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Effects of a couple-based intervention to reduce risks for HIV, HCV, and STIs among drug-involved heterosexual couples in Kazakhstan: A randomized controlled trial

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Abstract

Objective—Project Renaissance is a randomized controlled trial of an HIV/HCV/STI prevention intervention conducted in Almaty, Kazakhstan. We hypothesized that couples assigned to the intervention of interest will have lower incidence of HIV, HCV, sexually transmitted infections (STI), rates of unprotected sex, and unsafe injection over the 12-month follow up period compared to those assigned to an attention control arm.

Design—A total of 300 couples (600 participants) where one or both partners reported injecting drugs in the past 90 days were randomized to one of two arms: (1) a five-session HIV/HCV/STI prevention intervention (Risk Reduction: RR), or (2) a five-session Wellness Promotion (WP) intervention.

Results—Over the 12-month follow up period, assignment to RR compared to WP significantly lowered the incidence of HCV infection by 69% (IRR=0.31, 95% CI=0.10 – 0.90, p=0.031). Although differences were not statistically significant, RR participants had a lower incidence of HIV infection by 51% (IRR=0.49, 95% CI=0.16 – 1.48, p=0.204) and any STI by 37% (IRR=0.63, 95% CI=0.21 – 1.93, p=0.418) than WP participants. RR participants reported significantly fewer numbers of unprotected vaginal sex acts with their study partners (IRR=0.58, 95% CI=0.36 – 0.93, p=0.024) and more consistent condom use (OR=2.30, 95% CI=1.33 – 4.00, p=0.003) over the entire follow-up period compared to WP participants.

Conclusion—Project Renaissance demonstrated a significant effect for biological and behavioral endpoints. Findings draw attention to an HIV/HCV/STI prevention intervention

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strategy that can be scaled up for drug-involved couples in harm reduction programs, drug treatment, and criminal justice settings.

Keywords

HIV/AIDS; HCV; Injection Drug Use; Kazakhstan

Introduction

Kazakhstan has one of the world's highest prevalence rates of injection drug use, which has fueled co-occurring epidemics of HIV and Hepatitis C (HCV) infection [1–5].

Approximately one percent of Kazakhstani adults inject drugs; however, this proportion exceeds 10% in towns along major drug trafficking routes [6]. Kazakhstan is also experiencing one of the fastest growing HIV epidemics in the world [1,2,7]. Although parenteral transmission is responsible for the majority of HIV cases in Kazakhstan, heterosexual transmission surpassed injection drug use as the leading cause of new cases in 2011, suggesting that HIV is spreading to sexual partners of people who inject drugs (PWID) [8]. HCV poses a major disease burden in countries that have heroin epidemics, such as Kazakhstan, other Central Asian and East Asian countries, Eastern Europe, and Russia [9]. Research suggests that high rates of unsafe injection and unprotected sex among PWID in Kazakhstan have led to elevated rates of HIV and HCV infection [10–13].

The dual threats of drug-related and sexual risk behaviors among PWID and their sexual partners underscore the need for innovative couple-based behavioral interventions that bring intimate partners together in a safe environment to learn how to address risks. A couple-based modality allows the pair to learn and practice couple communication and negotiation skills together, as well as problem-solving, joint goal setting to work through challenging risk situations, and technical skills, including condom use and safe injection practices. Processing information and developing personalized strategies with a facilitator promotes accountability and increases commitment to change [14–17].

Research conducted over the past two decades has found that couple-based behavioral interventions are efficacious in reducing sexual [16–21] and drug-related risk behaviors [16,19,20]. However, to date, none of these studies have been found to have a significant effect on incidence of HIV and HCV infection. Only three studies have focused exclusively on drug-using couples or specifically addressed injection-related risks or drug-related triggers for unsafe sex and none have focused on HCV prevention [16,19,20].

