Computerized Brief Alcohol Intervention in HIV infected and At Risk Women Attending an Urban STD Clinic, Phase 2: The Randomized Controlled Trial

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1. Abstract

The major risk factor for HIV acquisition among women is high-risk heterosexual sex, including unprotected vaginal and anal sex, and sex with a high-risk partner. Hazardous alcohol use has been associated with high risk sexual behaviors and prevalent gonorrhea among women attending an urban STI clinic, both of which increase a woman's vulnerability to HIV acquisition and transmission. This application proposes a randomized controlled trial (RCT) of a culturally tailored computer-directed brief alcohol intervention (CBI) enhanced with cell-phone booster calls using interactive voice response technology (IVR) and text messaging among HIV-infected and at-risk women attending an urban STI Clinic. Hazardous drinking women (N=450) presenting to the clinic will be randomized to one of three arms: 1) usual clinical care/attention control, 2) clinic-based, CBI, or 3) clinic-based, CBI + 3 booster calls using IVR supplemented with text messages. The CBI, an evidence-based method for behavior change uses principles of motivational interviewing, to counsel on: 1) alcohol use and 2) associated HIV/STI risk behaviors. Primary outcomes, measured at 3, 6, and 12 month intervals, include alcohol-related risk behaviors (number of binge drinking episodes, drinking days/week, and drinks per drinking day), sexual risk behaviors (number of partners, episodes of unprotected vaginal/anal sex, episodes of sex while high), and occurrence of HIV/STI biomarkers. We hypothesize that a computer-delivered intervention will reduce alcohol use and high risk sexual behaviors among women attending an urban STD clinic. Prior to implementing the RCT, the CBI and IVR software and text messages have been revised to 1) include the association between hazardous alcohol use and risky sexual behaviors, and 2) ensure their relevance and acceptability using quantitative/qualitative feedback from a sample of women attending a Baltimore City STI clinic. The proposed research focuses on a particularly vulnerable population of urban HIV at-risk and HIV-infected women seeking treatment in a public STI clinic and examines novel BI intervention delivery strategies specifically tailored to be culturally/socially relevant to this population. If the intervention(s) prove to be effective, study findings will offer "real life" specialty care clinics a screening and intervention package that is practical, low cost, and easy to implement.

2. Objectives (include all primary and secondary objectives)

This application proposes a randomized controlled trial (RCT) of computer-delivered BI and telephone booster calls using IVR or text messaging for hazardous or binge drinking (>3 drinks/occasion) HIV-infected and HIV-at risk women (N=450) seeking care for either HIV or STIs in an urban STI Clinic. Study groups reflect three levels of intervention: 1) usual care/attention control, 2) clinic-based, computer-delivered, BI + text message boosters, and 3) clinic-based, computer-delivered, BI + 3 booster calls using IVR. Outcomes will be assessed at baseline, 3, 6, and 12 month intervals and will include alcohol-related risk behaviors (number of binge drinking episodes, drinking days/week, and drinks/occasion), sexual risk behaviors (multiple partners, episodes of unprotected vaginal/anal sex, alcohol before/during sex), and occurrence of HIV and other STIs.

Aim 1: To determine the effectiveness of computer-delivered BI (CBI), enhanced with IVR and booster text messages in decreasing alcohol risk behaviors among hazardous/binge drinking women attending an urban STI Clinic.

Hypothesis 1a: Women receiving BI + IVR/text will have fewer binge drinking episodes and lower alcohol consumption (number of standard drinks/week, number of drinking days/week) compared to usual care.
Hypothesis 1b: Women receiving BI will have fewer binge drinking episodes and lower alcohol consumption (number of standard drinks/week, number of drinking days/week) compared to usual care.
Hypothesis 1c: Women receiving BI + IVR will have fewer binge drinking episodes and lower alcohol consumption (number of standard drinks/week, number of drinking days/week) compared to BI only.

Aim 2: To determine the effectiveness of computer-delivered BI enhanced with IVR and text messaging boosters in decreasing sexual risk behaviors among hazardous/binge drinking women attending an urban STI Clinic.

Hypothesis 2a: Women receiving CBI + IVR/text will report fewer 1) sexual partners,2) episodes of unprotected vaginal or anal intercourse, 3) episodes of sex while high compared to control.
Hypothesis 2b: Women receiving CBI only will report fewer 1) sexual partners,2) episodes of unprotected vaginal or anal intercourse, 3) episodes of sex while high compared to control.
Hypothesis 2c: Women receiving BI + IVR/text report fewer 1) sexual partners,2) episodes of unprotected vaginal or anal intercourse, 3) episodes of sex while high compared to those receiving CBI only.

Aim 3: To observe the impact of computer-delivered BI enhanced with IVR and text messaging boosters on incidence rates of HIV and STI biomarkers and HIV among hazardous/binge drinking women attending an urban STI Clinic.

Hypothesis 3a: Women receiving CBI + IVR/text will have lower rates of incident gonorrhea, Chlamydia or HIV compared to control.

Hypothesis 3b: Women receiving CBI only will have lower rates of incident gonorrhea, Chlamydia or HIV compared to control.

Hypothesis 3c: Women receiving BI + IVR/text will have lower rates of incident gonorrhea, Chlamydia, or HIV compared to those receiving CBI only.

3. Background

3.a HIV among African American Women

African American (AA) women comprise only 12% of the US female population, and yet account for 66% of new HIV infections[1]. Of the 126,964 women living with HIV/AIDS, 64% are black, 19% are white, The rate of AIDS diagnosis for black women (45.5/100,000 women) is approximately 23 times the rate for white women[2] In fact, HIV/AIDS related conditions are now the leading cause of death from AA women aged 25-34[1]. High risk heterosexual sex is the major risk factor for HIV acquisition among AA women, including unprotected vaginal and anal sex, and sex with a high-risk partner. Faced with these staggering statistics, new, culturally competent, HIV prevention interventions are critical to improve the health and well-being of AA women.

3.b HIV among women in Maryland

In Maryland, HIV/AIDS cases attributable to heterosexual transmission have been increasing steadily since 1994, surpassing infections attributable to injection drug use in 2002[3]. In 2003, 36% of incident HIV cases were reported among women, 68.5% of which were attributable to heterosexual exposure.[3] AA women account for 85% of prevalent HIV cases among women in Maryland[4]. In 2006 there were 1022 newly diagnosed cases of HIV in Baltimore City, 87% among AA, and 37% among women[3]. Historically, the vast majority of Maryland residents with HIV infection have first been diagnosed at the Baltimore City Health Department's (BCHD) STI Clinics. Baltimore's two public STI clinics represent the highest volume sites for confidential HIV testing in the state of Maryland with 13,500 tests performed annually. HIV incidence is very high among those accepting testing, and is estimated at 1.5% per year.[5] Baltimore also ranks among the top US cities in STI morbidity; approximately 50% of STI clinic patients have a treatable STI at first clinic presentation[6]. Baltimore City STI clinic patients are at high risk for HIV in a region of high HIV prevalence; therefore, this medical setting is a critical site for HIV prevention.

3.c STIs and HIV risk among Women

STIs disproportionately affect AA women. In 2006, the *Neisseria gonorrhea* rate among AA women was 14 times higher than that among white women (618.1and 44.4 per 100,000 population, respectively). The rate of *Chlamydia trachomatis* among AA women was more than seven times higher than the rate among white women.[7] STIs can adversely affect a woman's health since they are often asymptomatic and difficult to diagnose. The health complications from STIs in women are frequent and a significant cause of reproductive health morbidity, including pelvic inflammatory disease, and infertility.[8, 9] Furthermore, genital lesions serve as an entry point for HIV, resulting in an increased vulnerability to acquisition and transmission of HIV infection. The presence of certain STIs can increase the risk of acquiring HIV infection from 2 fold to 5 fold[10, 11]. Women attending an STI clinic are at particular risk for acquisition and transmission of HIV.

3.d Alcohol Use Is Linked to HIV, Sex and Drug Risk Behaviors among Women

The prevalence of HIV infection among alcoholics is higher than that in the general population.[12, 13] Studies report over 40% prevalence of alcohol problems among HIV-infected individuals.[14, 15] These findings underscore the importance of understanding the impact of alcohol use on unsafe sexual behaviors in HIV-infected and HIV at-risk individuals particularly since sexual transmission of HIV is, in principle, preventable. Among HIV-infected and HIV at-risk women, those who are hazardous drinkers are more likely to have: (1) multiple or casual sex partners;[16-21] (2) unprotected sexual intercourse[22-24]; (3) intravenous drug use (IDU) sex partners or sex trading partners for money or drugs.[25, 26] Importantly, as the amount or frequency of alcohol increases, so does the likelihood of risky sexual behavior.[27-31] In global studies of general population women, alcohol use is linked to increased likelihood of having multiple sex partners as well as unprotected sex.[32, 33] Event level studies, assessing the association between alcohol use during sex and condom use, have been contradictory, although it appears more that some inconsistency stems from recall bias on the part of inconsistent condom users[34] and/or omission of partner substance abuse.[35] Such findings underscore the importance of using careful timeline follow back methods as well as assessing the partner intoxication status at the time of sex. Alcohol use is also associated with increased rates of HIV drug risk behaviors. Concurrent alcohol and IDU or sharing injection equipment is common.[36] Stein and colleagues [37-39] studying IDU in a needle exchange program found that individuals

with a history of hazardous alcohol use were over two times more likely to share needles, after controlling for demographic and behavioral factors associated with needle sharing. Using event specific analysis, needle sharing days were directly linked with alcohol use days. Alcohol use independently increases the risk of engaging in unsafe sexual behaviors and in drug use.

3.e. Alcohol Use Is Linked to STIs/HIV among Women

Alcohol use is associated with Chlamydia, and gonorrhea, even when behavioral risk factors are controlled.[40-42] Alcohol may alter biological susceptibility to HIV or STIs. Clinical and experimental studies have demonstrated that excessive alcohol consumption can result in impairment of the immune system, and can impact several immune functions including immune tolerance and host defense against opportunistic infections.[43] In a representative household survey of US adults, hazardous alcohol use, independent of high risk sexual activities, was the most important variable marking STI history and predicting future STIs.[44] Alcohol use is also associated with a reported history of STIs among community-recruited AA adults [45]. In a large household survey, the likelihood of having an STI in the past year was related to the frequency of alcohol use during the past month. Among young women aged 18 to 25, 2.1 percent of those who did not drink alcohol in the past month had a past year STI compared with 4.2 percent of those who were binge drinkers (>4 drinks per occasion in the past 30 days), and 7.3 percent of heavy alcohol drinkers (>4 drinks on the same occasion on each of 5 or more days in the past 30 day). *Importantly*, alcohol consumption appears to directly increase the risk of HIV infection. A large scale study of more than 8,000 women in Rakai, Uganda found that consuming alcohol before sexual intercourse increased the risk of acquiring HIV by 40% for women. The study also found that if both partners consumed alcohol, the risk increased by 81% for women.[46] Whether mediated by biologic or behavioral variables, alcohol abuse can enhance risk of HIV acquisition.

