

Computer-Based Alcohol Reduction Intervention for Alcohol-Using HIV/HCV Co-Infected Russian Women in Clinical Care: Study Protocol for a Randomized Controlled Trial

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Abstract

Background: Russia has a high prevalence of HIV. In 2018, over one million persons were living with HIV (PLWH); over a third were women. A high proportion of HIV-infected women are co-infected with Hepatitis C virus (HCV); and many consume alcohol, which adversely affects HIV and HCV treatment and prognosis. In spite of the triple epidemics of alcohol use, HIV and HCV, and the need for interventions to reduce alcohol use among HIV/HCV co-infected women, evidence-based alcohol reduction interventions for this vulnerable population are limited. To address this gap, we developed a clinical trial to evaluate the efficacy of a computer-based intervention to reduce alcohol consumption among HIV/HCV co-infected women in clinical care.

Methods: In this two-arm parallel randomized clinical trial, we propose to evaluate the efficacy of a culturally-adapted alcohol reduction intervention delivered via a computer for HIV/HCV co-infected Russian women. The study population consists of women 21-45 years old, with confirmed HIV/HCV co-infection who currently use alcohol. Intervention efficacy is assessed by a novel alcohol biomarker, ethyl glucuronide (EtG) and biomarkers of HIV and HCV disease progression. Women are randomized to trial conditions in a 1:1 allocation ratio, using a computer-generated algorithm to develop the assignment sequence, and concealment of allocation techniques to minimize assignment bias. Women are randomized to either: (1) the computer-based alcohol reduction intervention, or (2) the standard-of-care control condition. We will use an intent-to-treat analysis and logistic and linear generalized estimating equations to evaluate intervention efficacy, relative to the standard-of-care, in enhancing the proportion of women with a laboratory-confirmed negative EtG at each research study visit over the 9-month follow-up period. Additional analyses will evaluate intervention effects on HIV (viral load, and CD4+ levels), and HCV markers of disease progression (FibroScan).

Discussion: The proposed trial design and analysis provides an appropriate conceptual and methodological framework to assess the efficacy of the computer-based intervention. We propose to recruit 200 participants.

The intervention, if efficacious, may be an efficient and cost-effective alcohol reduction strategy that is scalable and can be readily disseminated and integrated in clinical care in Russia to reduce women's alcohol consumption and enhance HIV/HCV prognosis.

Trial registration: ClinicalTrials.gov, NCT03362476. Registered 5 December 2017, <https://clinicaltrials.gov/ct2/show/NCT03362476>

Introduction

Background and rationale {6a}

The HIV and Hepatitis C virus (HCV) epidemics are intertwined with increasing prevalence in Russia. As of 2018, over one million persons were living with HIV (PLWH) in the Russian Federation (Russia).¹ Women

made up 37% of new HIV diagnoses, almost tripling the 2006 prevalence rate.¹

The severity of the HIV epidemic is compounded by the intersecting HCV epidemic. Eastern Europe has the largest proportion of PLWH with serological evidence of HCV infection (27%).² The prevalence of HIV/HCV co-infection is markedly higher among individuals with a history of injection drug use (PWID). A recent review estimated an HCV prevalence of 69% among PWID compared to 4.6% among PLWH without a history of injection drug use in Russia.³ Among HIV-infected women in Saint Petersburg, Russia, a study by our group observed that 57.1% were HCV co-infected.⁴ Behaviors related to injection drug use, such as needle sharing, have contributed to the rapid spread of HIV/HCV co-infection among PWID globally,⁵ including in Saint Petersburg, Russia.⁶⁻⁸