This study represents the first randomized controlled trial (RCT) to test the efficacy of a behavioral couple-based intervention designed to reduce incidence of HIV, HCV, and STIs and decrease unprotected sex and unsafe injection among PWID and their partners in Kazakhstan and Central Asia. A total of 300 couples (N=600 participants) were randomized to one of two arms: (1) a five-session Risk Reduction intervention (RR), or (2) a five-session Wellness Promotion (WP) intervention. We hypothesized that couples in the RR arm compared to WP will have (1) lower incident rates of HIV, HCV, and STI seroconversions, (2) lower number and proportion of unprotected sex acts, (3) higher rates of consistent

condom use, (4) lower rates of needle or syringe sharing, and (5) lower number and proportion of unsafe injection acts.

Methods

Participants and trial design

This RCT was conducted between 2009 and 2012 in Almaty, Kazakhstan (see Figure 1 for CONSORT Flow Diagram). Recruitment occurred via word-of-mouth from participants to their injecting network members. Trained research assistants also recruited potential study participants from health clinics, syringe and harm reduction service locations serving PWID, and neighborhood locations where PWID gather. Couples were eligible to participate if they met the following criteria: (1) both partners were aged 18 or older; (2) both partners identified each other as their main intimate partner of the opposite sex; (3) their relationship had lasted for at least six months; (4) both partners reported intending to remain together for at least 12 months; (5) at least one partner reported having had unprotected vaginal or anal intercourse with the other partner in the previous 90 days; and (6) at least one partner reported injecting drugs in the past 90 days. Couples were excluded if either partner: (1) showed evidence of significant psychiatric, physical, or neurological impairment that would limit effective participation as determined during informed consent; (2) reported severe physical or sexual violence perpetrated by the other partner in the past year; (3) reported that the couple was planning a pregnancy within the next 18 months; or (4) was not fluent in Russian as determined during the informed consent process.

After providing informed written consent and being enrolled in the study, participants completed a pre-intervention baseline assessment and follow-up assessments at three, six, and 12 months post-intervention. During each assessment participants completed an Audio Computer Assisted Self-Interview (ACASI) conducted in Russian in a private room. We conducted bio-specimen testing for HIV, HCV, gonorrhea, and Chlamydia immediately after participants completed the baseline, six, and 12-month follow-up ACASI interviews.

A Clinical Research Coordinator (CRC) performed individual pre-test counseling related to HIV, HCV, and STIs and took biological samples. Within two weeks from the interview, the CRC notified each participant privately of his or her test results, conducted post-test counseling, and provided referrals and navigation to treatment when applicable. During the post-test counseling session, after providing the test results, the CRC asked each participant whether he or she would notify his or her partner and encouraged them to share their status so both partners could receive treatment. Then the CRC invited the participant's partner into the room and recorded whether or not the participant informed the partner of the diagnosis in the presence of the CRC. The CRC further conducted follow-up of phone calls and in-person appointments during which accompanied treatment and assistance with disclosure were offered.

At baseline, all participants in both study conditions who tested positive for HIV, HCV, or an STI were referred to care and treatment. Research staff followed up with phone calls, in-person appointments, and by accompanying positive participants to treatment clinics throughout the 12-month follow up period to ensure that participants who tested positive

received confirmatory tests when needed and were linked with treatment. During the RR and WP sessions, participants were provided with a list of resources on services in the community by the intervention facilitators. Participants also learned skills on how access treatment and care in the community and how to talk to medical providers in the RR and WP sessions. Those who were HIV negative were encouraged to access testing every 6 months.

The Columbia University Institutional Review Board and the Kazakhstan School of Public Health Institutional Review Board under the Ministry of Health approved the study. Participants received \$10 USD (1500 tenge) for completing the ACASI interview and bio-testing for each assessment visit to cover their time, as well as \$5 USD (750 tenge) for travel at each intervention session.

