STATISTICAL ANALYSIS PLAN

Title: Brief Electronic Intervention for Heavy Drinking and Sex Risk Among Men who have sex with Men Seeking HIV Testing

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C. DESCRIPTION OF THE STUDY

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C.1 Significance and Specific Aims of Project

The annual rate of new HIV infections among men who have sex with men (MSM) in the United States continues to grow rapidly, despite stability or decline among other groups[1]. Population-level HIV prevalence among MSM in North America is estimated at 15.4%[2], far and away the highest of any group. These data reflect the pressing need to continue developing and testing new tools for prevention among MSM that are well-positioned to reach those at highest risk. Responding to these risks is also consistent with goals identified in the *US National Strategy on AIDS* aimed at reducing new infections and overall health disparities among MSM[3]. Although a number of sex risk reduction interventions exist for MSM, barriers to dissemination and/or implementation limit their reach, and they fail to address pivotal factors that lead to high-risk behavior, such as alcohol use[4; 5]. Alcohol has been referred to as 'the forgotten drug in HIV/AIDS"[6], and reviews of the HIV epidemiology literature have highlighted the role of alcohol in fueling HIV transmission among MSM[7]. To date, only 7 interventions have been rigorously tested for efficacy in reducing heavy alcohol use among MSM[8], and all involve lengthy treatment protocols that present substantial barriers to their widespread use.

We propose a three-year study to develop and pilot test a brief, combined behavioral prevention intervention to reduce heavy drinking and unprotected anal intercourse (UAI) among HIV-negative MSM who are seeking HIV testing services offered in community settings. Individual-level behavioral interventions (BIs) can often be administered in a single session and offer a potentially effective solution for both providing prevention services in resource-constrained contexts and reaching MSM at highest risk for HIV acquisition[9; 10]. Brief BIs have been independently shown to be effective in reducing HIV risk in MSM and in reducing hazardous alcohol use in other populations. Our preliminary research supports the efficacy of a combined intervention for heavy drinking and sex risk, guided by the principles of motivational interviewing (MI), among HIV+ MSM and other high-risk groups. As such, combining existing interventions into a multi-component BI could yield robust prevention outcomes, particularly in MSM, among whom both behaviors are prevalent[2; 11]. Moreover, adapting each of these approaches into a technology-based format and optimizing them for use with tablet computers could leverage existing technology in order to maximize the reach and impact of the intervention on this priority population, one that eludes traditional public health and clinical interventions.

The proposed research has two phases: ***Phase 1*** *involves an iterative development process, based on qualitative research, that focuses on: (a) adapting existing combined, MI-based alcohol and sex risk intervention components to a technology-based format, and (b) understanding and addressing challenges in implementation, feasibility, and acceptability with high-risk MSM in community settings. Initial versions of the intervention (pre-alpha and alpha versions) created during Phase 1 will be heavily informed by Co-PIs, consultants, and developers. Subsequent (beta) versions will be informed by Phase 1 research, using focus*

groups, individual interviews, and theatre tests with high-risk MSM and other stakeholders. ***Phase 2*** *entails conducting a randomized-controlled pilot test of the intervention to explore its effects on HIV-risk behavior and alcohol use among MSM seeking testing in community-based outreach venues.*

Proposed Study and Specific Aims

Specific Aim 1: *Adapt existing protocols for MI-based combined BIs – which have previously been shown to reduce unsafe sex and heavy drinking – for use on tablet computers with MSM in community settings.* This will be accomplished in an iterative developmental process using qualitative methodologies with target group members and local stakeholders to produce a feasible and acceptable brief, technology-based intervention program for pilot testing in Phase 2.

Specific Aim 2: Conduct a small randomized-controlled pilot study ($N = 40$) examining the preliminary effects of an adapted and integrated tablet-based BI, compared against an attention-matched control, in reducing sexual risk and alcohol use among a sample of high-risk MSM seeking HIV testing in a community venue. We will evaluate our primary HIV-related outcomes (sexual risk behavior and alcohol use) at 1-, 3-, and 6-month follow-ups and conduct process evaluation to examine implementation procedures. Quantitative and qualitative data will be used to inform any further modifications that might be necessary for conducting a larger, randomized controlled trial of the intervention.

Overall, this research will produce the first known combined, theory-based, technology-adapted intervention for alcohol and HIV risk among high-risk MSM in community settings. Use of a tablet-based, portable platform for intervention delivery is a particularly innovative feature that offers a number of important advantages over traditional intervention approaches. Should pilot data provide initial evidence of efficacy, this research will provide the groundwork for a future full-scale randomized controlled trial that tests the effects of this intervention on co-occurring HIV and alcohol risk behaviors and biological indicators of risk in MSM.

C.2 Participant Population

Across all phases of the research, data will be collected from two groups: (1) Key informants (including health/social service providers, volunteer testing staff, and commercial sex venue staff; for Focus Groups, Phase 1a) and (2) high-risk MSM attending local commercial sex venues. Thus, 24 key informants, and 75 high-risk MSM participants (Individual interviews, $N = 35$; Pilot study, $N = 40$) will be recruited as a part of this research. Key informants will be recruited based upon existing community contacts and referrals. High-risk MSM participants will be recruited from the target venues after they have completed HIV testing and they report non-reactive results. All participants will be individuals aged 18 and older. The use of participants older than 18 is appropriate to ensure applicability of findings to adult populations of men who have sex with men (MSM) at risk for HIV infection. No special or vulnerable populations, as defined by 45 CFR Part 46 (e.g., prisoners, pregnant women, fetuses) are involved.

