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Is cannabis use associated with HIV drug and sex risk behaviors among Russian HIV-infected risky drinkers?

Arina Tyurina¹, Evgeny Krupitsky^{1,7}, Debbie M. Cheng^{2,3,1}, Sharon M. Coleman⁴, Alexander Y. Walley², Carly Briden², Natalia Gnatienco², Edwin Zvartau¹, Anita Raj⁵, and Jeffrey H. Samet^{2,6,*}

¹Laboratory of Clinical Pharmacology of Addictions, St. Petersburg Pavlov State Medical University, Lev Tolstoy St. 6/8, St. Petersburg 197022, Russia

²Department of Medicine, Section of General Internal Medicine, Clinical Addiction Research and Education (CARE) Unit, Boston University School of Medicine/Boston Medical Center, 801 Massachusetts Avenue, 2nd Floor, Boston, MA 02118-2605, USA

³Department of Biostatistics, Boston University School of Public Health, 801 Massachusetts Avenue, 3rd Floor, Boston, MA 02118-2605, USA

⁴Data Coordinating Center, Boston University School of Public Health, 801 Massachusetts Avenue, 3rd Floor, Boston, MA 02118-2605, USA

⁵Division of Global Public Health, Department of Medicine, University of California at San Diego, IOA Building, 10111 N. Torrey Pines Rd., San Diego, CA 92137, USA

⁶Department of Community Health Sciences, Boston University School of Public Health, 801 Massachusetts Avenue, 2nd Floor, Boston, MA 02118-2605, USA

⁷Department of Addictions, Bekhterev Research Psychoneurological Institute, Bekhtereva St., 3, St. Petersburg 192019, Russia

Abstract

Background—While cannabis use has been associated with increased HIV drug and sex risk behaviors, its impact on risk behaviors among HIV-infected individuals has not yet been established.

Methods—This study examined data from Russian HIV-infected risky drinkers enrolled in a randomized controlled trial of a behavioral intervention. The primary independent variable was cannabis use (current [past 30 days use], recent past [use but not in past 30 days] vs. no past year use). Primary outcomes were needle sharing and number of unprotected sexual episodes. Secondary outcomes were drug injection, number of injections, and multiple sex partners. Longitudinal regression analyses controlled for age, gender, marital status, education, CD4 count, ART use, risky alcohol use, other drug use, depressive symptoms and randomization group.

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*Corresponding Author: Phone: 617-414-7288, Fax: 617-414-4676, jsamet@bu.edu.

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Results—Cannabis use was common with 20% current and 26% recent past use at baseline. In longitudinal analyses current, but not recent past, cannabis consumption was significantly associated with needle sharing (AOR 2.23 current vs. none, 95% CI: 1.46, 3.36), drug injection (AOR 3.05 current vs. none, 95% CI: 2.06, 4.53) and number of injections (adjusted IRR 1.50 current vs. none, 95% CI: 1.19, 1.89). Current and recent past cannabis use were significantly associated with multiple sex partners but not with number of unprotected sex episodes.

Conclusion—Cannabis use was associated with drug and sex risk behaviors among Russian HIV-infected risky drinkers. Inquiry about cannabis use among HIV-infected patients may reveal a patient group at higher risk for sex and drug use behaviors that lead to HIV transmission.

Keywords

Cannabis use; HIV; sex risk behavior; drug risk behavior; Russia

1. Introduction

Cannabis is the most frequently used illicit drug in the world according to the United Nations Office on Drugs and Crime (United Nations Office on Drugs and Crime, 2010). Unfortunately, no national statistics on cannabis use in Russia exist, but based on regional reports, it may be the most used illicit drug in this country as well, with its use increasing (United Nations Office on Drugs and Crime, 2007). Despite the high prevalence of cannabis use, published reports about its association with HIV risk behaviors are few and none focus on an HIV-infected cohort.

Cannabis usage is related to the use of other drugs and often precedes injection drug use, such as cocaine and heroin (Lynskey et al., 2003; Fergusson et al., 2006). A previous study by this Russian-US research team examined Russian injecting drug users (IDUs) and found that cannabis use was associated with risky drug use (i.e., higher mean drug Risk Assessment Battery [RAB] score; Walley et al., 2008). Only a minority of these individuals were HIV-infected.