Among HIV-infected women alcohol use is prevalent and has been associated with increased STI. Among a sample of predominantly AA HIV infected women, 52% had a positive score on the CAGE questionnaire. Among these women, a +CAGE was associated with 1) *trichomonas vaginalis* and 2) having sex only while drinking alcohol or having sex with their partner when they both had been drinking.[47] In addition, alcohol use has recently been shown to be associated with HIV-1-RNA vaginal shedding among women on antiretroviral therapy. Among an urban sample of HIV infected women, moderate to hazardous levels of alcohol use were associated with vaginal shedding of HIV-RNA (>50 copies/ml) after adjustment for HIV viral load, immunosuppression and antiretroviral adherence.[48] These two studies suggest that hazardous alcohol use in an important target for intervention among HIV infected women.

3.f. Alcohol Use Is a Barrier to HIV Prevention Interventions and Treatment Adherence

Alcohol use is a barrier to HIV prevention interventions. In the NIMH National Multisite HIV Prevention Trial of 3,104 participants from 37 clinics in 7 regional sites, alcohol problems were a significant predictor of relapsed and unprotected patterns of sexual behavior among participants in the intervention condition over 1 year. The authors concluded that, "HIV preventive intervention efforts should include a focus on alcohol abuse".[49] Patients who are HIV+ and drink at hazardous levels have lower rates of antiretroviral therapy use and worsening virologic and immunologic status.[50]

3.g. Treatment for Hazardous Alcohol Use Can Reduce HIV Risk Behaviors

Treatment of hazardous alcohol use, however, can be effective in reducing sexual and drug risk behaviors and HIV transmission. Among alcoholic patients, HIV risk behavior decreased when treatment was provided for alcohol abuse[51, 52]. Stein and colleagues performed motivational interviewing as a brief intervention to reduce alcohol intake among needle exchange participants. They found an average reduction in drinking days from 12 at baseline to 8.3 at six months.[53] Importantly, a subsequent analysis demonstrated a reduction in HIV risk by decreased injection equipment sharing in the brief intervention group.[54]Thus, alcohol treatment can be considered primary HIV prevention.

3.h Alcohol Use among Women

Women are important targets for alcohol interventions. Women are more sensitive to alcohol impairment than men. Controlling for body weight, women achieve higher blood alcohol levels than men after drinking equivalent amounts. [55] Although women are less likely than men to develop alcohol abuse or

dependence, they are over represented among harmful/hazardous drinkers.[56] The threshold for harmful alcohol effects is strikingly low in women, with more than one drink per day placing women at risk for negative health consequences.[57] Women make up one-third of the estimated 14 million Americans who abuse or are dependent upon alcohol. While men drink alcohol in larger amounts than women do, alcohol-dependent women often experience greater physical impairment, sooner, once they begin to drink heavily.[58, 59] Women alcoholics develop alcohol-related liver disease, heart disease, and brain disorders earlier in their drinking careers than men. Heavy/ hazardous alcohol use is less likely to be detected in women receiving health services.[60] Women may be less likely to seek and or engage in alcohol treatment services,[61] making nontraditional care settings particularly important for reaching this population. Furthermore, women who abuse alcohol are less likely to be identified[60], and over the lifetime, less likely to enter treatment compared to men .[62]

3.i. Brief Alcohol Interventions for Women

Most alcohol-related health consequences are experienced not by alcohol-dependent persons but by the much larger group of hazardous drinkers whose problems are at an early or milder stage. This has led to increased efforts to identify and intervene with these at-risk drinkers earlier in their drinking careers before symptoms and problems advance. Brief advice on setting safe drinking limits can have significant and sustained impact on drinking levels in this at-risk population. These brief interventions (BI) begin with a focused assessment of alcohol and drug use and related problems. Next in a brief, interaction, the interventionist 1) provides personalized feedback based on assessment findings (e.g., elevated liver function test results or other medical problems, absenteeism or lateness at work, marital distress) 2) discusses pros/cons of drinking and 3) offers specific drinking reduction strategies, such as goal setting for "sensible" drinking..

A recent Cochrane Review of the BI literature has confirmed its overall effectiveness in reducing alcohol intake[63] and long-term consequences of hazardous alcohol use, especially in men. Booster phone calls reinforcing intervention content have also been shown to improve efficacy of BI; however, the key implication noted in this review was that *more evaluative research on women and minorities was needed*. Manwell and colleagues[64] presented long-term results of a randomized clinical trial of BI for hazardous drinking women of childbearing age (i.e., averaged more than 11 drinks/week; reported heavy drinking [more than 4 drinks/occasion] during the preceding month; or reported 2 or more symptoms on the CAGE). Out of almost 6,000 women screened in 17 primary care clinics, 12% met the definition of problem drinking. The intervention consisted of two physician-delivered sessions.. Overall, there were significant reductions in average weekly drinking and binge drinking in the intervention group compared to the control group. Specifically, a 47% reduction in mean drinks/week (14.1 to 7.5) occurred within 6 months of the intervention and was sustained over 48-month follow-up.[65] Similarly, binge drinking in the last month decreased from 93% to 68% of the sample and there was a corresponding reduction in the number of binge drinking episodes from 5.1 to 3.0 per month. More recently, BI produced reductions in hazardous alcohol use among postpartum women. In intent-to-treat analyses, women in the BI group, compared with controls, reported significantly greater reductions from baseline to 6 months in number of standard drinks consumed (14.2-drink reduction versus 5.1), number of drinking days (3.4-day reduction versus 1.2), and number of heavy drinking days** (1.8-day reduction versus 0.5;).[66] These studies confirm the significant number of women of childbearing age who are experiencing problem drinking and the effectiveness of a brief physician-based intervention to produce long-term, sustainable reductions in drinking. They also reflect that while brief and effective, these interventions do require clinical and staff resources that may lead to difficulty in translation to “real-world” clinical settings.

3.j. Computer-Directed Interventions

One alternative approach to counselor- or health practitioner-delivered interventions is computer-directed BI. *Computer-directed BIs offer tremendous advantages in reducing the multiple barriers that to-date have impeded translation of brief interventions from research studies to clinical practice*, even though such approaches cannot replicate the human elements of traditional interventions. Specifically, they offer tremendous advantages in terms of: Reach (computer-based interventions (CBIs) can be economically and

quickly implemented with large groups of patients); Replicability (CBIs offer perfect replication so that fidelity monitoring is no longer necessary); Anonymity (our team and others have shown patients are more willing to disclose sensitive information to a computer[67]) Flexibility (range of strategies can be "programmed" and matched to patient characteristics with empirically-derived decision rules); Functionality (software can be modified quickly and easily (as proposed in the current grant application); Cost and Time (single touch screen laptop can intervene with thousands of patients annually with little time and effort from busy medical staff); and Rigor (replicability is at the core of CBIs).

3.k. The Motivation Enhancement System (MES)

Drs. Svikis (Consultant) and Ondersma have developed a specific computer-directed screening and intervention program that targets substance use in individuals identified through medical settings. The intervention component of MES is based primarily on Motivational Interviewing principles[68], which are themselves derived from a range of conceptual models, including Decisional Balance theory;[69] ;Self-Perception theory;[70] and Self-Regulation theory.[71] The core components of the BI/MES that assist clients in reducing/abstaining from alcohol are to: 1) create dissonance between the client identified costs and benefits of drinking and 2) develop client generated methods to address drinking triggers therefore building self-efficacy to change behavior. The goal of the MES is to facilitate self-change and/or treatment engagement via a single intervention session. It consists of screening, assessment and intervention modules which are presented using a Tablet PC (a laptop computer with an integrated touch screen).

The screening component requires 10 minutes to complete and identifies patients at risk for hazardous drinking using a visually attractive screen that provides only the most pertinent information. No keyboarding is required; all answers are provided by choosing responses from a list or by touching a visual analogue scale. A mobile three-dimensional cartoon character (Peedy the Parrot) is capable of over 50 specific animated actions and does the "talking" for the entire program. Peedy the Parrot reads each item for the participant, acts as narrator and guide throughout the process, and provides occasional comic relief. Participants listen to Peedy via headphones to ensure privacy. The MES is thus completely private and requires no computer or reading literacy; and in studies to-date, participants have consistently given it near-perfect ratings for ease of use. For those who screen positive for alcohol/drug risk, the assessment component requires 20-30 minutes to complete and obtains detailed information about smoking, drinking and drug use (recent and lifetime) and problems associated with use. It also obtains baseline estimates of a patient's level of interest and motivation to change substance use as well as the extent to which the person feels he/she can make a change.

Research to-date with MES has targeted primarily post-partum women. The intervention component, presented as a 20-minute "Patient Health Check-Up"., consists of three components: (a) feedback regarding substance use, the negative consequences of substance use reported by the participant, and the participant's self-reported readiness to change; (b) elicitation of the pros and cons of substance use and related change, in which the participant chooses from a list of options the positive and negative aspects of the substance use for them; and (c) a summary and query regarding the participant's interest in change, followed by optional goal-setting regarding their substance use (and provision of a menu of change options/ strategies). Throughout the intervention Peedy (the animated parrot narrator) "reflects" back the participant's answers and helps to establish a constructive atmosphere in which the participant can consider the possibility of behavior change.

Based on human factors research and experiences from earlier NIDA-funded software development, the MES software was designed to meet five primary requirements. First, flexibility was paramount in order to minimize the time and cost of future modifications. Second, the MES had to have a "clean" appearance, with minimal distractions, a small number of total colors, and an expressive narrator/guide. Third, the MES had to be easy to use for persons at any level of reading or computer literacy; this meant that all instructions, questions, answers, and interactions had to be presented aurally as well as visually. Fourth, the MES had to replicate the key elements of a traditional brief intervention as much as possible. Fifth and finally, the MES had to be brief in order to fit easily within the health care setting.

3.l. Summary and Significance of MES to the Proposed RCT

For the current application, the potential significance of MES is clear. First, MES is a proactive, low-cost intervention that can reach a large number of primary care patients. Second, it requires only a single session and can be delivered in conjunction with a primary care appointment. Third, it is perfectly replicable with no need for staff training and fidelity monitoring and issues of resistance are no longer relevant. Fourth, since the initial investment has already been made in the development of MES software, modification and revision to target specific patient groups can occur with minimal time and effort. Fifth, similar populations to the one we are studying have found this technology simple and easy to use.

3.m. IVR and its use among hazardous drinking individuals

Using behavioral counseling through IVR to augment computer-delivered BI is innovative, has the potential to improve outcomes, and allows for widespread implementation of behavioral interventions among vulnerable and underserved populations that do not have routine access to primary care providers for disease management. Furthermore, IVRIVR is a telephone based technology that uses touch tone phones to allow the user to interact with a computer using the keypad or voice response system. IVR has gained increased attention in the implementation of behavioral interventions because of its ease of use, accessibility, efficiency and immediacy. Recent studies on its effectiveness for a variety of chronic health problems, including obesity, pre-diabetes, and smoking cessation are promising. [72-75] In addition, IVR has generally been found to be as reliable in obtaining clinical information as structured clinical interviews.[76] Reports of alcohol consumption using IVR have been found to highly correlate with blood alcohol concentration and reports from a cohabitating partner.[77] Generally, for the management of alcohol use disorders, IVR has been used as a means of daily self-report of drinking and has been found to be associated with overall decreases in alcohol consumption.[78] Recently, IVR was tested in an HIV setting where 31 hazardous drinking HIV infected individuals received a brief alcohol intervention followed by automated daily telephone self-monitoring and feedback (graphical display of drinking) at 30 days. The authors found the intervention to be feasible among this population, and an overall reduction in alcohol use although due to the nature of the study there was no control group.[79] While this study did not use IVR for personalized counseling/tailored counseling, it did demonstrate the feasibility of using IVR among hazardous drinking HIV+ persons.