Alcohol use poses a marked and persistent health threat to women living with HIV/HCV co-infection. In spite of significant reductions in alcohol use over the past two decades,⁹ problem alcohol use is prevalent in Russia and adversely impacts the treatment and prognosis of women living with HIV/HCV by accelerating HIV and HCV progression.¹⁰ A recent meta-analysis estimated that 55% [95% confidence interval (CI): 16%-88%] of Russian participants engaged in heavy episodic drinking and 58% (95% CI: 49%-67%) met diagnostic criteria for alcohol use disorder.¹¹ A World Health Organization study estimated that among Russian women, 43.7% of those who drank were heavy episodic drinkers compared to 19.9% in Europe as a whole.¹² A recent study among PLWH in Saint Petersburg found that, overall, 45.3% of women reported drinking in the past week, and of those 21.6% reported at least one heavy episodic drinking episode (4 or more drinks).¹³

Among HIV/HCV co-infected individuals, alcohol use may also lead to a variety of adverse health outcomes. HIV/HCV co-infected individuals develop liver disease earlier and more severely than those who are HIV mono-infected.¹⁴⁻¹⁶ Excessive alcohol consumption is a major contributor of liver-related mortality among persons with HIV/HCV co-infection.¹⁷ The adverse impact of alcohol use may be worse for women, who are more prone to rapid fibrosis progression and cirrhosis than men.¹⁸ In addition to direct health complications, alcohol may heighten health risks to PLWH by interacting with antiretroviral (ARV) therapy. For example, alcohol and ARV interactions may contribute to hepatotoxicity and liver disease,^{16,19} which may be accelerated by co-morbid HCV infection.²⁰ Furthermore, a history of alcohol use may impede persons with HIV/HCV co-infection from benefiting from the new generation of HCV treatments, such as direct acting anti-HCV drugs.²¹ Current recommendations are for individuals with HIV/HCV co-infection to abstain from alcohol use given that safe drinking levels have not been defined for this population.²² There is conflicting evidence with respect to the health effects of moderate alcohol consumption among HCV mono-infected and HCV/HIV co-infected persons, with some studies finding that even moderate amounts of alcohol may accelerate disease progression, while other studies identify no such association.^{23,24}

In spite of the need for interventions to reduce alcohol use among HIV/HCV co-infected women, there are few evidence-based interventions.^{25,26} A recent review of interventions to reduce alcohol consumption

among PLWH identified limited evidence that interventions reduced binge drinking frequency, alcohol use disorders, or alcohol dependence symptoms.²⁵ Furthermore, most of the interventions did not target alcohol use exclusively, but addressed other high-risk behaviors (e.g., reducing sexual risk behaviors) or included a focus on substance use more broadly. In addition, the majority of interventions were conducted in the U.S.; to our knowledge, none were implemented and evaluated in Russia.²⁵

In this two-arm parallel randomized clinical trial, we propose to evaluate the efficacy of a brief, culturally-adapted, computer-delivered alcohol reduction intervention for Russian women with HIV/HCV co-infection. The intervention includes modules utilizing cognitive behavioral and motivational enhancement principles to reduce alcohol consumption. Brief interventions based on cognitive behavioral therapy that include personalized feedback about alcohol use, establishment of personal drinking goals and tracking of goal progress coupled with behavioral strategies to reduce alcohol use have shown to be efficacious.^{29,30}

The proposed intervention will be brief and delivered via a computer-platform. Computer-delivered alcohol reduction interventions have been found to be effective in lowering problematic alcohol use, albeit with small effect sizes^{31,32} and may be more cost-effective and feasible to integrate to clinical care settings than existing interventions delivered by experienced trained clinical providers. A mounting body of evidence points to the promise of integrating treatment for alcohol use within comprehensive HIV-care services.³³ If efficacious, our intervention may be a scalable and cost-effective strategy to reduce alcohol use among women with HIV/HCV co-infection within the framework of comprehensive HIV care, in line with current strategies to strengthen HIV-care delivery.

Objectives {7}

The study objectives are:

1. To evaluate the efficacy of a computer-based alcohol reduction intervention condition, relative to the standard of care condition, in enhancing the proportion of HIV/HCV co-infected women detected with laboratory-confirmed negative alcohol biomarker over a 9-month follow-up period.
2. To evaluate the efficacy of a computer-based alcohol reduction intervention condition, relative to the standard of care condition, in reducing HIV/HCV co-infected women's HIV and HCV biomarkers of disease progression over a 9-month follow-up period.