Prior research has examined the association between cannabis use and sex risk behavior, again without a focus on HIV-infected populations. Studies conducted among adolescents in detention (Kingree et al., 2000; Kingree and Phan, 2001; Kingree and Betz, 2003), street youths (Bailey et al., 1998), and men who have sex with men (MSM; Bailey et al., 1998; Clutterbuck et al., 2001) found that cannabis use was associated with less condom use. However, among young heterosexual adults (Brodbeck et al., 2006) and adults in a substance use jail diversion program (Leigh et al., 2008), cannabis use was not associated with condom use. Another study found that among a representative sample of the Spanish population, cannabis use was associated with having multiple sexual partners but not associated with failure to use condoms (Castilla et al., 1999). Liao et al. found that adolescents who had positive toxicology tests for cannabis were more likely to test positive for gonorrhea and chlamydia (Liao et al., 2002). The limitation of most of these studies was the failure to classify timing of cannabis use resulting in the inability to detect a relationship between recent cannabis consumption and sexual risk and sexually transmitted infections.

Russia's spread of HIV infection over the past dozen years has been rapid, with an estimated one million infected (UNAIDS, 2010), and HIV risk behaviors are common. Although the Russian HIV epidemic has been propelled primarily by injection drug use, transmission via unprotected sexual contact has been increasing (Burchell et al., 2008; Goliusov et al., 2010). In 2007, sexual intercourse accounted for 34% of new infections compared to 18% in 2002 (Goliusov et al., 2008). Data show that condom use at last sex episode was reported by just 37% of Russian IDUs, a low proportion similar to that seen in other countries in Eastern

Europe and Asia (Mathers et al., 2009). Hence, Russia is an appropriate country to pursue this study's objective: to assess the longitudinal association between cannabis use and HIV drug and sex risk behaviors in a cohort of HIV-infected persons reporting risky drinking and unprotected sex. This study will test the hypothesis that HIV-infected Russian risky drinkers who use cannabis are more likely to engage in drug and sex risk behaviors.

2. Methods

2.1 Participants

We analyzed data from a cohort of 700 HIV-infected participants in the *HIV's Evolution in Russia - Mitigating Infection Transmission and Alcoholism in a Growing Epidemic (HERMITAGE)* randomized controlled trial conducted between 2007 and 2011 in St. Petersburg, Russian Federation (Lunze et al., 2012). The main eligibility criteria included the following: HIV-infection; 18-70 years old; any risky drinking by National Institute on Alcohol Abuse and Alcoholism (NIAAA) criteria in the past 6 months (National Institute on Alcohol Abuse and Alcoholism, 2007) and unprotected vaginal or anal sex in the past 6 months. Institutional Review Boards of Boston Medical Center and St. Petersburg Pavlov State Medical University approved this study.

2.2 Assessment

All participants were assessed at baseline (n= 700), at 6 month follow-up (n= 523; 75%) and at 12 month follow-up (n= 492; 70%) by assessors blinded to the individual's randomization status. Assessments were administered by a trained research associate (RA) in a face-to-face interview. Participants were asked to answer a variety of questions related to sex and drug risk behaviors. This study analyzed data obtained from the following instruments: Composite International Diagnostic Interview Short-Form (CIDI-SF; Robins et al., 1988), Risk Behavior Survey (Weatherby et al., 1994; Needle et al., 1995), sex risk questions used in Kalichman's original Healthy Relationship Interventions (HRI) study (Kalichman et al., 2001) and modified Addiction Severity Index (ASI; McLellan et al., 1985). Additional information was obtained from medical record review (e.g., current ART treatment, CD4 cell count). All instruments used were translated into Russian using protocols based on the six-step process of the WHO Gender, Alcohol and Culture: An International Study (GENACIS; Obot and Room, 2005) which includes translation as well as pre-testing in the desired, culturally relevant population.