High-risk MSM participants will be recruited through their indication of interest in participating in a research study on a standard "exit" assessment form that is collected by AIDS Project Rhode Island (APRI) after conducting rapid oral HIV testing and counseling at the venues. To ensure anonymity during the testing procedure, participants will only be approached by research staff after all standard HIV testing and counseling procedures are completed, and after APRI staff and participants verbally confirm a negative HIV testing result. This procedure

will ensure both that the anonymity of testers is maintained and that only those that are HIV-negative are recruited. Given that those seeking testing from these settings come from diverse racial/ethnic backgrounds, we expect that the proposed research will be capable of recruiting a similarly diverse sample.

Inclusion criteria for the research (Phases 1 and 2) are as follows:

1. Biologically male
2. Aged 18 or older
3. Fluent English speaker
4. Unprotected anal sex with a casual male partner at least once in the past 3 months
5. Heavy alcohol use during the past 2-weeks (>14 drinks per week, or at least one occasion of 5+ drinks on a given occasion)
6. Breath alcohol concentration (BrAC) of .000 at the time of enrollment
7. No history of complex alcohol withdrawal
8. Score of <4 for methamphetamine and <3 for cocaine and heroin/opiates on the SDS
9. HIV-negative

Exclusion criteria:

1. Individuals who are HIV-positive
2. Individuals who participated in other phases of the research
3. Individuals who report being coerced to participate

C.3 Recruitment Procedures

We will recruit participants who have sought and consented to voluntary, rapid oral-swab HIV counseling and testing (VCT) and subsequently test negative. Testing is free, anonymous, and conducted by APRI at two sites from which we will recruit: (1) AIDS Project Rhode Island offices and (2) a local Providence, RI bathhouse (Megaplex). See Appendix C for consent documents for individual interview participants. See Appendix D for consent documents for pilot study participants. Staff at both venues have arranged for private, quiet spaces in the venue that allow patrons to enter and complete testing anonymously. After testing, standard APRI protocol involves administration of a brief, anonymous questionnaire regarding testers' risk behavior and other concerns. An item inquiring about participants' potential interest in participating in the study will be added to this questionnaire and will signal to the APRI tester to refer the patron to study staff. Research staff, after confirming a negative HIV-test, will enter the private testing area and discuss the research with the participant in further detail. Upon consenting and enrolling in the research, research staff will collect minimal identifying data for the purposes of scheduling an interview session (Phase 1-b, individual interviews) or contact to encourage retention and provide payment (Phase 2, pilot study), including names, telephone numbers, and e-mail addresses. These data will be stored according to protocols for handling sensitive information, and we will destroy all identifying information after the study is completed. Study participants will be reimbursed for participation. Reimbursement amounts are determined according to the amount of time involved in each phase of research, and are consistent with standard reimbursement amounts for research involvement at the Center for Alcohol and Addiction Studies and Center for AIDS Research at Brown, thus posing little risk of coercion. Those

participating in Phases 1-b (individual interviews) will be paid $50, and those in Phase 1-c (theatre testing) will be paid $30. Those participating in Phase 2 will receive $50 for completing the baseline session (consisting of the intervention and baseline assessment), and $50 for each of the 1-, 3-, and 6-month follow-ups, with an extra $50 bonus for completing all three assessments. Phase 2 participants will be paid in cash after each follow-up appointment, with a bonus payment added after the 6-month appointment is complete

C.4 Design and Methods

PHASE 1: INTERVENTION DEVELOPMENT/REFINEMENT

C.4.1. Initial Development (α-version). Phase 1 will begin with the study team meeting to identify the core components of MI-based alcohol and sex risk interventions and developing an initial flow of the intervention content. These discussions will guide the construction of feature sets, wireframes, and flows to provide to web developers to aid them in creating a preliminary version of the intervention's components. This process will result in production of a preliminary □-version of the tablet-based intervention.

BI for sex risk reduction. Brief BIs for reducing HIV-risk behavior based on principles of MI focus on exploring current behavior and its consequences, and examining whether this behavior is congruent with one's goals. Based upon these goals, the intervention then provides a menu of options available for behavior change, and discusses various ways of initiating that change and reducing harm based on personal goals. PCC[9; 10], one of the only brief BIs for reducing HIV-risk among MSM to date, involves exploring the motivational, interpersonal, and behavioral precursors and effects of a specific unsafe sex episode, and whether these factors contribute to behaviors that are commensurate with one's goals. To facilitate this, PCC uses a uses a questionnaire to guide later education, feedback, and risk reduction planning tailored specifically to participant responses, and thus is highly algorithm-based. As such, elements of PCC are highly amenable to computerization, while achieving optimal relevance to individual participants (see 3C.6. Pilot Data, for more detail about our preliminary adaptation of PCC components). Rather than incorporating all components of PCC (which may result in an overly long intervention), we will incorporate those aspects of PCC that are most consistent with an MI-focus, using these components to support participants' identification/monitoring of factors that contribute to behavior that is discrepant with their goals.