Trial design {8}

The proposed study is a parallel two-arm randomized control trial to evaluate the efficacy of a culturally-adapted computer-based alcohol reduction intervention for HIV/HCV co-infected Russian women in clinical care.

Following receipt of informed consent and enrollment in the study, 200 women are randomized to one of two conditions following a 1:1 allocation ratio: (1) standard-of-care plus the adapted computer-based

intervention condition (n=100), or (2) the standard-of-care control condition alone (n=100).

Data are being collected at baseline, prior to randomization, and at 3-, 6- and 9-month follow-up during scheduled research visits via self-report surveys. In addition, biological markers are collected at baseline and at each follow-up to obtain objective and quantifiable measures of alcohol use and HIV and HCV disease status. The proposed trial design provides an appropriate conceptual and methodological framework to determine the efficacy of the intervention in reducing alcohol use and HIV and HCV disease progression (See Figure 1).

Methods: Participants, Interventions And Outcomes

Study setting {9}

The intervention is implemented in HIV clinical care facilities in Saint Petersburg, Russia. Saint Petersburg is the second largest city in Russia, with a population of approximately 5 million, and has a high prevalence of PWID, a key risk behavior associated with HIV/HCV acquisition.⁶ An estimated 40,000 PLWH live in Saint Petersburg, with about 2000 new cases diagnosed annually.³⁶ There is high prevalence of HCV infection among Russian PLWH.⁴ The current study includes women seeking HIV care at two clinical care sites: the [redacted] and the [redacted]. Both sites offer comprehensive HIV care, including mental health care, for HIV-infected women.

Eligibility criteria {10}

Eligible participants must: 1) be women ages 21-45 years old; 2) have chart-documented HIV and HCV infection; 3) be currently prescribed ARV therapy; 4) have a positive point-of-care ethyl glucuronide (EtG) or self-report alcohol use in the past 30 days. Women who are medically, cognitively, or psychologically incapable of study participation, as assessed by a research clinician, are excluded, as those who do not provide written informed consent to participate.

Who will take informed consent? {26a}

A research staff member explains the study, reviews the consent form with participants, and answers any questions before women provide written consent to participate in the study. All eligible participants must complete consent procedures prior to enrollment and randomization. Measures are being implemented to protect study participants. Study staff are instructed to highlight confidentiality and assure participants that their responses would not be shared with clinic staff or would in other way adversely affect service provision.

Compensation

Participants receive a 1000-ruble (~16USD) valued gift card at baseline and at the 9-month follow-up visit and a 500-ruble (~8 USD) valued gift card for each completed intermediary assessments (3- and 6-month research visits).

Interventions

Explanation for the choice of comparators {6b}

This trial compares the efficacy of standard clinician-delivered alcohol reduction counseling to a computer-delivered alcohol use reduction intervention. We hypothesize that the computer-delivered intervention may be less costly, less demanding on human resources and more feasible to integrate to clinical care than the current standard-of-care, with comparable results.

Intervention description {11a}

Intervention condition

Women in the intervention condition receive a brief computer-based intervention to reduce alcohol use that is guided by cognitive behavioral principles. The computerized intervention includes modules to: (a) provide an overview of the intervention and information regarding the impact of alcohol use on disease progression; (b) assess current levels of drinking and provide feedback on alcohol use; (c) set alcohol reduction goals and enhance motivation to modify drinking behaviors; (d) address challenges associated with achieving drinking goals; and (e) provide strategies to reduce alcohol use. The computerized intervention was adapted to be culturally appropriate and incorporates vignettes to illustrate intervention content. At the conclusion of each computer-based session, a study clinician meets with participants to establish drinking goals and discuss strategies to achieve these goals during a brief one-on-one motivational enhancement session. Participants randomized to the intervention condition also continue to receive the standard of care for alcohol use provided in the clinic.