3.n. Text messaging and its use among hazardous drinking individuals

The use of text messaging has risen dramatically in the past five years, with ¾ of the US adults using text messaging with a median of 10 texts per day (Pew Internet. http://www.pewinternet.org/Reports/2011/Cell-Phone-Texting-2011.aspx)

Using short messaging services (SMS) technology, text messages can be sent to participants to reinforce content from behavioral interventions. To date, text messaging has been used to support smoking cessation, weight loss, medication adherence, and diabetes management (Fledjsoe 2009). In a recent pilot study, Weitzel et al investigated the use of tailored text messages to reduce alcohol related consequences among college students. Among 40 participants, those randomized to the text messaging group reported significantly fewer drinks per drinking day during the study period. These results demonstrate preliminary feasibility of delivering alcohol related interventions via text messages and the rationale for further testing text messaging counseling among hazardous drinking individuals.

3.0 STI Clinics as a venue for intervention

Brief HIV/STI prevention counseling delivered at the Baltimore and other STI clinics has been effective in reducing HIV risk behaviors and STIs;[80, 81] however there is a need to integrate sex and substance abuse risk reduction programs since these two behaviors are so frequently associated.[82-84] Data from our clinic (in studies C.2.1) and others suggest that these patients have high rates of hazardous alcohol use and that this is associated with sexual risk behaviors and STIs.[85, 86] Thus, testing the effectiveness of a combined alcohol and sexual risk reduction intervention is more feasible in a setting where rates of behaviors are high and where STIs can feasibly be diagnosed. As STIs are irrefutable biomarkers of high risk sexual behavior or linkage to a high risk sexual network an STI diagnosis can validate self-reported behavioral change and is a surrogate marker of behavioral risk reduction [87]. Importantly, the feasibility and

acceptability of integrating substance abuse services into primary care at an STI clinic and sustaining such services has been demonstrated.[88]

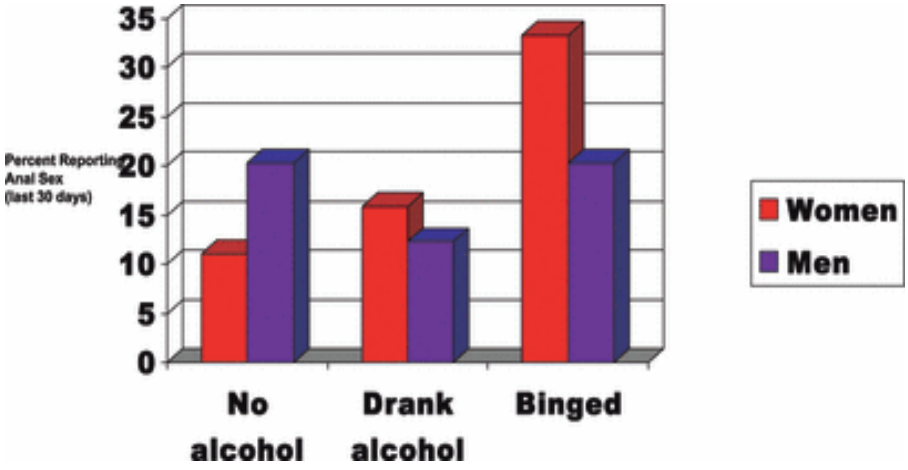
Summary

This proposed research has high scientific and public health significance. First, the study population will be predominantly African-American women, a group at exceptionally high risk for HIV. Second, it examines the effectiveness of empirically validated, brief alcohol interventions delivered using highly novel and innovative technology. Third, it tailors the intervention to enhance the cultural and social relevance of the content to more effectively engage this vulnerable population of urban women. Fourth, it implements the intervention in a STI clinic, a potentially important venue for delivering such care given the overrepresentation of alcohol and sexual risk behaviors in this setting. Finally, computer-directed BI and telephone counseling through IVR/text messaging offer a low-cost, efficient means of intervention delivery with high potential for widespread dissemination.

3.p. Preliminary Studies

Representative Research Findings Relevant to the Proposed Research. The following paragraphs highlight some of the research contributions of various members of our research team and demonstrate our group's history of collaboration and expertise and ability to successfully complete the proposed research

3.p.1.Gender, binge drinking, high risk sex, and sexually transmitted infections (Hutton, McCaul, Erbelding) We examined the association between binge drinking and risky sexual behaviors/STIs among patients attending the STI Clinics of the Baltimore City Health Department (BCHD). A total of 671 STI clinic patients were tested for STIs, and queried about recent alcohol/drug use and risky sexual behaviors using audio computer-assisted-self-interview. The association between binge drinking and sexual behaviors/STIs was analyzed using logistic regression adjusting for age, employment, and drug use. Binge drinking was reported by 30% of women and 42% of men. 21% reported having sex while drinking. Gender differences were found in rates of receptive anal sex which increased linearly with increased alcohol use among women but did not differ among men (see Figure 1). Within gender analyses showed that women binge drinkers engaged in anal sex at more than twice the rate of women who drank alcohol without binges (33.3% vs. 15.9%; $p < 0.05$) and 3 times the rate of women who abstained from alcohol (11.1%; $p < 0.05$). Having multiple sex partners was more than twice as common among women binge drinkers than women abstainers (40.5% vs. 16.8%; $p < 0.05$). Gonorrhea was nearly 5 times higher among women binge drinkers compared to women abstainers (10.6% vs. 2.2%; $p < 0.05$). The association between binge drinking and sexual behaviors/gonorrhea remained after controlling for drug use. Among men, rates of risky sexual behaviors/STIs were high, but did not differ by alcohol use. Rates of binge drinking among STI clinic patients were high. Among women, binge drinking was uniquely associated with risky sexual behaviors and an STI diagnosis. *These findings support the need to routinely screen for binge drinking as part of clinical care in STI clinics. Women binge drinkers, in particular, may benefit from interventions that jointly address binge drinking and risky sexual behaviors. Developing gender-specific interventions could improve overall health outcomes in this population.*[98]



ACASI vs. Face-to-Face Interview: Assessing Response Bias

Another substudy in the same BCHD STI clinic population (N=669) demonstrated the feasibility of using an ACASI-formatted survey, and its superiority to face to face interviews (FFI) as a data collection tool for

sensitive sexual risk behaviors (61). All participants initially underwent ACASI, and subsequently a FFI. A series of questions on illicit drug use and sexual risk behaviors were asked. In comparing responses to similar questions between the two interview modes (FFI compared to using the ACASI), participants reported 1) sensitive sexual behaviors such as same sex contact, receptive rectal sexual exposure, orogenital contact, and 2) a greater number of sex partners in the last month more frequently with the ACASI. The study demonstrated that patient reporting of sensitive sexual risk behaviors (same sex contact, exchange of drugs/money for sex, number of sexual partners in the month) in FFI was highly susceptible to social desirability bias. *We concluded that the ACASI might be a more reliable assessment method for reporting of sexual behaviors than face-on interviews with the STI clinician and that use of the ACASI within this setting was feasible.[99] This study, which was conducted on the same population that will be recruited for this proposal highlights the importance of including ACASI to minimize the extent of response bias among the participants.*

3.p.2 Alcohol use remains prevalent among women attending an urban STI clinic and is associated with risky sex (Chander, Hutton, Finklestein, McCaul, Erbelding). We recently (July 2008) conducted a pilot study among 200 women attending the BCHD STI Clinic to determine the prevalence of alcohol use. Participants were recruited from the waiting area and through flyers handed out by patient registration staff. Alcohol use was queried through the AUDIT-C. In this sample 88% of women were AA, 27% had less than a high school education, 34% graduated from high school, and the remaining 40% had some college or greater. Among this sample, the overall prevalence of any alcohol use was 57%; 25% reported binge drinking (≥ 4 drinks per occasion) and 29% met NIAAA criteria for hazardous drinking (> 7 drinks per week or ≥ 4 drinks per occasion). 52% of women had a score of 3 or greater on the AUDIT-C, reflecting hazardous alcohol use. Overall, 38% of women had risky sex, defined as either 1) a diagnosis of a sexually transmitted infection at the time of the survey or 2) reporting unprotected anal or vaginal intercourse while high. Binge drinking (Adjusted OR: 2.04 [95% CI:0.99-4.26], hazardous use (AOR: 2.10 [1.01-4.35]) and a positive AUDIT-C (AOR:2.54 (1.28-5.03) were all associated with high risk sexual behaviors even after adjusting for age, race, education, and illicit drug use. *These findings affirm that binge drinking and hazardous alcohol use continue to be problems in the STI clinic setting. Further, the study confirms the team's ability to recruit patients from the STI clinic lobby areas while waiting to see their practitioners.*

3.p.3 Cell phone use is more common than internet use among women attending an urban STI Clinic. In the same pilot study discussed above, women were asked about their cell phone and internet use. Of those surveyed, 93% used cell phones (Table 1). Neither alcohol nor drug use were associated with cell phone use. In contrast to the high percentage of cell phone use, only 48% of women used the internet once per week or greater. Not surprisingly, some college or graduate school (AOR: 5.13 (2.22-11.85)) and a high school degree (AOR: 2.71 (2.25-6.39) were associated with an increased odds of internet use compared to those with less than a high school education, while older age was associated with decreased internet use. Women were also asked if they would be interested in receiving health advice over the telephone (either cell phone or text messaging). Sixty nine percent of women stated they would be interested. These data demonstrate that cell

Table 1:Cell Phone and Internet Use Among 200 Women Attending an Urban STI Clinic

Internet usage	Total Sample (N=200)	Hazardous drinkers (N= 109)
Never	39 (20%)	27 (25%)
Once per month	32 (16%)	18 (17%)
Less than once per week	32 (16%)	17 (16%)
1-6 days per week	32 (16%)	17 (16%)
Daily	61 (31%)	27 (25%)
Cellular telephone usage		
Yes	185 (92.5%)	97 (89%)
No	15 (7.5%)	12 (11%)
Sends or Receives Text Messages		
Yes	156 (78%)	78 (72%)
No	44 (22%)	31 (28%)

phones use is widespread within this population and suggests that interventions via cell phone may be more accessible to urban women with low levels of internet use. Moreover, the majority of women surveyed stated that they would be interested in receiving health advice delivered by a cell-phone.

