Protocol

1. Project Title:

Advancing New Computer-based Health Outreach Regarding Sexual behavior (ANCHORS) Study: UH2 Project

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3. Abstract:

Despite clinical and public health efforts, the rate of new HIV infections in the United States (U.S.) remains unacceptably high[1] with an estimated 44,000 Americans diagnosed in 2014[1]. About 1.2 million Americans are living with HIV[2] leading to 23 billion dollars in annual public health costs[3]. The state of Florida (FL) carries an inordinate burden. As of 2013, FL ranked first in new HIV infections per year and second in total cases[1].

HIV has declined this past decade[1], but not equally across groups. Men who have sex with men (MSM) remain the highest risk group and primary intervention target[1,3]. Black MSM were the most affected racial group, making up 2/3 of new diagnosesl[1]. In the past decade, new diagnoses have risen among Hispanic MSM as well. Young adults also suffer disproportionately with over 40% of new infections among 18-30 year olds[4]. Elevated rates are due in part to overlapping risk behaviors like heavy drinking that tend to reduce safer sex[5].

Prevention is critically important[6]. About 1 in 8 HIV-positive people are unaware of their diagnosis[7], meaning they may infect others without their knowledge. This unaware population further increases prevention need. If more of these individuals could be reached for prevention pre-infection, the spread of HIV would be curbed[8].

New prevention efforts must address alcohol and HIV and be directed to the highest-risk groups[3,9,10]. While interventions have targeted MSM, few have targeted young MSM specifically[11]. Young people and MSM bring particular challenges[5]. Thus, it is important that prevention be targeted to them and developed with their input[5]. To that end, the goal of this project is to lay the groundwork for a synergistic, mobile intervention to reduce alcohol use and risky sex and prevent HIV among young adult MSM. This research study is made up of three related sub-projects: 1) a web-based survey; 2) a series of focus groups and 3) a small, preliminary acceptability and usability to study to test the mobile intervention. The proposed intervention to be tested on a preliminary basis in this study combines brief motivational intervention [24,46] with daily interactive voice response (IVR)[61] monitoring including personalized feedback[65]. Ultimately, this combined intervention will also include pre-exposure prophylaxis (PrEP)[47-49], however there will be no medication in this particular study. Each of these components has efficacy in enhancing treatment adherence, reducing alcohol and/or HIV risk but requires other interventions to maximize its potential benefit. Combining them will capitalize on the strength of each, leading to a higher impact alcohol and HIV preventive intervention.

4. Background:

Brief Interventions to Reduce Alcohol Use and Risky Sexual Behavior

Computer and web-based brief intervention based on motivational interviewing tenets have efficacy in reducing young adult alcohol use comparable to in-person interventions[23,24]. Computer/web-based interventions offer convenience and privacy[26,27] and young adults prefer them[28,29]. Recently, evidence has shown very brief (10 minute or less) web-based interventions, a subset of computer-based interventions, have efficacy and high dissemination potential[30]. Tertiary Health Research Intervention via Email (THRIVE), developed by Consultants Kypri and Hallet[31-33] is a very brief web-based alcohol intervention with efficacy based on multiple large trials overseas. These were followed by a study to develop and test an American version (US-THRIVE), which also yielded evidence for its efficacy[34] (see Preliminary Studies). Despite their efficacy, no studies have tested brief, web-based intervention in heavy drinking MSM, or evaluated how such interventions may reduce HIV risk.

Personalized normative feedback[35-37] is a key part of brief motivational intervention[24]. Evidence supports added utility of normative data that pertains closely to the study population[38]. This requires survey data to ascertain alcohol use and risky sex in a relevant sample, in this case young adult MSM. Protective behavioral strategies (PBS; cognitive behavioral techniques to reduce alcohol use and related harms) are also valuable intervention components[39-42]. Leeman et al.[34] showed that the type of PBS presented as part of US-THRIVE mattered as a version including only indirect PBS targeting behaviors ancillary to drinking (e.g., carrying a condom/protection while drinking) was associated with greater efficacy than control (see Preliminary Studies). Brief intervention for young MSM may be enhanced by including indirect PBS pertinent to drinking in relation to risky sex.

Brief motivational interventions have efficacy in reducing sexual risk including concurrent alcohol use and risky sex. In HIV-positive MSM, in-person motivational interviewing had efficacy in reducing concurrent alcohol use and unprotected sex[43]. A brief variant of the RESPECT counseling modality related to significant increases in condom use and reductions in sexually transmitted diseases (STDs) compared to control[44]. The HIV preventive component of the present intervention will be based partly on RESPECT. A multiple-module web intervention was linked to greater risky sex reduction among MSM[45]. Consultant Lewis[46] found web-based personalized normative feedback on alcohol-related risky sex related to reductions in this behavior in college students.

Pre-exposure Prophylaxis (PrEP): An Under-Utilized Intervention Strategy that Requires Strong Adherence

Evidence supports the efficacy of pre-exposure prophylaxis (PrEP) via once per day oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) to prevent HIV in high-risk groups like MSM[47-49,82]. In 2012, the FDA approved FTC/TDF for HIV prevention. Despite strong evidence; data indicating physician openness to prescribing[10]; and evidence of acceptability in MSM[47,50], uptake has been poor[51]. In a recent large survey, 1% of young adult MSM reported lifetime PrEP use[54]. Uptake in minority MSM has been particularly slow[53]. Rather than more placebo-controlled trials, research is needed to enhance PrEP uptake and adherence among MSM[10,54,55].

Findings with PrEP have shown regular adherence is needed with trials having lower adherence producing null results[10,57]. Daily assessment via interactive voice response (IVR) has been related to greater medication adherence[57,89] and drinking reduction[60,64], including in HIV/risky

sexual behavior studies. However, positive changes are typically associated with a combination of daily assessment and other intervention elements to enhance motivation to change[58] and/or with longer assessment periods[59-61] than the short-term (30-day) period in the proposed study[62,63]. In a study by Consultant Hasin, IVR data were used to create personalized feedback on alcohol use, which when combined with motivational interviewing showed greater decreases in alcohol use at longer-term follow-up than motivational interviewing only in alcohol dependent, HIV-positive patients[64].

IVR has pragmatic advantages including convenience, accessibility to anyone with phone access and cost-effectiveness[61,64] plus research advantages in enhancing data accuracy[20,64]. While cell/smartphones are common, some rural and lower socioeconomic people may not have one or be restricted in data use or texting. Further, text messaging adherence interventions in a recent review were not efficacious[57]. Though it has been used with young MSM[52], IVR has not been used for intervention or to enhance adherence in PrEP research.

An ultimate goal of this line of research is to develop a multi-component intervention one goal of which will be to enhance uptake and adherence to PrEP. Accordingly, several of the questions posed in this study will concern participants' views and knowledge regarding PrEP. However, there will be no medication taking in this particular study.

Barriers to medication adherence

Youth, risk perception, motivation and alcohol/substance use are barriers to uptake and adherence addressed in the proposed study. Younger age has been the most common factor tied to weaker PrEP adherence[5,10,65]. Thus, we opted to target young adults using web and mobile intervention components they prefer[29,52]. Daily IVR monitoring will provide additional help to enhance adherence given young adults' difficulties in this area.

Low perceived risk and motivation to change make young adults a challenging intervention population[18]. Relatedly, low perceived infection risk has been identified as a barrier to PrEP uptake and adherence[10]. Thus, along with intervention for PrEP adherence, an intervention component is needed to increase perceived risk and enhance motivation to initiate and continue medication use and decrease risky sex. Alcohol/substance use is another factor limiting adherence to PrEP[65] and antiretroviral treatment (ART)[67,68]. Along with effects on adherence, alcohol increases unprotected sex[69] in MSM[70]. Likewise, alcohol (especially heavy use) increases HIV risk[71] in MSM[72]. Thus, substance interventions can be considered primary HIV prevention for MSM[73].