Randomization and masking

We randomly assigned couples in a one-to-one ratio to receive the five-session RR intervention or a five-session WP intervention, which served as a comparison condition. The computer-generated randomization algorithm was designed to balance the number of couples per study arm as well as the number of HIV serodiscordant couples per arm via an adaptive, biased-coin procedure [22]. The investigator who designed the randomization program was not involved in the conduct of the trial, but consulted on the statistical analysis. Investigators were masked to treatment assignment until the final 12-month follow-up assessment was completed. Data were locked on February 1, 2013 at which point the study arms were unmasked.

Procedures

The Risk Reduction (RR) intervention was adapted from Project Connect II, an evidence-based HIV prevention intervention that was designed and tested by the authors of this paper with couples in New York City where one or both partners used drugs [14,23]. In adapting Project Renaissance, we modified the delivery style. In Project Connect, all sessions were delivered to each couple by a facilitator. For Project Renaissance, we delivered the intervention using three single-gender group sessions for female and male partners followed by two couple sessions for each couple. We also added new content in Project Renaissance on overdose response and prevention, given that the rate of death from overdose is the leading cause of death among people who inject drugs in Kazakhstan. Finally, we adapted the content and language of the scenarios, activities, and role plays used in the sessions to enhance contextual relevance to people who use drugs in Kazakhstan [19]. The content in the single gender group sessions and couple sessions covered similar core components (see figure 2). This dual modality delivery design was informed by the pilot study and formative qualitative work conducted by the authors, where couples suggested separate gender specific preparation was needed prior to participation in couple sessions [19]. Same gendered group sessions introduced ways to discuss sexual behaviors using an equitable communication model in preparation to discuss personal risk and commitment to harm reduction in couple sessions.

Both study arms consisted of five two-hour sessions spaced at least five days apart: the first three sessions were single gender groups for male partners and female partners led by same

gender facilitators. These single gender groups were conducted simultaneously in separate rooms. These group sessions were followed by two single couple sessions. The couple-based Risk Reduction intervention was guided by social cognitive theory and a relationship-oriented ecological framework [24]. The core components of this intervention focused on strategies to reduce risk behaviors for HIV, HCV, and STIs: (1) encouraging both partners to disclose and identify mutual drug-related and sexual risks; (2) modeling, role-playing, and practicing couple communication, negotiation, and problem solving skills that both partners could employ together to reduce their drug-related and sexual risks; (3) practicing technical condom use placement skills along with learning about a broader repertoire of pleasurable safer sex activities and needle/syringe disinfection skills as well as strategies for obtaining new syringes from pharmacies or harm reduction programs; and (4) identifying and addressing risks for opiate overdose using peer administration of naloxone, an opiate antagonist.

The couple-based Wellness Promotion (WP) comparison intervention was designed to control for non-specific effects (e.g., modality and dosage). Core components of this psycho-educational intervention focused on maintaining a healthy diet, promoting physical fitness in daily routines, improving access to health care services and drug treatment by identifying and addressing service barriers, learning stress-reduction exercises, and setting and following up on personal health goals. For ethical reasons, this intervention also included the same naloxone-based overdose prevention activity described above.

Measures

Biological endpoints—At baseline, six, and 12-month follow up visits we used biological assays to test for HIV, HCV, gonorrhea, and Chlamydia. Urine specimens were collected from participants and shipped to the Almaty Oblast Skin and Venereal Disease Dispensary to be tested for Chlamydia trachomatis and Neisseria gonorrhea using molecular/DNA amplification assay (BD ProbeTec ET System) with a sensitivity of 99.9% and specificity of 99.9%. For HIV and HCV testing, a study nurse administered a finger prick to collect blood for a dried blood spot (DBS) sample. A whole blood spot was applied to five printed circles on DBS filter paper cards, and sent to the reference laboratory at the Republican AIDS Center (RAC). For the serologic surveillance of HIV and HCV, a standard enzyme-linked immunosorbent assay (ELISA) was used [25]. Tests for all three biomarkers were conducted using a serial two-test strategy, as recommended by the World Health Organization and routinely used at the Kazakhstan RAC. U.S. manufactured Abbott Murex Biotech tests were used for the second test. According to the RAC Guidelines for Serological Surveillance, the Murex anti HIV ABBOTT and Murex anti HCV ABBOTT have a reported sensitivity of 99.9 % and specificity of 99%.