2.3 Independent Variable

2.3.1 Cannabis Use—The CIDI-SF 12 month survey (Robins et al., 1988) asked patients about their cannabis use during the past 12 months. Cannabis use in the last 30 days and past 6 months was assessed using the RBS, which we modified for the Russian setting by asking about drugs commonly used in Russia (Weatherby et al., 1994; Needle et al., 1995). For the purpose of the analysis, participants were grouped into three categories at each time point (baseline, 6, and 12 months): current cannabis user (any cannabis use in the past 30 days), recent past cannabis user (no cannabis use in the past 30 days but cannabis use in the past year reported at baseline; for the 6 and 12 month time points the timeframe was past 6 months), and cannabis non-user (no cannabis use reported in the past year for baseline; again for the 6 and 12 month time points the timeframe was past 6 months). Cannabis use was modeled as a time-dependent variable (i.e., the value was updated at each follow-up time). In order to determine if frequency of cannabis use during the preceding 30 days is associated with risk behaviors, participants were grouped into four categories: no use in past 30 days; low use (1-2 times in past 30 days); moderate use (3-5 times in past 30 days) and high level of use (6-30 times in past 30 days). The latter three categories were defined based on tertiles of the distribution.

2.4 Outcomes

2.4.1 Drug risk behavior—The primary drug risk behavior outcome was any “needle sharing” modeled as a dichotomous variable. Needle sharing at least once in the past 30 days could be either receptive (“using a needle/syringe that you know had been used by somebody else”) or distributive (“let someone else use your syringe/needle after you used it”). These data were obtained using the RBS (Weatherby et al., 1994; Needle et al., 1995), which we modified to ask specifically about receptive and distributive needle sharing. As secondary outcome variables, we examined past 30 days “injected drugs” as a dichotomous variable and “number of times injected drugs” as a continuous variable. All outcomes were assessed at baseline, six months and twelve months.

2.4.2 Sex risk behavior—All HERMITAGE cohort participants were asked questions about sex practices in the past 3 months using a set of questions developed by Kalichman et al. (2001). Participants provided detailed information about the 5 most recent partners, identified as a “main/regular” partner or an “other” partner. Participants were asked about total number of partners, sex episodes and condom use. The primary sex risk behavior outcome was the number of unprotected sexual contacts in the past 3 months and the secondary outcome was having multiple sex partners (≥ 2 vs. <2 partners) in the past 3 months. All outcomes were assessed at each of the 3 study time points.

2.5 Covariates

The following covariates were included in the regression analyses to control for potential confounding: sociodemographic characteristics (age, gender, marital status [married or living with partner vs. other] and education [$<$ high school graduation]), CD4 count ≥ 350 , current antiretroviral therapy (ART) use, depressive symptoms in the past 2 weeks in quartiles via the Beck Depression Inventory-II (Beck), risky alcohol use assessed via 30-day Timeline Follow-back (TLFB; Sobell and Sobell, 1992, 1995), and randomization group. In addition, use of other drugs besides cannabis in the past 30 days was assessed using the modified RBS. Analyses for sex risk outcomes were controlled for use of all other drugs except cannabis. Sex trade was included as an additional confounder in sex risk outcome analyses. Questions about sex trade were taken from the HIV Risk Assessment Battery (RAB; Navaline et al., 1994; Metzger et al., 2001).

2.6 Data Analysis

For this study we analyzed 1,715 observations obtained from 700 subjects. Descriptive statistics were calculated to characterize baseline variables overall and stratified by the main independent variable, cannabis use. Prior to regression modeling, potential collinearity among covariates was assessed by calculating the correlation between variables, and no pair of variables had a Spearman correlation >0.40 . GEE overdispersed Poisson regression models were used to analyze count outcomes (number of injections, number of unprotected sex episodes) and GEE logistic regression models were used for binary outcomes (e.g., any needle sharing). We used an independence working correlation structure and reported results using empirical standard errors. The regression models controlled for all covariates described above. Risky alcohol use, use of other drugs besides cannabis, and depressive symptoms were incorporated into the regression models as time-varying covariates. Due to a large number of missing values for CD4 count (approximately 30% of the sample), an additional category was created to include those with a missing value. For the sex risk outcomes, confirmatory analyses were conducted including sex trade (buying or selling sex for drugs or money) as an additional covariate. Exploratory analyses were also performed to assess gender as a potential effect modifier. All analyses were conducted using two-sided tests and a significance level of 0.05. Pairwise comparisons were not made unless the global

p-value for cannabis use was statistically significant. The statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc., NC, USA).