Standard-of-care condition

Women receiving treatment for HIV/HCV at the two clinical care sites are routinely asked about their alcohol and other substance use and counseled to avoid alcohol and other substances by clinical staff. When the treating clinician deems appropriate, women are referred to community-based care for substance use treatment. In addition, all women receive an educational brochure with information describing the adverse effects of alcohol use for persons with HIV/HCV co-infection and a list of community-based resources to seek further help.

Criteria for discontinuing or modifying allocated interventions {11b}

A staff psychiatrist assesses women's mental health as part of routine care and as requested by a treating clinician, and refers women diagnosed with alcohol dependence to substance use treatment. The psychiatrist may recommend discontinuation of participation in the trial if a participant is deemed psychologically incapable of continued participation.

Strategies to improve adherence to interventions {11c}

The intervention consists of taking a brief computer-based program; therefore, the key strategy to promote adherence are the outreach efforts to invite women back to the clinic to complete the first and follow-up sessions. To improve adherence, research staff will call participants to schedule visits, using contact information on file at the clinical sites.

Relevant concomitant care permitted or prohibited during the trial {11d}

All routine treatment procedures for women in care for HIV and HCV, as deemed appropriate by the patient's treating clinicians, are permitted during the trial.

Provisions for post-trial care {30}

Trial participation does not present more than minimal risk to subjects beyond those encountered as part of routine care. Therefore, no special provisions for post-trial care were included.

Outcomes {12}

Biomarkers (EtG and PEth) will be used to assess the efficacy of the intervention on alcohol use patterns and two associated health outcomes, HIV and HCV, as described below.

The primary outcome measure used to evaluate the efficacy of the adapted computer-based alcohol reduction intervention condition, relative to the standard of care condition, will be the proportion of women who test EtG negative at each of the follow-up assessments over 9-months.

HIV disease progression is evaluated based on changes in HIV viral load and CD4+ count over the 9-month follow-up period in the intervention arm relative to the control arm. HCV disease progression is assessed using two noninvasive biomarkers collected routinely as part of ongoing HCV care. The first is FibroTest which uses six separate biomarkers (α 2-macroglobulin, haptoglobin, γ -glutamyl transpeptidase, apolipoprotein A1, alanine transaminase, and total bilirubin) to generate a score that is correlated with the degree of liver damage.⁴³ The second is FibroScan, a specialized ultrasound that measures degree of fibrosis and steatosis in the liver, providing objective and quantifiable measures of HCV-associated liver damage.⁴⁴ The procedure is painless and performed at point of care.

Participant timeline {13}

[Insert FIGURE 2]

Sample size {14}

The samples size of 200 women (1:1 allocation ratio) was arrived at based on a power analysis. The most conservative hypothesis compares differences between trial conditions in the proportion of participants detected with a negative EtG test over the 9-month follow-up. EtG was selected for the power analysis because it is a sensitive biological test of alcohol use, and has a broad alcohol detection

window (5 days). The power calculations for the negative EtG test were based on our previous pilot study in which 30% of HIV/HCV-infected Russian women were identified with a negative alcohol use biomarker. Our study is powered to detect a small effect ($\delta = -0.2$; odds ratio = 0.3) in number of women testing EtG negative under a repeated measures logistic regression analysis framework, assuming an intra-cluster correlation of 0.10.

Recruitment {15}

Recruitment is conducted at two affiliated clinical sites that provide comprehensive HIV care. The study coordinator in Russia, a medical doctor with specialization in infectious diseases, reviews medical records to assess for potential eligibility. A clinician at each clinic then invites participants to the study and schedules a follow-up visit with a research staff member.

Assignment of interventions: allocation

Sequence generation and Concealment mechanism {16a} {16b}

We use concealment of allocation techniques to promote unbiased randomization.³⁵ A computer algorithm is used to generate a random allocation sequence prior to the study initiation. The random allocation sequence is generated in the U.S. and shared with Russian staff to implement.