In addition to content related to reducing sex risk behavior, the intervention will also be well-positioned for facilitating patrons' connection with other existing prevention resources (e.g., PrEP, STI screening, further testing). As such, based on the respondents' individual risk profile and previous engagement with these services, additional information will be provided concerning how and where specific resources can be located (see Appendix F for info card).

BI for alcohol use. Personalized feedback interventions (PFIs) involve delivering feedback on a range of data including comparisons of one's drinking with that of relevant proximal norms, challenging personally-relevant alcohol-related expectancies, conducting decisional balances related to use, presentation of practical use consequences (e.g., time and money spent, calories consumed), as well as strategies for harm reduction[47]. PFIs are frequently delivered electronically and used in conjunction with motivational interviewing (MI)[48]. These interventions can be readily tailored to MSM-specific needs and integrated with sex risk reduction components in an MI-consistent manner. Dr. Kahler's clinical trial with HIV-infected MSM uses this approach.

Combined BI. The proposed combined BI would utilize aspects of existing evidence-based BIs for alcohol use and HIV-risk behavior, and integrate their components to discuss the relationships between the two behaviors, including how engaging in alcohol use can potentiate HIV-risk behavior and how beliefs and attitudes about alcohol can affect this relationship. Combined BIs can also address how one's goals (e.g., health) and change efforts can be relevant to both behaviors. Table 1 presents an initial, brief outline of possible intervention components. The intervention will first involve a brief assessment completed via tablet, which will ask briefly about sex risk behavior, motivation for reduce drinking and sexual risk (including "stage of change"), collect a 30-day Timeline Follow-Back[91] of alcohol use and sexual behavior, and ask about engagement with other biomedical prevention activities (e.g., PrEP, STI screening). These items will be used to both determine eligibility and inform the content of the intervention. Although the intervention components are separated into discrete topic areas (alcohol use vs. HIV-risk), each component provides an opportunity to present content about how these behaviors intersect. For example, the expectancies module can address alcohol-related sex expectancies, which may promote both drinking and sex risk among MSM[29]. See Appendix A for additional detail. This process of development will result in a single-session BI, lasting approximately 50 minutes (based on our initial timing of several components; see 3C.3).

Table 1. Proposed Initial Intervention Components

Alcohol use

1.) Profile and norms
2.) Practical costs/consequences & gains from change
3.) Challenging alcohol-related expectancies
4.) Decisional balance (Pros and cons)
5.) Menu of options for changing drinking and plan for change

HIV risk reduction

1.) Profile and norms
2.) Decisional balance
3.) Feedback about sex risk reduction motivation and goal choice
4.) Factors contributing to past sex risk
5.) Risk reduction planning

Technical development. The intervention components will be presented via a web application (hosted on Brown University's web servers), and will be designed to be engaging, visually-appealing, and entertaining. The application will be dynamically optimized for tablet, mobile, or desktop-based delivery based on data from the device's web browser. Study-specific logins will be used to access the program from tablets at the study site. Participants can then use the application to navigate through the BI's components, including introduction, initial assessment, each module, and follow-up. User-provided data will be collected via baseline assessments, interactive modules during the intervention, and items within each component. These data will be used to tailor the intervention content to each participant, and will be accomplished using MySQL. To ensure that the application is entertaining and engaging, an animated cartoon "doctor" will guide participants through the assessment and intervention components, using humor where appropriate. Consistent with the spirit of MI, this character's narration will also involve a non-confrontational, non-judgmental tone, and will be specifically tailored to the needs of MSM. Interactive graphics, charts, videos, and "games" will also be used throughout. All animation and interactive web components will be produced using HTML5.

C.4.2.1. Procedures for Refinement. After the α-version is produced, we will use qualitative methods to elicit narrative feedback from key informants (focus groups; Phase 1a), individual interviews with MSM testing in these settings (clinic/bathhouse; Phase 1b) and from a small sample of theatre testers, who will use the software at the proposed study site (Phase 1c). These data will provide rich contextual information on key issues relevant to conducting interventions with high-risk MSM, the cultural appropriateness of the α-version intervention, conducting prevention activities in a community/outreach-based context. These data will also provide initial ratings of satisfaction, feasibility, and acceptability. We anticipate that several areas will need to be adapted based on this formative research, including: (1) use of relevant, local behavioral/social terminology, (2) adapting core components to match those identified as important by interviewees, (3) adjusting particular components (voice of the narrator, visual aids, etc.) based on logistical issues identified, (4) reviewing applicability of evaluation measures, (5) identifying strategies to enhance recruitment, follow-up, and retention, (6) altering the program to fit within the existing community setting-based VTC protocol, and (7) optimizing the methods for delivering summary feedback at the conclusion of the intervention (e-mail vs. hardcopy print-out). Based on this formative research and precise timing of the intervention components in Phase 1, we will also cut back on intervention content in order to arrive at a 50-minute BI, consistent with a standard clinical hour. After analyzing Phase 1 data, the study team will suggest revisions to the intervention based on our findings, and meet with developers in order to incorporate the recommended changes. This process will ultimately result in production of a □-version with all features integrated that will then be used for Phase 2 pilot testing.