3.p.4 Randomized Trial of Brief Alcohol Interventions Among HIV-Infected Women (McCaul, Chander, & Hutton). In this RCT (R01 AA14500), hazardous/binge drinking HIV infected women receiving care in the Johns Hopkins HIV clinic were randomized to a therapist delivered brief alcohol intervention versus usual care. All participants undergo an ACASI interview at 0, 3, 6, & 12 months and those randomized to the intervention received a brief alcohol intervention + 2 booster phone calls . Outcome measures included: alcohol/drug use, engagement in substance abuse treatment services, HIV-risk behaviors, HIV disease markers and medication adherence, and psychiatric symptoms. Early testing of our BI curriculum revealed the participants' observation that their heavy drinking was often a "trigger" for having sex that was not typical (e.g. rougher sex, casual sex, or unprotected sex). This underscored the importance of targeting the combination of sex and alcohol use in future risk reduction applications.

3.p.5 Development and Pilot Testing of Computer-Delivered Screening and Brief Intervention Software (Ondersma, Chase, Svikis, & Schuster, 2005). This three-study series was conducted to determine the acceptability and preliminary efficacy of a computer-based brief motivational intervention (the Motivation Enhancement System, or MES).[100, 101] In Study 1, quantitative and qualitative feedback from 30 post-partum women and 17 women in treatment for drug use were used to modify the software. In Study 2, 50 urban post-partum women who reported drug use in the month prior to pregnancy completed the intervention and provided repeated within-session ratings of state motivation. In Study 3, a total of 30 women were randomly assigned to intervention or control conditions with 1-month follow up. Overall, women rated the MES as highly acceptable and easy to use and reported significant increases in state motivation at post-intervention and at one-month follow-up (d = .49). These preliminary results were encouraging and suggested that further work in this area was warranted.

3.9.6Randomized Clinical Trial of Screening and Brief Intervention Software With Post-Partum Women (Ondersma, Svikis, & Schuster, 2007). This randomized trial built upon the successful development work cited above, and was based on the principle that implementation of brief interventions with this population could be greatly facilitated by computer-based interventions.[102] Participants were 107 post-partum women recruited from an urban obstetric hospital primarily serving a low-income population. Women were randomized into assessment only vs. assessment plus brief intervention conditions; 76 (71%) returned for follow-up evaluation, with the intervention being a 20-minute, single-session computer-based brief motivational session (based on Motivational Interviewing methods) combined with two non-tailored mailings. At four-month follow-up, the frequency of illicit drug use other than marijuana increased slightly for the control group, but declined among intervention group participants ($p < .05$, between-groups Mann-Whitney U; d = .50); the magnitude of intervention effects on changes in marijuana use frequency was similar, but did not reach statistical significance. Point-prevalence analysis at follow-up did not show significant group differences in drug use. However, trends under a range of assumptions regarding participants lost to follow-up all favored the intervention group, with most effect sizes in the moderate range (OR's 1.4 to 4.7). Alcohol use was not the primary outcome of this study. However, among this sample, there was also significantly less alcohol use at a level of weekly or greater among the intervention group (7%) versus the control group (29%). Adjusting for baseline alcohol use, in logistic regression, the control group had a significantly lower odds of consuming alcohol less than weekly (compared to weekly or greater) than the intervention group (OR: 0.162). *These results supported the efficacy of this high-reach, replicable brief intervention and demonstrate the research team's ability to conduct RCTs using MES in medical settings. Since a "standard care, no treatment" control group was not included, effect sizes may be conservative as research suggests the assessment only condition may have served as an intervention, leading to greater reductions in substance than expected with routine practice.*

3.p.7 Interactive Voice Response Technology (Finkelstein) Dr. Finkelstein has significant experience in development and systematic evaluation of patient-centered information technology, including IVR. IVR is

a telephone based technology that uses touch tone phones to allow the user to interact with a computer using the keypad or voice response system. One study with high relevance to this proposal carried out usability testing of two automated home-based systems designed to monitor patients' health status and improve self-care. [103] TLC-DietAid, an IVR system that uses computer telephony to carry out totally automated telephone conversations with patient users, monitors dietary behavior of dyslipidemia (cholesterolemia) patients in their homes and provides them with nutrition information, advice, and behavioral counseling, principally to lower saturated fat in their diets and thus lower low-density lipoprotein cholesterol (LDL-C) in their sera. During weekly conversations, TLC-DietAid speaks to patients over the telephone using computer-controlled digitized human speech. The patients, in turn, communicate with TLC-DietAid using the touch-tone keypad of their telephones. In usual practice, patients call TLC-DietAid once a week, however, for this evaluation study they used it every day for 2 weeks. Conversations typically last between 5 and 10 min, depending on the number or complexity of the topics addressed and the user's responses. After each conversation, TLC stores the information recorded by patients in a database, for use in tailoring future conversations. The systems were evaluated in two separate qualitative studies.[104] The qualitative analysis
uncovered "medium-specific" and "content-specific" issues that addressed either the process of the interaction or its content. The results demonstrated that patient-users tended to evaluate each system on the basis of how it fit into everyday life and corresponded to personal preferences. The methodology also allowed the system designers to understand users' concerns and the context of adoption in order to design changes to address such concerns. *This study demonstrates Dr. Finkelstein's ability to design and implement an IVR system, and his use of qualitative methods to modify the system. An important finding from this work was that users evaluated the system on its compatibility with their lives. Because cell phone use is prevalent in our proposed sample (93% surveyed used cell phones), this mode of intervention delivery may be particularly acceptable and may be more accessible to individuals who may not regularly access the health care system..*

3.p.8 Results from the Development Phase of this R01 Proposal

Development and Pilot Testing of Computer-Delivered Screening and Brief Intervention Software in the Baltimore City STI Clinic

In the development phase of this study we performed 20 in-depth interviews with women attending the BCHD STD clinic who reported binge drinking or having sex while under the influence of alcohol. The goal of these interviews was to obtain information from women about their alcohol use, alcohol expectancies, and alcohol use within their community to tailor the computerized intervention to women attending the BCHD STD clinic. Thematic saturation was reached. Drs. Chander and Hutton performed these in-depth interviews and the data have been independently coded and analyzed and used to tailor/modify the existing computerized BI to ensure its relevance to the STD clinic population
Initial software modifications were made by programmers at VCU, tested by investigators, followed by additional modifications and then piloted among women attending the BCHD STD clinic. Results from our first 10 pilot participants demonstrated that the intervention is twenty minutes in length. Peedy the parrot, the motivational interviewer/interventionist is well-liked by participants and the intervention is well accepted. Three participants felt that Peedy the parrot's voice was either too slow, or difficult to understand, and software modifications were made to address this.

The attention control, which consists of content related to dental health, has been developed and is twenty minutes in length to match the length of the CBI.

In addition to performing the in-depth interviews, and subsequently modifying the computerized brief intervention, we also developed and pilot tested the audio computer administered self interview (ACASI) to be used for screening, baseline and follow-up assessments. This has been piloted among 10 women who

have responded favorably to the ACASI. The women have filled out confidential questionnaires on survey content and there have been no complaints of questions being too personal. The baseline length of time varies between 07 and 30 minutes based on participants' familiarity with computers (see table 4).

Table 3: Evaluation of ACASI by Pilot Participants	
Median Time to Complete Baseline Assessment	10 minutes, range 7-30 minutes
Like working with the computer	1/10 did not like using the computer
Ease of computer use	10/10 said using the computer was easy
Comfort with questions	1/10 participants was uncomfortable answering questions about anxiety/mood
Confusing questions	0/10 said any questions were confusing
Irritating questions	0/10 said that any of the questions were irritating
Questions too personal	0/10 said questions too personal

3. Summary

Hazardous/binge alcohol use is prevalent among women attending Baltimore City STI clinics and associated with particularly high risk behaviors: unprotected sex, multiple sex partners, and anal intercourse**.** The MES system, based on the principles of motivational interviewing, offers an innovative, and replicable means of delivering brief alcohol/STI interventions among the vulnerable population of HIV-infected and HIV-at risk women. Enhancement of this intervention with cell-phone based telephone counseling using IVR and text messaging has the potential to reach individuals who may not routinely engage regular health care. The investigative team brings a depth and diversity of experience that will allow them to tailor the MES, IVR and text messaging intervention delivery systems and content to the target study population of urban women.

4.Study Procedures

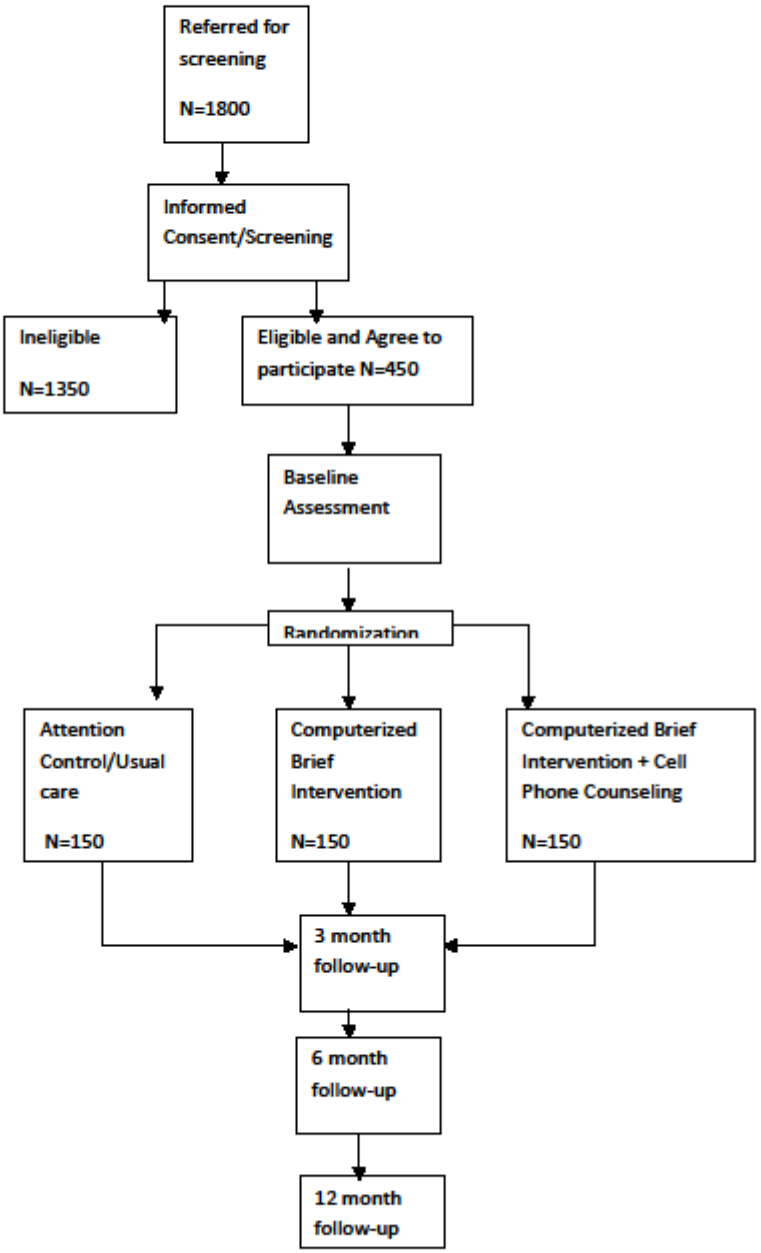
All procedures are for research purposes only.