The Proposed Study

According to the National HIV/AIDS Strategy[3], MSM, young adults, Black and Latino men and people in the Southern U.S. are at highest HIV risk and should be targeted with cost-effective, scalable interventions. We propose a synergistic mobile intervention to reduce alcohol and HIV risk in young adult MSM that combines 3 efficacious approaches. Brief interventions enhance motivation and risk perception but effect sizes are small to medium[24]. IVR has strengths in medication adherence[57,89] but daily monitoring typically requires additional intervention to observe behavior change in a short time period[58]. PrEP is highly efficacious, but uptake has been poor[57] suggesting a need for enhanced motivation and risk perception. High adherence PrEP is required[10,57], supporting a need for daily monitoring. An intervention including these elements will offer the strengths of all 3 while compensating for the limitations of each, yielding a combined intervention with great potential impact. This intervention will be readily accessible and amendable to use in clinical practice.

The present study represents the first phase (UH2) of what we anticipate to be a two phase project, building toward a randomized controlled trial in the next phase (UH3). Again, the goal of this, the UH2 phase study is to lay the groundwork for this combined intervention, one focus of which will be to enhance uptake and adherence to PrEP. However, there will be no medication taking in this particular study.

To that end, the UH2 phase study will be made up of three related sub-projects: 1) a web-based survey; 2) a series of focus groups and 3) a small, preliminary acceptability and usability to study to test the mobile intervention. The web survey will yield normative data to be included in the intervention. Focus group participants will be provided the web-based component of the combined preventive intervention and offer suggestions to tailor it to be culturally appropriate to MSM. Based on this input, the web-based intervention will be finalized and tested with IVR daily monitoring for usability in preparation for a follow-up randomized controlled trial (UH3), which will be proposed at a later date if the UH2 project is completed successfully.

The UH2 studies are innovative in that they address a lack of data regarding PBS use in young, heavy drinking MSM and a lack of focus group data regarding young MSM views on mobile prevention. Most importantly, the studies will provide critical data to inform the combined intervention to be tested in UH3, which is highly innovative.

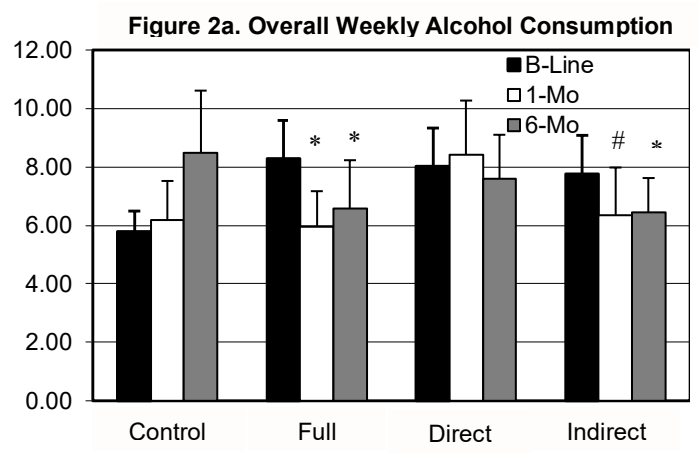
Preliminary Studies

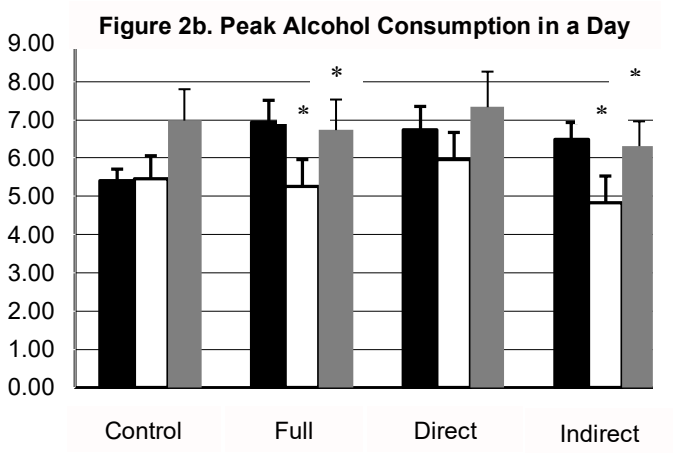
Preliminary Study 1: Initial US-THRIVE study. We tested the feasibility and preliminary efficacy of THRIVE[31-33] in U.S. college students. We modified THRIVE by changing Australian slang, standard drink units, normative data, web links, referrals and relevant laws (see Appendix) and compared this adaptation to an electronic brochure/assessment control. In addition to testing a Full/Replication variant with all protective behavioral strategies (PBS) from the original THRIVE, we tested variants containing short, focused lists of only Direct or Indirect PBS. Direct PBS focus on manner of drinking itself (e.g., slowing the pace of drinking). We predicted Direct PBS use would be too difficult to change based on a very brief intervention and thus Indirect PBS would be a more appropriate target. This was the first study to systematically vary types of PBS in a brief intervention.

Methods: Undergraduates reporting ≥1 heavy drinking day in the past 30 days were randomized. Those who completed the initial assessment/intervention were followed up 1- and 6 mos. later.

Results: The sample (N=208) was 36% Male, 68% White. There were significant condition x time effects for drinks per week (Fig. 2a) and peak drinks in a day (Fig. 2b). After 1-mo., the Indirect PBS-only condition had about a 25% decline in peak drinking and drinks per week compared to no decrease in Control. The difference between Indirect-only and Control for peak drinking was significant (*d*=.56) with a trend for drinks per week (*d*=.26). At 6-mos., both were significant (*d*=.45-.57). The Direct PBS-only condition did not differ from Control.

Conclusions: Results suggest efficacy for our U.S. adaptation. As predicted, the Indirect-only





variant showed significant decreases in alcohol use, but the Direct-only variant did not. Based on our findings we incorporated US-THRIVE as part of the intervention in the proposed study and opted to focus on provision of Indirect PBS.

Preliminary Study 2: PrEP knowledge, acceptability and alcohol use among MSM in Florida. We used recent data from an ongoing NIAAA-funded cohort study led by Co-Investigator Dr. Cook (U24AA022002) to address PrEP awareness and attitudes. These participants differ from the proposed study in that they are HIV-positive, but research has shown myriad similarities between HIV-positive and high-risk HIV negative individuals in demographics including race/ethnicity, risky sexual behaviors and alcohol use[76].

Methods: Data were from baseline and follow-up for the ongoing Florida Cohort study on relationships among substance use, mental health, health services use and HIV. Participants have been enrolled in-person from clinics and community settings in 7 Florida locations including rural and lower socio-economic sites.

Results: To date, 867 participants have enrolled (47% MSM). Among them, 71 (18%) were 18-30 years old (48% non-Hispanic Black, 27% Hispanic, 17% non-Hispanic White, 8% Other). Among MSM older than 30, non-Hispanic Whites were more common (41%) and non-Hispanic Black less common (41%). Among young adult MSM, 36% reported at least one past-month heavy drinking day, with 47% reporting non-heavy drinking. PrEP questions are in an ongoing follow-up including 133 MSM (n=22 ages 18-30). Among young adult MSM, 77% had heard of PrEP compared to 55% older MSM. Given small numbers thus far, we examined attitudes among all MSM who had heard of PrEP (n=76). Of these, 74% rated it at least “somewhat safe”; 61% stated they were at least “somewhat confident” it would reduce HIV and 63% reported they were at least “somewhat likely” to recommend PrEP. Most (61%) believed daily PrEP taking would be “not” or “somewhat” not difficult.

Conclusions: Enrollment of 405 MSM supports the recruitment capability of Dr. Cook’s group. Given a minority were young adults, we considered all data in projecting racial/ethnic breakdown. A considerable percentage of young MSM reported heavy drinking, but there was a range. The results support our ability to recruit racially diverse, young MSM with varied drinking for the UH2 web survey and heavier drinking for UH3. Young MSM tended to have heard of PrEP with positive attitudes. About 40% expressed uncertainty with ease of daily use.

Preliminary Study 3: IVR in HIV-positive rural Southerners. Co-investigator Tucker led research with daily substance use, sex and ART use reports from HIV-positive people in the rural South (R21-DA021524)[20,61,63].

Methods: Using IVR, they assessed the prior day's substance use in a 5-minute assessment. Participants accrued points for completing assessments in a timely manner, which were modestly reimbursed[77].