Phase 1a: Key informant focus groups. We plan to conduct three focus groups (N=8) with key informants, including health/social service providers, volunteer testing staff, commercial sex venue staff, and community leaders. Eligibility criteria will include being 18 years or older, with a qualified understanding of local MSM community needs. Participants will be recruited from organizations or groups that work within MSM communities, identified through referrals and existing relationships. Focus groups will be digitally recorded, facilitated by a senior investigator (Dr. Operario), and attended by a member of the research staff, who will take notes. Focus groups will take place in private research rooms to maximize confidentiality, will last roughly 2 hours, and members will receive $50 for participating, an amount consistent with similar research studies conducted in Providence. Focus group members will involve both general discussion about HIV-risk behavior in MSM and the role of alcohol in this process, as well as provide specific feedback about each component of the □- version BI.

Phase 1b: MSM individual interviews. We will also recruit a sample of 25 MSM from within the Providence bathhouse to participate in individual qualitative interviews. Individual interviews will inform the further refinement of the intervention, and provide preliminary data on acceptability and feasibility. Eligibility criteria will include being (1) male, (2) 18 years or older, (3) fluent in English, (4) HIV-negative, (5) residing in the greater Providence, RI area, and (6) reporting unprotected anal sex with a casual male partner at least once in the past 3 months[12]. In these interviews, a semi-structured protocol will first guide participants through the α-version intervention and ask them to comment on each of the core intervention components, with a particular eye on optimally adapting existing protocols to the realities of high-risk MSM. In addition, interviews will ask participants about their perceptions of prevention efforts conducted in bathhouses and other MSM-oriented venues (bars, nightblubs, adult bookstores), and ask them

to reflect on specific challenges that might affect the uptake of risk reduction efforts in the target settings (e.g., ability to attend, overall length). Interviews will last 2 hours, and participants will receive $50 for their participation.

Phase 1c: Theatre testing of BI alpha-version. We will recruit a sample of 10 MSM, using the eligibility criteria from Phase 1b, to conduct a "theatre test" of the BI. MSM who participated in earlier phases will be excluded to provide different perspectives. Participants who are seeking HIV testing at the target venues will be recruited using a screening item concerning their interest in the study that will be included on the standard post-test assessment, and their participation will be anonymous. Interested participants will simply wait in the testing room for study staff after VCT is complete. Staff will then provide them with a tablet and headphones in order to complete the full intervention. Afterward, participants will complete a brief questionnaire and interview about their perceptions of the acceptability and feasibility of delivering a BI in this environment, as well as comments they have about each BI component. Participants will receive $30 for completing the theatre test.

Qualitative analysis. Recordings of all focus groups and interviews will be transcribed via commercially available software. Data will be analyzed using modified grounded theory methods[90], with two independent coders arriving at a consensus on major themes identified. This qualitative data will allow us to refine the assessment instruments and BI components for population sensitivity. As such, the study team will review the analysis, and assess the strengths/weaknesses of each of the components based on these findings.

C.4.2. PHASE 2: PILOT TESTING

Specific Aim 2 is to conduct a pilot randomized controlled trial of our BI, and explore preliminary evidence of its efficacy for reducing sexual risk and alcohol use among a sample of high-risk MSM seeking HIV testing in community venues. As such, we will randomize 40 MSM who receive HIV testing at the identified venues to either the standard VCT group + attention-matched control (AC), or the VCT + Intervention (BI) group. We will test the hypothesis that those in the BI group will report reductions in sex risk outcomes, sex under the influence of alcohol, and alcohol use at 1-, 3-, and 6-month follow-ups compared to the VCT+AC group.

C.4.2.1. Methods

Eligibility. Criteria for inclusion in this portion of the study are: (1) Male, (2) age 18 or older, (3) fluent in English, (4) self-reported unprotected anal sex with a casual male partner at least once in the past 3 months[12], (5) heavy alcohol use during the past 2-weeks (>14 drinks per week, or at least one occasion of 5+ drinks)[13], (6) register a breath alcohol content of .000 upon recruitment, (7) no history of complex alcohol withdrawal, (8) scoring < 4 on severity of dependence scale (SDS) for methamphetamine[14], and < 3 on the SDS for cocaine and heroin/opiates[15; 16], (9) HIV-negative as indicated during their preliminary HIV testing, and (10) willing to provide phone and email contact information (see Design Considerations section below for further detail). Participants who test HIV+, score highly on the SDS, or participated in Phase 1 of the research will be excluded from participation. Those testing HIV+ will be referred to a comprehensive care clinic at the Miriam Hospital for treatment, as per the standard protocol of our collaborating agency. Those with high SDS scores will be provided with lists of local MSM-friendly drug treatment providers.

Recruitment. We will recruit participants from among those seeking HIV testing at the identified community-based venues. Patrons who are interested in participating indicate this on

their standard HIV testing "exit" form, which is anonymous. After APRI staff deliver negative results, participants will remain in a private room, where our research study staff will enter and provide further information about the study.

Baseline Assessment. All assessments will be completed on the tablet and administered by a research assistant that is blind to experimental condition. Study staff will first acquire informed consent and deliver the tablet to begin collecting baseline/screening measures. While ineligible participants will be informed of this on the assessment screen, eligible participants will then proceed directly to complete other baseline measures. Participants will receive $50 for the baseline session, which may take up to 90 minutes.