4.a. Study design,

4.a.1. Overview of Study Design:

We propose a randomized controlled trial (RCT) of computer-delivered BI and telephone booster calls using interactive voice technology and text messaging for hazardous/binge drinking women seeking care for sexually transmitted infections in the Baltimore City Health Department STI Clinic (BCHD STI) (N=450). The arms of the RCT will reflect three levels of intervention: 1) usual care/attention control, 2) clinic-based, computer-delivered, brief alcohol intervention, and 3) clinic-based, computer-delivered, brief alcohol intervention + 3 booster calls using IVR supplemented with counseling text messages. The primary outcomes will be measured at baseline, 3, 6, and 12 month intervals and will include alcohol-related risk behaviors (number of binge drinking episodes, drinking days/week, and drinks per occasion), sexual risk behaviors (number of partners, and number of unprotected vaginal and/or anal sex occasions, sex while high), and occurrence of STI biomarkers. See Study Design Overview Below

Study Design Overview



4.a.2. Study Setting and Participants

This study will take place at the BCHD STI Clinic. The Eastern District STI clinic of the BHCD processes over 12,000 Clinic patient visits per year (Table 5).

Table 5: Demographic Characteristics BCHD STI Clinic: Eastern District

Characteristic	BCHD STI Clinic: (n=12,768 visits)
Gender	
Male	6744 (52.8)
Female	6024 (47.2)
Race/Ethnicity	
African	10776 (84.4)
American	796 (6.2)
White	1002 (7.8)
Hispanic	194 (1.4)
Other	
Age	
<15	11 (.1)
15-19	1136 (8.9)
20-24	3307 (25.9)
25-29	2629 (20.6)
30-34	1464(11.4)
35-39	1096(8.5)
40-44	1279(10)
45+	1848(14.4)

The majority of patients who use the BCHD STI Clinics seek episodic treatment primarily for gonorrhea, syphilis, HIV, and chlamydial infections but also for other STIs such as trichomonas, non-gonococcal urethritis, herpes simplex virus infections, and human papilloma virus (HPV) infections. The Eastern STI Clinic is easily accessible to public transportation services, and is located in high prevalence areas for STIs and HIV infection. The clinic is staffed by 6-8 nurse practitioners and physician assistants trained in STI diagnosis and treatment, contraceptive care and counseling, HIV risk assessment, and pre-and post-test HIV counseling. The clinics operate Monday through Friday, 8:30 a.m. to 5:00 p.m. Individuals attend the clinic on a "walk-in, first-come, first served" basis and are assigned an appointment time for that day as they register. Clinicians are trained to provide HIV prevention counseling to all patients within their clinical encounter so that care is delivered according to an integrated HIV/STI treatment and prevention model. Our study focuses on women seeking STI services within this setting. Characteristics of the population are described in the Table. Forty seven percent of visits are made by women and 5% are HIV infected.

4.a.3. Recruitment

We plan to screen 1800 women receiving care at the BCHD STD Clinic over 30 months with the goal of recruiting approximately 15 women per month. Study participants will be identified by four mechanisms.

1) Women registering in the BCHD STI clinic will be given a standard form with the following question: "Have often in the last year have you had more than three drinks of alcohol on one occasion?" This form has already been integrated into the routine registration procedures at the Druid Hill STD Clinic, and will be added to the procedures at Eastern STD Clinic. This form will be reviewed by the study research assistant, and for those women who have had more than three alcoholic drinks on one occasion in the past year, a sticker will be placed on the form asking the provider to discuss referral to the study with the patient. This form will be included in the registration packet given to clinicians irrespective of the patient's drinking status.
2) Flyers will be posted in the clinic waiting room.

3) Participants will be recruited by provider referral. In addition to screening for alcohol use at registration, providers in the STD clinic ask all patients the following two questions as part of routine clinical care. These questions are integrated into the electronic medical record/standard history and physical form used at all patient encounters: 1) "In the last month: have you had sex when you were intoxicated on alcohol? 2) "In the last one month: Have you had more than 3 drinks on one occasion?" If a woman answers yes to either of these questions, providers may refer her for screening.

4) Waiting room recruitments: a table will be set up in the waiting room of the STD clinics where a research assistant will be seated with flyers advertising the study. The research assistant will follow a standard script that asks if a participant would like to screened for a study examining a computer delivered intervention to focusing on healthier behaviors (see attached script in supplemental study documents). In the waiting room, there will be no mention of alcohol or sexual risk behaviors. If a woman is willing to undergo screening, she will be taken to a private room, where more information can be given about the study, as well as screening and consent. In the event that a table is not available, a research assistant will be seated in the waiting room with recruitment flyers and any discussion of the study will only include information detailed on the attached script.

4.a.4.Informed Consent

Women who present for study screening will undergo informed consent in a private office in the BCHD STD Clinic. Consent will be obtained during usual clinic hours and 15 minutes will be allotted for obtaining consent. The consent forms will specify that the purpose of the study is to test the effectiveness of a computer-delivered brief intervention (with or without follow-up phone calls) among women with hazardous alcohol use. They will be informed that they will be randomly assigned to 1 of 3 study conditions (usual care, computer-directed brief alcohol intervention, or computer-directed brief alcohol intervention + booster phone calls) and that they may choose to leave the study at any time without compromising their health care at the BCHD. They will also be informed that if they consent to the study, they will participate in 4 research interviews including baseline, 3, 6 and 12 months. Risks and benefits of the study will be clearly explained as will alternate therapies. Participants will also be informed that that the study will have a confidentiality certificate administered by the National Institute of Alcohol Abuse and Alcoholism. After the consent form is reviewed, the participant will be asked questions regarding the consent form reflecting key study procedures, including randomization, for example, 1) what is the purpose of the study? 2) What are the study risks? 3) How will study group be determined? 4) What will be done to protect her confidentiality. The participant must answer all of these questions correctly to ensure adequate understanding of the consent form. If questions are not answered correctly, the research assistant will review the study procedures until the participant demonstrates understanding.

We will not be enrolling women who do not speak English. Because the intervention has an audio component, we will not be enrolling individuals who are hearing impaired.

4.a.5 Screening and Eligibility:

Women will be screened for the study in a private office in the BCHD STD Clinic. We anticipate screening 1800 women, with 25% meeting study eligibility. The screening will be comprised of the following questions to determine study eligibility.

1) Age
2) Patient of the BCHD STD Clinic
3) Quick Drinking Screen (a measure of daily quantity and weekly frequency of alcohol use)
4) Sex while under the influence of alcohol in the past 3 months
5) Sexually active with men
6) Pregnant
7) Able to speak and read English
8) Currently enrolled in alcohol treatment
9) Own a cell phone
10) Uses text messaging
11) Not moving out of the area in the next 12 months.

<u>Inclusion Critieria</u>

Age >=18 and
Patient of BCHD STD Clinic and
Sexually active with men in the last 90 days and any 1 of the following three criteria:

Average of 8 or more drinks per week or
Two heavy drinking episodes (4 drinks/occasion) in past 3 mos/90 days or
Sex while under the influence of alcohol in last 3 months/90 days on two or more occasions

Exclusion Criteria

Actively Psychotic or severe mental health symptoms
Unable to speak or read English
Pregnant
No cell phone
Does not text message and not interested in starting
Currently enrolled in alcohol treatment

Women who are ineligible for the study will receive $5.00 for their time. Women who are eligible for the study will participate in the baseline assessment described below in section 4.a.8.

4.a.6. Randomization

After women undergo their baseline assessment they will be randomized to one of three study arms: 1) Computerized Brief Intervention (CBI) + Cell phone counseling/text messages 2) CBI only 3) Attention Control/Usual Care. Randomization will be stratified by current illicit drug use.

4.a.7. Study Arms

Attention Control/Usual Care

An attention control arm has been created for this study to ensure that intervention effects are not a result of the increased attention one receives from participating in behavioral interventions. For participants randomized to the attention control arm the RA will record their group assignment and bring Peedy the Parrot onto the screen. They will then participate in computer-delivered informational intervention on oral health. Specifically, individuals will watch a series of videos on the importance of brushing and flossing teeth. In addition, they will receive educational information on gingivitis, gum disease, links between gum disease and overall health. Finally they will receive instruction on how to properly brush and floss teeth. The rationale for including dental information in the attention control arm is that poor oral hygiene has been identified as a major public health problem in Baltimore City.

Participants in all three arms will receive a "Healthy Woman" pamphlet that includes local resources including a comprehensive list of federally qualified health centers in Baltimore City and local resources for free dental care, psychiatric care, primary medical care, substance abuse treatment programs (including tobacco), AA and NA meetings, and domestic violence. This will be submitted to the IRB once it is complete.

Computerized Brief Intervention

Women randomized to either the CDI + IVR/text or CBI only will receive the computer-delivered brief intervention targeting alcohol use and risky sexual behaviors. Participants will interact with the computer via Peedy, a three dimensional animated character. Peedy the Parrot has been found in previous research to be well-understood and well-liked. The 20-minute intervention will be delivered as an ACASI, with participants listening to Peedy using headphones. The computerized intervention will focus on 1) providing feedback on the participants alcohol use and HIV risk behaviors, 2) emphasizing personal responsibility for change, 3) providing clear advice to change risky behaviors, 4) providing a menu of options for change, 5) using empathy as a counseling style, and 6) enhancing self-efficacy. The MES is heavily based on

Motivational Interviewing principles.[68] It thus includes traditional motivationally-oriented intervention components: feedback, pros and cons, and optional goal-setting. The MES tailors more thoroughly on present willingness to change. Thus, the above components are primarily presented to participants who are unwilling to initiate a change attempt. Those who are willing move directly into optional goal-setting, which includes a menu of change options as well as elements normally found in a "change plan worksheet" (specification of goals, problem-solving regarding how to address possible obstacles, etc.). It also provides expanded options for additional information, for addressing self-efficacy with participants whose willingness is high but confidence is low; and for assistance with relapse prevention—all presented only for participants who indicate interest in this information. The current MES also includes the ability to utilize the participant's first name, following data from Dijsktra[108] indicating that just this simple addition results in additional perceptions of personal relevance, with consequent increases in efficacy. Finally, women will be given a brief handout summarizing ways to avoid, cope and escape risky moods and situations associated with alcohol use (uploaded as supplemental document).

For the present study, these components have been tailored to the target women served by BCHD STI Clinic based on in-depth interviews done with women attending the clinic, and on feedback on the intervention after the MES was revised to reflect content from in-depth interviews. For example, the benefits of continuing to use alcohol (e.g., social network of alcohol using friends, helps person cope with stress, alcohol expectancies, avoidance of withdrawal) will also be discussed in conjunction with the benefits of reducing or stopping use (e.g., improved physical and psychological health, reductions in family conflicts and problems, reductions in high risk sexual and drug related behaviors). Opportunities to look at what life will be like five years in the future if the person continues to use alcohol as compared to making a choice to cut down or stop using alcohol are provided. Finally, participants have the chance to set goals to reduce or stop using alcohol either on their own or with assistance from AA, or another substance abuse program of their choice. The CBI script that was programmed into the MES software is attached as an appendix to this proposal.

