	no	196	76%	37	60%	.011
	yes	63	24%	25	40%	
Sex with MSM	no	257	99%	61	98%	0.476
	yes	2	1%	1	2%	
Sex with PLWH	no	117	45%	16	26%	.005
	yes	142	55%	46	74%	
Sex with commercial partner	no	253	98%	61	98%	1.000
	yes	6	2%	1	2%	
Exchange money or drugs for sex	no	251	97%	60	97%	1.000
	yes	8	3%	2	3%	
Condom use	Always/frequent	72	28%	11	18%	0.249
	50/50	86	33%	22	35%	
	Rare/never	101	39%	29	47%	
Education	School	151	58%	29	47%	.035
	Technical	66	25%	26	42%	
	College or university	42	16%	7	11%	
Employment	Employed	124	48%	42	68%	.044
	Unemployed	59	23%	10	16%	
	Student	53	20%	7	11%	
	Other	23	9%	3	5%	
Family status	Single/separated	196	76%	39	63%	.041
	Married	63	24%	23	37%	
Intimate partner violence	no	228	91%	44	71%	.000
history	yes	23	9%	18	29%	

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