Results: Over 70 days, the primarily low-income sample (N=44, 65% male, 43% African American) used the system to a similar extent as higher-SES populations[78-80]. Compared to non-callers, IVR callers were younger and less likely to be heterosexual. Baseline risk behaviors, including substance use, and sexual practices, did not predict IVR use. Odds of reporting risky sex and illicit drug use decreased by 3.0% (OR = 0.970, $p < 0.0001$), and 1.3% per IVR call day, respectively (OR = 0.987, $p = 0.014$). Odds of reporting alcohol use were not significantly altered as number of IVR call days increased (OR = 0.998, $p = 0.63$).

Conclusions: Findings support the utility of IVR as a way of obtaining valid, daily data and a means to deliver interventions to hard-to-reach populations living with or at risk for HIV. Younger, non-heterosexuals as in the proposed study were likely to access the system. IVR monitoring alone did not affect reports of alcohol use.

Summary and relevance. These studies demonstrate our group's skill and expertise pertinent to the proposed study, in web-based survey and brief intervention in alcohol; recruitment of young adults including young MSM; assessment of alcohol, sexual behavior and PrEP-related attitudes; including IVR-based assessment.

5. Specific Aims:

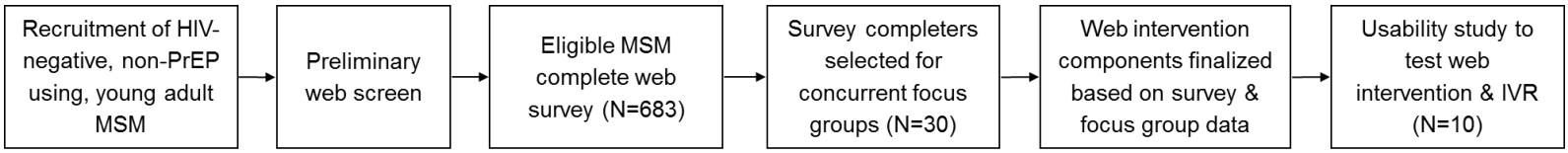
Aim 1. Collect alcohol and sexual activity data via web survey from 683 young MSM to yield normative data for the alcohol and HIV preventive intervention in a follow-up study (UH3). The survey will also help to establish feasibility.

Aim 2. Conduct focus groups (N=30) with young MSM who drink regularly to inform the content of the alcohol and HIV preventive intervention tested in the UH3 phase and ensure the intervention is culturally appropriate for MSM.

Aim 3. The combined alcohol/HIV preventive intervention will be finalized based on the web survey and focus groups. Preliminary testing (N=10) will establish usability, acceptability and correct any functionality issues.

6. Research Plan:

Figure 1. Overview of steps in UH2 Phase Project



Overview

For the UH2 phase project, we will screen a total of 1093 individuals in order to ultimately recruit 683 MSM for a brief web survey to yield data for personalized normative feedback included in the

intervention to be tested in a future study. The web survey will also allow us to demonstrate feasibility by inclusion of sufficient numbers of higher risk MSM from our geographic area. Thirty survey completers will be chosen for a focus group to provide opinions and suggestions to enhance the cultural appropriateness of the web-based intervention component for MSM. With data from the web surveys and focus groups, the brief web-based component will be finalized. A small sample will be enrolled to test usability and acceptability of the combined intervention and correct any technical flaws. With these steps completed, we will move to a separate study that recruits higher-risk MSM (UH3 Phase).

Procedures

This study (UH2) will be made up of three components. At the outset, an initial version of the brief, web-based alcohol and HIV intervention component will be developed based on existing interventions[33,34,44,46,64]. This will enable us to provide it to focus group participants subsequently for their input. Recruitment of respondents for the web survey will also begin at this time. The IVR system will be implemented in a REDCap system using REDCap's native IVR services. The REDCap IVR service uses the telephony service, Twilio Inc., to initiate phone calls to the participants, read survey questions, relay touch-tone responses back to the REDCap survey. This service will configured and tested internally over the first 6 months of UH2. This will enable us to test the IVR system combined with the brief web-based alcohol and HIV intervention component, revised based on web survey and focus group results, in a usability study in the last few months of UH2.

Web survey. Respondents will be recruited 3 ways: 1) at bars, clubs, clinics and community events and organizations (e.g., GatorWell) attended by MSM using flyers, palm cards and promotional items (e.g., pens, adhesive wristbands) with the study web address and QR code, which will be left at these locations; 2) ads on social media and other sites used by MSM (e.g., Grindr). Similar in-person methods have been used in the Florida Cohort study (Preliminary Study 2) and similar online approaches are used in studies of MSM[45,53,54]; 3) the study will be posted on Amazon M-Turk to recruit respondents through the M-Turk worker pool; and 4) the study will be posted on ResearchMatch.org to recruit ResearchMatch volunteers.

Those visiting the study web page can read an overview and complete electronic consent, followed by a pre-screener for eligibility. Before starting the pre-screener, participants will review a brief message to emphasize the goals of the research and its importance, along with the related importance of honest survey responses. The goal is to deter people from completing the survey multiple times and/or providing invalid contact information. Participants will be told that some respondents to the brief survey will be chosen for a 30-minute survey with possible invitation to a focus group. IP addresses will be recorded and only one pre-screen will be allowed per address. Respondents meeting inclusion criteria will be informed they were selected for the longer survey and continue to the survey. Upon completion, the survey will generate a study ID that respondents will provide to study staff with additional contact information via phone, text or email to be compensated. Participants who complete the 30-minute survey have the option to select whether or not they are interested in additional participation in the study. Those individuals who expressed interest will be contacted through email and given the opportunity to recruit peers to participate in the study. Interested individuals will be provided unique referral codes to distribute to peers "like yourself". We have based these procedures on approved protocol # 201601365 with Dr. Jalie Tucker (who is a Co-Investigator and PI Proxy on this protocol) as PI. The recruits who complete the screener survey will insert a unique referral code on the 1-minute screener survey. Current participants will be compensated based on the number of unique individuals who submit a screener survey with their referral code. Compensation will not be based on the referred individual's eligibility for the 30-minute

survey, or completion of the 30-minute web survey. Therefore, referral compensation will be based on referral only, not eligibility. Participant referrals will be entirely voluntary. In addition, those individuals referred to the survey may also elect (or not) to participate in the web survey.

Focus groups. After the first 50 respondents complete the survey, participants will be chosen randomly for the first of 4 focus groups. Randomly selected participants will be informed they are invited to give opinions on an alcohol and HIV preventive intervention for young MSM in a small group of peers. On the date of each group, after informed consent, participants will complete the web-based intervention component. Afterward, participants will be engaged by an experienced facilitator in a discussion of aspects of the intervention they liked and disliked and suggestions they have for enhancing its cultural appropriateness to young MSM. Local participants will also have the opportunity to participate in focus groups without first being recruited through the web survey. Flyers and advertisements will be posted in the Gainesville, FL area. Advertisements will direct participants to call, text, or email to learn more about the focus group participation.

Usability study. In the final 4 months of UH2, a small study will be conducted to test usability and acceptability of the combined alcohol and HIV preventive intervention including IVR-based monitoring and personalized feedback. Key goals will be to identify any issues and learn what aspects of it participants find more and less beneficial. PrEP will not be included and there will be no control condition. Participants (N=10) will be recruited from survey completers.

Participants will be invited to the office to complete the web-based alcohol and HIV intervention component and for IVR training. Participants will give convenient times and the best phone number to reach them and the IVR system will call up to 3 times/day until successful. Participants can also call back at a dedicated phone number using a personalized code. The 5-min. assessment will include items on alcohol, sex and medication taking. Given PrEP is not included, participants will report on another medication or health activity. Staff will remind participants by phone or text message if they miss a day. Participants will return 30 days later to give input and suggestions.

Participants

HIV-negative men ages 18-30 who report no lifetime PrEP use and past-3-month sexual activity with another man will be enrolled for a 30-minute web survey. Open criteria are needed to ensure the survey produces normative data with a range of alcohol use and sexual activity and mean scores reflecting moderate drinking and sexual activity. Efforts will be made to ensure the sample is representative in terms of age and race/ethnicity. Of those completing the survey, randomly selected participants will be invited for a focus group (N=30) each including up to 7-8 participants. Individuals who have prior experience taking PrEP can be enrolled directly in a focus group even though they are not eligible for the web survey or usability study. Similarly, a broader age range of 18-35 will be implemented for the focus groups. After the combined web-based alcohol and HIV preventive intervention is finalized with information from the survey and focus groups, 10 higher-risk MSM will be recruited to test the combined web-based intervention and IVR monitoring system to establish usability.