CBI + Booster phone calls using Interactive Voice Response Technology (IVR) and text messaging

This enhanced CBI arm, will use the MES-delivered brief intervention described above and be followed by three booster phone calls using IVR. The booster calls will occur 2, 4, and 6 weeks after intervention delivery. Participants randomized to this arm, will be informed that they will receive these calls. They will be asked if there are specific days of the week they would prefer to be called and if specific times of the day. The booster calls will reinforce the intervention content, query participants regarding drinking behaviors and goals, and build self-efficacy. The IVR used for this study has been developed by Dr. Finkelstein (Co-I). This computer-based telecommunications system uses computer telephony to carry out automated telephone conversations with patient users. The system is programmed with branching logic that responds to the respondents answer to a particular question. The system speaks to patients over the telephone using computer-controlled digitized human speech. Individuals randomized to this arm of the trial will be given, instructions, and the schedule for their receiving calls from study staff.

IVR Procedures: When a woman is called through the IVR system, the woman is asked to enter the last 4 digits of her social security number to verify her identity. Once her identity is confirmed, she will then undergo the counseling session.

Intervention content for booster phone calls: Content of the calls is based on content from the CBI. Women will be asked if they met their goals for safer alcohol use and safer sex, and based on their response, they will be branched into different counseling algorithms. The duration of the call is 5 minutes. The content of the call which has been programmed into the IVR is attached to this application as an appendix.

Text message boosters

Text messages will be delivered over 6 weeks. Participants randomized to this arm will be informed that they will be receiving these text messages. Text messages will be sent in the morning and evening and on weekends. The content of the texts is theory based. Individuals will receive three text messages per week

after receiving the intervention. Text messages are attached to this proposal in the supplemental study documents.

4.a.8. Research Assessments

Consented subjects will participate in a baseline assessment prior to randomization, and at 3 month, 6-months and 12 months follow-up. All research interviews and questionnaire administrations will be conducted by the Research Assistants who are blind to study condition and ACASI. The Research Assistants will be trained and receive day-to-day supervision on the assessment instruments by Dr. Hutton.Assessment instruments will characterize subjects using data obtained by self-report questionnaires, interviews, and objective physical measures. We have included this breadth of measurement strategies to increase the accuracy and scope of our findings. Subjects are breathalyzed before the interview to ensure that they are sober at the time of the research assessment. Also, should a subject appear impaired either from other drug use or illness, the research interview will be rescheduled. Subjects will receive bus tokens or cab fare to facilitate their transportation to and from their appointments.

Assessment instruments were selected to balance the need for study data across several outcome domains with the length and duration of the data collection. Since assessment alone can modify behavior, it is important to reduce the length/intensity of the assessment battery.

The following assessments will be performed. The baseline and follow-up assessments are uploaded as supplemental study documents to this proposal.

Table 6:STUDY ASSESSMENTS	**Baseline**	**Follow-up Visits**		
		3 Mos	**6 Mos**	**12 Mos**
Informed Consent	X			
Demographics	X			
General Health (Dental Questions)	X	X	X	X
Health and Lab Assessments				
Pregnancy	X	X	X	X
Contraception (Medical Record Abstraction)	X			X
Urine Gonorrhea and Urine Chlamydia	X	X	X	X
History of STI (Medical Record Abstraction	X			X
Rapid HIV Test (per BCHD STD Clinic procedure)	X		X	X
Alcohol and Drug Assessments				
Breath Alcohol	X	X	X	X
Alcohol Use Disorders Identification Test	X	X	X	X
Time Line Follow Back*	X	X	X	X
Quick Drinking Screen	X	X	X	X
Readiness Ruler	X	X	X	X
Alcohol Expectancy	X	X	X	X
Alcohol Treatment Entry	X	X	X	X
Urine Drug Screen	X	X	X	X
Heavy Smoking Index	X	X		X
MINI Alc	X			
Psychiatric				
Patient Health Questionnaire (depression)	X	X	X	X

GAD-7 (anxiety)	X	X	X	X
Primary Care PTSD	X	X	X	X
Patient Health Questionnaire for Panic	X	X	X	X
Sexual Risk Assessment				
Time Line Follow-Back	X	X	X	X
NIDA Risk Behavior Assessment (Modified)	X			X
HIV Assessment (HIV+ individuals only)				
ART Adherence VAS	X	X	X	X
ART Persistence	X	X	X	X
CD4 count/HIV-RNA (Medical Record Abstraction)	X		X	X
HAART Regimen (Medical Record Abstraction)	X	X		X

*** The Time Line Follow Back Interview may be audiotaped for fidelity checks.**

a) Demographics and Sexual History: Participants will be asked a range of demographic questions including their age, race-ethnicity, highest grade in school, marital status, employment, income, housing status, age of sexual debut, prior history of STI, sexual orientation, pregnancy history

b) Alcohol/Drug Use/Sexual Behaviors: The Time-line Follow-back will be used to obtain a detailed recent history of alcohol and drug use and sexual risk behaviors. Using structured interview prompts, the TLFB quantifies alcohol, and drug use and sexual activity on each day during the last thirty days. TLFB yields detailed quantity/frequency data including type of alcohol consumed, number of drinking days, mean number of drinks/drinking day, and number of binge drinking days, type of drug use, quantity and frequency of use and number of drug using days. Sexual risk behaviors that will be queried will include the number of sexual encounters in the 30days, types of sexual encounters (main or casual or exchange), type of intercourse (anal, oral, vaginal), condom use, sex while high, and drug and alcohol use by partner at time of sex.

c) Alcohol/sex expectancies will be measured using a modified version of the Revised Alcohol Expectancy Questionnaire[122, 123]. Items are rated on a scale of 1 (*disagree strongly*) to 6 (*agree strongly*). An example includes "I enjoy having sex more if I've had some alcohol"

d)Psychological distress: will be assessed based on the Patient Health Questionnaire (PHQ) for depression, panic, and anxiety (GAD-7)

e) Readiness to Change will be assessed using readiness rulers.

f) Alcohol Treatment Entry: Admission to off-site alcoholism treatment programs and engagement in Alcoholics Anonymous or Narcotics Anonymous will be assessed during the follow-up interviews

g) Breath Alcohol Concentration (BAC) will be obtained using an Alcosensor IV.

h) Urine Pregnancy Testing: Urine pregnancy testing will occur at baseline, 3, 6, and 12 months. Urine pregnancy testing is performed on-site by the laboratory staff at the BCHD Eastern STD Clinic.

i) Urine toxicology specimens. The following drug classes will be included: opiates (methadone, buprenorphine, morphine, dilaudid, codeine, demerol); sedatives/ tranquilizers (barbiturates and

benzodiazepines); stimulants (amphetamine and cocaine); and marijuana. Urine specimens will be collected at screening and each follow-up visit.

j) Gonorrhea and Chlamydia: Urine STI testing will occur at baseline and 3, 6, and 12 months after intake, and at all voluntary (unscheduled) clinic visits. We will record whether STI infection occurs at each of these visits, as well as reason for presentation at voluntary visits. Urine specimens will be obtained and tested for urine gonorrhea and Chlamydia using the Gen Probe. The Gen-Probe APTIMA Combo 2 (Gen-Probe, San Diego, CA) assay detects both *C. trachomatis* and *N. gonorrhea*. The test is highly sensitive and specific for the detection of both organisms and is comparable to a cervical swab collected by a clinician. Urine STI testing is performed by the laboratory at the BCHD Druid STD Clinic.

k) Rapid HIV testing will per performed using the OraQuick Advance Rapid HIV1/2 antibody test. Participants will be offered this test at baseline, 3, 6 and at 12 month follow-up. This testing is offered routinely in the BCHD STI Clinic to all individuals presenting for an STI exam. Women agreeable to HIV testing will be referred to the HIV testing and counseling services in the BCHD STD clinic. Testing will not be done by our study staff. Permission to obtain results of rapid HIV testing performed by the STI clinic staff will occur at the time of study consent.

l). HIV medication adherence: Among persons with HIV, this will be assessed using an ART Adherence Visual analog scale and an ART Persistence Questionnaire.

m) Medical record abstraction: At the time of consent we will obtain permission to access participant's BCHD medical record. We will review the medical record at baseline and at their twelve month follow-up to determine past STIs, contraception use, and pregnancy. For those who are HIV infected, we will access the medical record to collect CD4, HIV-RNA and use of antiretrovirals.

O) Phosphatidylethanol (PEth):[148] At the 12 month visit, we will collect blood spot for the measurement of PEth, a direct ethanol metabolite that is detectable in the blood for more than 2 weeks after sustained ethanol intake. This will be collected on a sub-sample of women enrolled in the trial to validate self-reported alcohol consumption. Participation will be voluntary and we will obtain separate consent for this. PEth has been shown to be a sensitive and specific marker for recent alcohol consumption. We anticipate collecting this biomarker on approximately 60 women. Collection occurs via finger-stick using Lancet. Participants providing a blood sample for PEth will receive $5.00 in remuneration.

While the majority of follow-up assessments at 3, 6, and 12 months will occur in person, if a participant requests that a follow-up assessment be completed over the telephone, via SKYPE, or through the US mail, we will allow for this on a case-by-case basis. We will ensure that any assessment over SKYP or the telephone is performed in a private office, in the 1830 E. Monument Street Bldg, 8th floor.

4.a.12. Follow-Up Procedures

We have previously been successful in obtaining consent and research participation from individuals attending the BCHD STI Clinic. In our previous study, a subset of individuals was invited to undergo a SCID interview. Of those consenting for study and who completed initial interview (N=671), 233 agreed to SCID interview and 201 (86%) returned to complete it. In other studies (see Appendix 3) taking place in the BCHD STI clinics, recruitment has generally exceeded projected numbers and retention has ranged from 71-95% . In our trial of BI among HIV-infected AA women, follow-up rates to date have exceeded 93%. Based on our prior research experience, and our extensive follow-up procedures detailed below, we expect to achieve research follow-up rates exceeding 75% at 12 months.

Follow-up assessments will be scheduled at the time of enrollment and confirmed prior to, and at each follow-up assessment visit. To optimize follow-up rates at all assessment time points (3, 6, & 12 months) we will follow a standard protocol. At the time of enrollment, a participant tracking form will be filled out, which includes the participants primary contact information (address, telephone number),

secondary and tertiary addresses, and two to three alternate contacts. Names, addresses, telephone numbers and releases of information for all three collateral informants will be obtained and entered into the data system at enrollment. Whenever possible, these contact persons are varied in their type of involvement with the participant; that is, a contact person may be a family member, a social worker, a parole or probation officer, or a close personal friend.