3. Results

3.1 Baseline Characteristics and Follow-up Cannabis use

Cannabis use in this group of HIV-infected Russians was common, occurring at baseline as follows: current (past month) 20% (n=143); recent past (not past month but in past year) 26% (n=183); and no past year use 54% (n=374). Baseline socio-demographic, health and behavioral characteristics of the study cohort are described in Table 1. Participants were 59% male with a median age of 29 years. Most participants (81%) reported past month risky alcohol use, completed more than 9 grades of education (78%) and were not married (64%). Cannabis use was less common in women compared to men (28% vs. 72%). Risky behaviors in the past 30 days included the following: injecting drugs 42% (n=294); needle sharing 23% (n=164); and past 3 month multiple sexual partners 27% (n=189). Cannabis use was also common at the two follow-up assessments: current 12% and 11% (n=61 and 56); recent past 9% and 9% (n=49 and 44); and no past year use 79% and 80% (n=413 and 392) at 6 and 12-months, respectively. Differences existed between participants who did and did not complete all study visits. Those with depressive symptoms and with risky drinking at baseline were less likely to complete all study visits; participants with a CD4 count greater than 200 and on ART were more likely to complete all follow-up assessments.

3.2 Drug risk behavior outcomes

Current cannabis use was significantly associated with the primary outcome, needle sharing, (adjusted odds ratio [AOR] 2.23 current vs. none, 95% C.I: 1.46, 3.36; $p<0.001$), and the secondary outcomes, past month injection drug use (AOR 3.05 current vs. none, 95% C.I: 2.06, 4.53; $p<0.001$), and number of injections (adjusted incidence rate ratio [AdjIRR] 1.50 current vs. none, 95% C.I: 1.19, 1.89; $p<0.001$; Table 2). However, no statistically significant associations were found between recent past cannabis use (no past month use but use in past 6 or 12 months) and drug risk behaviors. Additional analyses found statistically significant associations between frequency of cannabis use in the past month and needle sharing and frequency of cannabis use and injection drug use, as noted in Table 3.

3.3 Sex risk behavior outcomes

Cannabis use was not found to be significantly associated with the primary sex risk outcome, the number of unprotected sex episodes (adjusted IRR 1.22 current vs. none, 95% C.I: 0.85, 1.74; IRR 0.93 recent past vs. none, 95% C.I: 0.69, 1.26; global $p=0.48$; Table 4). However, cannabis use was significantly associated with the secondary sex risk outcome, multiple sex partners, (AOR 1.68 current vs. none, 95%CI: 1.15, 2.46, $p=0.01$; AOR 1.54 recent past vs. none, 95%CI: 1.11, 2.15, $p=0.01$; Table 4). In confirmatory analyses including sex trade as an additional covariate, we observed similar results for number of unprotected sex episodes (IRR 1.20 current vs. none, 95% C.I: 0.84, 1.72; IRR 0.92 recent past vs. none, 95% C.I: 0.68, 1.24, global $p=0.48$) and multiple sex partners (AOR 1.59 current vs. none, 95%CI: 1.07, 2.36, $p=0.02$; AOR 1.45 recent past vs. none, 95%CI: 1.01, 2.08, $p=0.046$). In exploratory analyses assessing gender as a potential effect modifier, a significant interaction between cannabis use and gender was not found for any of the outcomes. No statistically significant associations were detected between frequency of cannabis use in the past month and sex risk behavior; however, a clinically important association was observed between high frequency of cannabis use and number of unprotected sex episodes (Table 3).

4. Discussion

This study addresses the relationship between cannabis use and HIV risk behaviors in an HIV-infected cohort, a relationship previously examined only in mostly non-HIV-infected populations. In Russia, we found cannabis use to be common, with almost half of our sample reporting such use in the past year, and associated with most but not all drug and sex risk behaviors.