Randomization/Design. Participants will be randomly assigned to either the control or intervention groups by the software. Those randomized to the BI condition will complete the intervention, which will be delivered on a Windows tablet (with noise-cancelling headphones). Those randomized to the AC group (attention control) will watch a set of videos on the tablet on improving dietary and exercise habits. At the end of their session, participants in both groups will complete brief exit interviews and confirm contact information.

Follow-up Assessments. Follow-up assessments will be conducted at 1-, 3-, and 6-months following the intervention session. At each of these intervals, study staff will call participants and ask to schedule an appointment to come to the research offices. At these 45-minute appointments, participants will complete an assessment battery delivered on a tablet. Participants will receive $50 for each assessment appointment, plus a $50 bonus for completing all follow-up assessments.

C.4.2.2. Measures (see Appendix E)

Baseline/Eligibility Assessments. The SDS[17] will be used to assess symptoms of substance dependence for methamphetamine, cocaine, heroin/opiates, and alcohol. The SDS has demonstrated good validity and excellent reliability with respect to these drugs (α=0.80-0.85)[14; 15; 17]. In addition, a 30-day Timeline Follow Back (TLFB)[18; 19], administered online, will be used to assess alcohol use and sexual behavior during that period. The TLFB presents a calendar of each recall period, and participants respond by clicking on a box that represents a given day, answering several questions about that day. Questions will assess the number of standard drinks consumed on that day, the number of hours over which these drinks were consumed, the total number of sex partners, their relationship with each (e.g., steady vs. casual), the HIV status of each (e.g., HIV+, HIV-, or unknown), whether they asked about their partner's HIV/STI status or the last time they were tested, sex acts performed with each, condom use for each act, and whether sexual activity took place while under the influence of alcohol. Meta-analyses have shown that TLFBs for assessing alcohol use and sex behavior are reliable when administered electronically and online[20]. Other studies explicitly comparing online vs. in-person TLFBs for sexual behavior[21], and comparing the TLFB to biological measures for alcohol use[22] have confirmed the validity of online TLFBs. TLFB data will be used to determine participants' drinking eligibility, while single items will assess all other eligibility criteria. Finally, stages of change will be assessed using the Stages of Change (Short Form)[23] and a 4-item stages of change measure for HIV-risk[24-26].

Efficacy outcomes. Our primary outcomes will be the number of unprotected anal sex events, number of sex events under the influence of alcohol, frequency of drinking, and the

number of heavy drinking days over the past month. Outcomes will be assessed via 30-day Timeline Follow Back (TLFB)[91; 93] at each follow-up.

Secondary outcomes. We will also assess whether participants talked to their partners about their HIV/STI status and recent testing, and whether during each follow-up window, participants engaged in self-initiated HIV testing, sought STI screening, or sought information about pre-exposure prophylaxis. Change motivation and stages will also be explored as secondary outcomes.

Exploratory Mediators. As exploratory measures, we will include brief measures of possible mediators of the intervention effect, based on mediators identified in the original BIs. These will include HIV-related knowledge, perceived risk for HIV, peer safe sex norms, and safe sex behavioral skills (e.g., condom negotiation, partner communication skills, self-efficacy)[27-29].

General participant characteristics. Participants will also provide information about general demographic characteristics (e.g., age, ethnicity, income, educational level); general health; current relationship status and relationship history; self-reported history of other sexually transmitted infections (chlamydia, genital warts, gonorrhea, herpes, syphilis, trichomoniasis, Hepatitis B, Hepatitis C); drug use behaviors (SDS), and utilization of other health and social services. We will also administer the Client Satisfaction Questionnaire, a brief 8-item measure assessing satisfaction with services[95].

C.4.2.2. Data Analysis Plan

Descriptive/Exploratory analyses. Behavioral data (e.g., alcohol use and sex risk behaviors) will be tabulated using contingency tables within each condition at baseline and for each follow-up period. We will examine study retention rates at each follow-up and generate a CONSORT flow-diagram.

Primary analyses. Our hypotheses related to Specific Aim 2 are that participants in the intervention group will report (1) fewer unprotected anal sex events, (2) fewer events involving sex while under the influence of alcohol, and (3) lower frequency of drinking and a reduced number of heavy drinking days versus the control group. These hypotheses will be evaluated using an intention-to-treat comparison of the rates of our primary outcomes at 1-, 3-, and 6-month follow-ups, using a incidence rate ratio (IRR) and 95% CI. Given the count nature of the data, we will use a Poisson regression covarying for key baseline covariates, and compare IRRs across the two treatment conditions at each time point. As conclusions about statistical significance will be limited due to the small sample, clinically meaningful differences in the pattern of IRRs and means (for alcohol use variables) across groups will be used to evaluate our hypotheses. However, if available data produce stable results, generalized estimating equations (GEEs) using binomial distributions and logit-link functions will also be used to explore differences in these outcomes across time and treatment condition. We will also explore the potential influence of the intervention on secondary outcomes and exploratory mediators. IRRs and descriptive data will be used to compare the groups in terms of their frequency of talking to partners about their status, whether they sought additional HIV testing, STI screening or information about PrEP. Descriptive mean comparisons and linear regressions controlling for baseline values will be used to compare whether HIV knowledge and perceived risk, peer safe sex norms, and safe sex behavioral skills differ across the groups.