Reminder cards will be mailed two weeks prior to the scheduled appointment, and telephone calls (made cell phones and alternate contact numbers) will be made one week, and 24 hours prior to the scheduled assessment. In addition, text messages will be sent to remind women of their upcoming appointments 24 to 48 hours prior to their scheduled visit, and if a participant agrees, we will email appointment reminders. To keep the study "fresh" in the minds of the participants, birthday cards and holiday cards will be mailed. Reminder cards and birthday cards will be submitted to the IRB once their design is complete.

In addition to our standard protocol for participant tracking and follow-up, we will also be hiring a disease intervention specialist (DIS). DIS are currently used by the BCHD STI clinic to track individuals with positive STI tests who fail to return for follow-up. Using established BCHD STI clinic procedures for tracking and follow-up, the DIS will locate individuals who fail to attend their scheduled follow-up assessments and participants who have positive STI tests at a study assessment and are unable to be reached by telephone. The DIS will first call the individual and if unable to leave a message, will call alternate contacts. If unsuccessful, she will conduct a field visit to the home. If no success, she will conduct field visits to alternate contact addresses. If unsuccessful, she will call again at a different time of day, and if no return call after 48 hours, a second field visit will occur. If still unsuccessful, the DIS will send a registered letter to the participant at the addresses listed at the time of enrollment. If the DIS is able to establish contact during the field visit, the DIS will schedule the next study follow-up.

4b.Study duration and number of study visits required of research participants.

The study duration is 12 months, with study visits occurring at baseline, 3 months, 6 months and 12 months.

4c.Blinding

Because this is a behavioral intervention that involves counseling, participants will not be blinded to their study condition; however, research assistants performing the Time Line Follow Back Interview will be blinded to the participant's assigned study condition, as will the Principle Investigator and Co-Investigators. The Study coordinator will be aware of group assignment, but will not be assessing patient outcomes.

4d. Justification of why participants will not receive routine care.

All participants in the study will receive routine care offered by the BCHD STD Clinic. No current therapy will be stopped.

4e.Justification for inclusion of a placebo or non-treatment group.

This study does include an attention control group which will receive all of the usual care provided by the STD clinic, along with computer delivered information of the importance of regular dental care. This usual care group/attention control is included because it is essential to understand the efficacy of the computer delivered brief alcohol intervention alone, compared to usual care. Because not all women will have access to cell phones or text messaging, or they may not choose to engage in cell phone based counseling, it is important to establish whether a single computer delivered brief alcohol intervention decreases alcohol use and high risk sexual behaviors. In addition, the attention control condition is needed to determine the effects of our assessment on participant's drinking behaviors.

4f.Definition of treatment failure or participant removal criteria.

Participants will only be removed from the study if they become pregnant. The rationale is as follows: pregnant women should be referred for more extensive counseling on alcohol use to prevent alcohol exposure to the fetus and Fetal Alcohol Spectrum Disorders.

4g.Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely.

If the study ends prematurely, all enrolled participants will still receive routine care offered by the BCHD STD Clinic. Women interested in receiving counseling for alcohol use will be referred to local treatment programs and Baltimore City Community Psychiatry.

5.Inclusion/Exclusion Criteria

Inclusion Critieria

Age >=18 and
Patient of BCHD STD Clinic and
Sexually active with men in the last 90 days and any 1 of the following three criteria:

Average of 8 or more drinks per week or
Two heavy drinking episodes (4 drinks/occasion) in past 3 mos/90 days or
Sex while under the influence of alcohol in last 3 months/90 days (on at least two occasions)

Exclusion Criteria

Actively Psychotic or servere mental health symptoms
Unable to speak or read English
Pregnant
No cell phone
Does not text message and not interested in starting
Currently enrolled in alcohol treatment

6.Drugs/ Substances/ Devices

a. NA

5. Study Statistics

a. Primary outcome variable.
   1.Binge drinking episodes
   2.Drinks per drinking day
   3. Drinking days in the past week

b. Secondary outcome variables.
   1. Unprotected vaginal or anal sex
   2. Number of sexual partners
   3. Episodes of unprotected sex while high
   4. Incident STI

c. Statistical plan including sample size justification and interim data analysis.

Power Estimates for Sample Size Determination and Statistical Analysis

Our primary alcohol-related outcome is a reduction in hazardous drinking among HIV at-risk AA women across twelve months. We have defined hazardous drinking as >7 drinks per week or >3 drinks per occasion (also defined as binge drinking). Our data from the BCHD STI clinic indicate that 29% of women drink at hazardous levels. These women are the target population for our research.

Power estimates were derived using existing ACASI data from an earlier study in the STI clinic (Prelim Studies C.2.1 & C.2.3) and a recent pilot study in the same clinic during July 2008. Expected intervention effect sizes for alcohol-related outcomes were estimated from published studies of computerized BI with urban post-partum women ,[126] and from brief alcohol interventions among women of child-bearing age.[127] Ondersma and colleagues randomized 107 postpartum women with illicit drug use to computerized BI or control. Their trial was designed to determine preliminary efficacy of a one-time computer-delivered BI on drug use. The intervention was found to have a moderate effect size with odds ratios from 1.4 to 4.7. Manwell and colleagues[128] presented long-term results of a randomized clinical trial of BI for problem drinking women of childbearing age (i.e., averaged more than 11 drinks/week; reported heavy drinking [more than 4 drinks during a single drinking episode] during the preceding month; or reported 2 or more symptoms on the CAGE). Out of almost 6,000 women screened in 17 primary care clinics, 12% met the definition of problem drinking. Overall, there were significant reductions in average weekly drinking and binge drinking in the intervention group compared to the control group. Specifically, there was a 47% reduction in mean drinks per week (14.1 to 7.5) that occurred within 6 months of the BI and was sustained over the 48-month follow-up period. [129] Similarly, binge drinking in the last month decreased from 93% to 68% of the sample and there was a corresponding reduction in the number of binge drinking episodes from 5.1 to 3.0 per month.

Expected intervention effect sizes for sexual risk behavior outcomes were estimated from published studies of sexual risk reduction among individuals in alcohol treatment, and among individuals attending at STI clinic. Avins and colleagues examined sexual risk behaviors before and after alcohol treatment among 112 sexual active individuals. [130] In this study, the proportion of individuals using condoms consistently increased from 22% before treatment to 35% after alcohol treatment. Project Respect, a three arm randomized trial, tested behavioral counseling (enhanced counseling vs. brief counseling vs. didactic messages only) to reduce STI and risky sexual behaviors. In this study, both counseling arms demonstrated a decreased incidence of STI compared to control group that received didactic messages. Specifically, 149 participants (10.4%) in the didactic messages arm had new STDs compared with 103 (7.2%) in the enhanced counseling arm (RR, 0.69; 95% CI, 0.54-0.88) and 107 (7.3%) in the brief counseling arm (RR, 0.71; 95% CI, 0.58-0.89). Through the 12-month visit, 211 participants (14.6%) in the didactic

messages arm had developed new STDs, compared with 165 (11.5%) in the enhanced counseling arm (RR, 0.78; 95% CI, 0.64-0.94) and 173 (12.0%) in the brief counseling arm (RR, 0.81; 95% CI, 0.67-0.98). The 2 interactive counseling interventions had very similar cumulative incidence of STD through the 6- and 12-month visits.[131]

Primary Outcomes

AIM 1: To determine the effectiveness of computer-delivered BI and IVR/text in decreasing alcohol risk behaviors among hazardous/binge drinking African/American women attending an urban STI Clinic.

Hypothesis 1a: Women receiving BI + IVR/text will have fewer binge drinking episodes and lower alcohol consumption (number of standard drinks/week, number of drinking days/week) compared to usual care.

Hypothesis 1b: Women receiving BI will have fewer binge drinking episodes and lower alcohol consumption (number of standard drinks/week, number of drinking days/week) compared to usual care.

Hypothesis 1c: Women receiving BI + IVR will have fewer binge drinking episodes and lower alcohol consumption (number of standard drinks/week, number of drinking days/week) compared to BI only.

Power Analysis. For these outcomes, power calculations for a given sample size were derived on the basis of maximum effect size to be detected over time between the three study arms assuming a repeated measures analysis (baseline and three follow-up periods) and a balanced design. The calculation was performed for varying sample sizes, three levels of ES (0.2-, 0.4, and 0.5)[132] or effect size[133] three levels of rho or within-person correlation between measurements, and an alpha level of 0.0167 (0.05 experiment-wise error rate Bonferroni type adjustment[134] for three pair-wise hypothesis comparisons at 6 months with earlier and later treatment effects tested at an unadjusted alpha of 0.05)). Table 7 shows the resulting power calculations for 150 and 100 participants per study arm under these options.

Table 7. Power estimates^a for projected study arm sample sizes for count outcomes

Sample size per arm	rho	Effect size (ES)		
N=150 (450 total)		0.3	0.4	0.5
	0.3	.85	.97	.99
	0.4	.78	.98	.99
	0.5	.72	.95	.99
N=100(300 total)				
	0.3	.64	.91	.99
	0.4	.56	.86	.98
	0.5	.50	.80	.96
^a Experiment-wise alpha = 0.05				

Thus for the primary outcomes, the sample sizes of 150and 100 (with 30% potential loss-to-follow up), under consideration provide adequate power for medium effect sizes regardless of the assumed within-person correlation between measurements. For these outcomes we assume

an effect size of 0.35 (between small and medium). As a generalized concept, ES represents the mean difference between two groups normalized by a pooled group standard deviation,

Seconday Outcomes: Sexual risk outcomes Aims 2 & 3
AIM 2: To determine the effectiveness of computer-delivered BI and IVR/text in decreasing sexual risk behaviors among hazardous/binge drinking African/American women attending an urban STI Clinic.

Hypothesis 2a: Women receiving BI + IVR will report fewer 1) sexual partners,2) episodes of unprotected vaginal or anal intercourse, 3) episodes of sex while high compared to those receiving usual care.

Hypothesis 2b: Women receiving BI only will report fewer 1) sexual partners,2) episodes of unprotected vaginal or anal intercourse, 3) episodes of sex while high compared to those receiving usual care.

Hypothesis 2c: Women receiving BI + IVR report fewer 1) sexual partners,2) episodes of unprotected vaginal or anal intercourse, 3) episodes of sex while high compared to those receiving BI only.

Power Analysis. The power calculations for episodes of unprotected vaginal or anal intercourse with a given sample size and episodes of sex after or while drinking alcohol were derived using the effect size approach in Table 6. Estimates of the mean number of such episodes for the usual care group at baseline and standard deviation are 2.03 and 2.06, respectively. For a medium effect size, this would translate to being able to detect a difference of 1 episode. The number of sexual partners was considered as a proportion of participants having only one partner versus more than one partner. The power calculations for this proportional outcome for a repeated measures analysis were derived using equations in Diggle et al.[135] The calculations were performed with parameters similar to those for the primary outcomes, using a range of proportion differences from the usual care group estimate. Table 8 shows examples of the power calculations for this outcome.