Previous researchers have examined the impact of cannabis use on HIV risk behaviors among non-HIV-infected individuals and found positive associations but some findings have been inconsistent. It is possible that the inconsistencies relate to the methodology employed. For example, researchers did not consider different time frames of past cannabis use (e.g., current vs. recent past use; Budney et al., 1998; Walley et al., 2008). Budney et al. (1998) found that current cannabis use is significantly associated with needle sharing and drug dealing. A limitation of this study was the authors' categorization of cannabis users as current and non-users, without noting the recency of the use. In the current study, HIV-infected Russian "recent past" users do not behave exactly like current or non-users and hence timing of use merits closer examination. Another study classified non-HIV-infected individuals as regular and non-regular cannabis users and examined syringe sharing (Jutras-Aswad et al., 2010). This study revealed that on the day when participants used cannabis, non-regular cannabis users were five times more likely to share syringes than regular cannabis users. This finding suggests differing behaviors among intermittent and regular users. In the present study, we examined the difference between three categories of cannabis users (current cannabis use, recent past use and none), a novel approach that yielded distinct findings among the groups, providing additional data about the use of cannabis and its association with HIV risk behaviors. Also similar to past research in non-HIV-infected IDUs, we found that the frequency of use was associated with drug risks in this population (Valdez et al., 2008; Jutras-Aswad et al., 2010).

Findings regarding the associations between cannabis use and risky sexual behavior were less consistent; we did not find an association of cannabis with number of unprotected sex episodes, but did find a positive association with having multiple sexual partners. Lack of association between cannabis use and unprotected sex has been observed in other studies among substance using populations without specified HIV status (Leigh et al., 2008), though studies inclusive of non-substance users indicate such associations (Simons et al., 2010; Dirks et al., 2012). It may be that in the context of other substance use, cannabis does not elevate the risk for an increased number of unprotected sex episodes. However, whether such findings in non-HIV-infected individuals would be applicable in HIV-infected is not known, as awareness of one's positive HIV infection status among IDUs was associated with using condoms more frequently than those who are not HIV-infected or unaware of their status (Ruiz et al., 1996; Bravo et al., 1999). Thus, it is important to consider the association of cannabis use and sex risk behavior specifically among HIV-infected persons. In fact, we conjecture that the absence of an association between cannabis use and unprotected sex episodes may be related to this cohort being composed entirely of HIV-infected individuals, given the protective effects of knowing one's HIV status. Nonetheless, this lack of findings is notable given that cannabis did increase risk for having more sex partners, a finding observed in other research studies, as well (Bellis et al., 2008; Smith et al., 2010). When examining the specific risk for HIV transmission, although having multiple sex partners is taken as an indicator of risky behavior, in fact the risk is only increased if condoms are not used. Thus, if a person has more than one sexual partner, and does not use condoms during sexual intercourse, the behavior is risky (Leigh et al., 1993). Early in the HIV epidemic, the use of cannabis among high risk populations was found to increase the likelihood of HIV infection risk behaviors (van Griensven et al., 1987). As in this early study among

uninfected persons, we found an association between cannabis use and multiple sex partners. It is quite possible that these findings are not related directly to cannabis use, but rather that cannabis use is a marker for a riskier lifestyle, attributes of which are multiple sexual partners and use of illegal drugs. The findings of a significant association between frequency of cannabis use and HIV drug risk behaviors further bolster these results by suggesting a “dose-response” relationship.

This study had limitations. First, the observational nature of this study design limits our ability to make causal inferences regarding the impact of cannabis use on drug and sex risk behaviors. Second, the information about cannabis use was collected through self-report only and not confirmed through toxicological measurements. Lastly, participants with depressive symptoms, risky drinking, lower CD4 count and not on ART were less likely to complete all study visits. It is unclear how this may have impacted our study results but may have introduced a potential bias. However, this analysis did include the entire HERMITAGE cohort since the repeated measures analyses that were conducted allowed us to include subjects with partial follow-up information even if they did not complete all visits.