C.4.3. Recruitment

We will recruit participants who have sought and consented to voluntary HIV counseling and testing (VCT) with APRI on-site at outreach venues, and subsequently test negative. The staff at both settings (APRI offices/bathhouse) have arranged for private, quiet spaces in the venues that allow patrons to enter and complete testing anonymously. After testing, standard APRI protocol involves administration of a brief, anonymous questionnaire regarding testers' risk behavior and other concerns. An item inquiring about participants' potential interest in participating in the study will be added to this questionnaire and will signal to the APRI tester to refer the patron to study staff. Research staff, after confirming a negative HIV-test, will enter the private testing area and discuss the research with the participant in further detail. Upon consenting and enrolling in the research, research staff will collect minimal identifying data for the purposes of scheduling an interview session (Phase 1-b, individual interviews) or contact to encourage retention and provide payment (Phase 2, pilot study), including names, telephone numbers, and e-mail addresses. These data will be stored according to protocols for handling sensitive information, and we will destroy all identifying information after the study is completed. Study participants will be reimbursed for participation. Reimbursement amounts are determined according to the amount of time involved in each phase of research, and are consistent with standard reimbursement amounts for research involvement at the Center for Alcohol and Addiction Studies and Center for AIDS Research at Brown, thus posing little risk of coercion. Those participating in Phases 1-b (individual interviews) will be paid $50, and those in Phase 1-c (theatre testing) will be paid $30. Those participating in Phase 2 will receive $50 for completing the baseline session (consisting of the intervention and baseline assessment), and $50 for each of the 1-, 3-, and 6-month follow-ups, with an extra $50 bonus for completing all three assessments. Phase 2 participants will be paid in cash after each follow-up appointment, with a bonus payment added after the 6-month appointment is complete. Recruitment and reimbursement procedures will follow protocols approved by the Brown University Research Protections Office IRB.

C.4.4. Human Subjects Involvement, Characteristics, and Design

Across all phases of the research, data will be collected from two groups: (1) Key informants (including health/social service providers, volunteer testing staff, and commercial sex venue staff; for Focus Groups, Phase 1a) and (2) high-risk MSM seeking test at one of the community-based outreach venues. Thus, 24 key informants, and 75 high-risk MSM participants (Individual interviews, N = 25; Theatre testing, N = 10; Pilot study, N =40) will be recruited as a part of this research. Key informants will be recruited based upon existing community contacts and referrals. High-risk MSM participants will be recruited from among those seeking HIV testing at APRI offices and a local bathhouse. All participants will be individuals aged 18 and older. The use of participants older than 18 is appropriate to ensure applicability of findings to adult populations of men who have sex with men (MSM) at risk for HIV infection. No special or vulnerable populations, as defined by 45 CFR Part 46 (e.g., prisoners, pregnant women, fetuses) are involved.

High-risk MSM participants will be recruited through their indication of interest in participating in a research study on a standard "exit" assessment form that is collected by AIDS Project Rhode Island (APRI) after conducting rapid oral HIV testing and counseling at APRI offices/the bathhouse. To ensure anonymity during the testing procedure, participants will only be approached by research staff after all standard HIV testing and counseling procedures are

completed, and after APRI staff verbally confirm a negative HIV testing result. This procedure will ensure both that the anonymity of testers is maintained and that only those that are HIV-negative are recruited. Given that those seeking testing in these settings come from diverse racial/ethnic backgrounds, we expect that the proposed research will be capable of recruiting a similarly diverse sample.

Inclusion criteria for the research (Phases 1-b, 1-c and 2) are as follows:

10. Biologically male
11. Aged 18 or older
12. Fluent English speaker
13. Unprotected anal sex with a casual male partner at least once in the past 3 months
14. Heavy alcohol use during the past 2-weeks (>14 drinks per week, or at least one occasion of 5+ drinks on a given occasion)
15. Breath alcohol concentration (BrAC) of .000 at the time of enrollment
16. No history of complex alcohol withdrawal
17. Score of <4 for methamphetamine and <3 for cocaine and heroin/opiates on the SDS
18. HIV-negative

Exclusion criteria:

4. Individuals who are HIV-positive
5. Individuals who participated in other phases of the research
6. Individuals who report being coerced to participate

Types of Data. This study will involve collecting four types of data:

1. Focus groups (N = 24) in Phase 1-a, generating written notes, digital recordings, and transcripts.
2. Qualitative process interviews for both individual interviews (Phase 1-b, N = 35), generating written notes, digital recordings, and transcripts, written, open-ended questionnaire data.
3. Quantitative data on clinical outcomes for the pilot sample (Phase 2, N = 40), obtained via electronically-administered questionnaires.

All study procedures, including data collection, will be conducted by either the Contact PI/Project Director (Dr. Wray), Co-PIs (Drs. Operario and Kahler) or a Research Assistant. Research Assistants will receive intensive training in all study procedures from Dr. Wray and other PIs. Procedures for assigning individual participants to trial arms in Phase 2 will be based on a computer-generated randomization sequence that is completed automatically by the software. A randomized design is appropriate for our goal of pilot testing a behavioral intervention.