Behavioral endpoints—The Risk Behavior Assessment (RBA) [26,27] was used to assess sexual and drug risk behaviors. The assessment was employed at the baseline, three, six, and 12-month visits. Self-reported data on sexual behaviors with the study partner and with other partners in the prior 90 days were collected, including number of vaginal and anal intercourse acts, number of unprotected vaginal and anal intercourse acts, and consistent condom use during vaginal intercourse. The interview also assessed the number of times

participant's shared needles or syringes and unsafe injection behaviors in the past 90 days. Unsafe injection was defined as engaging in one or more of the following behaviors: using unclean syringes or needles; sharing cookers, cotton, rinse water, or other paraphernalia; splitting drug solutions with other injectors through front-loading, back-loading, or use of the same cooker/spoon; or adding their own or someone's else blood into an injected drug.

Statistical Analysis

Power analyses suggested that a sample size of 565 would achieve 80% power to detect a clinically meaningful 50% reduction in HIV or HCV seroconversions or STI incidence using the following additional parameters which were based on estimates from the pilot study [19]: 5% and 20% for a background seroconversion rate for HIV and HCV respectively with 80% and 20% for the proportion of the sample that would be either HIV-negative or HCV-negative for the respective analysis; background annual incident rate of 4.5 per 100 person years for STIs and .05 for the alpha and two-sided hypothesis testing. Estimated power for all other outcomes was substantially higher.

Consistent with an intent-to-treat approach, we estimated intervention effects by analyzing participants based on their experimental assignment. We used all available data on randomized participants at any follow-up visit in the statistical models. Mortality was high over the course of the follow-up period, with 46 deaths, including 11 due to drug overdose, nine to hepatocirrhosis, four to myocardial infarction, three attributed in part to AIDS, and the remainder to other causes. These 46 participants did not significantly differ from the other 554 participants on socio-demographic characteristics. Of the participants who died during the follow-up period, 29 completed the three and/or six-month follow-up assessment and these data were included in the statistical analysis. The overall retention rate over the entire follow-up period up was 88%. Attrition analyses revealed that no baseline measures were significantly different between those who attended vs. those who missed assessments for all follow-up time points.

For the biological outcomes, we calculated person-year incidence rates for HIV, HCV, and any STI by experimental assignments. Any STI was defined as any new infection of gonorrhea or Chlamydia that was detected at the six or 12-month follow-up visit. Covariance adjustment for unsafe injection in the 90 days prior to the baseline assessment was included to obtain incidence rate ratios (IRR) and corresponding 95% confidence intervals (CIs). For sexual and drug-related risk behavioral outcomes, we employed multilevel mixed-effects models to handle non-independence in observations. Although data were collected from each participant, responses were nested within couples. The analytical approach we used included couple as a random effect in the multilevel mixed effects models. Each observation at the first level of the model represents an individual measurement at one of the three post-treatment time points. Random effect parameters in the model accounted for dependencies from couple grouping and repeated measures over time. The models to estimate intervention effects at each follow-up visit also included follow-up time, the interaction between treatment condition and follow-up time, covariate adjustments for gender, and measures of the outcome variable reported at the baseline assessment. We used multilevel mixed-effects Poisson regression to estimate effects of the intervention on

the number of unprotected vaginal intercourse acts and the number of times sharing needles or syringes. We report estimates of effects as incident rate ratios (IRR) and corresponding 95% CIs. We also used multilevel mixed-effects logistic regression to estimate effects of the intervention on consistent condom use during vaginal sex and report of any unsafe injection. For these effect estimates, we report odds ratios (OR) and 95% CIs. We used Stata (version 12.0) for statistical analyses.