Participants will meet the following inclusion and exclusion criteria:

Inclusion

Web-survey:

1) Male sex at birth
2) Ages 18-30

3) Ability to read and write English
4) 1 or more instances of sexual activity with another man in the past 3 months
5) HIV-negative

Focus group:

1) 18-35
2) All other inclusion criteria will be the same as the web survey

Usability phase:

Along with inclusion criteria above (#1-5), the usability study will have more specific self-reported criteria, to recruit a higher-risk sample:
1) 5 or more drinks in a day in the past month
2) Past-month intercourse with another man without a condom
3) Willingness to try PrEP, but have never tried it before

Exclusion

Web Screen:

No subject may have lifetime use of PrEP

Focus group:

1) A current undergraduate or graduate student at any level in one of the 3 departments that make up the College of Health and Human Performance (HHP) at the University of Florida (UF), where Dr. Leeman's faculty appointment is.
2) Do not want to engage in open discussion regarding substance use or sexual activity/orientation in a group setting. It will be possible for participants to contribute to focus group discussions without providing detailed information about their own substance use or sexual activity, however focus group participants must have a degree of openness to discussing these topics with others. These groups will take place with 6-7 other people and some people may be made uncomfortable by the discussions that may take place with regard to participants' drinking, substance use or sexual behavior.
3) Not willing to be recorded via an electronic recording device

Usability phase:

In addition to #1 under web screen, those who do not wish to provide a phone number where they can be reached reliably will be excluded

Sample size estimation. In the UH2 phase, we will recruit men ages 18-35 who report HIV-negative status and sex with another man for focus groups (N=30). Additionally, we will recruit men ages 18-30 who report HIV-negative status and sex with another man for a web survey (N=683) to yield normative data for the personalized feedback component of the intervention, which will then be modified, IRB approved and tested initially for usability (N=10). Completion of each aim is a benchmark of the UH2 phase's success and feasibility of the UH3 phase.

Statistical power. The survey sample size was identified based on Hulley et al.[96]. A sample of 683 is needed to estimate with high precision 95% confidence intervals for mean endorsement levels of alcohol use and risky sex, thereby yielding accurate normative data for the personalized normative feedback. Another goal of analyses in this study is to add items regarding protective behavioral strategies to avoid alcohol-related sexual risk to the existing Protective Strategies Questionnaire. One key part of this process is to conduct

confirmatory factor analysis (CFA) of the measure including the new items. For CFA, the sample needed to evaluate model fit depends on model degrees of freedom (df). Models with 100 df need a sample of 132 for testing close model fit with power over .80. Power increases with df[97]. We will include up to 16 items in the revised PSQ loaded on 2 factors, in which case df will be 103. Thus, 683 respondents will yield excellent power to test the PSQ measurement model. Model fit will be evaluated with the Comparative Fit Index (>.95), Root Mean Square Error of Approximation (<.06) and Chi-square[98]. Thirty is a common minimum initial sample size for a focus group study[66,75]. Ten has been identified as an appropriate usability study sample size for technological tools with Faulkner[99] reporting a sample this size uncovered an average of 95% of problems.

Procedures

Milestones and timelines

Mos.	Task
1-3	Reword brief web-based preventive intervention component to make appropriate for MSM
1-6	Develop IVR system based on prior work by Drs. Tucker and Hasin, test among study staff
1-12	Set up, then begin web-survey to obtain normative data. Our benchmark is 450 respondents in Year 1. Recruitment will focus initially on FL. If 50% of the goal is not reached after 6 mos., recruitment will be expanded to other states in the Southeastern U.S. If after 6 mos., the sample is not representative in terms of younger/older age, targeted web ads will be focused on the needed age. If the sample is not suitably diverse, ads will be oriented to include more actors of the needed race. Identifiers other than study ID and IP address will be destroyed once individuals' study participation is complete. IP addresses will be retained only until the conclusion of the study, at which point this information will be destroyed as well.
4-12	Conduct focus groups to get opinions on intervention. Four focus groups are planned but if thematic saturation (no new themes discussed) is not reached[66], additional groups will be scheduled.
13-18	Continue web-survey to obtain normative data with a benchmark of 233 respondents. Over the 18 mos., recruitment of 80 MSM from the area who will likely be eligible for the subsequent UH3 study (i.e., report past-month heavy drinking and unprotected sex, openness to PrEP) is a feasibility benchmark.
13-18	Analyze focus group data, synthesize suggestions for changes to web-based intervention component and present to collaborators, then make any final decisions on changes
19-20	Analyze survey data to obtain normative data and conduct CFA to evaluate new PSQ items on avoiding sexual harms, revise web intervention to include normative data and focus group input
21-24	Conduct usability study (N=10), then make further changes to web intervention and IVR accordingly

Screening.

Preliminary screening via web screen: Respondents will be recruited 3 ways: 1) at bars, clubs, clinics and community events and organization (e.g., GatorWell) attended by men who have sex with men (MSM) using flyers, palm cards and promotional items (e.g., pens, adhesive wristbands) with the study web address and QR code that will be left at these locations; 2) ads

on social media and other websites used by MSM (e.g., Grindr). Some of the same in-person methods have been used in the Florida Cohort study (Preliminary Study 2) and similar online approaches are often used in studies recruiting MSM; 3) the study will be posted on Amazon M-Turk to recruit respondents through the M-Turk worker pool; and 4) the study will be posted on ResearchMatch.org to recruit ResearchMatch volunteers. Registered ResearchMatch volunteers between the ages of 18-30 that live in the Southeastern United States will be sent a brief message about the web survey. If volunteers indicate interest, they will be sent the screener survey link via the UF email server. At that point, they can voluntarily visit the link and complete the survey as described next. Those visiting the study web page can read an overview and provide electronic informed consent. As part of the consent process, respondents will be informed of efforts to protect their confidentiality including a Certificate of Confidentiality and that they may decline to participate or refuse to answer any questions without explanation. Individuals will be informed that some survey respondents will be chosen for a 30-minute survey with possible invitation to a subsequent study if they so choose. Should respondents omit on the pre-screener a response that is needed to determine eligibility, they will be informed that they were not selected for the full survey. IP addresses will be recorded as part of the survey. No identifiers other than IP address will be retained for individuals who complete the pre-screener but are not eligible to complete the 30-minute web survey. For those who complete the 30-minute survey, identifiers other than study ID and IP address will be retained only for those who want to be considered for participation in a subsequent study and are within a 50-mile radius of Gainesville. IP addresses will be retained only until the conclusion of the study in order to prevent individuals from completing multiple web surveys. At the conclusion of the study, IP address information for all participants will be destroyed as well. Identifiers will be recorded on paper forms including the paper-based master list including both study ID and identifiers. At the conclusion of the study, these paper records containing identifiers will be shredded.

Screening for focus groups: Those invited to take part in focus groups will be selected randomly from among web survey completers or from participants recruited locally. Prospective participants will initially be contacted by phone, text or email but the focus group process will be explained to them in some detail by phone. Upon initial phone contact and again during informed consent procedures on the day of the session, they will be informed that the goal of the focus groups is to get theirs and their peers' opinions on a web-based alcohol and HIV preventive intervention for men who have sex with men. The format of the focus group session will be detailed with prospective participants, first on the phone and then as part of informed consent. They will first complete the web-based intervention, which includes questions regarding their alcohol and other substance use along with their sexual behavior and that they will receive some information about these behaviors based on their responses. They will then be asked to discuss the opinions and suggestions regarding the intervention with a particular focus on ways in which the intervention can be made appropriate for men who have sex with men. It will be explained that they may know other participants in the focus group but that since the goal of the focus group is to get their opinion on an intervention, they need not discuss personal information during the focus groups. They may also opt not to respond to any particular discussion question during the focus group. They may also decline to continue should they recognize another participant and opt not to continue for this or any other reason. In order to participate, participants must agree to being part of an audio recording of the focus group, but study staff will not use their name or any other identifiable information during the recording, which will only be made available to investigators working on the study. Instead, participants will be referred do during focus group meetings and on the audio recordings by participant number. Participants are informed that if they are not comfortable with any aspect of the focus group process, that they should decline to participate. They will also be informed that they are allowed to omit any question they are uncomfortable answering.