Assignment of interventions: Blinding

Who will be blinded {17a}

Because the intervention entails completing a computer-based program, neither providers nor participants are blinded to the intervention assignment; however, the statisticians conducting the efficacy analyses will be blinded to allocation. Research members in Russia will assign a code to each of the two arms; which will be undisclosed to U.S.-based data analysts.

Data collection and management

Plans for assessment and collection of outcomes {18a}

Data for efficacy assessment is collected at baseline, and 3-, 6- and 9-months post-intervention initiation using multiple data-capture modalities. Participants complete a brief self-report survey assessing basic demographics, and history of alcohol and other substance use. The trained attending clinicians, one at each clinic, collect two biomarkers: 1) a urine sample from each woman at each study visit for EtG analysis, which assesses recent alcohol use; and 2) a dried blood spot at the 9-month follow-up for phosphatidylethanol (PEth) analysis, which measures alcohol use over the past 21-days. A research staff member abstracts via medical record review the following data: (a) length of HIV and HCV infection, (b) HIV viral load, (c) CD4+ count, (d) FibroTest score (based on liver function biomarkers, such as

apolipoprotein A1, alanine transaminase, and total bilirubin, etc.), (e) prescribed ARV regime, and (f) HCV treatment.

Plans to promote participant retention and complete follow-up {18b}

Based on a previous trial in this population³⁷ and on pilot work during adaptation of the computerized intervention, we expect loss-to-follow-up to be minimal and to not exceed 10%. Factors to improve intervention adherence and prevent loss-to-follow-up over the 9-month follow-up period are that all research personnel and clinical staff are highly qualified and trained in working with PLWH; that most patients have a trusting relationship with study clinicians; and that all research staff are from Saint Petersburg. In addition, staff will call participants to schedule subsequent research visits. Participants' contact information is on file at the clinical care sites.

Data management {19} and Confidentiality {27}

In accordance with the National Institutes of Health (NIH) requirements, the clinical trial established a data and safety monitoring plan to ensure participants' privacy and confidentiality during the trial and as part of data collection and storage. The plan is overseen by a four-member committee composed of the principal investigators and a study coordinator in Russia.

The data safety and monitoring plan stipulates that all records pertaining to the study and all original and electronic data files are to be securely stored off-site, in a locked metal file cabinet, accessible only to one of the Russian-based principal investigator. This is also true for completed and signed consent forms. To ensure participants' safety as well as the data's validity and integrity, only staff with extensive experience in the area of HIV/HCV treatment will be hired. All research staff will receive training on data collection, management and storage procedures (including of survey data and biomarkers), as well as confidentiality and research ethics. On an ongoing basis, the Russian-based study coordinator will review the data to ensure data quality, including checking range of values, and identifying any inconsistencies in the data. No names or other identifying information appears on data documents or in data files. Pen and pencil surveys will also contain no identifiers. Only designated staff will have access to the data at each site. Presentations and publications will not disclose the name of the sites where the research took place. When the final dataset is made publicly available, data will not contain identifying information.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

At baseline and at each follow-up assessment, women provide a urine sample, which is analyzed for EtG at the [redacted]. The limit of detection is >500 ng/mL. In addition, at 9-month follow-up, clinicians collect dried blood spot samples, which will be analyzed for PEth using U.S. Drug Testing Laboratory standardized procedures (USDTL, Des Plaines, IL). The PEth samples are analyzed at the [redacted] in Irkutsk, Russia. The limit of detection is 8 ng/mL; any result above this threshold is considered positive for alcohol consumption within the last 21 days. Urine samples will be disposed of immediately following

analysis at point of care. The dried blood spot cards will be labelled with a participant number to protect the participants' identity and stored at -30 degrees Celsius at the main clinical site, until shipped to Irkutsk for processing. These biological specimens will be destroyed after processing.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