Results

Enrollment and baseline characteristics are described elsewhere [12]. We screened 971 individuals of whom 728 (N=364 couples) met eligibility criteria and completed the baseline assessment. Of these 364 couples, 300 were enrolled and randomized. There were no significant differences between study arms with respect to overall retention rates (RR=87% v. WP=89%, $p=0.29$; please refer to the Consort Form for the retention rate at each follow-up assessment) and mortality rates (RR=6.6% v. WP=8.7%, $p=0.33$) over the entire follow-up period.

Table 1 describes socio-demographic characteristics and bio-testing results at baseline assessment for 600 participants by intervention assignment. The mean age of participants was 35.2 years (SD=7.7). Two-thirds of study participants self-identified as Russian and 11% identified as Kazakh. Other participants identified primarily as Uighur, Tatar, Uzbek, Dughan, and Korean. A majority of participants were married (87%, including common-law marriage) and had completed high school (77%). One-quarter were employed and nearly half (49%) reported having insufficient money to buy food in the prior three months. Two-thirds of participants (67%) reported ever being arrested. One-quarter (26%) tested positive for HIV, 77% tested positive for HCV, and 6% tested positive for any STI (gonorrhea, and/or Chlamydia) at the baseline. Of the 156 HIV positive participants, 98 participants (i.e. 49 couples) were in sero-concordant relationships and 58 participants were sero-discordant (38 men and 20 women were positive while their partners were negative). Of the 117 participants who knew of their HIV positive status prior to the baseline visit, less than one-fifth ($n=21$, 18%) reported currently taking ARV medication. Socio-demographic characteristics, baseline biologically confirmed HIV, HCV, and STI status, and ARV status did not differ significantly between the treatment arms.

Hypothesis tests for HIV, HCV, and STI seroconversion endpoints

Table 2 reports per 100 person-year incidence rates for HIV, HCV, and any STI by arm. There were nine newly detected HCV cases with 42.25 person-years in WP (i.e. 19.9 per 100 person-years) and five new cases with 67.25 person-years in RR (i.e. 7.4 per 100 person-years) over the one-year follow-up period, with an adjusted incident rate ratio of 0.31 (95% CI=0.10 – 0.90), after adjusting for unsafe injection. The difference between study arms indicated that participants in the RR arm had a 69% lower incidence of HCV infection compared to WP participants. There were nine newly detected HIV cases with 173 person-years in WP (i.e. 5.2 per 100 person-years) and five new cases with 187 person-years in RR (i.e. 2.7 per 100 person-years) over the one-year follow-up period, although the adjusted incident rate ratio for HIV between study arms was not statistically significant (IRR=0.49,

95% CI=0.16 – 1.48). For any STI (gonorrhea or Chlamydia), there were eight newly detected STI cases with 242.25 person-years in WP (i.e. 3.3 per 100 person-years) and five new cases with 240 person-years in RR (i.e. 2.1 per 100 person-years) over the one-year follow-up period. The study arms did not significantly differ on STI incidence (IRR=0.63, 95% CI=0.21 – 1.93).

Hypothesis tests for behavioral endpoints

Table 3 presents descriptive statistics regarding sexual and drug-related risk behaviors at the baseline, three, six, and 12-month follow-up assessments by intervention assignment. Table 4 reports the findings of multilevel models to estimate quantitatively the effect of assignment to RR vs. WP on sexual and drug-related risk behaviors over the entire follow-up and at each follow-up assessment. Over the entire follow-up period, participants who were assigned to RR compared to WP participants had a 42% lower incidence of unprotected acts of vaginal intercourse with their study partners (IRR=0.58, 95% CI=0.36 – 0.93) as well as an increased likelihood of reporting consistent condom use with their study partners (OR=2.30, 95% CI=1.33 – 4.00). Although the overall model was significant in sexual risk reduction, reductions in sexual risk behaviors were primarily seen at 3-month follow-up, and not at the 6 and 12-month follow-up periods. The findings from the models of sexual risk behaviors with all partners were similar to the findings from the models of sexual behaviors with study partners.