In conclusion, this study reveals a strong association between cannabis use and injection drug risk behaviors as well as having multiple sex partners, and thus identifies a subpopulation of HIV-infected persons at higher risk for transmitting HIV. Further understanding of whether the association between cannabis and HIV risk behaviors is causal would be valuable. This relationship has implications for both IDU-related and heterosexual HIV transmission. Cohort studies with detailed longitudinal information on cannabis use and risk behaviors, that include innovative designs, such as case crossover, could further illuminate whether this relationship is causal. If future studies were to find that cannabis use resulted in riskier behaviors, behavioral interventions directed at reducing cannabis use could be a novel approach to reducing HIV transmission.

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Table 1
Baseline socio-demographic, health and risk behavior characteristics of Russian HIV-infected risky drinkers

Characteristic	Total n=700	Current Cannabis (Past 30days) n=143	Recent Past Use (in Past Year but not 30days) n=183	No cannabis Use n=374	p-value
Socio-demographic					
Age, mean (SD)	30.1 (5.2)	29.4 (4.5)	28.7 (4.3)	31.0 (5.6)	<0.001
Female	285 (40.7%)	38 (26.6%)	54 (29.5%)	193 (51.6%)	<0.001
Male	415 (59.3%)	105 (73.4%)	129 (70.5%)	181 (48.4%)	
< 9 grades of education	156 (22.3%)	29 (20.3%)	54 (29.5%)	73 (19.5%)	0.02
Current married or living with partner	251 (35.9%)	46 (32.2%)	42 (23.1%)	163 (43.6%)	<0.001
Physical and mental health					
CD4>=350 cells/mm3 (n=491)	254 (36.3%)	35 (24.5%)	68 (37.2%)	151 (40.4%)	<0.001
Receiving ART	121 (17.3%)	15 (10.5%)	24 (13.1%)	82 (21.9%)	<0.01
Beck Depression Inventory-II score					
0-13 None	249 (35.6%)	42 (29.4%)	69 (37.7%)	138 (36.9%)	0.22
14-19 Mild	157 (22.4%)	39 (27.3%)	42 (23.0%)	76 (20.3%)	
20-28 Moderate	173 (24.7%)	42 (29.4%)	44 (24.0%)	87 (23.3%)	
29-63 Severe	121 (17.3%)	20 (14.0%)	28 (15.3%)	73 (19.5%)	
Risky drinking	569 (81.3%)	132 (92.3%)	144 (78.7%)	293 (78.3%)	<0.001
Using stimulants past 30 days	75 (10.7%)	44 (30.8%)	14 (7.7%)	17 (4.5%)	<0.001
Drug risk behavior					
Any needle sharing (distributive and receptive) past 30 days among entire sample (n=700)	164 (23.5%)	65 (45.5%)	32 (17.5%)	67 (18.0%)	<0.001
IDU in past 30 days (n=700)	294 (42.0%)	107 (74.8%)	66 (36.1%)	121 (32.4%)	<0.001
Number of times injected drugs past 30 days mean (SD)	21.2 (37.1)	40.3 (46.2)	15.4 (31.2)	16.7 (33.4)	<0.001
Sex risk behavior					
Number of unprotected sex episodes past 3 months, mean (SD)	15.9 (34.8)	20.9 (47.7)	14.6 (26.0)	14.6 (32.5)	0.36
Having multiple sex partners	189 (27.0%)	55 (38.4%)	60 (32.8%)	74 (19.8%)	<0.001
3 Month sex trade	107 (15.3%)	33 (23.1%)	36 (19.7%)	38 (10.2%)	<0.001

Table 2
Longitudinal analyses evaluating the association between cannabis use and HIV drug risk behaviors among 700 HIV-infected Russian drinkers