Screening for usability phase: Prospective participants will be selected randomly from among web survey completers and individuates recruited locally outside of the web survey. These individuals will invited to take part in a 30-day usability study with a goal of obtaining their opinions and suggestions regarding a combined mobile alcohol and HIV preventive intervention. In addition to the minimal risk that was associated with completing the web survey, the IVR daily assessment system will be explained to participants along with the need to provide a phone number so that they can be reached by the system. Participants will be informed that they are free to refuse participation, to stop participating entirely at any time or to omit any question they do not feel comfortable answering.

Intervention during focus group and usability phase. The intervention that will be developed initially and tested in this initial UH2 phase will include a brief web-based alcohol and HIV preventive intervention, then daily monitoring via IVR with personalized feedback for 30 days.

Alcohol intervention: US-THRIVE[34] with wording changes to make it more appropriate for young adult MSM. US-THRIVE begins with an introductory screen, then assessments of demographics; past-month drinking; hazardous use (Alcohol Use Disorders Identification Test [AUDIT][83]; height and weight to calculate estimated blood alcohol content [eBAC]). Immediately after assessments, US-THRIVE gives personalized feedback on 1) risk level based on AUDIT score; 2) eBAC from their peak past month drinking day; 3) a comparison between their typical alcohol use and normative data from age-matched MSM; and 4) estimated money spent on alcohol. For the initial version to be used in the focus groups, normative data will be estimated based on results in the literature, but for the small usability study and subsequent UH3 phase, these estimates will be replaced with normative data from the US2 web survey. Tabs at the top of the screen and clickable arrows will direct them to 3 other pages: “Tips,” “Facts,” and “Support.”

PBS will be in the “Tips” tab. In Leeman et al.[34], 96% accessed this tab. We will provide indirect PBS only, based on prior findings that provision of indirect PBS only was associated with similar outcomes as a full list of PBS. Each PBS will have a title in bold (e.g., “flock together,”) and brief description. The same 4 indirect PBS from Leeman et al.[34] will be included in the version provided to focus groups (Appendix). For the usability study and subsequent UH3 phase, additional PBS to avoid alcohol-related sexual risk will be added from among new items in the web survey (see measures below). Additional PBS will be added based on psychometric analysis and participant acknowledgment of openness to using each of these PBS (see data analytic section below).

The “Facts” screen contains standard alcohol-related information including local alcohol related laws. The “Support” screen contains standard web-based resources and local referrals for treatment options.

The original Australian THRIVE took 9 minutes to complete, on average[31,84], thus, the alcohol portion of the intervention should take less than 10 minutes on average.

HIV prevention: The web-based HIV preventive component will contain intervention material pertaining to risk for HIV and overlap between alcohol and risky sex. The HIV part will be a combination of web-based material from the single session version of the efficacious RESPECT intervention[44], followed by personalized normative feedback on alcohol-related sexual risk based on an intervention developed by Consultant Dr. Lewis[46].

Similar to US-THRIVE, the HIV preventive intervention will begin with a brief assessment of past-30-day sexual behavior including sex after alcohol use, Perceived Risk of HIV Scale (PRHS)[85] and Penn Risk Assessment Battery (RAB)[86]. The participant will be taken to material

adapted from RESPECT based on the intervention's 3 goals: 1) determine what behaviors put the participant at HIV risk; 2) use a "teachable moment" to enhance risk perception: and 3) develop risk-reduction strategies. Participants scoring over normative mean on the PRHS will get feedback that their perceived HIV risk is likely accurate but contrasts with their recent experiences of unprotected sex. Those with PRHS scores below the mean will get feedback that their risk perception may not be accurate. On the next page, participants will describe briefly a recent sexual encounter that may have put them at risk. On the page after, they will think back to prior sexual situations and steps they took to reduce risk. There will be several options given (e.g., wore a condom) and they will be able to give their own responses. Next, participants will be given their RAB score and an interpretation, in relation to a benchmark associated with elevated HIV risk[55]. Lastly, participants will return to their recent high-risk situation and think of one aspect of it that could have been changed to reduce risk (see Appendix). Based on the skill of IT professionals from the Clinical and Translational Science Institute (CTSI) who will program the web-based version of RESPECT; evidence supporting RESPECT's efficacy[44], and comparable efficacy between in-person and web-based interventions[23,24] we have confidence in the efficacy of this web version.

After RESPECT, based on Lewis et al.[46], participants will be presented personalized normative feedback summarizing 4 types of information on separate screens with a combination of text and graphs comparing the participant's responses with normative results from MSM of a similar age: 1) number of sexual partners; 2) number of instances of unprotected sex; 3) number of times having drank alcohol before sex; and 4) number of drinks typically consumed before sex (see Appendix). For the initial version in focus groups, normative data will be estimated.

Assessments contributing to personalized feedback should require a few minutes and participants in Dr. Lewis' study needed less than 1.5 minutes on average to view their feedback. The initial RESPECT session requires about 20 minutes, thus the web version should require this time or less. Thus, the HIV part should entail 25 minutes or less, with the combined alcohol/HIV intervention requiring no more than 35 minutes.

IVR: Cumulative personalized normative feedback will be generated weekly based on IVR responses. Similar to the web component, participants will get feedback with text and graphs on 1) drinks per week compared to normative data; 2) days with protected/unprotected sex compared to normative data; 3) number of days taking medication/completing other health activity; 4) comparisons between instances of sex (protected/unprotected) following alcohol versus not; and 5) medication taking/other health activity on drinking vs. non-drinking days. Feedback will be mailed to a postal address or posted to a secure, password-protected webpage.

Focus Group.

Sources of materials: Research data are derived from the on-line questionnaires as in the web survey and from discussion about the web-based alcohol and HIV intervention component during the focus groups. Discussion will be recorded using an electronic recording device and later transcribed verbatim, hard copies of which will be reviewed by study staff. All data are obtained strictly for research purposes and with the informed consent of subject participants, and are confidential.

In-person focus group: Participants who are selected randomly from among web-survey completers in the Gainesville area or recruited locally will be invited to take part in a focus group. These sessions will take place either in Yon Hall North or Florida Gymnasium on the UF campus. The Florida Gym and Yon Hall North facilities are centrally located on campus, both

connected to Ben Hill Griffin Stadium. These research facilities have dedicated, free parking for research participants. With the convenient location and parking, the research facilities are also readily accessible by emergency personnel in the unlikely event of an emergency. Focus group sessions will last about two hours. Compensation will be $35. Written informed consent will be obtained at the outset of the appointment.

Transportation will be provided via Uber, Lyft, or a taxi service for participants who would like to participate in an in-person focus group, but are limited by transportation. Individuals invited to participate in a focus group but are unable to attend in person will be given the opportunity to participate remotely via Zoom PHI. For those individuals who are interested in participating in a focus group but have limited availability or feel uncertain about taking part in a focus group with other participants, we will offer the opportunity for them to participate in an in-person one-on-one interview in place of the focus group.

Usability Study.

Sources of materials: Research data are derived from the on-line questionnaires and from responses provided to the interactive voice response system (IVR), which will also be developed and maintained using the same REDCap system as the web-based surveys. All data are obtained strictly for research purposes and with the informed consent of subject participants, and are confidential.

Procedures for identifying participants: Participants will be selected randomly from among web survey completers from a 50 mile radius of Gainesville, FL. Participants who completed a focus group may also be eligible for the usability portion should they be interested. Participants may also be recruited directly from this geographic area, outside of the web survey. Those selected will be invited to complete another preliminary web screener including items on frequency of any alcohol use; frequency of consumption of 5 or more drinks in a day in the past month; past-month intercourse with same and opposite sex partners; past month intercourse with same and opposite sex partners without a condom; HIV-negative status; no lifetime PrEP use; willingness to try PrEP.

Initial appointment: Eligible participants will be invited to the office to provide informed consent, to complete the web-based alcohol and HIV intervention component along with baseline assessments and for training in how to use the IVR system. Participants will give convenient times and the best phone number to reach them for the daily IVR assessments.