Although both RR and WP participants reported a substantial reduction in rates of needle sharing and unsafe injections from baseline to the 12-month follow up, no significant differences between conditions with respect to injection drug risks over the follow up period were found. The multilevel models of injection drug risk outcomes were also conducted among participants who reported ever injecting drugs and yielded similar findings with no significant differences between RR and WP. When conducting multilevel models to examine the differences in injection drug behaviors between the baseline and each follow-up assessment among participants from both study arms (including interaction terms between study arms and each follow-up), findings demonstrate a significant reduction of injection drug behaviors at each follow-up assessment. For example, in respect to the unsafe injection, the odds ratios at each follow-up were significantly less than 1 (OR=0.17, 0.11 and 0.10 at the 3, 6 and 12-month follow-ups respectively, with all p-values<0.01), indicating a significantly lower likelihood of unsafe injection at each follow-up when compared to behaviors at the baseline assessment.

Discussion

To our knowledge, Project Renaissance is the first RCT in which a couple-based HIV/HCV/STI intervention demonstrated a significant effect for both biological and behavioral endpoints. Over the one-year follow up period, participants in the RR intervention had a 51% lower incidence of HIV infection and a 69% lower incidence of HCV infection, although the IRR for HIV was not statistically significant.

Statistically significant effect sizes averaged over the one-year follow-up period were observed for the primary sexual behavioral outcomes. Participants who were randomized to

the RR arm had a 42% lower incidence of unprotected acts of vaginal intercourse with their study partners, compared to participants in the WP arm over the follow-up period, although statistically significant differences were found at 3 months but not at 6 or 12 months. These findings demonstrate the strength of the RR intervention in reducing risky sexual behaviors early on, and suggest that additional efforts such as booster sessions may be helpful in maintaining gains in behavior change over time, although additional research would be needed to examine when and how many booster sessions may be effective. The lack of significance in sexual behavior outcomes at 6 or 12 months may also be related to repeated assessment reporting bias, or to the strength of the Wellness intervention arm in promoting healthy behavior. Of note in this context is the rare opportunity for drug-involved couples to take part in behavioral interventions. It is not surprising that the WP would also demonstrate some effect in risk reduction through the support mechanisms offered through group and couples meetings.

Participants in both arms significantly reduced the incidence of sharing needles and unsafe injection practices. We speculate that this reduction in drug risks can be attributed to the overdose prevention and health related content that was included in both arms of the study.

The observed magnitude and consistency of findings for HCV endpoints and behavioral outcomes support the major hypotheses of the study and provide evidence for the efficacy of Project Renaissance in reducing HCV incidence and sexual risk behaviors. The significant behavioral effects observed at 3 months may have led to differences in biological outcomes between arms at 12 months. Although positive behavioral effects were found for reducing sexual risks for RR, both conditions significantly reduced injection risk, which is known to influence HCV transmission. However, 16.7% of people who did not report injecting drugs tested HCV positive. This may suggest that HCV infection may be linked to sexual risk behaviors [28]. The link between sexual risk behaviors, particularly unprotected anal sex, and HCV transmission has been found in some recent studies [29,30], however, other research suggests that unprotected sex is not associated with HCV transmission [31].

The study has two major limitations. As in other HIV clinical trials, we recruited eligible participants through non-random sampling procedures, which limits the generalizability of the study results to other injection drug users in Central Asia, particularly those who are not in committed intimate relationships. Inclusion of overdose prevention content in both study arms may have limited our ability to determine the effect of the intervention on drug use practices, although specific content on injection-related HIV and HCV risk reduction was not included in the WP arm.

Despite these limitations, recruitment through street outreach and within harm reduction and health clinic settings resulted in a hard to reach sample of people who use drugs, engage in multiple risky behaviors, and are not in drug treatment. The high participation, retention, and attendance rates achieved in this study demonstrate the feasibility and importance of including participants who have been excluded from many HIV related clinical trials.