C.4.4.1. Sources of Materials

In Phase 1a, we will collect data directly from informants using focus group methodology. These methods will produce qualitative data in the form of digital recordings (which will be recorded using a digital voice recorder [DVR]) and transcripts for analysis. Focus groups will be moderated by Dr. Operario and will generate data in the form of written notes, which will contain no individual participant identifiers. We will use the Phase 1a data to adapt

intervention protocols for use with the target populations and settings.

In Phase 1b, we will collect qualitative data in the form of digital recordings (recorded using DVR), transcripts for analysis, and open-ended, paper-and-pencil questionnaires. These interviews will be conducted by a trained RA, with PIs providing comprehensive training and supervision. Interviews will also generate data in the form of written notes, which will contain no individual participant identifiers. We will also collect discussion data directly from participants by asking them to comment and "think aloud" in response to the elements presented to them as they navigate the intervention; these discussions will also be digitally recorded and transcribed. Analyses of these qualitative data will be used to refine the intervention protocol.

In Phase 2, we will collect quantitative data directly from participants using computer-delivered assessments at baseline, 1-month, 3-months, and 6-months. These assessments will produce data on alcohol use and sexual risk behavior during the follow-up periods, and as such, participants will be provided with private spaces within the research offices to complete these measures. All staff members will receive training on ethical follow-up contact and retention strategies. This data will be used as a preliminary evaluation of the intervention on relevant outcomes.

Throughout the study, all procedures and data collection undertaken in face-to-face format will take place in locations that are convenient and private. APRI has arranged for private space to be available for the purposes of conducting the research in both venues. For data collected via computerized assessments, participants will be given privacy to complete these measures. For Phases 1-b and 2, participant contact information will be collected in order to arrange for study sessions, allow contact for any follow-ups, and encourage retention. Confidentiality of participants in these phases will be maintained by assigning them each a unique code number that will be associated with their identifying information in an electronic database that will itself be password-protected and stored on encrypted, secure Brown University servers. Only essential study staff will have access to this file. Participants in Phase 1-c will participate anonymously. Data collected and stored on physical mediums (written notes, digital recordings, written questionnaire data) will be kept in locked file cabinets at Brown University. All personal identifying information collected over the course of the research will be destroyed after the study is completed.

D. RISKS/BENEFITS OF PARTICIPATION

Participation in this study involves no physical risk above those ordinarily encountered in daily life. However, there may be several non-physical risks:

1. There is a small risk of loss of privacy and confidentiality of data, including data that is sensitive (sexual risk-taking, alcohol and drug use, psychological characteristics). We take this risk seriously, and will take steps to protect participants' confidential data and anonymity, as detailed in Section E. We will ensure that personal identifiers are removed from the data and any publications arising from the study. Informed consent documents will bring confidentiality risks to participants' attention.

2. Participants may also experience psychological discomfort while completing the intervention procedures and some of the quantitative assessment measures, since

these involve discussion and disclosure of sexual behavior and alcohol/drug use. We will take steps to minimize this discomfort by framing intervention messages as sensitively and non-directively as possible. Research staff will also be trained in a prepared crisis management protocol and have access to additional supervision from Dr. Kahler, who is a licensed psychologist. Research staff will also have lists of referrals to local agencies to address potential psychological problems that may arise in study participants.

D.1. Adequacy of Protection Against Risk

We will make every attempt to minimize risks to participants throughout the study protocol, including loss of privacy or confidentiality and psychological discomfort.

D.1.1. The risk of loss of privacy will be controlled (as described above) by using unique participant ID numbers on all data, rather than participant names. Transcription will be performed by study staff, who will be trained to maintain the confidentiality of interview data by omitting any identifying information when storing data. Only essential staff members will have access to data and research files. Specific forms of data will be protected as follows:

Digital Audio Recordings and Transcripts. Focus groups and interviews in Phases 1a-c will be recorded using digital voice recorders (DVRs). After each day of recording, the Research Assistant will transfer all new recordings from the DVRs to a password-protected computer in a locked project office. They will label files with the number of each focus group (for focus groups) or the Study ID of the individual participant (for participants in the individual interview phase, 1-b). They will listen to the recording in the digital file, and will use audio editing software to edit out any names or identifying information that may appear in the recordings. To store these data, the Research Assistant will then burn these edited files onto a data CD, which will be kept in a locked cabinet in a locked office (which is in a locked suite in a building with a security guard). After burning the voice recording onto these two data CDs, they will delete the original recording from the DVRs. The DVRs will always be kept in the locked cabinet in the RAs office when they contain original recordings. All original recordings will be removed from the recorders before starting a new interview or focus group, and no recording will remain on the DVR for longer than three days. Transcript files will be encrypted and stored securely in a password-protected file, on the password-protected computer in the Contact PI's locked office. Data CDs will be destroyed at the conclusion of the study, once transcription is complete and there is no longer any need for a physical copy of the recording.