30-day intervention period: Participants will be asked to complete assessments using the IVR system daily for a 30-day period. The IVR system will call up to 3 times/day using the number provided by the participant until successful. Participants can also call back at a dedicated phone number using a personalized code. The 5-minute assessment will include items on alcohol, sex and medication taking. Given PrEP is not included, participants will report on another medication or health activity. Staff will remind by phone or text message if they miss a day. Based on the participant's IVR responses, study staff will produce a cumulative personalized feedback document that will be posted to a secure site on the web to which only that study participant will have access, or it will be mailed to the participant's postal address, based on their preference.

Follow-up appointment: After the end of the 30 day IVR field period, participants will return for a follow-up appointment. At this appointment, they will complete another web-based TLFB assessment and repeat the rest of the measures from baseline. They will also be asked to give their views on each component of the intervention including how much they liked using it; how

useful they believe each part was in prompting them to change their behaviors and to offer suggestions for improvement, particularly ways to enhance the appropriateness of the intervention components for young adult MSM.

Assessments. On the pre-screen to indicate eligibility for the full survey, participants will be asked demographics (birth sex, age range); number of instances of intercourse in the past 3 months with same and opposite sex partners; HIV status and whether have taken PrEP. The following will be included in the full survey:

Demographics: The full survey includes questions on age, race, ethnicity, highest educational attainment, employment type, marital status, personal and household income.

Alcohol/substance use & sexual activity: Participants will complete an online *TLFB*[81] covering past-month alcohol and other substance use, adapted to include sexual activity[20,87]. Participants record memorable anchor events on calendars that serve as recall aids, then report daily drinking of beer, wine, and liquor and use of licit and illicit substances[88]. Participants report daily instances of sexual activity including whether day-to-day activity was with the same or different partners. On days when they indicate activity, they will be asked whether the partner was same or opposite sex, whether protection was used, and number of drinks before sex.

Sexual risk behaviors: The reliable and valid sexual risk subscale of the RAB[86] will be used, which contains 8 items each with 4 response options addressing sexual behaviors over the past 6 months.

Perceived HIV risk: The PRHS[85] is a reliable and valid 8-item measure of perceived risk of HIV infection that captures likelihood estimates, intuitive judgments and salience of risk.

HIV testing history. Participants will be asked to report the number of times they have taken any type of HIV test in the past 12 months and in their lifetimes.

Sexually transmitted infection history items: Participants will be asked to report regarding whether they have been diagnosed with 4 types of STIs in the past 12 months or prior.

Hazardous drinking: The Alcohol Use Disorders Identification Test* (AUDIT[83]) is an established, 10-item scale including items on alcohol use and DSM-IV dependence criteria that has been used in college samples[90,91].

Protective behavioral strategy use: The revised Protective Strategies Questionnaire (PSQ) contains 11 direct and indirect protective behavioral strategies. Participants rate the extent to which they use each on a 7-point scale. Additional items will be added to extend measurement of protective strategies to avoid additional alcohol-related sexual harms. In addition to the aforementioned questions, additional questions also on 7-point scales will ask participants about their openness to using each of the 16 strategies in the future.

PrEP knowledge and attitudes: These items will be taken from Co-Investigator Dr. Cook's Florida Cohort study. Participants will report whether they have heard of PrEP and openness to future use. On 5-point scales, those who have heard of PrEP will report perceptions of its safety, effectiveness, and difficulty in taking it daily.

Motivation: On 100-point visual analog scales, participants will report their interest in immediately making the following behavior changes: drinking less alcohol; quitting alcohol use altogether; having less sexual activity altogether; having less unprotected sexual activity; having sex less frequently following alcohol/substance use.

The UPPS Impulsive Behavior Scale[92,93] is a reliable, valid 59-item measure that assesses 5 subdimensions of impulsivity (premeditation, positive urgency, negative urgency, sensation seeking and perseverance).

Measures for usability study: The same assessments will be administered at baseline and conclusion of the 1-month usability study. In addition, usability study participants will be asked their liking of the intervention and agreement t is useful on 7-point scales and there will be an open-ended item where they can provide written input. Usability study participants will also complete the following assessments via the IVR system:

IVR assessment: Questions will concern behaviors the preceding day. Similar to Tucker et al.[20,61], participants will report number of drinks; whether they used a substance other than alcohol to get high; and whether they had sexual activity. If they reply "yes," follow-up questions will ask whether it was with a same or opposite sex partner; with their main, non-main or anonymous partner; type of activity (anal, oral, vaginal); whether or not protection was used; and whether or not a transaction for money or goods was involved. For those reporting alcohol or other substance use and sexual activity, a follow-up question will ask if substance use occurred before or after sex. The IVR system will include a question on PrEP use though usability study participants will respond according to another medication or health behavior. TLFB[81] will provide data for missing IVR days.

Compensation. Web survey compensation will be $25 in an electronic gift card. Participants will receive $10 in an electronic gift card per completed referral for the 1-minute screener survey. Participants will receive $35 for a focus group in a gift/cash card. Usability study participants will receive $30 at the first appointment. The IVR compensation strategy will be taken from Searles et al.[77] and implemented by Co-Investigator Tucker[20,21]. Participants receive $1 per day, banked in an electronic account plus an extra 10 bonus "points" ($2 value each) for completing 7 of 7 days in a week. If participants miss a day, they lose bonus points for the week but can recover 7 lost points for weeks with missing data if they do not miss more than 2 consecutive days. Should participants miss a day, they can call a separate number and leave the prior day's responses in a voicemail. Participants receive daily payment for "makeup" calls but are not figured into bonus eligibility. The system rewards consistent reporting while limiting punishment for missing minimal days. Maximum compensation for completing IVR assessments is $110. Participants are compensated $35 for the interview at the end, making maximum compensation $175.

7. Possible Discomforts and Risks:

Web Screen

Web-based assessments. The assessments in this study deal with some sensitive issues including participants' experiences of alcohol-related problems and risky sexual behavior. Potential disadvantages of these assessments are the time taken to complete them and possible breach of confidentiality. There is a slight possibility that completion of these measures may cause participants to experience stress or anxiety regarding their drinking, substance use or sexual behavior.

Possible breach of confidentiality. The chief risk to participants in the study is that their responses regarding alcohol/other substance use and sexual behaviors and/or their identities as research participants will be compromised, however extensive steps will be taken to avoid such breaches (see below).

Stress or anxiety. There is a slight chance of participant stress or anxiety stemming from answering questions regarding their substance use and sexual behavior. Steps will be taken to mitigate these risks (see below).

Focus Group

Web-based assessments and intervention materials. Risk associated with web-based assessments is the same as in the web survey with the exception that focus group participants will also complete the web-based alcohol and HIV intervention component being developed for the subsequent UH3 phase intervention study, based on existing intervention components. There is a possibility that completion of the intervention may cause participants to experience stress or anxiety regarding their drinking, substance use or sexual behavior.

Possible breach of confidentiality*.* In addition to a slight risk that their data collected via the web may be compromised, which is the same as in the web survey, there is an additional breach of confidentiality risk due to participants' completion of the focus group with 6-7 other participants. Efforts will be taken to avoid scheduling participants who reside close to each other, based on web survey respondents' postal addresses provided to study staff for compensation purposes, however study staff do not have any additional material they can use to avoid scheduling people who know each other for the same focus group. Web survey completers who are selected randomly for a focus group will be apprised of this risk when they are contacted initially by study staff and again as part of informed consent procedures. Also as part of informed consent procedures, participants will be asked to respect the confidentiality of their fellow participants' identities (to the extent that participants will be made aware of other participants' identities since they will not be required to provide their name or other personal details during the focus group discussions), responses and opinions stated during the focus group sessions.

Stress or anxiety. Participants may experience a degree of stress or anxiety due to the sensitive nature of some survey items or due to realization that their alcohol use and/or sexual behavior is problematic based on information presented in the personalized feedback portion of the web-based intervention. Participating in the focus group with other participants may also cause a degree of stress or anxiety. Steps will be taken to mitigate these risks (see below).

Usability Phase

Web-based surveys, IVR system and intervention materials. Risk is the same as in the other studies with the exception that usability study participants will also provide daily responses regarding alcohol and other substance use, sexual behavior and medication use or another health-related activity given that there is no medication involved with the usability study. The potential sensitivity of the IVR items is the same as in the prior web surveys. Use of the IVR system brings with it a slight increase in risk of confidentiality breach. The IVR calls will be managed through a cloud-based telephony services provider, Twilio Inc. Twilio's systems will initiate phone calls to the participants, read survey questions, relay touch-tone responses back to the REDCap survey. This process exposes the participant's phone number, the content of the survey questions, and the participant's responses to the Twilio's systems. Twilio does *not* maintain a record of these details. Twilio does record a log of what numbers where called when, but REDCap mitigates that risk by deleting the call log from the Twilio moments after completion using Twilio's own software interface libraries.