In conclusion, study findings draw attention to an HIV/HCV/STI prevention intervention strategy that has shown promise in addressing sexual risk behaviors and HCV incidence

among drug-involved couples. Such prevention strategies with heterosexual, drug-using couples in low-income urban neighborhoods with concentrated epidemics are essential to lowering transmission of the co-occurring epidemics of HIV, HCV, and STIs and can be incorporated into harm reduction programs, drug treatment, criminal justice systems, and other settings. In the past few years, there have been a number of calls for combination prevention (biomedical and behavioral) for people who inject drugs (PWID) [4,5,32,33]. Additional research is necessary to determine how long term gains in sexual risk reduction and HIV incidence can be achieved, and to identify how such behavioral approaches can be combined with early ART and other biomedical treatments (PREP, circumcision, microbicides) to improve maintenance of PWID in the test, treat, and retain continuum of HIV, HCV, and STI care.

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Figure 1.
CONSORT Form

Risk Reduction (RR)	Wellness Promotion (WP)
Perceived risk of HIV, HCV, and other STIs [initial session for both single gender group (SGG*) and couple sessions (CS*)]	Develop individualized health risk assessment (SGG and CS)
Information on the levels of infectivity and HIV transmission (viral load, acute infection, ART, PREP and impact on transmission risk) (SGG and CS)	Introduce the concept of body mass index and healthy weight assessment
Couple communication skills to enhance understanding and commitment to healthier choices as a dyad (speaker listener technique) (SGG and CS)	Knowledge of tobacco and alcohol health risk and review other common diseases (SGG and CS)
Options for HIV testing and care, including the rationale for testing over time and, potentially, testing together (SGG and CS)	Knowledge of healthy nutrition and associated foods (SGG and CS)
Practice condom technical skills and address barriers to use condoms (SGG and CS)	Strategies to improve and maintain health including nutrition, exercise, yoga, relaxation techniques (SGG and CS)
Problem-solving model to identify risks and develop an action plan with goals for sexual risk reduction and harm reduction strategies such as sterile syringe usage (SGG and CS)	Help seeking skills to address health problems by identifying and addressing service barriers to health care and drug treatment (SGG)
Gender roles and expectations related to sexuality, reproductive health, and safer sex practices (SGG and CS)	Stress-reduction exercises and setting personal health goals (SGG and CS)
Social support, risk networks, and goal setting to increase sustainability of healthier behaviors (SGG and CS)	Overdose (OD) response and prevention including knowledge and skills to utilize naloxone (CS)
Knowledge of risk associated with drug use including HIV risk of sharing syringes/needles and other equipment (SGG and CS)	
Triggers for unsafe sex, drug use, and drug-related risks (SGG and CS)	
Overdose (OD) response and prevention including knowledge and skills to utilize naloxone (CS)	

*SGG=single gender group, CS=couple session

Figure 2.
Intervention Core Components

Table 1

Socio-demographic Characteristics and Bio-testing Results at the Baseline by Intervention Assignments

	Total (N=600)	WP (n=298)	RR (n=302)
Age in years (mean, SD)	35.2 (7.7)	34.9 (7.4)	35.4 (8.0)
Ethnicity			
Russian	395 (66%)	187 (63%)	208 (69%)
Kazakh	67 (11%)	38 (13%)	29 (10%)
Married (& common-law marriage)	521 (87%)	258 (87%)	263 (87%)
High school	464 (77%)	229 (77%)	235 (78%)
Employed	157 (26%)	82 (28%)	75 (25%)
Homeless	80 (13%)	39 (13%)	41 (14%)
Insufficient money for food	291 (49%)	148 (50%)	143 (47%)
Ever arrested	402 (67%)	201 (67%)	201 (67%)
HIV positive	156 (26%)	83 (28%)	73 (24%)
HCV positive	461 (77%)	236 (79%)	225 (75%)
Any STI positive	35 (6%)	20 (7%)	15 (5%)
Gonorrhea positive	14 (2%)	7 (2%)	7 (2%)
Chlamydia positive	23 (4%)	13 (4%)	10 (3%)