Table8. Power estimates^a for projected study arm sample sizes for proportion outcomes

Sample size per arm	rho	Change in proportion having sex after or while drinking alcohol/week (decrease from 20.5%)			Change in proportion of 1 (vs > 1) sexual partner/week (increase from 59.5%)		
		6%	8%	10%	10%	15%	20%
N=150 (450 total)							
	0.2	.51	.79	.95	.77	.98	.99
	0.5	.34	.59	.81	.56	.91	.99
	0.8	.25	.45	.68	.43	.81	.97

Aim 3: To observe the impact of computer-delivered BI enhanced with IVR and text messaging boosters on incidence rates of HIV and STI biomarkers and HIV among hazardous/binge drinking women attending an urban STI Clinic.

Hypothesis 3a: Women receiving CBI + IVR/text will have lower rates of incident gonorrhea, Chlamydia or HIV compared to control.

Hypothesis 3b: Women receiving CBI only will have lower rates of incident gonorrhea, Chlamydia or HIV compared to control.

Hypothesis 3c: Women receiving BI + IVR/text will have lower rates of incident gonorrhea, Chlamydia, or HIV compared to those receiving CBI only.

3.The proportion of having at least one STI biomarker versus none was employed in deriving the power calculations as in Aim 3. The calculations were performed with parameters similar to those for the primary outcomes, using a range of proportion differences from the usual care group estimate. For the outcome of the proportion of participants having at least one STI biomarker versus none (estimated at 19.2% for the usual care group at baseline), the power for 150, at sample sizes under consideration, is reasonable (close to 80%) for a 50% decrease in the proportion, that is, about 9%.

Statistical Analysis. The principal statistical analyses for the three primary outcomes will proceed in two phases for each outcome separately: a cross-sectional evaluation of the study arms at baseline and full longitudinal evaluations of study effectiveness. The baseline comparisons of the participants in the study arms will be performed on demographic characteristics and outcome measurements. The analyses will include chi-square tests, and parametric and non-parametric analysis of variance appropriate to the characteristic or outcome being compared, and will evaluate the baseline comparability of the participants in the study arms. Study effectiveness will be evaluated through longitudinal analyses of marginal treatment differences performed with general linear model formulations using the generalized estimating equations technique[135] and parameters based on the underlying distribution of the outcome (e.g., Normal or Poisson or negative binomial). All dependent variables (number of binge drinking episodes, number of drinks per week, number of drinking days per week, number of sexual partners, number of episodes of sex while high, episodes of unprotected sex) will be analyzed as individual models with treatment group as the primary independent variable. All models will include baseline illicit drug use, age, HIV status, and psychiatric symptoms to adjust for potential imbalances in strata co-factors. Interaction terms will be created (including, but not limited to, prior STI, psychiatric symptoms, time) to test if specific covariates modify intervention effects and any interaction at a significance of $p \leq 0.1$ will be further tested.

All available information from participants will be included in the analyses regardless of participation level. Diagnostics will be employed to evaluate the appropriateness of model assumptions and covariance structure, with alternate strategies (e.g., transformations, non-linear models, non-parametric methods, alternate covariance structure) used if necessary. Individual contrasts will be employed to examine pair-wise differences between groups and between the baseline and follow-up measurement periods. Tests will be conducted at a two-sided alpha = 0.05 level of significance, pair-wise comparisons between the study groups will be conducted with an experiment-wise alpha = 0.05, and estimates will be provided with 95% confidence intervals. All efficacy outcome measures will be analyzed under the intent-to-treat principle, and the sample analyzed will include all subjects who are randomized regardless of whether they actually received the study treatment to which they were assigned or completed the study. Non-compliance will not be a large factor as the intervention is given at a short period of time (a single time point for the brief intervention and over 6 weeks for those with the IVR). However, it is probable that some individuals will drop out of the trial. In this case it is possible that there could be a selection bias. [136] To address this potential bias, we will use inverse probability of dropout weights (this is analogous to the inverse probability of censoring weights that have been used in observational studies. [136-142] Briefly, a subject specific weight that corresponds to the inverse probability that the individual remains in the trial up to time *t* (the scheduled visits at 3, 6, 9 and 12 months). These weights are then applied to the generalized linear model with GEE that was previously used for the intent-to-treat analysis.[136, 143] The weights act such that each individual not only represents themselves but also for those with similar characteristics but have removed themselves from the study.[136]. Thus individuals who are over-represented as they are the most likely to remain within the trial are down weighted, whereas those who have a higher tendency to withdraw from the study are up-weighted.

Essentially a pseudopopulation (based on the original study population) is constructed in which the selection bias is removed.[136] . The weights are constructed by applying a pooled logistic model assessing the probability of dropout by time using baseline and time-varying covariates to construct the model.[137, 138] An important assumption (not unique to these methods) is that there are no unmeasured confounders that are missing from these models. To assess the impact of possible unmeasured confounders, sensitivity analyses for marginal structural models will be applied. [144, 145]. Analyses will be performed primarily using SAS v9.1 (SAS Institute, Inc. Cary NC).

d. Early stopping rules.

We do not plan to conduct interim analyses of the dependent measures.

6. Risks

There are two primary risks to this study: breach of confidentiality and psychological distress. Participants will be asked to provide sensitive information related to alcohol and drug use, and high risk sexual behaviors. Every effort will be made to ensure confidentiality, including the use of ACASI, and a federal certificate of confidentiality. Psychological/emotional distress may occur during assessment interviews or during the brief intervention as issues related to drugs, alcohol, and sexual risk behaviors may be emotionally difficult.

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.

1) Confidentiality: Participants will be asked to provide sensitive information related to alcohol and drug use, and high risk sexual behaviors. We will obtain a federal Certificate of Confidentiality to protect the participant against the release of private/sensitive information. In addition, all participants will be assigned unique study identification numbers. A master file linking study identification numbers to participant names/contact information will be kept in a password protected file that only the investigators and project manager will have access to. In addition, all paper files and data will be kept in a locked filing cabinet.

   Confidentiality of Cell Phone Counseling and Text Messaging: Individuals will be counseled via their cell phone using IVR technology and text messages. In the event that a cell phone is misplaced or borrowed by another individual there is the risk of breaching confidentiality. To avoid this, prior to the delivery of cell phone counseling, women will be required to enter the last 4 digits of their social security number. In addition, IVR counseling calls originate from a secure Johns Hopkins Server, maintained by Dr. Finkelstein's research group. Thus no calls will be linked to the STD clinic. Similarly, for text messaging, no personal identifiers will be linked to text messages. Because text messages originate from a secure Johns Hopkins server, text messages will not be linked to the STD clinic.

All study outcomes will be reported as aggregate data. In addition, all investigators and members of the research team will have completed Johns Hopkins University on-line modules on Human Subjects Research and HIPAA. HIV testing and counseling are performed routinely within the BCHD STI Clinic. All women who undergo HIV testing and counseling will be informed that the result of their test is confidential but that there will be mandatory reporting of new cases to the State of MD. We expect breach of confidentiality to be a rare or infrequent event.

2) A second risk to this study is psychological distress. A participant may become uncomfortable while answering sensitive questions related to drug and alcohol use, sexual risk behaviors, mood, anxiety or during the brief intervention. If a woman experiences significant distress during the interview, the research assessment will be stopped, and Dr. Heidi Hutton, a PhD in Clinical Psychology, or Dr. Geetanjali Chander a general internist, will evaluate the participant, and assess if she is at risk for harming herself or others. If necessary, they will either personally escort her or if need be

engage emergency escort to the Johns Hopkins University Emergency Department which is less than one-quarter mile from the STI clinic. We expect this risk to be occur infrequently.

b. Steps taken to minimize the risks.
To minimize risks associated with breach of confidentiality, each participant will be assigned a unique study ID. A master file linking study identification numbers to participant names/contact information will be kept in a password protected file that only the investigators and project manager will have access to. In addition, all paper files and data will be kept in a locked filing cabinet. All study outcomes will be reported as aggregate data. All IVR and text message counseling will originate from a secure Johns Hopkins Server, and thus will not be linked to the STD clinic. In addition, all investigators and members of the research team will have completed Johns Hopkins University on-line modules on Human Subjects Research and HIPAA. HIV testing and counseling are performed routinely within the BCHD STI Clinic.

c. Plan for reporting unanticipated problems or study deviations.
Study deviations and unanticipated problems will be reported to the Johns Hopkins IRB by the Principal Investigator.

An adverse event (AE) is any untoward medical occurrence in a subject, not necessarily having a causal relationship with the study. A serious adverse event (SAE) is any untoward medical occurrence that a) results in death, b) is life-threatening, c) requires inpatient hospitalization or prolongation of existing hospitalization, d) results in persistent or significant disability/incapacity, or e) is a congenital anomaly/birth defect.
AE's may be graded as: Mild (no limitation of usual activities), Moderate (some limitation) or Severe (inability to carry out usual activities). The relationship of the AE to the study procedures is classified as: Not related, Unlikely, Possible, Probable, or Definite. The principal investigator will be responsible for distinguishing between an AE and SAE. SAE will be reported by telephone to the Johns Hopkins Medical Institute (JHMI) IRB, NIAAA project officers, and the Baltimore City Health Department (BCHD) within 48 hours of a SAE. The same classification and procedures will be applied to any SAE or AE occurring during the 12-month participant follow-up period.

Annual reports will be submitted by the principal investigator to the NIAAA project officer, the IRB, and BCHD summarizing all adverse events and how they were addressed by the study team.

d. Legal risks such as the risks that would be associated with breach of confidentiality.
We will obtain information on drug use, an illegal behavior that may place subjects at legal risk if confidentiality is breached. We have obtained a certificate of confidentiality from the NIH National Institute on Alcohol Abuse and Alcoholism to reduce this risk.

e. Financial risks to the participants.
There is no cost to participants of study participation. All study procedures are paid for by the research grant.

7. Benefits

Participants in the study may have the opportunity to receive counseling for hazardous alcohol use. Both the assessments and the interventions will result in an increased awareness of health behaviors. Benefits to others include increased knowledge of the effectiveness of brief alcohol intervention among high-risk women. In addition, if effective, computer-directed brief intervention may be adopted for more widespread use in STI clinics.

Ultimately if computer-directed brief alcohol/sexual risk reduction intervention or telephone counseling via IVR is found to be effective in reducing hazardous alcohol use and/or risky behaviors and improving health outcomes, this technology can be transferred to STI clinic settings for widespread implementation. Furthermore, if the intervention(s) prove to be effective study findings will offer "real life" specialty care clinics a screening and intervention package that is practical and would require no additional staff time and resources for implementation

8. Payment and Remuneration

Randomized participants will receive $30 for participation in the baseline assessment In addition, all participants, regardless of group assignment, will be paid for follow-up assessments at 3-mos ($35); 6-mos ($40) and 12-mos ($50) with a $20 bonus for completing all three assessments. These procedures have yielded high rates of participation in other RCTs with substance abusing populations. Also, subjects will receive bus tokens to facilitate their transportation to and from the interviews. Individuals who complete the 15 minute screening but do not qualify for the intervention will receive $5 for their time. Individuals who receive and respond to booster calls will be reimbursed for their cell phone minutes at $5 per call. They will also receive an additional $5 to cover the expense of text messages.

9. Costs

There are no costs of the study procedures to participants.

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