	Needle Sharing (observations=1,711)		IDU (observation=1,709)		Number of Injections (observation=1,709)	
	AOR (95% CI) *	p-value	AOR (95% CI) *	p-value	AdjIRR (95% CI) *	p-value
Cannabis (Time varying) ***		<0.001 **		<0.001 **		<0.001 **
None (ref)						
Recent Past Use	0.93 (0.62, 1.40)	0.72	1.15 (0.82, 1.62)	0.41	0.79 (0.60, 1.03)	0.09
Current Use	2.23 (1.46, 3.36)	<0.001	3.05 (2.06, 4.53)	<0.001	1.50 (1.19, 1.89)	0.001
Timepoint						<0.001
Baseline (ref)		0.15		0.66		
Six Months	0.78 (0.57, 1.09)		0.89 (0.69, 1.15)		0.56 (0.45, 0.70)	<0.001
Twelve Months	1.02 (0.74, 1.41)		0.94 (0.72, 1.23)		0.72 (0.58, 0.90)	<0.01
Age	0.97 (0.94, 1.01)	0.10	1.00 (0.98, 1.03)	0.77	0.99 (0.96, 1.01)	0.36
Gender Male	0.88 (0.61, 1.27)	0.50	0.88 (0.64, 1.21)	0.43	0.83 (0.65, 1.05)	0.11
Education level < 9 grades	1.05 (0.70, 1.59)	0.81	0.83 (0.56, 1.21)	0.33	0.92 (0.69, 1.22)	0.56
Marital Status						
Never or not currently married (ref)						
Married or living with partner	0.60 (0.41, 0.89)	0.01	0.61 (0.43, 0.85)	0.002	0.71 (0.55, 0.91)	0.004
Baseline CD4 count						
<350 (ref)						
350	1.95 (1.26, 3.00)	0.003	1.14 (0.77, 1.68)	0.51	0.98 (0.71, 1.36)	0.91
Current ART (Baseline)	0.41 (0.23, 0.72)	<0.001	0.27 (0.17, 0.44)	<0.001	0.31 (0.19, 0.51)	<0.001
BDI II (Time varying)		<0.001 **		<0.001 **		<0.001 **
No Depression (ref)						
Mild	2.08 (1.41, 3.05)	<0.001	2.02 (1.46, 2.80)	<0.001	1.26 (0.95, 1.67)	0.11
Mod	2.65 (1.80, 3.91)	<0.001	2.93 (2.11, 4.09)	<0.001	1.68 (1.26, 2.23)	<0.001
Severe	4.45 (2.94, 6.74)	<0.001	4.26 (2.95, 6.16)	<0.001	2.41 (1.79, 3.23)	<0.001
Risky Drinking (Time varying)	1.52 (1.10, 2.10)	0.01	1.46 (1.12, 1.91)	0.005	1.10 (0.86, 1.41)	0.42
Stimulant Use in past 30 days	2.18 (1.34, 3.55)	0.004	9.06 (5.00, 16.40)	<0.001	1.79 (1.39, 2.31)	<0.001

	Needle Sharing (observations=1,711)		IDU (observation=1,709)		Number of Injections (observation=1,709)	
	AOR (95% CI) *	p-value	AOR (95% CI) *	p-value	AdjIRR (95% CI) *	p-value
Randomization Group Control (ref)						
Intervention	0.95 (0.67, 1.33)	0.74	0.98 (0.73, 1.33)	0.91	1.04 (0.83, 1.29)	0.74

* From GEE logistic regression model

** Global p-value, pairwise comparison reported only if global p-value significant at < 0.05

*** None – no use in past year or 6 months (at visit 6 and 12 follow up)

Recent Past Use – use past year or 6 months (at visit 6 and 12 follow up) but not in past 30 days

Current Use – past 30 days

Adjusted for marital status, CD4 count, risky drinking (time-varying), age, gender, current ART baseline, use of other drugs besides cannabis (past 30d) (time-varying), educational status, and BDI-II (time-varying)

AOR=adjusted odds ratio

CI=confidence interval

IRR=incidence rate ratio

Table 3
Longitudinal analyses evaluating the association between cannabis use frequency and HIV drug and sex risk behaviors among 700 HIV-infected Russian drinkers

	Needle Sharing (observation 1,691)		IDU (observations =1,693)		Sex Episodes (observations=1,694)		Multiple Sex Partners (observations=1,695)	
	AOR (95% CI) *	p-value	AOR (95% CI) *	p-value	AdjIRR (95% CI) *	p-value	AOR (95% CI) *	p-value
Cannabis								
Frequency ***		<0.01 **		<0.001 **		0.08 **		0.14 **
None (ref) (n=1,455)								
Low (n=81)	1.95 (1.12, 3.39)	0.02	1.97 (1.12, 3.46)	0.02	0.87 (0.60, 1.26)		1.22 (0.69, 2.16)	
Moderate (n=80)	2.05 (1.13, 3.71)	0.02	3.79 (2.07, 6.94)	<0.001	0.82 (0.56, 1.20)		1.43 (0.84, 2.43)	
High (n=82)	3.17 (1.74, 5.77)	<0.001	3.63 (1.96, 6.47)	<0.001	2.08 (1.16, 3.70)		1.89 (1.11, 3.24)	