Possible breach of confidentiality. The chief risk to participants in the study is that their responses regarding alcohol/other substance use and sexual behaviors and/or their identities as research participants will be compromised. Similar steps will be taken as in the other studies, however the usability study also entails use of the IVR system. In order to be called by the

system, participants will be required to provide a phone number where they can be reached reliably. This identifier must be shared with the IVR provider, Twilio Inc., to deliver IVR portion of the usability study.

Stress or anxiety. Slight risk of stress or anxiety is the same as in the other UH2 phase studies. Steps will be taken to mitigate these risks (see below).

Procedures to Protect against or Minimize Potential Discomforts and Risks

Web-survey protections against risk.

Participant rights and minimizing burden from web-based surveys: While items in these surveys cover some sensitive topics, our past experience with these measures indicates that they are acceptable to participants. As part of informed consent, participants are advised that their participation is voluntary and that they are free to decline participation. They will also be informed that they are allowed to omit any question they are uncomfortable answering. In order to minimize participant burden, we have made an effort to limit the length of the survey. The full survey should not require more than 30 minutes to complete.

Ensuring confidentiality: Several steps will be taken to ensure participants' confidentiality. The web survey will be created and managed using the REDCap secure web application. Data transmission will be encrypted and all data will be stored on a secure web-based research server. Identifiers entered into the survey will be minimal: randomly selected study ID number and the IP address of the computer used by the respondent will be entered into the survey in order to minimize submission of multiple surveys by the same individual. When respondents complete the survey, the study ID number will be generated automatically by the survey. Respondents will then be instructed to make separate contact with study staff by email, or telephone to provide the study ID number and additional information (name, postal address) so that they may be compensated for completing the survey. This separate correspondence will not be linked to respondents' survey data at any point, though it is necessary to maintain a paper-based master list matching participant names and study ID numbers in order to maintain payment records; to ensure there are no duplicate or other inappropriate study enrollments; and to contact randomly selected participants for focus groups or the usability study. Respondent information will be entered separately into the University of Florida's (UF) secure online payment system, however this system is in no way connected to the research data. The Project Coordinator will keep a running paper record of study ID numbers and participant contact information, however this paper record will be stored in a locked cabinet in a locked room that is part of Dr. Leeman's research space in Yon Hall and will only be accessible to Dr. Leeman and senior study staff.

Web survey data collected via REDCap at UF are backed by UF Health's computing and data center facilities, which has a powerful, reliable, and secure computer environment for researching, storing, analyzing and securing large sets of data. The data center is housed in a dedicated, climate controlled, and secure facility with guard patrolled physical security and electronically controlled access. Power is conditioned and provided with dedicated battery and generator backup for high availability. Servers run on enterprise operating systems with modern network infrastructure. The UF Data Center employs the latest security technology including the most current enterprise class virus scanning software and network firewall to monitor and protect all network activity.

Minimizing stress or anxiety: A secondary risk is stress or anxiety regarding one's drinking, other substance use or sexual behavior that may occur as a result of responding to questions on the web survey. As part of the informed consent process, participants will be informed that they can

contact research staff including the Principal Investigator for clinical referrals should they be concerned and want to pursue treatment.

Focus group protections against risk.

Participant rights and minimizing burden: While items in these surveys cover some sensitive topics, our past experience with these measures indicates that they are acceptable to participants. As part of informed consent, participants are advised that their participation is voluntary and that they are free to decline participation. They will also be informed that they are allowed to omit any question they are uncomfortable answering. In order to minimize participant burden, we have made an effort to limit the length of the web-based intervention, which should not require more than 35 minutes to complete. The focus group discussion should require no more than 1 hour.

*Ensuring confidentiality***:** Similar steps will be taken to ensure confidentiality of participants' data collected via the web. Several steps taken to ensure participants' confidentiality during the focus group were described above as part of the informed consent procedures. Before the focus group begins, participants will be asked to keep all information shared as part of the focus group confidential. Participants will not be referred to by their name or any other identifiable information during the focus group and in the transcript created from focus group discussions, any names or other personally identifiable information will be redacted and participants will instead be referred to by study ID only. Use of a trained, experienced focus group facilitator will enhance the quality of discussion, the resulting data and further minimize any threats to confidentiality. Audio recordings from focus group sessions will be transcribed verbatim. Once a printed record is created, which will be absent any identifiers other than study ID, the audio recordings will be destroyed.

Minimizing stress or anxiety: A secondary risk is stress or anxiety regarding one's drinking, other substance use or sexual behavior that may occur as a result of responding to questions on the assessment portion of the web-based intervention or from the personalized feedback and other intervention materials. Participants will receive treatment referrals as part of the intervention should participation raise concerns that lead them want to change their substance use or sexual behaviors. In terms of stress or anxiety stemming from focus group participation, participants are ensured that any statements they make will be kept confidential. They will be informed about the nature of the focus group, which involves discussion with a small group of peers and a trained focus group leader and that they need not provide personal information during the focus group and they can opt not to participate should they recognize another participant or feel uncomfortable with any aspect of the process.

Usability study protections against risk.

Participant rights and minimizing burden: Participant rights and the manner in which we inform them of these rights will be the same as in the other UH2 phase studies. Participant burden will be minimized by keeping appointments and assessments as short as possible. The IVR assessment will only require about 5 minutes per day.

Ensuring confidentiality: In addition to similar steps taken in the other UH2 phase studies, identifiers recorded in the IVR system (participant phone number and study ID) will be stored securely with the REDCap web application. Phone numbers are solely for the purpose of the system contacting participants on a daily basis to complete their assessment. Phone numbers will be deleted from the IVR provider's system logs upon completion of each call. At the conclusion of the study, the telephone numbers will be removed from the data. Consequently, participant phone number will not appear as part of any data set that will be analyzed by any study collaborator. HIPAA principles will be in place as in the other UH2 phase studies and a Certificate of Confidentiality has been obtained.

Minimizing stress or anxiety: Similar steps will be taken to minimize participant stress or anxiety

Confidentiality (overall). In order to be compensated, participants' identifiable information will be entered into a secure, online system maintained by the University of Florida. Participants' names, street addresses and social security numbers will be entered into this system, however no study data will be entered and study id will not be included either thus preventing study data from being linked to the identifiers stored in this system. Use of this system enables us to compensate participants via a debit or gift card to which funds can be added as participants complete different stages of the study. Social security numbers will be collected only for the purpose of providing payment.

In order to facilitate data analysis, electronic data sets not containing any identifiers other than study ID will be stored on the P.I.'s desktop computer in his office at Florida Gym, on computers in the research facility in Yon Hall North and on space in a secure server maintained by the University of Florida College of Health and Human Performance. At the conclusion of each of the three individual studies, data will be deidentified. Any data from this study that is shared with collaborators or other qualified individuals from institutions outside the University of Florida will first be de-identified. Thus, no investigators outside the University of Florida will have access to any protected health information collected in this study.

With participants' consent, the focus group will be recorded using a portable recording device. Participants' will not be referred to by name on these recordings and it will not typically be necessary to discuss protected health information in the course of this discussion. Recordings will be transferred from the recording device to a secure server maintained by the UF College of Health and Human Performance and to the P.I. Dr. Leeman's desktop computer and desktop computers in Dr. Leeman's laboratory space. A study staff member will subsequently transcribe each focus group session verbatim for subsequent thematic analysis. After audio recordings are transcribed, they will be destroyed.

A Certificate of Confidentiality has been obtained from NIH/NIAAA. This certificate will protect the confidentiality of all research records generated by this study. Individually identifiable health information will be protected in accordance with the Health Insurance Portability and Accountability Act of 1996. All research personnel will be trained on human subjects' protection and HIPAA procedures.