We will use an intent-to-treat analysis and logistic and linear generalized estimating equations to evaluate intervention efficacy, relative to the standard-of-care, in enhancing the proportion of women with a laboratory-confirmed negative EtG over the follow-up period, thus evaluating whether there was a significant reduction in alcohol use in the intervention group, compared to the control group. Given that there is no consensus regarding safe levels of alcohol use among HIV/HCV-infected individuals^{45,46} and current recommendations are to abstain from alcohol use,⁴⁷ a key outcome is the proportion of women who test EtG negative (<500 ng/mL) over the 9-month follow-up in each trial condition. To triage results with self-reported patterns of alcohol use and EtG, we will also use a novel alcohol use biomarker, PEth collected once at follow-up. We will conduct multilevel regression analyses to account for clustering effects of the two sites, and between- and within-subject variation. Following the conventions in most trials, we will model treatment differences as a fixed-effect and use random effects for modeling the clustering effects of cohort and repeated measures data.

We will utilize a similar analysis to assess whether the intervention resulted in differences in liver disease progression by assessing changes in indirect serum markers of liver function based on mean FibroTest scores and direct biomarker of disease progression, FibroScan, and whether the intervention had an effect on HIV disease progression by assessing changes in mean viral load and CD4+ levels between the two conditions.

Oversight and monitoring

Steering and data monitoring committee {5d} {21a}

A four-member oversight committee, composed of the principal investigators and the Russian-based study coordinator was formed, and is in charge of quality assurance and compliance with recruitment and study procedures. The committee meets virtually on a monthly basis to assess project progress, review modifications, and monitor compliance with guidelines from the relevant institutional ethics committees and The Office for Human Research Protections of the U.S. Department of Health and Human Services. The committee is independent from the sponsor and none of the members have competing interests to declare.

Adverse event reporting and harms {22}

A system for monitoring and reporting of adverse events was put in place. All research team members were trained on the recognition and documentation of any unusual events or circumstances that may

occur during data collection. Researchers will record their observations on comment cards that will be reviewed by the study coordinator. Should a serious adverse event occur, the study coordinator will immediately inform the principal investigators who, in turn, will immediately inform New York University's Institutional Review Board (IRB). If an adverse event appears to be research-related, it will be reported to the Office for Human Research Protections of the U.S. Department of Health and Human Services and to the funding institution project officer, along with summaries of discussions concerning the event. The funding institution project officer will be informed of any IRB action taken concerning any adverse event. Research staff will be monitored closely by the principal investigators and the study coordinator. Staff deficits will be addressed via additional training, close monitoring for proficiency, and if not adhering to established protocols and procedures, will be terminated.

Frequency and plans for auditing trial conduct {23}

Semi-annual field visits will be conducted by the principal investigators to assess that procedures are being implemented as planned at all sites. These audits are independent from the sponsor and will entail observation of data collection efforts.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

Changes to the proposed protocol will require a re-submission to the IRB of both institutions, as well as updates to the trial registry. If changes to the protocol are different from what was explain to participants during consent, participants will be duly informed of the modifications and re-consented by research staff before continuing in the study.

Dissemination plans {31a}

Trial results will be shared in peer-reviewed publications that are open-access as well as at national and international research and policy conferences. The final data set will be available through an open access data repository.

Discussion

If efficacious in reducing alcohol use, this brief computer-delivered intervention for alcohol using HIV/HCV co-infected women in Russia would have a number of advantages. First, the computer-based platform affords participants greater confidentiality, thus encouraging participants to set realistic goals without perceiving pressure from healthcare providers. The digital platform offers greater flexibility of administration, for example, participants can go through the program at their own pace. Importantly, the participants' ability to replay segments of the intervention as needed may reinforce risk reduction by enhancing learning and alcohol reduction messages.

The proposed intervention is novel in several ways. First, it is delivered through a computer-based platform. Computer-delivered alcohol reduction interventions have been found to be effective in reducing

problematic alcohol use, albeit with small effect sizes,^{31,32} and may be more cost-effective than existing interventions delivered by experienced clinical providers. A computer-based platform offering a brief intervention is less labor- and cost-intensive than traditional interventions, and has the potential to be more feasible for integration into the clinical care setting. Third, the study collects two alcohol use biomarkers to assess intervention efficacy, rather than relying on self-report, which is prone to reporting biases. Data from a previous study with this population indicated that alcohol use was often underreported.⁴⁸ It will also utilize objective markers of liver function and HIV and HCV disease progression.