* From GEE logistic regression model

** Global p-value, pairwise comparison reported only if global p-value significant at < 0.05

None – No use in past 30 days
Low – 1-2 times in past 30 days
Moderate – 3-5 times in past 30 days
High – 6-30 times in past 30 days

Adjusted for marital status, cd4 count, risky drinking (time-varying), age, gender, current ART baseline, use of stimulants (past 30d) (time-varying), educational status, and BDI-II (time-varying)

AOR=adjusted odds ratio

AdjIRR=adjusted Incidence rate ratio

CI=confidence interval

Table 4
Longitudinal analyses evaluating the association between cannabis use and HIV Sex risk behavior among 700 HIV-infected Russian drinkers

	Number of Unprotected Sex Episodes (observations=1, 709)		Multiple Sex Partners (observations=1, 711)	
	AdjIRR (95% CI)*	p-value	AOR (95% CI)*	p-value
Cannabis (Time varying)***		0.48**		0.01**
None (ref)				
Recent Use	0.93 (0.69, 1.26)		1.54 (1.11, 2.15)	0.01
Current Use	1.22 (0.85, 1.74)		1.68 (1.15, 2.46)	0.01
Timepoint		<0.001		0.04
Baseline (ref)				
Six Months	0.80 (0.61, 1.04)	0.09	1.02 (0.77, 1.37)	0.89
Twelve Months	0.60 (0.46, 0.77)	<0.001	0.74 (0.55, 0.99)	0.04
Age	0.96 (0.93, 0.99)	0.01	0.99 (0.96, 1.02)	0.47
Gender Male	0.81 (0.63, 1.04)	0.11	1.34 (1.01, 1.78)	0.04
Education level < 9 grades	1.12 (0.80, 1.56)	0.51	1.21 (0.87, 1.66)	0.25
Marital Status		0.004		<0.001
Never or not currently married (ref)				
Married or living with partner	1.51 (1.14, 2.00)		0.43 (0.31, 0.59)	
Baseline CD4 count				
<350 (ref)				
350	1.20 (0.86, 1.68)	0.28	1.64 (1.15, 2.33)	0.01
Current ART (Baseline)	0.87 (0.63, 1.21)	0.39	1.10 (0.75, 1.62)	0.62
BDI II (Time varying)		<0.001		0.92**
No Depression (ref)				
Mild	0.97 (0.68, 1.38)	0.86	0.90 (0.64, 1.26)	
Mod	0.58 (0.44, 0.76)	<0.001	0.96 (0.68, 1.35)	
Severe	0.85 (0.53, 1.36)	0.52	0.91 (0.61, 1.35)	
Risky Drinking (Time varying)	1.36 (1.04, 1.79)	0.02	1.96 (1.47, 2.63)	<0.001
Drug use in past 30 days (Time varying)		0.94		0.11
(Other than cannabis)	0.99 (0.73, 1.35)		1.29 (0.95, 1.75)	
Randomization Group		0.84		0.52
Control (ref)				
Intervention	1.03 (0.78, 1.35)		0.91 (0.69, 1.21)	

* From GEE logistic regression model

** Global p-value, pairwise comparison reported only if global p-value significant at < 0.05

*** None – no use in past year or 6 months (at visit 6 and 12 follow up)

Recent Use - use past year or 6 months (at visit 6 and 12 follow up) but not in past 30 days

Current Use - past 30 days

Adjusted for marital status, cd4 count, risky drinking (time-varying), age, gender, current ART baseline, use of other drugs besides cannabis (past 30d) (time-varying), educational status, and BDI-II (time-varying)

AOR=adjusted odds ratio

CI=confidence interval

IRR=incidence rate ratio