In case of injury. If a participant is injured as a direct result of participation in this study and is clearly in need of immediate emergency treatment, 911 will be called right away. Efforts will be made to assist participants in obtaining any necessary treatment. If injury is a direct result of study participation, healthcare will be provided at the University of Florida Health Science Center at no charge. The participant and/or his or her insurance carrier will be expected to pay the costs of any further treatment, including any treatment at Shands Hospital. No additional financial compensation for injury or lost wages is available. Participants will not waive their legal rights by participating in this study. Participants will be provided with this information as part of the informed consent process.

8. Possible Benefits:

Web Survey

The web survey was designed to yield data that will benefit science and society and inform personalized normative feedback that is part of the combined alcohol and HIV preventive intervention to be tested in the subsequent UH3 phase. The survey was not designed to have

individual benefit to research participants. However, survey completers may be selected to participate in a focus group or the usability study subsequently and they may benefit from this.

Importance of the knowledge to be gained. The web survey will yield valuable data about correlates to heavy alcohol use and risky sexual behavior among MSM. Importantly, data from this survey will yield normative data to be incorporated in the subsequent intervention. Participants for the subsequent focus groups and usability study will be selected among survey completers and these studies will also yield valuable knowledge that will contribute to the intervention to be tested in the UH3 subsequent phase. Lastly, conduct of the web survey will support the feasibility of the UH3 phase intervention study. This is based on our expectation that at least 80 (the proposed sample size for the UH3 phase intervention study) of the 683 survey completers will be from a 50-mile radius surrounding UF and give responses indicative of eligibility for the subsequent UH3 phase intervention study. These include reporting at least one past-month heavy drinking day (i.e., 5 alcoholic drinks or more); unprotected sex with a man in the past month; and openness to trying PrEP. Participation in the web survey carries minimal risk, which is far outweighed by the potential benefit of the knowledge to be gained.

Focus Group

Participants may benefit from information about their alcohol and sexual risk behaviors from completing the web-based preventive intervention. They may also benefit from treatment referrals should they opt to change their drinking, other substance use or sexual risk behaviors. The focus groups offer great benefit to the project as they provide an opportunity to get input from the study population regarding what they liked and disliked about the web-based preventive intervention, along with their suggestions, particularly regarding how it can be made to be more culturally appropriate for men who have sex with men. Technical issues with the web-based intervention may also be detected as a result of focus group participants completing it.

Importance of the knowledge to be gained. The focus groups will yield valuable data regarding MSM views on mobile interventions. They will also provide input and enable detection of any technical issues. Any needed changes to the web-based intervention can then be made in advance of the UH3 phase intervention study.

Usability Phase

As with the focus group study, participants have the opportunity to benefit from intervention material provided as part of the brief web-based alcohol and HIV preventive intervention. In addition, the participants will receive personalized feedback based on their IVR responses, thus there may be some additional benefit to participants in this study compared to the focus group study.

Importance of the knowledge to be gained. This study will yield information valuable to this project. At the conclusion of 1-month, participants will inform study staff regarding what they liked and disliked about the combined intervention and any changes they recommend. The usability study will also provide an opportunity to uncover technical, legal, and regulatory issues with the web-based intervention component or the IVR monitoring system.

9. Conflict of Interest:

None.

10. Data Safety and Monitoring Plan:

Web Survey

This study is not a Phase 3 clinical trial and does not require a data safety monitoring board. Given the minimal risk nature of this web survey, the likelihood of a serious adverse event is remote. Risk of breach of confidentiality is minimal given the preventive steps described. The Principal Investigator is responsible for monitoring the data and assuring protocol compliance. During the review process the Principal Investigator will evaluate whether the study should continue unchanged, require modification/amendment, continue or close to enrollment. Either the Principal Investigator or the UF IRB have the authority to stop or suspend the study or require modifications. Data quality will be ensured through making the questions in the web-based surveys in the study as clear as possible, primarily through use of established measures that have been determined to be reliable and valid. This will increase the likelihood that participants will give valid responses.

Focus Groups

The focus group study is not a Phase 3 clinical trial and does not require a data safety monitoring board. Given the minimal risk nature of participation, the likelihood of a serious adverse event is slight. Risk of breach of confidentiality will be minimized through the preventive steps described. The Principal Investigator is responsible for monitoring the data and assuring protocol compliance. During the review process the Principal Investigator will evaluate whether the study should continue unchanged, require modification/amendment, continue or close to enrollment. Either the Principal Investigator or the UF IRB have the authority to stop or suspend the study or require modifications. Data quality will be ensured through use of clearly worded discussion questions for use during the focus groups and through use of a trained, experienced facilitator. After focus group discussions are transcribed, they will be read carefully on multiple occasions, in part so that any errors can be corrected. Regarding data quality of the web-based alcohol and HIV preventive intervention, data quality is ensured by making the questions and instructions in the web-based forms as clear as possible. This will increase the likelihood that participants will give valid responses and benefit from the intervention material.

Usability Study

This study is not a Phase 3 clinical trial and does not require a data safety monitoring board. Given the minimal risk nature of this study, the likelihood of a serious adverse event is remote. Risk of breach of confidentiality is minimal given the preventive steps described. The Principal Investigator is responsible for monitoring the data and assuring protocol compliance. During the review process the Principal Investigator will evaluate whether the study should continue unchanged, require modification/amendment, continue or close to enrollment. Either the Principal Investigator or the UF IRB have the authority to stop or suspend the study or require modifications. Data quality will be ensured through making the questions in the web-based surveys and the IVR assessment as clear as possible, primarily through use of established measures that have been determined to be reliable and valid. This will increase the likelihood that participants will give valid responses.

Designation of serious adverse events. Dr. Robert Leeman, the PI, has primary responsibility for monitoring the data, assuring protocol compliance, and conducting regular safety reviews throughout the study. Dr. Leeman will be responsible for distinguishing serious from non-serious adverse events and has sufficient clinical research expertise to make this distinction. In addition to his own experience conducting clinical research for several years, Dr. Leeman will also base determination of serious adverse events on consultation with Co-investigators Dr. Tucker and

Dr. Cook who have extensive and varied clinical and research experience. Dr. Leeman will consult with Dr. Cook regarding any medical issues associated with a Serious Adverse Event.

Reporting of serious adverse events. Should a serious adverse event occur, Dr. Leeman would report such events in writing within 48 hours to the NIAAA Project Officer as defined by NIAAA and to the UF IRB following their policies. The investigator will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project through regular weekly study meetings. An annual report will be submitted to the NIAAA Project Officer summarizing all adverse events.

Procedures for data quality assurance and confidentiality. The Principal Investigator is responsible for monitoring the data and assuring protocol compliance. During the review process, the Principal Investigator will evaluate whether the study should continue unchanged, require modification/amendment, continue or close to enrollment. Either the Principal Investigator or the UF IRB have the authority to stop or suspend the study or require modifications.

Data quality will be ensured through making the questions in the web-based surveys, IVR and clinical interviews in the study as clear as possible, primarily through use of established measures that have been determined to be reliable and valid. On the web survey, respondents will review a brief summary emphasizing the importance of providing honest and valid responses while completing the survey. They will also be encouraged to respond to the survey only once and discouraged from providing invalid contact information. This will increase the likelihood that participants will give valid responses. All research staff will be carefully trained by the Principal Investigator. Drs. Cheong and Leeman, who are experienced data analysts, will be primarily responsible for conducting the preliminary and final data analyses with advice from collaborators and with support from Ms. Jung.

Right to privacy for participation in this research will be protected through coding of data using study-assigned identification numbers and proper storage of research records. Access will be limited to the P.I. and his designates involved in the study. Hard copy master lists linking study IDs to research participants' contact information will be stored in locked cabinets at the Yon Hall research facility and in Dr. Leeman's office in Florida Gymnasium. These lists will be stored separately from other study materials. Identifiers will be destroyed when the study is completed. All email contact with participants will occur with the use of secure UF email accounts only. Web-based data collection will be encrypted and stored on secure servers, but will not contain any identifiers other than study ID and in the case of the web survey, IP address. A Certificate of Confidentiality has been obtained from NIAAA for this study. This certificate protects the confidentiality of all research records generated by this study. Individually identifiable health information will be protected in accordance with the Health Insurance Portability and Accountability Act of 1996. All research and medical personnel will be trained on human subjects' protection and HIPAA procedures.

Clinicaltrials.gov requirements. This study will be registered on clinicaltrials.gov.

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