**
p<0.01,*
p<0.05

Table 2

Per 100 person-year HIV, HCV and any STI incidence rates by intervention assignments

	Arm	Person year	# Positive	Per 100 persons per year incidence rates	Incidence rate ratio ^a
HIV (n=375)	WP	173	9	5.20 [2.71, 10.00]	0.49 [0.16, 1.48] (p=0.204)
	RR	187	5	2.67 [1.11, 6.42]	
HCV (n=122)	WP	45.25	9	19.89 [10.35, 38.23]	0.31 * [0.10, 0.90] (p=0.031)
	RR	67.25	5	7.43 [3.09, 17.86]	
Any STI (n=500)	WP	242.25	8	3.30 [1.65, 6.60]	0.63 [0.21, 1.93] (p=0.418)
	RR	240	5	2.08 [0.87, 5.01]	

Note:

**
p<0.01,*
p<0.05^a A baseline measure of unsafe injection in the past 90 days was included as covariance adjustment.

Table 3

Sexual and drug injection behaviors in the past 90 days among 600 participants by intervention assignments: mean (SD) or frequency (%)

	Arm	Baseline (n=600)	3-month (n=469)	6-month (n=468)	12-month (n=458)
Number of unprotected vaginal intercourse acts with study partner	WP	36.37 (40.34)	29.11 (38.68) **	17.43 (25.11)	16.69 (29.40)
	RR	41.56 (44.81)	19.17 (32.60) **	19.00 (31.79)	18.62 (36.92)
Consistent condom use during vaginal intercourse with study partner	WP	48 (16.1%) **	79 (32.2%) *	103 (44.8%)	113 (49.3%)
	RR	27 (8.9%) **	96 (42.9%) *	122 (51.3%)	125 (54.6%)
Number of times sharing needles/syringes ^a	WP	6.71 (24.92) *	1.15 (6.86)	0.81 (5.05)	1.33 (9.23)
	RR	3.42 (12.54) *	0.44 (2.58)	1.37 (7.55)	1.30 (8.73)
Unsafe injection ^a	WP	170 (57.4%)	64 (26.1%)	50 (21.7%)	43 (18.8%)
	RR	166 (55.5%)	67 (29.9%)	56 (23.5%)	44 (19.2%)

Note:

**
p<0.01,

*
p<0.05

^a There were five missing values at the baseline assessment.

Table 4

Multilevel models of sexual and injection drug behaviors on intervention (RR vs. WP): Effects, 95% confidence intervals and p-values

VARIABLES	Entire Follow-up	3-Month	6-Month	12-Month
Number of unprotected vaginal intercourse acts with study partner: <i>IRR</i>	0.58* [0.36 – 0.93] (p=0.024)	0.47* [0.24 – 0.94] (p=0.034)	0.56* [0.34 – 0.91] (p=0.020)	0.77 [0.34 – 1.75] (p=0.537)
Consistent condom use during vaginal intercourse with study partner: <i>OR</i>	2.30** [1.33 – 4.00] (p=0.003)	2.93** [1.31 – 6.55] (p=0.009)	2.45** [1.38 – 4.34] (p=0.002)	1.72 [0.70 – 4.24] (p=0.236)
Number of times sharing needles/syringes: <i>IRR</i>	0.98 [0.39 – 2.50] (p=0.971)	0.82 [0.21 – 3.14] (p=0.768)	0.95 [0.36 – 2.46] (p=0.909)	1.27 [0.25 – 6.32] (p=0.773)
Unsafe injection: <i>OR</i>	1.28 [0.87 – 1.88] (0.204)	1.40 [0.81 – 2.40] (0.229)	1.30 [0.88 – 1.92] (0.185)	1.13 [0.58 – 2.20] (0.712)

Note:

**
p<0.01,

*
p<0.05

^a Couple and time were set as random effects.

^b Adjusted covariates were gender and the baseline measure of the outcome.