As the HIV and HCV epidemics continue to grow, increasing the number of people in care, the computerized intervention program may allow for more patients to receive critical messages related to alcohol use, while reducing the burden on trained healthcare providers in an already heavily demanding clinical care setting. A computer-based intervention may be as or more efficacious (the objective of this trial is to assess efficacy relative to standard care) than other service delivery modalities but less labor intensive and less costly to implement and sustain. Because of the ubiquity and affordability of Wi-Fi and portable technology in clinical care settings in Russia and the limited demand of the intervention on healthcare providers' time, this computer-based intervention may be a feasible and cost-effective option for scale-up and dissemination to other HIV centers in Russia, and even to other clinical settings where alcohol use may be problematic, such as at obstetrician-gynecologist clinics and maternity hospitals. If efficacious, our intervention may be a feasible and cost-effective way to reach women with problematic drinking patterns at point of care and integrated to comprehensive HIV-delivery services.

Trial Status

All women have completed baseline assessment and we are currently working on scheduling women for follow-up assessments. Protocol version number 6, October 29, 2019. Recruitment began in January 2018 and was completed in October 2019. The protocol was submitted after the end of recruitment but prior to the end of the last patient visit. No significant modification were made to the protocol following the end of recruitment.

Abbreviations

ARV antiretroviral

EtG ethyl glucuronide

HCV hepatitis C virus

HHS U.S. Department of Health and Human Services

HIV human immunodeficiency syndrome

ICPSR Inter-University Consortium for Political and Social Research

IRB institutional review board

NIH National Institutes of Health

NYU New York University

OHRP Office for Human Research Protections

PEth phosphatidylethanol

PLWH person living with HIV/AIDS

PWID person who injects drugs

USDTL U.S. Drug Testing Laboratory standardized procedures

Declarations

Acknowledgements

Not applicable.

Authors' contributions {31b}

RJD, JLB, VR and NB are the principal investigators who conceived the study and led the proposal and protocol development, and were responsible for quality assurance and oversight.

EB was the Russian project coordinator, monitoring data collection, and in charge of patient follow-up.

LVG and NBK are the clinicians in contact with patients and in charge of collecting data

AC, NR, and JMS supported protocol implementation and U.S.-based coordination support

AC wrote the first draft of the manuscript. RJD and JLB edited and made substantial contributions to the manuscript.

All authors read and approved the final manuscript.

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The funding body had no role in the design of the study; collection, analysis, and interpretation of data; or in writing the manuscript.

Availability of data and materials {29}

We will deposit the final data set and codebook with the Inter-University Consortium for Political and Social Research (ICPSR) located at the University of

Michigan. ICPSR confidentiality requirements will be followed

(<http://www.icpsr.umich.edu/irb/index.html>). ICPSR will make the data permanently available to over

700 academic member institutions, permitting other researchers to conduct secondary analyses using the data set. Data availability will be announced at the ICPSR website.

Ethics approval and consent to participate {24}

The institutional review boards of New York University (number IRB-FY2019-2519) and Saint Petersburg State University (number 02-186) approved all study protocols. Written, informed consent to participate is obtained from all participants.

Consent for publication {32}

Not applicable.

Competing interests {28}

The authors declare that they have no competing interests.