Paper-and-pencil Questionnaire Data and Notes. Physical versions of qualitative data collected via handwritten notes taken by research staff and open-ended questionnaire responses (Phases 1a-c) will be labeled with study IDs only, and no identifying information will be recorded. Hard copies of these documents will be stored in locked file cabinets located in Brown University research facilities as long as the study is ongoing, but destroyed upon completion of the research.

Computerized assessment data. Screening data will be collected during Phase 1b, and consist of a small pool of items assessing study inclusion criteria. Quantitative data collected in Phase 2 will be more extensive, and assess screening criteria, responses to items during the intervention, and assessments administered during follow-ups. Screening, intervention-based, and baseline session assessment data will be gathered via online assessments delivered over the tablet. Follow-up assessments will be completed during in-person appointments conducted at the

Brown University research offices. However, all assessments will be delivered via computer, either via Qualtrics® online survey tools (which stores data securely) or via items built-in to the study's custom software. This data will be identified by participants' study IDs only, and will be downloaded weekly and stored in password-protected files on Brown University's servers, which are encrypted. This data will be kept in a separate location from files that link participants' identifying information with their unique study IDs.

Monitoring. The PIs will provide ongoing supervision and training to essential study staff at weekly meetings, which will also ensure continued compliance with data safety protocols. The PIs will also discuss human subjects issues at weekly meetings. Participants in human subjects research inevitably give up some privacy to share data about their individual experiences. However, we believe our data safety and monitoring plan will minimize the risks of any breach of privacy or confidentiality. The PIs will be responsible for ensuring that study protocols for maintaining confidentiality are followed.

Adverse Events. If an Adverse Event is reported, the Contact PI (Dr. Wray) will complete an Adverse Events form and report the event to The Brown University IRB and the NIH funding institute within 24 hours. The Contact PI will gather any information needed to investigate the event and to determine subsequent action. The Contact PI will document and report any subsequent action to institutional IRBs and the NIH program officer. DSMBs will also be informed of any adverse events and remedial actions needed. The Contact PI will also generate a brief report of adverse events for the study record each year, and we will forward the report to the institutional IRBs and the NIH funding institute.

D.1.2. The risk of psychological discomfort will be controlled by providing research staff with training on crisis management. Dr. Kahler, a licensed psychologist, will also be available to provide supervision. We will also identify MSM-friendly professional clinical and counseling services that can provide urgent services if needed, and will establish a Memorandum of Understanding with these agencies. During the informed consent process, we will clearly describe the nature of the intervention to participants, which includes discussion of alcohol/drug use and sexual behavior. We will closely monitor any indication of adverse events that might arise from participation in the intervention, and will respond promptly and appropriately by notifying the Brown University IRB.

D2. Potential Benefits

There are no direct benefits to study participants in Phase 1; possible indirect benefits for participants include learning about HIV prevention, testing, and treatment, and having opportunities to discuss their experiences and feelings regarding HIV prevention with investigators. In Phase 2, direct benefits may include opportunities to reflect on HIV risk and drinking behavior with the intervention and receive linkage to further preventive care. However, the MSM community as a whole will likely benefit from the development of the first brief tools for reducing heavy drinking and sex risk. We have instituted multiple procedures to minimize the risks associated with the loss of confidentiality and any discomfort during the study processes. These risks substantially outweigh the potential benefits of the proposed research.

The study will fill critical gaps in the research on interventions for reducing sex risks and related risk factors (heavy drinking) for MSM by providing the first, brief intervention that is

adapted for use in community-based settings. As such, our study will provide important insight into the feasibility and appropriateness of behavior change interventions delivered via tablet in MSM. To our knowledge, no known studies have tested a brief, combined heavy drinking and sex risk reduction intervention in MSM, nor has any published study described the potential for delivering these interventions in a technology-assisted format that can be delivered outside of healthcare settings. As such, this research will result in the development of the first highly disseminable and scalable tool for reducing heavy drinking and sex risk in high-risk MSM.

E. Informed Consent

The informed consent process will be conducted by trained staff members that possess research experience working with the target populations and who are also trained in the ethical treatment of human subjects. Staff members will also be trained in more advanced research topics, such as protocol adherence, quality assurance, data management, and so on. The process of informed consent involves presenting a detailed verbal description of the study as it is described on the printed, IRB-approved consent forms (Appendices C & D). Staff will emphasize that participation is voluntary, and that participants can refuse to answer any question and/or can discontinue participation at any time without penalty. Interviewers will ask whether participants have experienced any coercion to take part in the study; those that describe any pressure or coercion to participate will be excluded. Potential subjects receive an item-by-item reading of the consent form by the study interviewer. Participants will be informed of the procedures for ensuring their confidentiality, including: the use of unique non-personally identifying ID numbers instead of names on research materials, and maintenance of data in locked computer databases and in locked filing cabinets in locked rooms. Compensation for participation will be explained. All participants will be given the contact numbers of the Principal Investigators and IRB Chairs to answer questions about the study or one's rights as a human subject as well as a research site contact number. All consenting participants will be offered a copy of the informed consent form.

Appendices

Appendix	Content
A	Feature Set and Wireframes for Experimental Intervention Content
B	Attention Matched Control Content
C	Informed Consent Document (Individual Interview participants)
D	Informed Consent Document (Pilot study participants)
E	Study Measures
F	Follow-up Resources Info Card
G	Protocol Checklist & Submission Procedures

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