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Figures

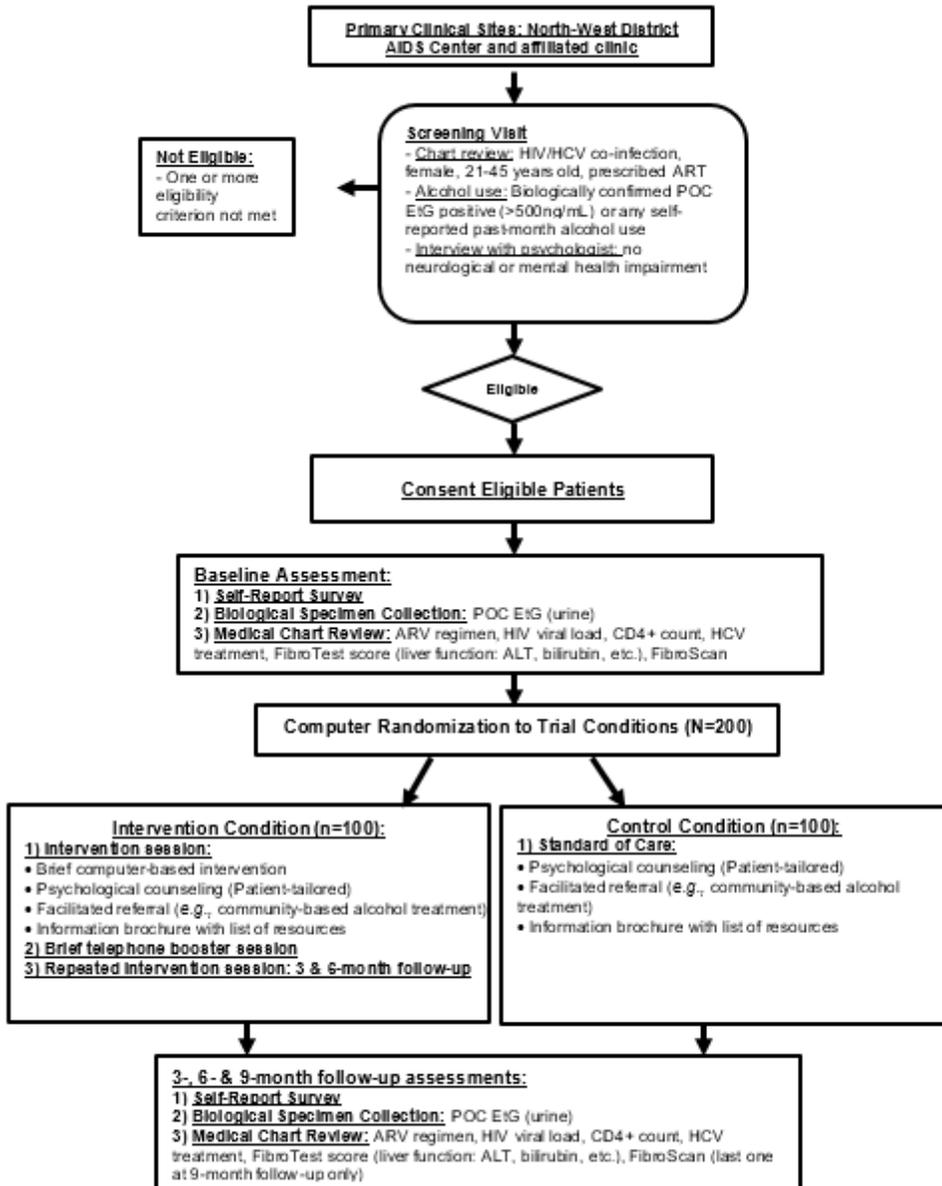


Figure 1

Trial flow diagram

	Enrolment	Allocation	Post-allocation				
	T0	T0	T1	T2	T3		
ENROLMENT:							
Eligibility screen	X						
Informed consent	X						
Allocation		X					
INTERVENTIONS:							
<i>Standard of care</i>			X				
<i>Computer based intervention</i>			X	X	X		
ASSESSMENTS:							
<i>Socio-demographic data</i>	X						
<i>ETG</i>	X		X	X	X		
<i>PEth</i>				X	X		
<i>FibroScan</i>	X		X	X	X		
<i>HIV viral load</i>	X		X	X	X		
<i>CD4+ count</i>	X		X	X	X		
<i>Self-reported alcohol use</i>	X		X	X	X		
<i>ARV regime</i>	X		X	X	X		

Figure 2

Standard Protocol Items; Recommendations for Interventional Trials (SPIRIT) schedule of enrollment, interventions, and assessments